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Prevalence, sociodemographic risk factors, and coverage of myopia correction among adolescent students in the central region of Portugal

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#### **Abstract**

## Background

Knowing the prevalence of myopia at school age is essential to implement preventive measures and appropriate interventions, ensure access to vision care, promote a healthier educational environment and improve academic performance. The purpose of this study was to determine the prevalence of myopia and its associated sociodemographic risk factors, as well as to estimate the coverage of myopia correction among adolescents in center of Portugal.

#### Methods

This cross-sectional study evaluated 1115 adolescents from the 5th to the 9th year of school, with an average of 12.9 years (SD = 1.5) ranging from 10.0 to 18.0 years. Optometric evaluations were carried out in a school environment and consisted of the evaluation of distance visual acuity, assessed using a logarithmic visual acuity chart (ETDRS charts 1 and 2) at 4 m, and measured by refractive error with a pediatric autorefractometer (Plusoptix), by non-cycloplegic. Myopia was defined as spherical equivalent (SE  $\leq$  -0.50 diopter (D)) and uncorrected visual acuity (UVA  $\leq$  95VAR). Adjusted logistic regression analysis was applied to investigate risk factors.

#### Results

We found a myopia rate of 21.5% and a high myopia rate of 1.4%. Higher school level and attendance at urban schools were associated with myopia, but no association was found with age or sex. Only 34.6% of myopic adolescents use the best optical correction and 26.4% do not use any type of optical correction.



Data on the prevalence of refractive problems in Portugal are scarce and heterogeneous. This study, although regional, provides a valuable contribution with a clear and reproducible methodology, following international guidelines and filling gaps in the existing literature. The results show that the rate of myopia in this age group is similar to reports from other European studies. The high rate of adolescents with uncorrected or under-corrected myopia in Portugal is a problem that deserves attention.

**Keywords:** Adolescence, Myopia, Sociodemographic factors, Visual acuity, Myopia correction coverage, Urban-suburban disparity

# Background

Myopia is a refractive condition that tends to develop in pre-adolescence, worsening during puberty and progressing into early adulthood  $[\underline{1}]$ . The greater the degree of myopia, the greater the risk of ocular complications that can lead to vision loss that is not recoverable  $[\underline{2}]$ .

The definition of myopia, the methods used to measure ocular refraction and the inconsistent use of cycloplegics, influence the quantifications of myopia prevalence. In most epidemiological studies, myopia is defined by  $SE \le -0.50D$  and high myopia by  $SE \le -5.00D$ , with cycloplegic refraction [3]. However, the literature often uses non-cycloplegic refractive techniques and considers the same myopia definition [4–6]. Large-scale myopia studies rarely use cycloplegics, so there is a tendency to overestimate the rate of myopia [5].

The prevalence rates of myopia, when assessed using refractive techniques with cycloplegia, are higher in Asia than in compared to Europe [7]. Studies reporting non-cycloplegic refractive measurements show a similar pattern of differences but at even higher rates [4, 8]. Although cycloplegic refraction is considered the most appropriate technique for myopia studies, the use of cycloplegic means it takes a long time to measure refraction and can cause temporary side effects, such as blurred near vision and photophobia, which reduces adherence. [9].

Autorefractometers (AR) are instruments frequently used to obtain ocular refraction in epidemiological studies, but closed-field AR's induce an overestimation of myopia. The use of openfield AR allows us to obtain refractive measurements close to cycloplegic refractive methods since it eliminates the stimulation of accommodation caused by instrument proximity [5]. It has also been recommended to measure non-cicloplegic autorefraction and visual acuity (VA) without correction, for higher accuracy in detecting myopia [9, 10]. The World Health Organization recommends measuring distance VA in vision screenings [11]. Employing a pinhole test in these screenings can reveal unmet refractive needs, as an improvement in VA with pinhole suggests the presence of correctable refractive errors [2, 11].

Although the magnitude of this problem presents geographic differences, an increase in the prevalence, incidence and progression rates has been observed globally. In Europe, population prevalence rates are estimated at around 40.0% and in certain parts of East Asia, rates exceed 60.0%, and there is strong evidence that these rates vary greatly with age [7]. This vision eye condition has become a growing concern in eye health, especially among school-age children and adolescents. Current trends show that children and adolescents are becoming myopic at an earlier age and that the degree of myopia continues to progress as these children age [2, 12]. The scientific literature reports that the prevalence of myopia tends to increase from the age of 6 years [7]. East Asia exhibits the highest rates of myopia, while Africa and South America have lower reported rates [13].

Health promotion and screening interventions are essential to prevent myopia and other refractive errors by identifying vision problems early. In addition, these actions can change behaviors by educating about the importance of spectacles and addressing common reasons for non-adherence to their use, such as discomfort or social stigma, thus improving acceptance and appropriate management of vision eye conditions. In Portugal, there is little data allowing to know the real extent of myopia. The National programme for eye health estimates that around 20.0% of children and around 50.0% of the adult population suffer from refractive errors in general, including myopia and other refractive conditions [14]. A study carried out with Portuguese university students recorded an increase in the prevalence of myopia from 23.4 to 41.3% between 2002 and 2014 [15]. Another study, based on the analysis of prescription and sales of ophthalmic lenses, estimated an increase in myopia from 40.0% in 2010 to more than 50.0% in 2020 [16].

The prevalence of refractive problems in Portugal is a topic where available data is relatively scarce and presents significant heterogeneity. Furthermore, these studies often present methodological descriptions that can be considered insufficiently detailed. This work aims to estimate the prevalence of myopia in adolescents who attend school from the 5th to the 9th year in the central region of Portugal. We also intend to understand the association of myopia with some sociodemographic parameters in these adolescents, and to estimate the coverage of myopia correction among this population.

#### Methods

## Study design and participants

This is an epidemiological, cross-sectional and observational study. Participants were children and adolescents attending the 2nd cycle of basic education (5th and 6th grades) and the 3rd cycle of basic education (7th, 8th and 9th grades) in Covilhã, a city in the central area of Portugal.

All schools in the urban area of the municipality where the study was conducted were included, covering 2 schools from the second cycle and 4 schools from the third cycle of basic education. Due to the small number of students in suburban schools and their significant geographic dispersion, 2 from each educational cycle in suburban area were selected based on having the highest number of enrolled students. All children enrolled in the participating schools were invited to join the study, with those receiving authorization from their legal guardians included, without participant randomization.

The inclusion criteria were being a child /adolescent attending the 2nd or 3rd cycle of basic education, aged between 10 and 18 years old, having the authorization from their legal tutor and providing verbal consent on the day of the screening. Incomplete screening records or those with poor cooperation were excluded from the data analysis. Students undergoing treatment with orthokeratology or atropine were also excluded, as this treatment can temporarily influence visual acuity and myopia measurement.

#### Procedures

The study protocol consisted of the acquisition of refractive measurements in eye screening actions in schools. The study was approved from the Ethics Committee of the National School of Public Health (CEENSP  $n^{\circ}$  29/2023) and was previously authorized by the Ministry of Education ( $n^{\circ}$ 

1307100001). Data were collected between November 2023 and February 2024. The examination and vision testing was performed by AN and MC.

Socio-demographic data were collected, such as age, sex, school level, school location (urban or suburban area), place of birth, and special educational needs.

All study volunteers underwent monocular distance visual acuity measurement and ocular refraction assessement using an autorefractometer Additionally, for participants who wore spectacles on the screening day, the prescription value of the spectacles was also recorded.

## Visual acuity

VA was measured with ETDRS (Original Series Chart 1 and Chart 2; Good-Lite; USA) at 4 m under photopic lighting conditions. The lighting in the room was measured with a digital luxmeter (Luxmeter PCE-L335; PCE instruments; Tobarra, Spain) and values equal to or greater than 400 lx were considered acceptable [17]. The ETDRS charts are considered reliable, repeatable and easy to use in screening actions [18]. All VA were recorded on the Visual Acuity Rating scale (VAR), which is a more intuitive system for using a logarithmic charts and allows scoring letter by letter instead of line by line [18, 19]. In this rating system, each letter has a score of 1VAR; each line has 5VAR and the decimal VA = 1.0 is equivalent to 100VAR, and decimal VA = 0.8 is equivalent to 95VAR.

The protocol recommended by the WHO was followed to calculate the effective refractive correction coverage rate [2]. To determine UVA, all children were assessed monocularly and without any refractive correction. Visual acuity with usual correction (VAUC) was assessed in all children who wore glasses or contact lenses with their usual correction. In cases where the presented visual acuity (PVA) - defined as UVA for those not wearing corrective lenses or VAUC for those who did was less than 95VAR, pinhole visual acuity (phVA) was also assessed. The diametre of pinhole was 1.5 mm. The same procedure was applied to record all visual acuity measurements. The patient started at the 80VAR line on the chart (equivalente 0,4 logMAR) and continued reading downwards until reaching a line where they could no longer correctly identify at least three letters. If the patient couldn't read the 80VAR line, they started at the top of the cgart. The final score was based on the number of letters correctly identified. A different card was used for each eye to avoid learning effects.

#### Autorefraction

AR was performed under non-cycloplegic conditions, using the PlusOptix, model A09 (PlusOptix; Nuremberg, Germany). The PlusOptix is a device that measures ocular refraction at a distance of 1 m from the eyes, reducing the effects of instrumental myopia compared to closed-field AR. The refraction obtained with the PlusOptix A09 has shown agreement with the refraction of cycloplegic retinoscopy and is indicated as a screening method in myopic children [20, 21]. The ocular refraction of each participant was measured three times and the mean value of the SE of the three measurements was calculated. The SE was obtained by adding the spherical component to half the cylindrical component of the ocular refraction measured with the AR. When PlusOptix reported that the participant's ocular refraction exceeded its measurement capacity, the refraction of the student's usual spectacles was considered.

## Definition of myopia

In screening activities, some authors recommend the combined use of refraction and VA, recognizing that this combination maximizes the sensitivity of screening in signaling myopia [10, 11, 22]. For children over 6 years of age, some authors recommend a decimal VA  $\geq$  1.0, equivalent to 0.0logMAR or 100VAR [23, 24], other authors recommend a decimal VA  $\geq$  0.8, equivalent to 0.1logMAR or 95VAR [9, 24].

In this study, the criteria of UAV < 95VAR and SE $\leq$ -0.50D were used to define myopia. To facilitate comparison with other studies, only the SE $\leq$ -0.50D criterion was also used. To characterize severity, we considered high myopia SE $\leq$ -6.00D, moderate myopia – 6.00D < SE $\leq$ -3.00D and mild myopia – 3.00D < SE $\leq$ -0.50D.

## Statistical analysis

The data were analyzed using SPSS version 28 (IBM SPSS Statistics; New York, USA). Continuous variables were expressed as mean (SD) and categorical variables were presented as counts or proportions. The study of differences between the eyes for the continuous variables was carried out using the paired samples t-test. Chi-square test was used to compare categorical variables between groups. A multivariate logistic regression analysis was carried out using a stepwise backward method to explore the sociodemographic factors associated with myopia. The results of the logistic regression were reported as odds ratios (OR). For all analyses, a two-sided *p-value* < 0.05 was considered statistically significant. Confidence intervals (CI) were calculated at 95%.

## Results

A total of 1115 students from urban and suburban schools took part in the study. The average age was 12.9 (SD = 1.5) years, ranging from 10.0 to 18.0 years. The male sex represented 50.9% of the total sample, and 67.4% of the students attended urban schools. There was also a rate of 11.7% of adolescents flagged in school files as having special educational needs (SEN) and 15.6% of participants were from other countries. The majority of migrant students originated from America (n = 99, with 92 from Brazil) and Africa (n = 49, with 43 from Angola). There were 19 adolescents from other European countries and 7 from Asia. The origin of 2 migrant students was not documented. The characteristics of the sample according to various factors are presented in Table 1. The results of the study of the differences between the groups, as well as the prevalence of myopia according to each of the factors analyzed, are also included.

Table 1
General characteristics of the sample

Characteristics		Size	Age	UVA [< 95VAR] N(%)	Myopia				
		[N (%)]	[years] (Average ±		SE≤-0.50I	)	SE≤-0.50D and UVA < 95VAR		
			SD)		N(%)	p-value ( $\chi^2$ )	N(%)	p-value ( $\chi^2$ )	
Total samp	le	1115(100)	12.7 ± 1.5	516(46.3)	262(23.5)		240(21.5)		
Sex	Male	568(51.0)	12.7 ± 1.5	245(43.1)	133(23.4)	0.957	121(21.3)	0.857	
	Female	547(49.0)	12.7 ± 1.5	271(49.5)	129(23.6)		119(21.8)		
Nature	Portuguese	941(84.4)	12.6 ± 1.5	438(46.5)	221(23.5)	0.982	201(21.4)	0.756	
	Migrants	174(15.6)	12.8 ± 1.5	78(44.9)	41(23.6)		39(22.4)		
School	2nd cycle	437(39.2)	$11.2 \pm 0.7$	190(43.5)	77(17.8)	< 0.001**	74(16.9)	0.003**	
level	3rd cycle	678(60.8)	$13.6 \pm 1.0$	326(48.1)	185(27.3)		166(24.5)		
SEN	Positive	131(11.7)	$13.0 \pm 1.4$	74(56.5)	29(21.1)	0.686	25(19.1)	0.469	
	Negative	984(88.3)	12,6 ± 1.5	442(44.9)	233(23.7)		215(21.8)		
School	Urban	751(67.4)	12.8 ± 1.5	360(47.9)	195(26)	0.005**	176(23.4)	0.026*	
location	Suburban	364(32.6)	12.5 ± 1.5	156(42.9)	67(18.4)		64(17.6)		

N - counts; % - proportions; SD - standard deviation - UVA - uncorrected visual acuity; VAR - visual acuity rating scale; SE - spherical equivalent; SEN - special educational needs

# Prevalence of myopia and risk factors

The mean values for UVA were  $90.6 \pm 17$ VAR and  $89.4 \pm 17$ VAR for the right and left eyes respectively, and this difference was statistically significant (t = 5.656, p < 0.001). The visual acuity of the worst eye was used to classify myopia. An UVA worse than 95VAR in at least one eye occurred in 516 participants (46.3%; 95% CI: 42.4-50.4%) (Table  $\underline{1}$ ).

For the SE $\leq$ -0.50D criterion, a prevalence of myopia was found to be 23.4% (95% CI: 21.0–26.0%), and for the SE $\leq$ -0.50D and UAV < 95VAR criteria, it was 21.5% (95% CI: 18.9–24.4%). The average value of the SE of the myopic population (n = 262) was – 2.70D (SD = 1.86), in a range between – 0.50D and – 10.37D. Considering SE $\leq$ -6.00D, we account for 16 cases, that is a rate of 1.4% (95% CI: 0.9–2.3%) was found for high myopia. The average value of the SE in high myopia was – 7.52 (SD = 1.32).

The proportion of myopic participants was not significantly different between girls and boys, between Portuguese and migrant students or between participants with and without SEN. However, it was significantly different between the school level, with a higher proportion of adolescents with

<sup>\*</sup>Significant at 0.05 level; \*\* significant at 0.001 level

myopia in the 3rd cycle; as well as between schools in urban and rural areas, with a higher proportion found in schools in the urban areas. These results was observed for both myopia classification criteria.

The association between the presence of myopia and age, sex, geographical location of the school and school level was studied using the odds ratio (OR) (Table  $\underline{2}$ ).

Table 2

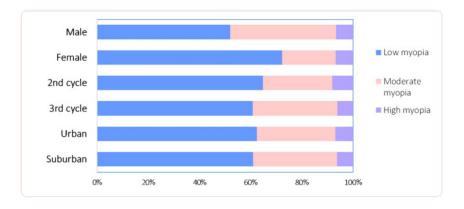
Myopia risk factors

Factor	OR crude (95% CI)	<i>p</i> -value	OR Adjusted (95% CI)	<i>p</i> -value
Age (numeric)	1.097 (0.996-1.208)	0.061	0.924 (0.786-1.085)	0.336
Sex	1.027 (0.772-1.367)	0.854	1.008 (0.756-1.344)	0.958
[male vs. female]				
School location [suburban vs. urban]	1.435 (1.044-1.973)	0.026*	1.409 (1.022-1.941)	0.036*
School level	1.590 (1.172-2.158)	0.003**	1.889 (1.152-3.097)	0.012*
[2nd cycle vs. 3rd cycle]				

<sup>\*</sup>Significant at 0.05 level; \*\* significant at 0.001 level

The crude OR revealed an association between myopia and the school location, as well as between myopia and the school level. The adjusted OR showed that adolescents from urban schools were 1.4 times more likely to have myopia than those from rural schools, after adjusting for age, sex and cycle of studies. Adolescents in the 3rd cycle of studies were also 1.9 times more likely to have myopia than adolescents in the 2nd cycle, after adjusting for age, sex and school location.

Figure 1 shows the distribution of myopia severity, according to sociodemographic characteristics. Low myopia is more common in all subgrups, but there were sex differences ( $\chi^2$  = 11.868, p = 0.003). Low myopia is more common in both boys and girls, but of the universe of myopic boys (121), 52.0% have low myopia and 41.3% have moderate myopia, while of the universe of myopic girls (119), 72.3% have a low degree of myopia and 21.0% have moderate myopia. In the studied sample, boys have the highest proportion of moderate myopia. The distribution of myopia severity did not reveal differences between adolescents at different school levels ( $\chi^2$  = 1.077, p = 0.584) ou between school location ( $\chi^2$  = 0.109, p = 0.947).



<u>Fig. 1</u>

Myopia distribution by severity. *Legend* (Low myopia, Moderate myopia, High myopia). The number in the bars corresponds to the number of adolescents with the condition

## Covarage of myopia correction

We found that 35.8% of the screened population reported wearing spectacles or contact lenses (n = 400). There were significant differences between sex in the use of spectacles, with a higher proportion of girls (218 girls, 54,5% and 182 boys, 45.5%) reporting the use of these devices ( $\chi^2 = 6.409$ , p = 0.011). However, no significant differences were found between urban and suburban areas, nor among different levels of education. Among the adolescents who reported using some optical correction, 13.0% (95% CI: 9.7–16.3%) did not show up with their usual correction on the screening day (n = 53). Among the adolescents who attended with their usual optical correction (n = 347), the majority (n = 212) used a myopic prescription, with SE  $\leq$ -0.50D. However, 36 of the students who use myopia correction do not meet the myopia criterion (UVA  $\leq$  95VAR AND AR SE  $\geq$ -0.50D). Hence, of the 240 students with myopia that have been identified, 176 use optical correction. In summary, we found a myopia rate of 21.5% (95% CI: 18.9–24.4%), of which 73.3% (95% CI: 67.8–78.9%) already use some optical correction. Moreover 3.2% (95% CI: 0.8–5.6%) of the sample use prescriptions for myopia while they not need it. It was also noted that the majority use monofocal lenses, with only 12 reported cases using myopia control lenses. There were no records of orthokeratology or atropine usage.

Table 3 shows the counts and proportions of adolescents who habitually use optical correction, according to presenting VA (UVA for those who do not use any correction, or VAUC for those who have spectacles or contact lenses). It also shows the number of cases in which VA improved when measured with the pinhole. It can be observed that only 34.6% (95% CI: 28.6–40.6%) of the myopic population is optically well corrected. Of the myopic teenagers who already use optical correction, a large percentage use insufficient correction to achieve a good vision. It was observed that 38.7% (95% CI: 32.5–44.9%) of the myopic population uses partial correction and 26.7% (95% CI: 21.1–32.3%) does not use any type of correction. The assessment of VA with pinhole in uncorrected or partially corrected myopic adolescents (n = 157) revealed that in 80.3% (95% CI: 74.1–86.5%) of cases it is possible to improve vision with adequate optical correction.

#### Table 3

Counts and proportions of myopic adolescents who already use some optical correction, according to the limits of uncorrected visual acuity (UVA) and corrected visual acuity (VAUC). SE – spherical equivalent; PhVA – pinhole visual acuity

Criteria	N	%
SE≤ ( -0.50D) and UVA < 95VAR	240	100
VAUC≥95VAR [already wear spectacles or Contact lenses]	83	34.6
VAUC < 95VAR [already wear spectacles or Contact lenses]	93	38.7
UVA < 95VAR [do not wear spectacles or Contact lenses]	64	26.7
PhVA (N= (93+64)) [improved]	126	80.3%

#### Discussion

This study evaluated the prevalence of myopia in adolescents attending school from the 5th to the 9th year. For the SE $\leq$ -0.50D and UVA < 95VAR criteria, there was a prevalence of myopia of 21.5% (95%CI:18.9–24.4%) and for high myopia there was a prevalence of 1.4% (95%CI:0.9–2.3%). Attending the 3rd cycle of studies and attending schools in urban areas were factors associated with a higher prevalence of myopia, while age and sex were not associated with increased odds of myopia. We also observed that only 34.6% (95% CI: 28.6–40.6%) of myopic students were well-corrected and 26.7% (95% CI: 21.1–32.3%) did not use any optical refraction.

Myopia is notably more prevalent in Asia, with scientific literature indicating that children and adolescents in East Asia experience exceptionally high rates of myopia. In some regions, the prevalence has been reported to exceed 80.0% [25]. Given the limited information on myopia prevalence among adolescents in Portugal, it is more practical to analyze and compare myopia trends within the European context, where data are more robust. While extensive research exists in regions such as China, utilizing data from European countries provides a more relevant comparison to Portugal's situation and enables a more immediate and applicable analysis of local trends and predictors.

Studies on the prevalence of myopia in European children and adolescents are few, and those we found that had been published in the last 5 years report rates ranging from 10% in Sweden to 24.8% in Austria [ $\underline{26}$ ,  $\underline{27}$ ]. When cycloplegic refraction is used, rates are lower [ $\underline{26}$ ,  $\underline{28}$ ,  $\underline{29}$ ] than when cycloplegia is not used [ $\underline{27}$ ,  $\underline{30}$ ]. It should also be noted that most studies use SE $\leq$ -0.50D as the definition of myopia [ $\underline{22}$ ,  $\underline{26}$ ,  $\underline{28}$ - $\underline{30}$ ] but some studies use a more myopic cutoff point [ $\underline{31}$ ] and the joint assessment of autorefraction and visual acuity [ $\underline{32}$ ].

The myopia rate found in the present study is similar to that reported in other studies from European countries. A comparison of our results with reports from other studies that used more conservative criteria to define myopia (e.g.,  $SE \le -0.50$  and  $UVA \le 95VAR$ ) reveals that myopia is slightly more prevalent among adolescents in Portugal (21.5%) than in Bulgaria (19.0%) [26], and very similar to the prevalence reported in Germany (21.5%), where the definition of myopia used a cutoff point  $SE \le -0.75D$  [31]. For a broader comparison with the  $SE \le -0.50D$  criterion, we found a prevalence rate of 23.4%. This value is very close to that reported by other studies with children

and adolescents in Europe, which used the same definition of myopia. In Austria, a rate of 24.8% was found between the ages of 15 and 18, and in Spain, a rate of 20.1% was reported in children aged 6 to 7 [22, 30].

The prevalence of myopia and associated risk factors among children has not yet been determined. It is known that genetic and environmental factors play a role in its etiology. Risk factors for myopia may include a combination of genetic, environmental and lifestyle factors, with the most obvious being genetics, time outdoors, near work and sex [33]. The literature also reports that the prevalence of myopia increases with age, is more frequent in girls and in the urban areas [22, 34]. In the present study, there was no association between myopia and age, but an association was found with school level, with a higher prevalence of mypia in the 3rd cycle. Although a higher school level necessarily requires an older age, the age-adjusted multivariate analysis revealed that age has no association and that the probability of myopia is 1.9 times greater in adolescents in the 3rd cycle. We believe that this association is influenced by other factors that also contribute to myopia, such as the intensity of close work and excessive use of digital screens [34]. Adolescents in the 3rd cycle of studies have a greater academic workload, which requires them to dedicate more time to tasks with near vision. Furthermore, the excessive use of digital screens, both for academic support and leisure, tends to be greater among older adolescents [35].

Regarding sex, there is no consensus in the literature, with older studies reporting that men have a higher prevalence of myopia, while more recent studies report that women show higher prevelances [34]. Other authors also report finding no association between sex and myopia [36], in line with the results from our study. The urban environment is also described as a factor associated with myopia and urban-rural differences tend to be stronger where there is a greater disparity in living conditions [37, 38]. This study also found this association, with adolescents attending an urban school being 1.4 times more likely to have myopia than those attending a suburban school. In a study carried out in India, where the location of the school was also taken into account, it was observed that the rate of myopia was 1.3 times higher in urban schools than in suburban schools [39].

Multi-ethnic population-based studies suggest that the prevalence of myopia varies according to ethnicity. The scientific literature reports that the prevalence of myopia is highest in Asian populations (above 50.0%), and lowest in African regions (around 15.0%) and shows values between 20.0 and 40.0% in Europe and America [3, 13]. In our study, no significant differences were found in myopia rates between Portuguese and migrant adolescents. For the most conservative criterion, SE $\leq$ -0.50D and UVA < 95VAR, the prevalence of myopia was 21.4% for the Portuguese and 22.4% for the migrants' adolescents. The migrant population in this study was mostly from Brazil and African countries, with a low rate of students from Asia. We believe that the low representation of Asian adolescents is the main reason why the migrant population had a prevalence rate similar to that of adolescents born in Portugal.

Scientific literature reports that children with special educational needs have a higher prevalence of vision dysfunction when compared to population samples, and one of the main causes of this disability is refractive errors [40]. In our study, there were no significant differences in the proportion of myopic adolescents between those with (vs. without) SEN. Since adolescents with low levels of autonomy and low capacity for collaboration in the acquisition of measurements have been excluded from the study, adolescents from the SEN group with greater potential for vision impairment may have been left out of our sample. On the other hand, this analysis is limited to myopia, and refractive errors such as hyperopia or astigmatism in individuals with SEN may be more frequent [41].

Another finding from our study that deserves reflection concerns the use of optical correction. Other authors report that the use of corrective spectacles improves the cognitive and educational well-being, psychological well-being, mental health, and quality of life of school-age children and adolescents [42]. Several authors have reported high rates of uncorrected myopia in school-age children [24, 43]. Our study found that only 34.6% of adolescents with myopia were well-corrected, with 38.7% being under-corrected, and 26.7% not using any correction. According to WHO recommendations, in screening activities, an improvement in visual acuity with a pinhole means that the problem of vision impairment can be solved with the use of suitable spectacles [11]. In the present study, when evaluating visual acuity with the pinhole in uncorrected or undercorrected myopic participants, an improvement was obtained in 80.3% of cases, which means that these adolescents can see their vision improved with a simple pair of appropriately prescribed spectacles. We also found that there is a significant percentage of teenagers who report having spectacles, but who do not use them regularly (13.0%). Several studies have explored compliance to spectacle use in impairement vision due to refractive errors, and a systematic review reveals that non-adherence rates in children are hiegh, even when glasses are freely provided. The reasons for non-adherence are varief, including factors such as broken glasses, forgetfulness, parental perceptions, and peer pressure [44, 45]. The design of the present study did not allow us to explore the reasons for this behavior, but it reinforces the message that teenagers' refusal to wear prescribed spectacles puts their eye health and their professional and academic future at risk [42]. Health professionals and the educational community must come together to raise awareness of the risks of non-compliance with spectacles, promote educational campaigns, and debunk myths and beliefs.

The main strength of this work lies in its analysis of data on myopia from a large sample of adolescents in the central region of Portugal, providing valuable insights into the prevalence of myopia in Portugal. However, there are also some limitations. One of the main limitations of this study is the fact that cycloplegic refraction was not used. Nevertheless, we sought a methodological design that would minimize this aspect, looking for a reliable alternative. An open-field autorefractometer was used, an instrument that is described as the closest technique to cycloplegic refraction [21, 37]. Another important measure was to combine the spherical equivalent measurement with uncorrected visual acuity, as proposed by others authors [9, 10], enabling to confer more confidence to the myopia prevalence values found in the present study. The definition of a refractive threshold and a visual acuity threshold as a cut-off point for myopia is therefore an added value and strengthens the findings of this study. The selection of the eye with poorer visual acuity may have contributed to some overestimation of myopia prevalence compared to studies that consider only one eye. However, this approach has also been adopted in similar studies [28, 32]. The association between myopia prevalence and the presence of modifiable environmental risk factors (e.g., shorter distance and longer time spent for near work) was not addressed in this study, representing an opportunity for future work. Studying modifiable environemental risk factors is fundamental for understanding which habits and behaviors of adolescents are associated with the development of myopia, providing relevant evidence for the development of recommendations for its prevention and management.

# Conclusions

This paper is a cross-sectional study of myopia in adolescents at a center in Portugal. It shows that myopia in adolescence is comparable to that reported by other European countries, being at the upper end of reported rates (above 20.0%). Moreover, it showed that mypia was higher among higher school levels and among students of urban schools.

The high prevalence of uncorrected or under-corrected myopia is a worrying aspect. Another pertinent aspect concerns non- compliance with spectacles, as a considerable number of students who reported having spectacles were not wearing them at the time of the assessment. Adolescents' refusal to wear their usual spectacles puts their ocular health and their school and professional future at risk.

The epidemiological burden of myopia among schoolchildren necessitates a cross-sectoral approach, involving both health and education sectors, to ensure systematic screening, effective refractive error services, optical correction, and ongoing follow-up for affected children. Our results also highlight the critical need for public education on eye care and the development of an effective and sustainable school-age vision screening program to prevent vision impairment and blindness. By integrating public education with practical screening initiatives, we can ensure early detection and treatment, ultimately safeguarding children's vision health.

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## **Abbreviations**

SE Spherical equivalent

AR Autorefroctometer

VA Visual acuity

ETDRS Early Treatment of Diabetic Retinopathy Study

UVA Uncorrected visual acuity

VAUC Visual acuity with usual correction

PhVA Pinhole visual acuity

VAR Visual Acuity Rating

OR Odds ratio

CI Confidence interval

SEN Special educational needs

#### Author contributions

AFN, MCBS and CAG contributed to the concept of the study. AFN and MC acquired and analyzed the data. AFN and CAG helped with the interpretation of the data. AFN and MC drafted the manuscript. MCBS and CAG supervised the study. All authors read and approved the final manuscript.

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# Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

# **Declarations**

Ethics approval and consent to participate

This study conformed to the principles of the Declaration of Helsinki, and informed consent was signed by the participants' parents. The Ethics Committee of the National School of Public Health, approved this study (approval number CEENSP  $n^{\circ}$  29/2023).

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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# Systematic review and meta-analysis of myopia prevalence in African school children

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Aleksandra Barac, Editor

#### **Abstract**

#### Purpose

Increased prevalence of myopia is a major public health challenge worldwide, including in Africa. While previous studies have shown an increasing prevalence in Africa, there is no collective review of evidence on the magnitude of myopia in African school children. Hence, this study reviews the evidence and provides a meta-analysis of the prevalence of myopia in African school children.

#### Methods

This review was conducted using the 2020 Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. Five computerized bibliographic databases, PUBMED, Scopus, Web of Science, ProQuest, and Africa Index Medicus were searched for published studies on the prevalence of myopia in Africa from 1 January 2000 to 18 August 2021. Studies were assessed for methodological quality. Data were gathered by gender, age and refraction technique and standardized to the definition of myopia as refractive error ≥ 0.50 diopter. A meta-analysis was

conducted to estimate the prevalence. Significant heterogeneity was detected among the various studies ( $I^2 > 50\%$ ), hence a random effect model was used, and sensitivity analysis was performed to examine the effects of outliers.

#### Results

We included data from 24 quality assessed studies, covering 36,395 African children. The overall crude prevalence of myopia over the last two decades is 4.7% (95% CI, 3.9–5.7) in African children. Although the prevalence of myopia was slightly higher in females (5.3%, 95%CI: 4.1, 6.5) than in males (3.7%, 95% CI, 2.6–4.7; p = 0.297) and higher in older [12–18 years 5.1% (95% CI, 3.8–6.3) than younger children (aged 5–11 years, 3.4%, 95% CI, 2.5–4.4; p = 0.091), the differences were not significant. There was a significantly lower prevalence of myopia with cycloplegic compared with non-cycloplegic refraction [4.2%, 95%CI: 3.3, 5.1 versus 6.4%, 95%CI: 4.4, 8.4; p = 0.046].

## Conclusions

Our results showed that myopia affects about one in twenty African schoolchildren, and it is overestimated in non-cycloplegic refraction. Clinical interventions to reduce the prevalence of myopia in the region should target females, and school children who are aged 12–18 years.

#### Introduction

Uncorrected refractive error is the most common cause of visual impairment affecting an estimated one billion people globally [1]. Myopia is the most common refractive error and an important cause of ocular morbidity, particularly among school-aged children and young adults. Worldwide, myopia is reaching epidemic proportions linked to changing lifestyles and modern technology, particularly mobile devices [2]. Globally, myopia affected 22.9% of the world's population in 2000, with projections of an increase to 49.8% by 2050 affecting 4.8 billion people [2], representing a 117% increase over 50 years. According to a 2015 report, it was estimated that globally, about 1.89 billion people are myopic and 170 million have high myopia [3].

The reported prevalence of myopia in children aged 5–17 years ranges from 1.2% in Mechi Zone, Nepal, to 73.0% in South Korea  $[\underline{4},\underline{5}]$ . Over 15 years, the prevalence of myopia increased from 79.5% to 87.7% in Chinese high school children with an average age of 18.5  $\pm$  0.7 years  $[\underline{6}]$ . In South African school children aged 5–15 years, the reported prevalence of myopia was only 2.9% with retinoscopy and 4.0% using autorefraction  $[\underline{7}]$ . The authors reported that this prevalence increased to 9.6% at age 15 years.

The increase in myopia prevalence will have a significant economic impact because of associated ocular health problems and visual impairment. Uncorrected myopia of between– 1.50 D and– 4.00 D can significantly affect vision to be regarded as a cause of moderate visual impairment and blindness, respectively [8]. Apart from its direct impact on visual impairment, high myopia [usually defined as a spherical equivalent  $\geq 5.00$ D [4, 9, 10] of myopia, although the definitions used to grade myopia are variable] increases the risk of potentially blinding ocular pathologies such as retinal holes; retinal tears; retinal degeneration; retinal detachment; and myopic macular degeneration [3, 11]. Uncorrected myopia has huge social, economic, psychological and developmental implications [12]. The economic cost of refractive errors, including myopia, has been estimated to be approximately US\$ 202 billion per annum [13], far exceeding that of other eye diseases.

The increasing prevalence of myopia has led to research in the study of the possible mechanism for myopia development, which has generated two broad themes: the role of nature (genetic influences) and nurture (environmental influences including lifestyle). Understanding the mechanism for the development of myopia is also being explored in the control of myopia. Epidemiologic data from Southeast Asia has given credence to the association between near work and myopia, given the number of hours children from this region spend doing near work. Due to vast regional differences in culture, habits, socioeconomic status, educational levels and urbanization, there is uncertainty as to the exact magnitude of the myopia burden among African school–aged children and its trend over time [14].

In the last few decades, there has been a change in the lifestyle and behavior of people in Africa as a result of increasing urbanization [15]. Africa's urban population grew from 27 million in 1950 to 567 million in 2015 (a 2,000% increase), and now 50% of Africa's population live in one of the continent's 7,617 urban agglomerations of 10,000 or more inhabitants [16]. Consequently, more children and young adults in Africa are increasingly engaged in indoor and near work activities compared to earlier generations [17]. Children spend long hours doing schoolwork and, following the advent of technology, increasingly use mobile devices for gaming and other activities [18, 19]. These factors are thought to promote myopia development and/or progression [20–23].

Africa is the world's second largest and second most populous continent, after Asia, and it accounts for about 16% of the world's human population. While every global region will experience a decline in population by 2100, the African population is expected to triple. Africa's population is the youngest amongst all the continents, the median age in 2012 was 19.7 years compared to the global median of 30.4 years. This young population is an important asset for the continent's development. The challenges of the young population must be addressed in time as they constitute the bulk of the productive age of the economy. While rising myopia is a cause for global concern, it is not given due attention in Africa due to a lack of adequate prevalence data and prospective studies tracking the trend of myopia over decades [24]. Due to this, the representation of Africa is poor in studies predicting global trends of myopia [24]. The aim of this study was to systematically review the evidence and provide a meta–analysis of the prevalence of myopia in African school children which will address the knowledge gap and help understand the prevalence of myopia among this group in Africa.

## Materials and methods

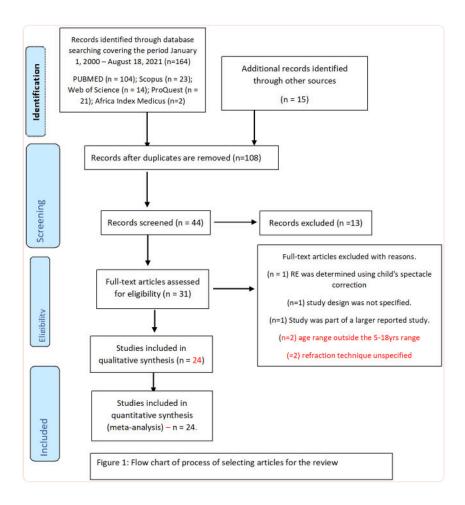
This systematic review followed the framework of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA. See Checklist in <u>S1 File</u>) [25]. The protocol for the review was registered with PROSPERO (#CRD42020187609).

## Search strategy and quality assessment

Two review team members (GO and BE) performed an independent systematic search and review of myopia in Africa using published data spanning the last two decades. Refractive error came into reckoning as a cause of visual impairment in the last two decades, following the change in the definition of visual impairment which was based on presenting visual acuity [26]. The search was conducted on 25th May and 18th August 2021. A third reviewer, KO, adjudicated where there were disagreements. The quality of each selected article was assessed using the checklist developed by Downs and Black [27] and each included article was assessed and scored on a 10-item scale (scoring is shown in S1 Table). The search was restricted to articles available online, articles

mentioning prevalence of myopia in any region of Africa, and articles published in the English language. Searches included the following databases: Web of sciences, PubMed, ProQuest, MEDLINE, Scopus, and African Index Medicus from 1<sup>st</sup> of January 2000 to August 18, 2021.

We searched these databases using the following MeSH (Medical Subject Heading) terms and keywords: Refractive AND error AND Africa AND children AND prevalence. A number of iterations of these search terms were used, for example, "refractive error AND Africa AND children AND prevalence" or "refractive error AND Africa AND children". Further details about search strategy and MeSH terms are available in the (S2 File). A broader search also used terms such as epidemiology, myopia, and school children. We also identified and included relevant studies by manually searching through the reference lists of identified papers. The PRISMA flowchart presented in Fig 1 shows the process used for selecting articles.



 $\label{eq:fig1} \hline Flow chart of process of selecting articles for the review.$ 

#### Inclusion and exclusion criteria

Studies published between 2000 and 2021, investigating the prevalence of refractive error in male and female school children aged 5 to 18 years of age were included in the review. Studies that employed an observational cross-sectional study design; had a clear description of the sampling technique; stated the method of measuring refractive error (cycloplegic or non-cycloplegic refraction), as well as objective or subjective refraction; stated the criteria for defining myopia (spherical equivalent  $\geq 0.50$  D of myopia [2, 28–30]; the study was either school-based or

population-based; and were published in English language, were included in the review. The decision as to whether the articles met the inclusion criteria was made independently by the two reviewers (GO and BE) and where there was a disagreement, a third reviewer (KO) was consulted.

Studies where the criteria for defining myopia were not specified; the ages of the participants were either not specified or outside the age range specified for this review; or which reported findings from a hospital/clinic-based sample were excluded from the review.

## Data extraction

The data extracted from each article included the following: Authors; year of publication; country of study; study design; sample size; sampling technique; the age of study participants; criteria for defining myopia; method of refractive error assessment (cycloplegic vs non-cycloplegic); method of refractive error assessment (objective vs subjective); prevalence of myopia; and the proportion of refractive error due to myopia. Where the reported prevalence was not clearly defined, the corresponding author in the published article was contacted for clarification.

## Statistical methods

Meta–analysis was conducted using Stata version 14.0 (StataCorp, College Station, TX, USA). The syntax "metaprop" in Stata was used to generate forest plots and each forest plot showed the prevalence of myopia in school children, by gender, age and refraction technique in individual studies and its corresponding weight, as well as the pooled prevalence in each subset and its associated 95% confidence intervals (CI). A heterogeneity test obtained for the different studies showed a high level of inconsistency (I² > 50%) thereby indicating the use of a random effect model in all the meta–analyses conducted. Sensitivity analysis was carried out by examining the effect of outliers, by employing similar method to that used by Patsopoulos et al. [31], which involves the process of comparing the pooled prevalence before and after eliminating one study at a time. The funnel plot was used to report the potential bias and small/large study effects and Begg's tests was used to assess asymmetry. The prevalence was subdivided into separate datasets based on overall prevalence, males or females, cycloplegic or non-cycloplegic refraction for a more detailed analysis of the prevalence of myopia. Also, to study a possible variation of the prevalence of myopia in terms of age, the age groups in the reported studies were divided into two categories: 5–11 years and 12–18 years. Their respective funnel plots are shown as (\$3-\$57 Files).

## Results

# Summary of included studies

From the described search strategy, a total of 164 potentially relevant titles/abstracts of articles were initially identified. Fig 1 presents the flowchart of the article screening and selection process. Following a quick inspection of identified studies and removal of duplicate articles, 44 relevant articles were assessed for eligibility. Using the pre–defined inclusion and exclusion criteria, 24 of 30 articles that underwent detailed review were eligible, and data from these studies were included in this study. A breakdown of the eligible studies as well as their quality assessment scores (maximum of 10) are presented in Table 1. S1 Table shows how the quality assessment scores were calculated.

 $\label{thm:continuous} Table\ 1$  Characteristics of studies that reported the prevalence of myopia in school-aged children in Africa and were included in the meta-analysis.

First Author	Year of study	Study Country <sup>†</sup>	Age group (years)	Mean age (year		Total Sample size	Cycloplegia	-	Prevalence of myopia (%)	Comm refrac error
Atowa [32]	2017	Nigeria	8-15	11.5 2.3	±	1197	Yes	Objective	2.7	
Wajuihian [ <u>33</u> ]	2017	South Africa	13-18	15.8 1.6	±	1586	No	Objective	7	
Chebil [ <u>34</u> ]	2016	Tunisia	6-14	10.1 1.8	±	6192	Yes	Objective	3.71	
Kedir [ <u>35</u> ]	2014	Ethiopia	7–15	Not report	ed	570	No	Subjective	2.6	
Soler [ <u>36</u> ]	2015	Equatorial Guinea	6-16	10.8 3.1	±	425	Yes	Objective	10.4	
Kumah [ <u>37</u> ]	2013	Ghana	12-15	13.8		2435	Yes	Objective	3.2	
Mehari [ <u>38</u> ]	2013	Ethiopia	7–18	13.1 2.5	±	4238	No	Objective	6	
Jimenez [ <u>39</u> ]	2012	Burkina Faso	6-16	11.2 2.4	±	315	No	Objective	2.5	
Naidoo [ <u>7</u> ]	2003	South Africa	5-15	Not report	ed	4890	Yes	Objective	2.9	
Yamamah [ <u>40</u> ]	2015	Egypt	6-17	10.7 3.1	±	2070	Yes	Objective	3.1	Astign
Nartey [ <u>41</u> ]	2016	Ghana	6-16	10.6		811	No	Subjective	4.6	
Anera [ <u>42</u> ]	2006	Burkina Faso	5-16	10.2 2.2	±	388	Yes	Objective	0.5	
Chukwuemeka [ <u>43</u> ]	2015	South Africa	7–14	9.9 2.2	±	421	No	Objective	18.7	Astign
Alrasheed [44]	2016	Sudan	6-15	10.8 2.8	±	1678	Yes	Objective	6.8	Myopi
Abdul-Kabir [45]	2016	Ghana	10-15	Not report	ed	208	No	Objective	22.6	Myopi
<b>Ebri</b> [ <u>46</u> ]	2019	Nigeria	10-18	13.3 1.9	±	4241	Yes	Objective	4.8	Astign
<b>Ezinne</b> [ <u>47</u> ]	2018	Nigeria	5-15	9.0 2.5	±	998	Yes	Objective	4.5	Myopi

 $<sup>^{\</sup>dagger}$  = country the study was conducted;

 $<sup>^{\</sup>mbox{\scriptsize $^{$}$}}$  = authors provided data for only those aged 5–18 years.

The included studies comprised of the following: six (25.0%) studies from Ghana, four (16.7%) each from South Africa, and Nigeria, three from Ethiopia (12.5%), two (8.3%) from Burkina Faso, and one (4.2%) each from Sudan, Egypt, Equatorial Guinea, Somalia and Tunisia (Table 1). Of the reviewed articles, 84.2% (n = 21) were school-based, cross-sectional studies, two (8.3%) were population-based, cross-sectional studies, while one (4.2%) employed a cross-sectional study design but did not report whether it was school or population-based.

## Method of measuring refractive error in African school-aged children

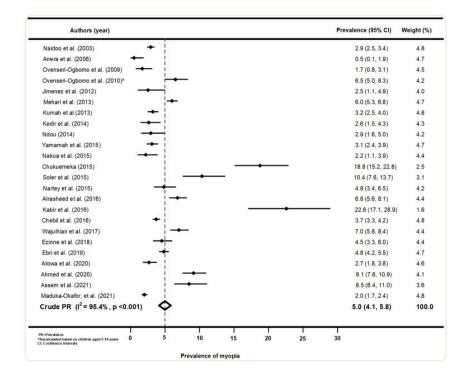
Of the reviewed studies, 13 (54.2%) performed cycloplegic refraction to determine the refractive error status of the children, while non-cycloplegic refraction was used in 11 (45.8%) of the studies. Regarding the technique used for refractive error measurement, over three–quarters of the studies (n = 20, 83.3%) performed objective refraction, with about one–sixth (n = 4, 16.7%) performing subjective refraction.

# Prevalence of myopia in African school-aged children

The number of children aged 5–18 years included in the study ranged from 208 for a study conducted in Ghana [ $\underline{45}$ ] to 6192 for another study conducted in Tunisia [ $\underline{34}$ ,  $\underline{55}$ ]. The prevalence of myopia reported in these studies ranged from 0.5% [ $\underline{42}$ ] to 10.4% [ $\underline{36}$ ,  $\underline{52}$ ] with cycloplegic refraction. In studies where non–cycloplegic refraction was used to determine refractive error refraction in school children, the reported myopia prevalence ranged from 1.7% [ $\underline{51}$ ] to 22.6% [ $\underline{45}$ ].

# Meta-analysis of myopia prevalence in children ag 5–18 years in Africa (2000–2021)

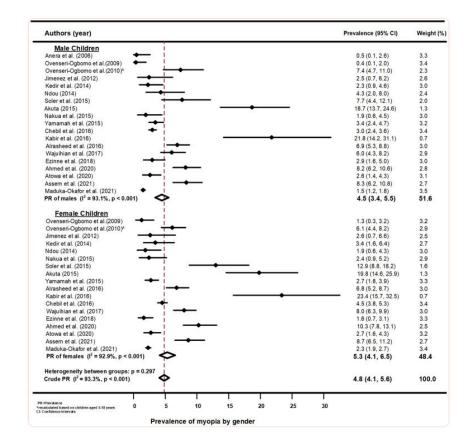
Myopia prevalence among school children in Africa Fig 2 shows a forest plot of the prevalence of myopia among African school children aged 5–18 years. The pooled estimate of myopia in the African region was significant (5.0%, 95%CI: 4.1, 5.8; p<0.001) and about 37.5% of the studies (n = 9) reported significantly higher prevalence of myopia and 50% (n = 12) reporting significantly lower prevalence compared with the pooled estimate across Africa. The study by Abdul–Kabir found the highest prevalence (22.6%) of myopia among Ghanaian children (95%CI: 17.1, 28.9) [45], while Anera et al. found the lowest prevalence among children in Burkina Faso (0.5%, 95%CI: 0.1, 1.9) [42]. The pooled prevalence estimates of myopia was similar to the study by Ebri [46] and Ezinne [47] (4.8%, 95%CI:4.2, 5.5), both involving children from Nigeria [46, 47]. Funnel plots and using Begg's test for Myopia in Africa indicated homogeneity (S3 File) and meta–regression analysis of myopia by year of publication indicated that publication of year increased as the proportion of myopia decreased but this relationship was not statistically significant (p = 0.423, S7 File).



 $\frac{Fig\,2}{Forest\ plot\ of\ myopia\ prevalence\ from\ the\ meta-analysis\ of\ African\ studies.}$ 

# Myopia prevalence by gender of the School children in Africa (2000–2021)

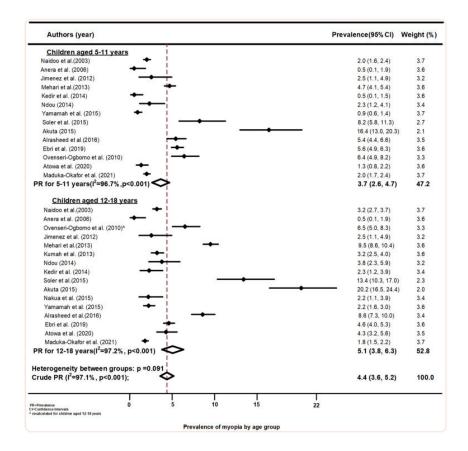
Fig 3 is a forest plot for prevalence of myopia by gender among school children aged 5–18 years in Africa. The prevalence estimates varied significantly between studies in both male and female children (p<0.001, per gender), and the overall pooled prevalence of myopia by gender was 4.8% (95%CI: 4.1, 5.6) and similar between male and female estimates (p = 0.297). Compared with the overall pooled estimate, the prevalence of myopia was slightly higher in male (4.5%, 95%CI: 3.4, 5.5) children than females (5.3%, 95%CI: 4.1, 6.5) but the difference was not significant as indicted by the overlapping of the CIs with that of the overall pooled estimate. Funnel plots and using Begg's test for Myopia by gender reported absence of publication biases (5.4% File).



 $\frac{Fig\,3}{Forest\ plot\ of\ myopia\ prevalence\ by\ gender\ from\ the\ meta-analysis\ of\ African\ studies.}$ 

# Myopia prevalence by age group of the school children in Africa (2000–2021)

The forest plot of the prevalence of myopia in children aged 5–11 years and 12–18 years is presented in Fig 4. The pooled estimate of myopia in school children aged 5–11 years and 12–18 years was lower (3.7%, 95%CI 2.6, 4.7) and higher (5.8%, 95%CI 3.8, 6.3) respectively, than the pooled estimate but none was significant as they overlapped with the pooled estimate in Africa (4.4%, 95%CI 3.6, 5.2). The heterogeneity between the groups was approaching significant (p = 0.091) but older children had a higher prevalence of myopia than younger children. Among those aged 5–11 years, the highest significant prevalence was reported in a Ghanaian study (16.4%, 95%CI: 13.0, 20.3) and a study conducted in Equatorial Guinea (8.2%, 95%CI: 5.8, 11.3) while school children in Ethiopia (0.5%, 95%CI: 0.1, 1.5) had the lowest significant prevalence estimate of myopia. Among those aged 12–18 years, children in Ghana also showed the highest significant prevalence of myopia (20.2%, 95%CI: 16.5, 24.4), but the lowest prevalence was reported among School children in Burkina Faso (0.5%, 95%CI: 0.1, 1.9). The heterogeneity of these studies by age as subgroups analysis were low (S5 File).



 $\label{eq:fig4} \mbox{Forest plot of myopia prevalence by age group across African studies}.$ 

# Myopia prevalence by mode of refraction among school children in Africa (2000–2021)

The forest plot displayed in Fig 5 shows the pooled estimate of myopia prevalence among school children in Africa. Using cycloplegic refraction, studies have reported significantly lower prevalence estimates of myopia among school children in Africa compared with those that used non–cycloplegic refraction (4.2%, 95%CI: 3.3, 5.1 versus 6.4%, 95%CI: 4.4, 8.4; p = 0.046). From the plot, it can be seen that studies that used non cycloplegic technique to determine refraction had greater variabilities in the reported myopia prevalence (ranging from 1.7 to 22.6%), but those that performed cycloplegic refraction had smaller between study variability in the reported prevalence of myopia (range from 0.5 to 10.4%). Funnel plots and the Begg's test for Myopia by refraction technique shown in S6 and S7 Files, respectively, found no publication biases.

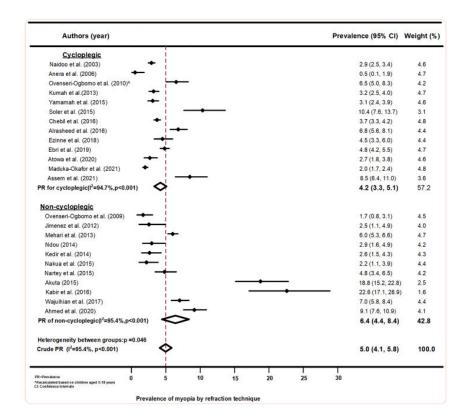


Fig 5

Forest plot of myopia prevalence by refraction technique among school children in Africa.

#### Discussion

# Prevalence of myopia

The present study provided recent estimates of the myopia prevalence in African children using data from twenty eight studies conducted over two decades. The prevalence of myopia defined as SER  $\geq$  0.50D of myopia in school children across African countries was 4.7% (95%CI, 3.9, 5.7%) and there were wide variations within and between African countries. A significantly higher prevalence rate was observed in Ghana [45] and South Africa [43], with significantly lower rates in Burkina Faso [42] and Ethiopa [56]. In some countries like Ghana, the variation in the reported prevalence of myopia between studies reached 21% [37, 41, 45, 48, 51, 52]. Although the regional variations in myopia prevalence found in this study are consistent with the statement of Foster and Jiang who remarked that "Considerable regional difference exists from country to country even within the same geographical area" [57], it remains unclear why these variations exist. While the criteria for defining refractive error is often cited as the reason for the variation in the prevalence of refractive errors, including myopia, between studies, this may not be the case in our study because only studies that defined myopia as spherical equivalent of  $\geq$  0.50 D were included.

The overall low prevalence of myopia found across Africa is consistent with other studies that reported lower myopia prevalence in African children compared with Asian children [5, 58]. It is instructive to note that in four of the studies that were included in the current review [36, 43, 45, 52], the reported prevalence of myopia was greater than 10%. Of these, two studies [36, 52] used cycloplegic refraction, which is thought to more accurately estimate the prevalence of myopia [59]. The lower prevalence of myopia in Africa compared with the other regions may be related to the

differences in genetic predisposition to myopia development, and to culture [60–62]. Although the role of genetics in the development and progression of myopia is reported to be small [12], it is believed to have a role in an individual's susceptibility to environmental risk factors for myopia [63]. In addition, several studies have shown the major involvement of environmental factors such as near work (writing, reading, and working on a computer) in myopia development [60, 63]. In many African countries, children do not start education and learning at the same early age as in other countries of Asia. African children are therefore exposed to less near work and are more involved with outdoor activities, resulting in less risk of developing myopia compared with their Asian counterparts. This assertion is supported by the fact that in 2010, the pre-primary school enrolment rate in the most populous country in Africa (Nigeria) was 41.83% compared to 89.12% in 2012 in China (the most populous country in Asia) [64]. We acknowledge that a recent investigation [65] has shown that more precise objective measures are required to make definitive conclusions about the relationship between myopia and near work.

Notwithstanding the relatively low prevalence of myopia found among African children, there is a need to monitor myopia prevalence among children in this region given the increasing access to, and use of, mobile devices among African population [19], including children. This is important considering the reported higher increase in the prevalence of myopia in black children living in Africa (2.8% to 5.5%) compared with other black children not living in Africa (4.8% to 19.9%) after 10 years [58]. It is assumed that black children not in Africa may have more access and exposure to near work, including mobile devices, and less outdoor activities than their counterparts in Africa.

## Age and gender-based differences in myopia prevalence

There was a 34.6% increase in the prevalence of myopia between the age groups with the older age group having a higher prevalence of 5.2%. The slightly higher prevalence of myopia between the two age groups shows there is a tendency for myopia prevalence to increase with age which is consistent with previous studies from elsewhere [58, 66, 67]. This increase in myopia prevalence is thought to be associated with the increasing growth of the eyeball. Although the pooled prevalence of myopia in female children was slightly higher than in male children (4.7 versus 3.7%), the difference did not reach statistical significance. The influence of gender on the prevalence of myopia has not been unequivocal in the literature [68–72] with some suggesting that the slightly higher prevalence in females may be related to the different ages of onset of puberty between boys and girls [73]. Other factors that could account for the reported apparent higher prevalence of myopia in girls include limited outdoor activity time than boys [74].

# Prevalence of myopia by refraction technique (cycloplegic and non-cycloplegic)

The present study demonstrated that cycloplegic refraction resulted in significantly lower estimates of myopia prevalence than non-cycloplegic refraction, which was consistent with previous studies [75–78]. It has been reported that non-cycloplegic refraction overestimates the prevalence of myopia, yields a non-reliable measurement of association of myopia risk factors [59, 76], and hence cycloplegic refraction is regarded as the gold standard for measuring myopia [59]. Over half of the studies in this review utilised cycloplegic refraction, which is particularly important in this age group where the difference between the cycloplegic and non-cycloplegic refraction is quite high [77, 78]. The fact that non-cycloplegic refraction often results in overestimation of myopia may have, in part, accounted for the high prevalence reported in one study from Ghana [45]. Furthermore, we have demonstrated that cycloplegic refraction results in a lower variability of measured refractive error than non-cycloplegic refraction (see Fig 5), which may reflect the variable accommodative state

during the refraction of children of different ages. This finding underscores the need to appropriately control accommodation when performing refraction especially in young children who have a higher amplitude of accommodation and in whom accommodation is more active.

## Implications of the study

This is the first systematic review and meta-analysis to estimate the prevalence of myopia among school children in Africa and its variation with age, gender and refraction technique. As previously reported, the prevalence of myopia in Africa appears low compared to other regions such as South East Asia. This study also provides baseline data for comparison and future prevalence studies to establish a trend in myopia epidemiology in this population. A further remarkable finding in this review is the demonstration that non-cycloplegic refraction overestimated the prevalence of myopia and results in more variable estimates of refractive errors compared with cycloplegic refraction. The interpretation of myopia prevalence data obtained from non-cycloplegic refraction may be potentially misleading to researchers and policymakers. As a result, it is recommended that cycloplegic refraction be used in all studies investigating the prevalence of myopia in children.

## Strengths and limitations of the review

This review has certain limitations. Firstly, this review did not investigate the trend in the prevalence of myopia among school children in Africa due to the limited number of studies. Secondly, the selection of English-only studies likely biased the results towards studies in Anglophone countries or countries where the findings were reported in English. Thirdly, the current review did not explore the various factors influencing the epidemiology of myopia in this population. Despite these limitations, a major strength of this study is the selection of studies that used a uniform definition of myopia (i.e.  $\geq 0.50$ DS of myopia) which allowed for a better comparison in the reported prevalence of myopia. In addition, the study excluded studies that were conducted in unselected groups such as hospital-based studies and studies that did not report any evidence of sampling in the study. In addition, the selected studies were evaluated for robustness in the study designs employed in each study.

# Conclusions

In summary, this systematic review and meta-analysis have shown that the prevalence of myopia among schoolchildren in Africa is lower than other regions of the world. The use of non-cycloplegic refraction for estimation of myopia prevalence can be misleading as it returns higher and more variable prevalence estimates. There is a need to monitor the trend of myopia as more children in this region are increasingly being exposed to identified risk factors for myopia development including access to mobile devices, increased near work, increased online or remote learning, and limited time outdoors. Future studies are needed to understand the role of ethnicity on the myopia prevalence in Africa as the inclusion and comparison of the different ethnicities (Black vs White vs Asian) in the same region would add useful information about whether significant differences in the prevalence of myopia among different ethnicity in Africa exists.

# Supporting information

S1 Table
Quality assessment of full-text articles included in review.
(DOCX)
Click here for additional data file. (23K, docx)
S1 File
PRISMA 2020 checklist.
(DOCX)
Click here for additional data file. (32K, docx)
S2 File
Search terms for refractive error Africa children prevalence filters (2000–2021).
(DOCX)
Click here for additional data file. (13K, docx)
S3 File
Funnel plots and 95% confidence intervals of Myopia.
(DOCX)
Click here for additional data file. (15K, docx)

S4 File
Funnel plots and 95% confidence intervals of Myopia by gender.
(DOCX)
Click here for additional data file. (15K, docx)
S5 File
Funnel plots and 95% confidence intervals of Myopia by age in categories.
(DOCX)
Click here for additional data file. (15K, docx)
S6 File
Funnel plots and 95% confidence intervals of Myopia by refraction technique.
(DOCX)
Click here for additional data file. (15K, docx)
S7 File
A meta-regression analysis of Myopia by year of publication.
The vertical axis is the log proportion of Myopia, and the horizontal axis represents year of publication. Each dark dot represented one selected study, and the size of each dark dots corresponds to the weight assigned to each study. Given the slope of the regression line has descending slightly in this figure, this could be interpreted as publication of year increased, the proportion of myopia decreased and, this relationship did not differ statistically (p = 0.5512).

(DOCX)

Click here for additional data file. (37K, docx)



Data used in the analysis.

(XLSX)

Click here for additional data file. (46K, xlsx)

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The authors recieved no specific funding for this work.

# **Data Availability**

All relevant data are within the paper and its <u>Supporting information</u> files.

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### Decision Letter 0

Aleksandra Barac, Academic Editor

13 Dec 2021

PONE-D-21-28841Systematic Review and Meta-analysis of Myopia prevalence in African School children.PLOS ONE

Dear Dr. Osuagwu,

Thank you for submitting your manuscript to PLOS ONE. After careful consideration, we feel that it has merit but does not fully meet PLOS ONE's publication criteria as it currently stands. Therefore, we invite you to submit a revised version of the manuscript that addresses the points raised during the review process.

Please submit your revised manuscript by Jan 27 2022 11:59PM. If you will need more time than this to complete your revisions, please reply to this message or contact the journal office at <a href="mailto:plosone@plos.org">plosone@plos.org</a>. When you're ready to submit your revision, log on to <a href="https://www.editorialmanager.com/pone/">https://www.editorialmanager.com/pone/</a> and select the 'Submissions Needing Revision' folder to locate your manuscript file.

Please include the following items when submitting your revised manuscript:

- A rebuttal letter that responds to each point raised by reviewers. You should upload this letter as a separate file labeled 'Response to Reviewers'.
- A marked-up copy of your manuscript that highlights changes made to the original version. You should upload this as a separate file labeled 'Revised Manuscript with Track Changes'.
- An unmarked version of your revised paper without tracked changes. You should upload this as a separate file labeled 'Manuscript'.

If you would like to make changes to your financial disclosure, please include your updated statement in your cover letter. Guidelines for resubmitting your figure files are available below the reviewer comments at the end of this letter.

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We look forward to	receiving your	revised	manuscript.
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Kind regards,

Aleksandra Barac

Academic Editor

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Reviewers' comments:

Reviewer's Responses to Questions

#### **Comments to the Author**

1. Is the manuscript technically sound, and do the data support the conclusions?

The manuscript must describe a technically sound piece of scientific research with data that supports the conclusions. Experiments must have been conducted rigorously, with appropriate controls, replication, and sample sizes. The conclusions must be drawn appropriately based on the data presented.

Reviewer #1: Yes

Reviewer #2: Yes

\*\*\*\*\*

2. Has the statistical analysis been performed appropriately and rigorously?

Reviewer #1: Yes

Reviewer #2: Yes

\*\*\*\*\*

3. Have the authors made all data underlying the findings in their manuscript fully available?

The <u>PLOS Data policy</u> requires authors to make all data underlying the findings described in their manuscript fully available without restriction, with rare exception (please refer to the Data Availability Statement in the manuscript PDF file). The data should be provided as part of the manuscript or its supporting information, or deposited to a public repository. For example, in addition to summary statistics, the data points behind means, medians and variance measures should be available. If there are restrictions on publicly sharing data—e.g. participant privacy or use of data from a third party—those must be specified.

Reviewer #1: Yes

Reviewer #2: No

\*\*\*\*\*\*

4. Is the manuscript presented in an intelligible fashion and written in standard English?

PLOS ONE does not copyedit accepted manuscripts, so the language in submitted articles must be clear, correct, and unambiguous. Any typographical or grammatical errors should be corrected at revision, so please note any specific errors here.

Reviewer #1: Yes

Reviewer #2: Yes

\*\*\*\*\*

5. Review Comments to the Author

Please use the space provided to explain your answers to the questions above. You may also include additional comments for the author, including concerns about dual publication, research ethics, or publication ethics. (Please upload your review as an attachment if it exceeds 20,000 characters)

Reviewer #1: The authors conducted a review and meta-analysis of articles on the prevalence of myopia in African children.

This study follows the recommendations for this type of review.

Several points of detail should be reported

- $1\,^{\circ}$  In the inclusion criteria, the authors report having excluded studies in which the ages of the participants were either not specified or outside the age range specified. But they did not clearly define the age ranges of this review themselves.
- 2 ° Two articles have been included but pose a problem in my opinion.
- They did not report whether it was school- or population-based. The inclusion / exclusion criteria are not clear at this level
- They did not specify the method used to determine the refractive error. However, it is clearly specified in the inclusion criteria "stated the method of measuring refractive error cycloplegic or non-cycloplegic refraction, as well as objective or subjective refraction"

I think we should exclude these articles or change the inclusion criteria

- $3^{\circ}$  in the table, in addition to the age limits, the median or average of the ages must be included in each article. Moreover, the authors specify it for an article: In another study (43) however, the children were aged 4 24 years but with a mean age of 12 years.
- 4° in the discussion, when the authors evoke the fact that fewer children await early education and learning in many African countries, compared with Asian countries, means that the children do less near work and are more involved with outdoor tasks, nuances must be made.

In a meta-analysis, Gajjar (Acta ophtahlmol 2021) show that the role of near vision is still questionable and that the study of the literature does not allow a conclusion. On the other hand, Tang Y (J Glob Health. 2021) shows the existence of a difference in the prevalence of myopia in China depending on whether the children live in the city or in the countryside.

5° The authors said that "he apparent higher prevalence of myopia in girls may be due to girls having ... shorter axial length than boys". That surprising !!!

Reviewer #2: This is a good Meta-analysis regarding the myopia prevalence in Africa

it is good structured and well-written; however, it would be better if you add a figure showing prevalence of myopia by ethnicity (black vs white vs asian in the same region) to show if it affects the prevalence of myopia or not

\*\*\*\*\*\*

6. PLOS authors have the option to publish the peer review history of their article (what does this mean?). If published, this will include your full peer review and any attached files.

If you choose "no", your identity will remain anonymous but your review may still be made public.

**Do you want your identity to be public for this peer review?** For information about this choice, including consent withdrawal, please see our <a href="Privacy Policy">Privacy Policy</a>.

Reviewer #1: No

Reviewer #2: No

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# Author response to Decision Letter 0

13 Jan 2022

Response to Reviewers comments

Dear Aleksandra Barac

Thanks for the very useful comments which has strengthened our manuscript. We have revised the article according to the suggested comments. We have provided a point-by-point response to all reviewers comments for clarity.

The changes made in the revised manuscript and supplementary files were highlighted using red font for easy identification.

Journal Requirements:

When submitting your revision, we need you to address these additional requirements.

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Response: Done

Comments to the Author

1. Is the manuscript technically sound, and do the data support the conclusions?

The manuscript must describe a technically sound piece of scientific research with data that supports the conclusions. Experiments must have been conducted rigorously, with appropriate controls, replication, and sample sizes. The conclusions must be drawn appropriately based on the data presented.

Reviewer #1: Yes

Reviewer #2: Yes

2. Has the statistical analysis been performed appropriately and rigorously?

Reviewer #1: Yes

Reviewer #2: Yes

\_\_\_\_

3. Have the authors made all data underlying the findings in their manuscript fully available?

The PLOS Data policy requires authors to make all data underlying the findings described in their manuscript fully available without restriction, with rare exception (please refer to the Data Availability Statement in the manuscript PDF file). The data should be provided as part of the manuscript or its supporting information, or deposited to a public repository. For example, in addition to summary statistics, the data points behind means, medians and variance measures should be available. If there are restrictions on publicly sharing data—e.g. participant privacy or use of data from a third party—those must be specified.

Reviewer #1: Yes

Reviewer #2: No

Response: We have included the study data used in the analysis as a spread sheet inline with PlosOne policy

\_\_\_\_\_

4. Is the manuscript presented in an intelligible fashion and written in standard English?

PLOS ONE does not copyedit accepted manuscripts, so the language in submitted articles must be clear, correct, and unambiguous. Any typographical or grammatical errors should be corrected at revision, so please note any specific errors here.

Reviewer #1: Yes

Reviewer #2: Yes

#### 5. Review Comments to the Author

Please use the space provided to explain your answers to the questions above. You may also include additional comments for the author, including concerns about dual publication, research ethics, or publication ethics. (Please upload your review as an attachment if it exceeds 20,000 characters)

#### Reviewer #1:

The authors conducted a review and meta-analysis of articles on the prevalence of myopia in African children.

This study follows the recommendations for this type of review.

Several points of detail should be reported

 $1^{\circ}$  In the inclusion criteria, the authors report having excluded studies in which the ages of the participants were either not specified or outside the age range specified. But they did not clearly define the age ranges of this review themselves.

Response: Agreed and we have excluded the 4–24year-old range study (Yareed et al) and the 5-19 year study (Ovenseri-Ogbomo et al) as they do not meet our stipulated inclusion criteria of 5-18 year.

- 2 ° Two articles have been included but pose a problem in my opinion.
- They did not report whether it was school- or population-based. The inclusion / exclusion criteria are not clear at this level. They did not specify the method used to determine the refractive error. However, it is clearly specified in the inclusion criteria "stated the method of measuring refractive error cycloplegic or non-cycloplegic refraction, as well as objective or subjective refraction"

Response: The inclusion and exclusion criteria were made clearer and as suggested, we excluded these studies as the two stipulated criteria are not specified [Rushood (39) and Woldeamanuel (47)]

 $3^{\circ}$  in the table, in addition to the age limits, the median or average of the ages must be included in each article. Moreover, the authors specify it for an article: In another study (43) however, the children were aged 4 - 24 years but with a mean age of 12 years.

Response: We have included the mean age in Table 1 and the study with age range 4-24years was excluded based on the exclusion criteria.

4° in the discussion, when the authors evoke the fact that fewer children await early education and learning in many African countries, compared with Asian countries, means that the children do less near work and are more involved with outdoor tasks, nuances must be made.

Response: In a meta-analysis, Gajjar (Acta ophthalmol 2021) showed that the role of near vision is still questionable and that the study of the literature does not allow a conclusion. On the other hand, Tang Y (J Glob Health. 2021) showed the existence of a difference in the prevalence of myopia in China depending on whether the children live in the city or in the countryside. However, we agree with the reviewer and have made the following revision in the discussion section:

In addition, several studies have shown the major involvement of environmental factors such as near work (writing, reading, and working on a computer) in myopia development(62, 65). In many African countries, children do not start education and learning at the same early age as in other countries of Asia. African children are therefore exposed to less near work and are more involved with outdoor activities, resulting in less risk of developing myopia compared with their Asian counterparts. This assertion is supported by the fact that in 2010, the pre-primary school enrolment rate in the most populous country in Africa (Nigeria) was 41.83% compared to 89.12% in 2012 in China (the most populous country in Asia) (66). We acknowledge that a recent investigation(67) has shown that more precise objective measures are required to make definitive conclusions about the relationship between myopia and near work.

5° The authors said that "he apparent higher prevalence of myopia in girls may be due to girls having ... shorter axial length than boys". That surprising !!!

Response: Zadnik et al study was referring to a specific context in their study, where they found that girls tended to have steeper corneas, stronger crystalline lenses, and shorter eyes/axial length than boys. These findings are specific to their study and cannot be used to explain any result where a higher prevalence of myopia in girls is found. For example, we know that shorter axial length is generally associated with hyperopia and not myopia.

However, the new analysis after removing the 4 studies, showed no statistically significant difference in myopia prevalence between gender. Therefore, we have removed this statement and the revised section now reads:

The influence of gender on the prevalence of myopia has not been unequivocal in the literature (70-74) with some suggesting that the slightly higher prevalence in females may be related to the different ages of onset of puberty between boys and girls (75). Other factors that could account for the reported apparent higher prevalence of myopia in girls include limited outdoor activity time than boys (76).

Reviewer #2

This is a good Meta-analysis regarding the myopia prevalence in Africa. It is good structured and well-written; however, it would be better if you add a figure showing prevalence of myopia by ethnicity (black vs white vs asian in the same region) to show if it affects the prevalence of myopia or not

Response: Thanks for the suggestion. Although the inclusion and comparison of the different ethnicities (Black vs White vs Asian) in the same region would add useful information about the differences in the prevalence of myopia between ethnic groups in Africa, studies that have been conducted in Africa did not specify the different ethnicities. However, we think there is need for such comparison between black vs white vs Asian and this could be another research interest with a different research aim for another manuscript. We have suggested this in the conclusion for future study direction. The section now reads:

Future studies are needed to understand the role of ethnicity on the myopia prevalence in Africa as the inclusion and comparison of the different ethnicities (Black vs White vs Asian) in the same region would add useful information about whether significant differences in the prevalence of myopia among different ethnicity in Africa exists.

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Reviewer #1: No

Reviewer #2: No

Response. Thanks for your comments

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# Decision Letter 1

Aleksandra Barac, Academic Editor

17 Jan 2022

Systematic Review and Meta-analysis of Myopia prevalence in African School children.

PONE-D-21-28841R1

Dear Dr. Osuagwu,

We're pleased to inform you that your manuscript has been judged scientifically suitable for publication and will be formally accepted for publication once it meets all outstanding technical requirements.

Within one week, you'll receive an e-mail detailing the required amendments. When these have been addressed, you'll receive a formal acceptance letter and your manuscript will be scheduled for publication.

An invoice for payment will follow shortly after the formal acceptance. To ensure an efficient process, please log into Editorial Manager at <a href="http://www.editorialmanager.com/pone/">http://www.editorialmanager.com/pone/</a>, click the 'Update My Information' link at the top of the page, and double check that your user information is up-to-date. If you have any billing related questions, please contact our Author Billing department directly at <a href="mailto:authorbilling@plos.org">authorbilling@plos.org</a>.

If your institution or institutions have a press office, please notify them about your upcoming paper to help maximize its impact. If they'll be preparing press materials, please inform our press team as soon as possible -- no later than 48 hours after receiving the formal acceptance. Your manuscript will remain under strict press embargo until 2 pm Eastern Time on the date of publication. For more information, please contact <a href="mailto:onepress@plos.org">onepress@plos.org</a>.

Kind regards,

Aleksandra Barac

Academic Editor

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# Acceptance letter

Aleksandra Barac, Academic Editor

24 Jan 2022

PONE-D-21-28841R1

Systematic Review and Meta-analysis of Myopia prevalence in African School children.

Dear Dr. Osuagwu:

I'm pleased to inform you that your manuscript has been deemed suitable for publication in PLOS ONE. Congratulations! Your manuscript is now with our production department.

If your institution or institutions have a press office, please let them know about your upcoming paper now to help maximize its impact. If they'll be preparing press materials, please inform our press team within the next 48 hours. Your manuscript will remain under strict press embargo until 2 pm Eastern Time on the date of publication. For more information please contact <a href="mailto:onepress@plos.org">onepress@plos.org</a>.

If we can help with anything else, please email us at <u>plosone@plos.org</u>.

Thank you for submitting your work to PLOS ONE and supporting open access.

Kind regards,

PLOS ONE Editorial Office Staff

on behalf of

Dr. Aleksandra Barac

Academic Editor

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# Recent Epidemiology Study Data of Myopia

Zhao-Yu Xiang 1 and Hai-Dong Zou 1, 2

#### Abstract

Myopia, a pandemic refractive error, is affecting more and more people. The progression of myopia could cause numerously serious complications, even leading to blindness. This review summarizes the epidemiological studies on myopia after 2018 and analyzes the risk factors associated with myopia. The prevalence of myopia varies in different regions, age, and observation time. East Asia has been gripped by an unprecedented rise in myopia, and other parts of the world have also seen an increase. The prevalence of myopia in children continues to rise and aggravates with age. The prevalence of high myopia has also increased along with myopia. Racial dependence and family aggregation can be seen frequently in myopia patients. Increased outdoor activities are proven to be protective factors for myopia, as near-distance work and higher education levels affect in the opposite. The impact of gender or urbanization on myopia is controversial. The relationship between nutrition, digital screens, Kawasaki disease, pregnant women smoking during pregnancy, and myopia is still not clear for lack of sufficient evidence. Understanding the various factors that affect myopia helps to clarify the mechanism of myopia formation and also to formulate reasonable prevention and control measures of myopia to protect people's health, especially for adolescents.

# 1. Introduction

Uncorrected refractive error is not only the second leading cause of global blindness but also the leading cause of preventable visual impairment in children [1]. Myopia, the main manifestation of refractive error, is now an alarming pandemic: 2.5 billion people could be affected by myopia by the end of this decade [2]. In many regions, such as eastern China, myopia is often addressed as a "simple" refractive error, instead of a disease [3]. However, it undeniably increases the risk of diseases of blindness such as macular degeneration, retinal detachment, cataracts, and glaucoma [4-6]. Almost 15 years ago, myopic macular degeneration had already driven myopia to become the leading cause of permanent monocular blindness in Japan [7] and the most frequent cause of severe visual impairment and blindness in the elderly Chinese population in Taiwan [8]. Apart from its deleterious effects on functional vision, the loss of visual acuity associated with uncorrected myopia or permanent vision loss significantly affects all aspects of an individual's quality of life. The constraints that affected individuals experience are likely to further limit their independent choices

and pose additional monetary and physical burdens [9]. Furthermore, the economic and financial burden of myopia on families incorporate both the cost of optical devices or other refractive modalities and the need for frequent and long-term management of the condition by an eye-care practitioner [10]. For Chinese urban migrant families, merely the cost of spectacles deters the parents from providing refractive error correction for their children [11], resulting in an increase in myopia and deteriorating functional vision that will certainly damage the future lives of the young. Naidoo et al. reported that the potential global productivity loss associated with the burden of visual impairment was estimated at US\$244 billion from uncorrected myopia in 2015 [12]. Controlling myopia, therefore, should be emphasized as a major worldwide public health objective.

# 2. Global Prevalence of Myopia and High Myopia

In 2016, Holden et al. estimated that the global prevalence of myopia was 1.406 billion people worldwide (22.9% of the global population), and that 163 million people had high myopia in 2000. They also concluded that, by 2050, there will be 4.758 billion people with myopia (49.8% of the global population), and 938 million will have high myopia [13]. In accordance with Holden's methodology, we searched PubMed (National Library of Medicine) on March 1, 2020, for epidemiological studies on myopia after January 1, 2018, regardless of the original language of publication. Population-based studies were chosen because they reflect the real-world data of the epidemic. Countries were grouped based on the continent they belonged to. A summary of the data is given in Table 1, showing that the prevalence of myopia varies significantly between different regions, ages, and observation times.

Table 1

Population-based epidemiology study results of myopia and high myopia published from January 1, 2018, to March 1, 2020, in PubMed (National Library of Medicine) database.

_	Region,	_	Age range, year/cohort	Cycloplegia	Mean age (SD), year	Myopia	
	country					Definition	Prev (95% %
Chen et al. [ <u>14</u> ]	East Asia, China (East)	43858	Third-year high school students	No	18.4 (0.7) overall	SE < -0.5 D	79.5 in 20 87.7 in
Huang et al. [ <u>15</u> ]	East Asia, China (Taiwan)	6069	6-15	No	10.5 (2.3)	SE < 0.0 D	76.6
Wang et al. [ <u>16</u> ]	East Asia, China (East)	4801	5–20	No	12.3 (3.8)	$SE \le -0.5 D +$ $UCVA \le 20/25$	63.1 6
Thorn et al. [ <u>17</u> ]	East Asia, China (East)	13220	5–16	No	9.4 (1.9)	SE≤-1.0 D	49.5
Choy et al. [ <u>18</u> ]	East Asia, China (Hong Kong)	1396	6–13	No	8.8 (N/A)	SE ≤ −0.5 D	37.7 4
Wang et al. [ <u>19</u> ]	East Asia, China (southwest)	1626	40-80	No	N/A	SE < -0.5 D	26.4 2 ov 31.5 35 Hai 16.8 20.8
Wang et al. [ <u>20</u> ]	East Asia, China (Inner Mongolia)	2090	40-80	No	N/A	SE < -0.5 D	29.4 3 ov 31.8 34 Hai 23.0 26 Mor
Yam et al. [21]	East Asia, China (Hong	10137 (4257	6-8 and parents	No*	7.6 (1.0) in children and	$SE \le -0.5 D$ (in children) and	25.0 in cl

SE, spherical equivalent; N/A, not available; UCVA, uncorrected visual acuity. \*Cycloplegic measurements in patients needed a detailed eye examination. †Cycloplegic measurements in 135 patients. <sup>‡</sup>The last recorded refraction including autorefraction, cycloplegic refraction, and/or subjective refractions. <sup>§</sup>Cycloplegic measurements in 633

According to epidemiological surveys from the past two years, the prevalence of myopia varies depending on the continent, country, and region. East Asia has been gripped by an unprecedented rise in myopia, and other parts of the world have also seen an increase. As Morgan et al. referred to in their review, the highest rates occur in China, Japan, and Singapore [46]. In China, the highest prevalence occurs in the eastern areas, which are the economically developed parts of China, as shown in Table 1. In South Asia, the prevalence is much lower than in East Asia. In India, the prevalence of myopia is similar to that of the nearby Tibetan province of China where the prevalence is nearly the lowest in all of China. A meta-analysis concluded that only 5.3% of children younger than 16 years of age are myopic in India [47]. The prevalence of myopia in Europe and North America ranges from 6.2% to 26.2% (Table 1).

At present, most of the epidemiological studies of myopia are based on cross-sectional data, while there are relatively few cohort studies. Cohort studies are more informative since they present the annual incidence and progress of myopia, and currently, they all suggest that the prevalence of myopia is increasing every year. According to the published research, the prevalence of myopia among 12- to 17-year-old students in the United States from 1971 to 2004 increased from 12.0% to 31.2%, and over the past 30 years, the prevalence in all ages has increased significantly [48]. A retrospective study of myopia in Taiwan showed that the average prevalence in 7-year-olds increased from 5.8% in 1983 to 21% in 2000; at the age of 12, the prevalence of myopia was 36.7% in 1983 and increased to 61% by 2000 [49]. In southern China, a 5-year follow-up survey was conducted on 6- to 15-year-old children. The cumulative average annual myopia progression was -2.20 D, and the annual change rate of myopia was -0.43 D [50]. Another study in Beijing, North China, showed that the annual incidence of myopia was 7.8%, and the progression of myopia was -0.17 D [51].

A critical parameter for the epidemiological analysis of myopia is age, since prevalence rates have been known to increase significantly with age, as shown in Table 1. In Finland, a total of 240 myopic school children with a mean spherical equivalent (SE) of -1.43 D at baseline were followed up for 22 years, at the end of which, the mean SE of the more myopic eye was -5.29 D. About 32% of the children receiving their first myopic glasses between and around 11 years of age had high myopia (SE  $\leq$  -6.00 D in one eye) in adulthood. A younger onset age of myopia predicted a greater prevalence of high myopia after 22 years, suggested by a prevalence of 65% for those with baseline ages between 8.8 and 9.7 years and 7% for those aged between 11.9 and 12.8 years [52]. An epidemic of high myopia occurs parallel to myopia, as shown in Table 1, perhaps because early-onset myopia progresses more and more before it stabilizes [46].

## 3. The Risk Factors of Myopia

The pathogenesis of myopia is not entirely clear from the current research, and more is believed to be the result of genetic and environmental interactions [53]. The rapid development of the modern economy, the process of industrialization, and the improvement of living standards have all affected the occurrence and development of myopia. Similar to other chronic eye diseases, the risks of myopia can be classified as genetic or environmental factors, the latter of which includes outdoor activities, near-distance work, education, gender, and urban environment, among others, as shown in Table 2.

Table 2
Risk factors for the prevalence of myopia.

Risk factors	Reference	Region, country	Odds ratio: prevalence with factor vs. without factor
Parental myopia	Atowa et al. [ <u>54</u> ]	Africa, Nigeria	6.80 for one myopic parent and 9.47 for two myopic parents
	Yang et al. [ <u>43</u> ]	North America, Canada (suburban)	2.52
	Harrington et al. [ <u>36</u> ]	Europe, Ireland	2.4 (paternal)
	Kim et al. [ <u>55</u> ]	East Asia, Korea	1.84 for myopia and 3.48 for high myopia
Low outdoor activity	Singh et al. [ <u>28</u> ]	South Asia, India (North)	19.73 (<1.5 hours per day)
	Hagen et al. [ <u>34</u> ]	Europe, Norway	1.96 (less sport outdoors) and 0.67 (less other outdoors)
	Atowa et al. [ <u>54</u> ]	Africa, Nigeria	1.25
	Yang et al. [ <u>43</u> ]	North America, Canada (suburban)	1.17
Time spent on near work/studying/playing	Harrington et al. [ <u>36</u> ]	Europe, Ireland	3.7 (using screens >3 hours per day) and 2.2 (frequently reading/writing)
	Singh et al. [ <u>28</u> ]	South Asia, India (North)	2.94 (reading/writing > 4 hours daily) and 8.33 (playing video games > 2 hours daily)
	Wang et al. [ <u>16</u> ]	East Asia, China (East)	1.88 (moderate school workload) and 2.36 (high school workload)
	Chiang et al. [ <u>41</u> ]	North America, U.S.	1.27 (watched 2 hours of television daily) and 1.28 (used the computer for 1 hour daily)
High level of education	Wang et al. [ <u>19</u> ]	East Asia, China (Southwest)	2.50 (undergraduate/graduate)
	Wang et al. [ <u>20</u> ]	East Asia, China (Inner Mongolia)	1.52 (middle/high school) and 3.77 (undergraduate/graduate)
	Chiang et al. [ <u>41</u> ]	North America, U.S.	1.79 (senior high school graduate education)
	Yang et al. [ <u>32</u> ]	Europe, Austria	1.3–1.7 (≥graduated from professional training or served an apprenticeship) in 2013–2017
	01 1	r 1	4.47.6.40 1 3

The common characteristics of hereditary diseases are race-dependency and familial aggregation, both of which are often seen with myopia. A study based on children of different races found that Asians had the highest prevalence of myopia (18.5%), followed by Hispanics (13.2%), and Caucasians had the lowest prevalence (4.4%) [56]. The apparent familial aggregation of myopia can be shown by the high ratio of parental myopia. A study of Chinese children with an average age of 11.45 years found that the prevalence of myopia in children with one or two myopic parents was 2-3 times higher than that in subjects without parental myopia [53]. In Poland, if both parents are myopic, the odds ratio (OR) of the children having high myopia in adulthood has been shown to be 3.9 [52]. Children with parental myopia also have larger SEs and longer eye axial lengths. To a large extent, family association is considered a genetic factor of myopia, rather than inheritance, because family members have the same environment. However, genetic change cannot explain the rapid changes in prevalence that have taken place over the past one or two generations. Genetics play an important role in early-onset myopia and impose a level of baseline risk, while changes in the environment, especially education and outdoor activities, are the main cause of the emergence of myopia epidemics  $[\underline{46}]$ . To date, more than 25 myopic loci have been discovered via linkage analyses, most of which are on autosomal chromosomes. These loci can be found in the Online Mendelian Inheritance in Man (OMIM) database [57]. A few reports have indicated an interactive effect between genetic predisposition and environmental stress [58]; however, the underlying mechanism remains unclear.

# 3.2. Outdoor Activity

Increasing outdoor activity has been proven to be a protective factor for myopia in many epidemiological investigations, as shown in <u>Table 2</u>. In Guangzhou, 3 years after an increase in outdoor activity in the first grade of a primary school, the accumulation of myopia was 37% lower than that in students without the intervention, and the difference was statistically significant (P > 0.05) [59]. Similar results were found in school children in North Ireland, Brazil, and Poland [60–62]. Ho et al. even suggested that 120 min/day of outdoor light exposure during school can prevent the incidence of myopia [63].

The protective mechanism of outdoor activities in relation to myopia is complicated and includes higher illuminance, reduced peripheral defocus, vitamin D, chromatic spectrum of light, physical activity, circadian rhythms, spatial frequency characteristics, and less near-distance work [64]. Among them, higher illuminance is the most well-established theory with evidence shown in both animal and human studies. Norton and Siegwart used animal models to study the relationship between refractive status and light conditions and found that low light (1 to 50 lux) and darkness (<1 lux) are conducive to the extension of the eye axial length, leading to myopia. Strong light (1000–2800 lux), however, delays the occurrence and development of myopia [65]. This effect may be a result of an increase in dopamine receptor D1 activity in the ON pathway [66]. Additionally, Landis et al. measured the amount of time 102 children spent in scotopic (<1-1 lux), mesopic (1-30 lux), indoor photopic (>30–1000 lux), and outdoor photopic (>1000 lux) light during both weekdays and weekends using wearable light sensors, and they found that rod pathways stimulated by dim light exposure are also important in human myopia development. They then suggested that the optimal strategy for preventing myopia with environmental light includes both dim and bright light exposure [67]. Apart from illuminance, many more studies have emerged that focus on the "outdoor light-dopamine" mechanism. Dopamine is a key regulator of both circadian rhythms and eye growth [68]. Natural light from outdoor activities stimulates the retina to secrete more dopamine, and this dopamine was found to control eye growth [69].

We believe that some reported risk factors for myopia may be ascribed to outdoor activity, for example, the seasonal change of myopia growth. Gwiazda et al. found that the speed of myopia progression changes from month to month and is slower from April to September. Therefore, the average progress in winter is higher than that of summer, and the difference is statistically significant (P < 0.0001), which may be due to children spending more time outdoors in summer than in winter [70]. In Czech, Rusnak et al. observed 398 eyes of 12-year-old children and found significantly higher axial length growth during the winter period than the summer period. They suggested that the lack of daylight exposure in winter may lead to myopia progression [71].

### 3.3. Near-Distance Work

Many studies have shown that near-distance work is an important risk factor for myopia, such as reading, writing, and working on a computer, as shown in Table 2. Sherwin et al. demonstrated that children working at a distance less than 30 cm had 2.5 times the rate of myopia than those working at longer distances. Additionally, children who would read for more than 30 min at a time had a higher incidence of myopia than children who read for less than 30 min [72]. Research on the effect of near-distance work and eye movement parameters on myopia has speculated that long-term near-distance work maintains the retina image in a defocused state for a long time. Adjusting to the blurred image, then, results in an increased adjustment lag, which, together with other parameters that make chronic hyperopia defocused for a long time, induces the retina to produce some neurotransmitters or growth factors to regulate the inappropriate growth of the eye axial length, leading to the progression of myopia [73]. Working long hours at a close distance and with a low frequency of breaks during study may also be risk factors for myopia, but further research is still needed.

### 3.4. Education

Studies in Singapore, Germany, and other countries found that higher levels of education increase the prevalence of myopia [74, 75]. Previous studies have even shown that the higher the level of education, the higher the prevalence of myopia, as shown in Table 2. Better schools or cram schools have also been shown to be risk factors for myopia [76, 77]. A study that tested the biological interaction of genetic predisposition and the education level on myopia risk found that individuals with high genetic risk combined with a college education have a high risk of myopia, and patients with high genetic risk but only primary education have a much lower risk of myopia [78]. Education may reflect a complex combination of higher levels of exposure to near-reading and correspondingly lower levels of outdoor physical activity, leading to an upregulation of high-risk genes, excessive eye growth, and the development of myopia.

# 3.5. Others

Other myopia-related risk factors such as gender, urbanization, nutrition, digital screens [79, 80], Kawasaki disease [81], and maternal grandmother smoking during pregnancy [82] have been reported, but most of them lack sufficient evidence. Data concerning the effect of gender or urbanization on myopia prevalence, for example, is conflicting. In one study in India on children younger than 16 years old, girls living in urban areas were significantly more likely to have myopia than boys [47], whereas Reed et al. found the opposite to be true [39]. In the same report from Indian, the prevalence of myopia was shown to be higher in urban areas compared to rural areas (OR 2.12) [47], supporting the idea that severe air pollution in cities may accelerate myopia progression [83]. However, Morris et al. did not find strong evidence associating urban or rural

status with the incidence of myopia in a United Kingdom cohort of 3,512 children. In that study, the association between the geographical setting and myopia was considered to be potentially driven by underlying confounding factors such as education and time spent outdoors [84].

Nutrition is important for eye development in children and has been suggested to play a role in the incidence of myopia in early life. For example, children who were breastfed during the first 6 months of life were found to be less likely to have myopia [85]. However, the association between diet and myopia is controversial [86, 87]. Recently, there was no significant correlation between an infant's diet at 6, 9, and 12 months and SE, axial length, or myopia at age three years in a Singapore cohort study [88].

### 4. Conclusions

In summary, myopia not only affects the physical and mental health of individuals but also puts a great burden on society. Myopic adolescents are more likely to be anxious than those without myopia [89]. Knowing the various factors that affect the occurrence and development of adolescent myopia is conducive to clarifying the mechanism of myopia formation and also to formulating reasonable prevention and control measures of myopia to protect the health of adolescents.

# Acknowledgments

This work was funded by the Chinese National Nature Science Foundation (81670898 and 82071012), The Project of Shanghai Shen Kang Hospital Development Centre (SHDC2018110), The Science and Technology Commission of Shanghai Municipality (20DZ1100200), Shanghai Municipal Education Commission-Gaofeng Clinical Medicine Grant Support (20172022), Shanghai General Hospital, Clinical Research (CTCCR-2018Z01), Shanghai Engineering Research Center of Precise Diagnosis and Treatment of Eye Diseases, Shanghai, China (19DZ2250100), National Key R&D Program of China (2016YFC0904800 and 2019YFC0840607), and National Science and Technology Major Project of China (2017ZX09304010).

# Conflicts of Interest

The authors declare that they have no conflicts of interest.

# **Authors' Contributions**

Xiang Zhao-Yu contributed to the literature search, manuscript preparation, manuscript editing, and manuscript review. Zou Hai-Dong contributed to the concept, design, definition of intellectual content, literature search, data acquisition, data analysis, manuscript preparation, manuscript editing, and manuscript review.

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# Recent Epidemiology Study Data of Myopia

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#### Abstract

Myopia, a pandemic refractive error, is affecting more and more people. The progression of myopia could cause numerously serious complications, even leading to blindness. This review summarizes the epidemiological studies on myopia after 2018 and analyzes the risk factors associated with myopia. The prevalence of myopia varies in different regions, age, and observation time. East Asia has been gripped by an unprecedented rise in myopia, and other parts of the world have also seen an increase. The prevalence of myopia in children continues to rise and aggravates with age. The prevalence of high myopia has also increased along with myopia. Racial dependence and family aggregation can be seen frequently in myopia patients. Increased outdoor activities are proven to be protective factors for myopia, as near-distance work and higher education levels affect in the opposite. The impact of gender or urbanization on myopia is controversial. The relationship between nutrition, digital screens, Kawasaki disease, pregnant women smoking during pregnancy, and myopia is still not clear for lack of sufficient evidence. Understanding the various factors that affect myopia helps to clarify the mechanism of myopia formation and also to formulate reasonable prevention and control measures of myopia to protect people's health, especially for adolescents.

# 1. Introduction

Uncorrected refractive error is not only the second leading cause of global blindness but also the leading cause of preventable visual impairment in children [1]. Myopia, the main manifestation of refractive error, is now an alarming pandemic: 2.5 billion people could be affected by myopia by the end of this decade [2]. In many regions, such as eastern China, myopia is often addressed as a "simple" refractive error, instead of a disease [3]. However, it undeniably increases the risk of diseases of blindness such as macular degeneration, retinal detachment, cataracts, and glaucoma [4-6]. Almost 15 years ago, myopic macular degeneration had already driven myopia to become the leading cause of permanent monocular blindness in Japan [7] and the most frequent cause of severe visual impairment and blindness in the elderly Chinese population in Taiwan [8]. Apart from its deleterious effects on functional vision, the loss of visual acuity associated with uncorrected myopia or permanent vision loss significantly affects all aspects of an individual's quality of life. The constraints that affected individuals experience are likely to further limit their independent choices

and pose additional monetary and physical burdens [9]. Furthermore, the economic and financial burden of myopia on families incorporate both the cost of optical devices or other refractive modalities and the need for frequent and long-term management of the condition by an eye-care practitioner [10]. For Chinese urban migrant families, merely the cost of spectacles deters the parents from providing refractive error correction for their children [11], resulting in an increase in myopia and deteriorating functional vision that will certainly damage the future lives of the young. Naidoo et al. reported that the potential global productivity loss associated with the burden of visual impairment was estimated at US\$244 billion from uncorrected myopia in 2015 [12]. Controlling myopia, therefore, should be emphasized as a major worldwide public health objective.

# 2. Global Prevalence of Myopia and High Myopia

In 2016, Holden et al. estimated that the global prevalence of myopia was 1.406 billion people worldwide (22.9% of the global population), and that 163 million people had high myopia in 2000. They also concluded that, by 2050, there will be 4.758 billion people with myopia (49.8% of the global population), and 938 million will have high myopia [13]. In accordance with Holden's methodology, we searched PubMed (National Library of Medicine) on March 1, 2020, for epidemiological studies on myopia after January 1, 2018, regardless of the original language of publication. Population-based studies were chosen because they reflect the real-world data of the epidemic. Countries were grouped based on the continent they belonged to. A summary of the data is given in Table 1, showing that the prevalence of myopia varies significantly between different regions, ages, and observation times.

Table 1

Population-based epidemiology study results of myopia and high myopia published from January 1, 2018, to March 1, 2020, in PubMed (National Library of Medicine) database.

_	Region,	_	Age range, year/cohort	Cycloplegia	Mean age (SD), year	Myopia	
	country					Definition	Prev (95% %
Chen et al. [ <u>14</u> ]	East Asia, China (East)	43858	Third-year high school students	No	18.4 (0.7) overall	SE < -0.5 D	79.5 in 20 87.7 in
Huang et al. [ <u>15</u> ]	East Asia, China (Taiwan)	6069	6-15	No	10.5 (2.3)	SE < 0.0 D	76.6
Wang et al. [ <u>16</u> ]	East Asia, China (East)	4801	5–20	No	12.3 (3.8)	$SE \le -0.5 D +$ $UCVA \le 20/25$	63.1 6
Thorn et al. [ <u>17</u> ]	East Asia, China (East)	13220	5–16	No	9.4 (1.9)	SE≤-1.0 D	49.5
Choy et al. [ <u>18</u> ]	East Asia, China (Hong Kong)	1396	6–13	No	8.8 (N/A)	SE ≤ −0.5 D	37.7 4
Wang et al. [ <u>19</u> ]	East Asia, China (southwest)	1626	40-80	No	N/A	SE < -0.5 D	26.4 2 ov 31.5 35 Hai 16.8 20.8
Wang et al. [ <u>20</u> ]	East Asia, China (Inner Mongolia)	2090	40-80	No	N/A	SE < -0.5 D	29.4 3 ov 31.8 34 Hai 23.0 26 Mor
Yam et al. [21]	East Asia, China (Hong	10137 (4257	6-8 and parents	No*	7.6 (1.0) in children and	$SE \le -0.5 D$ (in children) and	25.0 in cl

SE, spherical equivalent; N/A, not available; UCVA, uncorrected visual acuity. \*Cycloplegic measurements in patients needed a detailed eye examination. †Cycloplegic measurements in 135 patients. <sup>‡</sup>The last recorded refraction including autorefraction, cycloplegic refraction, and/or subjective refractions. <sup>§</sup>Cycloplegic measurements in 633

According to epidemiological surveys from the past two years, the prevalence of myopia varies depending on the continent, country, and region. East Asia has been gripped by an unprecedented rise in myopia, and other parts of the world have also seen an increase. As Morgan et al. referred to in their review, the highest rates occur in China, Japan, and Singapore [46]. In China, the highest prevalence occurs in the eastern areas, which are the economically developed parts of China, as shown in Table 1. In South Asia, the prevalence is much lower than in East Asia. In India, the prevalence of myopia is similar to that of the nearby Tibetan province of China where the prevalence is nearly the lowest in all of China. A meta-analysis concluded that only 5.3% of children younger than 16 years of age are myopic in India [47]. The prevalence of myopia in Europe and North America ranges from 6.2% to 26.2% (Table 1).

At present, most of the epidemiological studies of myopia are based on cross-sectional data, while there are relatively few cohort studies. Cohort studies are more informative since they present the annual incidence and progress of myopia, and currently, they all suggest that the prevalence of myopia is increasing every year. According to the published research, the prevalence of myopia among 12- to 17-year-old students in the United States from 1971 to 2004 increased from 12.0% to 31.2%, and over the past 30 years, the prevalence in all ages has increased significantly [48]. A retrospective study of myopia in Taiwan showed that the average prevalence in 7-year-olds increased from 5.8% in 1983 to 21% in 2000; at the age of 12, the prevalence of myopia was 36.7% in 1983 and increased to 61% by 2000 [49]. In southern China, a 5-year follow-up survey was conducted on 6- to 15-year-old children. The cumulative average annual myopia progression was -2.20 D, and the annual change rate of myopia was -0.43 D [50]. Another study in Beijing, North China, showed that the annual incidence of myopia was 7.8%, and the progression of myopia was -0.17 D [51].

A critical parameter for the epidemiological analysis of myopia is age, since prevalence rates have been known to increase significantly with age, as shown in Table 1. In Finland, a total of 240 myopic school children with a mean spherical equivalent (SE) of -1.43 D at baseline were followed up for 22 years, at the end of which, the mean SE of the more myopic eye was -5.29 D. About 32% of the children receiving their first myopic glasses between and around 11 years of age had high myopia (SE  $\leq$  -6.00 D in one eye) in adulthood. A younger onset age of myopia predicted a greater prevalence of high myopia after 22 years, suggested by a prevalence of 65% for those with baseline ages between 8.8 and 9.7 years and 7% for those aged between 11.9 and 12.8 years [52]. An epidemic of high myopia occurs parallel to myopia, as shown in Table 1, perhaps because early-onset myopia progresses more and more before it stabilizes [46].

## 3. The Risk Factors of Myopia

The pathogenesis of myopia is not entirely clear from the current research, and more is believed to be the result of genetic and environmental interactions [53]. The rapid development of the modern economy, the process of industrialization, and the improvement of living standards have all affected the occurrence and development of myopia. Similar to other chronic eye diseases, the risks of myopia can be classified as genetic or environmental factors, the latter of which includes outdoor activities, near-distance work, education, gender, and urban environment, among others, as shown in Table 2.

Table 2
Risk factors for the prevalence of myopia.

Risk factors	Reference	Region, country	Odds ratio: prevalence with factor vs. without factor
Parental myopia	Atowa et al. [ <u>54</u> ]	Africa, Nigeria	6.80 for one myopic parent and 9.47 for two myopic parents
	Yang et al. [ <u>43</u> ]	North America, Canada (suburban)	2.52
	Harrington et al. [ <u>36</u> ]	Europe, Ireland	2.4 (paternal)
	Kim et al. [ <u>55</u> ]	East Asia, Korea	1.84 for myopia and 3.48 for high myopia
Low outdoor activity	Singh et al. [ <u>28</u> ]	South Asia, India (North)	19.73 (<1.5 hours per day)
	Hagen et al. [ <u>34</u> ]	Europe, Norway	1.96 (less sport outdoors) and 0.67 (less other outdoors)
	Atowa et al. [ <u>54</u> ]	Africa, Nigeria	1.25
	Yang et al. [ <u>43</u> ]	North America, Canada (suburban)	1.17
Time spent on near work/studying/playing	Harrington et al. [ <u>36</u> ]	Europe, Ireland	3.7 (using screens >3 hours per day) and 2.2 (frequently reading/writing)
	Singh et al. [ <u>28</u> ]	South Asia, India (North)	2.94 (reading/writing > 4 hours daily) and 8.33 (playing video games > 2 hours daily)
	Wang et al. [ <u>16</u> ]	East Asia, China (East)	1.88 (moderate school workload) and 2.36 (high school workload)
	Chiang et al. [ <u>41</u> ]	North America, U.S.	1.27 (watched 2 hours of television daily) and 1.28 (used the computer for 1 hour daily)
High level of education	Wang et al. [ <u>19</u> ]	East Asia, China (Southwest)	2.50 (undergraduate/graduate)
	Wang et al. [ <u>20</u> ]	East Asia, China (Inner Mongolia)	1.52 (middle/high school) and 3.77 (undergraduate/graduate)
	Chiang et al. [ <u>41</u> ]	North America, U.S.	1.79 (senior high school graduate education)
	Yang et al. [ <u>32</u> ]	Europe, Austria	1.3–1.7 (≥graduated from professional training or served an apprenticeship) in 2013–2017
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The common characteristics of hereditary diseases are race-dependency and familial aggregation, both of which are often seen with myopia. A study based on children of different races found that Asians had the highest prevalence of myopia (18.5%), followed by Hispanics (13.2%), and Caucasians had the lowest prevalence (4.4%) [56]. The apparent familial aggregation of myopia can be shown by the high ratio of parental myopia. A study of Chinese children with an average age of 11.45 years found that the prevalence of myopia in children with one or two myopic parents was 2-3 times higher than that in subjects without parental myopia [53]. In Poland, if both parents are myopic, the odds ratio (OR) of the children having high myopia in adulthood has been shown to be 3.9 [52]. Children with parental myopia also have larger SEs and longer eye axial lengths. To a large extent, family association is considered a genetic factor of myopia, rather than inheritance, because family members have the same environment. However, genetic change cannot explain the rapid changes in prevalence that have taken place over the past one or two generations. Genetics play an important role in early-onset myopia and impose a level of baseline risk, while changes in the environment, especially education and outdoor activities, are the main cause of the emergence of myopia epidemics  $[\underline{46}]$ . To date, more than 25 myopic loci have been discovered via linkage analyses, most of which are on autosomal chromosomes. These loci can be found in the Online Mendelian Inheritance in Man (OMIM) database [57]. A few reports have indicated an interactive effect between genetic predisposition and environmental stress [58]; however, the underlying mechanism remains unclear.

# 3.2. Outdoor Activity

Increasing outdoor activity has been proven to be a protective factor for myopia in many epidemiological investigations, as shown in <u>Table 2</u>. In Guangzhou, 3 years after an increase in outdoor activity in the first grade of a primary school, the accumulation of myopia was 37% lower than that in students without the intervention, and the difference was statistically significant (P > 0.05) [59]. Similar results were found in school children in North Ireland, Brazil, and Poland [60–62]. Ho et al. even suggested that 120 min/day of outdoor light exposure during school can prevent the incidence of myopia [63].

The protective mechanism of outdoor activities in relation to myopia is complicated and includes higher illuminance, reduced peripheral defocus, vitamin D, chromatic spectrum of light, physical activity, circadian rhythms, spatial frequency characteristics, and less near-distance work [64]. Among them, higher illuminance is the most well-established theory with evidence shown in both animal and human studies. Norton and Siegwart used animal models to study the relationship between refractive status and light conditions and found that low light (1 to 50 lux) and darkness (<1 lux) are conducive to the extension of the eye axial length, leading to myopia. Strong light (1000–2800 lux), however, delays the occurrence and development of myopia [65]. This effect may be a result of an increase in dopamine receptor D1 activity in the ON pathway [66]. Additionally, Landis et al. measured the amount of time 102 children spent in scotopic (<1-1 lux), mesopic (1-30 lux), indoor photopic (>30–1000 lux), and outdoor photopic (>1000 lux) light during both weekdays and weekends using wearable light sensors, and they found that rod pathways stimulated by dim light exposure are also important in human myopia development. They then suggested that the optimal strategy for preventing myopia with environmental light includes both dim and bright light exposure [67]. Apart from illuminance, many more studies have emerged that focus on the "outdoor light-dopamine" mechanism. Dopamine is a key regulator of both circadian rhythms and eye growth [68]. Natural light from outdoor activities stimulates the retina to secrete more dopamine, and this dopamine was found to control eye growth [69].

We believe that some reported risk factors for myopia may be ascribed to outdoor activity, for example, the seasonal change of myopia growth. Gwiazda et al. found that the speed of myopia progression changes from month to month and is slower from April to September. Therefore, the average progress in winter is higher than that of summer, and the difference is statistically significant (P < 0.0001), which may be due to children spending more time outdoors in summer than in winter [70]. In Czech, Rusnak et al. observed 398 eyes of 12-year-old children and found significantly higher axial length growth during the winter period than the summer period. They suggested that the lack of daylight exposure in winter may lead to myopia progression [71].

### 3.3. Near-Distance Work

Many studies have shown that near-distance work is an important risk factor for myopia, such as reading, writing, and working on a computer, as shown in Table 2. Sherwin et al. demonstrated that children working at a distance less than 30 cm had 2.5 times the rate of myopia than those working at longer distances. Additionally, children who would read for more than 30 min at a time had a higher incidence of myopia than children who read for less than 30 min [72]. Research on the effect of near-distance work and eye movement parameters on myopia has speculated that long-term near-distance work maintains the retina image in a defocused state for a long time. Adjusting to the blurred image, then, results in an increased adjustment lag, which, together with other parameters that make chronic hyperopia defocused for a long time, induces the retina to produce some neurotransmitters or growth factors to regulate the inappropriate growth of the eye axial length, leading to the progression of myopia [73]. Working long hours at a close distance and with a low frequency of breaks during study may also be risk factors for myopia, but further research is still needed.

### 3.4. Education

Studies in Singapore, Germany, and other countries found that higher levels of education increase the prevalence of myopia [74, 75]. Previous studies have even shown that the higher the level of education, the higher the prevalence of myopia, as shown in Table 2. Better schools or cram schools have also been shown to be risk factors for myopia [76, 77]. A study that tested the biological interaction of genetic predisposition and the education level on myopia risk found that individuals with high genetic risk combined with a college education have a high risk of myopia, and patients with high genetic risk but only primary education have a much lower risk of myopia [78]. Education may reflect a complex combination of higher levels of exposure to near-reading and correspondingly lower levels of outdoor physical activity, leading to an upregulation of high-risk genes, excessive eye growth, and the development of myopia.

# 3.5. Others

Other myopia-related risk factors such as gender, urbanization, nutrition, digital screens [79, 80], Kawasaki disease [81], and maternal grandmother smoking during pregnancy [82] have been reported, but most of them lack sufficient evidence. Data concerning the effect of gender or urbanization on myopia prevalence, for example, is conflicting. In one study in India on children younger than 16 years old, girls living in urban areas were significantly more likely to have myopia than boys [47], whereas Reed et al. found the opposite to be true [39]. In the same report from Indian, the prevalence of myopia was shown to be higher in urban areas compared to rural areas (OR 2.12) [47], supporting the idea that severe air pollution in cities may accelerate myopia progression [83]. However, Morris et al. did not find strong evidence associating urban or rural

status with the incidence of myopia in a United Kingdom cohort of 3,512 children. In that study, the association between the geographical setting and myopia was considered to be potentially driven by underlying confounding factors such as education and time spent outdoors [84].

Nutrition is important for eye development in children and has been suggested to play a role in the incidence of myopia in early life. For example, children who were breastfed during the first 6 months of life were found to be less likely to have myopia [85]. However, the association between diet and myopia is controversial [86, 87]. Recently, there was no significant correlation between an infant's diet at 6, 9, and 12 months and SE, axial length, or myopia at age three years in a Singapore cohort study [88].

### 4. Conclusions

In summary, myopia not only affects the physical and mental health of individuals but also puts a great burden on society. Myopic adolescents are more likely to be anxious than those without myopia [89]. Knowing the various factors that affect the occurrence and development of adolescent myopia is conducive to clarifying the mechanism of myopia formation and also to formulating reasonable prevention and control measures of myopia to protect the health of adolescents.

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# Conflicts of Interest

The authors declare that they have no conflicts of interest.

# **Authors' Contributions**

Xiang Zhao-Yu contributed to the literature search, manuscript preparation, manuscript editing, and manuscript review. Zou Hai-Dong contributed to the concept, design, definition of intellectual content, literature search, data acquisition, data analysis, manuscript preparation, manuscript editing, and manuscript review.

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Global variations and time trends in the prevalence of childhood myopia, a systematic review and quantitative meta-analysis: implications for aetiology and early prevention

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#### **Abstract**

The aim of this review was to quantify the global variation in childhood myopia prevalence over time taking account of demographic and study design factors. A systematic review identified populationbased surveys with estimates of childhood myopia prevalence published by February 2015. Multilevel binomial logistic regression of log odds of myopia was used to examine the association with age, gender, urban versus rural setting and survey year, among populations of different ethnic origins, adjusting for study design factors. 143 published articles (42 countries, 374 349 subjects aged 1–18 years, 74 847 myopia cases) were included. Increase in myopia prevalence with age varied by ethnicity. East Asians showed the highest prevalence, reaching 69% (95% credible intervals (CrI) 61% to 77%) at 15 years of age (86% among Singaporean-Chinese). Blacks in Africa had the lowest prevalence; 5.5% at 15 years (95% CrI 3% to 9%). Time trends in myopia prevalence over the last decade were small in whites, increased by 23% in East Asians, with a weaker increase among South Asians. Children from urban environments have 2.6 times the odds of myopia compared with those from rural environments. In whites and East Asians sex differences emerge at about 9 years of age; by late adolescence girls are twice as likely as boys to be myopic. Marked ethnic differences in age-specific prevalence of myopia exist. Rapid increases in myopia prevalence over time, particularly in East Asians, combined with a universally higher risk of myopia in urban settings, suggest that environmental factors play an important role in myopia development, which may offer scope for prevention.

**Keywords:** Epidemiology, Child health (paediatrics), Optics and Refraction, Public health

#### Introduction

Myopia is the most common cause of correctable visual impairment in the developed world in adults and children<u>1–5</u> and is a leading cause of preventable blindness in developing countries.<u>6</u>
Approximately one in six of the world's population is myopic.<u>7</u> This represents a substantial burden

worldwide with an appreciable unmet need for visual correction especially in poorer countries.8 Myopia begins in early life and increases in frequency and severity through childhood and adolescence into adulthood. High myopia affects up to 20% of secondary school children in East Asia, and is associated with sight-threatening pathologies that are irreversible. In white European populations the prevalence of myopia is relatively low affecting approximately 3–5% of 10-year olds 10-12 and up to 20% aged 12-13 years. 2 13-15 In contrast, studies from Asian populations suggest rapid increases in the prevalence of childhood myopia (in terms of prevalence and absolute levels of myopia), affecting 80–90% of school-leavers in East Asia. 9 16–19 However, not all Asian populations appear to be undergoing this myopic transition. 12 20–23 There are marked ethnic and geographical differences in myopia prevalence, which seem to have changed over time. There is a need to bring together the evidence to quantify population differences in myopia prevalence over time. However, quantifying the degree of ethnic differences in myopia is often hampered by interstudy differences in methodology, where different age groups, sampling methods and definitions of myopia are used. Hence, we undertook a systematic review of geographical and ethnic variations in myopia prevalence in childhood over an extended time period using a quantitative Bayesian meta-regression of studies that reported myopia prevalence. We provide estimates of myopia prevalence by age, ethnicity and sex, and examine trends over time. The influence of interstudy differences in study design on estimates of myopia prevalence was investigated as well as gender differences, and living in urban versus rural environments.

# Methods

The systematic review followed the Meta-analysis Of Observational Studies in Epidemiology guidelines for the conduct of systematic reviews and meta-analysis of observational studies. 24 A combination of text words for myopia (short\$sight\*/myopi?/myope\$/refractive error\$/ocular refraction), childhood (child/childhood/children/adolescent/adolescence/teenage) and epidemiological terms (incident/incidence/prevalen\*/population\$/survey\$) were combined with the related medical subject headings in MEDLINE (1950 to February 2015), and subject headings EMBASE (1980 to February 2015) and Web of Science (1970 to February 2015) databases (full search strategy is available in the online supplementary material). Validity of the search strategy was verified by its ability to identify all studies known to the investigators and those identified in recent qualitative reviews of myopia. 7 9 25 26

# Inclusion and exclusion criteria

Studies were included if they provided quantitative estimates of myopia prevalence in populations with a clearly defined sampling strategy. Surveys or audits of hospital eye departments or clinics were excluded. Studies that did not report ethnicity of the participants were excluded. Review articles were excluded to avoid duplication of data from individual studies, but were used to check that relevant studies were identified. Studies inviting non-specific volunteers, that relied on self-reported myopia or carried out refractive assessment in a subset, that is, only in those with reduced vision, were excluded.

# Studies identified and data extraction

All data extraction was carried out independently by three reviewers (ARR, VVK and CGO), with independent extraction in a subset. Disagreements in data extraction were resolved by discussion.

Data were extracted on a number of key indicators of study quality, identified a priori. These included methods of assessment (including subjective refraction/retinoscopy and open or closed field autorefraction and use of cycloplegia) and case definition of myopia. In the presence of multiple definitions for myopia within a study, the definition with spherical equivalent refraction/sphere refraction closest to '-0.5 D or less' was used. Some studies reported prevalence based on subjective refraction separately from those on autorefraction. In these situations we included only data from the autorefractor measurements to avoid double counting data from the same study. When prevalence was reported with and without the use of cycloplegia, estimates obtained after the use of cycloplegia were used preferentially.

Data were also extracted on study response rates, habitation type (urban, rural or mixed) and year of survey (midpoint when a study period was reported), geographical location (region/city and country), number of children examined, number with myopia, estimates of myopia prevalence by gender and ethnic/racial group where available. For longitudinal studies, prevalence estimates from follow-up visits were not included in the analyses as our analyses are based on myopia prevalence not incidence.

Among studies that reported ethnicity, most studies were conducted on indigenous population groups (migrant populations were classified according to the reported ethnicity). Ethnicity was classified into the groups listed below, broadly following definitions of the United Nations (UN) and WHO:

- I. Whites: individuals of white European ancestry residing in Europe, America, Australia and New Zealand
- II. East Asian (eg, Chinese, Japanese, Mongolian, Taiwanese, and Chinese children in Hong Kong and Singapore)
- III. South Asian (eg, Indian, Pakistani, Bangladeshi and Nepalese)
- IV. South-East Asian (eg, Malaysian, Thai, Cambodian, Lao)
- V. Blacks in Africa (eg., children from Burkina Faso, Madagascar, South Africa and Tanganyika)
- VI. Blacks not in Africa (eg, blacks in UK or America)
- VII. Middle Eastern or North African (eg, Iranian, Israeli, North African and Tunisian)
- VIII. Hispanic or Latino (eg, Chilean, Colombian, Mexican, Puerto Rican and Ecuadorian)
  - IX. Native Hawaiian or other Pacific Islander (eg, Aborigines and children from Vanuatu)
  - X. American Indian or Alaska native

Ethnic specific estimates of prevalence were extracted if available; otherwise the reported prevalence of myopia was linked to the predominant ethnicity of the study population.

# Statistical analysis

All statistical analyses were carried out using OpenBUGS (V.3.2.2)27 and R (V.3.1.1).28 We used Bayesian multilevel binomial logistic regression to investigate the associations between the log odds of myopia in either eye and potentially modifying factors, including age, gender, ethnicity, year of survey, and study design factors such as methods of assessment and habitation type.

Associations with age were non-linear and varied by ethnicity therefore the model allowed for a quadratic association with age that differed by ethnic group by including an interaction term in the models. Note, quadratic associations on the log odds scale translate into flexible non-linear

associations on the prevalence scale, which encompass exponential associations with an asymptote. Ethnic specific time trends in reported myopia prevalence were investigated using year of survey.

Missing data on survey year were imputed for studies by subtracting 3 years from the year that the article was published (based on the median time to publication, in studies with available data). There were sufficient data to analyse time trends in whites, East Asians and South Asians only. We estimate ORs for rural versus urban and rural versus mixed habitation settings assuming a common OR across ethnicity; however we present sensitivity analyses by ethnicity.

We allowed for potential systematic differences between studies using different methods of refractive assessment by including study level covariates for the use of cycloplegia or not and whether refraction was based on (1) subjective refraction/retinoscopy (this included studies that performed autorefraction and subjective refraction/retinoscopy) or (2) open field autorefraction or (3) closed field autorefraction. This investigation was performed on a subset of studies with available data adjusting for ethnic specific associations with age and survey year, as well as habitation type. Additional analyses investigated an interaction between age and use of cycloplegia.

The difference in myopia prevalence between boys and girls was estimated from a separate model using the subset of studies that reported data separately for boys and girls, adjusting for study design factors and ethnic specific associations with age. All analyses took into account the hierarchical data structure arising from repeated measures of prevalence within the same study population by fitting 'study population' as a 'level' in all our models. A study population was defined as the same ethnicity examined at the same point in time in the same geographical location. A full description of the model appears in the online supplementary statistical appendix. We present median prevalence estimates and ORs with 95% credible intervals (95% CrI), which represent the range of values within which the true value of an estimate is expected to lie with 95% probability.

Modelled age and ethnic specific prevalence estimates were standardised to urban populations and applied to UN demographic data for 2015 and 2025.29 We selected the dominant ethnic group for the following UN defined regions (1) Black—Africa and the Caribbean, (2) White—Europe, North America, Western Asia, Australia and New Zealand, (3) Hispanic—Central and Southern America, (4) Other/mixed—Melanesia, Micronesia and Polynesia. More detailed ethnic division was possible for Asia where (5) East Asian was used to represent Eastern and Central Asia, (6) South Asian—Southern Asia, and (7) South-East Asian—South-Eastern Asia. Using UN population data by 5-year intervals (from 0 year to 19 years) the mid age band prevalence estimates at ages 2 years, 7 years, 12 years and 17 years were applied to the corresponding population data, to obtain population numbers with myopia, overall and by region, with associated 95% CrIs as described previously.30 A description of the statistical model is available online (see online supplementary statistical appendix).

#### Results

The article selection process is outlined in <u>figure 1</u>. In total 143 articles reported age-specific prevalence of myopia in 164 separate study populations (374 349 participants, 74 847 cases of myopia) from cross-sectional surveys published between 1958 and 2015 in 42 different countries. Online <u>supplementary table</u> S1 summarises the key features of the articles contributing to this review along with the citation. <u>Table 1</u> summarises the numbers of subjects and cases of myopia by ethnicity contributing to the analysis. Data extracted on myopia prevalence by ethnicity showed stark differences overall (<u>figure 2</u>) and a non-linear increase in myopia prevalence with age. We therefore modelled ethnic specific quadratic associations with age. There were sufficient data to

estimate trends over time in myopia prevalence in whites, East Asians and South Asians only. Estimated over an extended time period there appears to have been a marginal decline in the odds of myopia in white children and adolescents after adjustment for age and environmental setting (estimates per decade in table 2). However, the 95% CrI for this result is wide and compatible with stable myopia prevalence over time. In contrast, evidence suggests a 23% increase per decade in East Asians (95% CrI 1.00 to 1.55), with weak evidence of an increase in myopia prevalence over time in South Asians (table 2). There was no evidence to suggest that time trends were not linear. In addition, among East Asians time trends did not appear to vary by geographical location.

Table 1
Summary of the number of study populations with data on myopia prevalence by ethnic group

						Survey years	
Ethnicity	No. study populations	Published articles	K	N	x	Range	Mean*
White	34	34	87	54 324	3444	1958 to 2011	1994
East Asian	65	55	310	157 879	60895	1983 to 2013	2000
South Asian	23	20	72	46 012	2648	1992 to 2014	2002
South-East Asian	9	7	18	19 134	2076	1987 to 2010	2006
Black in Africa	10	5	24	8491	262	1961 to 2009	1993
Black not in Africa	5	5	15	5038	371	1997 to 2008	2006
Middle Eastern or North African	16	16	67	41 812	2679	1990 to 2011	2008
Hispanic or Latino	10	10	26	33 408	1503	1976 to 2007	1995
Native Hawaiian or other Pacific Islander	6	6	15	5794	529	1967 to 2008	1987
American Indian or Alaska	4	4	9	2457	440	1967 to 2002	1985
Unknown/other/mixed	3	3	3	323	42	2001 to 2008	2004

K, total number of available estimates of prevalence.

N, total number of participants (published or estimated).

X, total number of cases of myopia using definition closest to 'spherical equivalent refraction/sphere refraction of

<sup>-0.50</sup> D or more myopia'

<sup>\*</sup>Mean survey year weighted by study population size.

Table 2

ORs for trends over time, environmental setting and methods of refractive assessment

		Adjusted odds ratio*	
Factor	Number of study populations	(95% credible interva	
Calendar Time			
Per decade in whites	34	0.85 (0.69, 1.05)	
Per decade in East Asians	65	1.23 (1.00, 1.55)	
Per decade in South Asians	23	1.05 (0.45, 2.63)	
Environmental setting			
Rural	37	1.00	
Urban	115	2.61 (1.79, 3.86)	
Mixed†	12	2.71 (1.63, 4.68)	
Study design characteristics			
Cycloplegia—yes	109	1.00	
Cycloplegia—no	43	2.12 (1.76, 2.52)	
Subjective refraction/retinoscopy	85	1.00	
Closed field autorefraction	54	2.18 (1.79, 2.73)	
Open field autorefraction	12	1.30 (0.89, 1.85)	

<sup>\*</sup>ORs are the medians (95% credible intervals in parenthesis) of the posterior distributions from the Bayesian multilevel binomial logistic regression of the log odds of myopia adjusting for ethnic specific associations with age, ethnic specific associations with survey year (for white, East Asian and South Asian children, only) and environmental setting. The multilevel model took into account that some study populations provide only one age-specific estimate whereas others contribute data for several age groups. ORs for the study design characteristics are based on a subset of studies that specifically reported whether cycloplegia was used. ORs for environmental setting and study design characteristics were assumed to be common across ethnicities.

#### Figure 1

Summary of article selection process from MEDLINE, EMBASE and Web of Science.

<sup>†</sup>Mixed refers to studies that reported myopia prevalence for urban and rural groups combined.

#### Figure 2

Prevalence (%) of myopia for boys and girls combined by age and ethnic group. Data extracted on the age-specific prevalence (as a percentage) of myopia for all study populations are plotted against age for girls and boys combined, by ethnic group. The vertical axis is plotted on the logit scale. Data points from the same study population are joined by a straight line. The size of each symbol is inversely proportional to the SE of the estimate of prevalence.

<u>Table 3</u> provides estimates of myopia prevalence by age and ethnicity standardised to children residing in urban environments. For whites, East Asians and South Asians estimates are also standardised to 2005. For other ethnic groups there were insufficient data to model time trends and therefore estimates are indicative of data available for the 'average' survey year given in <u>tables 1</u>. East Asians have the highest prevalence of myopia reaching 80% by 18 years of age. In contrast, the lowest myopia prevalence in late adolescence is in black children in Africa (5.5% of 15 year olds).

Table 3

Estimated prevalence of myopia by age and ethnicity in boys and girls combined

	Prevalence (%) of myopia by age				
Ethnicity	5 years	10 years	15 years	18 years	
White	1.6 (1.0, 2.5)	6.7 (4.1, 10.3)	16.7 (10.6, 24.5)	22.8 (14.6, 32.7)	2005*
East Asian	6.3 (4.4, 9.2)	34.5 (26.7, 44.0)	69.0 (60.6, 76.8)	79.6 (73.0, 85.4)	2005*
South Asian	5.3 (2.9, 9.6)	9.2 (5.2, 15.7)	13.0 (7.4, 21.6)	13.9 (7.7, 23.5)†	2005*
South-East Asian	6.7 (2.9, 14.4)‡	11.5 (5.3, 23.3)	23.7 (11.7, 41.8)	28.0 (13.8, 48.2)†	2006§
Black in Africa	2.8 (1.5, 5.0)	1.8 (1.1, 2.7)	5.5 (3.1, 9.0)		1993§
Black not in Africa	4.8 (4.0, 5.7)	8.2 (6.8, 9.8)	19.9 (14.3, 26.5)¶		2006§
Middle Eastern or North African	3.5 (2.0, 5.7)	5.5 (3.4, 8.8)	19.6 (12.8, 28.6)	47.1 (34.2, 60.4)	2008§
Hispanic or Latino	5.0 (1.9, 11.6)	4.7 (1.8, 11.0)	14.3 (5.8, 29.8)		1995§
Native Hawaiian or other Pacific Islander	2.6 (0.5, 11.6)‡	5.5 (1.4, 20.3)	23.0 (6.9, 57.6)		1987§
American Indian or Alaska native**	11.3 (3.3, 31.4)	20.2 (6.0, 49.9)	29.8 (10.7, 59.7)††		1985§

Prevalence estimates are medians (95% credible intervals in parenthesis) of the posterior distributions for predicted prevalence from the Bayesian multilevel binomial logistic regression of the log odds of myopia adjusting for ethnic specific associations with age, ethnic specific associations with survey year (for white, East Asian and South Asian children, only) and environmental setting. The multilevel model takes into account that some study populations provide only one age-specific estimate whereas others contribute data for several age groups. Estimates correspond to urban populations.

Children living in predominantly urban environments have 2.6 times the risk of myopia compared with children living in rural environments (<u>table 2</u>, OR 2.61, 95% CrI 1.79 to 3.86). Studies that reported prevalence for a mixed (urban+rural) population are a very heterogeneous group and the estimate should be interpreted with caution. There was no evidence of heterogeneity in the OR of urban versus rural environment by ethnicity. For all ethnic groups, except whites, an urban

<sup>\*</sup>Survey year fitted in the model.

<sup>†</sup>Estimate at age 16.5 years (upper limit of available data).

<sup>‡</sup>Estimate at age 7 years (lower limit of available data).

<sup>§</sup>Mean survey year weighted by study population size.

<sup>¶</sup>Estimate at age 12.5 years (upper limit of available data).

<sup>\*\*</sup>Estimates correspond to rural populations as there were no data in an urban setting for this ethnic group.

<sup>††</sup>Estimate at age 14.5 years (upper limit of available data).

environment is associated with an increased risk of myopia, especially in blacks in Africa, South Asians and South-East Asians (<u>figure 3</u>). However, exclusion of one outlying study in western Newfoundland whites <u>31</u> residing in a rural community weakened the OR for urban versus rural in whites to 0.99 (95% CrI 0.26 to 5.01).

#### Figure 3

ORs for urban versus rural setting are from a Bayesian multilevel binomial logistic regression stratified by ethnicity, adjusting for the quadratic association with age and year of survey (for white, East Asian and South Asian children, only). The common OR is from a Bayesian multilevel binomial logistic regression model using all the data from all ethnic groups combined that adjusts for the ethnic specific quadratic association with age, ethnic specific associations with survey year (for white, East Asian and South Asian children, only) and environmental setting, assuming common OR for urban versus rural settings across ethnicities (as presented in table 2).

Studies that did not use cycloplegia reported double the odds of myopia than those that did use cycloplegia (after allowing for age, ethnicity, survey year and environmental setting, table 2). We examined an interaction between use of cycloplegia and age and found that the OR for 'no cycloplegia' versus cycloplegia was stronger at younger ages than at older ages (see online supplementary table S2). Method of measurement of refraction was also associated with myopia prevalence. Studies defining myopia based on autorefraction reported a higher prevalence of myopia (especially closed autorefraction) than studies using retinsocopy or subjective refraction (either exclusively or in addition to autorefraction).

The meta-regression comparing boys and girls is based on 64 study populations with 146 996 participants and 36 958 cases of myopia. We examined differences between boys and girls for each ethnic group separately. At about age 9 years gender differences begin to emerge in whites and East Asians and become more pronounced with age showing a higher prevalence of myopia in girls than in boys (see online <a href="supplementary table">supplementary table</a> S3). By 18 years of age white girls are approximately twice as likely as white boys to be myopic (OR 2.03 95% CrI 1.40 to 2.93). A similar picture emerged for East Asians (OR 2.30 95% CrI 2.01 to 2.61). There was no clear evidence of gender differences in South Asians or in Hispanic/Latinos and there was insufficient data in the other ethnic groups to estimate gender differences by age.

There were sufficient data to investigate geographical variations in age-specific myopia prevalence in whites, East Asians and South Asians. In whites there was no clear evidence of differences in myopia prevalence in studies from Europe, USA and Oceania. Among East Asians the highest prevalence of myopia is among those residing in Singapore (86% of 15 year olds, table 4). Rates are very similar in Hong Kong and Taiwan (~80% of 15 year olds), lower in China (~59% of 15 year olds) and Australia (41% of 15 year olds). Rates are lowest in a rural population of Mongolia (table 4). Estimates in Japan are based on data from the 1990s and may not be representative of contemporary Japanese children. South Asian children residing in Australia, England or Singapore are approximately five times more likely to be myopic than their counterparts living in Nepal or India (table 4). At 15 years of age approximately 40% of migrant South Asians are myopic compared with 9% of indigenous South Asians.

Table 4

Estimated prevalence of myopia by age in boys and girls combined (1) stratified by country for East Asians, and (2) stratified by continent for South Asians

	Prevalence (%) of myopia by age						
	5 years	10 years	15 years	18 years	Year		
East Asians by country							
Australia	1.9 (0.8, 4.2)*	13.6 (6.2, 26.5)	40.6 (22.3, 60.9)*	_	2005†		
China	3.9 (2.9, 5.9)	24.9 (19.8, 34.3)	59.0 (51.7, 69.3)	71.9 (65.4, 80.0)*	2005†		
Hong Kong	9.2 (5.4, 15.7)	45.3 (31.8, 60.7)	78.2 (66.8, 87.1)	86.4 (78.2, 92.2)*	2005†		
Japan	1.7 (0.7, 3.8)	12.2 (5.8, 24.3)	37.6 (21.1, 58.2)	51.7 (32.1, 71.2)*	1990‡		
Malaysia	4.6 (1.4, 14.5)*	28.4 (10.4, 58.1)	63.2 (33.5, 85.7)	75.3 (47.2, 91.4)	1990‡		
Mongolia	0.3 (0.1, 0.9) *§	2.7 (0.8, 7.2)§	10.8 (3.5, 25.0)§	17.7 (5.9, 37.2)*§	2003‡		
Singapore	14.9 (9.9, 22.4)	59.0 (47.2, 70.2)	86.2 (79.4, 91.1)	91.7 (87.2, 94.8)*	2005†		
Taiwan	10.1 (5.9, 19.8)¶	48.0 (34.0, 67.4) ¶	80.0 (69.0, 90.0)¶	87.6 (79.9, 94.0)¶	2005†		
USA	4.9 (1.9, 12.0)	-	-	_	2005†		
South Asians by continent							
Living in South Asia	3.6 (2.2, 5.7)	6.4 (4.0, 9.7)	9.1 (5.7, 13.7)	10.3 (5.8, 17.0)*	2005†		
Not living in South Asia	20.4 (10.6, 36.0)*	31.6 (17.8, 50.1)	40.5 (24.1, 59.5)	43.8 (25.2, 63.9)*	2005†		

Numbers express medians and 95% credible intervals in parenthesis.

Estimates correspond to urban populations standardised where possible to 2005. For Japan and Malaysia, estimates are indicative of 1990 and for Mongolia estimates are for a rural population in 2003.

Cells without estimates of prevalence indicate insufficient data to obtain estimates.

Estimates of the global myopia prevalence and number of cases by region were attained by applying modelled age and ethnic specific prevalence estimates to UN defined population data for calendar years 2015 and 2025 and ages 0 year to <19 years (see online <u>supplementary table</u> S4). Global estimates suggest a burden of 312 million myopic cases in 2015 (95% CrI 265 million to 369 million), rising to 324 million (95% CrI 276 million to 382 million) in 2025. Population prevalence of myopia in childhood (0 year to <19 years) is highest in East Asia (35%) with nearly 80% of cases in Asia. The global share of myopia cases will remain high in Asia in 2025 with a marginal increase in Africa due to more rapid expansion of this age group in Africa than in other regions.

<sup>\*</sup>Estimate obtained by extrapolation.

<sup>†</sup>Survey year as fitted in the model.

<sup>‡</sup>Mean survey year weighted by study population size.

<sup>§</sup>Estimates correspond to rural populations.

<sup>¶</sup>Estimates correspond to mixed populations in terms of urban/rural environmental setting.

This is the first systematic review and quantitative meta-analysis of the worldwide prevalence of myopia in childhood and adolescence. We have quantified the striking ethnic differences in myopia prevalence that become more marked with age. In particular, East Asians show the highest prevalence with over 90% of East Asians living in Singapore and 72% of East Asians living in China aged 18 years exhibiting myopia (defined as at least -0.5 D of myopia). Overall South Asians had much lower rates with limited evidence of trends over time. However, there were marked differences between those living in South Asia compared with migrant South Asian populations. There was no strong evidence of time trends in myopia prevalence among white populations. Nonlinear associations between age and the log odds of myopia captured a large proportion of the ethnic variation in myopia prevalence. Some ethnic groups show a rapid increase with age in the early years that flattens (East Asians, whites, South Asians), suggesting that levels of myopia may have plateaued, reaching saturated levels. 32 In others the increase in myopia prevalence was almost linear with age (South-East Asian, American Indian or Alaska Native, Native Hawaiian Pacific Islanders). In other groups the increase with age did not emerge until after about 8 years of age (Hispanics, blacks (in and outside of African) and Middle Eastern or North Africans). We have shown that living in an urban rather than rural environment is associated with almost a tripling in the risk of myopia and this pattern is seen among all ethnic groups. As expected, studies that did not use cycloplegia reported higher myopia prevalence (especially at younger ages) as did studies that relied on autorefractor findings, particularly closed field instruments. We also showed that sex difference in the age-specific prevalence of myopia exist in whites and East Asians, emerge at about 9 years of age and become more marked through adolescence showing double the odds of myopia in girls compared with boys.

The increase in myopia prevalence seen in urban compared with rural populations agrees with others that have explicitly examined this in children with the same ethnic ancestry. 20 21 33-46

Although there was no formal evidence of a difference in urban-rural differences across ethnic groups, some populations showed marginally larger ORs compared with others. Stronger urban-rural differences in South Asians and South-East Asians may reflect greater disparity in living conditions compared with high-income countries. These findings are consistent with the results of studies in population groups that migrate from rural to urban settings, which tend to adopt myopia rates of the host population, for example, Pacific Islanders that migrated to Taiwan;47 South Asian children living in the UK have higher rates of myopia12 than South Asian children residing in predominantly rural communities in India;21 39 Indians in Singapore have prevalence rates more similar to Singaporean Chinese than to Indians in India.48 49 The apparent decreased risk of myopia associated with urban environment in whites was explained by inclusion of western Newfoundland whites residing in a rural community with shared genetic ancestry, who showed an unusually high prevalence of myopia.31 Removal of this single population reduced the OR for urban versus rural in whites towards the null.

Potential explanations have been suggested for the higher rates of myopia in children residing in urban settings compared with children from the same ethnic groups living in more rural settings including a more congested environment 33 44 and greater emphasis on education and hence near vision activities. 50–53 Several studies have shown a link between increased near vision activities and myopia, 19 38 54 55 but this is not a universal finding. 11 56 57 Years of education have also been related to myopia 25 and introduction of formal education at younger ages in some East Asian countries 57 58 may be a contributing factor. In Singapore 59 children from as young as 3 years and as young as 2 years in Hong Kong 32 actively participate in additional education classes before formal schooling education begins. In contrast, the prevalence of myopia is low in African

populations where literacy rates are low, and formal education does not start for most children until the ages of 6–8 years. 60 61 It is possible that the younger age of initial exposure to formal education patterns levels of myopia through childhood.

Further evidence is provided by the reported independent associations of population density on myopia prevalence, 33 44 which may suggest a contribution from a collection of risk factors associated with urban living environment. Time spent outdoors will differ between urban and rural communities and has been examined in relation to myopia. 56 58 62–67 Children who become myopic are less likely to participate in sports/outdoor activities. 68 In a 2-year prospective study there was a suggestion that longer durations spent outdoors were associated with slower axial elongation in non-myopic teenagers but not in pre-existing myopes. 69 A recent systematic review and meta-analysis showed a 2% reduction in the odds of myopia for every additional hour per week spent outdoors. 70 Biological mechanisms for an association include low accommodative demand outdoors coupled with increased depth of focus. 25 Time spent outdoors is also culturally patterned, and might be related to sibship; teasing out the independent, potentially causal, effects of time spent outdoors requires further study. 62 65 71 72

Despite the association between myopia prevalence and an urban environment, ethnic differences in myopia prevalence exist among populations drawn from the same living environment. 12 14 54 Whether these ethnic differences reflect genetic susceptibility to environmental factors or are due to ethnic differences in other factors is unclear. A previous meta-analysis of three British birth cohort studies including over 15 000 white children showed that various familial factors were related to the odds of reduced vision (a proxy for myopia) in childhood including social class, parental education, maternal age and birth order (with higher risk among first-born children). 10 All of these familial factors are likely to differ with level of urbanisation and ethnic group. It is also likely that intensity of near vision and emphasis on academic achievements are related to sibship and birth order.

Higher rates of myopia prevalence in girls compared with boys have been found in some individual studies, 10 18 57 73–78 but not in others. 12 21 23 79–81 The reason for disagreements between studies examining the association between myopia and sex is likely to be due to two factors (1) age of children studied, and (2) statistical power of a study which is influenced by the size of the study and the age-specific prevalence of myopia. The sex differences seem to emerge at about 9 years of age and become more pronounced with age, hence comparisons at younger ages are unlikely to show gender differences. Differences observed beyond the first decade of life have been attributed to a stronger emphasis on education/near distance related activities in girls compared with boys. 18 This gender difference may persist in adulthood. 5 53 82 83 It is well established that differences between cycloplegic and non-cycloplegic refractions are more marked at younger ages, 84–86 especially with closed field autorefraction. 87

This review has a number of strengths and limitations. By adopting a more inclusive approach, we were able to include more studies in the meta-analysis thereby increasing the sample size and representativeness. Adopting a more exclusive approach, that is, omitting studies with imperfect study methods, would result in loss of power and would not allow study design differences to be quantified. We took account of study level factors including environmental setting, year of survey and survey methods used to define cases of myopia, particularly use of cycloplegia. The increased numbers allowed us to quantify the marked differences in the age-specific prevalence of myopia between ethnic groups, between urban and rural environments as well as gender differences. Limitations of this study include the omission of study response rates in the analysis as reliable data were not routinely reported. Our analysis is based on summaries from published data rather than data from individuals, which may lack the granularity to determine associations. A meta-analysis

based on individual data would have yielded more precise results for the age-specific prevalence and could adjust for individual factors. Such an approach would be preferable if these data could be obtained for all relevant studies. However, the difficulty with an individual data meta-analysis is that it may represent a subset, biased towards well resourced studies, which are not representative of studies as a whole. Future work could examine trends in myopia incidence over time by meta-analysing estimates of incidence from longitudinal studies. This review did not examine within-person changes in spherical refraction over time which is likely to show different myopic refraction progression rates by ethnicity over time.

In summary, this meta-analysis provides the most comprehensive and current evidence on myopia prevalence in childhood and adolescence. It seems that populations that have experienced rapid economic transition (East and South Asians) have undergone the most rapid myopic transition. It will be important to monitor trends in myopia over time especially in relation to populations undergoing rapid transitions in myopia and to identify factors of the urban environment that are responsible. Understanding the aetiology of childhood myopia will give clues to prevention, potentially offering strategies to limit the economic impact of refractive error.

# Supplementary Material

#### Web supplement:

Click here to view. (255K, pdf)

#### **Footnotes**

**Collaborators:** All authors contributed substantially to the conception and design of this paper. ARR, VVK, AKW and CGO conducted the literature searches and extracted the data from published papers. ARR, VVK and CGO drafted the paper and carried out statistical analysis. All authors contributed to revising the manuscript and all authors approved the final version. ARR and CGO will act as guarantors. The guarantors accept full responsibility for the integrity of the work as a whole. All authors had access to the data, and approved the final version to be published.

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