

## Review Article

# The Association between Childhood Myopia Prevalence and Environmental Factors in China: A Metaregression Analysis

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**Background.** Myopia prevalence varies across the country among schoolchildren in China. Recently, environmental factors have been shown to be important in myopia development and progression. Given China's geographical diversity with variable environmental factors, we investigated whether environmental factors could explain the regional variations in myopia in mainland China. **Methods.** We searched PubMed, Web of Science, and Chinese Science Periodical Databases for studies with reports of myopia prevalence in schoolchildren in mainland China from the years 1979 to 2019. Data on environmental factors (annual sunshine hours, temperature, and population density) were obtained from past records. A random-effect univariate metaregression analysis was used to investigate the association between the environmental factors and myopia prevalence and to determine the proportion of variation in regional myopia prevalence that can be attributed to each factor. **Results.** Forty-nine eligible studies were identified that included 666,864 schoolchildren aged 6 to 20 years. The pooled estimate of myopia prevalence was 32.88% (95% confidence interval: 26.69–39.08%). Univariate metaregression analysis indicated that annual sunshine hours (27.97% of variance), annual temperature (24.66%), and population density (7.06%) significantly contributed to regional myopia prevalence variation (each  $p < 0.05$ ), while seasonal variation in sunshine hours (1.54%,  $p = 0.604$ ) was not a significant predictor of myopia prevalence. However, only annual sunshine hours was significantly associated with myopia prevalence in the multivariate metaregression model. **Conclusion.** Myopia prevalence in children was higher in regions with low sunshine hours, and annual sunshine hours was significantly associated with regional variation in myopia prevalence in mainland China.

## 1. Introduction

Myopia is acknowledged to be a substantial public health concern due to its increasing prevalence in recent decades and the sight-threatening ocular complications associated with high myopia such as cataract, retinal detachment, maculopathy, and glaucoma [1, 2]. Although evidence suggests that myopia prevalence is increasing worldwide, analyses of global trends in myopia show marked regional differences in myopia prevalence, with developed East Asian and South-East Asian countries such as China, Japan, South Korea, Singapore, and Taiwan showing the greatest increase

in the prevalence of myopia [3, 4]. There have been reports of myopia prevalence of up to 80–90% in urban young adult populations (school leavers) in these countries, and approximately 10 to 20% of myopes in these countries have high myopia ( $>6D$ ), placing them at significant risk of ocular complications in later life [5].

Both genetic and environmental factors are thought to be involved in the aetiology of myopia. However, the rapid increase in myopia prevalence over the past few decades cannot be explained merely by genetic predisposition [6], and numerous studies suggest that environmental factors could be involved in the rise in myopia prevalence [7–9].

Several environmental factors have been proposed as playing important roles such as increased near work, less time engaged in outdoor activities, urbanization, or a combination of these factors [10–16].

Near work has long been considered as an environmental risk factor for myopia development since myopia is often associated with schooling and educational performance [13, 17, 18]. However, prospective longitudinal studies that have investigated the role of near-work activities in myopia development have shown that near work is a relatively weak predictor of myopia development in children [19, 20]. More recently, time outdoors has emerged as an additional environmental risk factor for myopia development with consistent evidence that less time spent outdoors is associated with a higher risk of myopia development [10, 16, 21–25]. Findings from animal [26, 27] and human studies [28–32] suggest that bright ambient light outdoors may underlie the association between greater time spent outdoors and less myopia progression. Recent prospective longitudinal studies (using objective light measurement techniques) in schoolchildren [29] and young adults [31] also showed that greater daily light exposure was associated with slower axial eye growth, suggesting that light exposure is an important environmental risk factor in eye growth. Myopia progression also exhibits a seasonal variation with slower progression noted in summer compared to winter [33, 34] with higher progression reported during periods with shorter daylight length [34]. Greater outdoor activities and higher levels of environmental light in summer have been hypothesized to drive the seasonal variation in myopia progression [16, 31, 35, 36] which further supports a role of light exposure in regulating eye growth.

Urbanization has also been shown to be associated with a higher prevalence of myopia [37], and this may be related to factors such as increased academic demands [11, 12, 21], more time in education [21], lack of outdoor activities [16], constricted living spaces [38], and higher population density [14, 39].

In China, the reported prevalence of myopia in primary schoolchildren varies across the country ranging from 5% in Tong Liao city [40] to 37% in Beijing [41]. China is a geographically large country with a wide diversity in its climate with varying sunshine hours and temperature across different provinces [42]. Given the association between myopia prevalence and bright light/time outdoors and urbanization/population density, it is possible that geographical differences in these environmental factors may explain some of the variations in myopia prevalence across China. Therefore, we performed a meta-analysis of myopia prevalence in primary and secondary schoolchildren from different provinces in mainland China and examined the influence of objective records of environmental factors such as annual sunshine hours, seasonal variation in sunshine hours, temperature, and population density on the prevalence of myopia to quantify the variability in regional myopia prevalence that can be accounted for by recorded environmental factors.

## 2. Methods

**2.1. Literature Review.** Studies identified for the meta-analysis reported myopia prevalence in primary and secondary schoolchildren from mainland China and were published between the years 1979 and 2019. Research papers in both English and Chinese languages were searched, since including only English language papers may lead to systematic error in the meta-analysis [43]. The literature search was conducted through PubMed, Web of Science, and China Science Periodical Databases (<http://www.cnki.net> and <http://www.wanfangdata.com.cn> and <http://www.cqvip.com>) and was completed in April 2019. The following text words were used to search relevant references in PubMed: ((“myopia”[MeSH Terms] OR “myopia”[All Fields]) OR (“refractive errors”[MeSH Terms] OR (“refractive”[All Fields] AND “errors”[All Fields]) OR “refractive errors”[All Fields] OR (“refractive”[All Fields] AND “error”[All Fields]) OR “refractive error”[All Fields])) AND (“epidemiology”[Subheading] OR “epidemiology”[All Fields] OR “prevalence”[All Fields] OR “prevalence”[MeSH Terms]) AND ((“china”[MeSH Terms] OR “china”[All Fields]) OR (“asian continental ancestry group”[MeSH Terms] OR (“asian”[All Fields] AND “continental”[All Fields] AND “ancestry”[All Fields] AND “group”[All Fields]) OR “asian continental ancestry group”[All Fields] OR “chinese”[All Fields])) AND ((“child”[MeSH Terms] OR “child”[All Fields] OR “children”[All Fields]) OR (“students”[MeSH Terms] OR “students”[All Fields])). The literature search through Web of Science and China Science Periodical Databases used the key indexing terms of myopia, prevalence, incidence, schoolchildren, primary schoolchildren, secondary schoolchildren, and visual acuity. The literature search was conducted by two authors (ZY and SU) independently, and the extracted studies were compared, and any inconsistencies were resolved by consensus. Reference lists from the included studies were also searched to identify other relevant studies.

Studies that directly reported myopia prevalence, or contained data allowing estimation of myopia prevalence, in primary schoolchildren, and/or primary and secondary schoolchildren in mainland China were considered for analysis. The following details were extracted from each study: author and year of publication, the year the study was conducted, study region and province, study population (sample size, age, and gender distribution), method of refractive error data collection (subjective refraction, autorefraction, and cycloplegic refraction), definition of myopia, and myopia prevalence.

### 2.2. Data Extraction and Quality Assessment

**2.2.1. Myopia Prevalence.** The quality of the studies included in this meta-analysis was evaluated using the methodological criteria for prevalence studies developed by Leboeuf-Y de and Lauritsen [44] and Walker [43]. Three aspects of each study were assessed, including (1) whether the final sample was representative of the target population, (2) quality of

data (were the data primarily from a prevalence study or were they taken from a survey not specifically designed for the purpose? Have the data been collected directly from the participants by means of a validated method such as subjective refraction or autorefractometry or cycloplegic refraction? Was the same mode of data collection used for all subjects?), and (3) a clear statement of the definition of myopia. For this meta-analysis, we defined myopia as spherical equivalent refractive error  $< -0.50$  D. When multiple publications from the same study or geographical location were available, we included only one study that best addressed the study inclusion criteria.

**2.2.2. Environmental Factors.** The primary aim of most of the studies included in the meta-analysis was to report the myopia prevalence, and therefore, data pertaining to environmental factors such as sunshine hours, temperature, and population density were not available directly from the studies. Therefore, we accessed the Chinese National Earth System Science Data Sharing Infrastructure website (<http://www.geodata.cn>, date last searched: 26 May 2019) to obtain past records of sunshine hours and temperature, recorded at meteorological stations for each of the study locations where the myopia prevalence was reported.

Sunshine hours are defined as the number of hours for which the direct solar irradiance exceeds  $120 \text{ W/m}^2$  in a given period, in a given location, and are typically expressed as an average over several years. In this study, average annual cumulative sunshine hours were derived for each cohort in the specified location, based on the age of the oldest subject reported in the cohort. For example, if a study reported myopia prevalence that was collected in primary schoolchildren (aged 6 to 12 years) in Shanghai in the year 2000, the annual cumulative sunshine hours were estimated and averaged from the years 1988 to 2000 (12 years). This estimation assumes that all the schoolchildren are residents in the location since birth and also assumes that the annual sunshine hours in a given location do not fluctuate substantially over the calculated years, since the younger children (6-year-olds when compared to 12-year-olds) would have experienced only the later years of sunshine (i.e., 1995 to 2000).

We also derived average cumulative sunshine hours for different seasons to examine whether seasonal differences in sunshine hours are associated with geographical variation in myopia prevalence. Based on the meteorology records, sunshine hours between the months of April and June were defined as summer sunshine hours, and sunshine hours between the months of July and September, October and December, and January and March were defined as autumn, winter, and spring sunshine hours, respectively. The mean annual temperature ( $^{\circ}\text{C}$ ) was also derived for each of the cohorts by averaging the annual temperature over a period of time (based on the oldest subject in the cohort) in the corresponding location.

Population density data during the study period were obtained from the records of the National Bureau of Statistics of China for each of the study locations. Similar to the

estimation of sunshine hours, the estimation of mean annual temperature and population density assumed that all the schoolchildren in a particular school were residents in the same location since birth.

**2.3. Data Analysis.** All statistical analyses were performed using STATA 15.0 (StataCorp LP, College Station, Texas, USA). Pooled myopia prevalence estimates with 95% confidence intervals were calculated using random-effects meta-analysis for all the included studies, and the pooled estimates were also calculated separately for primary and secondary schoolchildren. The  $I^2$  statistic was used to test for statistical evidence of heterogeneity across the studies ( $I^2$  values  $>50\%$  indicates a high-level heterogeneity) [45]. Univariate metaregression (random-effect model) was used to investigate sources of heterogeneity in the published prevalence estimates of myopia and to establish the factors accounting for differences in myopia prevalence. Similar to meta-analysis estimates, the metaregression analysis was also performed for all the included studies and separately for primary and secondary schoolchildren.

Several factors such as mean cumulative annual sunshine hours, mean annual temperature, population density, and seasonal variation in sunshine hours (the difference between the maximum and minimum seasonal cumulative sunshine hours) were considered, and each of these factors was analysed separately to determine the proportion of variance in myopia prevalence that can be attributed to each factor. All the factors identified in the univariate analysis that could significantly contribute to the variance in myopia prevalence were then entered into a multivariate metaregression model to estimate the overall variance that can be attributed to these factors. Pooled myopia prevalence estimates were then recalculated after stratifying the studies based on the factors that could significantly explain the variation in myopia prevalence between studies. Potential publication bias was assessed using the Egger test [46].

### 3. Results

**3.1. Characteristics of the Studies Included in the Analysis.** Of 856 studies identified through our literature search, 747 studies were excluded after abstract and full-text review. The majority of the excluded studies did not report myopia prevalence in mainland Chinese schoolchildren, and a few studies reported myopia prevalence in Chinese children living in other countries (Figure 1). The remaining papers were assessed, and 49 studies were included for the meta-analysis. Of the 49 studies, 31 studies reported the overall myopia prevalence (both primary and secondary schoolchildren), and 18 studies reported prevalence only in primary schoolchildren. Some studies ( $n=19$ ) that reported overall myopia prevalence allowed the estimation of myopia prevalence separately for primary (5 to 14 years of age) and secondary (12 to 20 years of age) schoolchildren, and therefore, we estimated the myopia prevalence and included these findings in the primary and secondary schoolchildren analyses. Overall, 49 studies were used in the combined

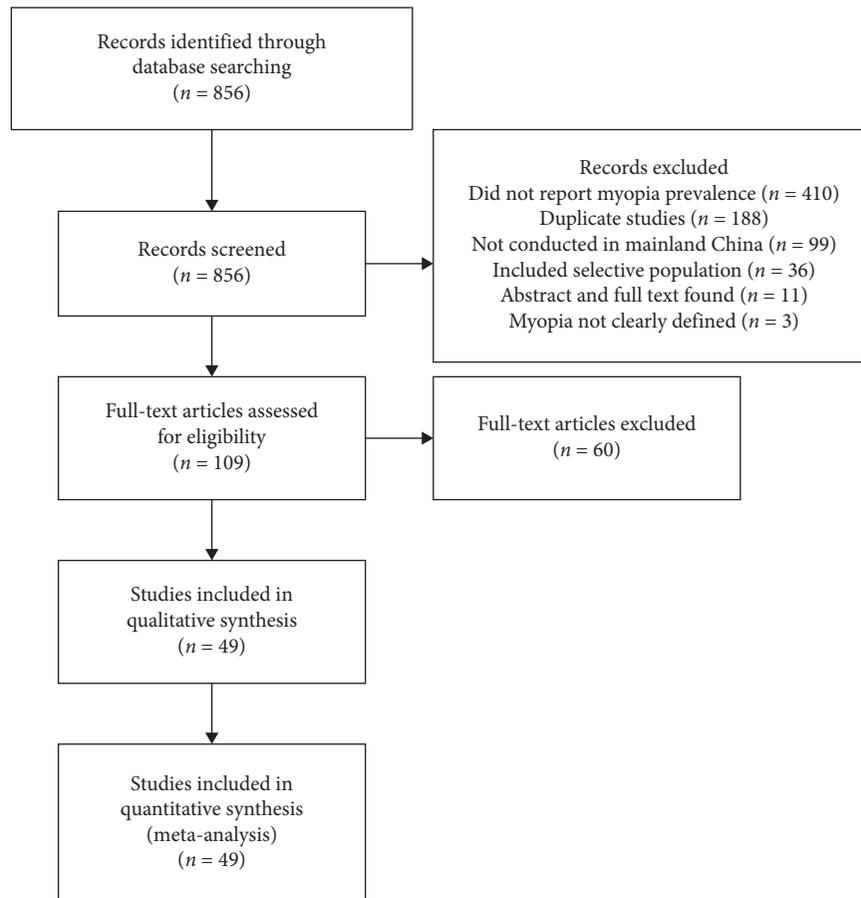


FIGURE 1: Flow diagram of the study selection process.

schoolchildren category (Table 1), 37 studies in the primary schoolchildren category, and 19 studies in the secondary schoolchildren category. Figure 1 shows a flowchart of the study selection process.

**3.2. Quality Assessment of the Included Studies.** All the included studies had sample size >600 (range 632 to 156,934 and total number of children of 666,864) and were assumed to be representative of the target population. Some studies were not primarily designed to estimate the myopia prevalence and reported the prevalence of several ocular diseases, but these studies were included since myopia prevalence was also reported. All the included studies used standard modes of data collection (subjective refraction, autorefraction, or cycloplegic refraction) and used a criteria of <-0.50 D as the criteria to define myopia.

**3.3. Meta-Analyses.** The pooled estimate of myopia prevalence from all the studies was 32.88% (95% confidence interval (CI) 26.69–39.08%). The pooled estimate of myopia prevalence from the studies that included only primary schoolchildren was 23.55% (95% CI: 19.87–27.22%), and the pooled prevalence from the studies that included only secondary schoolchildren was 60.05% (95% CI: 45.05–75.05%). Supplementary figures show the forest plots

of estimated pooled myopia prevalence in primary (Supplementary Figure 1) and secondary (Supplementary Figure 2) schoolchildren. The  $I^2$  statistic revealed that there was a high level of heterogeneity ( $I^2 > 99\%$ ) across the studies for all studies and also when only primary and only secondary schoolchildren studies were analysed.

**3.4. Univariate Metaregression.** The metaregression model quantified the influence of the covariates sunshine hours, annual temperature, population density, and seasonal variation in sunshine hours on myopia prevalence (Table 2). When all the studies were pooled together (both primary and secondary school students), the univariate metaregression revealed that the proportion of variance in myopia prevalence explained by cumulative annual sunshine hours was 27.97% (adjusted  $R^2 = 27.97$ ,  $p < 0.001$ ). Additional univariate metaregression analysis indicated that 24.66% of variance in myopia prevalence could be explained by mean annual temperature (adjusted  $R^2 = 24.66$ ,  $p < 0.001$ ). A separate univariate analysis revealed that population density was also significantly associated with the regional myopia prevalence variation and represented 7.06% of variance in myopia prevalence (adjusted  $R^2 = 7.06$ ,  $p = 0.036$ ). Seasonal variation in sunshine hours was not significantly associated with the myopia prevalence in this population and explained only 1.54% of variation in myopia prevalence in the

TABLE 1: Characteristics of all the studies included in the meta-analysis.

Authors (year of publication)	Myopia prevalence (combined or primary or secondary school ages)	Study location (city)	Age range (years)	Gender distribution (% males)	Sample size	Prevalence of myopia (%)	Annual sunshine hours (total hours)
Yuan et al. (2005) [47]	C, P	Kunming	6–12	NA	10312	36.59	2126
Zhong (2014) [48]	C	Guiyang	6–20	50%	12907	50.55	883
Liu et al. (2003) [49]	C, P	Dongguan	NA	NA	5650	31.88	1716
Zhang et al. (2014) [50]	C, P	Beijing	5–14	52%	4249	36.71	2520
Xie et al. (2013) [51]	C, P, S	Qinghai Yunnan Shandong Wenzhou Shanghai	NA	55%	19139	31.60 <sup>†</sup>	2830 <sup>†</sup>
Guo et al. (2017) [52]	C	Greater Beijing	6–18	51.1%	35745	70.90	2512
Yu et al. (2003) [53]	C, P, S	Shanwei	6–19	NA	1502	54.79	1752
Wei et al. (2014) [54]	C, P	Nanning	6–12	NA	6315	35.70	1277
Tu et al. (2013) [55]	C, P	Shaoxing	6–15	49%	2002	25.72	1893
Luo et al. (2013) [56]	C, P	Baotou	7–12	NA	4276	14.92	2681
Liu et al. (2009) [57]	C, P, S	Shaoyang	NA	48%	1000	58.70	1504.5
Yu et al. (1982) [58]	C, P, S	Fuzhou	NA	54%	1579	39.30*	1762
Chen and Liu (2010) [59]	C, P, S	Zibo	NA	52%	156934	51.91	2403
Xiong (2013) [60]	C, P, S	Shiyan	NA	50%	2088	58.64	2003
Wang et al. (2014) [61]	C, P, S	Maanshan	6–15	53%	4062	38.00	1953
Gui et al. (2013) [62]	C, P, S	Wuhu	6–17	50%	94963	43.43	1938
Xin-fu et al. (2015) [63]	C, P	Sanya	6–13	51%	1218	25.12	1888
Si et al. (2006) [64]	C, P	Yongdeng Tianzhu	NA	53% (Yongdeng) 55% (Tianzhu)	56386	12.69 <sup>†</sup>	2909 <sup>†</sup>
Zhao (2007) [65]	C, P, S	Jinan	NA	50%	4737	60.10	2446.8
Zhang (1994) [66]	C, P, S	Zhongwei	NA	50%	4762	25.49	2955
Zhang et al. (2003) [67]	C, P	Otog Banner	NA	50%	10365	19.62	2831.9
Shang et al. (2009) [68]	C, P	Shenyang	7–14	53%	636	28.07*	2420
Jia (2005) [69]	C, P	Jinzhou	NA	50%	30510	14.34	2769
Wu (2011) [70]	C, P	Weinan	NA	NA	2683	27.32	2242
Liu et al. (1979) [71]	C, P	Xining	NA	NA	919	12.19	2759.3
Chen et al. (1990) [72]	C, P	Shigatse	6–14	54%	1770	2.99	3142
Cui and Fang (2002) [73]	C, P	Baicheng	8–13	50%	2236	14.22	2923
Liu et al. (2017) [74]	C, P	Tongcheng	6–13	54%	1802	15.59	2452
Yu et al. (2015) [75]	C	Jiading	6–16	51%	6321	29.68	2033
Li and Li (2010) [76]	C	Hami	6–18	56%	3197	25.81	3211
He et al. (2009) [37]	C	Zhongshan	7–18	47%	5622	52.70	1647
Liu et al. (2012) [77]	C, P, S	Chengdu	NA	51%	3162	57.75	1016.2
Bai et al. (2004) [78]	C, P, S	Daqing	NA	50%	13725	36.03*	2424

TABLE 1: Continued.

Authors (year of publication)	Myopia prevalence (combined or primary or secondary school ages)	Study location (city)	Age range (years)	Gender distribution (% males)	Sample size	Prevalence of myopia (%)	Annual sunshine hours (total hours)
Wei et al. (2007) [79]	C, P, S	Wuhan	6–20	51%	1061	44.67	1861.9
Yin et al. (2013) [80]	C	Karamay	NA	49%	658	26.44	2697
Chen et al. (2007) [81]	C, P, S	Emin	NA	48%	18061	23.08	2993.5
Guo et al. (2016) [82]	C	Guangzhou	NA	52%	3055	47.30	1499
Dong et al. (2007) [83]	C, P, S	Tongliao	7–18	50%	71888	4.89	3083
Aerke et al. (2014) [84]	C	Kashmir Alkasu	7–18	50%	5737	12.95 <sup>†</sup>	2904 <sup>†</sup>
Du (2009) [85]	C, P, S	Baoji	8–19	55%	5489	49.41	2039.1
Gao et al. (2011) [86]	C, P, S	Lianyungang	6.5–20	49%	2480	33.27	2287
Song et al. (2010) [87]	C	Beijing	NA	49%	15316	53.87	2553.6
Wei et al. (2016) [88]	C	Heze	7–18	50%	2400	55.58	2231.7
Wu et al. (2013) [89]	C	Weihai and Guanxian	4–18	53%	6026	36.90	2462
Li et al. (2015) [90]	C, P, S	Shenzhen	6–17	58%	20568	37.01	1857
Qian et al. (2016) [91]	C	Mangshi	5–16	51%	7681	39.10	2029
Chin et al. (2015) [92]	C	Turpan	4–19	43%	632	17.25	2948
Li et al. (2014) [93]	C	Central Heilongjiang	5–18	54%	1675	5.01	2455
Pi et al. (2012) [94]	C	Chongqing	6–15	52%	3079	13.71	988

NA: not available from the study. The second column provides the age group of each study: C represents combined myopia prevalence for both primary and secondary schoolchildren, P represents primary only, and S represents secondary schoolchildren only. \*Prevalence was calculated based on the number of myopic eyes versus the total number of eyes. <sup>†</sup>Average myopia prevalence and annual sunshine hours from all the study locations.

TABLE 2: Relationship between covariates and myopia prevalence from univariate metaregression analyses in all the studies (5–20 years), studies involving only primary schoolchildren (5–14 years), and only secondary schoolchildren (12–20 years).

Covariates	All studies ( $n = 49$ ) $R^2$	Primary schoolchildren ( $n = 37$ ) $R^2$	Secondary schoolchildren ( $n = 19$ ) $R^2$
Annual sunshine hours	<b>27.97</b>	<b>58.32</b>	<b>28.74</b>
Annual temperature	<b>24.66</b>	<b>49.70</b>	<b>18.12</b>
Population density	<b>7.06</b>	<b>8.94</b>	0.287
Seasonal difference in sunshine hours	1.54	<b>12.54</b>	2.21
Year of publication	4.04	<b>8.26</b>	1.93

$R^2$ : coefficient of determination. The values highlighted in bold indicate a significant association.

combined group of all children (adjusted  $R^2 = 1.54$ ,  $p = 0.604$ ). However, for primary schoolchildren, the seasonal variation explained 12.54% of the variance which was statistically significant (adjusted  $R^2 = 12.54$ ,  $p = 0.018$ ).

Myopia prevalence was not significantly associated with the year of study publication, which accounted for only 4.04% of variation in myopia prevalence (adjusted  $R^2 = 4.04$ ,  $p = 0.089$ ). Overall, the univariate metaregression analyses indicated that cumulative annual sunshine hours, mean annual temperature, and population density were statistically significant determinants of myopia prevalence, while seasonal variation in sunshine hours and year of publication did not significantly influence the variation in myopia

prevalence when all the studies were pooled together. Figure 2 shows the association between myopia prevalence and each of the predicting factors. It can be observed that there was a significant negative association between myopia prevalence and annual sunshine hours, while significant positive associations existed between myopia prevalence and annual temperature and population density.

**3.5. Multivariate Metaregression.** Since annual sunshine hours, annual temperature, and population density were significant predictors of myopia prevalence, these factors were added to a multivariate metaregression analysis to

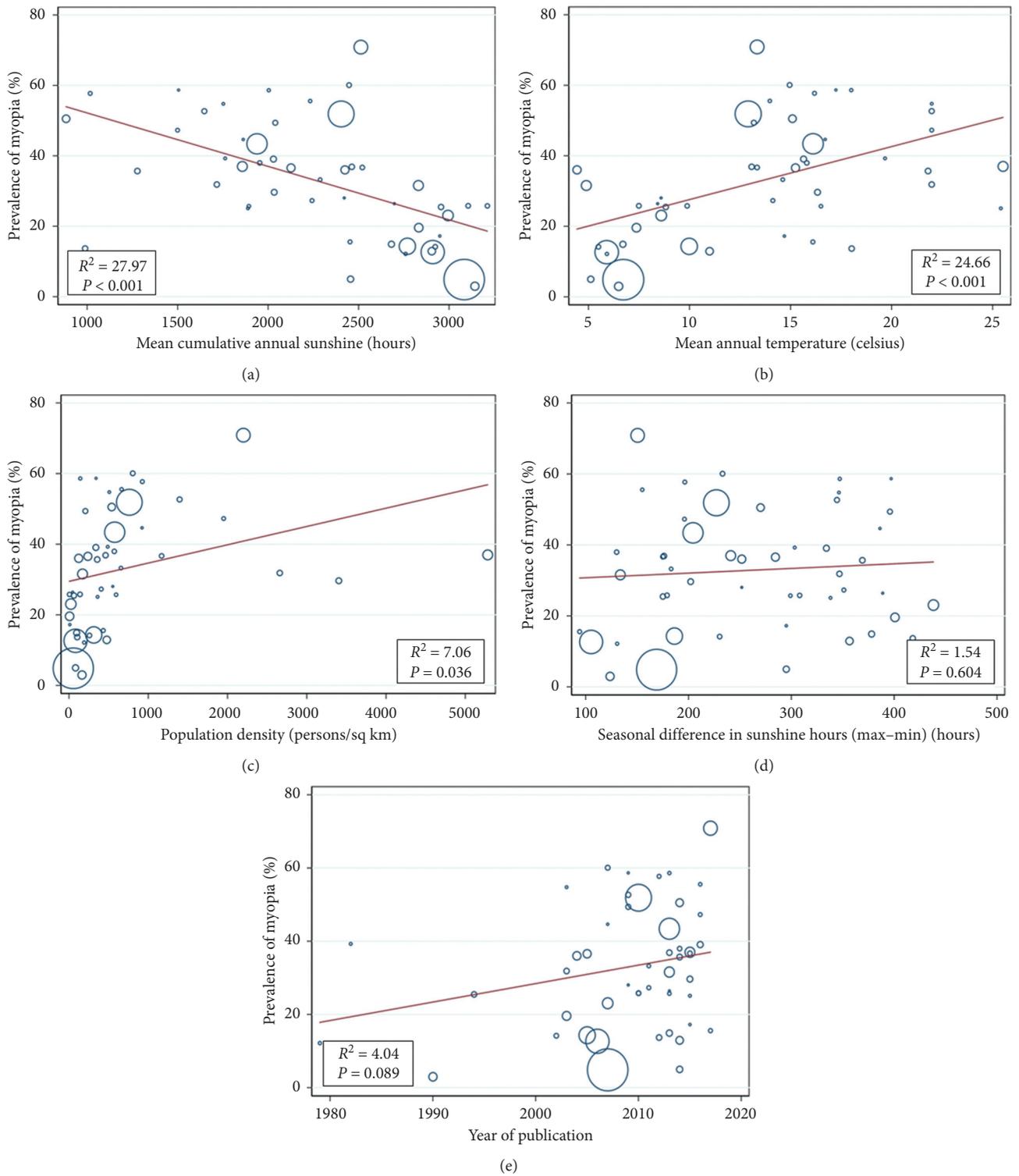


FIGURE 2: Metaregression plots showing the relationship between myopia prevalence and environmental factors: mean cumulative annual sunshine hours (a), mean annual temperature (b), population density (c), seasonal variation in sunshine hours (d), and year of publication of the paper (e) for all studies. The size of each circle is proportional to the weight (number of subjects) of the studies. The solid line indicates best fit regression line.

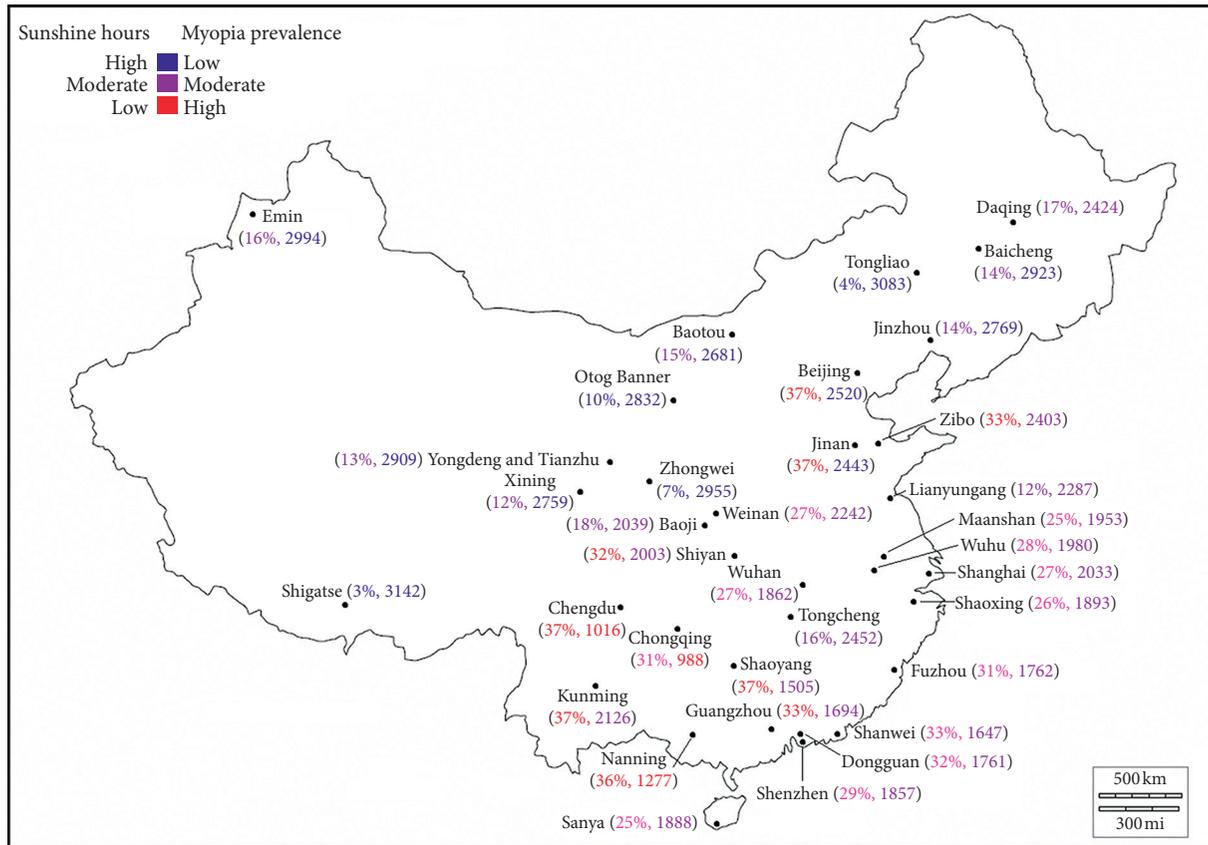


FIGURE 3: Myopia prevalence in primary schoolchildren and mean annual sunshine hours in mainland China. Blue colour font indicates regions with lower myopia prevalence and higher annual sunshine hours. Red colour font indicates regions with higher myopia prevalence and lower annual sunshine hours.

estimate the overall variation in the myopia prevalence that can be attributed to these factors. This analysis revealed that the overall proportion of variance that could be explained by these covariates in the model was 28.01% (adjusted  $R^2 = 28.01\%$ ,  $p < 0.001$ ). Annual sunshine hours was found to be a statistically significant predictor of myopia prevalence in the multivariate model ( $p = 0.049$ ), whereas the association between myopia prevalence and annual temperature ( $p = 0.379$ ) and population density ( $p = 0.562$ ) was not statistically significant. Metaregression analyses were also repeated separately for myopia prevalence in primary schoolchildren only and for secondary schoolchildren only. In each of these categories, only annual sunshine hours was a significant predictor of myopia prevalence in the multivariate model. Figure 3 shows the myopia prevalence in primary schoolchildren and mean annual sunshine hours in different cities of mainland China.

**3.6. Myopia Prevalence Estimates Based on Annual Sunshine Hours.** A second meta-analysis was performed by stratifying the regions based on a tertile split of annual sunshine hours. The regions were classified as habitually experiencing high annual sunshine hours (annual sunshine hours  $>2517.4$  hours,  $n = 17$ ), moderate (annual sunshine hours between 1995.0 and 2517.4 hours,  $n = 16$ ), and low annual sunshine hours (annual sunshine hours  $<1995.0$  hours,  $n = 16$ ). The

regions with low and moderate annual sunshine hours had a similar myopia prevalence (low annual sunshine hours: 41.00%, 95% CI 36.25–45.74 and moderate sunshine hours: 39.64%, 95% CI 31.18–48.09) that was higher than the prevalence in regions with high annual sunshine hours (18.86%, 95% CI 14.61–23.12).

**3.7. Publication Bias.** There was no significant publication bias when all the studies were included ( $p = 0.06$ ) and when only primary ( $p = 0.446$ ) and only secondary schoolchildren ( $p = 0.162$ ) were included.

## 4. Discussion

The study examined the variations in regional myopia prevalence in schoolchildren in mainland China by analysing the association between myopia prevalence and environmental factors such as sunshine hours, population density, and annual temperature. Using multivariate metaregression analyses, we found that objective records of sunshine hours are significantly associated with myopia prevalence, with higher prevalence observed in regions with lesser sunshine hours. The annual sunshine hours accounted for ~28% of the regional variation in myopia prevalence in schoolchildren of mainland China.

Our findings of a strong association between higher myopia prevalence with lower sunshine hours are in agreement with several previous studies. Based on environmental data, Daubs [95] suggested that annual hours of sunshine had a strong negative association with high myopia. Cui et al. [13] also reported an inverse association between cumulative hours of daylight and eye elongation and myopia progression in Danish children. Many population-based studies have shown that children who spend less time outdoors (or less time exposed to bright outdoor light) are at higher risk of myopia development (Li et al. 2015) [10, 16, 22–25, 96, 97]. A recent prospective study that captured objective personal light exposure also found higher axial elongation/eye growth in children with lower ambient light exposure [29].

Prospective randomised controlled trials examining the influence of interventions to increase children's outdoor activities during school hours have reported a reduction in myopia development [23, 24, 32] and a reduced myopic shift in refraction in both myopic and nonmyopic children [32]. A prospective study is underway in China that is assessing the impact of a modified classroom design that allows more outdoor light exposure on myopia development and progression [32, 98].

The biological mechanism underlying the association between myopia prevalence and sunshine hours is yet to be determined. A widely proposed hypothesis is that bright light levels stimulate retinal dopamine release [99] which in turn modulates eye growth [100]. Our finding of a significant association between greater sunshine hours and lower myopia prevalence would be consistent with this hypothesis. Studies that have investigated the role of vitamin D in myopia development have reported that while vitamin D is a biomarker for time spent outdoors, it does not appear to independently mediate the antimyopia effect of time outdoors [101]. The role of physical activity in the association between time spent outdoors and myopia development has also been widely investigated, and several studies have reported that it does not independently predict myopia prevalence [102]. Other theories propose that the spectral content of sunlight including higher ultraviolet light levels could play a role in the association [103] or that the eye is more able to focus at far distances when outdoors [8], but these hypotheses are yet to be fully tested.

Seasonal variation in sunshine hours was not significantly associated with myopia prevalence for combined studies of primary and secondary school-age children, but when the studies of primary school-age children were considered separately, there was a weak but significant positive association (predicting 13% of the variance in myopia prevalence in univariate analysis) between seasonal differences in sunshine hours and myopia prevalence. Vannas et al. [104] observed a trend toward a higher prevalence of myopia in Finnish military conscripts who originated from above the Arctic Circle (where the seasonal fluctuations are higher) compared to the rest of Finland, suggesting a higher prevalence of myopia in regions with higher seasonal variations in natural outdoor light exposure. In contrast, countries which are geographically located close

to the equator, such as Singapore, have low seasonal fluctuations in light yet have very high myopia prevalence [3]. It may be that seasonal variations in light are not a strong factor in the development of myopia or that personal light exposure patterns are more important.

Population density significantly influenced the myopia prevalence, except in analyses of only secondary schoolchildren, where it contributed to <1% of the variation in myopia prevalence in the univariate analysis. Other studies that have investigated the association between living space in urban areas and myopia prevalence have produced mixed results. Ip et al. [14] and Choi et al. [38] have reported higher myopia prevalence in children who lived in smaller, confined houses/apartments, while Zhang et al. [39] found no association between myopia prevalence and dwelling space and the proximity of other structures, after controlling for accommodative demand (due to near-work activities) in Chinese schoolchildren. A cross-sectional study by Guo et al. [105] found that rural children spent significantly greater time outdoors (nearly twice) compared to urban children in China. It is possible that the limited open space available in urban zones and the population density could potentially restrict children from spending more time outdoors, thereby limiting the bright light exposure. Multivariate regression analysis for the combined schoolchildren and primary schoolchildren groups also indicated that only annual sunshine hours was a significant risk factor. Since annual sunshine hours is a measure of the available bright sunshine (a binary measure above a threshold value) in a specific geographic location, and we have no data on personal exposure, we cannot determine from our data if the effect is related to children spending more total time outdoors or if there is a dose-related effect, where brighter daylight gives a greater antimyopia effect in a shorter time spent outdoors.

Ambient temperature was not a significant factor in the multivariate analysis which was due to a strong negative correlation (colinearity) between annual temperature and annual sunshine hours ( $r = -0.78$ ,  $p < 0.001$ ). Presumably, higher temperatures were associated with greater cloud cover that reduced the annual sunshine hours [106], although it is possible that other environmental factors such as air pollution could influence this association.

The studies included in the analysis were published between the years 1979 and 2017, and the year of publication accounted for only ~4% of the variation in myopia prevalence (and ~8% in the primary schoolchildren category). The overall weak positive trend ( $p = 0.09$ ) indicated an increase in myopia prevalence over time from 1979 to 2017, but most of the studies (45 of 49) were in a relatively narrow time band between 2002 and 2017.

When we considered the risk factors separately for the primary and secondary school-age children, we found that for the primary schoolchildren, the association between sunshine hours and myopia prevalence strengthened and accounted for ~58% of the regional variation in myopia prevalence, whereas the association weakened and contributed to ~29% in secondary schoolchildren. It may be that primary school-age children are more susceptible to the

environmental factors when they are first developing myopia and that these environmental factors become less important at older ages of onset. Since our data only consider the prevalence of myopia and not its progression, we cannot say if these environmental factors influence the progression of myopia.

Annual sunshine hours and population density factors accounted for ~35% of the regional variation in myopia prevalence in these 5- to 20-year-old Chinese children, but there are clearly other factors that are influencing the myopia prevalence. Parental myopia is an obvious factor and it contains information about not only the genetic risk but also the environmental risks associated with a shared parent-offspring lifestyle [107, 108]. Near work is often identified as a risk factor for myopia development [11, 12, 15, 109, 110]. We speculate that the time spent in near-work activities during school hours is unlikely to contribute significantly to the variation in regional myopia prevalence in this study since the school hours and academic syllabus are typically consistent in primary and secondary schools across China. However, near-work activities outside school hours are likely to vary between children in different geographic regions, for example, based on socioeconomic factors, and this is likely to modify the risk of myopia development.

A major limitation of the results reported in the metaregression analysis is that the environmental data were obtained retrospectively and represent regional averages of data rather than personal exposure. However, the large number of studies and high sample size (49 studies and a total combined sample size of 666,864 subjects) included in the analysis improves the reliability of the metaregression. By including data only from China, we ensured that the participants were probably well matched for ethnicity, although some regional variations are likely to have been present. The estimated environmental effects may not provide an accurate assessment of lifetime exposure in all of the children in a geographic location since some of the children may not have resided permanently in the same location. It should also be noted that the annual sunshine hours represent only the potential exposure to bright outdoor light, but not the actual exposure. Similarly, the urban density experienced by the children in the studies depends on their individual experience and not the geographical mean urban density. The analysis also provides an estimate of some environmental factors associated with myopia prevalence, but not the progression of myopia. A few studies ( $n=3$ ) included in the meta-analysis have reported average myopia prevalence from multiple study locations, but the regional variations in the environmental factors are unlikely to influence the study results since the locations are geographically close (within 50 km radius). However, one study reported average myopia prevalence from five locations which are geographically diverse, and the annual sunshine hours in these locations ranged from 1780 to 2491 hours. Presumably, the use of average annual sunshine hours in these cases would have minimized the impact of regional sunshine hour variation on the study results.

## 5. Conclusions

With the aim to explore the factors associated with the variation in regional myopia prevalence in mainland China, we found that myopia prevalence is higher in regions with lower sunshine hours and higher population density. Although the underlying mechanisms could not be determined, the findings support the concept that increased time spent outdoors and/or exposure to bright outdoor light levels may help to reduce or delay myopia onset.

## Data Availability

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

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

## Supplementary Materials

Supplementary Figure 1: forest plot showing the random-effect meta-analysis of the pooled myopia prevalence from the studies that involved only primary schoolchildren. Supplementary Figure 2: forest plot showing the random-effect meta-analysis of the pooled myopia prevalence from the studies that involved only secondary schoolchildren. Supplementary Table 1: PRISMA checklist. (*Supplementary Materials*)

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