

Original Investigation

Effect of Time Spent Outdoors at School on the Development of Myopia Among Children in China

A Randomized Clinical Trial

Mingguang He, MD, PhD; Fan Xiang, MD, PhD; Yangfa Zeng, MD; Jincheng Mai, BSc; Qianyun Chen, MSc; Jian Zhang, MSc; Wayne Smith, MD, PhD; Kathryn Rose, PhD; Ian G. Morgan, PhD

IMPORTANCE Myopia has reached epidemic levels in parts of East and Southeast Asia. However, there is no effective intervention to prevent the development of myopia.

OBJECTIVE To assess the efficacy of increasing time spent outdoors at school in preventing incident myopia.

DESIGN, SETTING, AND PARTICIPANTS Cluster randomized trial of children in grade 1 from 12 primary schools in Guangzhou, China, conducted between October 2010 and October 2013.

INTERVENTIONS For 6 intervention schools (n = 952 students), 1 additional 40-minute class of outdoor activities was added to each school day, and parents were encouraged to engage their children in outdoor activities after school hours, especially during weekends and holidays. Children and parents in the 6 control schools (n = 951 students) continued their usual pattern of activity.

MAIN OUTCOMES AND MEASURES The primary outcome measure was the 3-year cumulative incidence rate of myopia (defined using the Refractive Error Study in Children spherical equivalent refractive error standard of ≤ -0.5 diopters [D]) among the students without established myopia at baseline. Secondary outcome measures were changes in spherical equivalent refraction and axial length among all students, analyzed using mixed linear models and intention-to-treat principles. Data from the right eyes were used for the analysis.

RESULTS There were 952 children in the intervention group and 951 in the control group with a mean (SD) age of 6.6 (0.34) years. The cumulative incidence rate of myopia was 30.4% in the intervention group (259 incident cases among 853 eligible participants) and 39.5% (287 incident cases among 726 eligible participants) in the control group (difference of -9.1% [95% CI, -14.1% to -4.1%]; $P < .001$). There was also a significant difference in the 3-year change in spherical equivalent refraction for the intervention group (-1.42 D) compared with the control group (-1.59 D) (difference of 0.17 D [95% CI, 0.01 to 0.33 D]; $P = .04$). Elongation of axial length was not significantly different between the intervention group (0.95 mm) and the control group (0.98 mm) (difference of -0.03 mm [95% CI, -0.07 to 0.003 mm]; $P = .07$).

CONCLUSIONS AND RELEVANCE Among 6-year-old children in Guangzhou, China, the addition of 40 minutes of outdoor activity at school compared with usual activity resulted in a reduced incidence rate of myopia over the next 3 years. Further studies are needed to assess long-term follow-up of these children and the generalizability of these findings.

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Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Mingguang He, MD, PhD, Zhongshan Ophthalmic Center, Guangzhou 510060, China (mingguang_he@yahoo.com).

Myopia has reached epidemic levels in young adults in some urban areas of East and Southeast Asia.¹ In these areas, 80% to 90% of high school graduates now have myopia and approximately 20% have high myopia (defined as ≤ -6 diopters [D]).² Myopia also appears to be increasing, albeit more slowly, in populations of European and Middle Eastern origin.^{3,4} The increasing prevalence of myopia is of worldwide concern.

Myopia poses a considerable personal and societal burden because of the need for correction of refractive errors to avoid visual impairment. In addition, early-onset myopia may progress to high myopia and the need for expensive treatment for its multiple sight-threatening pathological consequences, such as myopic macular degeneration.⁵

Currently, there is no effective intervention for preventing the onset of myopia. Attempts to slow myopic progression (the progressive increase in severity of myopia throughout childhood) by using corrective lenses have had only limited success,⁶ although low-dose atropine eyedrops show promise.^{7,8}

Recent studies suggest that time spent outdoors may prevent the development of myopia.^{9,10} The protective association appears to be related to total time spent outdoors, rather than engagement in sport activities, because time spent engaged in an indoor sport activity is not associated with lower likelihood of myopia.¹⁰ However, randomized trials are required to establish causality and to provide evidence of sufficient quality to inform public policy.

The purpose of this study, the Guangzhou Outdoor Activity Longitudinal Trial, was to assess the efficacy of increasing time spent outdoors in preventing the onset of myopia in Chinese children.

Methods

Study Design

This cluster randomized, school-based trial was conducted in Guangzhou, China, to assess the efficacy of increasing time spent outdoors in preventing the development of myopia over a 3-year period. Ethics approval was obtained from the human ethics committee of the Zhongshan Ophthalmic Center and the Guangzhou Ministry of Education. The study was conducted in accordance with the tenets of the World Medical Association's Declaration of Helsinki.¹¹

Since 1987, students in all grades in 30 government-operated primary schools in Guangzhou, China, have received annual visual acuity tests as part of a health surveillance program. Schools are located over the 6 districts of Guangzhou, providing a representative sample.¹²

In early 2009, all 30 schools accepted an invitation to participate in this trial. One school was excluded due to incomplete visual acuity data. The remaining 29 schools were stratified into 6 strata based on visual acuity distribution, assessed by a histogram of students with normal visual acuity (uncorrected visual acuity in right eye $>20/25$) with school level in 2008 from grade 1 to grade 6 (eFigure in Supplement 1). Each stratum represented different patterns of myopia with age. Two schools were randomly selected from each of the 6 strata, with 1 school allocated

to the intervention and 1 school allocated to the control. Schools in the intervention and control groups were matched closely in terms of longitudinal loss of visual acuity, which correlates closely with the development of myopia in children.¹² This randomization process was performed with a simple random sampling using SAS version 9.2 (SAS Institute Inc), which generated 12 schools in 6 strata as the participating schools for the study.

Cluster randomization by school was chosen as the study design because school-based interventions can change students' behavior through mandatory changes in curriculum. Randomization by class was considered, but it is not compatible with interventions involving a parent education campaign. With this study design, masking was not feasible.

Data at baseline were gathered on children in grade 1 (ages: 6-7 years), with annual follow-up to grade 4. Students in primary schools in China generally do not change schools.

Intervention and Supervision of Implementation

Information sessions were conducted for principals and head teachers of grade 1 in participating schools. Before baseline data collection, all 12 participating schools held information seminars for parents, in which study staff answered questions and collected consent forms. Only those who gave consent were enrolled at baseline. Given the potential discomfort after undergoing cycloplegic refraction, the parents were asked for additional consent before the examination at each follow-up visit. Cycloplegic refraction was performed only on those children who had parental consent. Otherwise, cycloplegic refraction was not performed; however, other assessments, including axial length and corneal curvature, were conducted.

Increasing time spent outdoors was implemented in 2 ways. First, an additional 40-minute outdoor activity class was scheduled at the end of each school day throughout the school year in the intervention schools (which was approximately 9½ months per year, with 2½ months as school holiday). The intervention started at the beginning of September 2009. Participation in these classes was compulsory whether or not there was consent for assessment. An outdoor activity program brochure was distributed to grade 1 classes. The supervising teacher and head teacher were asked to fill in forms to report the outdoor activities (eMethods 1 in Supplement 1). To maximize compliance, study staff went to 2 of the 6 intervention schools each day to inspect the outdoor classes without prior notice. The frequency of school visits was reduced to 1 day per week during the third year of the study. Details of compliance were recorded.

The second part of the intervention was aimed at increasing the engagement of children in outdoor activities after school hours, especially during weekends and holidays. This was promoted to parents and children by providing items such as school bags, umbrellas, water bottles, and hats with outdoor activity logos. Children were rewarded for completing a diary of weekend outdoor activities and a regular newsletter was distributed to parents. Children and parents in control schools continued their usual patterns of activity.

Measurements

The eye examinations were performed at school by 1 senior optometrist, 3 ophthalmic nurses, and 1 fellowship-trained oph-

thalmologist, who were not masked to the randomization group. Field work was preceded by training sessions and pilot exercises at 1 primary school. The examination protocols were based on protocols used in the Refractive Error Study in Children (which was a multicountry, population-based study in children organized by the World Health Organization).¹³ When possible, noncontact measurements were taken.

Height and weight were measured. Visual acuity was assessed by following standard procedures using tumbling E ETDRS charts (Precision Vision).¹³ Cover and uncover tests were used to identify tropia at both near and distance.

Cycloplegia was then induced with 3 eyedrops of 1% cyclopentolate administered to each eye at 0, 5, and 20 minutes. Pupil light reflex and pupil dilation were checked after an additional 15 minutes and recorded. Full cycloplegia was assumed if the pupil dilated to 6 mm or greater and the light reflex was absent. Before dilation, axial length and corneal curvature were measured by noncontact partial-coherence laser interferometry using the IOL Master (Carl Zeiss Meditec). Three measures were taken for the right eye only.

Autorefractometry using the Topcon 8800K was then performed, with 3 measurements taken on the right eye and 3 on the left eye. The mean value of 3 valid measurements was calculated. Follow-up examinations (during 2011-2013) were the same as at baseline in 2010 and conducted by the same examiners when possible and using the same equipment. The baseline and follow-up examinations were performed during the same time of year (October to November).

Information on risk factors for myopia, including family myopic status and the child's daily activities, was collected using questionnaires (eMethods 1 and eMethods 2 in Supplement 1), with annual response rates ranging from 92.4% in 2009 to 99.2% in 2011.

Outcomes

The primary outcome of the study was the 3-year cumulative incidence rate of myopia in the intervention and control groups. Myopia was defined as a spherical equivalent refractive error (sphere +½ cylinder) of at least -0.50 D. This definition was chosen based on the Refractive Error Study in Children.¹³ Incident myopia was defined as myopia detected in children who did not have myopia at baseline.

Secondary outcomes were the changes in mean spherical equivalent and axial length over 3 years. Data for the right eyes were primarily used for analysis because refraction and biometry in the right and left eyes were highly correlated; however, sometimes data were available only for the left eye and were used for analysis. Only the children with successful cycloplegic refraction were included in the analysis for the 3-year incidence rate of myopia. In the rare cases in which the participant was classified as having myopia based on cycloplegic refraction data at both the first- and second-year visit, but was without cycloplegic refraction data at the third-year visit, the participant was classified as having incident myopia. The analysis on the changes of axial length and corneal curvature did not require successful cycloplegic refraction.

Time per day spent outdoors outside of school hours was assessed from the questionnaire on children's daily activity.

The average daily time spent outdoors during the school semester days (T_{school}) was calculated using the time spent outdoors on weekdays (T_{wd}) and on weekends (T_{we}):

$$T_{school} = (T_{wd} \times 5 + T_{we} \times 2) \div 7$$

Time spent outdoors during the weekends (T_{we}) was used as a proxy for time spent outdoors during the summer and winter holidays (3 months per school year). Therefore, the average daily time spent outdoors during 1 school year (T_{year}) was calculated as:

$$T_{year} = (T_{school} \times 9 + T_{we} \times 3) \div 12$$

Examination forms and questionnaires were reviewed for accuracy and completeness before data entry at the Zhongshan Ophthalmic Center and checked with data cleaning programs. The study protocol is provided in Supplement 2.

Statistical Analysis

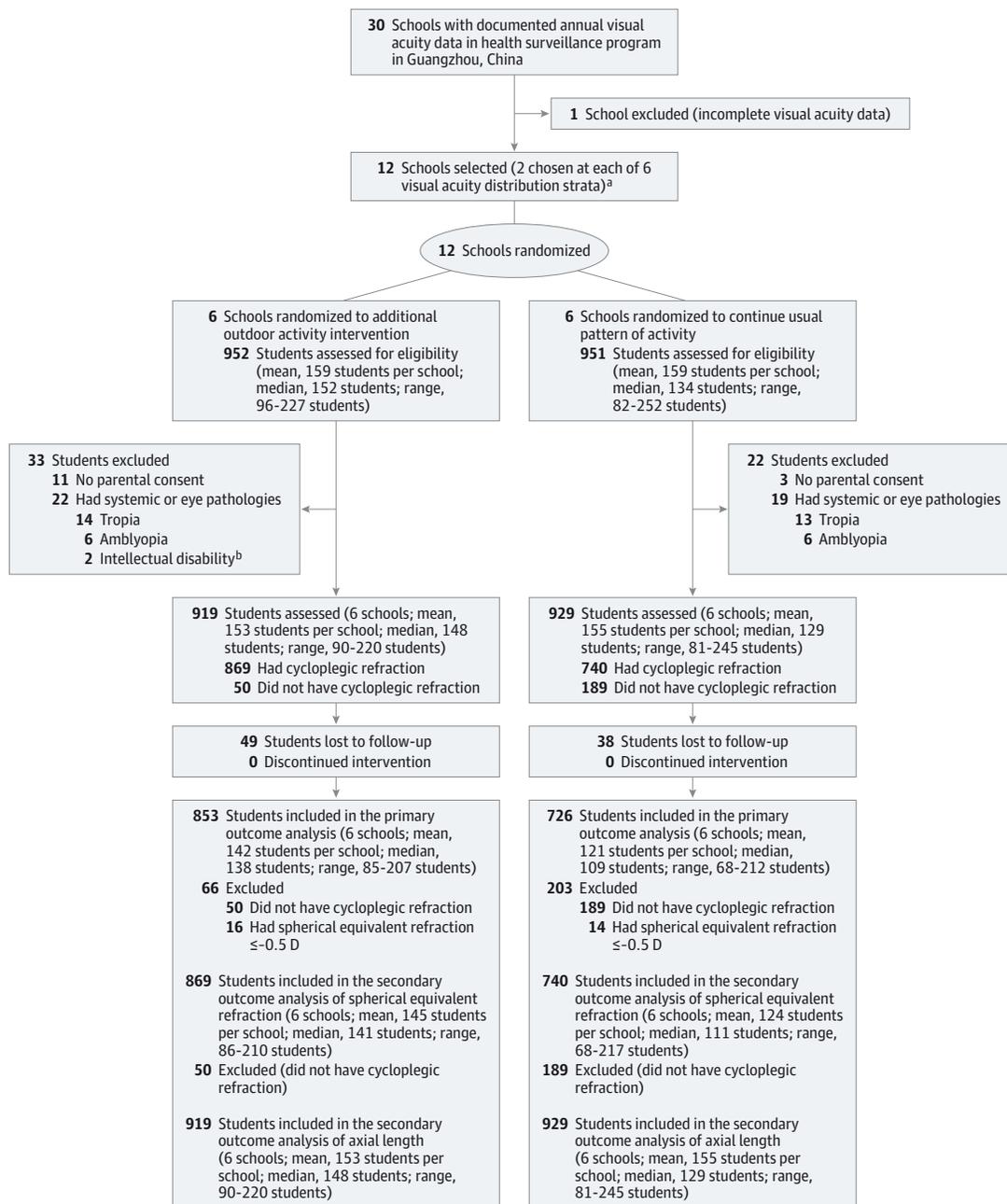
The sample size was calculated using a method that accounts for the intracluster correlation coefficient (which is the ratio of between-cluster variance to between- and within-cluster variance), the number of events, the expected effect size, and the intended power of the study. The cluster size was approximately 120 (which is the average number of students in grade 1 at each school); the rate of incident myopia was estimated to be 10% per year from grade 1 to grade 4³; the expected reduction in rate of incident myopia was set at 50%; and the intracluster correlation coefficient was assumed to be 0.02 based on a calculation from the Refractive Error Study in Children.¹³ This would require a total of 5 matched clusters, assuming a power level of 90% and a 2-sided α of .05. Further assuming participation rates of 90% and loss to follow-up of less than 5% per year led to a total of 6 matched clusters with 120 students per class.

In the descriptive analysis of baseline characteristics, the difference in spherical equivalent refraction and axial length between the intervention and control groups was assessed with standard parametric tests (t test) if data were normally distributed and nonparametric tests (Mann-Whitney test) if the data were not normally distributed.

The analyses on the primary and secondary outcomes were performed based on intent-to-treat principles. The primary outcome was the 3-year cumulative incidence rate of myopia among the students without established myopia at baseline. The students with unsuccessful cycloplegic refraction were considered as missing data. The difference in the cumulative incidence rate of myopia was calculated using exact unconditional methods based on the Farrington-Manning score statistic. Changes in spherical equivalent refraction and axial length were compared between the intervention and control groups using mixed-effects models with unstructured covariance structures after comparing other covariate structures, such as the variance component, compound symmetry, first-order autoregressive, and Toeplitz, based on the smallest Akaike information criterion and Bayesian information criterion values.

All of the model covariates were adjusted for age and sex. Treatment assignment, time, and treatment \times time interac-

Figure. Flow of Participants in the Guangzhou Outdoor Activity Longitudinal Trial



^a Subjectively stratified into 6 strata based on historic visual acuity distribution illustrated as a histogram of the percentage of students with normal vision.

^b Defined based on self-reported medical history.

tions were included as fixed effects. The cluster was considered as a random effect. Mean changes and 95% confidence intervals derived from the mixed models were calculated. Sensitivity analyses were conducted to assess alternate thresholds defining myopia (-0.75 D and -1.00 D). Post hoc regression analysis was conducted, adjusting for the presence of myopia in 1 or both parents.

For the primary outcome, a 1-sided P value was considered and the corresponding 1-sided significance level was .025.

All other P values were based on 2-sided tests ($P < .05$ considered significant). Statistical analyses were performed using Stata version 12 (StataCorp) and SAS version 9.2 (SAS Institute Inc).

Results

Twelve schools were randomized (6 to the intervention group and 6 to the control group; **Figure**). Of 1903 children

Table 1. Baseline Characteristics of Participants in the Guangzhou Outdoor Activity Longitudinal Trial

	Intervention Group (n = 919) ^a	Control Group (n = 929) ^a	P Value
Age, mean (SD), y	6.61 (0.33)	6.57 (0.32)	.01
Boys, No. (%)	489 (52.58)	509 (54.61)	.38
Height, mean (SD), cm	120.29 (0.17)	120.51 (0.16)	.36
Weight, mean (SD), kg	22.54 (0.15)	22.56 (0.14)	.93
Body mass index, mean (SD) ^b	15.48 (0.07)	15.45 (0.07)	.71
Wearing glasses, No. (%)	47 (5.11)	40 (4.31)	.41
Uncorrected visual acuity, median (IQR)	0.80 (0.80-0.80)	0.80 (0.80-1.00)	.16
Spherical equivalent refraction, mean (SD), D ^c	1.30 (0.97)	1.26 (0.81)	.42
Prevalence of myopia, No./total (%) ^c	16/869 (1.84)	14/740 (1.89)	.94
Axial length, mean (SD), mm	22.60 (0.71)	22.66 (0.70)	.05
Corneal radius of curvature, mean (SD), D	43.54 (1.64)	44.42 (1.40)	.08
Time spent outdoors outside of school hours, median (IQR), min/d	46.1 (30.00-68.04)	46.07 (30.00-67.50)	.34
Parental myopia, No. (%)			
0	376 (46.36)	273 (40.21)	
1	306 (37.73)	245 (36.08)	.001
Both	129 (15.91)	161 (23.71)	

Abbreviation: IQR, interquartile range.

^a Right eye data for students who had informed consent and completed baseline examination.

^b Calculated as weight in kilograms divided by height in meters squared.

^c Right eye data for children with cycloplegic refraction only.

Table 2. Refractive and Biometric Outcomes at 3-Year Follow-up of the Guangzhou Outdoor Activity Longitudinal Trial^a

	Intervention Group	Control Group	Difference (95% CI)	P Value
Cumulative incidence of myopia	259/853 (30.4) ^b	287/726 (39.5) ^b	-9.1 (-14.1 to -4.1) ^c	<.001
Cumulative change, mean (95% CI) ^d				
Spherical equivalent refraction, D	-1.42 (-1.58 to -1.27)	-1.59 (-1.76 to -1.43)	0.17 (0.01 to 0.33)	.04
Axial length, mm	0.95 (0.91 to 1.00)	0.98 (0.94 to 1.03)	-0.03 (-0.07 to 0.003)	.07

^a The calculation on all outcomes was based on right eye data only.

^b Cumulative number of cases of incident myopia/number of analyzed participants (%).

^c Expressed as a percentage and calculated using exact unconditional methods based on the Farrington-Manning score statistic.

^d Derived from mixed models.

(952 in the intervention group and 951 in the control group), 87 (4.6%) withdrew during the 3 years the trial was conducted (49 [5.1%] in the intervention group and 38 [4.0%] in the control group), primarily due to the children changing schools. Only the children with cycloplegic refraction were included in the analysis on incident myopia. Parental refusal for cycloplegic refraction was the reason for the majority of children who did not undergo the examination. The reasons cycloplegic refraction was not performed at each visit appear in eTable 1 in Supplement 1. The baseline characteristics of students in the intervention and control groups by consent or refusal for cycloplegic refraction appear in eTable 2 in Supplement 1; there were no statistically significant differences.

School visit compliance records indicated that among 734 school visits, successful implementation of the outdoor class were observed in 613 (83.5%). Among 121 visits with unsuccessful implementation, 64 (52.9%) were due to inclement weather, such as rain or extremely low temperatures during

the winter months. Detailed compliance data are summarized in eTable 3 in Supplement 1.

The characteristics of the students in the intervention and control groups at baseline were similar (Table 1). The mean (SD) age of the children was 6.57 (0.32) years in the intervention schools and 6.61 (0.33) years in the control schools ($P = .01$). There were no significant baseline differences between the intervention and control groups in sex, prevalence of myopia, or mean spherical equivalent refraction. The mean (SD) axial length was 22.60 (0.71) mm in the intervention schools and 22.66 (0.70) mm in the control schools ($P = .05$). The proportion of parents with myopia was lower in the intervention group (53.6%) compared with the control group (59.8%; $P < .001$).

The primary and secondary outcome measures in the 2 groups at the 3-year follow-up appear in Table 2. The 3-year cumulative incidence rate of myopia was 30.4% (259 incident cases among 853 eligible participants at baseline) in the intervention group and 39.5% (287 incident cases

Table 3. Time Spent Outdoors Outside of School Hours at Baseline and Follow-up Visits in the Guangzhou Outdoor Activity Longitudinal Trial

Time	Median (IQR), min/d		P Value ^a
	Intervention Group	Control Group	
Baseline	46.10 (30.00-68.04)	46.07 (30.00-67.50)	.34
Follow-up, y			
1	68.04 (47.41-97.86)	66.42 (46.07-94.29)	.21
2	61.07 (35.89-88.93)	60.00 (35.36-88.39)	.48
3	60.54 (33.21-88.39)	57.32 (33.21-88.93)	.82

Abbreviation: IQR, interquartile range.

^a Calculated using the Wilcoxon rank sum test.

among 726 eligible participants at baseline) in the control group (difference of -9.1% [95% CI, -14.1% to -4.1%]). The intracluster correlation coefficient was 0.023 for the primary outcome, 0.009 for spherical equivalent refraction, and 0.009 for axial length.

In the primary outcome analyses in which the threshold for defining myopia was changed to -0.75 D, the cumulative incidence rate of myopia was 24.2% in the intervention group and 31.1% in the control group (difference of -6.8% , which remained statistically significant; $P = .003$). In the analyses in which the threshold for defining myopia was -1.0 D, the cumulative incidence rate of myopia was 20.4% in the intervention group and 25.5% in the control group (difference of -5.1% ; $P = .02$; eTable 4 in Supplement 1). In a post hoc logistic regression model adjusting for parental myopia, the odds ratio for 3-year incidence rate of myopia in the intervention group compared with the control group was 0.73 (95% CI, 0.57 to 0.92; $P = .01$).

Cumulative change in spherical equivalent refraction (myopic shift) after 3 years was significantly less in the intervention group than in the control group (mean of -1.42 D vs -1.59 D, respectively; difference of 0.17 D [95% CI, 0.01 D to 0.33 D]; $P = .04$). Cumulative axial elongation was not significantly different.

In each year of the trial, children in the 2 groups reported similar amounts of time spent outdoors outside of school hours (Table 3).

Discussion

Increasing the amount of time that children spent outdoors at school resulted in statistically significant reductions in incident myopia and myopic shift in refraction over 3 years. Two other trials of shorter duration and with smaller sample sizes have reported similar results. A study of 571 students aged 7 to 11 years in Taiwan reported a 1-year reduction in the incidence rate of myopia of 8.4% in the intervention group vs 17.7% in the control group.¹⁴ A 1-year school-based trial of 80 students aged 7 to 11 years in Changsha, China, reported a reduction in myopia progression.¹⁵

Our study achieved an absolute difference of 9.1% in the incidence rate of myopia, representing a 23% relative reduction in incident myopia after 3 years, which was less than the anticipated reduction. However, this is clinically important because small children who develop myopia early are most likely to progress to high myopia (≤ -6 D), which increases the risk

of pathological myopia.¹⁶ Thus a delay in the onset of myopia in young children, who tend to have a higher rate of progression,¹⁷ could provide disproportionate long-term eye health benefits.

The education campaign directed at parents in the intervention group appears to have had no effect on time spent outdoors outside school hours (Table 3). Thus, the intervention length was approximately 40 minutes per day of increased time spent outdoors for 5 school days per week during school terms, which in China lasts 9½ months. Monitoring suggested that compliance was high in the intervention schools.

The school-based trial in Taiwan¹⁴ reported a reduction in incident myopia of approximately 50% in 1 year, but student behavior was not closely monitored. The intervention involved locking the children out of their classrooms during school recesses, possibly delivering as much as 80 minutes spent outdoors per day on school days. This is more than what was achieved in our trial, and appears to have produced a greater protective effect, suggesting a dose-response relationship.

The effect of these interventions should be compared with the effect sizes expected from epidemiological data in observational studies. In the Orinda Longitudinal Study of Myopia,¹⁰ spending 10 to 14 hours per week “engaging in outdoor and sport activities” compared with 0 to 5 hours per week was associated with approximately half the risk of developing myopia. If “engaging in outdoor and sport activities” is equivalent to time spent outdoors, approximately 90 minutes per day of additional time spent outdoors was associated with a 50% lower risk of developing myopia. In the Sydney Myopia Study 5-year follow-up,¹⁸ approximately 1 additional hour per day of time spent outdoors was associated with a reduction in the incidence rate of myopia from 23.3% to 8.3%. Thus, the magnitude of the effects in the randomized trials is broadly consistent with existing epidemiological data.

The limitations of this study should be noted. First, sample size estimation was based on a 50% reduction of incident myopia; however, we did not observe this amount of reduction. Given that the actual sample size was greater than planned, the results were nevertheless statistically significant. Second, incomplete participation due to refusal of cycloplegic refraction was more frequent in the control group, which could have biased the results; however, the data in eTable 2 in Supplement 1 suggest that participants who received cycloplegic refractions and those who did not

were generally similar. The effect on the primary outcome is also supported by the consistent findings for one of the secondary outcomes. Third, due to the nature of randomization by schools, it was not possible to mask the examiners, which may have led to observational bias. However, the primary and secondary outcomes relied on objective measurement with devices that automatically generate results, making observation bias likely minimal.

Conclusions

Among 6-year-old children in Guangzhou, China, the addition of 40 minutes of outdoor activity at school compared with usual activity resulted in a reduced incidence rate of myopia over the next 3 years. Further studies are needed to assess long-term follow-up of these children and the generalizability of these findings.

ARTICLE INFORMATION

Author Affiliations: State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China (He, Xiang, Zeng, Chen, Zhang, Morgan); Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, East Melbourne (He); National Centre for Epidemiology and Population Health, Australian National University, Canberra (Xiang); Guangzhou Student's Health Care Institute of the Guangdong City Department of Education, Guangzhou, China (Mai); Environmental Health Branch, NSW Department of Health, Sydney, Australia (Smith); Discipline of Orthoptics, Faculty of Health Sciences, University of Sydney, Sydney, Australia (Rose); Discipline of Orthoptics, Graduate School of Health, University of Technology Sydney, Sydney, Australia (Rose); Research School of Biology, Australian National University, Canberra (Morgan).

Author Contributions: Dr He had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: He, Xiang, Smith, Rose, Morgan.

Acquisition, analysis, or interpretation of data: He, Xiang, Zeng, Mai, Chen, Zhang, Smith.

Drafting of the manuscript: He, Xiang, Morgan.
Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Xiang, Zhang, Smith, Morgan.
Obtained funding: He.

Administrative, technical, or material support: He, Xiang, Zeng, Mai, Chen, Morgan.

Study supervision: He, Morgan.

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