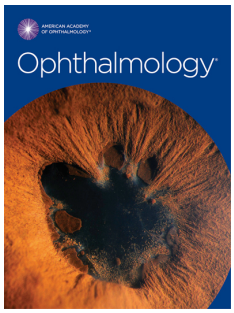

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Time Outdoors in Reducing Myopia: A School-Based Cluster Randomized Trial with Objective Monitoring of Outdoor time and Light Intensity

Running head: Time outdoors to reduce Myopia

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Abbreviations and Acronyms:

SE = spherical equivalent; AL = axial length; IRR = incidence risk ratio; CI = confidence interval; MMD = myopic macular degeneration; STORM = Shanghai Time Outside to Reduce Myopia trial; lux = luminance; UV = ultraviolet; SVM = support vector machine.

Abstract

Purpose： To evaluate the efficacy of time outdoors per school day over 2 years on myopia onset and shift.

Design： A prospective, cluster-randomized, examiner-masked, three-arm trial.

Participants： A total of 6295 students aged 6 to 9 years from 24 primary schools in Shanghai, China, stratified and randomized by school in a 1:1:1 ratio to control (n=2037), test I (n=2329), or test II (n=1929) group.

Methods： An additional 40 or 80-minutes of outdoor time was allocated to each school day for test I and II groups. Children in the control group continued their habitual outdoor time. Objective monitoring of outdoor and indoor time and light intensity each day was measured with a wrist-worn wearable during the second-year follow-up.

Main Outcome Measures： The 2-year cumulative incidence of myopia (defined as cycloplegic spherical equivalent [SE] of ≤-0.5 diopters[D] at the right eye) among the students without myopia at baseline and changes in SE and axial length (AL) after 2 years.

Results： The unadjusted 2-year cumulative incidence of myopia was 24.9%, 20.6%, and 23.8% for control, test I, and II groups. The adjusted incidence decreased by 16% [Incidence Risk Ratio (IRR)=0.84, 95%CI: 0.72~0.99; *P* =0.035] in test I and 11% (IRR=0.89, 95%CI: 0.79~0.99; *P* =0.041) in test II when compared with the control group. The test groups showed less myopic shift and axial elongation compared with the control group (test I: -0.84D and 0.55mm, test II: -0.91D and 0.57mm, control: -1.04D and 0.65mm). There was no significant difference in the adjusted incidence of myopia and myopic shift between the two test groups. The test groups had similar outdoor time and light intensity (test I: 127±30 minutes/day and 3557±970 lux/minute; test II: 127±26 minutes/day and 3662±803 lux/minute), but significantly more outdoor time and higher light intensity compared with the control group (106±27 minutes/day and 2984±806 lux/minute). Daily outdoor time of 120~150 minutes at 5000 lux/minutes or cumulative outdoor light intensity of 600,000~750,000 lux significantly reduced the IRR by 17%~31%.

Conclusions： Increasing outdoor time reduced the risk of myopia onset and myopic shifts, especially in nonmyopic children. The protective effect of outdoor time was related to the duration of exposure as well as light intensity. The dose-response effect

between test I and test II was not observed probably due to insufficient outdoor time achieved in the test groups, which suggests that proper monitoring on the compliance on outdoor intervention is critical if one wants to see the protective effect.

Key Words: Outdoor, Myopia, Cluster Randomized Trial, Children, School health

Trial Registration ClinicalTrials.gov Identifier: NCT02980445

Introduction

Myopia, a condition affecting nearly a quarter of the world's population, has been projected to double in prevalence by the year 2050.[1] The health and economic burden both to the individual and the society is substantial.[2,3] In many East Asian countries including China, there is a trend of an early onset of myopia in childhood fueled in part by educational demands, and more than half of school-aged students are affected, with around 80% myopic by the end of schooling.[4-7] Myopia shift in early years is more rapid and naturally longer,[8,9] thus an early onset increases the risk of high myopia and sight-threatening complications in later life such as myopic macular degeneration (MMD).[10] It has been projected that MMD could lead to 55.7 million people suffering from irreversible visual impairment and blindness globally in 2050.[11] Therefore, it is of importance to postpone myopia onset and slow myopia progression.

Prior evidence from controlled trials and systematic reviews has demonstrated the effectiveness of increased outdoor time in reducing the risk of myopia onset.[12-15] However, there remain several gaps in our understanding of the best and most feasible strategy to implement increased outdoor time for myopia prevention and control. Firstly, there was a lack of objective monitoring of outdoor exposure, thus the exact dose-response relationship and the threshold of its effect on myopia prevention have not been determined. Secondly, research indicated that the protective effect of outdoor exposure varied with light intensity.[12] Nevertheless, the effects of light intensity and their interrelations with outdoor time have not been clarified. Additionally, the effect of outdoor exposure on the myopia shift in already myopic individuals remains inconclusive. In addition, the optimal duration and light intensity of outdoor activities

remain unknown. These gaps impede the development of effective and practical intervention strategies.

Therefore, we aimed to evaluate the dose-response efficacy of increasing time outdoors on myopia onset and myopia shift in a two-year prospective, cluster-randomized, examiner-masked, and three-arm trial. A wrist-worn wearable light sensor was used to objectively monitor time outdoors and light intensity and investigate the relationship between outdoor exposure and myopia.

Methods

Study Design

The Shanghai Time Outside to Reduce Myopia trial (STORM) study is a prospective, cluster-randomized, examiner-masked, three-arm school-based trial conducted from October 2016 to December 2018 in Shanghai, China. A detailed study protocol and methodology were previously reported.[16] Briefly, this trial recruited from a possible 940 eligible public primary schools across the 16 districts of Shanghai, a region of 6340 square kilometers with mostly similar climatic conditions. The classroom structure, curriculum, and recess time were standard across schools following the standards developed by controlled the Shanghai Education Committee. Eight of 16 districts were randomly selected based on the location and socioeconomic status, thereafter, three public primary schools with similar prevalence of myopia (cycloplegic spherical equivalent [SE] in right eye $\leqslant$ -0.50 D)[17] were chosen from each of the eight districts and randomly assigned to one of the control, the test I, or the test II group at an allocation ratio of 1:1:1. This randomization process was performed using a simple random sampling package in SAS version 9.3 (SAS Institute, Cary, NC, USA).

School-based cluster randomization was chosen for the present trial because the intervention required mandatory changes in curriculum and school activities at the school level. Because of the school-based design, children were aware of the study allocation, however the outcome examiners, including technicians, optometrists, and statisticians were masked to the allocations.

The trial was approved by the Shanghai General Hospital Ethics Committee (No. 2016KY138) and adhered to the tenets of the Declaration of Helsinki. Written informed consent for each child was obtained from a parent/carer. This trial is registered with ClinicalTrials.gov, identifier: NCT02980445.

Participants

From each of the selected schools, all students from grades I and II (aged 6 to 9 yrs) were recruited and allocated to their assigned group. Students with strabismus or amblyopia, using any myopia control treatment strategies (including but not limited to atropine, orthokeratology lens), or those who refused cycloplegia were excluded. Included children and those excluded children totally and stratified by groups were comparable in terms of demographic and other factors.

Intervention

Increasing time outdoors was implemented at the school level. While children in the control group continued with their usual outdoor activities, children in the test I group had an additional outdoor time of 40-minute per school day (scheduled either during the mid-day break or at the end of school day) and children in the test II group had additional 80-minute outdoor time per school day delivered in 2 ways: a) 40-minute outdoor time similar to test I and b) another 40-minute over 5 recesses per school day. To ensure delivery and implementation of the outdoor time, we sought approval and support from Shanghai Education Bureau and Shanghai Health Bureau who issued an official statement inviting the schools and eye health departments to participate in and support the program. Intervention implementation was supervised at various levels (school, district, municipal, etc.), and information including content of the activities, attendance rate, and reasons for non-attendance was reported using a web-based application (APP). Reported information included the implementation of outdoor sessions, attendance rate, the content of the activities, and reasons for non-attendance. The intervention compliance was monitored and reported by an independent investigator in the research team. A wearable wrist-watch light sensor[18] was assigned to children to objectively collect the outdoor time and light intensity, which could serve as another supervision tool for intervention compliance. Both the questionnaire and

smart wrist-worn wearable data were analyzed immediately to improve compliance by providing feedback to each level (districts, schools, parents, and children, etc.).

Data collection

Examinations were conducted at the school by trained physicians included: visual acuity (retro-illuminated ETDRS chart, Guangzhou Xieyi Weishikang, Guangzhou, China,), slit-lamp examination (66 Vision Tech, Suzhou, China), intraocular pressure check (NT-1000; Nidek, Tokyo, Japan), cycloplegic autorefraction (KR-8900, Topcon, Tokyo, Japan) and axial length (AL) measurements (IOL Master, Carl Zeiss Meditec, Germany). AL was measured three times for each eye, and if the difference between any two measurements was greater than 0.05 mm, the process was repeated until the difference was below this value. Cycloplegia was induced with two (three if cycloplegia was insufficient after two) drops of 1% cyclopentolate (Cyclogyl; Alcon, Fort Worth, TX, USA) five minutes apart and refractive error assessment was conducted forty minutes later when pupils were larger than 6 mm with no light reflex. All examinations at baseline and annual follow-up visits were performed between November and December using the same protocol and equipment throughout. Investigators and examiners at each school involved in the trial were trained and certified prior to the trial commencement.

At baseline and each follow-up visit, parents/carers completed an online questionnaire providing basic information (age, parental myopia, etc.), out-of-school time spent outdoors, visual environment and activities, and myopia treatment if any.

At the end of the first-year, all included children received a smart wrist-mounted wearable device[18] and were required to wear it every day from 7:00 a.m. until 8:00 p.m. throughout the second year of the trial. The wearable was equipped with a light sensor, a global positioning system receiver module, and a pedometer. The light sensor sampled luminance (lux) and ultraviolet (UV) intensity at 20-second intervals. Data collected from the wearable were time (year/month/day/00:00:00), luminance, UV intensity, count of steps, weather, and wearing status. All data were automatically uploaded to a cloud-based server. The accuracy of the wearable device for time spent

outdoors and indoors, scenes involving sunny and cloudy days were evaluated against subjective records for adult participants, with an accuracy of 92.4%.[18]

Outcomes

The primary outcome was the 2-year cumulative myopia incidence. Secondary outcomes were the changes in mean SE and AL over two years. SE was defined as a sphere plus half-cylinder. Myopia was defined as SE ≤ -0.50 D. Incident myopia was defined as myopia development in children who were non-myopic at baseline. Hyperopia was defined as SE ≥+2.00 D, while emmetropia was defined as -0.50 D < SE ≤+0.75 D. The difference in SE and AL between the 2 year and baseline visits for both myopic and non-myopic children was calculated.

Statistical analysis

The sample size was calculated based on the cluster-randomized design that accounted for the intracluster correlation coefficient, the expected effect size, the power of the study, and the cluster size. The intracluster correlation coefficient was set at 0.015 (based on data from a refractive error study in children);[19] the cluster size was 300 (average number of grade I and grade II students in each school in Shanghai); the rate of incident myopia per year was 16%;[20-21] the expected reduction in the incident myopia was set at 33%.[15] A total of six matched clusters was required assuming a power of 85%, and a two-sided α of 0.05. Further considering a participation rate of 90%, loss to follow up of 10% per year, and exclusion rate of 5%, finally, eight matched clusters (each cluster including one control, test I and II) with 300 children per cluster were recruited .[17]

Compliance was summarized at the school level and computed as a percentage of the number of school days when the outdoor intervention was implemented. Noon break duration was calculated for each school based on the school timetable.

The efficacy analysis was performed at the individual level. Only right eye data were analyzed. Only children with full cycloplegia were included in the analysis of the myopia onset and myopic shift. The 2-year cumulative myopia incidence included those who became myopic either at the 1 or 2-year visits, while non-incident myopes were

non-myopic throughout the trial. Those who were non-myopic at baseline and 12-month visits but discontinued before the 24-month visit were considered as missing data.

Means and standard deviations were applied for continuous variables with normal distribution, medians with quantiles for continuous variables with skewed distribution, and frequencies with proportions for categorical data. The incidence between groups was compared with modified Poisson regression using the Generalized Estimating Equation (GEE) model with log link function and exchangeable correlation structure and robust sandwich estimator applied to account for the clustering effect. Baseline age, sex, parental myopia, refractive status, compliance, and duration of noon-break were included as confounders. Risk of myopia incidence in the test versus control groups was calculated using incidence risk ratio (IRR) and 95% confidence interval (CI). IRR is the cumulative incidence in the intervention group divided by the cumulative incidence in the control group. To ensure consistency of results, hazard ratios were computed using Cox proportional hazard regression model accounting for time to event.

Linear mixed-effects models were used to determine differences in the changes of SE and AL among groups after accounting for schools as random effects and adjusting for confounding factors of baseline age, sex, parental myopia, refractive status, compliance and duration of noon-break. Data of myopes and non-myopes that attended baseline and 24-month visits were used to fit these models.

A machine-learning based support vector machine model (SVM) classified data generated every 20 seconds by the wearable as either “outdoor” or “indoor” and summarized the time outdoor and indoor in minutes per day, [18] light intensity as lux per outdoor and indoor minute as well as cumulative outdoor and indoor lux per day for each participant. Indoor and outdoor time, as well as indoor and outdoor light intensity, were plotted for each day and compared between study groups using linear mixed models. The associations of outdoor time, outdoor light intensity, and cumulative outdoor lux per day with myopia incidence were analyzed using modified Poisson regression using GEE and incorporating confounding factors and clustering effects. We

also estimated the outdoor time, outdoor light intensity, and cumulative outdoor lux required to achieve various levels of efficacy for reducing myopia incidence. Statistical analysis was performed using SAS 9.3 (SAS Institute, Cary, NC, USA) and R3.2.0 (Vienna, Austria). Statistical significance was set at 5%.

Results

Participant characteristics

Of the 6967 screened participants, 6295 participants (2037, 2329, and 1929 from control, test I and II, respectively) were enrolled. At baseline, 429 (6.8%) were myopes, and 5866 were non-myopes. Baseline demographic data such as age, sex, out-of-school time spent outdoors, time spent near work, SE, AL, and myopia prevalence were comparable between groups and published previously.[16]

Figure 1 outlines the participant flow through the trial. A total of 1228 (19.5%) children withdrew over the two years [429 (34.9%], 451 (36.7%), 348 (28.3%) in the group of control, test I, test II, respectively], mainly due to refusal to accept cycloplegia [354 (28.8%)], absent [44 (3.6%)], and transferred schools [401 (32.7%)]. The rate of loss to follow-up was comparable among three groups (control: 21.1%; test I:19.4%; test II: 18.0%; P=0.140). Baseline characteristics of children who withdrew from the trial and those who completed the trial were similar, except for the myopia prevalence (9.5% versus 6.3%; P=0.014). A total of 5067 and 5340 participants were eligible for the 2-year cumulative incidence and progression analysis, respectively. Implementation of outdoor time was achieved for 84.6% and 88.0% of the school days for test I and II groups respectively.

Myopia incidence

The 2-year unadjusted cumulative myopia incidence was 24.9% (401/1608), 20.6% (387/1878), and 23.8% (376/1581) for the control, the test I and the test II groups. The difference between test I and the control group was -4.3% (95%CI -7.1%, -1.5%), and between test II and the control group was -1.1% (95%CI -4.1%, 1.9%; Table 1). After adjusting for baseline age, sex, parental myopia, refractive status, compliance, and duration of noon-break, the adjusted incidence decreased by 16% (incidence risk ratio

[IRR]=0.84, 95%CI: 0.72-0.99; *P*=0.035) in test I and 11% in test II (IRR=0.89, 95%CI: 0.79-0.99; *P*=0.041) when compared with the control group (Table 2). Similar IRR was observed between the two test groups (*P*=0.428). Longer noon-break duration at school was significantly associated with reduced risks of myopia onset (IRR=0.79, 95%CI: 0.67-0.92; *P*=0.003). Similarly, reduced hazard ratios were observed in both test groups when compared to the control group (Cox model over 2 years, test I: 0.81, 95%CI: 0.68-0.96, *P*=0.016; test II: 0.86, 95%CI: 0.73-1.01, *P*=0.066). The risk of myopia incidence was similar between tests I and II (*P*=0.522).

Change in SE and AL

Cumulative changes in SE over 2 years were not significantly different among three groups (control: -0.98±0.76 D; test I: -0.84±0.77 D; test II: -0.93±0.77 D; *P*=0.132; Table 1), while the cumulative changes in AL after 2 years were less in the test groups (test I: 0.55±0.33 mm; test II: 0.58±0.33 mm) than in the control group (0.62±0.33 mm; *P*=0.056; Table 1). Similarly, after adjusting for confounding factors, the adjusted change in SE was -1.04D (95% CI: -0.91~ -1.17D) in the control group, which was not significantly different from the two test groups (test I: -0.84 D, 95% CI: -0.72 - -0.96 D; test II: -0.91 D, 95% CI: -0.79D ~ -1.03D; *P*=0.131). Adjusted change in AL in the control group (0.65mm, 95% CI: 0.60 to 0.70 mm) was greater when compared to the two test groups (test I: 0.55 mm, 95% CI: 0.55 to 0.60 mm; test II: 0.57 mm, 95% CI: 0.52 to 0.62mm; *P*=0.044; Table 1).

Objective measurement of outdoor exposure

The wearable data for outdoor time (minutes) and light intensity (lux/outdoor minute) are summarized in Figure 2a to 2b. Overall, the study cohort spent an average of 120±30 minutes (2.0±0.5 hours) outdoors and 492±0.9 minutes (8.2±0.5 hours) indoors. The mean outdoor time was 106±27 mins/day, 127±30 mins/day, and 127±26 mins/day for the control, test I, and II groups, respectively (*P*=0.005). No differences existed between test I and II groups in terms of the mean outdoor time (*P*=0.430). Mean outdoor light intensity was greater in test I (3,557±970 lux/outdoor minute) and test II groups (3,662±803 lux/outdoor minute) compared to the control group (2,984±806 lux/outdoor minute; *P*=0.027), while similar outdoor light intensity was observed between the two test groups (*P*=0.369). The mean cumulative outdoor light exposure per day was

375,000±150,000 outdoor lux/day for the control group and 536,000±228,000 and 539,000±167,000 outdoor lux/day for test I and II respectively (*P*=0.069).

Association of outdoor exposure with myopia incidence and shift in SE and AL

Noncompliance was observed in the test groups. Therefore, we further pooled all participants together and performed a post-hoc analysis to investigate the relationship between outdoor exposure and myopia onset and myopic shifts in refractive error. Figure 3 presented the second-year myopia incidence by indoor and outdoor light intensity and outdoor time. There was no variation in myopia incidence by indoor light intensity; in comparison, a reduction in myopia incidence was observed with the increasing level of outdoor light intensity and increasing outdoor time. Analysis of individual time and light intensity variables showed that increasing time outdoors significantly decreased the risk of incident myopia, with an 18% reduction in IRR for every 60 outdoor minutes per day (Poisson regression model IRR: 0.82, 95%CI: 0.68-0.98; *P*=0.031). A cumulative of 300,000 lux per day reduced the risk of myopia onset by 20% (IRR: 0.80, 95%CI: 0.71-0.90; *P*<0.001) compared to no outdoor exposure. In comparison, myopia incidence was not associated with either time indoors (IRR: 1.04, 95%CI: 0.96-1.12; *P*=0.349) or indoor light intensity (IRR: 1.00, 95%CI: 0.99-1.00; *P*=0.746).

The second-year myopia shift for myopes and non-myopes was plotted by outdoor time (Figure 4) and demonstrated a reduced shift in SE and AL with increasing outdoor time. Increasing cumulative outdoor lux per day was also associated with a reduced myopic shift in SE and AL (outdoor exposure of 300,000 lux per day: SE: β=0.036 D; *P*=0.020; AL: β=-0.021 mm; *P*=0.001). Further, the protective effects of outdoor time on myopic shift in SE and AL were observed only in non-myopes (*P*=0.023 and 0.002 for SE and AL) but not in those who were already myopic (*P*=0.410 and 0.335, respectively). In comparing those already myopic to non-myopes, a difference in outdoor exposure was observed (121±28 mins/day vs 129±29 mins/day, a difference of 8 mins/day, *P*<0.001).

Pooled data of all participants together indicated that cumulative outdoor lux of 10000 per day reduced the risk of myopia onset (β= -0.007 for every 10,000 lux/day, IRR: 0.993, 95%CI: 0.989-0.996; *P*<0.001) compared to no outdoor exposure. The observed

cumulative outdoor lux difference of approximately 163,000 lux between the test groups and the control group (374,000 outdoor lux/day in the control group versus 536,000 and 539,000 outdoor lux/day in test I and II) equated to a 12% reduction in IRR for incident myopia when compared to control group. As shown in Table 3, we performed a simulation model and found that a 17%-31% reduction in myopia incidence would require 600,000~750,000 cumulative outdoor lux/day or 120-150 outdoor minutes at 5000 lux/min.

Discussion

In this cluster-randomized intervention trial, encouraging additional outdoor exposure in schoolchildren in test groups effectively reduced the risks of myopia onset. No differences in incident myopia were found between test I and test II, but this was not surprising given that the measured outdoor exposures were similar despite the different targets. Increasing outdoor exposure at school prevented myopic changes in non-myopic children, but not in children who already had myopia. Although this is consistent with other epidemiological evidence,[14] the lack of protective effect in pre-existing myopes is puzzling. Our results indicated that pre-existing myopes spent less time outdoors compared to non-myopes. Although this result might be suggestive of behavioural differences between myopes and non-myopes, the sample size for existing myopes was small to make any reasonable inference. The long-term objective monitoring of outdoor exposure including outdoor time and light intensity in the present trial lent further evidence on effects of outdoor for myopia control and prevention by providing greater insights about outdoor time and light intensity.

The present trial found increasing outdoor time effectively decreased the risk of myopia onset. Prior to this trial, outdoor exposure was already known to have protective effects on myopia development.[12,13,15] A meta-analysis confirmed the strong association between time outdoors and risk of the onset of myopia.[14] In previous studies, Wu et al found that increasing outdoor time during recess (approximately 80 mins/day) could reduce myopia incidence by 50% over one year (Wu et al 2013: 8.41% vs. 17.65%; Wu et al 2018: 14.47% vs. 17.40%),[12,13] while He et al found a relative decline of 23% over

3 years with the addition of 40 minutes of outdoor activity per day at school(30.4% vs 39.5%).[15] Our incidence reduction after a two-year intervention was 11%-16%, which was close to the effect observed in the study by He et al, with an increased time outdoors of around 20 minutes.[15] Of note, baseline age, sex, parental myopia, refractive status, compliance, and duration of noon-break were adjusted in final models to balance the baseline characteristics among groups.

The current study also showed more outdoor time slowed myopic changes in non-myopic children, but not in myopic children, which was consistent with previous epidemiological studies.[22,23] In contrast, Wu et al found the protective effects of outdoor time on myopic changes were noted in myopic children. [12,13] However, seasonal effects on progression, and acceleration of progression in covid lockdowns, suggested that progression could be regulated in some ways by environmental exposures.[24,25]

Despite test II being prescribed with greater outdoor duration, the two test groups were not different in their efficacy (IRR=0.84 and 0.89 compared with control). This may be due to a lack of difference between total outdoor time per day and light intensity between groups. Our objective wearable data confirmed that the time outdoors did not usually meet the intended targets, especially with test II. Additionally, periods of outdoor time coincided with both tests I and II (Figure 2). The reasons for reduced time outdoors despite reported compliance being high are uncertain. The physical space availability, opportunity for structured activities, cultural attitudes on sun exposure and academic performance, as well as weather (e.g., pollution) could play roles in the failure to meet targets. Furthermore, the numerous breaks which test II required included multiple transitions from outdoor to classroom which may have been challenging and difficult to implement, since teaching buildings in Shanghai are commonly multi-storey designed. For example, given the short nature of the break children may not have had the chance to be outdoors whilst on break. The aforementioned suggested increasing time outdoors may encounter bottlenecks in practical implementation. This finding also suggested that longer breaks might be needed to increase time spent outdoors more feasible.

Of note, the objective measurements in the present trial provide evidence-based clues for the formulation of specific intervention strategies that may be designed based on the requirements of the community. Data from previous studies implied a possible threshold for effective prevention,[14] but ours is the first which generated a model to quantify them. For example, one study found no protective effect with 360 minutes/week outdoors and others observed a lower risk of future myopia with 600-840 minutes or greater time outdoors/week. In contrast, our model indicated that a 25% to 30% reduction in myopia risk required approximately 770,000 to 860,000 cumulative lux per day at an outdoor light intensity of approximately 5000 lux with approximately 154-172 outdoor minutes. At a lower intensity (4500 lux) it increases to 170-190 minutes. Therefore, compared with controls, a 25% to 30% reduction in IRR requires approximately 65-85 extra outdoor minutes per day. In comparison, only an extra 20 minutes/day outdoors was achieved with test groups compared to the control. This new information, therefore, provides evidence-based clues to formulate intervention strategies that can be recalculated for communities based on their local light intensities.

Findings from our study have several public implications. Firstly, it accumulates evidence on the already known protective effects of outdoor exposure and suggests outdoor exposure should be a prescribed lifestyle modification for myopia prevention. Secondly, our findings derived from the objective measurements provide an evidence-based model which may calculate the outdoor exposure required for myopia risk reduction that can be personalized to a community's geographic light intensity and exposure. Thirdly, the outdoor exposure did not meet the intended targets in the test groups, especially in test II. This suggests the feasibility of implementing the outdoor exposure of more than 80 minutes is low in real-world settings and for this to be met more incentives are required to improve outdoor exposure among Chinese schoolchildren. The policy that eased the burden of excessive homework and off-campus tutoring for students undergoing compulsory education proposed by the education department can make it easier to achieve the goal of reducing the myopia rate, and extended school hours should also be used for outdoor activities rather than homework. Outdoor intervention programs should also enlist the support of parents and local community programs.

Several limitations should also be acknowledged. Firstly, a pre-specified 33% reduction in incident myopia was not detected given the pre-specified sample size. A failure to achieve outdoor targets and a reduced sample on enrolment with further loss to follow-up may have impacted the chance of finding an effect. Secondly, specific doses of outdoor time were prescribed for groups I and II, however, their impacts on participant behavior, particularly on time spent outdoors outside of school hours, were not considered. Thirdly, the use of the wearable may lead to some participants changing their behavior with increased compliance in the test groups during the second year (i.e., Hawthorne effect). Fourthly, the magnitude of light intensity recorded in this study differed from previous studies because of a difference in light sensors, limiting a direct comparison between studies. Furthermore, light exposure was recorded using a wrist wearable and may not directly relate to the light levels received at the eye. Fifthly, the dose-response relationship noted from the objective measurements of outdoor exposure should be interpreted carefully, as this was derived from pooling data rather than our RCT design. Therefore, the relationship could not imply causality. Finally, although 20.5% of the study cohort was lost to follow-up at 24 months, the rate of follow-up was not different between the groups (control: 21.1%; test I:19.4%; test II: 18.0%; P=0.137) and therefore, any impact on study outcome was minimal.

In summary, increasing outdoor time reduced the risk of myopia onset and myopic shift in refractive error, especially in nonmyopic children. However, there was a lower-than-expected effect of outdoor time and may be related to the insufficient levels of outdoor time that were achieved in the test groups. Efficacy was similar between test I and test II and is likely related to similar actual outdoor exposure between groups. Importantly, objective monitoring of outdoor time and light indicated that the protective effect of outdoor time was related to the duration of exposure as well as light intensity. The results also indicate that monitoring compliance is essential to affect the behavioural change required to increase time outdoors. These findings may assist in designing and implementing effective public health strategies that reduce the risk of myopia.

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Legends for figures

Figure 1. Flow of participants in the trial

Figure 2. a) Outdoor light exposure per min for each hour block for an average day across the three groups. b) Outdoor time in mins for each hour block across the day for the three groups.

Figure 3. Myopia incidence during 2nd year a) by indoor light intensity; b) outdoor light intensity and c) total outdoor time/day

Figure 4. The association between time outdoors and 2-year myopia progression of SE and AL stratified

Table 1. Myopia Incidence, change in SE(D) and AL (mm) over 2 years

	Control	Test I	Test II
Unadjusted Incidence of Myopia*	24.9% (401/1608)	20.6% (387/1878)	23.8% (376/1581)
Change in SE (D), mean ± SD	-0.98 ± 0.76	-0.84 ± 0.77	-0.93 ± 0.77
Adjusted change in SE(D), 95%CI	-1.04(-0.91 to -1.17)	-0.84(-0.96 to -0.70)	-0.91(-1.03 to -0.79)
Change in AL(mm), mean±SD	0.61 ±0.33	0.55 ± 0.33	0.58 ± 0.33
Adjusted change in AL(mm), 95% CI*	0.65(0.60 to 0.70)	0.55(0.51 to 0.60)	0.57(0.52 to 0.62)

*$p<0.05$ for the comparisons among three groups;CI: confidence interval; SE: spherical equivalent; SD: standard deviation; AL: axial length.

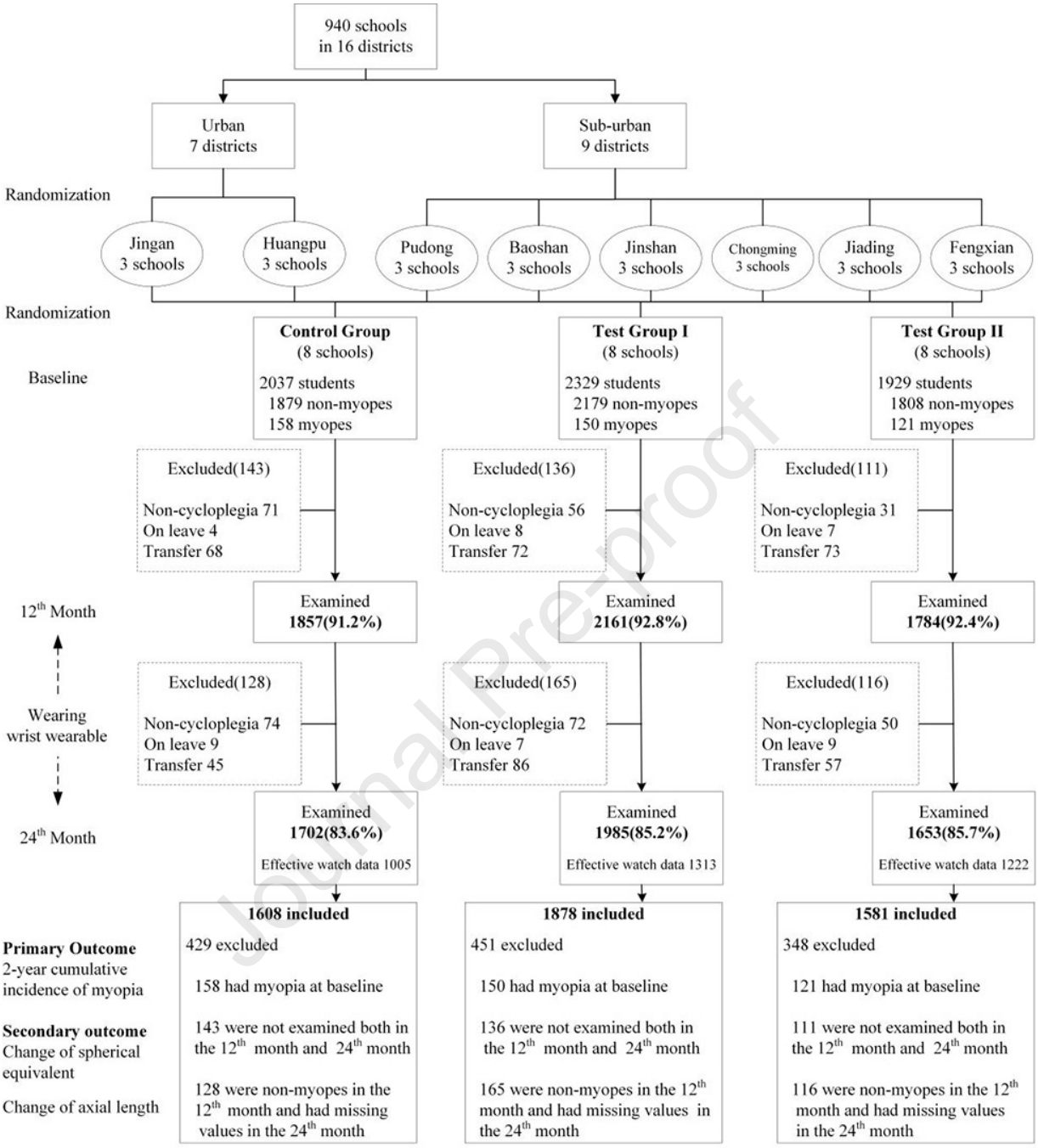
Table 2. Factors Associated with 2-year Cumulative Incidence of Myopia by Poisson Regression Model

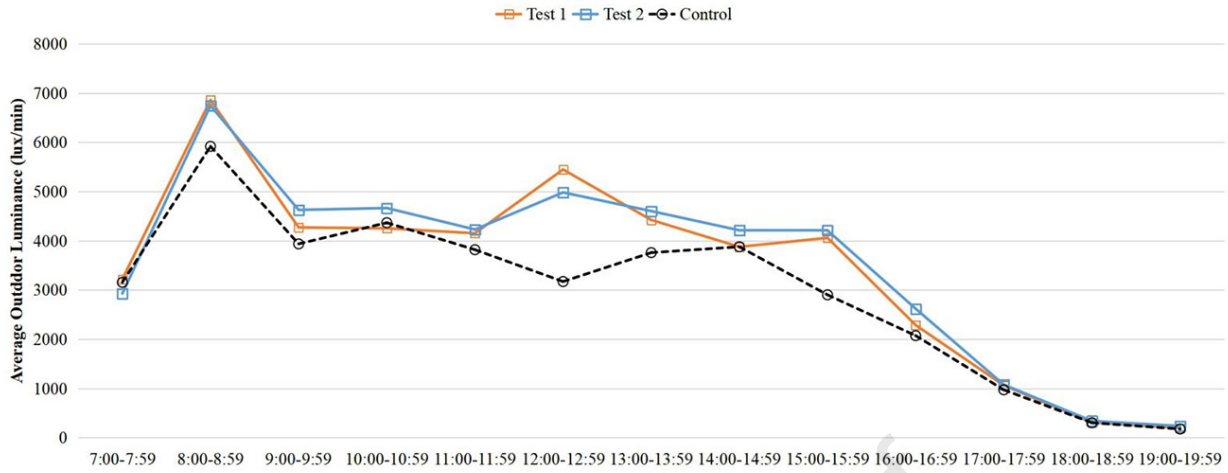
Parameter	IRR	95%CI Lower	95%CI Upper	*P value*
Group (Test I vs Control)	0.84	0.72	0.99	0.035
Group (Test II vs Control)	0.89	0.79	0.99	0.041
Age at baseline	0.97	0.90	1.04	0.356
Gender (Girl vs Boy)	1.20	1.12	1.30	<0.001
Parental myopia				
Parental myopia (one parent only vs neither)	1.12	1.03	1.22	0.008
Parental myopia (both parents vs neither)	1.40	1.28	1.53	<0.001
Compliance	0.70	0.42	1.17	0.172
RE status at baseline (hyperopia vs emmetropia at baseline)	0.12	0.10	0.15	<0.001
School level noon-break duration	0.79	0.67	0.92	0.003

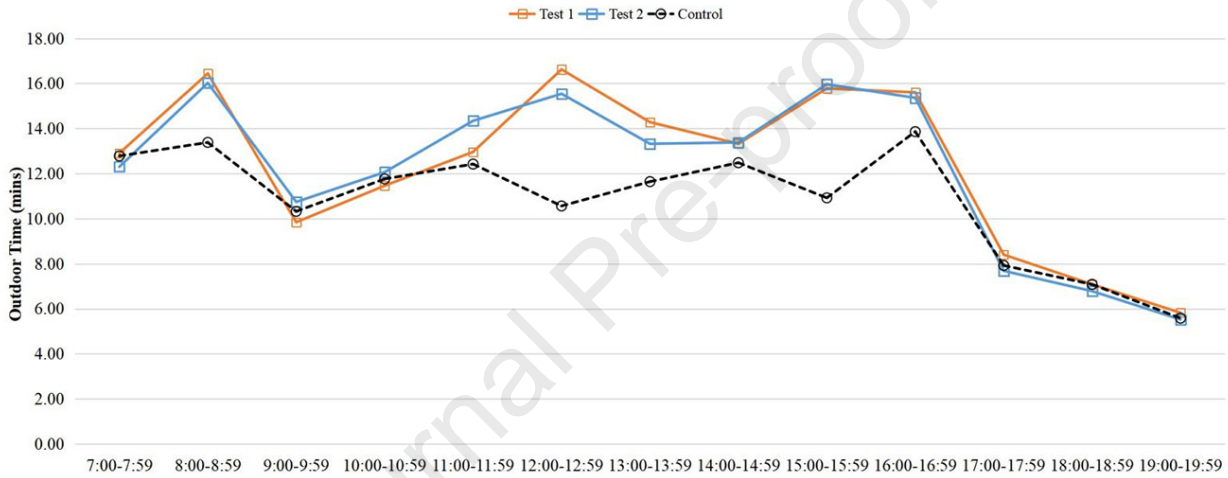
IRR: Incidence Risk Ratio; CI: confidence interval; RE: refractive error.

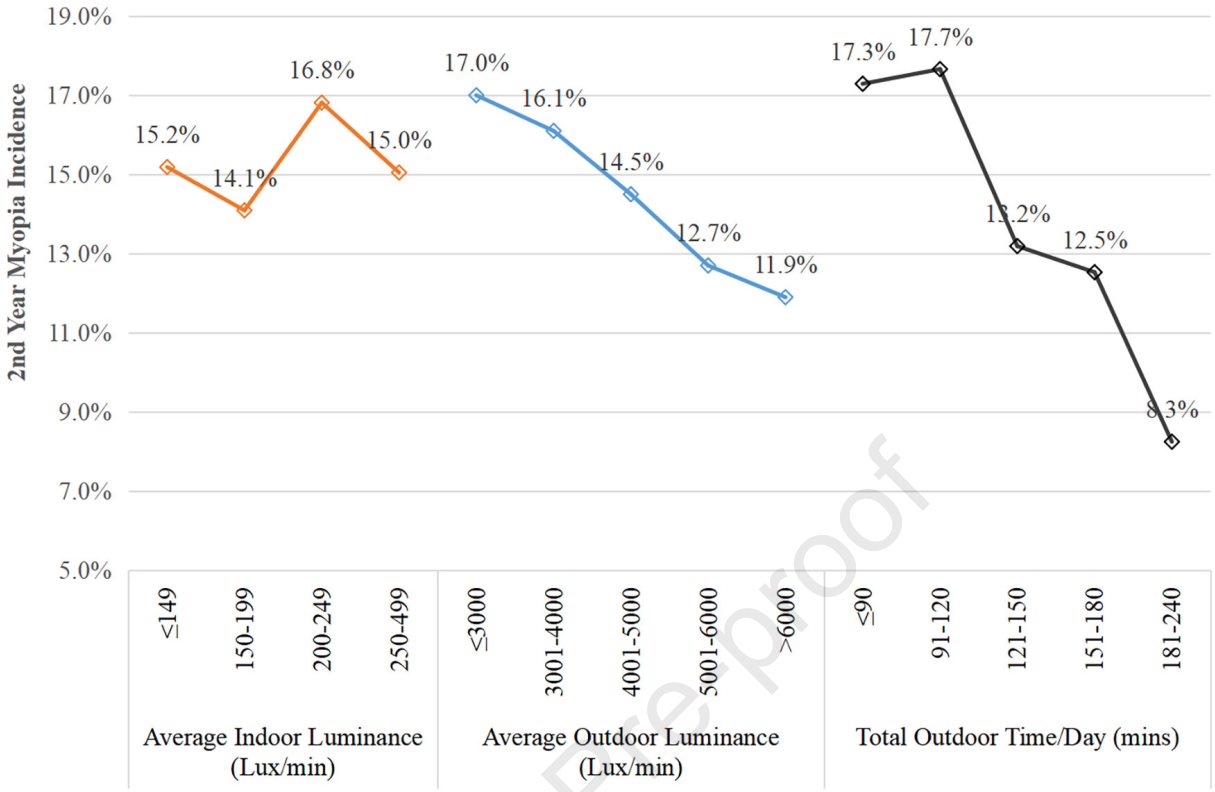
Table 3. Estimated reduction of myopia incidence within different scenarios of outdoor time and light intensity by simulation

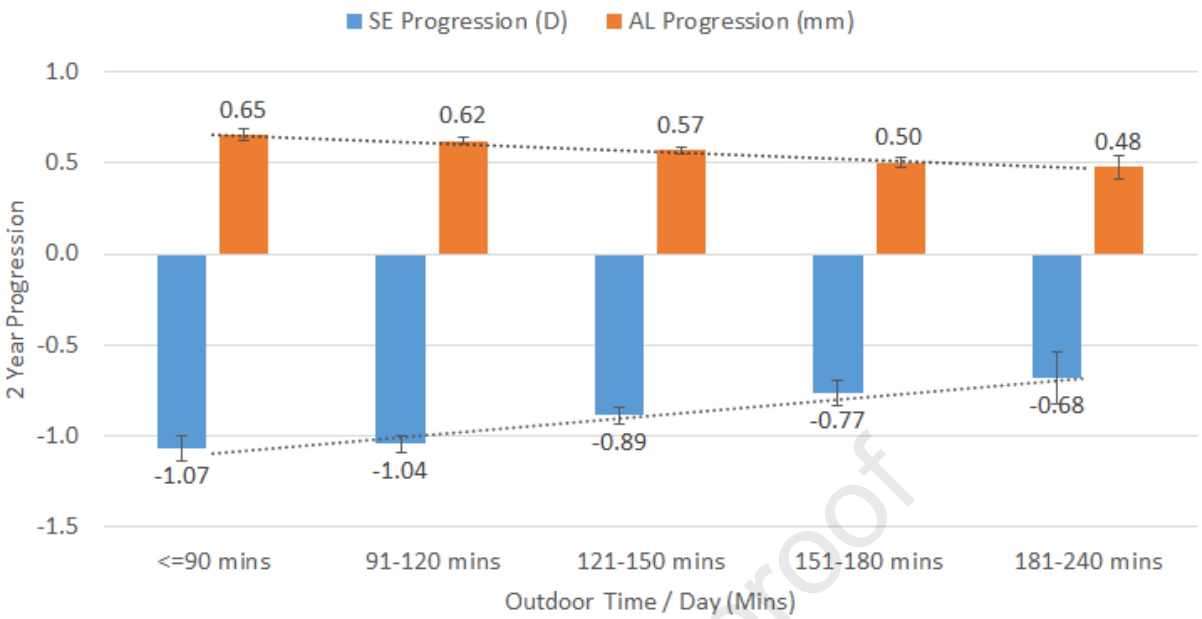
Cumulative outdoor lux per day	IRR compared to no outdoor exposure	% Reduction compared to Controls	Outdoor time in minutes relative to light intensity			
			Intensity: 5000 lux/minute	Intensity: 4500 lux/minute	Intensity: 4000 lux/minute	Intensity: 3500 lux/minute
375000	0.76	Reference Control experience	75	83	94	107
400000	0.74	-2%	80	89	100	114
450000	0.72	-5%	90	100	113	129
500000	0.69	-9%	100	111	125	143
550000	0.67	-13%	110	122	138	157
600000	0.64	-17%	120	133	150	171
650000	0.62	-22%	130	144	163	186
700000	0.60	-26%	140	156	175	200
750000	0.57	-31%	150	167	188	214
800000	0.55	-36%	160	178	200	229
850000	0.53	-41%	170	189	213	243











Increasing outdoor exposure at school prevented myopic changes in non-myopic children, but not in myopes. The protective effect of outdoor time was related to the duration of exposure and light intensity.