

The Association between Time Spent Outdoors and Myopia in Children and Adolescents

A Systematic Review and Meta-analysis

Justin C. Sherwin, MBBS, MPhil,^{1,2} Mark H. Reacher, MD,¹ Ruth H. Keogh, DPhil,³
Anthony P. Khawaja, MBBS, MPhil,¹ David A. Mackey, MD,^{2,4,5} Paul J. Foster, PhD^{6,7}

Objective: To summarize relevant evidence investigating the association between time spent outdoors and myopia in children and adolescents (up to 20 years).

Design: Systematic review and meta-analysis.

Participants: Results from 7 cross-sectional studies were pooled in a meta-analysis. A further 16 studies (8 cross-sectional not meeting criteria for meta-analysis; 7 prospective cohort studies; 1 randomized, controlled trial [RCT]) were reported in the systematic review.

Methods: The literature search included 4 databases (Medline, Embase, Web of Science, and Cochrane Central Register of Controlled Trials [CENTRAL]), and reference lists of retrieved studies. Estimates of association were pooled using random effects meta-analysis. We summarized data examining the association between time spent outdoors and prevalent myopia, incident myopia, and myopic progression.

Main Outcome Measures: Pooled odds ratios (ORs) and 95% confidence intervals (CIs) for myopia for each additional hour spent outdoors per week from a meta-analysis.

Results: The pooled OR for myopia indicated a 2% reduced odds of myopia per additional hour of time spent outdoors per week, after adjustment for covariates (OR, 0.981; 95% CI, 0.973–0.990; $P < 0.001$; I^2 , 44.3%). This is equivalent to an OR of 0.87 for an additional hour of time spent outdoors each day. Three prospective cohort studies provided estimates of risk of incident myopia according to time spent outdoors, adjusted for possible confounders, although estimates could not be pooled, and the quality of studies and length of follow-up times varied. Three studies (2 prospective cohort and 1 RCT) investigated time spent outdoors and myopic progression and found increasing time spent outdoors significantly reduced myopic progression.

Conclusions: The overall findings indicate that increasing time spent outdoors may be a simple strategy by which to reduce the risk of developing myopia and its progression in children and adolescents. Therefore, further RCTs are warranted to investigate the efficacy of increasing time outdoors as a possible intervention to prevent myopia and its progression.

Financial Disclosure(s): The authors have no proprietary or commercial interest in any of the materials discussed in this article. *Ophthalmology* 2012;xx:xxx © 2012 by the American Academy of Ophthalmology.



There is a wide variation in the prevalence of myopia worldwide. The prevalence exceeds 80% in some populations of East Asia, but is much lower in populations in Africa, Europe, Australia, and North America.¹ Myopia carries major social, educational, and economic consequences and adversely impacts quality of life.² Although the blurred vision associated with myopia is easily managed with corrective lenses or refractive surgery, currently there is no widely used intervention to retard the development or progression of myopia. High (or pathologic) myopia is associated with an increased risk of degenerative retinal conditions and retinal detachment, primary open-angle glaucoma, and early-onset cataracts, all of which pose a

substantial lifetime risk for severe visual impairment and blindness.³ Because the prevalence of high myopia attributed to “school myopia” is increasing, especially in East Asia, this form of high myopia may be more susceptible to environmental pressures than predominantly inherited forms.¹

For several decades, environmental factors have been believed to play an important role in the determination of refractive error.^{4–6} Even though a substantial proportion of myopia cases can be explained by inheritance,⁷ this does not exclude strong environmental influences being the driving force behind the rapid increases in the prevalence of myopia over time, especially in East Asia.⁸ Such changes are con-

sistent with an intrinsic plasticity in refractive error mediated by the refractive power of the cornea and lens, which could be influenced by environmental factors.¹ This raises the possibility of public health strategies to reduce the prevalence and possibly the severity of myopia.

Few consistently protective environmental factors for myopia have yet been identified, but the past decade has seen a large increase in the number of observational studies investigating the hypothesis that time spent outdoors protects against myopia. To our best knowledge, no systematic review or meta-analysis on the association between time spent outdoors and myopia has been published, or registered, to date. We have therefore undertaken a systematic review and meta-analysis to summarize and quantitatively combine all relevant evidence for an association between time spent outdoors and myopia and its progression.

Methods

Search Strategy and Inclusion Criteria

Our research question was, "What is the association between duration of time spent outdoors and myopia or myopic progression in children and adolescents aged up to 20 years?" Time spent outdoors was defined as the sum of general activities, leisure activities, and sports performed outdoors. Children and adolescents without myopia were defined as the sum of emmetropes and hypermetropes.

One author (J.C.S.) systematically conducted a search of 4 databases (Medline [1950–September 2011], Web of Science [1899–September 2011], Embase [1974–September 2011], and the Cochrane Central Register of Controlled Clinical Trials [CENTRAL; up to September 2011]). The following search strategy was performed in Medline and CENTRAL: myopi* OR "myopia"[MeSH Terms] OR "short-sight" OR "short-sighted" OR "short-sightedness" OR "short sight" OR "short sighted" OR "short sightedness" OR "near-sight" OR "near-sighted" OR "near-sightedness" OR "near sight" OR "near sighted" OR "near sightedness" OR "refractive errors"[MeSH Terms] OR refract*) AND (outdoor* OR outside OR "Leisure Activities"[MeSH Terms] OR sport* OR "physical activity" OR "Motor Activity"[MeSH Terms] OR hobb*). The same search was performed in Web of Science, but MeSH terms were not used. The following search strategy was used for Embase (exp degenerative myopia/ or exp myopia/ or exp high myopia/ OR exp refraction error/ OR myopi*.mp. OR short-sight*.mp. OR near-sight*.mp. OR refracti*.mp.) AND (physical activity.mp. or exp physical activity/or exp exercise/OR outdoor*.mp. OR outside.mp. OR hobb*.mp. OR exp leisure/).

Assessment of retrieved titles and abstracts involved a comparison against our research question. If considered potentially suitable, or if uncertainty regarding suitability remained after reading the title and abstract, full-text articles were subsequently retrieved. Two authors independently performed this assessment (J.C.S. and A.P.K.), and any inconsistencies were resolved by consensus. Reference lists from all identified studies were also examined. From the full-length articles, the studies were required to meet the following inclusion and exclusion criteria for the purposes of the meta-analysis. Inclusion criteria were (1) reported time spent outdoors in keeping with our exposure definition, (2) reported myopia (prevalent or incident) or myopic progression as the outcome measure, (3) reported a measure of the association either as an effect estimate with 95% confidence interval (CI) or standard error

(SE) or allowed for the calculation of it from raw data contained in the article, and (4) were limited to children and adolescents (aged up to 20 years). We excluded studies without a precise definition of myopia, animal studies, and conference abstracts. When multiple publications from the same study population were available for the same study design (e.g., cross-sectional), we included the publication that best addressed our research question. We did not limit studies according to study design, thus potentially including interventional as well as observational studies.

Studies that were appropriate to our research question but did not meet the criteria for the meta-analysis are reported in our systematic review, with reasons for exclusion outlined, and sources of bias and study limitations recorded. Additional studies were grouped according to the outcome(s) that were presented in the results: association between time spent outdoors and (1) incidence of myopia or (2) myopic progression. If studies addressed both of these outcomes, their results are presented separately. We did not produce a tally of "positive" and "negative" studies, because this can miss important sources of heterogeneity and obscure the role of bias.⁹

Data Extraction and Assessment of Study Quality

To appropriately report the systematic review and meta-analysis we were guided by the MOOSE checklist.¹⁰ For each study, the following characteristics were extracted: (1) last name of first author, (2) year of publication, (3) study design, (4) area of the study population (East Asian vs not East Asian), (5) number of subjects in the study, (6) participation rates, (7) age range of study subjects, (8) definition of time spent outdoors, (9) definition of myopia, (10) effect estimate plus 95% CI or SE, (11) which confounding factors were adjusted for, and (12) the latitude of the study location. If not presented in the original report, information on latitude was retrieved using an online resource.

Study quality was assessed with a tool outlined in a systematic review investigating the assessment of quality and bias in observational studies.¹¹ Variables assessed for quality included the methods for selecting study participants, methods for measuring exposure (time spent outdoors) and outcome (myopia), design-specific sources of bias (including but not limited to recall bias, interviewer bias, loss to follow-up, and masking), methods for controlling confounding, statistical methods (appropriate use of statistics for primary analysis of effect), and conflict of interest.

Statistical Methods for the Meta-analysis

All studies included in the meta-analysis reported odds ratios (ORs) and 95% CIs for myopia per increase of 1 hour per week or 1 hour per day in outdoors exposure. We estimated the SE of log OR estimates by the width of the confidence interval on the log scale divided by 2×1.96 .¹² For each study, we standardized results by obtaining the OR estimate on the hours per week scale. If the exposure variable was defined as hours per day, the log OR and its SE were divided by 7 to derive the corresponding hours per week estimate. For the purposes of the analysis, time spent outdoors (hours per week) was considered equal to time spent outdoors (hours per day) multiplied by 7.

We chose to use a random effects meta-analysis because of the expected heterogeneity in the included studies in terms of study population, definition of exposure and outcome, and degree of adjustment for confounders.¹³ DerSimonian and Laird¹⁴ pooled ORs that were obtained from random effects meta-analysis. Sensitivity analyses were also performed to assess the robustness of pooled estimates, including a prespecified subgroup analysis investigating the effect of geographic region (East Asia vs other).

We also performed post hoc subgroup analyses investigating the effect of age group, measurement of refractive error, and definition of time spent outdoors.

Tests for heterogeneity of effect estimates across studies were performed using the Q statistic, and the effect of study heterogeneity on the variation in the estimated pooled treatment effect was estimated using the I^2 statistic, which indicates the proportion of total variation due to heterogeneity.¹⁵ Meta-analyses were performed in Stata version 10.1 (StataCorp, LP, College Station, TX) using the *metan* program. Publication bias was assessed with the *metabias* program of Stata, by means of the adjusted rank correlation test of Begg,¹⁶ and the regression-based test of Egger et al.¹⁷ Extent of publication bias was also displayed graphically using a funnel plot.

Results

Identification and Selection of Reports for the Systematic Review and Meta-analysis

We identified 2912 articles from the database (55 from CENTRAL, 898 from Medline, 511 from Embase, and 1448 from Web of Science). After removal of 1289 duplicate publications, there were 1623 studies (Fig 1). In total, 46 articles were retrieved for full-text review, and 23 independent reports contained results pertinent to our research question. The 23 reports included 15 cross-sectional studies, 7 prospective cohort studies, and 1 randomized, controlled trial (RCT). Seven of the cross-sectional studies met the criteria for meta-analysis, and the remaining cross-sectional studies were

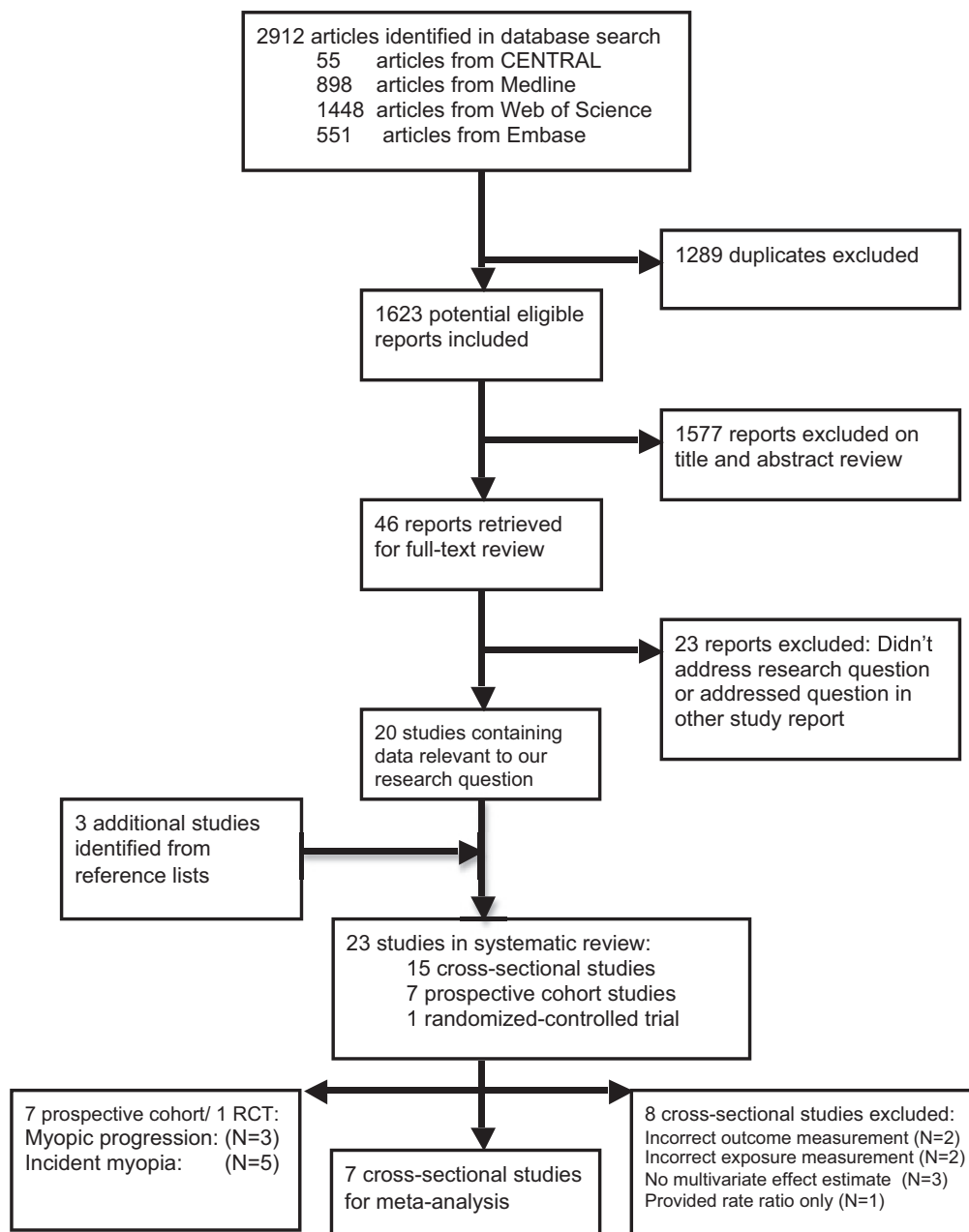


Figure 1. Flow diagram outlining the selection process for inclusion of studies in the systematic review and meta-analysis. CENTRAL = Cochrane Central Register of Controlled Trials; RCT = randomized, controlled trial.

summarized and are reported separately. We were unable to perform a meta-analysis of studies investigating the incidence of myopia or myopic progression as endpoints (7 prospective cohort studies; 1 RCT), because most failed to provide a multivariate measure of association or did not measure time spent outdoors as a continuous variable that would have allowed us to pool estimates together. There were 2 studies investigating incident myopia that could be pooled together statistically, and 2 studies investigating myopic progression as well, but we decided against performing this analysis because of the small numbers. We did not consider it appropriate to combine estimates of risk from prospective studies with ORs from cross-sectional studies.

Characteristics of Studies Included in the Meta-analysis of Cross-sectional Studies

Characteristics of the 7 cross-sectional studies included in the meta-analysis, including participation rates, age, and number of participants and definitions of exposure and outcome, are summarized in Table 1. The 7 studies comprised a total of 9885 individuals and comprised 6 studies of school-age children and 1 of children aged 6–72 months.¹⁸

Ascertainment and definition of exposure varied across studies. Five studies used self-reported time spent outdoors,^{19–23} and 2 used parental reporting using questionnaires.^{18,24} Three studies included sports in their definition of time spent outdoors,^{19,21,23} 2 included outdoor sports,^{18,22} and 2 studies used only outdoor sports as a measure of time spent outdoors,^{20,24} which is likely to have underestimated total outdoor exposure.

Three studies^{18,20,21} reported effect estimates as hours of time spent outdoors per day, with the remaining 4 studies reporting hours per week. Some studies provided extra details about their

exposure methods. For example, the study by Dirani et al²¹ recorded time spent outdoors separately on weekdays and weekends, the sum of which was then divided by 7 to obtain the daily estimate. However, other studies failed to differentiate between time spent outdoors on weekends and weekdays. Deng et al²³ recorded time spent outdoors during the school year and in the summer break separately.

Refractive error was assessed objectively using cycloplegic autorefraction in 5 studies, with 1 study using noncycloplegic retinoscopy by an experienced optometrist.²³ Khader et al²⁰ used self-reported myopia, but this was confirmed with health records. Prevalence estimates of myopia from cross-sectional studies were broad, ranging from 11.4%¹⁸ to 83.1%.²²

All 7 studies gave response rates and described sampling methods, albeit in varying degrees. However, only 2 studies outlined specific exclusion criteria and provided information on nonresponders.^{18,21} More comprehensive methodologies pertaining to some studies^{19,21–23} have been published elsewhere. Quality assessment of the 7 cross-sectional studies has been conducted (Table 2, available at <http://aaojournal.org>). Although individual study quality was variable, we did not considerate it appropriate to weight studies based on a “quality score” because it brings a rather arbitrary and subjective component to the meta-analysis.⁹

Pooled Estimates of the Association between Outdoor Activity and Prevalent Myopia

Table 3 shows the OR estimates (95% CIs) obtained from each study before converting into a standardized effect estimate for the meta-analysis, as well as covariates that were adjusted for in the individual multivariate analyses. Random effects meta-analysis yielded a pooled OR for myopia of 0.981 (95% CI, 0.973–0.990; $P_{OR} < 0.001$; $I^2 = 44.3\%$; $P_{\text{heterogeneity}} = 0.092$) per additional

Table 1. Characteristics of the 7 Cross-sectional Studies Included in the Meta-analysis of Time Spent Outdoors and Myopia

Study	Location (Name of Study)	Latitude	n (Participants)	Participation Rates (%)	Age	Definition of Time Outdoors	Definition of Myopia (D)
Deng et al ²³	New England, USA	46°32'N	147	NS	6–18 years	Hours per week in time outdoors or in sports	SER ≤ −0.5
Dirani et al ²¹	Singapore Singapore Cohort (Study of Risk Factors of Myopia [SCORM])	1° 14'N	1249	79.6	11–20 years	Hours per day spent on total outdoor activity, defined as sum of outdoor leisure and outdoor sporting activities	SER ≤ −0.5
Ip et al ¹⁹	Sydney, Australia (Sydney Myopia Study)	34° 0'S	2339	75.0	12–13 years	Hours per week on general activities, leisure activities, and outdoor sport	SER ≤ −0.5
Khader et al ²⁰	Amman, Jordan	31°57'N	1777	92.0	12–17 years	Hours per day playing sports	SER ≤ −0.5
Low et al ¹⁸	Singapore (Strabismus, Amblyopia and Refractive Error in Singaporean Children [STARS])	1° 14'N	3009	72.3	6–72 months	Hours per day in total outdoor activity per day	SER ≤ −0.5
Lu et al ²²	Quangdong Province, China (Xichang Pediatric Refractive Error Study)	20°13'–25°31'N	998	81.0	13–15 years	Hours per week of outdoor activity of all kinds	SER ≤ −0.5
Mutti et al ²⁴	USA (Orinda Longitudinal Study of Myopia)	37°52'N	366	84.0	13–14 years	Hours per week of sports activities	SER ≤ −0.75 in both vertical and horizontal meridians

NS = not specified; SER = spherical equivalent refraction.

Table 3. Individual Study Estimates of the Association between Time Spent Outdoors and Myopia in 7 Cross-sectional Studies Meeting Inclusion Criteria in the Meta-analysis

Author	OR (95% CI)	Units of Exposure	Adjusted Effect Estimate OR (95% CI)	Covariates Adjusted for in Model
Deng et al ²³	0.915 (0.843–0.994); a second effect estimate was calculated for summer months: 1.000 (0.969–1.033)	Hours per week	N/A	Age and number of myopic parents
Dirani et al ²¹	0.90 (0.84–0.96)	Hours per day	0.985 (0.975–0.994)	Age, gender, ethnicity, school, books read per week, height, parental myopia, father's education level, intelligence quotient
Ip et al ¹⁹	0.97 (0.95–0.995)	Hours per week	N/A	Age, gender, height, ethnicity, school type, parental myopia, highest parental education, continuous reading ≥ 30 minutes, close reading distance (<30 cm)
Khader et al ²⁰	0.89 (0.86–0.93)	Hours per day	0.983 (0.979–0.986)	NS; Other variables in the analysis (and hence likely covariates) were age, family history of myopia, reading and writing
Low et al ¹⁸	0.95 (0.85–1.07)	Hours per day	0.993 (0.977–1.010)	Familial clusters, age, gender, height, presence of myopic parents, reading stage
Lu et al ²²	1.14 (0.69–1.89)	Hours per week	N/A	NS; Other variables in the analysis (and hence likely covariates) were age, gender, parental education, homework, personal reading, watching television, and playing video games/computer use
Mutti et al ²⁴	0.936 (0.892–0.974)	Hours per week	N/A	Myopic parents, diopter-hours per week, sports, academic scores

CI = confidence interval; N/A = if units of exposure presenting as hours per week, the corresponding effect estimate was entered into the meta-analysis unchanged; NS = not specified; OR = odds ratio.

hour of time spent outdoors per week. The intrastudy effect estimates and overall pooled estimates are shown in Fig 2. Assuming that a 1-hour increase in time spent outdoors per day was equiv-

alent to 7 hours of increased time spent outdoors per week, the equivalent OR per 1 hour per day increase in time spent outdoors is 0.867 (95% CI, 0.811–0.930).

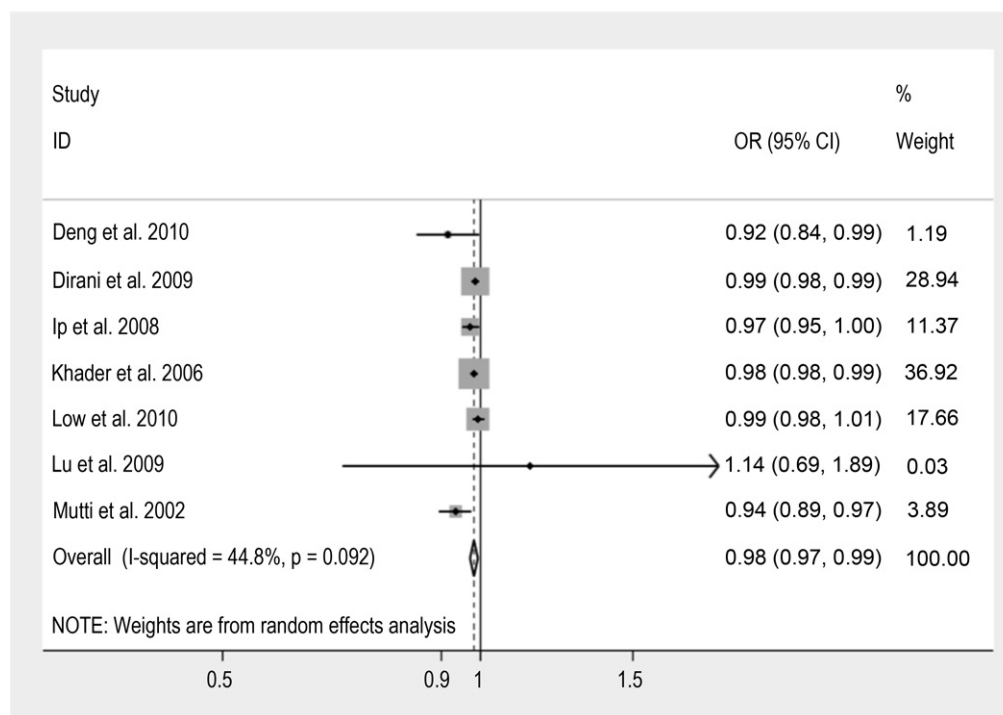


Figure 2. Random effects meta-analysis investigating the effect of time spent outdoors (hours per week) on prevalence of myopia. CI = confidence interval; OR = odds ratio.

Subgroup and Sensitivity Analyses

We performed a prespecified subgroup analysis on geographic location and a post hoc subgroup analysis on age.

Geographic Location. Three studies were performed in East Asia.^{18,21,22} In these studies, the pooled OR was 0.987 (95% CI, 0.979–0.995; $P_{OR} = 0.002$). A more protective association was found in the non-East Asian studies, where the pooled OR was 0.966 (95% CI, 0.944–0.989; $P_{OR} = 0.003$). However, there was greater heterogeneity among the non-East Asian studies ($I^2 = 64.9%$ [$P_{heterogeneity} = 0.036$] vs $I^2 = 0.0%$ [$P_{heterogeneity} = 0.608$]).

Age Group. Excluding the study involving younger children (aged 6–72 months)¹⁸ resulted in a slightly stronger protective association, giving a pooled OR of 0.978 (95% CI, 0.968–0.989; $P_{OR} < 0.001$; $I^2 = 46.4%$) per increase of 1 hour of exposure per week.

We also performed post hoc sensitivity analyses investigating the effect of differences in exposure and outcome measurement.

Measurement of Refractive Error. Excluding the study in which myopia was self-reported,²⁰ the pooled OR was slightly reduced: pooled OR was 0.976 (95% CI, 0.961–0.992; $P_{OR} = 0.004$; $I^2 = 54.0%$) per additional hour of exposure per week.

Definition of Time Spent Outdoors. When the 2 studies^{20,24} that considered time spent outdoors as synonymous with sports were omitted, the pooled effect size for an additional hour of time spent outdoors per week was very similar but the heterogeneity was lower: OR, 0.983 (95% CI, 0.971–0.995; $P_{OR} = 0.007$; $I^2 = 33.1%$). We also used the second effect estimate reported by Deng et al.²³ In the primary analysis, we used the OR from the school year, but here we present the pooled analysis when using the effect estimate that corresponds to time spent outdoors in summer months: OR, 0.983 (95% CI, 0.976–0.991; $P < 0.001$; $I^2 = 34.9%$).

Assessment of Publication Bias

We assessed for possible publication bias in the 7 cross-sectional studies with a funnel plot. Aside from the study by Lu et al,²² most studies were found near the apex of the funnel plot because of the much smaller SEs for effect estimates. There is some suggestion of asymmetry in the plot, with estimates from more studies appearing to the left of the pooled estimate. Any asymmetry in the spread of studies included in a funnel plot may occur because of publication bias, heterogeneity in the effect size across studies, or may be by chance. However, with only 7 studies neither Begg's test ($P = 0.652$) nor Egger's test ($P = 0.293$) suggest publication bias.

Estimates of Association in Cross-sectional Studies Excluded from Meta-analysis

Eight cross-sectional studies were obtained whose data could not be pooled for meta-analysis (Table 4, available at <http://aaojournal.org>). These studies involved >9000 children, although some of the subjects were participants in >1 publication. Three of the studies had <500 participants,^{25–27} with the 2 largest studies exceeding 2000 participants, each with complete refractive and questionnaire data.^{28,29} Excluding the study performed in Sydney (15.0% of participants had East Asian ethnicity), all of the remaining studies involved participants from East Asia.²⁸ Aside from the study by Tan et al,²⁷ all of the studies investigated children of school age. Tan et al investigated 414 children of kindergarten age in Singapore using noncycloplegic autorefractometry and parents completed activity questionnaires.²⁷ Time spent outdoors (≥ 7 vs <7 hours per week) was associated with a reduced prevalence of myopia,

although it was not significant (multivariate rate ratio, 0.81; 95% CI, 0.50–1.32). Some of the studies involved 2 different populations, for example, the Singapore-Xiamen study,³⁰ and comparison of children from Sydney and Singapore.³¹ These studies allowed for the investigation of risk factors that may explain the differences in myopia prevalence between the 2 sites/populations. It was found that differences in time spent outdoors was the most significant factor explaining differences in myopia prevalence between Singapore (prevalence of myopia, 29.1%) and Sydney (prevalence of myopia, 3.3%).³¹

Ma et al,³² using noncycloplegic autorefractometry, found that time spent outdoors during weekdays is associated with emmetropia (compared with myopia; OR, 1.145; 95% CI, 1.047–1.252; $P = 0.003$). Rose et al²⁸ investigated 3132 children from 2 school-year groups in Sydney. They found that, after adjustment for gender, ethnicity, parental myopia, near work, maternal and parental education, and maternal employment, a greater number of hours spent outdoors was associated with a more hyperopic mean spherical equivalent refraction (SER) in students in both years 1 ($P = 0.009$) and 7 ($P = 0.003$). Rose et al also addressed the interplay between near work and outdoor time, finding that the highest odds of myopia was found in students with high levels of near work and low levels of time spent outdoors, whereas the most hyperopic refraction was found with high levels of time spent outdoors and low levels of near work.²⁸ In a small study in Taiwan, Wu et al²⁵ found a highly protective association between outdoor activity (often vs seldom/none) and myopia. After adjustment for school year, gender, parental myopia, reading/writing, computer use, and other near-work activities, the adjusted OR for often spending outdoors was 0.3 (95% CI, 0.1–0.9; $P < 0.001$). In a separate study, Saw et al³⁰ found that although children with myopia spent less time outdoors, the association was not statistically significant after taking into account other factors. Zhang et al²⁹ did not find that time spent outdoors was associated with myopic refraction (increasingly negative SER) in either univariate or multivariate analysis.

Estimates of Association in Prospective Studies

Five prospective cohort studies investigated the relationship between time spent outdoors and incident myopia (Table 5). The 5 studies involved nearly 4000 subjects aged ≥ 6 years, with the oldest participants being medical students in Turkey. Three of the 5 studies presented multivariate analyses with incident myopia as an outcome variable. Jones et al³³ followed >1000 children without myopia aged 8 to 9 years for 5 years, during which 21.6% developed myopia (≥ -0.75 diopters [D] of myopia in both the horizontal and vertical meridians on cycloplegic autorefractometry). After adjustment for the number of myopic parents and reading, the OR of developing myopia for every 1 hour of sport/outdoor activity per week was 0.91 (95% CI, 0.87–0.95). There was a difference in the time spent outdoors per week (11.65 vs 7.98 hrs/wk; $P < 0.001$) between nonmyopes and future myopes, respectively. Receiver operating curve analysis demonstrated that the predictive ability of time spent outdoors was better than chance, although there was a significant interaction between time spent outdoors and the number of myopic parents. Jones et al³³ also found that higher risk of developing myopia in children with 1 or 2 myopic parents could be partially attenuated by increased participation in sports and outdoor activities, supporting a gene-environment interaction. Onal et al³⁴ followed 207 Turkish medical students for 1 year, finding a highly protective relationship between time spent outdoors conducted before and at age 7 (mostly outdoor vs mostly indoor activity) and incident myopia (SER between ≥ -0.75 D on autorefractometry). After adjustment for age, gender, parental myopia, studying habits,

Table 5. Cohort Studies Investigating the Relationship between Time Spent Outdoors and Incidence of Myopia

Author	Summary of Study	Reason for Exclusion from Meta-analysis	Results	Biases and Study Limitations
Jones et al ³³	Prospective cohort study of 1038 children with no myopia in the third grade of school (age 8–9 years), with 5 years of follow-up.	Meets inclusion criteria	After adjustment for number of myopic parents and reading, the odds ratio of developing myopia for every 1 hour of sport/outdoor activity per week (OR, 0.91; 95% CI, 0.87–0.95).	Only 1 exposure assessment performed; reliability of questionnaire not well established; there was a significant difference in exposure between those with and without complete follow-up.
Jones-Jordan et al ⁵³	Prospective cohort study comparing 731 incident myopes with 587 emmetropes in the United States. Subjects were 6- to 14-year-old participants in the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study.	No multivariate OR or RR was presented with myopia as an outcome	Hours per week spent in outdoor/sports activities were significantly less for children who became myopic 3 years before onset through 4 years after onset by 1.1–1.8 hours per week.	No multivariate analysis; broad age range; questionnaire responses from parents; only brief questionnaire used; possibility for recall bias; follow-up of our emmetropes with necessary data was shorter than that of myopes.
Onal et al ³⁴	Prospective cohort study of 207 Turkish medical students with 1-year follow-up.	Outdoor activity was measured as a categorical variable only	Highly protective relationship between outdoor activity conducted before and at age 7 (mostly outdoor vs mostly indoor activity) and incident myopia (multivariate OR, 0.44; 95% CI, 0.23–0.82; $P = 0.001$).	Small sample size; subjects were medical students; short follow-up (1 year); loss to follow-up of a large percentage of phase IV students; recall bias, as exposure preceded outcome by many years.
Peckham et al ⁵⁴	Birth cohort study of 383 children aged 7–11 living in England, Scotland, and Wales (1958 birth cohort).	No multivariate OR or RR was presented	Did not find any differences in outdoor activity between those with myopia and those without.	No multivariate analysis; lack of comprehensive exploration of exposure/outcome.
Saw et al ³⁵	Prospective cohort study (3 years' follow-up) of 994 Singaporean school children aged 7–9 years.	Meets inclusion criteria; however, it is not appropriate to combine RRs with ORs.	Multivariate RR of outdoor activity (hours per week) on incident myopia: RR, 1.01 (95% 0.98–1.04).	Potential misclassification of exposure from parental questionnaires.

CI = confidence interval; OR = odds ratio; RR = rate ratio/relative risk.

and parental myopia*activity before 7 years interaction, the OR for outdoor activity (mostly outdoor before age 7) was 0.44 (95% CI, 0.23–0.82; $P = 0.001$).³⁴ Saw et al³⁵ followed 994 children aged 7 to 9 years in Singapore, finding a multivariable risk ratio of 1.01 for time spent outdoors (95% CI, 0.98–1.04) for incident myopia after 3 years of follow-up (SER ≥ -0.75 D based on cycloplegic autorefraction).

There were 3 studies involving 463 children ≥ 6 years old (2 prospective cohort; 1 RCT) that investigated the relationship between time spent outdoors and myopic progression (Table 6). Yi and Lee³⁶ performed an RCT in China in which 80 children with myopia aged 7 to 11 years were randomized to either an intervention or control group and followed for 2 years. Children in the intervention group, who completed >14 hours of outdoor activities per week and reduced near and middle-distance work activities, had less myopic progression compared with control (mean annual progression 0.38 vs 0.52 D; $P < 0.01$). In the intervention group, increased time outdoors reduced myopic progression ($P < 0.05$). Parssinen and Lyyra³⁷ followed 240 children (mean age, 10.9 years) with myopia for 3 years, discovering that increasing time spent outdoors was significantly associated with reduced myopic progression and reduced final spherical equivalent in males, but not females, after adjustment for age, initial refraction, and near work. Boys and girls in the slowest progressing quartile spent more time outdoors than the fastest progressing quartile (mean difference, 0.7

hrs/d). In another prospective cohort study with 3 years of follow-up, Saw et al³⁸ found no relationship between increasing time spent outdoors and myopic progression.

Discussion

The purpose of this systematic review and meta-analysis was to summarize all of the available relevant evidence with reference to the relationship between time spent outdoors, a potentially modifiable lifestyle exposure, and myopia and its progression. Because we excluded more cross-sectional studies in the meta-analysis than we were able to include, this decreases the validity of our overall pooled estimate, but an interpretation of excluded cross-sectional studies is consistent with the findings of our meta-analysis. Additional evidence for a link between increasing time outdoors and myopia and myopic progression is seen in the interpretation of the results from cohort studies and 1 RCT. However, the numbers of prospective studies available were considerably fewer than cross-sectional studies. Taken together, we consider it possible that increasing time spent outdoors could confer a modest, but significant, reduced risk against

Table 6. Studies Investigating the Relationship between Time Spent Outdoors and Myopic Progression

Author	Summary of Study	Results	Biases/Limitations
Parssinen and Lyrra ³⁷	Prospective cohort study (nested in RCT) with 2 years' (apostrophe) follow-up of 238 myopes (mean age, 10.9 years)	The amount of time spent outdoors was associated with reduced myopic progression (regression coefficient, 0.23; $P < 0.01$) and reduced final spherical equivalent (regression coefficient, 0.17; $P < 0.05$) in boys, after adjustment for age, initial SER, and close work. Time spent outdoors was not significantly associated with myopic progression and final SER in girls in a multivariate model. There was a significant difference between groups time spent outdoors and the rate of myopic progression (ANOVA; $P = 0.009$) in girls, but not boys ($P = 0.326$). Boys and girls in the slowest progressing quartile spent more time outdoors than the fastest progressing quartile (mean, 3.2 ± 1.4 vs 2.5 ± 1.1 hours outdoors per day; $P = 0.003$).	Possible selection bias
Yi and Lee ³⁶	RCT investigating 80 children with myopia aged 7–11 years in China with 2 years' follow-up. Children were randomly assigned to either an intervention group or control group. Intervention group did near- and middle-vision activities < 30 hr/wk and > 14 – 15 hrs outdoor activities week.	The annual mean myopia progression (0.38 ± 0.15 D) in the intervention group was significantly lower than that in the control group (0.52 ± 0.19 D; $P < 0.01$). More time outdoors was inversely correlated with myopia progression ($P < 0.05$).	Small sample size
Saw et al ³⁸	Prospective cohort study (nested in RCT) of 143 students with myopia aged 6–12 years in Singapore with 2 years' follow-up.	There was no relationship between outdoor activity (hrs/wk) and myopic progression after adjusting for age, gender, and parental myopia: regression coefficient, 0.013 D per outdoor activity (hrs/wk; 95% CI, -0.013 to 0.04 ; $P = 0.33$).	Small sample size. The length of follow-up varied for each child (boys more likely to remain for longer period). Participants are volunteers in an ad, controlled trial with different socioeconomic backgrounds compared with the Singapore population

ANOVA = analysis of variance; CI = confidence interval; D = diopter; RCT = randomized, controlled trial; SER = spherical equivalent refraction.

development of myopia and its progression. Although causality cannot easily be determined from observational epidemiologic studies, the finding that increasing time outdoors reduced myopic progression in a small RCT supports a possible causal protective effect of being outdoors.

We found a significant protective association between increasing time spent outdoors and prevalent myopia in nearly 10 000 children and adolescents aged ≤ 20 years. Each increase in hours per week of time spent outdoors was associated with a 2% reduced odds of myopia, after adjustment for potential confounders (OR, 0.98; $P < 0.001$). Caution must be undertaken in the interpretation of this pooled effect estimate. Although the pooled effect size represents only a weak protective association, its interpretation depends on the unit of measurement. An increase in 7 hours of time spent outdoors per week (1 hr/d) equates to a much stronger protective association (OR, 0.87). There was a wide variation between studies regarding the levels of adjustment of potential confounders, and residual confounding may have affected individual effect estimates and the pooled OR. In addition, the pooled OR does not take into account the quality of the included studies that contributes to the overall estimate.

Studies included in the meta-analysis exhibited wide differences in their individual exposure definitions. Results of our sensitivity analyses suggest our findings were robust with regards to differences in classification of exposure and outcome. Conversion of effect estimates originally using hours of exposure per day to estimates referring to hours of exposure per week may have resulted in bias since it required the assumption that mean daily time spent outdoors multiplied by 7 was equal to the duration of weekly time spent outdoors.

Moderate heterogeneity between effect size estimates may reflect different study populations and geographic contexts, different eligibility criteria, the broad range of participation rates, and different definitions of exposure and outcome, as well as different levels of adjustment for potential confounders. A high percentage of all of the studies in this analysis were performed in East Asia, in keeping with the high prevalence of myopia in this region and associated research efforts. Although time spent outdoors seems to be protectively associated with myopia in East Asian populations, the strength of the association seems to be less marked than for the non-East Asian populations. This could reflect the narrower range of time spent outdoors by children living in East Asia,³⁸ rather than intrinsic ethnic differences. One

must be wary of generalizing results from this subgroup analysis, especially with the relatively few studies involved.

A fundamental drawback of cross-sectional studies is the inability to determine temporality of exposure and outcome, and reverse causality cannot be excluded. It remains possible that children with prevalent myopia are less likely to spend time outdoors than those without. This has been supported by studies of personality type between people with and without myopia,³⁹ plus the finding that myopes might be more likely to live in urban areas where there is less open space⁴⁰ and consequently are less able to participate in sports and outdoor activities. Time spent outdoors is influenced by many factors. To illustrate, time spent outdoors shows ethnic variation⁴¹ and is highly correlated between siblings.⁴² Furthermore, spending time outdoors may also be influenced by environmental factors such as the season/climate, levels of visible light, and one's school or work schedule.²³ Avoiding the problem of reverse causality can be dealt with using a prospective design of sufficient follow-up, and several prospective cohort studies have shown that increasing time spent outdoors is associated with a reduced risk of developing myopia (Table 4). Increasing time spent outdoors is also associated with a reduced axial length,²¹ an endophenotype of refractive error.

Publication bias is a well-recognized pitfall in the conduct of meta-analyses.⁴³ It refers to the publication (or lack of publication) of a study, based on the results of the study (results that are not statistically significant or have been previously published may be less likely to be published). Statistical tests for publication bias in the meta-analysis were not significant; however, such an analysis has a limited role given that we excluded more studies than we included, and it is important to appraise the totality of the evidence available, which transcends the pooled analysis of cross-sectional studies of individually variable quality. Notably, most of the studies that were not included in the meta-analysis were not included because of differences in measurement of exposure and/or outcome or failure to perform a multivariate analysis. We do not consider that the results of such cross-sectional studies differed greatly from the studies included in the meta-analysis; however, this may be different from the results of unpublished studies assessing this relationship.

Our overall findings from observational epidemiologic studies suggest that increasing time outdoors may be associated with a reduced risk of myopia and myopic progression. Therefore, our evaluation suggests a need for well-designed RCTs to investigate the effect of increasing time spent outdoors as a possible intervention to prevent the development of myopia and myopic progression in children and adolescents. Because it may not be ethical to conduct long-term RCTs, prospective cohort studies may also have an important role. Results of such studies will then allow a better picture of the possibility and feasibility of increasing time spent outdoors being used as a potential preventative strategy. At the time of the final literature search, only 1 RCT had been completed, suggesting that increasing time outdoors significantly reduced myopic progression.³⁶ However, the difference between the intervention and control groups was only modest and may not be clinically signifi-

cant. Our finding that increasing time outdoors is protectively associated with myopia in the meta-analysis, as well as the results from the other observational studies in the systematic review, support the results from this RCT.

Upcoming RCTs will afford the opportunity to answer several important questions. First, does increasing time outdoors prevent myopia and its progression? If increased time outdoors is shown to be an efficacious intervention, is the effect the same or different among children of different ages, ethnicities/populations, and environments (e.g., rural vs urban)? Is the effect the same or different according to family/genetic history of myopia or levels of near work? Such studies may have different lengths of follow-up and times at which the effect of the intervention is maximal. As the increased risk of blindness and visual impairment is typically, but not universally, limited to those with high myopia, knowledge of whether increasing time outdoors would reduce myopic progression even in high myopes (and incidence of ocular complications) is paramount.

Upcoming studies may wish to include a more objective definition of time spent outdoors and possibly biomarkers of outdoor exposure such as vitamin D or conjunctival ultraviolet autofluorescence.^{44,45} Alternatively, the use of subjective methods such as diaries, pager contact, or the experience sampling method⁴⁶ are preferred because they are less susceptible to reporting bias than standard questionnaires. Two clinical trials (identifiers NCR00848900 and NCT01388205) investigating physical activity, time spent outdoors, and myopia are currently registered at www.clinicaltrials.gov. Results from these studies, and others planned, will provide further answers about the relationship between time spent outdoors and myopia.

There are a myriad of possible mechanisms by which spending time outdoors may protect against the development and progression of myopia. They include increased release of retinal dopamine in response to sunlight (dopamine inhibits axial elongation in experimental myopia,⁴⁷ and the protective effect can be blocked by the dopamine antagonist spiperone⁴⁸), increased light intensity outdoors²⁸ (leading to pupil constriction, increasing depth of focus, decreasing blur, and slowing of eye growth), and the low accommodative demand for distance vision.²³ A further, but less likely, consideration is that increased time spent outdoors prohibits time spent on near work, resulting in a substitution effect.²⁸ It may also be the spectral composition of light, and not its intensity, that may be associated with a longer axial length and more myopia.⁴⁹ Despite a genetic basis,⁵⁰ current evidence suggesting a role for vitamin D in myopia pathogenesis is weak.⁵¹ It has also been proposed that insufficient ultraviolet radiation may be involved,⁵² although bright light has been shown to be protective of myopia in animal experiments using ultraviolet-free light.⁴⁸ Because there is no protective association between indoor sports and myopia,^{21,28} unlike outdoor sports, it suggests that physical activity may be a surrogate for outdoor activity. This is supported by a cohort study with 2 years of follow-up in 156 university students where physical activity time was higher in nonmyopes and associated with hyperopic refraction (0.175 D per hour of physical activity per day; $P = 0.015$) after adjustment for potential confounders,

although there were no differences in objectively measured physical fitness levels between myopes and nonmyopes ($P = 0.321$).

A precise understanding of the risk factors for myopia and its progression is required to implement strategies targeting the current and projected rise of myopia in the ensuing years. Findings from our systematic review and meta-analysis indicate that increasing time outdoors may be protective of prevalent and incident myopia and myopic progression. Consequently, there is a need for further study of this exposure–disease association in additional RCTs looking at incidence of myopia and myopic progression as primary endpoints.

Acknowledgments. The authors thank Isla Kuhn (Reader Services Librarian, University of Cambridge Medical Library) for assistance with the search strategy.

References

- Morgan I, Rose K. How genetic is school myopia? *Prog Retin Eye Res* 2005;24:1–38.
- Saw SM, Katz J, Schein OD, et al. Epidemiology of myopia. *Epidemiol Rev* 1996;18:175–87.
- Jeganathan VES, Saw SM, Wong TY. Ocular morbidity of pathological myopia. In: Beuerman RW, Saw SM, Tan DHH, Wong TY, eds. *Myopia: Animal Models to Clinical Trials*. Singapore: World Scientific; 2011.
- Morgan RW, Speakman JS, Grimshaw SE. Inuit myopia: an environmentally induced “epidemic”? *Can Med Assoc J* 1975;112:575–7.
- Johnson GJ, Matthews A, Perkins ES. Survey of ophthalmic conditions in a Labrador community. I. Refractive errors. *Br J Ophthalmol* 1979;63:440–8.
- Daubs J. Environmental factors in the epidemiology of malignant myopia. *Am J Optom Physiol Opt* 1982;59:271–7.
- Young TL, Metlapally R, Shay AE. Complex trait genetics of refractive error. *Arch Ophthalmol* 2007;125:38–48.
- Rose KA, Morgan IG, Smith W, Mitchell P. High heritability of myopia does not preclude rapid changes in prevalence. *Clin Experiment Ophthalmol* 2002;30:168–72.
- Greenland S, O’Rourke K. Meta-analysis. In: Rothman KJ, Greenland S, Lash TL, eds. *Modern Epidemiology*, 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:652–82.
- Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12.
- Sanderson S, Tatt ID, Higgins JP. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. *Int J Epidemiol* 2007;36:666–76.
- Chinn S. A simple method for converting an odds ratio to effect size for use in meta-analysis. *Stat Med* 2000;19:3127–31.
- Higgins JP, Thompson SG, Spiegelhalter DJ. A re-evaluation of random-effects meta-analysis. *J R Stat Soc Ser A Stat Soc* 2009;172:137–59.
- DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177–88.
- Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539–58.
- Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994;50:1088–101.
- Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
- Low W, Dirani M, Gazzard G, et al. Family history, near work, outdoor activity, and myopia in Singapore Chinese preschool children. *Br J Ophthalmol* 2010;94:1012–6.
- Ip JM, Saw SM, Rose KA, et al. Role of near work in myopia: findings in a sample of Australian school children. *Invest Ophthalmol Vis Sci* 2008;49:2903–10.
- Khader YS, Batayha WQ, Abdul-Aziz SM, Al-Shiekh-Khalil MI. Prevalence and risk indicators of myopia among school-children in Amman, Jordan. *East Mediterr Health J* 2006;12:434–9.
- Dirani M, Tong L, Gazzard G, et al. Outdoor activity and myopia in Singapore teenage children. *Br J Ophthalmol* 2009;93:997–1000.
- Lu B, Congdon N, Liu X, et al. Associations between near work, outdoor activity, and myopia among adolescent students in rural China: the Xichang Pediatric Refractive Error Study report no. 2. *Arch Ophthalmol* 2009;127:769–75.
- Deng L, Gwiazda J, Thorn F. Children’s refractions and visual activities in the school year and summer. *Optom Vis Sci* 2010;87:406–13.
- Mutti DO, Mitchell GL, Moeschberger ML, et al. Parental myopia, near work, school achievement, and children’s refractive error. *Invest Ophthalmol Vis Sci* 2002;43:3633–40.
- Wu PC, Tsai CL, Hu CH, Yang YH. Effects of outdoor activities on myopia among rural school children in Taiwan. *Ophthalmic Epidemiol* 2010;17:338–42.
- Saw SM, Hong RZ, Zhang MZ, et al. Near-work activity and myopia in rural and urban schoolchildren in China. *J Pediatr Ophthalmol Strabismus* 2001;38:149–55.
- Tan GJ, Ng YP, Lim YC, et al. Cross-sectional study of near-work and myopia in kindergarten children in Singapore. *Ann Acad Med Singapore* 2000;29:740–4.
- Rose KA, Morgan IG, Ip J, et al. Outdoor activity reduces the prevalence of myopia in children. *Ophthalmology* 2008;115:1279–85.
- Zhang M, Li L, Chen L, et al. Population density and refractive error among Chinese children. *Invest Ophthalmol Vis Sci* 2010;51:4969–76.
- Saw SM, Zhang MZ, Hong RZ, et al. Near-work activity, night-lights, and myopia in the Singapore-China study. *Arch Ophthalmol* 2002;120:620–7.
- Rose KA, Morgan IG, Smith W, et al. Myopia, lifestyle, and schooling in students of Chinese ethnicity in Singapore and Sydney. *Arch Ophthalmol* 2008;126:527–30.
- Ma M, Zhang Z, Song J, et al. [An epidemiological survey of refractive error and associated factors among middle school students in Deqing County of Zhejiang Province, China.] *Fudan University Journal of Medical Sciences* 2010;37:680–4.
- Jones LA, Sinnott LT, Mutti DO, et al. Parental history of myopia, sports and outdoor activities, and future myopia. *Invest Ophthalmol Vis Sci* 2007;48:3524–32.
- Onal S, Toker E, Akingol Z, et al. Refractive errors of medical students in Turkey: one year follow-up of refraction and biometry. *Optom Vis Sci* 2007;84:175–80.
- Saw SM, Shankar A, Tan SB, et al. A cohort study of incident myopia in Singaporean children. *Invest Ophthalmol Vis Sci* 2006;47:1839–44.
- Yi JH, Li RR. Influence of near-work and outdoor activities on myopia progression in school children [Chinese]. *Chinese J Contemp Pediatr* 2011;13:32–5.

37. Parssinen O, Lyyra AL. Myopia and myopic progression among schoolchildren: a three-year follow-up study. *Invest Ophthalmol Vis Sci* 1993;34:2794–802.
38. Saw SM, Nieto FJ, Katz J, et al. Factors related to the progression of myopia in Singaporean children. *Optom Vis Sci* 2000;77:549–54.
39. Young FA, Singer RM, Foster D. The psychological differentiation of male myopes and nonmyopes. *Am J Optom Physiol Opt* 1975;52:679–86.
40. Ip JM, Rose KA, Morgan IG, et al. Myopia and the urban environment: findings in a sample of 12-year-old Australian school children. *Invest Ophthalmol Vis Sci* 2008;49:3858–63.
41. Cheng D, Schmid KL, Woo GC. Myopia prevalence in Chinese-Canadian children in an optometric practice. *Optom Vis Sci* 2007;84:21–32.
42. Guggenheim JA, Pong-Wong R, Haley CS, et al. Correlations in refractive errors between siblings in the Singapore Cohort Study of Risk factors for Myopia. *Br J Ophthalmol* 2007;91:781–4.
43. Sutton AJ, Duval SJ, Tweedie RL, et al. Empirical assessment of effect of publication bias on meta-analyses. *BMJ* 2000;320:1574–7.
44. Sherwin JC, McKnight CM, Hewitt AW, et al. Reliability and validity of conjunctival ultraviolet autofluorescence measurement. *Br J Ophthalmol* 2012;96:801–5.
45. Sherwin JC, Hewitt AW, Kearns LS, et al. Distribution of conjunctival ultraviolet autofluorescence in a population-based study: the Norfolk Island Eye Study. *Eye (Lond)* 2011;25:893–900.
46. Rah MJ, Walline JJ, Lynn Mitchell G, Zadnik K. Comparison of the experience sampling method and questionnaires to assess visual activities in pre-teen and adolescent children. *Ophthalmic Physiol Opt* 2006;26:483–9.
47. McCarthy CS, Megaw P, Devadas M, Morgan IG. Dopaminergic agents affect the ability of brief periods of normal vision to prevent form-deprivation myopia. *Exp Eye Res* 2007;84:100–7.
48. Ashby RS, Schaeffel F. The effect of bright light on lens compensation in chicks. *Invest Ophthalmol Vis Sci* 2010;51:5247–53.
49. Mehdizadeh M, Nowroozzadeh MH. Outdoor activity and myopia. *Ophthalmology* 2009;116:1229–30; author reply 30.
50. Mutti DO, Cooper ME, Dragan E, et al. Vitamin D receptor (VDR) and group-specific component (GC, vitamin D-binding protein) polymorphisms in myopia. *Invest Ophthalmol Vis Sci* 2011;52:3818–24.
51. Mutti DO, Marks AR. Blood levels of vitamin D in teens and young adults with myopia. *Optom Vis Sci* 2011;88:377–82.
52. Prepas SB. Light, literacy and the absence of ultraviolet radiation in the development of myopia. *Med Hypotheses* 2008;70:635–7.
53. Jones-Jordan LA, Mitchell GL, Cotter SA, et al. Visual activity before and after the onset of juvenile myopia. *Invest Ophthalmol Vis Sci* 2011;52:1841–50.
54. Peckham CS, Gardiner PA, Goldstein H. Acquired myopia in 11-year-old children. *Br Med J* 1977;1:542–5.

Footnotes and Financial Disclosures

Originally received: May 19, 2011.

Final revision: April 3, 2012.

Accepted: April 17, 2012.

Available online: ●●●.

Manuscript no. 2011-751.

¹ Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK.

² Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, University of Melbourne, Department of Ophthalmology, Melbourne, Australia.

³ MRC Biostatistics Unit, Institute of Public Health, University Forvie Site, Cambridge, UK.

⁴ Department of Ophthalmology, Royal Hobart Hospital, University of Tasmania, Hobart, Tasmania, Australia.

⁵ Centre for Ophthalmology and Visual Science, University of Western Australia, Lions Eye Institute, Perth, Australia.

⁶ Division of Genetics & Epidemiology, UCL Institute of Ophthalmology, University College London, London, UK.

⁷ National Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital, London, UK.

Presented at: the 2011 American Academy of Ophthalmology Meeting, Orlando, FL (11-PP-30028853-AAO).

Financial Disclosure(s):

The authors have no proprietary or commercial interest in any of the materials discussed in this article.

Supported by the Centre for Eye Research Australia (CERA) (D.A.M. and J.C.S.) receives Operational Infrastructure Support from the Victorian Government. D.A.M. is a recipient of the Pfizer Australia Senior Research Fellowship.

Correspondence:

Justin C. Sherwin, Department of Public Health and Primary Care, Institute of Public Health, University of Cambridge, Forvie Site, Robinson Way, Cambridge CB2 0SR, UK. E-mail: justinsherwin@gmail.com.