Time Outdoors and Physical Activity as Predictors of Incident Myopia in Childhood: A Prospective Cohort Study

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Purpose. Time spent in "sports/outdoor activity" has shown a negative association with incident myopia during childhood. We investigated the association of incident myopia with time spent outdoors and physical activity separately.

Methods. Participants in the Avon Longitudinal Study of Parents and Children (ALSPAC) were assessed by noncycloplegic autorefraction at ages 7, 10, 11, 12, and 15 years, and classified as myopic (≤ -1 diopters) or as emmetropic/hyperopic (≥ -0.25 diopters) at each visit ($N = 4{,}837$–$7{,}747$). Physical activity at age 11 years was measured objectively using an accelerometer, worn for 1 week. Time spent outdoors was assessed via a parental questionnaire administered when children were aged 8–9 years. Variables associated with incident myopia were examined using Cox regression.

Results. In analyses using all available data, both time spent outdoors and physical activity were associated with incident myopia, with time outdoors having the larger effect. The results were similar for analyses restricted to children classified as either nonmyopic or emmetropic/hyperopic at age 11 years. Thus, for children nonmyopic at age 11, the hazard ratio (95% confidence interval, CI) for incident myopia was 0.66 (0.47–0.93) for a high versus low amount of time spent outdoors, and 0.87 (0.76–0.99) per unit standard deviation above average increase in moderate/vigorous physical activity.

Conclusion. Time spent outdoors was predictive of incident myopia independently of physical activity level. The greater association observed for time outdoors suggests that the previously reported link between "sports/outdoor activity" and incident myopia is due mainly to its capture of information relating to time outdoors rather than physical activity. (*Invest Ophthalmol Vis Sci.* 2012;53:2856–2865) DOI:10.1167/iovs.11-9091

Myopia arises from a mismatch between the axial length of the eye and the focal power of its refractive elements, the cornea and crystalline lens. This produces blurred distance vision that requires the use of spectacles, contact lenses or refractive surgery for correction. A high degree of myopia is associated with a number of sight-threatening pathologies.[1,2] Myopia is rare in infancy, but increases steadily in prevalence to affect approximately 25–50% of young adults in Western countries, and up to 80% of young adults in parts of South East Asia.[3,4]

Experiments in animals from a range of taxonomic orders, including primates, have shown that the visual environment can influence refractive development.[5–8] For instance, the deprivation of sharp vision ("form deprivation") induces axial myopia, as does the hyperopic defocus imposed by wearing a minus-power spectacle lens.[9,10] Genetic factors also have been shown to be important, because—at least in chickens—they are the major determinant of an individual animal's susceptibility to myopia induced by the visual environment.[11] The level of illumination during the day (and, indeed, the timing or complete absence of a light or dark phase) also can affect refractive development.[12–21]

Many studies in humans are consistent with the above findings (but not all,[22,23] perhaps due to the complexity of the visual environment). For example, a shift towards myopia has been observed during childhood in eyes exposed to form deprivation,[24] hyperopic defocus,[25–28] and specific alterations to daily illumination levels,[29–32] although some of the latter results appear not to generalize to the population at large.[33–35] Due to the high visual demands of reading, and the tendency for myopia to develop during the school years, the time children spend engaged in reading and other near work long has been considered as a potential contributor to myopia development, albeit with conflicting results.[36] Alongside near work, a number of more recent studies have documented a strong (negative) association between the amount of time children spend outdoors and their refractive error,[37–44] that is with myopia being more common in children who spend less time outdoors. However, like the association between time spent reading and myopia, this finding has not been observed universally either.[45–48]

Three of the studies whose findings support a negative association between time outdoors and myopia have been prospective in nature.[37,39,44] However, each of these studies have design features that complicate the interpretation of their findings. Pärssinen and Lyyra analyzed data from a randomized controlled trial (RCT) of an optical treatment for myopia in which boys, but not girls, who spent more time outdoors exhibited a slower rate of myopia progression.[37] Jones et al. found that the number of hours per week that children

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Table 1. Performance of Different Autorefraction "Cut-Points" in Identifying Subjects with a Subjective Refraction <-0.75D

Cut-Point	Sensitivity	Specificity	ROC Curve Area
Autorefraction <-0.75 D	0.92	0.84	0.88
Autorefraction <-1.00 D	0.91	0.92	0.92
Autorefraction <-1.25 D	0.83	0.97	0.90

The analysis was carried out for a sample of 344 children whose refractive error was assessed by noncycloplegic autorefraction at the 15-year clinic, and whose subjective refraction details (for an eye exam carried out within ±6 months of the clinic visit) were obtained from their optometrist, as described previously (McMahon G. The Genetics and Epidemiology of Myopia in the ALSPAC Cohort. School of Optometry & Vision Sciences. Cardiff, Wales: Cardiff University; 2010. Thesis).

engaged in parentally-reported "sports/outdoor activity" was predictive of incident myopia, with the degree of association varying with the number of parents with myopia, but not with the sex of the child.[39] An elegant, in-depth analysis of the data from the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) cohort carried out by Jones-Jordan et al. similarly reported that children who became myopic spent less time engaged in sports/outdoor activity during the years before their myopia onset than children who remained emmetropic.[44]

Generalization of the findings of Pärssinen and Lyyra[37] is limited by virtue of their RCT having been restricted to existing myopes, that is the results do not address the question of whether time spent outdoors is predictive of incident myopia. In contrast, the studies by Jones et al.[39] and Jones-Jordan et al.[44] provide clear evidence that time engaged in sports/outdoor activity is associated with incident myopia, but do not reveal whether it is being outdoors and/or engaging in physical activity that is predictive. The separation of the potential risks/benefits associated with time outdoors and engaging in physical activity is important, because physical activity is known to be predictive of myopia progression in young adults (medical students[49]), and myopic school children have been reported to engage in less physical activity than non-myopes.[50,51]

We analyzed data from a cohort for whom information on time spent outdoors and physical activity was available, allowing us to examine these exposures as separate predictive factors for incident myopia. Because time spent reading for pleasure has been shown previously to be associated with incident myopia at age 11 years in the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort,[52] we also considered this as a predictor of incident myopia at the later ages examined in our study.

METHODS

This was an opportunistic study, using a longitudinal data set that has been assembled as a resource for scientists investigating a wide range of topics within the biomedical and social sciences, called the ALSPAC birth cohort.[53]

Subjects

Pregnant women with an expected date of delivery between April 1, 1991 and December 31, 1992, resident in the former Avon health authority area in Southwest England, were eligible to participate in the study. A cohort of 14,541 pregnant women was established, resulting in 13,988 children who were alive at 12 months of age. Data collection has been via various methods, including self-completion questionnaires sent to the mother and her partner, and after age 5 to the child, as well as direct assessments and interviews in a research clinic, biological samples, and linkage to school and hospital records. Ethical approval for the study was obtained from the ALSPAC Law and Ethics committee and the three local research-ethics committees. This research adhered to the tenets of the Declaration of Helsinki.

Data Availability

Data on Outcome. All children still participating in ALSPAC were invited approximately yearly (starting at age 7 years) to sessions held at a central location, where a number of assessments and interviews took place. The nature of these assessments was different at different ages so as to try and cover key developmentally-appropriate topics and scientific priorities, but without overloading the participants (each assessment took 3–4 hours). Vision-related data were included in the assessments carried out at the 7-, 10-, 11-, 12-, and 15-year clinics, where refractive error was estimated by noncycloplegic autorefraction (Canon R50 instrument, Canon USA Inc., Lake Success, NY). We interpreted these data as screening for "likely myopia," rather than as a direct measure,[54,55] although for ease of reading in this study we refer to "myopia" and "incident myopia." After the removal of outlier readings, the mean spherical equivalent (MSE) refractive error was calculated as the autorefraction sphere power plus half of the cylinder power. At each of the 5 test ages, subjects were classified as myopic if the average of the MSEs in their right and left eyes was ≤ -1.00 diopter (D). Similarly, subjects were classified as emmetropic or hyperopic ("emmetropic/hyperopic") if the averaged MSE in their right and left eyes was ≥ -0.25 D. We selected the threshold of ≤ -1.00 D for detecting myopia, since for subjects aged 15 years this provided high sensitivity and specificity to detect individuals with a subjective refraction ≤ -0.75 D (Table 1), which corresponded to the criterion used to define myopia by Jones et al.[39] from their cycloplegic refraction measurements. We chose the ≥ -0.25 D threshold for detecting subjects who were emmetropic or hyperopic to match the value used by Jones-Jordan et al.[44]

Data on Exposures

Level of Physical Activity. Children attending the research clinic at age 11 years were asked to wear an Actigraph accelerometer (dimensions 45 × 35 × 10 mm, weight 43 g; model WAM 7164, Actigraph, Fort Walton Beach, FL) for the following 7 days, and return it by post in a prepaid envelope.[56] This type of accelerometer is worn at the right hip on an elasticized belt. Data from the returned accelerometers were downloaded and imported into a database. Children who did not provide at least 10 hours of valid data on at least 3 separate days were omitted from the analyses. Two physical activity variables were derived from the data[50,57]: Mean counts per min (CPM) for the whole week, and minutes of moderate to vigorous activity (MVPA) per day. Mean CPM for the whole week was used to estimate a child's total activity. It is likely that the accrued CPM will have been biased towards children who wore the monitor for longer but who not necessarily were more active. However, no adjustment was made for the duration of monitor wear to maintain consistency with previous work.[50] MVPA, which was defined as ≥3600 activity counts per minute,[58] was used to capture time engaged in active sports. In support of this reasoning, it has been reported that MVPA is associated more strongly with obesity than CPM.[59] Note, however, that time spent swimming would not have been captured by the activity monitors, as they would not have been worn for this pastime. Additionally, we also derived a variable representing sedentary behavior, as this has attracted increasing interest as a separate construct from physical activity (i.e., it is possible to meet recommendations for physical activity, yet spend large amounts of time sedentary) and may have independent associations with metabolic risk factors in children.[60] A lower threshold of 200 counts per minute was used to define sedentary time.[56]

Table 2. Subject Demographics

			Attended Research Clinic							
Research Clinic Visit	**Age Mean ± SD (Yrs.)**	**Sex (% Male)**	**Total**	**With Valid Refraction**	**With Valid Refraction and Full Covariate Information***	**Myopic at This Visit (%)**	**Myopic at Current or Any Preceding Visit (%)**	**Number of Myopic Parents (% 1/% 2)**	**Time Outdoors (% High)**	**Time Reading (% High)**
(age 7)	7.5 ± 0.3	50.6%	7747	7623	2929	188 (2.5%)	188 (2.5%)	40.9%/8.6%	90.7%	38.7%
(age 10)	10.6 ± 0.3	49.4%	7212	7095	3061	499 (7.0%)	542 (7.6%)	40.0%/8.7%	90.9%	38.8%
(age 11)	11.7 ± 0.2	49.1%	6499	6390	3025	561 (8.8%)	693 (10.8%)	40.1%/8.7%	90.8%	38.9%
(age 12)	12.8 ± 0.2	48.9%	6508	6394	2931	758 (11.9%)	931 (14.6%)	40.3%/8.7%	91.0%	39.4%
(age 15)	15.4 ± 0.3	47.1%	4837	4759	2363	821 (17.3%)	1030 (21.6%)	40.1%/9.1%	90.4%	41.1%

* For the predictor variables, number of myopic parents, time spent reading for pleasure, time spent outdoors, sex, and physical activity.

Time Spent Outdoors. When the study children were aged 8–9 years, a questionnaire was completed by their mother, which included four items asking, "On a (weekend day)/(school week day), how much time on average does your child spend each day out of doors in (summer)/(winter)." The response options for these questions were, "None at all," "1 hour," "1–2 hours," and "3 or more hours." Due to low numbers in some response categories for the 2 questions relating to time spent outdoors in *summer*, we classified children as either spending a "high" amount of time outdoors if the response was "3 or more hours," and as "low" otherwise. For the 2 questions relating to time spent outdoors in *winter*, we classified children as spending a "low" amount of time outdoors if the response was "None at all" or "1 hour," and as "high" otherwise. To avoid over-fitting models, we selected from the 4 time outdoors variables the one that displayed the strongest association with our outcomes of interest in univariate analyses. This was the variable corresponding to time spent outdoors on a weekend day in summer.

Potential Confounders. During pregnancy, each child's mother was asked to categorize her ethnicity as (using the groupings listed in the 1991 United Kingdom Census): white, black/Caribbean, black/African, black/other, Indian, Pakistani, Bangladeshi, Chinese, other. As approximately 98% of the responses to this question were "white," subjects whose mother categorized themselves as nonwhite were excluded due to the low numbers. Each subject's mother and her partner completed questionnaires that included the item, "How would you rate your sight without glasses?" The response options were, for each eye separately, "always very good," "can't see clearly at a distance," "can't see clearly close up," and "can't see much at all." Parents were classified as myopic if they answered "can't see clearly at a distance" for both eyes, and as nonmyopic otherwise. In the questionnaire completed by the mother when the study children were aged 8–9 years, they were asked, "On normal days in school holidays, how much time on average does your child spend each day reading books for pleasure," with response categories as for the time outdoors questions. Due to low numbers in the two extreme response categories for the first question, we classified children as either spending a "high" amount of time reading for pleasure if the response was "1–2 hours" or "3 or more hours," and as "low" otherwise.

Statistical Analysis

In an ideal setting, refractive information would have been collected for all participants at each exact target age during the 8-year period from age 7 to 15. In practice, many subjects missed one or more assessment sessions. The actual age for each child when they attended was recorded, and in several cases this was older than the expected age due to illness, holidays, and so forth. We used survival analysis to investigate which factors predicted the rate at which subjects became myopic within the cohort, as this allowed us to use all the data available despite some missing values.

We constructed a life table and used Kaplan-Meier plots for univariate analyses of the predictors of interest. We also used univariate and multivariate Cox regression models to observe the effect of adjusting the results for two predictors of interest (time outside and level of measured activity) for each other as well as for established predictors of myopia onset (number of myopic parents, sex, time spent reading for pleasure). These results are expressed as survival estimates, rate ratios, and hazard ratios with 95% confidence intervals (CI). Because we had only a single point estimate of time spent outdoors and of physical activity level during the observation period, we carried out secondary analyses to investigate whether these predictors remained associated with myopia development when considering only participants who became myopic after the potential risk/protective exposures were measured, namely between the 11- and 15-year clinics. We also used logistic regression to investigate factors predicting myopia onset after age 11, and we present these results as unadjusted and adjusted odds ratios (OR), respectively. The logistic regression analyses also were repeated after imputing missing values using the multiple imputation by chained equations (MICE) method.[61] Since the results were similar with and without imputation, only the nonimputed results are presented. Analyses were carried out using SPSS (v16.0.2 for Windows) and STATA/MP11.2 for Windows.

RESULTS

The subject demographics are presented in Table 2. Detailed illustrations depicting attendance of children across research clinic visits are shown in Figure S1 (Supplementary Information Online, http://www.iovs.org/lookup/suppl/doi:10.1167/iovs.11-9091/-/DCSupplemental). Overall, at least one refractive measure was available for 9109 children, of whom 1236 had myopia, giving a lower-bound myopia prevalence estimate of 13.6%. The first data point was for a child aged 6 and the latest for a child aged 17 years. The life table (Table 3) shows the ages at which myopia developed or the participants were last seen, and participants who were nonmyopic. These data also are presented in the form of a Kaplan-Meier survival curve in Figure 1, together with 95% CI for the survival curve. The 95% CI around the curve widened considerably after approximately 15½ years, corresponding to the marked reduction in subject numbers who were seen at older ages. These "stragglers" who had their assessments far later than planned may not be representative of the bulk of the participants.

Figure 2A shows the Kaplan-Meier curves for the two time outdoors groups (where "low" corresponds to <3 hours per day and "high" to 3+ hours per day, as reported by the mother for summer weekend days when the child was aged 8–9). Figures 2B–D show Kaplan-Meier curves for directly assessed physical activity/sedentary behavior at age 11, categorized as (1) CPM for the whole week, (2) minutes with sedentary counts, and (3) minutes with MVPA, respectively.

All of the aforementioned predictors were associated with the development of new cases of myopia. The rate ratio (RR,

TABLE 3. Life Table for Incident Myopia in ALSPAC Participants Who Attended One or More of the Assessment Clinics for 7, 10, 11, 12, and 15-Year-Olds

Age (Years)	Number Entering This Period of Observation	No. Became Myopic	No. Lost To Follow-Up	Remaining Participants Who Are Nonmyopic (%)	95% CI For Percentage Remaining Nonmyopic
6–7	9109	0	1	100.0	-
7–8	9109	72	929	99.2	99.0 to 99.3
8–9	8107	4	85	99.1	98.9 to 99.3
9–10	8018	2	22	99.1	98.9 to 99.3
10–11	7994	238	454	96.1	95.6 to 96.5
11–12	7302	132	570	94.3	93.7 to 94.8
12–13	6600	192	1517	91.2	90.5 to 91.8
13–14	4891	50	471	90.2	89.4 to 90.8
14–15	4370	5	18	90.1	89.3 to 90.8
15–16	4347	505	3569	72.3	70.8 to 73.8
16–17	273	36	233	55.7	50.6 to 60.4
17–18	4	0	4	55.7	50.6 to 60.4

ratio of how quickly the event of interest occurs in one group compared to another across the whole time period; 95% CI) for children spending a high versus low amount of time outside was 0.67 (0.56–0.81, $P < 0.001$). The results for the 3 activity variables were: (1) RR = 0.87 (0.83–0.92, $P < 0.001$) for each quartile of mean CPM compared to the next, (2) RR = 1.15 (1.10–1.22, $P < 0.001$) for each quartile of sedentary time compared to the next, and (3) RR = 0.90 (0.85–0.96, $P < 0.017$) per quartile of minutes of MVPA.

To investigate which of these related factors had the most predictive power, we carried out Cox regressions, including time spent outdoors and each of the activity variables (coded as continuous variables). The results are shown in Table 4. In Model 1, a univariate analysis, only a single predictor was included, while in Model 2, the number of myopic parents, time spent reading (maternal report at age 8–9 years), and sex also were included. In Model 3, both time outdoors and one of the three physical activity variables were included, along with the number of myopic parents, time spent reading, and sex. In the univariate and multivariable models, greater time spent outdoors was associated with a lower risk of myopia, as were greater average levels of overall physical activity (CPM) and MVPA, while an increase in sedentary time was associated with an increased risk of myopia development. The change in the physical activity hazard ratios (HR) was minimal after adjustment for time spent outdoors (Table 4), while the HR for time outdoors changed from 0.70 to 0.76 after adjusting for physical activity, corresponding to a reduction in effect size of approximately 10%. Table 5 shows the survival analysis results considering incident myopia developing after age 11, the age at which physical activity was assessed. The hours for time outdoors and the physical activity/sedentary behavior variables were similar to those in the analysis of all subjects (Table 4).

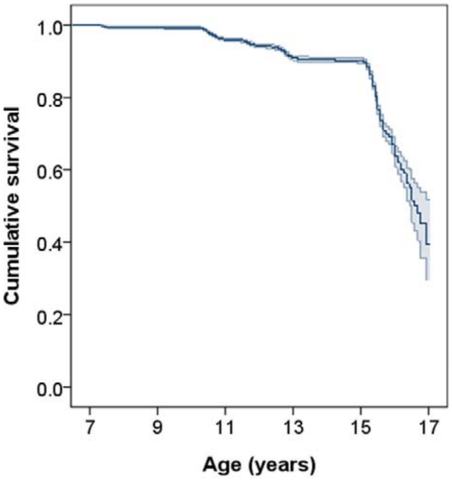

FIGURE 1. Kaplan-Meier survival curve for full dataset ($N = 9109$). The shaded region shows the 95% CI. Note the widening of the 95% CI beyond the age of 15 years, due to markedly reduced subject number for this period.

A set of logistic regression analyses also were carried out, again being restricted to children who were nonmyopic at age 11 (Table 6). There were 2005 such children with complete information on predictor variables, and who either were seen at the age 15-year clinic or who already were known to have become myopic when they attended the 12-year clinic (namely, 281 children who became myopic and 1724 who remained nonmyopic when seen at the 15-year clinic). Time spent outdoors (OR = 0.65, 95% CI 0.45–0.96) again was predictive, while there was less compelling evidence that this was the case for the three continuous variables representing physical activity/sedentary behavior (Table 6).

To confirm that our results were not influenced adversely by the misclassification of true myopes as nonmyopes, we carried out an additional set of analyses in which attention was restricted to children who were "emmetropic/hyperopic" at the 11-year clinic (Supplementary Tables S1 and S2). The risk/benefit associated with each predictor variable was similar in these restricted analyses, although the smaller sample size led to considerably wider confidence intervals.

Interestingly, our binary predictor variables time outdoors and time reading for pleasure were uncorrelated ($r = 0.01$, $P = 0.528$), suggesting that children who read for longer were equally likely to spend time outside as those who read less.

DISCUSSION

We used survival analysis to investigate whether time spent outdoors or time spent in physical activity was predictive of myopia development, using a multidisciplinary data set from a birth cohort study. We had available only single time-point estimates for the exposures of interest, whereas because these exposures are likely to vary across the time period, ideally we would have included data on outdoor exposure and physical activity measured at regular and frequent time-points. However, these were not available within the ALSPAC study. There is evidence that these behaviors track over time,[62,63] especially in the short-term, and so our single point estimates will have some association with the summed activity over the whole

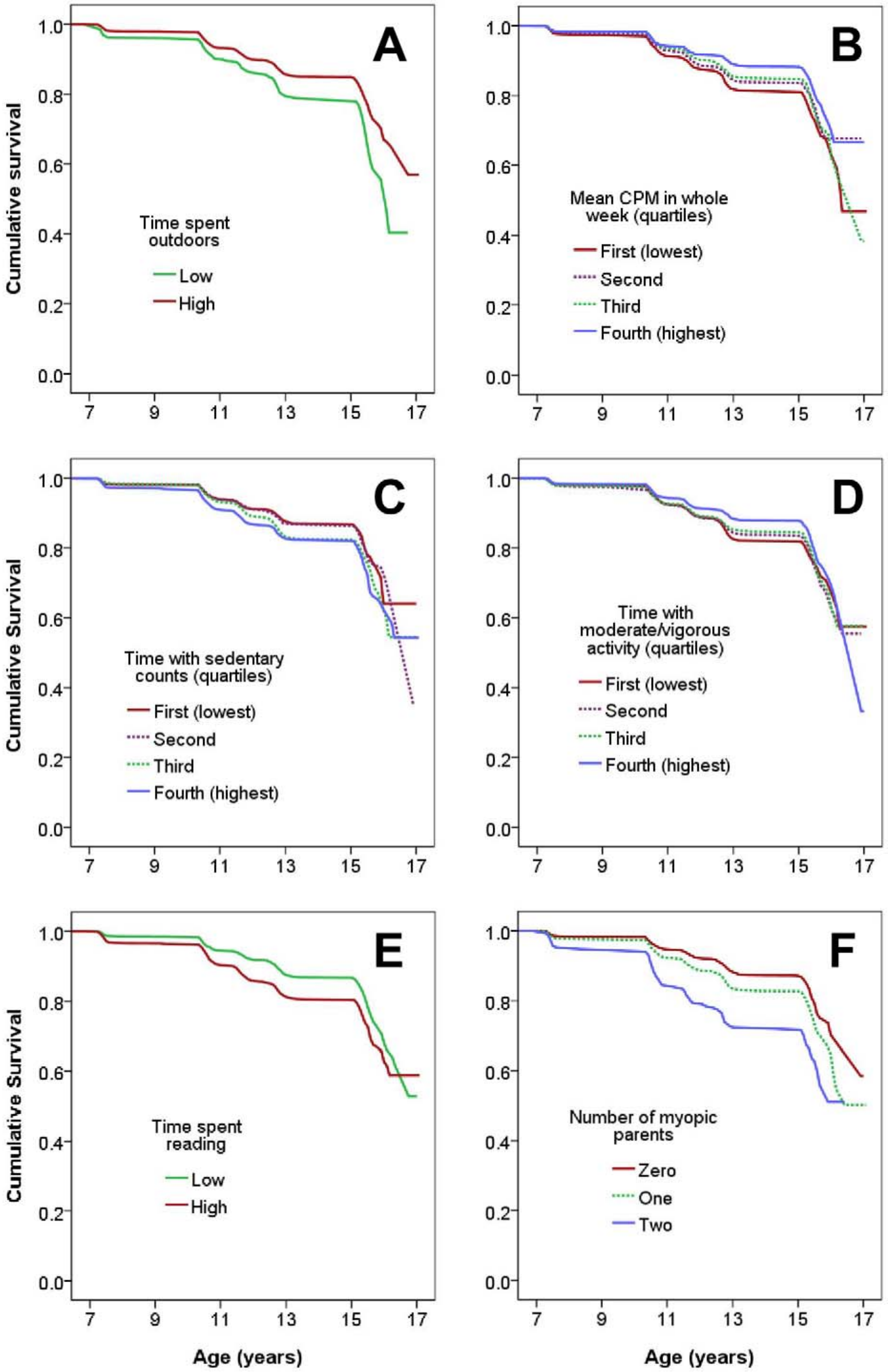

Figure 2. Kaplan-Meier survival curves for subgroups of children from the full dataset. Subjects were grouped according to: (**A**) Time spent outdoors ($N = 6961$). (**B**) Mean CPM physical activity in whole week ($N = 5733$). (**C**) Minutes with sedentary counts ($N = 5733$). (**D**) Minutes of moderate/vigorous physical activity ($N = 5733$). (**E**) Time spent reading ($N = 6947$). (**F**) Number of myopic parents ($N = 5675$).

time period. However, our analysis will not be as accurate as a more detailed data set would have been, resulting in some loss of power to detect associations.

To avoid reverse causation as an explanation for the link between our exposures of interest and incident myopia, we also used regression models that included only children in whom myopia developed only after the exposure data had been ascertained.

Despite its shortcomings, the questionnaire item on time spent outdoors was strongly predictive of incident myopia. Children classified as spending a "low" amount of time outdoors at age 8–9 years were (after converting from ORs to relative risks[64]) about 40% more likely to have myopia between the ages of 11 to 15 years, compared to those classified as spending a "high" amount of time outdoors. Physical activity was measured immediately after the refractive assessment at age 11, using an objective, quantitative monitoring device. Regardless of these favorable measurement attributes, there was more limited evidence for an association between physical activity and myopia onset after age 11. Moreover, the risk

Table 4. Cox Regression Analyses for Incident Myopia

	Model 1* ($N \geq 5733$)			Model 2† ($N \geq 3266$)			Model 3‡ ($N = 3241$)		
Predictor	**HR**	**95% CI**	***P* Value**	**HR**	**95% CI**	***P* Value**	**HR**	**95% CI**	***P* Value**
Time outdoors	0.66	0.56 to 0.78	<0.001	0.70	0.57 to 0.85	<0.001	0.76	0.60 to 0.96	0.023
Mean CPM	0.85	0.80 to 0.90	<0.001	0.86	0.80 to 0.94	<0.001	0.87	0.80 to 0.95	0.001
Sedentary time	1.17	1.10 to 1.24	<0.001	1.14	1.05 to 1.23	0.001	1.13	1.04 to 1.22	0.003
Time with MVPA	0.91	0.85 to 0.96	0.001	0.90	0.83 to 0.98	0.017	0.91	0.84 to 0.99	0.025

The predictor variable time spent outside was coded as "low" versus "high." The three physical activity/sedentary behavior variables were coded as standardized continuous values (mean zero, SD 1).

* Model 1 included only the predictor variable listed (univariate analysis).

† Model 2 included the predictors: number of myopic parents, time spent reading, sex, and the predictor listed.

‡ Model 3 included the variables in Model 2 plus time outdoors and, when time outdoors was the predictor listed, mean CPM (note the results were almost identical when one of the other two physical activity variables was used in place of mean CPM).

associated with different physical activity levels was modest. Children with a 1 SD below average increase in general physical activity (mean CPM) or MVPA were approximately 10% more likely to have myopia by the age of 15, as were children with a 1 SD above average increase in the time they spent being sedentary. Thus, our results suggested that time spent outdoors was a stronger predictor of incident myopia than time spent playing sports.

Our findings for time spent outdoors are qualitatively similar to those of Jones et al., who reported an OR = 0.91 (95% CI 0.87–0.94) for a parental questionnaire item ascertaining hours per week of sports/outdoor activity in 514 children aged 8–9 years, 111 of whom became myopic by the age of 13–14 years.[39] Children who remained nonmyopic engaged in an average of 11½ hours per week of sports/outdoor activity, compared to 8 hours per week in children with incident myopia. Our results also are consistent with the findings of Jones-Jordan et al.,[44] who followed the refractive development of a cohort of children aged 6–14 years, of whom 731 became myopic and 587 remained emmetropic. Subjects with incident myopia spent 10–20% less time engaged in parentally-reported sports/outdoor activity during each of the 4 years before myopia onset, and continued to spend a similarly lower amount of time in sports/outdoor activity after myopia onset. Our results suggested that it is the outdoor element of the "sports/outdoor activity" questionnaire response that is likely to have had the major predictive capacity in the studies of Jones et al.[39] and Jones-Jordan et al.[44]

For ALSPAC participants, time spent reading for pleasure also was associated with incident myopia, in keeping with a

Table 5. Prediction of Incident Myopia: Cox Regression Analysis Restricted to Children Who Were Nonmyopic at Age 11 ($N = 2542$)

Variable	HR	95% CI	*P* Value
Analysis 5a			
No. myopic parents			0.490
0 vs. 1 myopic parent	1.160	0.907 to 1.483	0.238
0 vs. 2 myopic parents	1.116	0.727 to 1.711	0.616
Time reading (low/high)	1.213	0.957 to 1.538	0.110
Time outdoors (low/high)	0.661	0.469 to 0.931	0.018
Sex (male/female)	1.042	0.816 to 1.332	0.740
Mean CPM for whole week (normal score)	0.877	0.772 to 0.996	0.043
Analysis 5b			
No. myopic parents			0.478
0 vs. 1 myopic parent	1.164	0.910 to 1.489	0.226
0 vs. 2 myopic parents	1.100	0.718 to 1.688	0.661
Time reading (low/high)	1.210	0.954 to 1.535	0.116
Time outdoors (low/high)	0.664	0.471 to 0.937	0.020
Sex (male/female)	1.095	0.863 to 1.390	0.455
Time with sedentary counts (normal score)	1.106	0.978 to 1.250	0.108
Analysis 5c			
No. myopic parents			0.500
0 vs. 1 myopic parent	1.157	0.904 to 1.479	0.246
0 vs. 2 myopic parents	1.118	0.729 to 1.715	0.609
Time reading (low/high)	1.222	0.964 to 1.549	0.098
Time outdoors (low/high)	0.657	0.466 to 0.926	0.016
Sex (male/female)	1.029	0.804 to 1.317	0.820
Time with MVPA (normal score)	0.868	0.764 to 0.987	0.031

Table 6. Prediction of Incident Myopia: Logistic Regression Analysis Restricted to Children Who Were Nonmyopic at Age 11 ($N = 2005$)

Variable	OR	95% CI	*P* Value
Analysis 6a			
No. myopic parents			0.481
0 vs. 1 myopic parent	1.175	0.900 to 1.533	0.236
0 vs. 2 myopic parents	1.143	0.718 to 1.818	0.574
Time reading (low/high)	1.323	1.023 to 1.712	0.033
Time outdoors (low/high)	0.653	0.446 to 0.958	0.029
Sex (male/female)	1.058	0.810 to 1.382	0.679
Mean CPM for whole week (normal score)	0.887	0.773 to 1.017	0.086
Constant	0.188		<0.001
Analysis 6b			
No. myopic parents			0.471
0 vs. 1 myopic parent	1.179	0.903 to 1.539	0.226
0 vs. 2 myopic parents	1.132	0.712 to 1.802	0.600
Time reading (low/high)	1.323	1.023 to 1.713	0.033
Time outdoors (low/high)	0.653	0.446 to 0.957	0.029
Sex (male/female)	1.110	0.857 to 1.437	0.429
Time with sedentary counts (normal score)	1.095	0.959 to 1.251	0.180
Constant	0.183		<0.001
Analysis 6c			
No. myopic parents			0.485
0 vs. 1 myopic parent	1.173	0.898 to 1.531	0.241
0 vs. 2 myopic parents	1.148	0.721 to 1.827	0.561
Time reading (low/high)	1.334	1.031 to 1.725	0.028
Time outdoors (low/high)	0.650	0.444 to 0.953	0.027
Sex (male/female)	1.043	0.797 to 1.366	0.759
Time with MVPA (normal score)	0.877	0.764 to 1.006	0.062
Constant	0.190		<0.001

number of prior studies,[37,65–69] but in contrast to the studies of Jones et al.[39] and Jones-Jordan et al.[44] Conversely, we found no evidence of a statistical interaction between time spent outdoors and the number of myopic parents in predicting incident myopia in the ALSPAC cohort (data not shown), unlike that observed by Jones et al.[39] We note also that not all studies have observed an association between time outdoors and incident myopia. In a cohort of children from Singapore ($N =$ 994), Saw et al. reported that the number of hours per week spent outdoors in games and activities was not predictive of myopia development (RR = 1.01; 95% CI 0.98 −1.04),[70] despite a weak association between these variables when they were examined concurrently.[42] One potential reason for the lack of association in the prospective study carried out in Singapore,[70] is that the prevalence of myopia had reached approximately 60% by the end of the study when the subjects still were only 10–12 years old (484 children already myopic at baseline, plus 454 incident myopes, in a total sample of 1478). This figure is much higher than the prevalence of myopia in the two previous US samples, and the UK ALSPAC subjects, suggesting that alternative environmental exposures might dominate any influence of time outdoors in children growing up in Singapore, or simply that there was too narrow a range of time spent outdoors between subjects to disclose an effect.

Limitations and Strengths of the Study

Our investigation had four main limitations. First, refractive error was measured infrequently, and by means of noncycloplegic autorefraction. Much greater precision in determining the exact time of myopia onset has been obtained in previous studies using annual cycloplegic autorefraction assessments.[44,70] Noncycloplegic autorefraction has relatively high sensitivity and specificity for detecting myopia in older children, but is likely to have led to a progressively greater proportion of nonmyopic subjects being classified wrongly as myopic at earlier ages, due to the tendency for younger subjects to accommodate more during the test.[55] However, we chose to maintain a consistent threshold (≤ -1.00 D) for classifying myopes, since this provided greater stringency in detecting, and thus excluding, children who already were myopic when we came to study incident myopia from the age of 11 years. In support of the validity of our myopia classification method, the risk of incident myopia was similar when we considered all subjects who were "nonmyopic" at age 11 years, and when we restricted our analysis to those categorized as "emmetropic/hyperopic" at this age. Second, we estimated time spent outdoors using a crude assessment method (parental questionnaire) administered at only a single time point. More frequent assessments,[44] and more precise, quantitative assessment methods[71,72] (Hewitt, A.J., et al. *IOVS* 2011;52:ARVO E-Abstract 1190) would provide the opportunity to quantify better the full extent of the association with time spent outdoors. Inaccurate parental questionnaire responses, or changes in the amount of time individual children spent outdoors over the period from age 11 to 15 years, would each act to lessen our statistical power to detect an association between time outdoors and myopia development, and cause us to underestimate this variable's effect size. Furthermore, our analyses relied on the assumption that children's prospectively measured exposures would tend to be consistent throughout the 11- to 15-year age interval of particular interest, in other words that a child's behavior would track forward, or that any causal effect associated with an exposure would occur after a delay that was within our 4-year follow-up period. Third, it was apparent that the subjects attending the research clinic at age 15 years were not a random sample of those attending the research clinic at age 11 years. Although the differences between the 15-year clinic attendees and nonattendees were small, they nevertheless limit the extent to which our results can be generalized more widely. Importantly, there also was substantial loss-to-followup over the 15+ years of the ALSPAC study. Coupled with the high rate of missing data for key predictor variables, this meant, for example, that only 2845 (Figure S1; Online) of the approximately 14,000 children who were alive at 1 year of age were available for inclusion in the analysis of incident myopia from the age of 11 years (note that of these, only the 2542 children not already myopic at age 11 years actually could be included). Because the relationship between time spent outdoors and myopia may have differed in the children who regularly attended clinics compared to those never/rarely attending, this is a further reason for caution in extrapolating from the observed results to the general population. This limitation relating to the sampling of subjects also is likely to apply to the other cohorts that have been used to examine the relationship between time outdoors and myopia. Indeed, since visual/refractive development is only one component of the ALSPAC study, it may be that our results are more representative than those obtained from cohorts whose sole purpose has been to study refractive development. Fourth, our study had a high rate of missing data for the key variables, parental myopia (31%), physical activity (14%), and time outdoors (12%). If these data were *not* missing-at-random, the fact that they were missing will have introduced bias into our results. This either could have strengthened or weakened the observed associations, depending on the relationships between data not missing-at-random compared to the data that were observed.

Nature of the Relationship Between Time Spent Outdoors and Myopia

RCTs are the ideal way to test whether the association between time spent outdoors and myopia onset/progression is causal in nature. To our knowledge, the results of only one such trial have been reported to date: The preliminary (1-year) findings from the Guangzhou Outdoor Activity Longitudinal (GOAL) study (Xiang F, et al. *IOVS* 2011;52:ARVO E-Abstract 3057). The intervention tested in the GOAL RCT was giving children ($N =$ 1789, age 6–7 years) 1 hour of additional time outdoors during each school day. Children receiving the intervention had less myopia (−0.25 ± 0.42 versus −0.34 ± 0.46 D) and less axial elongation (0.29 ± 0.18 versus 0.33 ± 0.23 mm) than controls, supporting a causal relationship. In other reports, the progression of myopia has been found to be slower during the summer than the winter,[73,74] and since children usually spend more time outdoors during the summer months, these results also are consistent with a causal relationship between time outdoors and incident myopia.

The nature of the relationship between time outdoors and myopia development has been considered widely.[39,41,44,48] Time outdoors does not seem to be a surrogate (reciprocal) variable for time spent reading since, except for one study in Taiwan,[43] it has been noted that children who spend longer time outdoors do not engage in less near work.[39,41,44,74] Accordingly, in ALSPAC participants, time outdoors and time reading for pleasure were uncorrelated. Instead, the high ambient light level encountered typically outdoors has received support as being a potential mediator of the effects attributable to time outdoors. In animal models, ambient light levels have been found to influence the rate of visually-induced form-deprivation myopia,[75,76] as well as the rate of compensation to monocularly-imposed myopic and hyperopic defocus.[20] The latter study suggests further that the effects of high ambient light levels are mediated by dopamine signalling, since administration of the D_2-receptor antagonist, spiperone, abolished differences in the rate of compensation to lens-induced defocus. Since the prevalence of myopia varies little across geographical latitudes that exhibit wide differences in day length and ambient light intensity,[31] it is likely that light levels regulate the eye's "gain" response to the visual cues that guide emmetropization rather than exerting a direct effect on eye growth. Additional experiments in animal models should prove useful in elucidating the range of light levels that offer most protection against myopic eye growth, and the daily duration of high intensity light that is required. Such research also should prove valuable in investigating the chronology of the exposure-effect relationship between high ambient lighting and refractive development. For instance, in a study of Turkish medical students, myopia progression was associated with (retrospectively surveyed) outdoor activity before or at the age of 7 years (OR = 0.44, 95% CI 0.23–0.82, in a multivariate analysis).[40] Assuming causality, this association between an exposure during childhood (lack of time outdoors) and myopia progression in early adulthood could represent a direct, but delayed, effect of time spent outdoors in childhood, or it may have resulted from greater myopic progression in early adulthood of individuals who started to develop myopia during their childhood. As well as the intensity of light differing between indoor and outdoor environments, the spectral composition of ambient lighting also has been posited as a potential reason for the association between time outdoors and myopia development.[77,78] Again, experiments in animal models should help to clarify this.[20,79] All of the aforementioned studies may be fruitful in informing the design of future studies of children.

In view of the quantitative nature of the physical activity/sedentary time assessments, and because they were ascertained at a time closer to the 11–15-year interval of particular interest, it is plausible that they captured information about the amount of time children spent outdoors over and above that captured by the binary variable derived from the mothers' questionnaire response. This means that the physical activity variables may have shown an association with incident myopia through their residual association with time outdoors (i.e., including the binary time spent outdoors variable in regression models would have been insufficient to control fully for its influence, hence allowing the physical activity variables to show association by virtue of their link to time spent outdoors). Alternatively, a causal relationship between physical activity and myopia onset also seems feasible, especially given the known links between eye growth, and glucose, glucagon, and insulin levels.[80–82]

CONCLUSION

In our prospective cohort study, greater time spent outdoors at age 8–9 years was associated with a reduced incidence of myopia development over the whole study period (ages 7–15 years), and specifically between the ages of 11 and 15 years. Time engaged in physical activity, which was assessed using a rigorous, quantitative method, also was associated with myopia onset, but to a lesser extent. Our findings support the preliminary results from the GOAL RCT, that spending a greater amount of time outdoors is partially protective against myopia development. Our results also suggest that any association between concurrently assessed refractive error and physical activity, such as that observed previously in the ALSPAC cohort,[50] may not be causal solely in the direction: *less physical activity → myopia*, but also in the direction: *myopia → less physical activity*, which, if true, is a nonvisual negative consequence of myopia deserving attention in its own right.

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