Early Childhood Refractive Error and Parental History of Myopia as Predictors of Myopia

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Purpose. To determine the utility of a child's first grade refractive error and parental history of myopia as predictors of myopia onset between the second and eighth grades.

Methods. Subjects were nonmyopic children in the first grade who were enrolled in the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study. Myopia was defined as −0.75 D or more myopia in both meridians (by cycloplegic autorefraction). The children were classified as having a high (versus low) risk of myopia with a cycloplegic sphere cutoff of +0.75 D or less (versus more) of hyperopia. Parental myopia was determined by a parent-completed survey. Discrete-time survival models predicted the risk of myopia.

Results. Of the 1854 nonmyopic first graders, 21.3% were at high risk of myopia. More high-risk subjects had two myopic parents, 25.4% compared with 16.5% in the low-risk group ($P < 0.0001$). The low-risk survival function was similar regardless of the number of myopic parents. Among high-risk eighth graders, the survival probability was lower than in the low-risk group, decreasing with an increase in the number of myopic parents. The sensitivity and specificity of first grade refractive error with the number of myopic parents as predictors for myopia onset were 62.5% and 81.9%, respectively.

Conclusions. First grade refractive error and the number of myopic parents can predict a child's risk of myopia; however, because the sensitivity of these factors is low, these two predictors may not be sufficient at this young age when a more accurate prediction of myopia onset is needed. (*Invest Ophthalmol Vis Sci.* 2010;51:115–121) DOI: 10.1167/iovs.08-3210

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Parental history of myopia has long been postulated to be an important risk factor for the development of myopia. The Orinda Longitudinal Study of Myopia (OLSM) showed an association between parental myopia and a child's refractive error and axial length before the onset of juvenile myopia.[1] Studies have shown a higher proportion of myopic children among families with two myopic parents compared with one- and no-myopic-parent families.[2–6] For example, Mutti et al.[4] found an odds ratio (OR) of 3.31 for myopia onset given one myopic parent compared with no myopic parents and an OR of 7.29 for myopia onset given two myopic parents compared with no myopic parents. In Singaporean children, Saw et al.[3] found an OR of 1.63 with either parent myopic and an OR of 1.70 with both parents myopic. Dirani et al.[7] provide a review of refractive error heritability in twins, reporting studies in which the heritability was lower than 0.25 in samples including children. Because children have not reached their final refractive error, measures of heritability may be affected by misclassification, perhaps reducing the level of heritability. Other studies have found higher heritability of refractive error in adult subjects or in age-matched subjects in twin studies.[8,9] Hammond et al.[8] found a heritability of myopia among adult twins of 0.90. Lyhne et al.[9] looked at refraction in twins 20 to 45 years of age and found a heritability between 0.89 and 0.94. These results all support some familial influence in the etiology of myopia.

Earlier work on predictors from the OLSM showed that the sphere component of the cycloplegic refractive error (in negative cylinder convention) in the third grade had 86.7% sensitivity and 73.3% specificity for the prediction of myopia by the eighth grade, with a cutoff point of +0.75 D or less hyperopia in initially nonmyopic children.[10] Earlier detection of the risk of onset of myopia may be desirable for a preventive intervention to be the most effective when applied over the longest time, beginning when differences between children who will become myopic and those who will not are small. Unfortunately, early detection may be difficult. Recent analyses suggest that differences between children who will become myopic and those who remain emmetropic appear only 3 to 4 years before onset.[11] Recent data from Gwiazda et al. (*IOVS* 2007;48:ARVO E-Abstract 2382) found that parental history of myopia and the refraction of 5-year-old subjects were predictive of development of myopia—a surprising result. In the present study, data from the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study were used to evaluate the refractive error of children in the first grade (average age, 6 years) and parental history of myopia as predictors of the onset of myopia by the eighth grade.

Methods

Data were drawn from the CLEERE Study, a multicenter, cohort study of school-aged children examined annually during school grades 1 through 8. Parents and children were provided an explanation of the study, and the parents provided written consent for their children. The children provided verbal assent. Data were collected at five clinical sites: Orinda, CA (University of California, Berkeley, 1989–2001); Eutaw, AL (University of Alabama, Birmingham, 1997–2006); Irvine, CA (Southern California College of Optometry, 1997–2006); Houston, TX (University of Houston, 1997–2006); and Tucson, AZ (University of Arizona, 2001–present). The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board at each clinical site. Children included in this analysis were first grade subjects examined between 1989 and 2005 who were nonmyopic in the right eye in the first grade and who had at least one additional examination each year in grades 2 through 8. Autorefraction was performed with two instruments (the R-1, Canon, Tokyo, Japan, from 1989 to 2000, and the WR-5100K, Takagi Seiko, Nagano, Japan from 2001 on). Myopia was defined as −0.75 D or more myopia in both the horizontal and vertical meridians measured by cycloplegic autorefraction in the right eye. Corneal anesthesia was used to minimize the discomfort from the cycloplegic drops. One drop of 0.5% proparacaine was followed by 2 drops of 1% tropicamide, 5 minutes apart, for cycloplegia in children with light irises (defined as grade 1 or 2 on the Seddon scale[12]). Children with dark irises received 1 drop of 0.5% proparacaine, 1 drop of 1.0% tropicamide, and 1 drop of 1.0% cyclopentolate. Ten measurements of refractive error were made 25 minutes after initial drop instillation. The average of these refractions was calculated by using the matrix method of Harris.[13]

A new case of myopia was defined when a subject had −0.75 D or more myopia measured in both meridians by cycloplegic autorefraction. This definition was chosen because −0.75 D of myopia is a clinically significant cutoff for providing a spectacle prescription, is likely to create symptoms of distance blur, and is beyond the measurement error of the autorefractors used to measure refractive error.[14]

Parents provided information on their own refractive error through a survey. Typically, one parent provided both parents' years of birth, whether they wore spectacles or contact lenses; the age when they were first prescribed spectacles if worn; and how they primarily used the spectacles at the time of the survey (for viewing at a distance, at near, or both). A parent was considered myopic if he or she used the spectacles primarily for distance or for both distance and near if the spectacles had first been prescribed before the parent was 17 years of age. This cutoff had a relatively high sensitivity and specificity (76% and 74%, respectively) in a validation study conducted by Walline et al.[15] The child's ethnic group designation was supplied by a parent on a medical history form containing six categories (based on the existing NIH categories): American Indian or Alaskan Native; Asian or Pacific Islander; black, not of Hispanic origin; Hispanic; white, not of Hispanic origin; and other or unknown.

Statistical Methods

Based on previous work,[10] children were classified into high- and low-risk myopia groups. High risk of myopia among nonmyopic children was defined as hyperopia of +0.75 D or less hyperopia in the cycloplegic sphere (in negative cylinder convention) in the first grade. Comparisons based on risk status and the number of myopic parents were made by using *t*-tests for variables that were continuous (mean ± SD). For categorical variables, percentages within each group are presented. The Jonckheere-Terpstra nonparametric test was used to test whether the relation between risk status and number of myopic parents was ordered. Discrete-time survival models were fitted to predict the risk of myopia in grades 2 through 8 with adjustment for gender, site, and ethnicity.[16] The modeling accounted for the discrete nature of the visits, which were not exactly equally spaced but were roughly 1 year apart. The survival models also allowed for the inclusion of subjects who did not complete the entire study. In the discrete-time survival model, the log odds that myopia will occur in a given grade are assumed to be a linear function of the predictors. The predictors included the potential risk factors (i.e., the number of myopic parents and the first grade refractive error, as well as the control variables gender, site, and ethnicity). The discrete survival models produced hazard and survival probabilities. The hazard probability specifies the probability that a subject who survived to a specific time point (i.e., grade in school) without the onset of myopia will become myopic by the next grade. The survival function is the probability of surviving up to or reaching a specific time point without becoming myopic.

Additional models included axial length and diopter-hours, a cumulative near work exposure variable, as predictors. Diopter-hours is defined as 3 × reading for pleasure hours + 3 × studying hours + 2 × computer/video games hours + TV hours.[4]

Results

There were 2158 subjects without myopia at the first grade visit. Of these, 1968 (91.2%) had myopia data from both parents. Twenty-four (1.2%) subjects were excluded from the 1968, because they missed one or more visits preceding the myopia onset visit, thereby making the actual grade at onset unknown, and 90 (4.5%) subjects had no visit after the first grade, leaving a total sample of 1854 children. The mean (±SD) length of follow-up was 5.32 ± 1.84 years. Table 1 shows the number of subjects who were seen in each grade level. With time, the subject count decreased either because a subject experienced the event (myopia) and left the data set or because the subject had no more follow-up visits. Of the 1854 children in the sample, 334 had become myopic by grade 8.

Figure 1 shows modeled survival probability curves for no, one, and two myopic parents. The model that generated the curves used the number of myopic parents as a predictor and gender, site, and ethnicity as control variables. For a given grade, the height of a curve provides the estimated probability that an individual will not be myopic in that grade. As expected, the highest survival probability across all grades was for subjects who had no myopic parents, followed by one myopic parent, then two myopic parents.

Table 2 shows myopia risk status by the number of myopic parents. Overall, 21.3% of the first graders fell into the high-risk group characterized by +0.75 D or less hyperopia (cycloplegic sphere). Almost half of the low-risk subjects had no myopic parents, whereas 16.5% had two. Among the high-risk group, the percentage of children with two myopic parents was 25.4%. The Jonckheere-Terpstra test was used to test whether more myopic parents were associated with the high-risk classification. The test of no association was rejected ($P < 0.0001$), indicating that the chance of a child being in the high-risk group increased with the number of myopic parents.

Table 1. Number of Subjects Examined in Each Grade

	Grade							
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Subjects, *n*	1854	1854	1723	1590	1341	1124	844	599

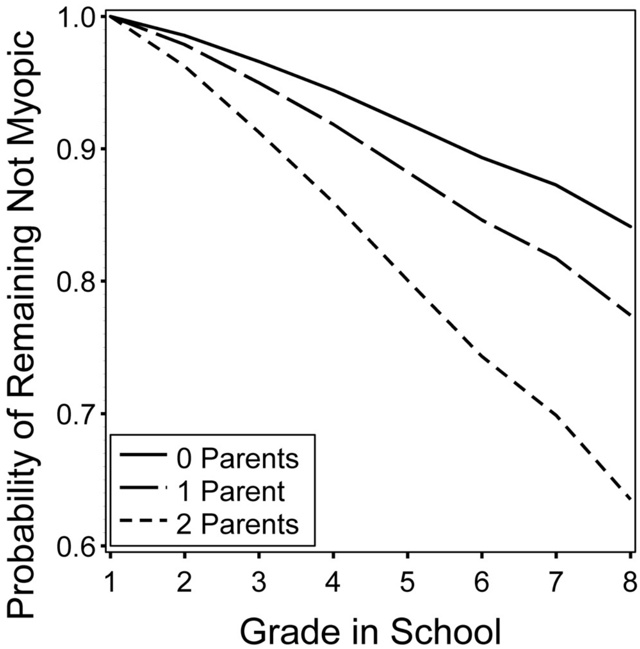

FIGURE 1. Survival curves for remaining nonmyopic by number of myopic parents.

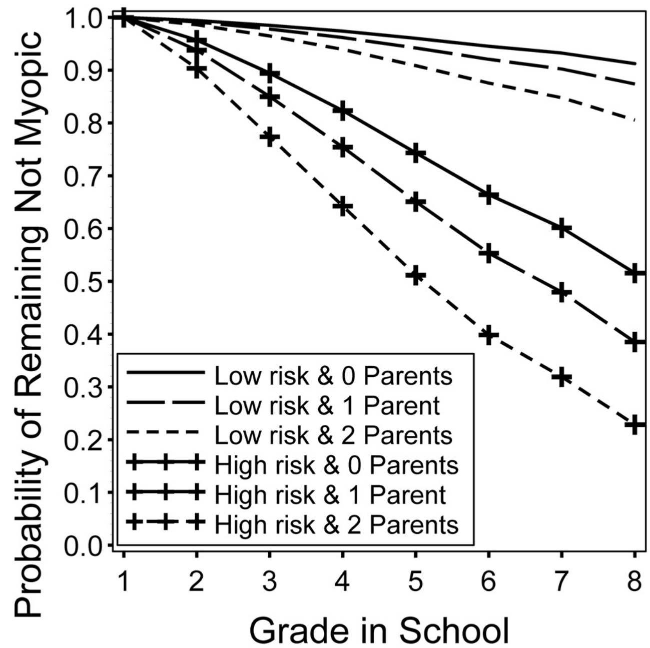

FIGURE 2. Survival probabilities for remaining nonmyopic by risk status and number of myopic parents.

Figure 2 shows survival probability curves for no, one, and two myopic parents as a function of risk group. The model that generated the survival function probabilities added the predictor myopia risk group to the model associated with Figure 1. Across grade levels for low-risk children, the survival functions remained fairly constant. Table 3 presents the estimated hazard ratio (HR) results for the development of myopia over the course of the study as a function of first grade myopia risk category and number of myopic parents. The HR for the development of myopia given the high-risk category was 7.56 (95% confidence interval [CI], 5.94–9.63; $P < 0.0001$). The HR differed between one and no myopic parents when adjusted for risk category ($P = 0.01$). The HR comparing subjects who had one or two myopic parents was also statistically significant (HR, 1.61; 95% CI, 1.18–2.21; $P = 0.003$). Children of two myopic parents had an increased HR of eventual myopia compared with children who had no myopic parents (HR, 2.38; 95% CI, 1.66–3.41; $P < 0.0001$). In a model adding an interaction between the number of myopic parents and myopia risk group, the interaction was not statistically significant.

The hazard and survival probabilities are presented in Table 4 by first grade refractive error risk status and the number of myopic parents. The statistically significant HR for two myopic parents compared to one or no myopic parents had little net effect, given the high survival rate for the low-risk group. Several features were noted in the high-risk group. The hazard probabilities were similar among those with no or one myopic parent and increased in children with two myopic parents. The chance of survival in the high-risk group, regardless of the number of myopic parents, was notably lower than that in the low-risk group, consistent with the large HR associated with risk group status.

Among those subjects who became myopic, 46.4% had myopic mothers and 38.3% had myopic fathers. Among children who did not become myopic, 37.4% had myopic mothers and 33.4% had myopic fathers. For the myopic group, Table 5 presents summary statistics by parental myopia group. Both the mean age at myopia onset and the mean amount of refractive error at the final study visit were similar across groups categorized by the number of myopic parents. Age at myopia onset and amount of myopia at the final visit were compared among the 109 children who had only a myopic mother or only a myopic father, to examine parental gender effects in one-myopic-parent families. Both age at onset and amount of myopia at the final visit were similar among children with myopic mothers only and myopic fathers only.

Table 6 presents the observed sensitivity and specificity for subjects in the two extremes of the risk factors—that is, the subjects with neither risk factor versus the subjects with both risk factors. Of those who remained nonmyopic, 81.9% were classified as low risk with nonmyopic parents (specificity), whereas of those who became myopic, 62.5% were in the high-risk group with at least one myopic parent (sensitivity).

Analyses by ethnic group were also completed; however, the small number of subjects with first grade visits who also had two myopic parents made analyses inadvisable in all ethnic groups but whites and Asians. Asian subjects were seen at the

TABLE 2. Risk Status (High vs. Low Risk of Myopia) by Number of Myopic Parents

Risk Status	Myopic Parents, *n* (%) None	One	Two	*P*
Low	697 (47.7)	522 (35.8)	241 (16.5)	<0.0001*
High	140 (35.5)	154 (39.1)	100 (25.4)	

* *P* from Jonckheere-Terpstra test.

TABLE 3. Modeled Hazard Ratios for the Development of Myopia over the Course of the Study

Variable	HR (95% CI)	*P*
High risk versus low risk	7.56 (5.94–9.63)	<0.0001
One versus no myopic parents	1.48 (1.09–1.99)	0.01
Two versus no myopic parents	2.38 (1.66–3.41)	<0.0001
Two versus one myopic parent	1.61 (1.18–2.21)	0.003

Table 4. Model Estimates for Myopia Risk Group and Number of Myopic Parents

Risk Status	Myopic Parents	Hazard Probability	Survival Function
Low	None	0.022	0.91
Low	One	0.031	0.87
Low	Two	0.050	0.81
High	None	0.143	0.52
High	One	0.197	0.39
High	Two	0.284	0.23

Irvine and Orinda, California sites, whereas the white subjects were from Irvine and Orinda, California and Houston, Texas. The model estimates in Table 7 for Asians and whites are similar to those shown in Table 4 for the group in its entirety. The eighth grade hazard probabilities and the survival function probabilities are shown side by side for easy comparison. The subgroups' pattern was similar to the overall pattern, where the low-risk group had a higher survival probability across the number of myopic parents than did the high-risk group. Asian survival probabilities differed from white survival probabilities by various amounts in the two risk groups. In the low-risk group, the survival probabilities across the number of myopic parents differed by 0.18 to 0.24 between the two ethnicities, from no myopic parents to two myopic parents. In the high-risk group the difference in the survival probabilities differed by 0.40, 0.25, and 0.19 for the no-, one-, and two-myopic-parent subjects, respectively, with a survival probability for an Asian in the high-risk group with two myopic parents of 0.15.

Looking at age at onset by the Asian and white subgroups, there was a significant difference in mean age for Asians ($P = 0.02$), with the age at onset being 10.9 years in children with no myopic parents, 9.1 years in children with one myopic parent, and 9.9 years in children with two myopic parents. There was no significant difference in the age of whites at onset of myopia. There also was a significant difference in refractive error at the first grade visit associated with the number of myopic parents for Asians with myopia. Among Asian subjects, the mean spherical equivalent at the first grade visit was 0.61, 0.26, and 0.04 D, respectively, in children with no, one, or two myopic parents. Mean refractive error among the whites with myopia was not significantly different among subjects with a differing number of myopic parents.

Table 8 presents the HRs for the model shown in Table 3 with the addition of axial length and diopter-hours and sport/outdoor activities. Axial length in the first grade was associated with an HR of 1.51 (95% CI, 1.24–1.85), indicating that longer eyes in first grade increased the odds of development of myopia. Diopter-hours did not confer an increased risk of myopia. These two variables did little to affect the HRs for the risk of myopia (slightly decreased HRs) or number of myopic parents

Table 6. Proportion of Subjects who Became Myopic in Relation to Risk and Number of Parents

Child Became Myopic	Low-Risk Group and No Myopic Parents, *n* (%)	High-Risk Group and at Least One Myopic Parent, *n* (%)
No	628 (81.9)	139 (18.1)
Yes	69 (37.5)	115 (62.5)

(slightly increased HRs) shown in Table 3. The second model in Table 8 inserted sports/outdoor activity hours in place of diopter-hours. Although the HRs for risk of myopia and number of myopic parents changed little, there was a statistically significant HR for sports/outdoor activity hours (HR, 0.98; 95% CI, 0.96–0.99). The hazard probabilities and the survival function shown in Table 4 are updated in Table 9 with the addition of axial length and diopter-hours. Neither the hazard probabilities nor the survival function underwent meaningful change. As a measure of the robustness of the findings to different definitions, similar analyses were run with alternative definitions of myopia (−0.75 D spherical equivalent and −0.75 D in both meridians). Both alternative definitions produced results consistent with the results presented herein (data not shown).

Discussion

Premyopic refractive error data from third grade can predict myopia with good sensitivity and specificity.[10] Extending this prediction to first grade using the cutoff of +0.75 D or less hyperopia on cycloplegic sphere for high myopia risk and combining it with the number of myopic parents showed that the survival probability for remaining nonmyopic in the eighth grade among high-risk children with two myopic parents is only 23%. Modeling the relationship of the occurrence of myopia with risk group and myopic parents, however, did not show evidence of an interaction between risk based on first grade refractive error and the number of myopic parents. It appears that the amount of refractive error in the first grade does not vary with the number of myopic parents (i.e., the data do not indicate a different effect on first grade refractive error based on the number of myopic parents).

These results are similar to those of Gwiazda et al. (*IOVS* 2007;48:ARVO E-Abstract 2382), who evaluated parental myopia and child's refractive error at age 5 years as predictors of juvenile-onset myopia. They found an increased risk of myopia onset in children with two myopic parents and 5-year-old refractions less hyperopic than +0.75 D. They also found that the risk of myopia did not differ with respect to the number of myopic parents among those children who were low risk by virtue of their hyperopic refractive error at age 5 years.

Table 5. Characteristics of Child's Myopia in Relation to Parents' Myopia

	No Myopic Parents	One Myopic Parent	Two Myopic Parents	*P*
Age at onset, y	10.4 ± 1.8	10.3 ± 1.9	10.4 ± 1.9	0.91
Spherical equivalent at final visit, D	−2.3 ± 1.2	−2.5 ± 1.2	−2.6 ± 1.4	0.17
	Mother Myopic		**Father Myopic**	***P***
Age at onset, y	10.1 ± 1.9		10.6 ± 1.7	0.18
Spherical equivalent at final visit, D	−2.6 ± 1.3		−2.3 ± 1.1	0.22

Data are the mean ± SD.

Table 7. Model Estimates for Myopia Risk Group and Number of Myopic Parents

Risk Status	Myopic Parents (*n*)	Hazard Probability		Survival Function	
		Asian	White	Asian	White
Low	None	0.087	0.012	0.76	0.96
	One	0.094	0.022	0.74	0.92
	Two	0.148	0.041	0.61	0.85
High	None	0.293	0.080	0.33	0.73
	One	0.312	0.143	0.30	0.55
	Two	0.431	0.239	0.15	0.34

As has been shown before,[2–5] the risk of myopia increases with the number of myopic parents. Consistent with prior findings, we found risk differences between no versus two myopic parents, between one versus two myopic parents, and between no versus one myopic parent. Children of nonmyopic parents are the most likely to remain nonmyopic.

We have also controlled for myopic parents by placing the refractive error risk group in the model, as parentage has already helped determine where their children fall along the refractive error continuum. Although it appears that the number of myopic parents has only a modest effect in our modeling, it is worthwhile to remember this original association when considering the magnitude of the actual effect of parental myopia. In an earlier analysis, for example, the OR for having two compared to no myopic parents was 5.07.[2]

One might suspect that children with myopic parents would become myopic earlier. Data from this sample do not show similar effects for the number of myopic parents. The average age at onset was similar among myopic children no matter how many myopic parents they had. Iribarren et al.[17] reported a similar lack of association between age of myopia onset and parental history of myopia in a group of adult subjects. The number of highly myopic parents was associated with age at first glasses in a group of subjects in a study by Liang et al.,[18] with the association strongest among those children who were also highly myopic. We did not find a significant difference between having only a myopic mother or only a myopic father on the average age of onset. This may be a result of not witnessing the onset of myopia in all those who were myopic, that is, the currently myopic children who may have had earlier onset were excluded.

Having myopic parents has been shown to be associated with greater myopic progression as well. Kurtz et al.[19] reported on 5 years of myopia progression among Correction of Myopia Evaluation Trial (COMET) subjects. In the single-vision lens group, there were differences in progression from unadjusted analyses between subjects with one or two myopic parents (0.55-D difference) and between subjects with two or no myopic parents (0.78 D difference). There was no difference in progression among subjects with one myopic parent and no myopic parents. Saw et al.[20] found that myopia progression was higher in Singaporean children with myopic parents (−0.63 D) compared with those without myopic parents (−0.42 D). They also found that parents with high myopia (defined as −6.0 D or more myopia) had a significant effect; children with no parents with high myopia had a mean progression of −0.56 D, children with one parent with high myopia, −0.67 D; and children with two parents with high myopia, −0.90 D.

Consistent with our findings, Ip et al.[21] found differences between 12-year-old European Caucasian and East Asian children in the amount of refractive error as a function of the number of myopic parents. Overall, children with no myopic parents had a mean refractive error of +0.70 D, those with one myopic parent had a mean refractive error of +0.34 D, and those with two myopic parents had a mean refractive error of −0.55 D. Among the Caucasians, the mean refractive error was +0.99 D for those with no myopic parents, 0.70 D for those with one myopic parent, and 0.32 D for those with two myopic parents. In the East Asian subjects, the corresponding mean refractive errors were −0.06, −0.91, and −2.29 D, respectively. Among their East Asian subjects, the association of parental myopia with the child's refractive error was quite strong. In comparison, in CLEERE subjects at their first grade visit who would eventually become myopic, the white subjects did not have a mean refractive error difference with respect to number of myopic parents—approximately 0.30 D in each group. A significant difference did exist among the Asians with myopia, whose refractive error was 0.61 D with no myopic parents compared with 0.04 D with two.

Our ability to address ethnicity in this particular analysis is limited because of the way the data were collected in the CLEERE Study. The analysis included subjects in the first grade. Recruitment varied by site, and during the first years of the study, recruitment was open to all grade levels before being

Table 8. Modeled Hazard Odds Ratios for the Development of Myopia

Variable	HR (95% CI)	*P*
Model 1		
High risk versus low risk	7.24 (5.58–9.39)	0.013
One versus no myopic parents	1.50 (1.09–2.07)	0.13
Two versus no myopic parents	2.56 (1.75–3.73)	<0.0001
Two versus one myopic parent	1.70 (1.23–2.36)	0.002
Axial length	1.51 (1.24–1.85)	<0.0001
Diopter-hours	1.00 (0.99–1.01)	0.14
Model 2		
High risk versus low risk	7.31 (5.68–9.41)	<0.0001
One versus no myopic parents	1.59 (1.16–2.17)	0.004
Two versus no myopic parents	2.50 (1.73–3.63)	<0.0001
Two versus one myopic parent	1.58 (1.15–2.17)	0.005
Axial length	1.56 (1.28–1.90)	<0.0001
Sports/outdoor activity hours	0.98 (0.96–0.99)	0.008

Table 9. Model Estimates for Myopia Risk Group and Number of Myopic Parents, Controlling for Axial Length and Diopter-Hours

Risk Status	Myopic Parents	Hazard Probability	Survival Function
Low	None	0.022	0.91
Low	One	0.033	0.87
Low	Two	0.055	0.80
High	None	0.141	0.54
High	One	0.198	0.40
High	Two	0.296	0.23

restricted to the first grade. At one site (Tucson, AZ) recruitment was not possible in the first grade due to a previous ongoing research study. For these reasons, the sample of available first graders was small in some ethnic groups, with the limited number of children with two myopic parents making it impossible to complete some analyses. From the analyses of the white and Asian children, there was a differing survival function for myopia by the eighth grade, with a result similar to that of Ip et al.[21] Among both the low- and high-risk groups, the survival probabilities decreased from no to two myopic parents in both ethnic groups. The difference in survival probabilities between the two ethnic groups is particularly striking in the high-risk myopia group.

A simple measure of the usefulness of the combination of risk group and parental myopia is to look at those with neither risk factor and those who have both risk factors, to assess the sensitivity and specificity of the test (Table 6). As can be seen, the specificity is good; approximately 82% of the subjects who remained nonmyopic through eighth grade were accurately assessed. On the other hand, the sensitivity of this test was poor, accurately identifying only 62.5% of those who became myopic by the eighth grade. The first grade criterion does not appear to have the ability to correctly identify those who will have myopia as accurately as our previous criterion using cycloplegic refractive error in the third grade. We presume that this is due to the lack of differentiation at the younger age, where the subjects are relatively homogeneous with regard to many of the variables under study.[10] The incipient onset of myopia may take place rapidly, making long-term prediction difficult. One may have suspected that a high-risk cutoff would be more sensitive, but this group appears to contain a large number of children who are destined to remain emmetropic. The criterion used was developed in the original OLSM sample and has been used previously by our group as well as others. It is probable that a different cutoff would improve sensitivity at the expense of specificity.

To attempt to account for the contributions of the ocular components and the potential impact of near work, axial length and diopter-hours were added to the model. Axial length was associated with a statistically significant increase in the odds of myopia (OR = 1.51), though when controlled for in models evaluating the hazard probability and survival function, there was little change in the probabilities. Sports/outdoor activity hours showed a decreased risk of myopia development (OR = 0.98), similar to our previous paper identifying predictors[2] and other cross-sectional studies in which sports/outdoor activities were associated with a lower occurrence of myopia.[22,23]

As a tool for communicating to parents whether their first grader will become myopic, cycloplegic sphere will give a fair idea of future myopia, with the increase in the HR more than seven times for a child in the high-risk group. Focusing on high-risk children with two myopic parents increases the ability to identify the potential for myopia, but the usefulness of the application of a preventive treatment would still depend on the efficacy and expense of the treatment and its potential side effects. If the objective were to identify children for a preventive treatment, the ability to differentiate between those who will and will not become myopic is not accurate enough, misclassifying approximately 20% of children in the high-risk and one- or two-myopic-parent categories as those who will become myopic. This amount of potential misclassification may make the application of some treatments undesirable—for instance, any pharmaceutical agent that would produce side effects such as chronic pupillary dilation.

References

1. Zadnik K, Satariano WA, Mutti DO, Sholtz RI, Adams AJ. The effect of parental history of myopia on children's eye size. *JAMA.* 1994;271:1323–1327.
2. Jones LA, Sinnott LT, Mutti DO, Mitchell GL, Moeschberger ML, Zadnik K. Parental history of myopia, sports and outdoor activities, and future myopia. *Invest Ophthalmol Vis Sci.* 2007;48:3524–3532.
3. Saw SM, Shankar A, Tan SB, et al. A cohort study of incident myopia in Singaporean children. *Invest Ophthalmol Vis Sci.* 2006;47:1839–1844.
4. Mutti DO, Mitchell GL, Moeschberger ML, Jones LA, Zadnik K. Parental myopia, near work, school achievement, and children's refractive error. *Invest Ophthalmol Vis Sci.* 2002;43:3633–3640.
5. Pacella R, McLellan J, Grice K, Del Bono EA, Wiggs JL, Gwiazda JE. Role of genetic factors in the etiology of juvenile-onset myopia based on a longitudinal study of refractive error. *Optom Vis Sci.* 1999;76:381–386.
6. Yap M, Wu M, Liu ZM, Lee FL, Wang SH. Role of heredity in the genesis of myopia. *Ophthalmic Physiol Opt.* 1993;13:316–319.
7. Dirani M, Chamberlain M, Garoufalis P, Chen C, Guymer RH, Baird PN. Refractive errors in twin studies. *Twin Res Hum Genet.* 2006;9:566–572.
8. Hammond CJ, Snieder H, Gilbert CE, Spector TD. Genes and environment in refractive error: the twin eye study. *Invest Ophthalmol Vis Sci.* 2001;42:1232–1236.
9. Lyhne N, Sjolie AK, Kyvik KO, Green A. The importance of genes and environment for ocular refraction and its determiners: a population based study among 20–45 year old twins. *Br J Ophthalmol.* 2001;85:1470–1476.
10. Zadnik K, Mutti DO, Friedman NE, et al. Ocular predictors of the onset of juvenile myopia. *Invest Ophthalmol Vis Sci.* 1999;40:1936–1943.
11. Mutti DO, Hayes JR, Mitchell GL, et al. Refractive error, axial length, and relative peripheral refractive error before and after the onset of myopia. *Invest Ophthalmol Vis Sci.* 2007;48:2510–2519.
12. Seddon JM, Sahagian CR, Glynn RJ, Sperduto RD, Gragoudas ES. Evaluation of an iris color classification system. The Eye Disorders Case-Control Study Group. *Invest Ophthalmol Vis Sci.* 1990;31:1592–1598.
13. Harris WF. Algebra of sphero-cylinders and refractive errors, and their means, variance, and standard deviation. *Am J Optom Physiol Opt.* 1988;65:794–802.
14. Zadnik K, Mutti DO, Adams AJ. The repeatability of measurement of the ocular components. *Invest Ophthalmol Vis Sci.* 1992;33:2325–2333.
15. Walline JJ, Zadnik K, Mutti DO. Validity of surveys reporting myopia, astigmatism, and presbyopia. *Optom Vis Sci.* 1996;73:376–381.
16. Singer J, Willett J. *Applied Longitudinal Data Analysis*. Oxford, UK: Oxford University Press; 2003:644.
17. Iribarren R, Balsa A, Armesto A, et al. Family history of myopia is not related to the final amount of refractive error in low and moderate myopia. *Clin Exp Ophthalmol.* 2005;33:274–278.
18. Liang CL, Yen E, Su JY, et al. Impact of family history of high myopia on level and onset of myopia. *Invest Ophthalmol Vis Sci.* 2004;45:3446–3452.
19. Kurtz D, Hyman L, Gwiazda JE, et al. Role of parental myopia in the progression of myopia and its interaction with treatment in COMET children. *Invest Ophthalmol Vis Sci.* 2007;48:562–570.
20. Saw SM, Nieto FJ, Katz J, Schein OD, Levy B, Chew SJ. Familial clustering and myopia progression in Singapore school children. *Ophthalmic Epidemiol.* 2001;8:227–236.
21. Ip JM, Huynh SC, Robaei D, et al. Ethnic differences in the impact of parental myopia: findings from a population-based study of 12-year-old Australian children. *Invest Ophthalmol Vis Sci.* 2007;48:2520–2528.
22. Rose KA, Morgan IG, Ip J, et al. Outdoor activity reduces the prevalence of myopia in children. *Ophthalmology.* 2008;115:1279–1285.
23. Dirani M, Tong L, Gazzard G, et al. Outdoor Activity and myopia in Singapore teenage children. *Br J Ophthalmol.* 2009;93(8):997–1000.

Appendix: The CLEERE Study Group (as of September 2008)

Clinical Centers

Franklin Primary Health Center, Inc.: Sandral Hullett (Principal Investigator, 1997–2007), Robert N. Kleinstein (Co-investigator, 1997–2007), Janene Sims (Optometrist, 1997–2001 and 2004–2007), Raphael Weeks (Optometrist, 1999–2007), Sandra Williams (Study Coordinator, 1999–2007), LeeAndra Calvin (Study Coordinator, 1997–1999), and Melvin D. Shipp (Co-investigator, 1997–2004). Drs. Kleinstein and Sims are affiliated with the University of Alabama at Birmingham School of Optometry.

University of California, Berkeley School of Optometry, Berkeley, CA: Nina E. Friedman (Principal Investigator, 1999–2001), Pamela Qualley (Study Coordinator, 1997–2001), Donald O. Mutti (Principal Investigator, 1996–1999), and Karla Zadnik (Optometrist, 1996–2001).

University of Houston College of Optometry: Ruth E. Manny (Principal Investigator, 1997–2007), Suzanne M. Wickum (Optometrist, 1999–2007), Ailene Kim (Optometrist, 2003–2007), Bronwen Mathis (Optometrist, 2002–2007), Mamie Batres (Study Coordinator, 2004–2007), Sally Henry (Study Coordinator, 1997–1998), Janice M. Wensveen (Optometrist, 1997–2001), Connie J. Crossnoe (Optometrist, 1997–2003), Stephanie L. Tom (Optometrist, 1999–2002), Jennifer A. McLeod (Study Coordinator, 1998–2004), Julio C. Quiralte (Study Coordinator, 1998–2005), and Gaby Solis (Study Coordinator, 2005–2007).

Southern California College of Optometry, Fullerton, CA: Susan A. Cotter (Principal Investigator, 2004–2007, Optometrist, 1997–2004), Julie A. Yu (Principal Investigator, 1997–2004; Optometrist 2005–2007), Raymond J. Chu (Optometrist, 2001–2007), Carmen N. Barnhardt (Optometrist 2004–2007), Jessica Chang (Optometrist, 2005–2007), Kristine Huang (Optometrist, 2005–2007), Rebecca Bridgeford (Study Coordinator, 2005–2006), Connie Chu (Optometrist, 2004–2005), Soonsi Kwon (Optometrist, 1998–2004), Gen Lee (Study Coordinator, 1999–2003), John Lee (Optometrist, 2000–2003), Robert J. Lee (Optometrist, 1997–2001), Raymond Maeda (Optometrist, 1999–2003), Rachael Emerson (Study Coordinator, 1997–1999), and Tracy Leonhardt (Study Coordinator, 2003–2004).

University of Arizona, Department of Ophthalmology, Tucson, AZ: J. Daniel Twelker (Principal Investigator, 2000–present), Dawn Messer (Optometrist, 2000–present), Denise Flores (Study Coordinator, 2000–2007, Rita Bhakta (Optometrist, 2000–2004), and Katie Garvey (Optometrist, 2006–present).

Resource Centers

Chairman's Office, The Ohio State University College of Optometry, Columbus, OH: Karla Zadnik, (Chairman, 1997–present), Jodi M. Malone (Study Coordinator, 1997–present).

Videophakometry Reading Center, The Ohio State University College of Optometry, Columbus, OH: Donald O. Mutti (Director, 1997–present), Vidya Subramanian (Reader, 2006-), Huan Sheng (Reader, 2000–2006), Holly Omlor (Reader, 2003–2006), Meliha Rahmani (Reader, 2004–2006), Jaclyn Brickman (Reader, 2002–2003), Amy Wang (Reader, 2002–2003), Philip Arner (Reader, 2002–2004), Samuel Taylor (Reader, 2002–2003), Myhanh T. Nguyen (Reader, 1998–2001), Terry W. Walker (Reader, 1997–2001).

Optometry Coordinating Center, The Ohio State University College of Optometry, Columbus, OH: Lisa A. Jones (Director, 1997–present), Linda Barrett (Data Entry Operator, 1997–2008), John Hayes (Biostatistician, 2001–2007), G. Lynn Mitchell, Biostatistician, 1998–present), Melvin L. Moeschberger, (Consultant, 1997–present), Loraine Sinnott (Biostatistician, 2005–present), Pamela Wessel (Program Coordinator, 2000–present), Julie N. Swartzendruber (Program Coordinator, 1998–2000).

Project Office, National Eye Institute, Rockville, MD: Donald F. Everett.

Committees

Executive Committee: Karla Zadnik (Chairman), Lisa A. Jones, Robert N. Kleinstein, Ruth E. Manny, Donald O. Mutti, J. Daniel Twelker, Susan A. Cotter.