Predicting the onset of myopia in children by age, sex, and ethnicity: Results from the CLEERE Study

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SIGNIFICANCE: Clinicians and researchers would benefit from being able to predict the onset of myopia for an individual child. This report provides a model for calculating the probability of myopia onset, year-by-year and cumulatively, based on results from the largest, most ethnically diverse study of myopia onset in the United States.

PURPOSE: This study aimed to model the probability of the onset of myopia in previously nonmyopic school-aged children.

METHODS: Children aged 6 years to less than 14 years of age at baseline participating in the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study who were nonmyopic and less hyperopic than +3.00 D (spherical equivalent) were followed up for 1 to 7 years through eighth grade. Annual measurements included cycloplegic autorefraction, keratometry, ultrasound axial dimensions, and parental report of children's near work and time spent in outdoor and/or sports activities. The onset of myopia was defined as the first visit with at least −0.75 D of myopia in each principal meridian. The predictive model was built using discrete time survival analysis and evaluated with *C* statistics.

RESULTS: The model of the probability of the onset of myopia included cycloplegic spherical equivalent refractive error, the horizontal/vertical component of astigmatism (J_0), age, sex, and race/ethnicity. Onset of myopia was more likely with lower amounts of hyperopia and less positive/more negative values of J_0. Younger Asian American females had the highest eventual probability of onset, whereas older White males had the lowest. Model performance increased with older baseline age, with *C* statistics ranging from 0.83 at 6 years of age to 0.92 at 13 years.

CONCLUSIONS: The probability of the onset of myopia can be estimated for children in the major racial/ethnic groups within the United States on a year-by-year and cumulative basis up to age 14 years based on a simple set of refractive error and demographic variables.

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Most children's refractive error changes slowly from low levels of hyperopia to emmetropia.[1–5] For one-third of adults in the United States, emmetropia in their childhood was not maintained but instead was followed by the onset of myopia.[6] The transition between emmetropia and myopia is characterized by an acceleration in axial elongation[7–10] and inadequate compensatory reductions in the power of the crystalline lens.[8,9,11–13] Accurate prediction of the transition between remaining emmetropic and crossing the threshold to become myopic would have substantial benefit in research and clinical practice. A predictive model would be useful for sample size planning in myopia prevention clinical trials, providing estimates of the likelihood of conversion from emmetropia to myopia, given different sample configurations of age, sex, race/ethnicity, baseline refractive error, or other significant covariates. A predictive model would help the clinician advise an individual child and their family on the probability of future refractive error. Recommendations for prevention strategies could be made based on a child's individual level of risk and age, translating into an opportunity for earlier myopia control intervention, e.g., encouraging emmetropic children to spend more time outdoors as early as possible. Increased time spent outdoors has consistently been shown to reduce the incidence of myopia,[14–20] and protective effects of more time spent outdoors have been traced to exposures in children as young as 3 years.[21] Early initiation of low-dose atropine therapy is another option. Effective in slowing myopia progression,[22–24] 0.05% atropine has also been shown to lower the probability of the onset of myopia.[25] The eye care provider might find probabilities for onset by age useful in identifying an appropriate window for preventive treatment with low-dose atropine or any other evidence-based approach.

Numerous predictive factors for myopia onset have been identified, including demographic, biometric, and accommodative variables.[10,15,26–30] However, the best single predictor of future myopia is a less hyperopic baseline spherical equivalent refractive error.[15,17,27,30] The increase in prediction accuracy from adding other variables as judged by a change in the area under a receiver operating characteristic (ROC) curve is often small, ranging from less than

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0.05 up to 0.10 compared with 0.64 to 0.93 for spherical equivalent refractive error alone.[15,17,27,29]

Area under the ROC curve analysis evaluates how well risk factors perform in terms of overall sensitivity and specificity. However, this analysis does not provide estimates of the probability of myopia onset based on individual data that would be needed for detailed sample size planning and individual patient counseling. A few studies have extended their analyses to provide these probabilities. The Wenzhou Medical University Essilor Progression and Onset of Myopia (WEPrOM) study identified older age, female sex, parental myopia, less hyperopic noncycloplegic spherical equivalent refractive error, longer axial length, and lower positive relative accommodation as independent predictive factors with an area under the ROC curve of 0.74 (95% confidence interval, 0.68 to 0.80).[29] Their web-based calculator does not include age or parental myopia but added corneal power to this list of factors. Inputting individual data results in estimated survival curves over a 4.5-year period and probabilities of myopia onset across that follow-up interval (https://myopia-risk-calculator.shinyapps.io/weprom/). The Northern Ireland Childhood Errors of Refraction (NICER) study and its Predicting Myopia Onset and progression (PreMO) risk worksheet use an individual child's age, parental history of myopia, cycloplegic spherical equivalent refractive error, and axial length to provide an ordinal risk score for future myopia onset.[10,31] The Singapore Cohort Study of the Risk factors for Myopia (SCORM) study developed a predictive model based on cycloplegic refractive error and parental myopia. The model performed well with a *C* statistic of 0.91 when validated using 1774 participants from SCORM who were enrolled at ages 7 to 9 years and followed for up to 9 years.[30]

The available risk calculators are therefore most applicable to young Chinese children or European White children. The PreMO ordinal risk score provides useful graded estimates of the probability of onset that extend from baseline ages of 6 to 8 years out to a final age of 16 years but has some limitations in that the scores are only provided for increments of 3 years of age and are not on a continuous scale. The WEPrOM calculator provides probabilities year-by-year in survival curves but is based on a limited length of follow-up and a narrow range of baseline ages using data from only one race/ethnicity. SCORM also provides ordinal risk scores along with figures depicting the probability of myopia onset as a function of baseline age, refractive error, and parental myopia; however, the prediction is only for 1 year from baseline.[30] Previous analysis of Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) data provided optimal cutpoints for spherical equivalent refractive error for predicting the onset of myopia.[17] The purpose of the current analysis was to improve risk calculation from CLEERE data by extending those dichotomous results to include specific probabilities of myopia onset year-by-year and cumulatively up to age 14 years using baseline cycloplegic refractive error at 6 to 13 years of age, sex, and race/ethnicity.

METHODS

The CLEERE Study was a multicenter, observational evaluation of ocular component development and risk factors for juvenile-onset myopia conducted in school-aged children (grades 1 to 8) at five clinical sites across the United States. CLEERE was an expansion of the Orinda Longitudinal Study of Myopia that began in 1989 in Orinda, California, a predominantly White community. To increase racial/ethnic representation and generalizability, four sites were added: in 1997, Eutaw, Alabama (Black); Irvine, California (Asian American); and Houston, Texas (Hispanic); and in 2001, Tucson, Arizona (Native American—Tohono O'odham). This research was reviewed by an independent ethical review board and conforms with the principles and applicable guidelines for the protection of human participants in biomedical research. Informed consent and assent were provided by the parents and children, respectively. Consent procedures and study protocols were approved by each site's institutional review board.

The CLEERE Study's measurement methods have been described previously in detail.[32] Measurements were made only on the right eye. Refractive error was measured using the average of 10 readings from autorefraction (Canon R-11989-2000, Canon R-1 [Canon, Lake Success, NY; no longer manufactured], Grand Seiko WR-5100K 2001-2010 [Shigiya (USA) Ltd., Schaumburg, IL]). Measurements were performed under cycloplegia, 30 minutes after one drop of proparacaine 0.5% and either two drops of tropicamide 1.0% if iris color was less than grade 2 or one drop each of tropicamide 1.0% and cyclopentolate 1.0% when iris color was grade 2 or darker.[33,34] Parents provided information about children's sex and race/ethnicity. For race/ethnicity, parents selected one of the six categories used by the National Institutes of Health in 1997 when CLEERE began: American Indian or Alaskan Native; Asian or Pacific Islander; Black, not of Hispanic origin; Hispanic; White, not of Hispanic origin; or Other.

As in our previous analysis, myopia was defined as being at least −0.75 D or more myopic in both principal meridians, the criterion used in CLEERE since its inception.[17] This amount was chosen for being outside of measurement error,[35] unambiguously myopic as opposed to possibly astigmatic, more likely to cause a reduction in visual acuity, and therefore more likely to be corrected clinically. Eight datasets were created for each age from 6 to 13 years. Children were included in a dataset if they had (1) a nonmyopic visit at that age, (2) at least one subsequent visit, and (3) no visit in which the spherical equivalent refractive error was +3.00 D or more hyperopic due to not being at risk for myopia onset. Data from the same child could appear in more than one dataset if they remained nonmyopic for more than 1 year.

Each age dataset was fit using separate discrete time survival models of the risk of myopia onset at or before age 14 years. The model outcome was the log of the odds of the probability of myopia at age *a* given that a child was nonmyopic and therefore still at risk of myopia onset between baseline and that age (i.e., the hazard odds, denoted logit $h(a)$). Models controlled for refractive error at the first visit in each dataset, ethnicity, and sex. Probability of onset was modeled as a function of spherical equivalent and the J_0 (horizontal/vertical) component of astigmatism. Other candidate variables were eliminated, and these two variables were identified as the best predictors of future myopia onset in a previous analysis of CLEERE data.[17] Their significance as independent variables was reconfirmed in the current analysis ($p<0.01$ for each variable at each baseline age, except $p=0.19$ for J_0 at age 6). Each age beyond baseline had its own associated ROC and area under the curve. The *C* statistic was an average of areas under the age-specific ROC curves, weighted by the amount of available data. The *C* statistic used every possible pairing of participants to estimate the probability that a participant from the myopia onset group had a higher risk of onset than an age-matched participant from the group that remained nonmyopic. Estimates of the *C* statistic were computed using the model predicted probabilities of myopia onset and 10-fold cross validation. A dataset was randomly divided into 10 groups, dividing those with and without onset separately to ensure each group had a sufficient number of onset events. A training set model was fit using 9 of the 10 groups. The test set comprised the remaining group, which was used to obtain predicted hazards from the fitted model. The role of test set was rotated across the 10 groups. The *C* statistic was then computed using predicted probabilities derived from the 10 test sets. The model fit had the following form:

$$\text{logit } h(a) = A_{i+k} + \text{Ethnicity}_i + \beta_1 \text{Female}_i + \beta_2 \text{SER}_i + \beta_3 J_{0i}$$

$$\text{logit } h(a) = \log \frac{h}{1-h}$$

TABLE 1. Number of children in each of the datasets by baseline age

	Future myope		
	No	Yes	
Baseline age (y)	n (%)	n (%)	Total n
6	484 (81.1)	113 (18.9)	597
7	1484 (80.1)	368 (19.9)	1852
8	1774 (81.5)	402 (18.5)	2176
9	1946 (83.3)	389 (16.7)	2335
10	1962 (85.6)	331 (14.4)	2293
11	1993 (89.3)	240 (10.7)	2233
12	1911 (92.4)	158 (7.6)	2069
13	1380 (95.0)	72 (5.0)	1452

The number of children is divided at each baseline age between those who remained nonmyopic and those who became myopic in any year after baseline up to age 14 years.

$$\frac{1}{1+e^{-\text{logit } h(a)}} = h = \text{probability of myopia onset at age}(i+k)$$

where i represents participant age and data at baseline and k represents the number of years after baseline. The range of $(i + k)$ was 7 to 14 years of age.

RESULTS

Of the 4027 total unique participants, between 597 and 2335 children were in each of the eight baseline age datasets (Table 1). The proportion of children who went on to develop myopia by age 14 years was highest for the younger baseline ages (18.9% at age 6 years, 19.9% at age 7 years) and decreased as children became older (5.0% at age 13 years; Table 1). The majority of children were White, followed by Hispanic, and Black. More of the Asian American children in the sample were younger (decreasing percentages at older ages), whereas Native American children were older (increasing percentages at older ages; Table 2). The overall sample was 49.9% female. The model $A_{(i+k)}$ coefficients for follow-up ages $(i + k)$ are given in Table 3. These represent the value of the log of the hazard odds for age $(i + k)$ when the categorical predictors are at their reference values, and the values of ocular predictors are 0. The baseline ages (i) are in the left-hand column. The follow-up age (k) is read from left to right. For example, the length of follow-up could range from 1 to 7 years before reaching a maximum age of 14 if the baseline age were 7 years. In that case, A_8 represents a value of $(k) = 1$, A_{12} a value of $(k) = 5$, and A_{14} a value of $(k) = 7$. However, the length of follow-up could range from 1 to 3 years before reaching a maximum age of 14 if the baseline age were 11 years. In that case, A_8 is not used, A_{12} represents the first possible follow-up coefficient with a value of $(k) = 1$, and A_{14} represents a value of $(k) = 3$. Table 4 lists the coefficients for the other model terms of ethnicity, sex (female = 1, male = 0), spherical equivalent refractive error, and the J_0 component of astigmatism.

Examples of model results for baseline ages of 7, 9, and 11 years are shown in Fig. 1. Asian females had the highest probability of becoming myopic, and White males had the lowest probability. The filled squares in the figure provide the probability of the onset of myopia at age $(i + k)$ given that the child had remained nonmyopic prior to that age. The different levels of spherical equivalent refractive error were included in the examples based on previously identified optimal cutpoints at each age: +0.50 D at age 7, +0.25 D at age 9, and 0.00 D at age 11.[17] J_0 was kept constant at +0.50 D. Given those baseline values of refractive error at age 7, the probability of the onset of myopia at age 14 was 0.15 for an Asian female who remained nonmyopic up to age 13 (filled squares in Fig. 1A) but only 0.020 for a White male (filled squares in Fig. 1D). These probabilities decreased with older baseline age. Given those baseline values of refractive error at age 11, the probability of the onset of myopia at age 14 was 0.079 for an Asian female who remained nonmyopic up to age 13 (filled squares in Fig. 1C) and 0.017 for a White male (filled squares in Fig. 1F).

Model results at each age can be used to provide the cumulative probability of myopia onset by a particular age. By subtraction, 1 − the probability of the onset of myopia at age $(i + k)$ yields the probability of being nonmyopic (survival) at age $(i + k)$. Multiplying these probabilities of survival over a series of (k) years yields the probability of remaining nonmyopic between baseline and age $(i + k)$. Again by subtraction, 1 − the probability of remaining nonmyopic between baseline and age $(i + k)$ yields the probability of becoming myopic between baseline and age $(i + k)$. These probabilities are also shown in Fig. 1. Given the same baseline values of refractive error at age 7, the probability of becoming myopic by age 14 for an Asian female with those baseline values of refractive error at age 7 was 0.55 (open circles in Fig. 1A) and at 0.09 for a White male (open circles in Fig. 1D). Therefore, the probability of remaining nonmyopic by age 14 for an Asian female was 0.45 (filled circles in Fig. 1A) and 0.91 for a White male (filled circles in Fig. 1D). The probabilities showed the expected change with older baseline age, namely, a higher probability of remaining nonmyopic and a lower probability of onset. If the baseline age was 11, the probability of becoming myopic would be 0.18 for an Asian female with the given baseline values of refractive error in this example (open circles in Fig. 1A) and 0.04 for a White male (open circles in Fig. 1D). The probability of remaining nonmyopic by age 14 would then be 0.82 for an Asian female (filled circles in Fig. 1C) and 0.96 for a White male (filled circles in Fig. 1F).

TABLE 2. Distribution of the sample by ethnicity at each baseline age

	White	Hispanic	Black	Asian American	Native American	Other
Baseline age (y)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
6	350 (58.6)	37 (6.2)	69 (11.6)	126 (21.1)	6 (1.0)	9 (1.5)
7	886 (47.8)	379 (20.5)	273 (14.7)	248 (13.4)	50 (2.7)	16 (0.9)
8	980 (45.0)	464 (21.3)	309 (14.2)	265 (12.2)	138 (6.3)	20 (0.9)
9	975 (41.8)	450 (19.3)	352 (15.1)	287 (12.3)	250 (10.7)	21 (0.9)
10	856 (37.3)	464 (20.2)	386 (16.8)	257 (11.2)	313 (13.6)	17 (0.7)
11	826 (37.0)	487 (21.8)	394 (17.6)	203 (9.1)	307 (13.7)	16 (0.7)
12	812 (39.2)	402 (19.4)	375 (18.1)	185 (8.9)	281 (13.6)	14 (0.7)
13	505 (34.8)	331 (22.8)	310 (21.4)	90 (6.2)	209 (14.4)	7 (0.5)

TABLE 3. Model $A_{(i+k)}$ coefficients for ages up to 14 years

Baseline age (i) (y)	Coefficients (A_{i+k})							
	A_7	A_8	A_9	A_{10}	A_{11}	A_{12}	A_{13}	A_{14}
6	−4.25 (−5.08 to −3.43)	−3.20 (−3.84 to −2.56)	−2.80 (−3.42 to −2.19)	−2.31 (−2.91 to −1.72)	−2.17 (−2.78 to −1.55)	−2.34 (−3.09 to −1.58)	−1.96 (−2.73 to −1.20)	−2.47 (−4.76 to −0.19)
7		−3.77 (−4.15 to −3.39)	−3.04 (−3.39 to −2.70)	−2.72 (−3.06 to −2.38)	−2.63 (−2.99 to −2.28)	−2.57 (−2.96 to −2.18)	−2.40 (−2.82 to −1.98)	−2.33 (−2.87 to −1.79)
8			−3.54 (−3.89 to −3.19)	−2.70 (−3.01 to −2.38)	−2.41 (−2.73 to −2.09)	−2.27 (−2.62 to −1.93)	−2.27 (−2.66 to −1.89)	−2.17 (−2.68 to −1.66)
9				−3.55 (−3.89 to −3.21)	−2.87 (−3.18 to −2.55)	−2.74 (−3.07 to −2.40)	−2.67 (−3.03 to −2.31)	−2.41 (−2.84 to −1.98)
10					−3.65 (−4.01 to −3.29)	−3.35 (−3.70 to −2.99)	−3.05 (−3.41 to −2.68)	−3.01 (−3.43 to −2.58)
11						−3.95 (−4.36 to −3.53)	−3.52 (−3.92 to −3.12)	−3.34 (−3.79 to −2.90)
12							−3.85 (−4.32 to −3.39)	−3.51 (−3.99 to −3.03)
13								−3.85 (−4.52 to −3.19)

The i represents participant baseline age, and k represents the number of years after baseline. The range of $(i + k)$ is between 7 and 14 years of age. The 95% confidence limits appear in the parentheses.

The effects of race/ethnicity, sex, and baseline refractive error on the probability of becoming myopic by age 14 are shown in Table 5. The effect of race/ethnicity can be seen by reading the results from left to right within a table. The probabilities were lowest for White children, similarly low for Black and Native American children, and highest for Hispanic and Asian American children. The effects of sex can be seen by comparing the table on the left to the one on the right within a baseline age group. For each baseline age, females had a higher probability of becoming myopic within each ethnic group, often by close to a factor of 2. The effect of less hyperopic baseline spherical equivalent refractive error can be seen by comparing the first two rows within each table. As expected, a lower amount of hyperopic buffer increased the probability of becoming myopic. The increase in probability of onset was by roughly a factor of 2 for younger children but by a factor of 5 to 10 for older children, although at a much lower level of probability. The effect of the J_0 component of astigmatism can be seen by comparing the second and third rows within each table. A decrease in J_0 (a shift away from with-the-rule astigmatism) increased the probability of becoming myopic. The increase was small for younger children and was more substantial for older children. More detailed results of the probability of becoming myopic by age 14 by baseline age, refractive error, and race/ethnicity can be found in Appendix Fig. A1, available at http://links.lww.com/OPX/A722; Fig. A2, available at http://links.lww.com/OPX/A723; Fig. A3, available at http://links.lww.com/OPX/A724; Fig. A4, available at http://links.lww.com/OPX/A725; and Fig. A5, available at http://links.lww.com/OPX/A726.

The predictive model performed well across baseline ages, with C statistics increasing from 0.83 at 6 years of age to 0.92 at age 13 years. The performance of the predictive model for each year beyond baseline ages of 7, 9, and 11 years is shown by the ROC curves in Fig. 2. Model performance was best when the follow-up was only 1 year from the baseline age and poorer when the follow-up extended to age 14 years. The areas under the curve ranged from a maximum of 0.96 for the 1-year intervals from 7 to 8 and 9 to 10 years of age to a minimum of 0.77 for the 7- and 5-year follow-up intervals from 7 to 14 and 9 to 14 years of age, respectively. The 1-year interval from 11 to 12 years of age had an area under the curve of 0.94, and the 3-year interval from 11 to 14 years of age had an area under the curve of 0.85.

DISCUSSION

The current analysis of the multiethnic CLEERE sample of 6- to <14-year-old children in the United States yields year-by-year estimates of the probability of myopia onset as well as the cumulative probability of onset up to age 14 years. The model uses a small set of variables readily obtained by clinical case history and objective measurement that could be performed in an eye examination: spherical equivalent refractive error, the horizontal/vertical component of astigmatism, age,

TABLE 4. Model coefficients (95% CI) for ethnicity, sex (female = 1, male = 0), spherical equivalent refractive error, and the J_0 component of astigmatism

Baseline age (y)	Coefficients (95% CI) for ethnicity, sex, and baseline refractive error						
	Asian American	Black	Hispanic	Native American	Female	Spherical equivalent	Astigmatism (J_0)
6	1.37 (0.89 to 1.86)	0.53 (−0.07 to 1.14)	0.77 (−0.16 to 1.7)	—	0.77 (0.35 to 1.2)	−2.42 (−2.86 to −1.97)	−0.44 (−1.09 to 0.21)
7	1.24 (0.92 to 1.57)	0.23 (−0.13 to 0.59)	1.07 (0.79 to 1.36)	0.30 (−0.48 to 1.08)	0.89 (0.66 to 1.13)	−2.35 (−2.57 to −2.13)	−0.77 (−1.07 to −0.47)
8	1.02 (0.7 to 1.35)	−0.03 (−0.4 to 0.33)	0.69 (0.4 to 0.97)	−1.02 (−1.62 to −0.41)	0.68 (0.45 to 0.91)	−3.07 (−3.33 to −2.82)	−1.05 (−1.33 to −0.77)
9	1.08 (0.73 to 1.42)	0.26 (−0.1 to 0.62)	0.34 (0.02 to 0.66)	−0.49 (−0.95 to −0.02)	0.51 (0.28 to 0.75)	−3.33 (−3.6 to −3.06)	−1.16 (−1.42 to −0.9)
10	1.05 (0.65 to 1.45)	0.17 (−0.23 to 0.56)	0.31 (−0.04 to 0.66)	−0.05 (−0.52 to 0.41)	0.53 (0.27 to 0.79)	−3.17 (−3.45 to −2.9)	−1.42 (−1.71 to −1.14)
11	0.97 (0.5 to 1.43)	−0.09 (−0.56 to 0.38)	0.26 (−0.13 to 0.66)	−0.15 (−0.71 to 0.4)	0.60 (0.3 to 0.91)	−3.22 (−3.55 to −2.89)	−1.38 (−1.7 to −1.05)
12	0.52 (−0.12 to 1.17)	−0.60 (−1.2 to 0.01)	0.060 (−0.44 to 0.56)	0.02 (−0.64 to 0.68)	0.40 (0.02 to 0.78)	−3.26 (−3.66 to −2.86)	−1.47 (−1.85 to −1.08)
13	0.67 (−0.31 to 1.66)	−0.38 (−1.22 to 0.46)	−0.05 (−0.82 to 0.71)	−1.19 (−2.52 to 0.13)	0.41 (−0.16 to 0.99)	−3.47 (−4.1 to −2.84)	−0.95 (−1.58 to −0.32)

The coefficient at age 6 years for Native American children could not be calculated due to a small number of participants within that table cell. CI = confidence interval.

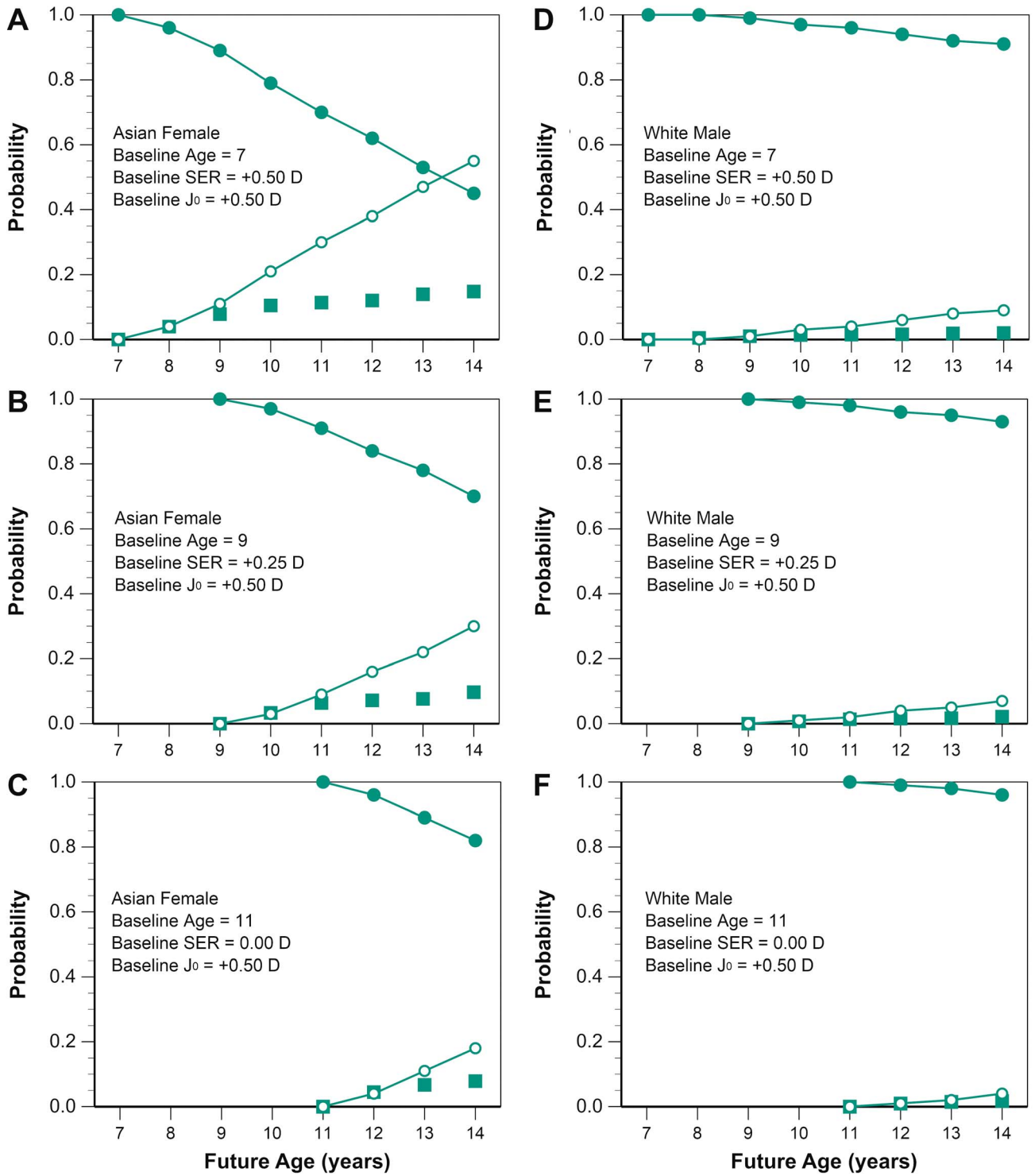

FIGURE 1. Model-derived probabilities at future ages ($i + k$) given the baseline data shown and baseline ages (i) of 7, 9, and 11 for Asian females (panels A–C) and White males (panels D–F). The probability of becoming myopic at a given age ($i + k$) given no previous myopia is shown by the filled squares ■. The probability of remaining nonmyopic by a given age ($i + k$) is shown by the filled circles —●—. The probability of becoming myopic by a given age ($i + k$) is shown by the open circles —○—.

sex, and race/ethnicity. Cycloplegia during measurement of refractive error is considered the gold standard for children but may be a limitation in countries where access to pharmaceuticals is restricted.[36]

Model performance was comparable to previous work. The *C* statistics in the current analysis ranged from 0.83 to 0.92, depending on the baseline age. In comparison, WEPrOM achieved areas under

TABLE 5. The probabilities of becoming myopic by age 14 years by sex, ethnicity, and selected baseline refractive errors at baseline ages of 7, 9, and 11 years

	Male					Female				
Baseline to final age	**7–14 y**					**7–14 y**				
SER (D), J_0 (D)	**White**	**Black**	**Native American**	**Hispanic**	**Asian American**	**White**	**Black**	**Native American**	**Hispanic**	**Asian American**
+0.75, +0.50	0.054	0.067	0.072	0.15	0.17	0.12	0.15	0.16	0.32	0.36
+0.25, +0.50	0.16	0.20	0.21	0.39	0.45	0.34	0.41	0.43	0.69	0.74
+0.25, 0.00	0.23	0.28	0.29	0.52	0.57	0.46	0.53	0.56	0.81	0.85
Baseline to final age	**9–14 y**					**9–14 y**				
SER (D), J_0 (D)	**White**	**Black**	**Native American**	**Hispanic**	**Asian American**	**White**	**Black**	**Native American**	**Hispanic**	**Asian American**
+0.50, +0.50	0.032	0.042	0.020	0.045	0.091	0.053	0.068	0.033	0.074	0.15
0.00, +0.50	0.16	0.20	0.099	0.21	0.38	0.24	0.30	0.16	0.32	0.54
0.00, 0.00	0.26	0.32	0.17	0.34	0.56	0.39	0.46	0.26	0.49	0.73
Baseline to final age	**11–14 y**					**11–14 y**				
SER (D), J_0 (D)	**White**	**Black**	**Native American**	**Hispanic**	**Asian American**	**White**	**Black**	**Native American**	**Hispanic**	**Asian American**
+0.25, +0.50	0.019	0.017	0.016	0.024	0.048	0.034	0.031	0.029	0.044	0.086
−0.25, +0.50	0.089	0.082	0.077	0.11	0.21	0.15	0.14	0.13	0.19	0.34
−0.25, 0.00	0.17	0.15	0.15	0.21	0.37	0.28	0.26	0.25	0.34	0.54

J_0 = the horizontal/vertical component of astigmatism; SER = spherical equivalent.

the curve of 0.74 for both 2 and 4.5 years of follow-up.[29,37] NICER found an area under the curve of 0.87 using baseline spherical equivalent in nonmyopic children at 6 to 7 years of age to predict myopia onset up to 9 years later.[10] SCORM found a *C* statistic of 0.91 for predicting myopia onset in the year following baseline based on cycloplegic refractive error and parental myopia.[30]

Refractive error is common to each of the other predictive models, but the number of additional terms varies. WEPrOM uses sex, spherical equivalent, axial length, corneal refractive power, and positive relative accommodation (which requires some clinical training to measure). It does not include age or race/ethnicity. The NICER PreMO worksheet uses age, parental history of myopia, cycloplegic or noncycloplegic spherical equivalent refractive error, and axial length, with axial length either measured directly or estimated from keratometer power and cycloplegic refractive error. Input data do not include sex or race/ethnicity. The SCORM risk scoring system for Chinese children uses age, sex, refractive error, and parental myopia or a combination of ocular component values in place of refractive error.[30] The CLEERE model does not include axial length, corneal power, or parental myopia because they did not add significantly to predictions based on refractive error.[17] Fig. 1 and Table 5 demonstrate how age, sex, and race/ethnicity alter the probability of onset: lower at older ages for a given refractive error, higher in females, and higher in Asian American children. The absence of demographic data from other calculators may limit their generalizability.

For a predictive model to be effective and parsimonious, input data should make independent contributions to the prediction. WEPrOM and PreMO include both refractive error and axial length, highly correlated variables, in the same predictive model. The value of including both refractive error and axial length as concurrent inputs has been noted previously and questioned.[38] The following comparison illustrates the concern. Using the CLEERE model without axial length, the probability of myopia onset in 3 years for a 7-year-old Asian American girl with a spherical equivalent refractive error of +0.50 D and J_0 of 0.00 D would be 0.28. The same scenario in WEPrOM, assuming an average corneal power of 43.75 D and average positive relative accommodation of −3.60 D, would be 0.32 for an axial length of 23.0 mm but 0.60 for an axial length of 23.5 mm. The underlying assumption is that a longer eye at a given age and nonmyopic refractive error increases the risk of onset by growing faster and reaching myopia sooner. The lack of significance for axial length in a multivariate model with refractive error suggests that this is not the case, at least in CLEERE results.[17] A model that requires both axial length and refractive error also means the added expense of having an axial length biometer.

Besides differences in model terms, the different baseline ages, lengths of follow-up, and racial/ethnic heritages across studies may also introduce variability among the current predictive models. Recruitment strategies vary considerably among studies—from enrollment of a single early grade in school,[26] two grades,[29] three grades,[27,30] six grades,[17] or separate cohorts of younger and older children.[15,28] The duration of follow-up also ranges from as low as 2 years to as high as 9 years.[10,29,30] The racial/ethnic composition also varies across these studies. Chinese ancestry is well represented in these datasets,[26–30] as are Australians of European descent,[15] children from Northern Ireland,[10] and children in the United States from several racial/ethnic groups.[17] A more formal comparison of predictive models would help to quantify the effects of these potential sources of variability.

A major purpose of predictive factors is to guide clinical care. A dichotomous risk score or discrete refractive error cutpoints might be one strategy for making decisions about whether to initiate preventive treatment. The dichotomous outcomes from CLEERE provided these optimal cutpoints, with *C* statistics ranging from 0.87 to 0.93, depending on the number of years of follow-up.[17] Remarkably, the SCORM cutpoints for myopia onset within 1 year from baseline were almost identical to those from CLEERE despite being conducted in different countries, namely, 0.00 D for baseline ages 6 to 8 years and −0.25 D for children older than 9 years.[30] Similar cutpoints can be seen for CLEERE as the leftmost points in the figure from Zadnik et al.[17] The more hyperopic points to the right in the CLEERE figure provided the cutpoints for myopia onset by the eighth grade: less hyperopic than +0.75 D for grade 1 (age 6 years), +0.50 D or less hyperopic for grades 2 and 3 (ages 7 and 8 years),

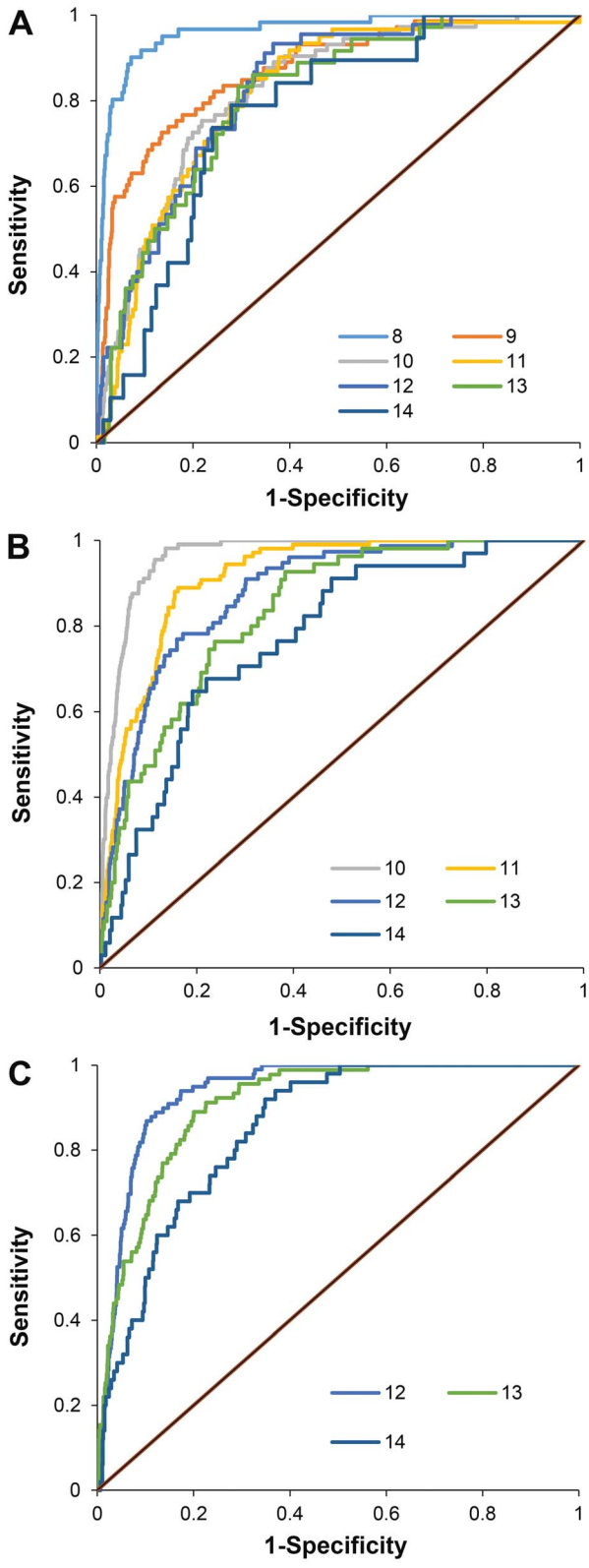

FIGURE 2. ROC analyses for myopia predictions year-by-year for three baseline ages: (A) 7 years, (B) 9 years, and (C) 11 years. Each line represents an additional year a child remained nonmyopic. Model performance was best when predicting myopia onset within 1 year from the baseline age and decreased with each additional year a child remained nonmyopic after the baseline age. The diagonal line represents a chance level of performance. ROC = receiver operating characteristic.

+0.25 D or less hyperopic for grades 4 and 5 (ages 9 and 10 years), and emmetropic or more myopic for grade 6 (age 11 years).[17] The longer time horizon from CLEERE of up to 7 years from baseline is arguably more clinically useful as it provides the opportunity for earlier intervention. Preventive strategies that have been studied are limited to increased time spent outdoors and low-dose atropine.[14–20,25] Time outdoors is an inexpensive option but should be implemented with appropriate attention to protection of skin and eyes from short-wavelength sunlight exposure. Low-dose atropine was used successfully to delay onset without significant side effects or undesirable shifts toward hyperopia.[25] Any preventive optical strategy would have to be extremely effective to overcome the irony of wearing a correction when emmetropic to avoid wearing a future correction for myopia.

Another strategy for making treatment decisions might consider the eventual probability of myopia onset rather than a dichotomous cutpoint. This approach raises the question: How high a probability in how many years into the future would lead clinicians or parents to initiate treatment? A spherical equivalent refractive error of +0.50 D may be an optimal cutpoint for a 7-year-old, but Fig. 1 shows very different eventual probabilities of myopia for a 7-year-old Asian American girl with a spherical equivalent refractive error of +0.50 D (0.54) compared with a White male (0.09). Perhaps those probabilities should be viewed relative to the expected prevalence for a given child's demographic data in order to make them more useful when deciding about initiating preventive treatment.

The CLEERE dataset has several strengths, a major one being the diversity in its representation of major racial/ethnic groups in the United States. The percentages of Black children were close to the 12 to 13% reported for the census data between 1990 and 2010 (www.census.gov), whereas Whites were underrepresented and Asian American, Hispanic, and Native American children were overrepresented. Refractive error was measured using an objective, validated, cycloplegic protocol.[34,39,40] Covariates that vary with time such as near work and time outdoors were considered in the current discrete time survival model and in the previous discrete time hazard models, as recommended, but were noncontributory.[17,38] Nonmyopic refractive errors spanned a wide range up to +3.00 D but excluded 100 children with +3.00 D or more hyperopia who were not at risk for myopia onset. The range of baseline ages in CLEERE was wider with longer follow-up compared with WEPrOM but not as wide as NICER.[10,29,31,37] However, the CLEERE data span the ages when most myopia develops.[41] A major limitation for CLEERE is that data collection occurred between 1989 and 2010. A considerable amount of epidemiologic data indicates that the prevalence of myopia has increased in recent decades.[6,42–44] The likely source of increased prevalence is time-varying environmental factors such as increased near work, decreased time outdoors, or some combination of the two. Changes in children's behavior imposed by COVID restrictions implicate both, with some indication from multivariate analysis of greater effects from limited time outdoors compared with increased near work.[45–47] Importantly, neither CLEERE nor other predictive models include these time-varying factors in the calculation of probability of myopia onset. More children may be at risk due to changes in behavior, but once a particular level of refractive error is reached,

the probability of myopia onset by sex and ethnicity may not have changed substantially. The list of risk factors for myopia onset has not changed over time, and the power of refractive error as a predictive variable is quite consistent across studies conducted more recently than CLEERE and in different parts of the world.[15,17,27,29,30] Efforts toward harmonization of prediction calculators will be useful as more longitudinal studies become available. In addition to providing a consensus predictive model, another aspect of harmonization of various longitudinal datasets would be to determine if the probabilities attached to the various risk factors have changed over time. The current CLEERE predicative model suggests that the probabilities for the onset of myopia across the diverse racial/ethnic heritages of children in the United States can be based on a simple set of refractive error and demographic variables.

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