Racial and Ethnic Differences in Myopia Progression in a Large, Diverse Cohort of Pediatric Patients

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Purpose. The purpose of this study was to characterize the differences in myopic progression in children by race/ethnicity and age.

Methods. Patients enrolled in Kaiser Permanente Southern California between 2011 and 2016 and between the ages of 4 and 11 years old with a documented refraction between −6 and −1 diopters (Ds) were included in this retrospective cohort study. Patients with a history of amblyopia, strabismus, retinopathy of prematurity, or prior ocular surgery were excluded from analyses. Patients' race/ethnicity and language information were used to create the following groups for analysis: white, Black, Hispanic, South Asian, East/Southeast Asian, Other Asian, and other/unknown. A growth curve analysis using linear mixed-effects modeling was used to trace longitudinal progression of spherical equivalents over time, modeled by race/ethnicity. Analyses adjusted for potential confounders, including body mass index (BMI), screen time, and physical activity.

Results. There were 11,595 patients who met the inclusion criteria. Patients were 53% girls, 55% Latino, 15% white, 9% black, 9% East/Southeast Asian, and 2% South Asian. Mean age (standard deviation [SD]) at the time of initial refraction was 8.9 years (1.6 years). Patients had an average (SD) of 3.4 (1.5) refractions, including the baseline measurement, during the study period. A three-way interaction model that assessed the effects of age at baseline, time since baseline, and race/ethnicity found that children of East/Southeast Asian descent showed significantly faster myopia progression across time ($P < 0.001$). East/Southeast Asian patients who presented with myopia between 6 to < 8 years progressed similarly to white patients in the same age group and significantly faster compared with white patients in other age groups.

Conclusions. Myopia progression differed significantly between East/Southeast Asian and white patients depending on the patients' age.

Keywords: myopia, pediatrics, refraction, ocular, race factors

Myopia is increasingly appreciated as a major global public health concern. Although myopia has long been established as a common cause of vision impairment,[1,2] myopia's growing prevalence, especially in East Asia, necessitates greater exploration into the risk factors for myopia onset and progression. Approximately one-third of American and European adults are myopic, whereas the prevalence of myopia in many East Asian countries now reaches 80–90%.[3–7] It is estimated that approximately 49.8% of the global population will have myopia by 2050 and 9.8% will have high myopia of -5.0 D or less.[2]

The concerns around myopia extend beyond the need for corrective lenses. Being myopic increases the patients' risk of irreversible vision loss from multiple secondary sequelae, including retinal detachments, maculopathy, choroidal neovascular membranes, and optic neuropathy.[8] Patients with high myopia (≤-10.0 D) experience diminished quality of life comparable to those with keratoconus.[9] Visual impairment from uncorrected myopia is estimated to result in a global potential productivity loss of US $244 billion dollars, with the Southern and Eastern parts of Asia taking on the greatest burden.[10]

The risk factors for myopia progression are multifactorial and incompletely understood. The risk factors driving myopia incidence in children are of particular importance as the incidence of childhood onset of myopia has increased.[11] Myopia that begins earlier in childhood has been shown to progress faster than adult-onset myopia.[12,13] Pärssinen et al. examined the risk factors for pediatric myopic progression into adulthood and found that higher myopia in adults was associated with less time spent on sports and outdoor activities during childhood and higher parental myopia.[14] Hu et al. found that older age, female sex, and lower initial refractive error were associated with faster myopia progression in Chinese patients.[15] Donovan et al.'s meta-analysis of children wearing single-vision spectacles found that myopia

progression rates were higher in urban Asians compared to urban Europeans with younger children and girls having greater annual rates of progression.[16]

Considerable research has examined interventions to slow myopia progression and a one-size-fits-all approach may not be appropriate. However, most studies on myopia follow ethnically homogenous cohorts, which limit the generalizability of results. Although racial differences in myopic progression have been examined previously, the exact role that race plays in the development and progression of myopia remains incompletely understood. Some studies have compared the prevalence of myopia across different geographic regions to assess racial differences. However, this approach generates questions around confounding variables as the diversity of countries and cultures bring about differences in risk factors other than race. In addition, as myopia often develops at younger ages, studying children will identify which groups are at greatest risk for progression.

The purpose of the current study is to compare progression data between races from a large real-world population. The value of using real-world population data is that the information comes from the same source population to minimize selection bias and confounding. This study is a retrospective cohort study that includes over 36,000 refractions from over 11,000 children with myopia. Information from this study may help in designing racially and culturally specific interventions and in planning clinical trials.

Methods

We conducted a retrospective cohort study of pediatric patients enrolled in Kaiser Permanente Southern California (KPSC), an integrated health care organization whose patient population is reflective of the socioeconomic and racial diversity of Southern California.[17] KPSC's electronic health records (EHRs) from 2011 to 2016 were used to identify study-eligible patients.

We focused on children with early onset myopia who were between 4 and 11 years old when they had a refraction measurement between -6 to -1 diopters (Ds). The first measurement where the refractive error was ≤-1 D defined the baseline measurement and all follow-up measurements were included in the analysis. Patients also must have at least one follow-up refraction ≥21 months after the baseline measurement and before the end of 2017. Patients with amblyopia, strabismus, or retinopathy of prematurity were identified through International Classification of Diseases (ICD) codes and excluded from the sample. Patients with strabismus or cataract surgery were identified by Current Procedural Terminology (CPT) codes prior to their first qualifying refraction measurement and were also excluded. Furthermore, patients whose medical records lacked information on gender were excluded from analysis ($n = 18$).

Patient information on race, ethnicity, and language preferences were abstracted from the KPSC EHR. Patients were surveyed on this information upon enrollment within KPSC and additional details could be added at any time during their care. For children under the age of 12 years old, parents were asked for this information. Patients older than 12 years old were asked to self-report this information. Patients born at KSPC had their maternal race and ethnicity used for identification purposes unless otherwise specified. For race, patients could identify as American Indian or Alaska Native, Asian, Black or African American, Hispanic or Latino, Native Hawaiian or Pacific Islander, white, decline to state, other, or unknown. For ethnicity, patients could select from a list of over 250 groups or select "Decline to State," "Other," or "Unknown." For our study, race/ethnicity categories were collapsed to white, Black, Hispanic, South Asian, East/Southeast Asian, other Asian, and other/unknown. Patients were classified as South Asian if the patient self-identified, or—in the case of children under the age of 12 years—were identified by their parent(s), as Afghan, Asian Indian, Bangladeshi, East Indian, Nepalese, Pakistani, or Sri Lankan, or indicated that their written or spoken language was Bengali, Gujarati, Hindi, Malayalam, Panjabi, Pashto, Punjabi, Sinhalese, Urdu, or Urdu Pakistan. Although other languages are spoken in South Asia, the aforementioned languages were the only ones that patients within this cohort identified as using. Patients were classified as East/Southeast Asian if they were identified as a racial/ethnic group related to or had a primary, spoken, or written language pertaining to East/Southeast Asia. The East/Southeast Asian group included the following racial/ethnic groups: Asian/Pacific Islander, Cambodian, Chinese, Filipino, Indonesian, Japanese, Kinh/Viet, Korean, Laotian, Malaysian, Tagalog, Taiwanese, Thai, and Vietnamese. Languages classifying a patient as East/Southeast Asian were the following: Burmese, Chinese, Dzongkha, Hakka, Japanese, Khmer, Korean, Laotian, Mandarin, Philippine, Tagalog, Thai, Toishanese, and Vietnamese. Patients who were identified as Asian race but were missing more specific race-ethnicity information, specified their language as English only, spoke languages not typically associated with South Asian or East/Southeast Asian regions, or lacked information to further classify the Asian group were categorized as other Asian.

Cycloplegic, manifest, final, and wearing refractions were included for analysis. If a patient had more than one refraction on the same day, the measurement was selected in the same order of priority. The eye with the more negative refractive error at baseline was chosen for analysis. Measurement or recording errors were possible and patients with a biologically implausible average yearly refraction change (calculated using the baseline and final measurements of refractive errors) of ≥ 10 D were excluded from analyses.

Covariates of interest included age, sex, race/ethnicity, body mass index (BMI), year of first examination, screen time, physical activity, and outdoor time. Age at baseline was defined as the patient's age at the time of the first refraction measurement. BMI was calculated using height and weight measurements closest to the date of the initial refraction. Screen time, physical activity, and outdoor time were abstracted from the EHR. At well-child visits, patients were asked whether they had < 2 hours of screen time per day, > 1 hour of physical activity per day, and > 2 hours of outdoor time per day. Responses from the visit closest to baseline were abstracted for analyses. Data on outdoor time were only available in 2017.

A growth curve analysis using linear mixed-effects models was used to trace longitudinal progression of spherical equivalents (SEs) over time by age at baseline. As this longitudinal model relies on person-time, this model traces an average trend across observations among patients of the same age or the same time since onset, rather than trac-

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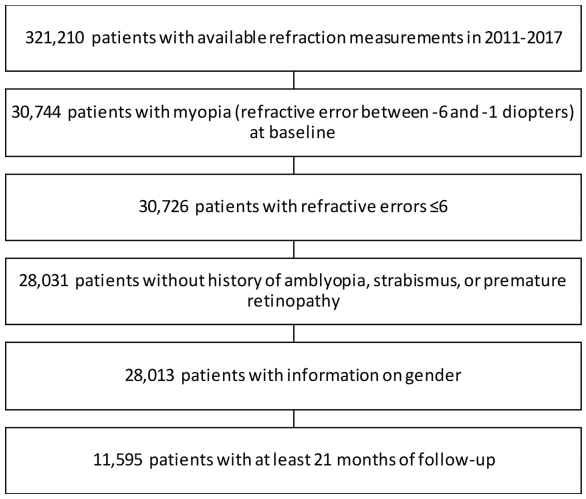

Figure 1. Flow chart of patient eligibility.

ing each individual's trajectory and then averaging those trajectories.

Analyses adjusted for potential confounders or proxies of confounders including BMI z-score percentiles (< 5%, 5–< 85%, 85–< 95%, and 95–100%), screen time (< 2 vs. ≥ 2 hours per day), and physical activity (≥ 1 vs. < 1 hour per day). We used a conditional growth model with refractive error as the outcome to estimate the fixed and random effects of time since baseline measure. These time effects allowed us to trace the trend of myopia progression by age at baseline and across time, conditional on potential confounders. The intrapatient correlation was specified as an autocorrelation structure of order 1. To understand whether the growth trajectory varied with different baseline ages and race/ethnicities, we included a three-way interaction between the time of refractive error measurement, age at baseline measurement, and race/ethnicity. The post hoc tests of pairwise comparisons of the estimated growth trends between race/ethnicity groups were performed using Tukey's method.[18] Patients missing data on screen time, physical activity, or outdoor time were categorized as unknown for these variables and were included in analyses. Analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R (R version 3.4.3).

Institutional Review Board (IRB) approval was obtained. This research also adhered to the tenets of the Declaration of Helsinki.

Results

A total of 11,595 patients met inclusion criteria (Fig. 1) and contributed 39,690 measurements for analyses. The cohort consisted of 6327 (55%) patients of Latino race/ethnicity and 6122 (53%) girls (Table 1). The average age at baseline (standard deviation [SD]) was 8.9 years (1.6 years). Of these children, 7% were between 4 and < 6 years of age, 21% were between 6 and < 8 years, 41% were between 8 and < 10 years, and 31% were between 10 and < 12 years. The average length of follow-up (SD) was 3.1 years (0.9 years) with a range of 1.8 to 5.9 years (Tables S1 & S3). Data on screen time and physical activity were missing for 13% and 10% patients, respectively. Among patients with available information, 90% patients reported < 2 hours of screen time per day and 94% patients had physical activity of ≥ 1 hour per day.

Patients underwent an average of 3.4 (SD = 1.5) refractions, including the baseline measurement, during the study period, and 75% patients had at least 3 measurements for analyses (see Table 1). The average SE at baseline was –2.0 (SD = 1.0) diopters (Ds) and varied between –2.2 and –1.9 D across race/ethnicity groups (see Table 1). Of all refractive errors at baseline, 5.8% were cycloplegic, 84.9% were final, 8.1% were manifest, and 1.1% were wearing (Table S1). Of all refractive errors used in the analysis, including baseline, 4.6% were cycloplegic, 85.7% were final, 5.1% were manifest, and 4.7% were wearing (Table S1). Among all 39,690 measurements, 26% of measurements were taken when the patient was between 12 and 16.2 years of age.

Of the 11,595 patients in the cohort, 26 children were missing information on BMI, leaving 11,569 children for the growth model analyses. Table 2 model A shows results for mixed-effects models controlling for potential confounders, such as screen time and physical activity. Model A shows that, on average, SE decreased by 0.37 D per year post-baseline. Boys had a slightly higher SE by 0.02 D compared to girls ($P = 0.007$). We did not find significant differences by levels of screen time and physical activity. Compared to younger patients between 4 and < 6 years of age, older patients were found to have more severe myopia (see Table 2, model A). Only children of Latino, East/Southeast Asian, and other Asian race showed significant differences in their severity of myopia compared to white children controlling for sex, age at baseline, and change over time.

Table 2 model B shows all significant effects of a three-way interaction model that assessed the effects of age at baseline, time since baseline, and race/ethnicity. Only children of East/Southeast Asian descent showed demonstrable different growth trajectory across time ($P = 0.001$).

Figure 2A traces the change over time and suggested that East/Southeast Asian children's myopia progressed faster than that of white children. Although the average SE at the time of initial refraction is more negative for white children than East/Southeast Asian children, crossover occurs at 1-year follow-up when progression is higher for East/Southeast Asian children compared to white children. Figure 2B used age at diagnoses and time since baseline to calculate myopia trajectories across age and by age of onset among white and East/Southeast children. A pairwise test of slopes (Table 3) showed that white children appeared to progress independently of the age of myopia onset. Conversely, East/Southeast Asian children had different trajectories across age and trajectories that varied significantly by age of onset, when compared to white children (see Table 3, model B). Overall, East/Southeast Asian children demonstrated a greater degree of progression compared to their white counterparts (see Table 2). Furthermore, East and Southeast Asian children who presented with myopia between 10 and < 12 years of age had significantly different changes over time compared to children of the same race who were diagnosed at younger ages (see Fig. 2, Table 3).

Discussion

The current study presents myopic progression data across race and ethnicity within one population. The study does show that race/ethnicity is a significant predictor for myopia

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Table 1. Descriptives of Sample by Race/Ethnicity

	White	Black	Latino	South Asian	East/ Southeast Asian	Other Asian	Other/ Unknown	Total
Number of children	1691	996	6327	215	1025	843	498	11,595
Age at baseline examination, y								
Mean (SD)	8.9 (1.6)	8.7 (1.7)	8.8 (1.6)	8.8 (1.7)	9.1 (1.4)	8.9 (1.5)	9.1 (1.5)	8.9 (1.6)
Age at baseline exam, *N* (%)								
[4, 6)	98 (6)	95 (10)	454 (7)	19 (9)	40 (4)	32 (4)	17 (3)	755 (7)
[6, 8)	338 (20)	218 (22)	1358 (21)	41 (19)	188 (18)	203 (24)	105 (21)	2451 (21)
[8, 10)	716 (42)	401 (40)	2574 (41)	93 (43)	454 (44)	363 (43)	205 (41)	4806 (41)
[10, 12)	539 (32)	282 (28)	1941 (31)	62 (29)	343 (33)	245 (29)	171 (34)	3583 (31)
Gender, *N* (%)								
Female	879 (52)	540 (54)	3400 (54)	119 (55)	501 (49)	412 (49)	271 (54)	6122 (53)
Male	812 (48)	456 (46)	2927 (46)	96 (45)	524 (51)	431 (51)	227 (46)	5473 (47)
BMI z-score								
N	1683	994	6319	214	1023	841	495	11569
Missing	8	2	8	1	2	2	3	26
Mean (SD)	0.6 (0.3)	0.7 (0.3)	0.7 (0.3)	0.5 (0.3)	0.6 (0.3)	0.5 (0.3)	0.6 (0.3)	0.7 (0.3)
Screen time < 2 h / day, *N* (%)								
Yes	1286 (76)	734 (74)	5077 (80)	178 (83)	767 (75)	653 (77)	378 (76)	9073 (78)
No	152 (9)	115 (12)	577 (9)	14 (7)	93 (9)	61 (7)	41 (8)	1053 (9)
Missing	253 (15)	147 (15)	673 (11)	23 (11)	165 (16)	129 (15)	79 (16)	1469 (13)
Physical play ≥ 1 h / day, *N* (%)								
Yes	1424 (84)	854 (86)	5492 (87)	186 (87)	826 (81)	692 (82)	409 (82)	9883 (85)
No	62 (4)	29 (3)	333 (5)	11 (5)	70 (7)	47 (6)	28 (6)	580 (5)
Missing	205 (12)	113 (11)	502 (8)	18 (8)	129 (13)	104 (12)	61 (12)	1132 (10)
Number of measurements at baseline and during follow-up								
Mean (SD)	3.6 (1.6)	3.1 (1.3)	3.3 (1.3)	3.8 (2.1)	3.6 (1.7)	3.7 (1.6)	3.6 (1.5)	3.4 (1.5)
Number of measurements at baseline and follow-up, *N* (%)								
2	399 (23.6)	364 (36.6)	1642 (26.0)	45 (20.9)	214 (20.9)	163 (19.3)	119 (23.9)	2946 (25.4)
3 or More	1292 (76.4)	632 (63.5)	4685 (74.0)	170 (79.1)	811 (79.1)	680 (80.6)	379 (76.1)	8649 (74.6)
Refraction error								
Mean (SD)	−1.9 (1.0)	−2.1 (1.0)	−2.0 (1.0)	−2.1 (1.0)	−2.2 (1.1)	−2.1 (1.0)	−2.1 (1.1)	−2.0 (1.0)
Average yearly change in refractive error from first to last measurement								
Mean (SD)	−0.4 (0.4)	−0.3 (0.4)	−0.3 (0.4)	−0.5 (0.3)	−0.5 (0.4)	−0.5 (0.4)	−0.4 (0.4)	−0.4 (0.4)
Length of follow-up in y								
Mean (SD)	3.2 (0.9)	3.1 (0.9)	3.1 (0.9)	3.2 (0.9)	3.2 (0.9)	3.3 (0.9)	3.1 (1)	3.1 (0.9)
Median (IQR)	3.1 (2.3, 3.9)	3 (2.3, 3.8)	3 (2.3, 3.8)	3.1 (2.4, 3.9)	3.1 (2.4, 4)	3.2 (2.4, 4)	3 (2.2, 3.9)	3.1 (2.3, 3.9)

BMI = body mass index; IQR = interquartile range; SD = standard deviation.

progression. Only East/Southeast Asian differed in terms of their overall trajectory from white children by having steeper declines in SE. White children tended to have similar degrees of myopia progression across ages of < 10 years.

Myopia is a complex and multifactorial disease that includes genetic and environmental factors. Increased outdoor time, low-dose atropine, and orthokeratology had been used with variable success to prevent the onset or progression of myopia.[19] Understanding which patients are at risk for myopia progression and at what ages can help focus attention on possible interventions to higher risk patients. Hu et al.'s Chinese cohort (n = 495, mean age 5.12 years) found that 35.8% of children demonstrated refractive stability over at least 2 years. Further, the authors found that older age, female sex, and lower initial refractive error were associated with faster myopia progression.[15] Donovan et al.'s meta-analysis of children wearing single-vision spectacles found that myopia progression rates were higher in urban Asians than urban European populations with younger children and girls having greater annual rates of progression.[16] Our findings support Donovan's finding in a cohort that shares the same physical environment. Consistent with the findings from Hu et al., we found that myopia progression is instantaneous from the time of baseline measure and continuous over time.

In our current study, information on screen time and physical activity had high proportions of missing data, 13% and 10%, respectively, and these proportions were larger than the proportion of patients with > 2 hours of screen time per day (9%) and patients with < 1 hour of physical activity per day (5%). Additionally, the available data showed little distinction between race-ethnicity groups and might be subject to recall or response bias. Given the high proportion of missing data and the lack of statistical significance of screen time and physical activity in the univariate results, we conducted a sensitivity analyses without these two variables. We found that the effect and significances of regression coefficients of time were consistent between the two models with and without physical activity and screen time (Table S4). In a prospective longitudinal study of 10,000 children between 5 and 15 years of age, Saxena et al. found that use of computers/video games and watching television had been found to be significant risk factors for myopia progression within 1 year.[20] Additionally, in a 2-year prospective cohort study

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Table 2. Results of Mixed Effect Models Predicting Refractive Error, Controlling for Potential Behavioral Confounders

	Model A			Model B		
	Beta Coefficient	Standard Error	*P* Value	Beta Coefficient	Standard Error	*P* Value
Intercept	0.56	0.03	<0.001	0.47	0.06	<0.001
Years from baseline	−0.37	0.00	<0.001	−0.37	0.04	<0.001
Gender						
Female		Reference			Reference	
Male	0.02	0.01	0.007	0.02	0.01	0.005
Race/ethnicity						
White		Reference			Reference	
Black	0.02	0.02	0.306	0.01	0.08	0.915
Latino	0.03	0.01	0.026	−0.01	0.06	0.932
South Asian	−0.04	0.03	0.262	0.04	0.14	0.800
East/Southeast Asian	−0.04	0.02	0.039	0.34	0.10	0.001
Other Asian	−0.09	0.02	<0.001	−0.09	0.11	0.421
Other/unknown	0.01	0.02	0.765	0.14	0.13	0.277
Screen time <2 h / day						
No		Reference			Reference	
Yes	−0.01	0.01	0.448	−0.01	0.01	0.573
Missing	0.02	0.02	0.408	0.02	0.02	0.324
Physical activity ≥ 1 h / day						
No		Reference			Reference	
Yes	0.02	0.01	0.071	0.02	0.01	0.105
Missing	0.01	0.02	0.664	0.00	0.02	0.906
Refractive error at baseline	1.00	0.00	<0.001	1.00	0.00	<0.001
Age at baseline, y						
[4, 6)		Reference			Reference	
[6, 8)	−0.23	0.02	<0.001	0.00	0.06	0.947
[8, 10)	−0.26	0.02	<0.001	−0.12	0.06	0.049
[10, 12)	−0.26	0.02	<0.001	−0.21	0.06	<0.001
BMI z-score percentile						
[0, 5)		Reference			Reference	
[5, 85)	0.01	0.02	0.761	0.01	0.02	0.766
[85, 95)	0.00	0.02	0.995	0.00	0.02	0.995
[95, 100)	0.02	0.02	0.410	0.02	0.02	0.418
Years from baseline*baseline age						
Years from baseline*baseline age [4, 6)	–	–	–		Reference	
Years from baseline*baseline age [6, 8)	–	–	–	−0.13	0.04	0.001
Years from baseline*baseline age [8, 10)	–	–	–	−0.04	0.04	0.257
Years from baseline*baseline age [10, 12)	–	–	–	0.06	0.04	0.129
Trajectories by race/ethnicity						
Years from baseline*White	–	–	–		Reference	
Years from baseline*Black	–	–	–	0.10	0.05	0.043
Years from baseline*Latino	–	–	–	0.16	0.04	<0.001
Years from baseline*South Asian	–	–	–	−0.13	0.09	0.146
Years from baseline*East/Southeast Asian	–	–	–	−0.24	0.07	<0.001
Years from baseline*Other Asian	–	–	–	−0.12	0.07	0.106
Years from baseline*Other/unknown	–	–	–	0.08	0.09	0.368
Baseline age [6, 8)*race/ethnicity						
Baseline age [6, 8)*White	–	–	–		Reference	
Baseline age [6, 8)*Black	–	–	–	−0.13	0.10	0.159
Baseline age [6, 8)*Latino	–	–	–	−0.07	0.07	0.339
Baseline age [6, 8)*South Asian	–	–	–	0.07	0.17	0.673
Baseline age [6, 8)*East/Southeast Asian	–	–	–	−0.31	0.11	0.006
Baseline age [6, 8)*Other Asian	–	–	–	0.05	0.12	0.655
Baseline age [6, 8)*Other/unknown	–	–	–	−0.02	0.15	0.901
Baseline age [8, 10)*race/ethnicity						
Baseline age [8, 10)*White	–	–	–		Reference	
Baseline age [8, 10)*Black	–	–	–	−0.13	0.09	0.133
Baseline age [8, 10)*Latino	–	–	–	−0.04	0.07	0.550
Baseline age [8, 10)*South Asian	–	–	–	−0.04	0.15	0.809
Baseline age [8, 10)*East/Southeast Asian	–	–	–	−0.31	0.11	0.003
Baseline age [8, 10)*Other Asian	–	–	–	0.06	0.12	0.582
Baseline age [8, 10)*Other/unknown	–	–	–	−0.15	0.14	0.281

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Table 2. Continued

	Model A			Model B		
	Beta Coefficient	**Standard Error**	***P* Value**	**Beta Coefficient**	**Standard Error**	***P* Value**
Baseline age [10, 12)*race/ethnicity						
Baseline age [10, 12)*White	–	–	–	Reference		
Baseline age [10, 12)*Black	–	–	–	−0.07	0.09	0.435
Baseline age [10, 12)*Latino	–	–	–	−0.02	0.07	0.762
Baseline age [10, 12)*South Asian	–	–	–	0.05	0.16	0.764
Baseline age [10, 12)*East/Southeast Asian	–	–	–	−0.33	0.11	0.002
Baseline age [10, 12)*Other Asian	–	–	–	0.10	0.12	0.385
Baseline age [10, 12)*Other/unknown	–	–	–	−0.11	0.14	0.445
Years from baseline*baseline age [6, 8)*race/ethnicity						
Years from baseline*baseline age [6, 8)*White	–	–	–	Reference		
Years from baseline*baseline age [6, 8)*Black	–	–	–	0.01	0.06	0.802
Years from baseline*baseline age [6, 8)*Latino	–	–	–	−0.05	0.04	0.304
Years from baseline*baseline age [6, 8)*South Asian	–	–	–	0.00	0.10	0.978
Years from baseline*baseline age [6, 8)*East/Southeast Asian	–	–	–	0.14	0.07	0.047
Years from baseline*baseline age [6, 8)*Other Asian	–	–	–	0.02	0.08	0.756
Years from baseline*baseline age [6, 8)*Other/unknown race/ethnicity	–	–	–	−0.16	0.10	0.109
Years from baseline*baseline age [8, 10)*race/ethnicity						
Years from baseline*baseline age [8, 10)*White	–	–	–	Reference		
Years from baseline*baseline age [8, 10)*Black	–	–	–	0.02	0.06	0.654
Years from baseline*baseline age [8, 10)*Latino	–	–	–	−0.10	0.04	0.016
Years from baseline*baseline age [8, 10)*South Asian	–	–	–	0.09	0.10	0.326
Years from baseline*baseline age [8, 10)*East/Southeast Asian	–	–	–	0.18	0.07	0.011
Years from baseline*baseline age [8, 10)*Other Asian	–	–	–	0.06	0.07	0.434
Years from baseline*baseline age [8, 10)*Other/unknown race/ethnicity	–	–	–	−0.08	0.09	0.374
Years from baseline*baseline age [10, 12)*race/ethnicity						
Years from baseline*baseline age [10, 12)*White	–	–	–	Reference		
Years from baseline*baseline age [10, 12)*Black	–	–	–	−0.03	0.06	0.549
Years from baseline*baseline age [10, 12)*Latino	–	–	–	−0.14	0.04	0.001
Years from baseline*baseline age [10, 12)*South Asian	–	–	–	0.03	0.10	0.730
Years from baseline*baseline age [10, 12)*East/Southeast Asian	–	–	–	0.21	0.07	0.002
Years from baseline*baseline age [10, 12)*Other Asian	–	–	–	0.06	0.08	0.408
Years from baseline*baseline age [10, 12)*Other/unknown race/ethnicity	–	–	–	−0.14	0.09	0.137
Model information	**Model A**			**Model B**		
Model fit						
AIC	79,746.56			79,169.20		
BIC	79,961.23			79,770.28		
Number of children in model	11,569			11,569		
Number of observations	39,609			39,609		

AIC = Akaike information criterion; BIC = Bayesian information criterion.
*An asterisk marks an interaction effect between variables.

of 156 medical students, Jacobsen et al. found a significant, inverse association between physical activity and refractive change toward myopia.[21] Although our current study found no association between screen time or physical activity and myopia progression, future work can investigate screen time using finer categories and physical activity in younger populations with the distinction between outdoor and indoor physical activity.

Our study has some limitations. Although our sample is larger than that of population-based cohort studies, such as the Guangzhou Twin Eye Study (GTES; $n = 1831$),[22] the Generation R study ($n = 3422$),[23] and the Avon Longitudinal Study of Parents and Children (ALSPAC; $n = 2833$),[24] and our results are similar to prior studies in many ways, results may not be fully generalizable to other white or East/Southeast Asian populations. As we were interested in the trajectories of children who present with myopia earlier in life, we did not recruit children older than 11 years into this study, leaving fewer, yet numerically sufficient numbers to estimate trends beyond ages 11 years. Another limitation is the study's real-world setting, where cycloplegic refractions were not performed routinely in patients with myopia in this age group. The lack of cycloplegia results in overestimation of myopia in young children and, as a result, the values presented herein may overestimate myopic error; however, the purpose of this study was not to characterize

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Table 3. *P* Values of Pairwise Comparisons of Growth Trends Between East/Southeast Asian and White Patients Across Baseline Age Groups, from Three-Way Interaction Model (Model B)

		White				East/Southeast Asian			
		[4, 6)	[6, 8)	[8, 10)	[10, 12)	[4, 6)	[6, 8)	[8, 10)	[10, 12)
White	[4, 6)		0.232	1.000	1.000	0.048*	<0.001*	0.435	1.000
	[6, 8)			0.064	<0.001*	0.972	0.274	1.000	<0.001*
	[8, 10)				<0.001*	0.087	<0.001*	0.181	0.427
	[10, 12)					<0.001*	<0.001*	<0.001*	1.000
East/Southeast Asian	[4, 6)						1.000	0.878	0.001*
	[6, 8)							0.040*	<0.001*
	[8, 10)								<0.001*
	[10, 12)								

Model B shows testing modification effect of age at baseline examination and years from baseline on racial/ethnic differences in myopia progression (3-way interaction between years from baseline, baseline age, and race/ethnicity; $n = 11{,}569$).

*Significant at $P < 0.05$.

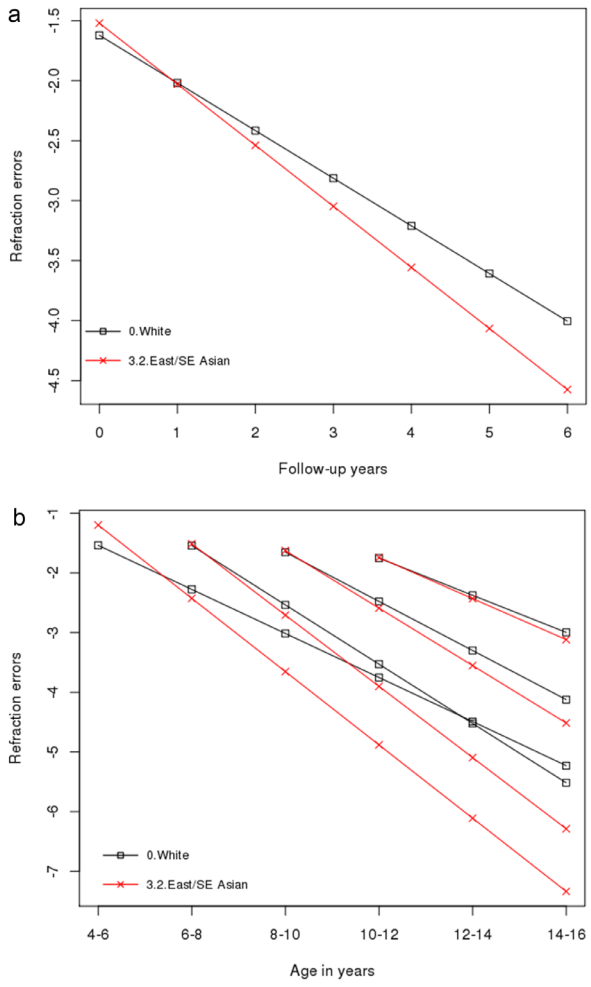

Figure 2. Refractive error by years of follow-up, as estimated by three-way interaction model, model B ($n = 11{,}595$). (**A**) Shows change in refractive error over time. (**B**) Refractive error by age. **B** uses results from model B on age, time since baseline, and age at baseline to calculate trajectories for East/Southeast Asian Children and white children by age at baseline.

absolute refractive error in children but instead to determine the differences in myopic trajectories based on race. Given cycloplegia was not the norm in children and there was no differential application between race and ethnic groups, we do not anticipate the lack of cycloplegia would affect the differences in progression seen between races. We also assumed that the progression was linear and we verified this assumption by reviewing a spaghetti plot of the refractive errors and performing a test for curvature, which was not significant.

The strength of our study lies in the real-world analysis of a large, racially and ethnically diverse cohort of 11,595 patients. Additionally, the use of an EHR-based dataset allows us to longitudinally assess refractive errors in a large cohort of patients, similar to the GTES and ALSPAC studies.[22,24] With the size and diversity of our cohort, we were able to analyze 39,690 refractive error measurements and identify differences in myopia progression between major race and ethnicity groups and groups within the Asian category. Such analysis has been able to reveal differences between groups that would have been masked with a smaller or less diverse study population.

Our findings suggested that prevention efforts and clinical trials should consider race. Attention on East and Southeast Asian children should be considered as they demonstrate higher progression of myopia than any other race.

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References

1. Chua J, Wong TY. Myopia-the silent epidemic that should not be ignored. *JAMA Ophthalmol*. 2016;134(12):1363–1364.
2. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology*. 2016;123(5):1036–1042.
3. Vitale S, Ellwein L, Cotch MF, et al. Prevalence of refractive error in the United States, 1999-2004. *Arch Ophthalmol*. 2008;126(8):1111–1119.
4. Williams KM, Verhoeven VJ, Cumberland P, et al. Prevalence of refractive error in Europe: the European Eye Epidemiology (E(3)) Consortium. *Eur J Epidemiol*. 2015;30(4):305–315.

5. Pan CW, Dirani M, Cheng CY, et al. The age-specific prevalence of myopia in Asia: a meta-analysis. *Optom Vis Sci*. 2015;92(3):258–266.
6. Pan CW, Ramamurthy D, Saw SM. Worldwide prevalence and risk factors for myopia. *Ophthalmic Physiol Opt*. 2012;32(1):3–16.
7. Ding BY, Shih YF, Lin LLK, et al. Myopia among schoolchildren in East Asia and Singapore. *Surv Ophthalmol*. 2017;62(5):677–697.
8. Tideman JW, Snabel MC, Tedja MS, et al. Association of axial length with risk of uncorrectable visual impairment for Europeans with myopia. *JAMA Ophthalmol*. 2016;134(12):1355–1363.
9. Rose K, Harper R, Tromans C, et al. Quality of life in myopia. *Br J Ophthalmol*. 2000;84(9):1031–1034.
10. Naidoo KS, Fricke TR, Frick KD, et al. Potential lost productivity resulting from the global burden of myopia: systematic review, meta-analysis, and modeling. *Ophthalmology*. 2019;126(3):338–346.
11. Rose K, Smith W, Morgan I, Mitchell P. The increasing prevalence of myopia: implications for Australia. *Clin Exp Ophthalmol*. 2001;29(3):116–120.
12. Chua SY, Sabanayagam C, Cheung YB, et al. Age of onset of myopia predicts risk of high myopia in later childhood in myopic Singapore children. *Ophthalmic Physiol Opt*. 2016;36(4):388–394.
13. Brodstein RS, Brodstein DE, Olson RJ, et al. The treatment of myopia with atropine and bifocals. A long-term prospective study. *Ophthalmology*. 1984;91(11):1373–1379.
14. Parssinen O, Kauppinen M, Viljanen A. The progression of myopia from its onset at age 8-12 to adulthood and the influence of heredity and external factors on myopic progression. A 23-year follow-up study. *Acta Ophthalmol*. 2014;92(8):730–739.
15. Hu Y, Ding X, Long W, et al. Longitudinal changes in spherical equivalent refractive error among children with preschool myopia. *Invest Ophthalmol Vis Sci*. 2019; 60(1):154–160.
16. Donovan L, Sankaridurg P, Ho A, et al. Myopia progression rates in urban children wearing single-vision spectacles. *Optom Vis Sci*. 2012;89(1):27–32.
17. Koebnick C, Langer-Gould AM, Gould MK, et al. Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. *Perm J*. 2012;16(3):37–41.
18. Tukey JW. Comparing individual means in the analysis of variance. *Biometrics*. 1949;5(2):99–114.
19. Modjtahedi BS, Ferris FL, 3rd, Hunter DG, Fong DS. Public health burden and potential interventions for myopia. *Ophthalmology*. 2018;125(5):628–630.
20. Saxena R, Vashist P, Tandon R, et al. Incidence and progression of myopia and associated factors in urban school children in Delhi: The North India Myopia Study (NIM Study). *PLoS One*. 2017;12(12):e0189774.
21. Jacobsen N, Jensen H, Goldschmidt E. Does the level of physical activity in university students influence development and progression of myopia?–A 2-year prospective cohort study. *Invest Ophthalmol Vis Sci*. 2008;49(4):1322–1327.
22. Liao C, Ding X, Han X, et al. Role of parental refractive status in myopia progression: 12-year annual observation from the Guangzhou Twin Eye Study. *Invest Ophthalmol Vis Sci*. 2019;60(10):3499–3506.
23. Enthoven CA, Tideman JWL, Polling JR, et al. Interaction between lifestyle and genetic susceptibility in myopia: the Generation R study. *Eur J Epidemiol*. 2019;34(8):777–784.
24. Shah RL, Huang Y, Guggenheim JA, Williams C. Time outdoors at specific ages during early childhood and the risk of incident myopia. *Invest Ophthalmol Vis Sci*. 2017;58(2):1158–1166.