Independent Influence of Parental Myopia on Childhood Myopia in a Dose-Related Manner in 2,055 Trios: The Hong Kong Children Eye Study

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• PURPOSE: To determine the effects on childhood myopia of parental myopia, parental education, children's outdoor time, and children's near work.

• DESIGN: Population-based cross-sectional study.

• METHODS: A total of 6,155 subjects in 2,055 family trios (1 child and both parents). Cycloplegic autorefraction was measured for children and noncycloplegic autorefraction for parents. Parental education, children's outdoor time, and near work were collected by questionnaires. Children were categorized into 10 groups based on parental myopia levels. Associations of the above factors with myopia were evaluated by regression analyses. The areas under the receiver operating characteristic curve (AUROCs) for myopia were evaluated.

• RESULTS: Mild parental myopia did not increase childhood myopia's risk, but the risk was 11.22-folds when both parents were highly myopic. Higher parental education (Father: OR 1.08, $P = .046$; Mother: OR 1.11, $P = .001$) and more reading time of children were risk factors (OR 1.21, $P = .044$). Reduced odds of myopia were associated with more time spent on outdoor activities (OR 0.78, $P = .017$). Notably, all these factors became insignificant after adjustment, except for parental myopia. Children with more severe parental myopia spent more time on reading, but less on electronic devices. Parental myopic status alone accounted for 11.82% of myopia variation in children. With age and parental myopia, the AUROC for myopia was 0.731.

• CONCLUSIONS: Among parental and environmental factors, parental myopia confers, in a dose-related manner, the strongest independent effect on childhood myopia. Therefore children with high risk of myopia can be identified for early prevention, based on parental myopia data. **(Am J Ophthalmol 2020;218:199–207.**

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INTRODUCTION

GLOBALLY, MYOPIA IS THE MOST COMMON OCULAR disorder, and predominantly so in Asian populations. However, there has been an increasing prevalence over the past decades also in the other populations.[1–4] It is predicted that nearly half of the world's population would be myopic by 2050, with as much as 10% being highly myopic.[5] High myopia is associated with excessive eyeball growth leading to sight-threatening complications, including presenile cataract, glaucoma, retinal detachment, choroidal neovascularization, myopic macular degeneration, and macular hemorrhage.[6–10] It is a major public health concern, posing heavy health and economic burden to the society.

Parental myopia is a known risk factor for childhood myopia development, indicating genetic contribution.[11,12] Zadnik and associates demonstrated that history of parental myopia was associated with children's ocular size.[13] Subsequent studies supported parental myopia as a risk factor for childhood myopia development.[14–18] However, genetic contribution may not be the only risk, and environmental factors could be linked to parental myopia, which of itself affects children's vision.[19,20] Myopic parents may create a myopigenic environment including habits of intensive near-work and limited time outdoors.[19] Some studies suggested that time outdoor would neutralize the impact of parental myopia on childhood myopia.[14,19] Furthermore, the impact of parents' myopia severity on children's myopia development has not been established as a result of limited quantitative parental data. Results of several studies, which are based on self-reported history of parental myopia without actual refraction data, indicated a possible relationship between parental and childhood myopia.[13–15,17,18,21]

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TABLE 1. Demographic Comparison of 2,055 Trios With the Hong Kong Children Eye Study Cohort

Characteristic	Current Study (N = 2,055)	HKCES (N = 4257)	*P*
Male-female ratio	1.08	1.1	.05
Children's age (years)	7.61 ± 0.95	7.62 ± 0.96	.992
Children's axial length (mm)	23.15 ± 0.95	23.15 ± 0.95	.876
Children's SER (Diopter)	0.15 ± 1.59	0.14 ± 1.59	.741
Children myopia rate (%)	24.8%	25.0%	.715
Parental SER (Diopter)	–2.70 ± 2.88	–2.71 ± 2.95	.339
Low family income rate (%)	25.2%	38.0%	<.001

HKCES = Hong Kong Children Eye Study, SER = spherical equivalent refraction.
Unless otherwise noted, values are mean ± SD. Low family income was defined as household income lower than 20,000 HKD.

Here we studied 2,055 family trios (1 child and both parents) from the Hong Kong Children Eye Study (HKCES). We investigated known myopic factors: refraction and education level of parents, as well as children's outdoor time exposure and near-work time. We aimed to establish whether the severity of parental myopia has an influence on childhood myopia, and to evaluate whether this effect is independent of such environmental factors as children's outdoor time and near work.

METHODS

• **SUBJECTS:** The study subjects were recruited from the HKCES, a population-based cohort study of eye conditions in 4,257 children of grade 1 to grade 3 (aged 6–8 years) from primary schools in Hong Kong.[22–24] In brief, the HKCES was designed to determine the prevalence of children's ocular disorders, including refractive errors, strabismus, amblyopia, and allergic eye diseases, and to identify the environmental and genetic determinants of these conditions. Sample selection was based on a stratified and clustered randomized sampling frame. In Hong Kong, all primary schools (n = 571) registered in the Education Bureau were stratified into 7 clusters according to population densities. In HKCES, the schools in each cluster region were randomly assigned an invitation priority according to the ranking numbers generated by computer. Invitations to participate in the cohort were sent according to the ranking numbers until the required sample was achieved in each cluster region.

All children and both parents were given complete ophthalmoscopic investigations and assessments of environmental factors by questionnaires. If only 1 parent, either mother or father, completed the assessment, the whole family was not included in this report. Siblings and twins were also not included. The project conformed to the tenets of the Declaration of Helsinki and obtained ethical approval from the Institutional Review Board of the Chinese University of Hong Kong. Informed consent was signed by all participants.

• **OCULAR EXAMINATIONS:** Refractive status was measured for each child before and after cycloplegia using an autorefractor (Nidek ARK-510A, Gamagori, Japan). Two cycles of 1% cyclopentolate (Alcon, Vilvoorde, Belgium) and 1% tropicamide (Santen, Osaka, Japan) are given at 10 minutes apart. Thirty minutes after the last drop, a third cycle of cyclopentolate and tropicamide drops would be administered if pupillary light reflex was still present or the pupil size was less than 6.0 mm. Three or more readings of spherocylindrical autorefraction were taken and averaged at 30 minutes after the last drop of cycloplegic agent. Subjective refraction and best-corrected visual acuity were measured by an optometrist in those children with presenting visual acuity <20/25 in either eye. Noncycloplegic refraction was measured for parents.

• **DEFINITIONS OF MYOPIA:** Spherical equivalent refraction (SER) was defined as spherical diopters (D) plus one-half cylindrical diopters. In children, myopia was defined as SER of –0.50 D or less, emmetropia as –0.50 D < SER < +0.50 D, and hyperopia as SER ≥ +0.50 D. Mild myopia was defined as –0.50 D ≥ SER > –3.00 D, moderate myopia as –6 < SER ≤ –3.00 D, and high myopia as SER ≤ –6.00 D. In adults, myopia was defined as SER of –0.75 D or less. Otherwise, the grading of myopia was similar with that of children. Only data from right eye were included in the analysis in view of the high correlation between both eyes.

• **QUESTIONNAIRE ON PARENTAL EDUCATION LEVEL, CHILDREN'S OUTDOOR ACTIVITIES, AND NEAR WORK:** Validated questionnaires used in our study derived mainly from the Chinese version of those used in the Sydney Myopia Study (SMS),[25,26] so as to facilitate comparison between the 2 studies. The protocol was previously published.[22] First, adjustments for cultural differences and local dialect were implemented by discussing with the

TABLE 2. Myopia Prevalence in Children for Different Severities of Parental Myopia

Parental Myopic Status	No. of Children	Mean (±SD) Age of Children	Myopia Prevalence in Children % (95% CI)
No myopia + No myopia	165	7.66 ± 0.97	12.12 (7.94-18.07)
No myopia + Mild myopia	379	7.56 ± 0.96	12.66 (9.67-16.42)
Mild myopia + Mild myopia	236	7.68 ± 0.93	13.98 (10.11-19.03)
No myopia + Moderate myopia	226	7.66 ± 0.93	22.12 (17.17-28.02)
Mild myopia + Moderate myopia	329	7.61 ± 1.01	27.36 (22.8-32.44)
Moderate myopia + Moderate myopia	157	7.55 ± 0.88	33.76 (26.77-41.53)
High myopia + No myopia	130	7.71 ± 0.94	30.77 (23.41-39.25)
High myopia + Mild myopia	190	7.59 ± 1.04	31.05 (24.86-38)
High myopia + Moderate myopia	183	7.61 ± 0.92	45.36 (38.26-52.64)
High myopia + High myopia	60	7.67 ± 0.93	56.67 (43.86-68.64)
Overall	2,055		24.82 (23.69-26.29)

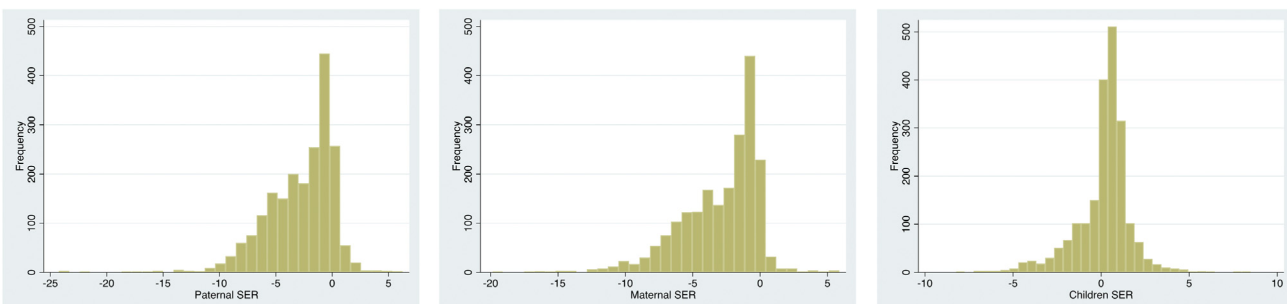

FIGURE 1. Distribution of refraction in father, mother, and children.

representatives of local teachers, parents, and ophthalmologists to make the questionnaires culturally appropriate and linguistically accurate. Second, a pilot study was performed among the parents of 100 children to verify the questionnaires' reliability and validity. For outdoor activity, it was found that the overall intraclass correlation coefficient between 2 repeated surveys (with an interval of 4 weeks) was 0.72, and that the Cronbach's alpha coefficient of each item was 0.68. Near-work activities included homework and pleasure reading. Watching television (TV), videos, digital video discs (DVDs), and playing computer games were classified as midrange activities. Diopter-hour was defined as follows: (hours spent studying + hours spent reading for pleasure) × 3 + (hours spent playing video games or working on the computer at home) × 2 + (hours spent watching television) × 1.[12] Total outdoor activities were divided into 2 categories, namely, outdoor for leisure (including walking, riding a bike, playing in park, and picnic) and sport activities. The average number of outdoor activity hours per day was calculated using the formula: [(hours spent on weekday) × 5 + (hours spent on weekend day) × 2]/7. Parental education was categorized according to Hong Kong's education system: primary school, secondary school, associate degree, bachelor's degree, and master's degree or higher.

Questionnaires were administered to parents for their completion with assistance by a trained staff in presence or on the telephone. All data of questionnaires were doubly entered to ensure integrity and precision. And for the missing data in the questionnaires, the parents would be further contacted for completion.

• **STATISTICAL ANALYSIS:** Prevalence and its 95% confidence interval were calculated for myopia in children. Parental influences on childhood myopia was evaluated as follows. First, parental myopia was categorized into 10 groups according to the combinations of paternal and maternal myopia severities. In each of the 10 groups, the prevalence of childhood myopia was determined. Odd ratios (ORs) of risk of childhood myopia in each group was calculated via logistic regression with adjustment for age and gender. Effect of (1) parental myopia; (2) parental education; (3) children's outdoor time; and (4) children's near-work time on childhood myopia development was evaluated separately via the logistic regression model with the adjustment of age and gender. Multiple logistic regression models were constructed to evaluate how each of the above factors contributes to childhood myopia. The areas under the receiver operating characteristic (ROC) curve of parental myopia, age, time of outdoors,

TABLE 3. The Influence of Parental Myopia and the Other Risk Factors on Children's Myopia

Factors	OR[a] (95% CI)	P^a Value	OR[b] (95% CI)	P^b Value	OR[c] (95% CI)	P^c Value
Parental myopic status						
No myopia + No myopia	Reference		Reference		Reference	
No myopia + Mild myopia	1.15 (0.65-2.02)	.168	1.09 (0.59-1.99)	.788	1.09 (0.6-1.99)	.78
Mild myopia + Mild myopia	1.27 (0.69-2.33)	.414	1.24 (0.65-2.35)	.514	1.23 (0.65-2.34)	.52
No myopia + Moderate myopia	2.20 (1.24-3.91)	.002	2.01 (1.08-3.74)	.027	2.02 (1.08-3.75)	.027
Mild myopia + Moderate myopia	3.09 (1.81-5.3)	<.001	3.08 (1.73-5.47)	<.001	3.10 (1.74-5.50)	<.001
Moderate myopia + Moderate myopia	4.31 (2.39-7.75)	<.001	4.23 (2.24-7.99)	<.001	4.25 (2.25-8.01)	<.001
High myopia + No myopia	3.43 (1.86-6.33)	<.001	3.54 (1.84-6.83)	<.001	3.55 (1.84-6.85)	<.001
High myopia + Mild myopia	3.74 (2.11-6.63)	<.001	3.84 (2.08-7.1)	<.001	3.84 (2.08-7.10)	<.001
High myopia + Moderate myopia	7.03 (3.99-12.37)	<.001	7.78 (4.19-14.46)	<.001	7.79 (4.20-14.47)	<.001
High myopia + High myopia	11.22 (5.49-22.93)	<.001	11.58 (5.35-25.06)	<.001	11.65 (5.38-25.23)	<.001
Paternal educational level	1.08 (1.00-1.17)	.046	0.90 (0.80-1.00)	.053	0.90 (0.81-1.01)	.068
Maternal educational level	1.11 (1.04-1.18)	.001	1.02 (0.92-1.15)	.699	1.02 (0.91-1.15)	.68
Time of outdoor	0.90 (0.8-1.02)	.092	NA	NA	1.00 (0.83-1.21)	.978
Outdoor for sports	0.94 (0.77-1.13)	.499	NA	NA	NA	NA
Outdoor for leisure	0.79 (0.65-0.96)	.017	NA	NA	NA	NA
Diopter*hour	0.99 (0.96-1.01)	.326	0.99 (0.95-1.03)	.721	1.00 (0.96-1.05)	.935
Total near-work time (hours per day)	1.06 (0.96-1.17)	.244	NA	NA	NA	NA
Watching TV	0.88 (0.76-1.01)	.074	NA	NA	NA	NA
Doing home work	1.02 (0.84-1.24)	.842	NA	NA	NA	NA
Reading	1.21 (1.01-1.48)	.044	NA	NA	NA	NA
Using computer	1.02 (0.86-1.21)	.804	NA	NA	NA	NA
Using electronic devices	0.80 (0.69-0.93)	.005	NA	NA	NA	NA
Total near-work time	1.06 (0.96-1.17)	.244	NA	NA	NA	NA

NA, not applicable.
[a]Age and gender were adjusted in the model.
[b]Age, gender, time of outdoors, parental education, and parental myopia status were in the model.
[c]Age, gender, diopter-hours of near work, parental education, and parental myopia status were in the model.

near work, and parental education level were evaluated with parametric ROC regression. The parametric ROC curve regression model was a probit model; a normal cumulative distribution function with input of a linear polynomial in the corresponding quantile function invoked on a false-positive rate.[27] A *P* value of less than .05 was considered statistically significant. All analyses were performed using Stata Statistical Software (version 14.0; StataCorp, College Station, Texas, USA).

RESULTS

A TOTAL OF 6,165 INDIVIDUALS FROM 2,055 FAMILY TRIOS were included in this study. The mean age of the children was 7.61±0.95 years (range 6-8); and for parents, 41.06±5.95 years (range 25-70). The overall myopia prevalence in children aged 6-8 years was 24.8% (Table 1). In parents, the prevalence of no myopia, mild, moderate, and high myopia was respectively 31.5%, 27.8%, 25.6%, and 15.2%. The demographics of this sample group were similar with the HKCES (Table 1), except family income. The proportion of low-income families of the current study was lower than that of the HKCES. The distributions of refraction in father, mother, and children were shown in Figure 1. The myopia prevalence in children increased with the severity of parental myopia (Table 2).

• SEPARATE EFFECT ON CHILDHOOD MYOPIA OF PARENTAL MYOPIA, PARENTAL EDUCATION LEVEL, CHILDREN'S OUTDOOR ACTIVITIES, AND CHILDREN'S NEAR WORK AFTER ADJUSTMENT OF AGE AND GENDER: Parental myopia has a dose-related effect on childhood myopia. Mild parental myopia conferred no effect (OR 1.15, 95% CI 0.65-2.02, $P = .168$; Table 3). The risk was 2.2-fold higher when one parent was moderately myopic (OR 2.20, 95% CI 1.24-3.91, $P = .002$; Table 3), and 11.22-fold higher when both parents were highly myopic (OR 11.22, 95% CI 5.49-22.93, $P < .001$; Table 3). The risk effect of myopia in children with a highly myopic parent may be reduced if the other parent was nonmyopic (OR 3.43, 95% CI 1.86-6.33, $P < .001$; Table 3) or mildly myopic (OR 3.74, 95% CI 2.11-6.63, $P < .001$; Table 3). Of note, the risk of childhood myopia was the same from paternal refraction (Beta coefficient: 0.12, $P < .001$,

FIGURE 2. Linear regression of children's refraction with paternal refraction status and maternal refraction status.

R^2=12.5%; Figure 2) and from maternal refraction (Beta coefficient: 0.13, P < .001, R^2=12.5%; Figure 2).

Paternal education level (OR 1.08, 95% CI 1.00-1.17, P = .046; Table 3) and maternal education level (OR 1.11, 95% CI 1.04-1.18, P = .001; Table 3) showed a positive association, that is, a higher parental education level conferring a higher risk.

The mean number of hours children spent on total outdoor activity was 1.45±0.63 hours/d, and was similar across different categories of parental myopic status (Table 4). We found a protective association of myopia with the outdoor time children spent specifically for leisure activities (OR 0.78, 95% CI 0.65-0.96, P = .017; Table 3), but not from total outdoor time (OR 0.90, 95% CI 0.80-1.02, P = .092; Table 3).

Children with more severe parental myopia spent more time on reading, but less on electronic devices (Table 4). Notably, time spent on reading showed a risk association with childhood myopia (OR 1.21, 95% CI 1.01-1.48, P = .044; Table 3), but time spent on electronic devices was a protective factor (OR 0.80, 95% CI 0.69-0.93, P = .005; Table 3). There was no significant association with the other near-work activities and diopter-hours of near work (Table 3).

• **MULTIPLE REGRESSION MODEL OF PARENTAL MYOPIA, PARENTAL EDUCATION, CHILDREN'S OUTDOOR TIME, AND CHILDREN'S NEAR WORK:** In the multiple regression model, association with parental myopia remained significant after adjustment of parental education, children's outdoor time, and children's near work (Table 3). The OR of parental myopic status became smaller for mild and moderate parental myopia, but larger for high-myopic parental group in the multiple regression model (Table 3). Of note, parental education, children's outdoor time, and children's near work were not associated with childhood myopia after the adjustment of parental myopia (Table 3). Factors such as parental education, children's time outdoor, and children's near work attributed altogether to 5.9% of the myopia variation in children (R^2=0.0587). Parental myopic status alone accounted for 11.8% (R^2=0.1182), and there was no enhancement of the model after adding other environmental factors.

• **THE AUROCS FOR MYOPIA:** The AUROCs were respectively 0.660 (95% CI 0.641-0.670; Figure 3), 0.670 (95% CI 0.641-0.697; Figure 3), 0.523 (95% CI 0.497-0.549; Figure 3), and 0.520 (95% CI 0.495-0.545; Figure 3), 0.501 (95% CI 0.471-0.532; Figure 3), 0.535 (95% CI 0.505-0.566; Figure 3), for the myopia differentiation with children's age, parental myopia, paternal education level, and maternal education level, children's outdoors time, and children's diopter-hour of near work. Taking children's age and parental myopia together, the AUROC values were 0.731 (95% CI 0.710-0.798) for myopia.

DISCUSSION

IN THIS POPULATION-BASED STUDY OF 2,055 FAMILY TRIOS, we evaluated parental myopia, parental education, children's outdoor time, and children's near work about their influence on childhood myopia development and revealed that parental myopia is the strongest independent factor associated with childhood myopia, posing a dose-related effect.

First, the association of parental myopia and childhood myopia development was independent of other environmental risk factors. After adjustment with confounding factors, the OR became smaller for parents with mild and moderate myopia, but larger for the highly myopic parents (2 mildly myopic parents: unadjusted OR 1.27; adjusted OR 1.23; vs 2 highly myopic parents: unadjusted OR 11.22; adjusted OR 11.65). Although the changes of ORs were small, this may potentially suggest that

TABLE 4. Time Spent Outdoors and Time Spent on Near Work

	Time Spent Outdoor (Hours per Day; Mean ± SD)			Time Spent on Near Work (Hours per Day; Mean ± SD)					
	Outdoor for Sports	Outdoor for Leisure	Total Outdoor Time	Watching TV	Doing Homework	Reading	Using Computer	Using Electronic Devices	Total Near-Work Time
Overall	0.87 ± 0.4	0.59 ± 0.38	1.47 ± 0.62	1.13 ± 0.51	1.36 ± 0.39	0.8 ± 0.36	0.59 ± 0.43	0.8 ± 0.48	2.75 ± 0.74
Parental myopic status									
No myopia + No myopia	0.87 ± 0.38	0.58 ± 0.39	1.45 ± 0.62	1.10 ± 0.50	1.39 ± 0.39	0.73 ± 0.37	0.65 ± 0.46	0.86 ± 0.47	2.77 ± 0.72
No myopia + Mild myopia	0.86 ± 0.41	0.59 ± 0.36	1.45 ± 0.6	1.16 ± 0.53	1.32 ± 0.39	0.75 ± 0.35	0.57 ± 0.44	0.86 ± 0.5	2.65 ± 0.72
Mild myopia + Mild myopia	0.89 ± 0.41	0.64 ± 0.4	1.52 ± 0.67	1.10 ± 0.51	1.35 ± 0.38	0.78 ± 0.34	0.57 ± 0.42	0.82 ± 0.47	2.7 ± 0.71
No myopia + Moderate myopia	0.93 ± 0.42	0.59 ± 0.38	1.51 ± 0.64	1.13 ± 0.52	1.32 ± 0.4	0.77 ± 0.33	0.58 ± 0.41	0.77 ± 0.49	2.67 ± 0.7
Mild myopia + Moderate myopia	0.86 ± 0.38	0.59 ± 0.38	1.45 ± 0.61	1.13 ± 0.49	1.38 ± 0.37	0.84 ± 0.36	0.58 ± 0.43	0.80 ± 0.48	2.79 ± 0.73
Moderate myopia + Moderate myopia	0.87 ± 0.37	0.61 ± 0.39	1.48 ± 0.65	1.09 ± 0.50	1.34 ± 0.37	0.88 ± 0.39	0.58 ± 0.44	0.72 ± 0.46	2.79 ± 0.84
High myopia + No myopia	0.92 ± 0.42	0.57 ± 0.4	1.48 ± 0.68	1.19 ± 0.55	1.38 ± 0.39	0.82 ± 0.42	0.66 ± 0.47	0.75 ± 0.49	2.87 ± 0.83
High myopia + Mild myopia	0.87 ± 0.4	0.61 ± 0.39	1.48 ± 0.62	1.12 ± 0.49	1.4 ± 0.41	0.82 ± 0.36	0.58 ± 0.44	0.81 ± 0.47	2.81 ± 0.76
High myopia + Moderate myopia	0.86 ± 0.38	0.59 ± 0.33	1.45 ± 0.53	1.13 ± 0.50	1.39 ± 0.39	0.85 ± 0.33	0.58 ± 0.39	0.76 ± 0.46	2.83 ± 0.7
High myopia + High myopia	0.79 ± 0.38	0.48 ± 0.34	1.26 ± 0.56	0.98 ± 0.51	1.33 ± 0.38	0.81 ± 0.31	0.57 ± 0.32	0.65 ± 0.38	2.73 ± 0.61
P value	.502	.414	.387	.361	.228	.0002	.521	.010	.048

The *P* values are the results of comparing environmental factors such as outdoor activities among children with different severities of parental myopia via analysis of variance.

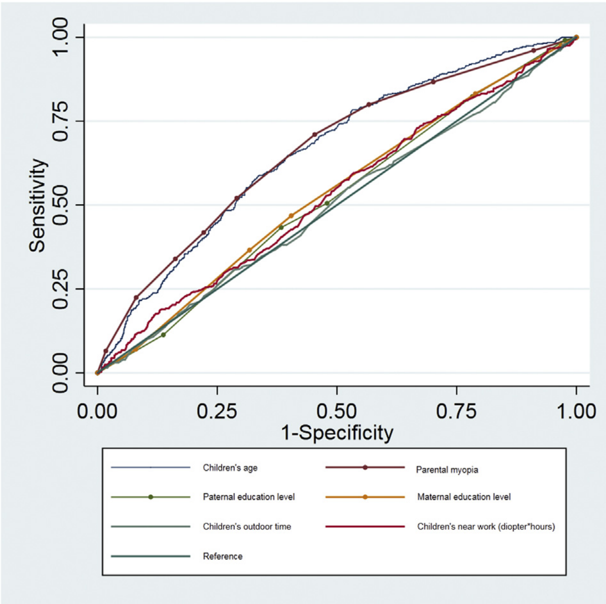

FIGURE 3. Areas under the receiver operating characteristic curve for myopia with children's age, parental myopia, parental education levels, children's outdoors time, and children's diopter-hour of near work. Parental myopia was an ordinal variable, classified into 10 groups according to the combinations of paternal and maternal myopia severities.

environmental factors play a heavier role in families without myopic parents or with mildly myopic parents, than in families with highly myopic parents. Further studies were warranted to ascertain these findings. Interestingly, our results also supported that parental myopia would contribute to environmental factors, as children with myopic parents tend to have more reading time but less usage of electronic devices. It is possible that higher-educated parents tend to provide an environment to children with more reading time and less free usage of electronic devices. The latter has been shown in the British Twins Early Development Study cohort to be associated with myopia in teens.[28] In this study, we found children's reading time a risk factor and electronic device usage a protective factor, but both became insignificant after adjustment of parental myopia. This finding about the protective effect of electronic device usage could be explained by the more restricted usage of the former by highly myopic parents than nonmyopic parents. Notably, parental myopia remained significantly associated with childhood myopia after adjustment of reading time, electronic device usage, time for outdoor activities, or parental education level. Parental myopia may therefore act independently as a genetic influence on childhood myopia, plus imposing environmental factors on near work.

Second, there is a dose-response relationship between childhood myopia and their parental myopia, both in the number of myopic parents, and their severity. Of note, the effect of paternal refraction on children's refraction was separate and similar as maternal refraction. This also suggested a genetic response more than an environmental effect, as a larger number of highly myopic parents may confer more accumulation of myopic genes. On the other hand, the environmental effect of one parent or both parents will be similar. Among those children with both parents being nonmyopic, there was a 12% myopia rate, though we also noted a much higher proportion (56%) in those with both highly myopic parents. In 2009, Lopes and associates have recruited 1152 monozygotic and 1149 dizygotic twin pairs and found that refractive errors showed high heritability of 77%, whereas the shared environmental effects accounted for 7% and the individual environmental effects account for 16% of the spherical equivalent variance, respectively.[29]

Third, our results provided quantitative risk stratification of childhood myopia based on parental myopia. One moderately myopic parent conferred a 2.2-fold increased risk of myopic children, and both parents being highly myopic would lead to a 11.22-fold increase in risk. In 1994, Zadnik and associates first revealed that, before the onset of juvenile myopia, children of myopic parents had longer eyeballs.[13] Based on the history of parental myopia, Mutti and associates showed that the OR of myopia in children with 2 myopic parents was 6.40, compared with those with nonmyopic parents, after the adjustment of outdoor time and near work, which implied that heredity was the most important factor associated with juvenile myopia.[12] Subsequently, Jones-Jordan and associates demonstrated that the number of myopic parents can predict the risk of childhood myopia; however, the sensitivity was low.[15] A recent study also showed that the number of myopic parents had been found to be highly associated with childhood myopia, but the same study showed that the number of myopic parents was weakly predictive of refractive error in children aged 7 years, $R^2 = 3.0\%$ (95% CI 1.8%-4.1%, $P < .0001$) and in those aged 15 years, $R^2 = 4.8\%$ (95% CI 3.1%-6.5%, $P < .0001$).[30] In 2012, Xiang and associates showed a progressive increase in the prevalence of myopia in children with increasing severity of parental myopia based on self-reported questionnaires.[17] Nevertheless, the impact of severity of parental myopia on their children's myopia development is still not established, because all these reports are based on history and self-reported questionnaires.

Another point to note is that subjects of our cohort were children aged 6-8 years. Myopia onset at this age range will very likely develop into moderate and high myopia. Recently, Mojarrad and associates analyzed the polygenic risk score of 1.1 million variants for myopia. The highest accuracy ($R^2 = 11.2\%$) was obtained with a P value threshold of .01 for a polygenic risk score derived from those variants. That polygenic risk score had AUROC values of 0.67 (95% CI 0.65-0.70) for any myopia, 0.75 (95% CI 0.70-0.79) for moderate myopia, and 0.73 (95%

CI 0.66-0.80) for high myopia.[31] In our study, with the age and parental myopia of children, the AUROC for myopia was 0.731, which means that the prediction accuracy was similar to the thousands of variants. Children's age and parental myopia status may provide clinical implications of myopia prediction and of early intervention for children aged 6-8 years, though currently the accuracy is not yet good enough.

This is a population-based study of 2,055 family trios, allowing direct analysis of parental and children information. Another strength of this study is its use of a strict cycloplegia protocol for children to ensure the accuracy of refraction. However, certain limitations should also be noted. First, parental refraction was based on noncycloplegic autorefraction, which may overestimate the prevalence of myopia in younger people, although this effect is likely small in adults. A difference of 0.29 D more hyperopic after cycloplegia in adults has been reported, and the effect was more prominent in hyperopic subjects than in myopic subjects.[32] In this study, we used a more stringent criterion of parental myopia of <-0.75 D instead of <-0.5 D. Second, measurement of children's near work and outdoors time was based on validated questionnaires, which is prone to recall bias. Further studies with more precise measurement, such as wearable sensors, will help provide objective information. Third, this is a cross-sectional study, and therefore only association but not causation could be determined. Fourth, the response rate of parents (70.0%) was relatively low in the HKCES, especially for the father. All together, we have 4257 children in the HKCES; however, only 2,055 pairs of parents have been recruited in the current study. Although there are no differences in ophthalmic parameters in complete trios compared to the overall population, in view of the fact that the average family income in the current study was higher than that in the HKCES, bias might be introduced into the study.

In conclusion, parental myopia plays a crucial role in the development of myopia of their children, which is independent of environmental factors such as outdoor time and near work, and in a dose-related manner. Children with high risk of myopia could be identified early based on parental myopia information for early prevention.

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