Relative Contribution of Risk Factors for Early-Onset Myopia in Young Asian Children

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Purpose. To investigate the associations of near work, outdoor activity, and anthropometric risk factors with early-onset myopia in Singaporean preschool children.

Methods. Pregnant women who attended their first-trimester clinic at two major maternity units were recruited for the GUSTO birth cohort ($n = 1236$). Cycloplegic autorefraction and axial length (AL) were obtained in 3-year-old children ($n = 572$). Parents completed detailed questionnaires on parental myopia, near work, and outdoor activities when the child was 2 years of age. Height and weight were measured in the children at various time points from birth to 3 years of age.

Results. Among the cohort of 572 children, 35 children (6.1%) had early-onset myopia. In multivariable regression models, compared to children whose parents were not myopic, those with two myopic parents were more likely to have a more myopic spherical equivalent (SE) (regression coefficient: −0.36; 95% confidence interval [CI]: −0.61 to −0.11) and longer AL (regression coefficient: 0.24; 95% CI: 0.10–0.39) and more likely to have myopia (odds ratio [OR] = 4.8; 95% CI: 1.4–16.6). Neither near work nor outdoor activity was associated with SE, AL, and myopia. Taller children were found to have longer AL at birth and at 12, 24, and 36 months, but there were no associations with SE.

Conclusions. Genetic factors may have a greater contribution to early development of refractive error compared to environmental factors.

Keywords: myopia, axial length, spherical equivalent, family history of myopia, near work activity and outdoor activity

Myopia is a major public health concern due to its high prevalence across urban Asian cities.[1,2] Among school-age children living in South China, the prevalence of myopia was 74.8%.[2] In Taiwan, up to 84% of high school children aged 16 to 18 years were myopic, and 21% had high myopia.[1] However, prevalence of myopia has been reported to be as low as 10.8% among 15-year-old children in New Delhi, India.[3] Adults with high myopia may develop ocular abnormalities such as retinal detachment, myopic macular degeneration, and glaucoma, which may result in severe and irreversible loss of vision.[4–6] Therefore, it is important to understand the etiology of myopia.

Genes as well as environmental factors such as near work and outdoor activities are risk factors for myopia.[7–13] In the Singapore Cohort Study of the Risk Factors for Myopia (SCORM) study, 994 children aged 7 to 9 years with both myopic parents had a 1.6 times higher risk of myopia compared to children with no myopic parent.[14] In SCORM, teenage children who spent more time outdoors were less likely to be myopic.[9] Similarly, in the Sydney Myopia Study (SMS) among 1765 six-year-old and 2367 twelve-year-old children, reduced amount of outdoor activity and longer time spent on reading were associated with a more myopic refraction.[8,15]

Body growth may play a role in myopia development, as the periods of critical body and eye growth occur simultaneously in early life. In the SCORM study of 1449 children aged 7 to 9 years, height was positively associated with axial length (AL). Taller girls were found to have more myopic refractions, but this association was not observed in boys.[16] The Strabismus, Amblyopia and Refractive Error in Singaporean Children (STARS) study of 3009 Singapore Chinese children aged 6 to 72 months reported that for every 1 cm increase in height, the spherical equivalent (SE) was more myopic by 0.01 diopters.[17] Although this finding was statistically significant, it may not be clinically significant.[17] In contrast, several other studies did not confirm the association between height and SE.[18–21] In a study of 106,926 Israeli male military recruits aged 17 to 19 years, body stature was not associated with myopia.[20] Similarly, body stature was not associated with refractive error in 23,616 nineteen-year-old Korean male military conscripts.[19] There was no association between height and refractive error among 1371 children aged 12 to 17 years from rural China.[21] Anthropometric measures were not associated with SE in 1765 Australian children aged 6 years, but height was positively associated with AL.

In this study, we evaluated the role of parental myopia, near work, outdoor activity, and height on SE, AL, and myopia in a birth cohort of 3-year-old Singapore children.

Methods

Study Population

The Growing Up in Singapore Towards Healthy Outcomes (GUSTO) birth cohort (naturally conceived) and the In Vitro Fertilization (IVF) cohort consist of offspring of pregnant women aged 18 years and above who attended their first-trimester antenatal ultrasound scan clinic at either one of the major maternity units, KK Women's and Children's Hospital (KKH) or National University Hospital (NUH), between June 2009 and September 2010.[22] This study had participants from the three main ethnic groups in Singapore, which are Chinese, Malay, and Indian, and included those who planned to reside in Singapore for the next 5 years. Children with eye conditions such as strabismus, facial nerve palsy, eye infection, eye injury, and other such eye-related conditions were excluded.

The Figure is a flow chart that shows the progress of participants throughout the study from recruitment to the third-year visit. The GUSTO study recruited 1236 women at the first-trimester antenatal clinic, and 1232 women attended the clinic at the 26- to 28-week gestational age visit. Of the 1236 participants recruited, 65 participants dropped out during the 26- to 28-week gestation visit. A total of 1171 infants were born between November 2009 and May 2011. After delivery, 85 participants dropped out. For the remaining 1086 participants, the number of participants seen at each postnatal visit is stated. A total of 161 participants did not attend the 3-year clinic visit. A total of 925 participants attended the 3-year visit.

The study was approved by the SingHealth Centralized Institutional Review Board and National Health Group's Domain Specific Review Board. It was conducted according to the tenets of the Declaration of Helsinki. Informed written consent was obtained from the children's parents after a verbal explanation of the study.

Antenatal Questionnaires

Questionnaires in English, Chinese, Malay, or Tamil were administered to the women at two time points, at the recruitment visit (<14 weeks) and 26 to 28 weeks of gestation.

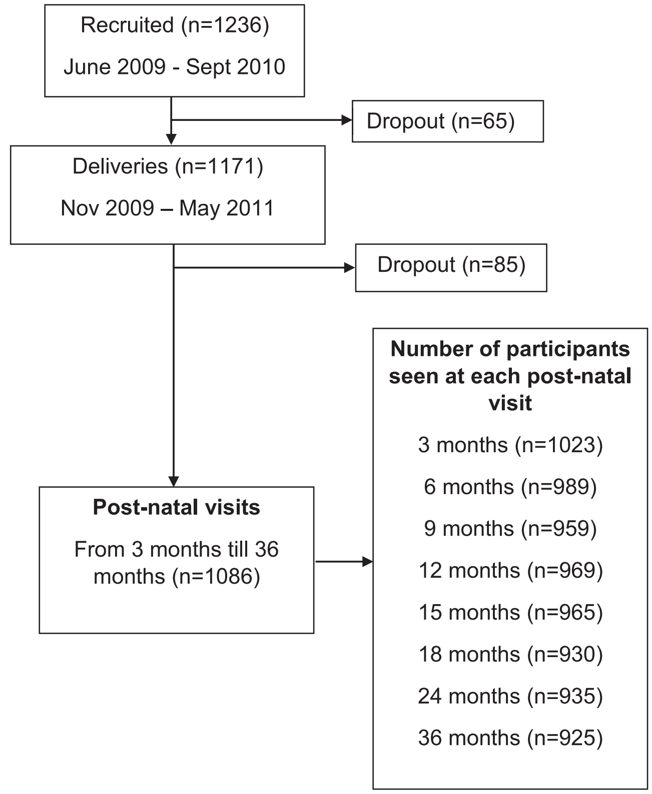

Figure. Progress of the GUSTO study.

Information such as ethnicity, parental educational level, and monthly household income was assessed during the recruitment visit. Parental educational level was classified into two categories: (1) secondary school or less and (2) GCE O-level and higher. The Singapore-Cambridge General Certificate of Education Ordinary Level (GCE O-level) examination is held once a year in Singapore, and examinations are set by the University of Cambridge Local Examinations Syndicate. Students usually take the examination at the end of their fourth or fifth year in secondary school, mostly at 16 years old.

Parental Myopia

At the 2-year postnatal clinic visit, a questionnaire was administered by a trained interviewer to obtain information about the refractive status of parents and the outdoor and indoor activities of the child. Parents gave details about whether they wore glasses or contact lenses and for what purpose. Parents were classified as myopic if glasses or contact lenses were worn for distant viewing or for both distance and near viewing. As the parents were young, the glasses worn for distance and near vision, were not for presbyopia corrections.

Near Work and Outdoor Activities

The types of near-work activities included reading or writing, coloring or drawing, playing with handheld devices, and using computers. Near-work activities were recorded in number of hours per day separately for weekdays and weekends. The total number of hours spent on near work per day was calculated from all the near-work activities. Reading habits, for example, if the child read alone, the age at which the child started reading and the number of books read per week, were collected. Additional information such as the age at which the child started attending child care and the number of hours spent in child care was obtained. Outdoor activities included physical activities (playing in the backyard, walking or riding a tricycle) and leisure activities (barbeque, picnic, going to the park or beach). Outdoor activities were recorded in number of hours per day separately for weekdays and weekends. The average number of hours of each activity per day was calculated (5/7 × hours per weekday + 2/7 × hours per weekend). These questionnaires on near-work and outdoor activities were similar to that used by SMS.[15] Some of the modifications of the SMS questionnaire were additional outdoor activities such as playing in the backyard or riding a tricycle, which were appropriate for a 2-year-old.

Birth Parameters and Anthropometric Measurements

After delivery, birth parameter data such as birth weight (kg), birth length (cm), and gestation age (weeks) were obtained. The child's anthropometric measures of early growth were measured by trained observers using standard protocol every 3 months from 3 months to 18 months, then again at 24 and 36 months. Recumbent length was used to measure infants and children aged less than 2 years using an infantometer (210 mobile measuring mat; Seca, Hamburg, Germany). Standing height was measured with a stadiometer (model 213; Seca). Weight of the child was measured using Seca model 803. All anthropometric measurements were taken twice with bare feet. If the length or height differed by 1 cm, a third measurement was taken for the average calculation. Similarly, a third measurement was taken if the weight differed by 200 g. Body mass index (BMI) was calculated using weight divided by the square of the height (kilograms per meter squared).

Eye Measurements Performed at 3 Years Old

After the instillation of one drop 0.5% proparacaine and one drop 2.5% phenylephrine, cycloplegia was achieved with three drops of 1% cyclopentolate instilled at 5-minute intervals. After an interval of at least 30 minutes after the last eye drop, cycloplegic autorefraction was performed with a table-mounted autorefractor (model RK-F1; Canon, Tokyo, Japan). Axial length measurements were obtained using an optical biometer (IOL Master; Carl Zeiss-Meditec, Oberkochen, Germany). The reliability of each AL measurement was assessed using signal-to-noise ratio (SNR), and a reading was accepted if SNR $\geq$ 2.0. Spherical equivalent refraction (SE) for each eye was calculated as sphere power plus half cylinder power. Myopia was defined as a SE of at least –0.5 diopters (D).

Statistical Analysis

As there is a high correlation between right and left eye (Spearman ρ 0.88 for SE and 0.96 for AL), only data from the right eye were used. Student's *t*-test and χ^2 test were used to compare baseline characteristics between participants with and without cycloplegic autorefraction for continuous and categorical variables, respectively. First, univariate models were constructed examining the association of early-life factors (exposures) with AL, SE, and myopia (outcomes). Subsequently, multivariate models were constructed additionally adjusting for other confounders. All *P* values are two-sided and were considered statistically significant when less than 0.05. Data analysis was performed with STATA 2009 (Stata Statistical Software, Release 11; StataCorp LP, College Station, TX, USA).

Results

Out of 1236 recruited participants, 925 children (74.8%) attended the third-year clinic visit. Axial length was measured in 760 children (61.5%) and could not be measured in 165 children for the following reasons: 87 children (7.0%) were uncooperative; home visits were conducted in 32 children (2.6%); optometrist was not available for 16 children (1.3%); Institutional Review Board approval was not in time for 18 children (1.5%); 6 children had eye conditions (0.5%); parents of 3 children (0.2%) did not consent; and parents were not with 3 children (0.2%) during clinic visits.

Cycloplegic refraction was performed in 572 children (46.3%), and SE measurement was not performed in 353 children for the following reasons: 189 children (15.3%) were uncooperative; parents of 102 children (8.3%) did not consent; home visits were conducted in 32 children (2.6%); optometrist was not available for 19 children (1.5%); 8 children (0.6%) had eye conditions; and parents were not with 3 children (0.2%) during clinic visits.

In comparison with the number among children who did not undergo cycloplegic autorefraction, there were more females who underwent cycloplegic autorefraction (50.2% vs. 41.6%; $P = 0.01$), but there were no significant differences in age ($P = 0.07$), ethnicity ($P = 0.28$), total time spent on near work (hours/day) ($P = 0.15$), total time spent outdoors (hours/day) ($P = 0.91$), maternal education level ($P = 0.21$), and parental myopia ($P = 0.48$) between the two groups (Table 1). There were 35 myopic children (6.1%), of whom 54.3% were males and 45.7% were females.

Table 2 shows the association of parental myopia with SE, AL, and myopia among the participants. After adjusting for age, sex, ethnicity, and maternal education level, a child was more likely to have a negative SE (regression coefficient: –0.26; 95% confidence interval [CI]: –0.43 to –0.08) and longer AL (regression coefficient: 0.16; 95% CI: 0.06–0.27) if the mother was myopic, compared to a child without a myopic mother. Children with parental history of myopia showed negative SE (regression coefficient: –0.29; 95% CI: –0.49 to –0.08), longer AL (regression coefficient: 0.15; 95% CI: 0.03–0.27), and higher odds of myopia (odds ratio [OR]: 3.3; 95% CI: 1.1–10.2).

The overall GUSTO cohort spent an average of 0.6 hours/day (SD 0.7) reading or writing, 0.4 hours/day (SD 0.5) coloring or drawing, 0.6 hours/day (SD 0.8) using handheld devices, 0.1 hour/day (SD 0.3) using a computer, and 1.7 hours/day (SD 1.5) on total near-work activities. On average, children started reading at 16.6 months (SD 4.6) and read 6 books (SD 8) per week at 2 years old with a parent reading to them or independently. The children started going to preschool at 17.8 months (SD 6.1). Time spent on near-work activities did not differ between children whose refractive error was measured compared to those not measured. Reading habits such as age the child started reading, number of books read per week, and age the child started preschool did not differ between the two groups. The children spent an average of 0.8 hours/day (SD 0.8) on outdoor physical activities, 0.6 hours/day (SD 1.1) on outdoor leisure activities, and 1.4 hours/day (SD 1.5) on total outdoor activities. There were no significant differences in outdoor physical activities, outdoor leisure activities, and total outdoor activities between those whose refractive error was measured and not measured.

Table 3 shows the relationship of near-work and outdoor activities with SE, AL, and myopia. The different types of near work and outdoor activities were not associated with the eye measurements after adjustment for confounders. Reading habits and preschool activities were not significantly associated with myopia. After adjusting for age, sex, ethnicity, and maternal education level, the average time spent on total near

Table 1. Comparison of Baseline Characteristics Between Participants With and Without Cycloplegic Refraction in GUSTO

Variables	Participants Who Underwent Cycloplegic Autorefraction at the 3-Year Clinic Visit, $N = 572$			Participants Who Did Not Undergo Cycloplegic Autorefraction at the 3-Year Clinic Visit, $N = 353$			
	N	Mean* or %*	SD	*N*	Mean* or %*	SD	*P* Value†
Child's age, mo	572	36.5	1.0	353	36.6	1.1	0.07
Child's sex							0.01
Female	287	50.2	–	147	41.6	–	
Child's ethnicity							0.28
Chinese	316	55.2	–	214	60.6	–	
Malay	150	26.2	–	82	23.2	–	
Indian	106	18.6	–	57	16.2	–	
Near-work activities							
Total time spent on near work, h/d	545	1.7	1.5	325	1.8	2.0	0.15
Outdoor activities							
Total time spent outdoors, h/d	572	1.4	1.5	353	1.4	1.4	0.91
Maternal education level							0.21
Secondary school or less	161	28.3	–	112	32.3	–	
GCE O-level and higher	408	71.7	–	235	67.7	–	
Parental myopia							0.48
None	144	26.4	–	93	28.6	–	
Either one	402	73.6	–	232	71.4	–	

* Mean (SD) for continuous variables and percentages for categorical variables.
† Student's *t*-test or χ^2 test (two-sided).

work was 1.7 hours/day among children whose parents were nonmyopic, 1.7 hours/day among children who had one myopic parent, and 1.4 hours/day among children whose parents were both myopic. There was no difference in time spent on near work among children with two myopic parents compared to children with no or one myopic parent ($P = 0.08$).

Table 4 shows the association of anthropometric measures with SE, AL, and myopia. Controlling for age, sex, ethnicity, maternal education level, and parental myopia, children who were taller at birth and at 12, 24, and 36 months showed longer AL. Similarly, the multivariate models at other periods such as 3 weeks and 3, 6, 9, 15, and 18 months showed significant positive relationships with AL. Height was subsequently categorized into quartiles, and there were significant increasing trends in AL when we compared the highest quartiles of height with the lowest quartiles. In the multivariate models, there were no significant associations between height with SE and myopia.

In the multivariate model, for every 1 SD increase in birth weight, AL increased by 0.12 mm (95% CI: 0.07–0.17).

Table 2. Multivariable Analysis of Parental Myopia With Spherical Equivalent, Axial Length, and Myopia at 36-Month Visit in GUSTO Participants

Variables	Spherical Equivalent, D			Axial Length, mm			Myopia, Defined as ≤−0.50 D)		
	N	β (95% CI)*	*P* Value	*N*	β (95% CI)†	*P* Value	*N*	OR (95% CI)*	*P* Value
Paternal myopia									
No	273	Reference		270	Reference		273	Reference	
Yes	271	−0.12 (−0.30, 0.06)	0.19	267	0.09 (−0.02, 0.19)	0.10	271	2.06 (0.95, 4.46)	0.07
Maternal myopia									
No	250	Reference		246	Reference		250	Reference	
Yes	294	−0.26 (−0.43, −0.08)	<0.01	291	0.16 (0.06, 0.27)	<0.01	294	2.10 (0.95, 4.64)	0.07
Parental myopia									
No	143	Reference		141	Reference		143	Reference	
Yes	401	−0.29 (−0.49, −0.08)	<0.01	396	0.15 (0.03, 0.27)	0.02	401	3.34 (1.10, 10.19)	0.03
No. of parents with myopia									
0	143	Reference		141	Reference		143	Reference	
1	237	−0.25 (−0.47, −0.04)	0.02	234	0.10 (−0.02, 0.23)	0.11	237	2.83 (0.89, 9.02)	0.08
2	164	−0.36 (−0.61, −0.11)	<0.01	162	0.24 (0.10, 0.39)	<0.01	164	4.79 (1.39, 16.55)	0.01
P trend			<0.01			<0.01			0.01

Parental myopia was obtained via questionnaires administered at 24-month visit.
* For the outcomes of SE and myopia, the multivariable models were adjusted for age, sex, ethnicity, and maternal education level.
† For the outcome of AL, the multivariable model was adjusted for age, sex, ethnicity, and maternal education level and height at 36 months.

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TABLE 3. Multivariable Analysis of Near Work and Outdoor Activities at 24 Months With Spherical Equivalent, Axial Length, and Child's Myopia at 36-Month Visit in GUSTO Participants

Variables	Spherical Equivalent, D			Axial Length, mm			Myopia, Defined as ≤−0.50 D		
	N	*β* (95% CI)*	*P* Value	*N*	*β* (95% CI)†	*P* Value	*N*	OR (95% CI)*	*P* Value
Near-work activities, h/d									
Reading or writing	533	0.06 (−0.07, 0.19)	0.36	527	−0.04 (−0.11, 0.04)	0.36	533	1.26 (0.80, 1.98)	0.31
Coloring or drawing	533	0.14 (−0.03, 0.32)	0.11	526	−0.06 (−0.16, 0.05)	0.31	533	0.71 (0.28, 1.78)	0.47
Handheld devices	541	−0.10 (−0.20, 0.0)	0.05	534	0.07 (0.01, 0.13)	0.03	541	1.04 (0.67, 1.61)	0.86
Computer	541	−0.09 (−0.34, 0.16)	0.46	534	0.01 (−0.13, 0.16)	0.86	541	0.92 (0.31, 2.74)	0.88
Total near work	543	−0.01 (−0.07, 0.05)	0.72	536	0.01 (−0.03, 0.04)	0.60	543	1.03 (0.81, 1.31)	0.80
Outdoor activities, h/d									
Playing time	544	0.07 (−0.04, 0.18)	0.19	538	−0.01 (−0.08, 0.05)	0.70	544	0.59 (0.32, 1.07)	0.08
Leisure time	544	−0.03 (−0.11, 0.04)	0.39	538	−0.01 (−0.05, 0.04)	0.76	544	1.00 (0.70, 1.44)	1.00
Total outdoors	544	0.0 (−0.06, 0.06)	0.98	538	−0.01 (−0.04, 0.03)	0.66	544	0.84 (0.61, 1.17)	0.31

Parental myopia was obtained via questionnaires administered at 24-month visit.

* For the outcomes of SE and myopia, the multivariable models were adjusted for age, sex, ethnicity, maternal education level, and parental myopia.

† For the outcome of AL, the multivariable model was adjusted for age, sex, ethnicity, maternal education level, parental myopia, and height at 36 months.

However, BMI at various periods was not associated with SE or myopia in the multivariate models. After adjusting for age, sex, ethnicity, maternal education level, and parental myopia, rate of growth in height from birth to 3 months ($P = 0.01$), birth to 6 months ($P < 0.01$), and birth to 9 months ($P < 0.01$) was associated with a longer AL.

DISCUSSION

In this study, we showed that in Asian preschool children aged 3 years, family history of myopia was significantly associated with myopia, a more myopic SE, and longer AL. In addition, height was associated with a longer AL. However, near work and outdoor activity were not significantly associated with myopia. These data suggest that family history may have a stronger role than environmental factors in causing early development of refractive error in Asian preschoolers. In contrast, there may be greater environmental influences detected in studies of older Asian primary schoolchildren.[23–25]

Previous studies have reported the impact of family history on the development of myopia in older individuals.[7,11,26] Few have examined the relationship between parental myopia as a risk factor for myopia in 3-year-olds.[17,27] Fan et al.[27] did not observe an association between parental myopia with SE or AL among preschoolers aged 2 to 6 years old in Hong Kong. The lack of association may be due to a small number of parents with myopia. However, Low et al.[17] suggested that preschool children aged 6 to 72 months had a 1.9 (95% CI 1.4–2.6) times increased odds of myopia if both parents were myopic compared to children without myopic parents.[17] In the SCORM study, it was shown, among 543 myopic children aged 7 to 9 years, that AL increased by 0.11 mm in children with parental myopia compared to children without parental myopia.[28] In line with these findings, our study showed that children with either myopic fathers or mothers tend to have a more myopic refraction or longer AL. This association was statistically significant for children with myopic mothers, but not myopic fathers. The mechanisms underlying the sex difference are unclear. The difference is unlikely to be sex linked, because myopia has not been shown to be a characteristic inherited through the female line. Although environmental factors were not associated to the development of early-onset myopia in our study, a possible reason for the sex difference observed may be attributed to shared environmental effects, as mothers may spend more time with their children compared to fathers. In contrast, the Orinda Longitudinal Study of Myopia did not report a difference in myopia risks for children with myopic fathers versus myopic mothers among 514 children aged 8 to 9 years.[29] Parental myopia may be significantly associated with myopia in the offspring either through shared genetic background or shared near-work environment.[30] Myopic parents may encourage their children to read more or to maintain high academic standards. To rule out shared near-work environment in our study, the amount of

TABLE 4. Multivariable Analysis of Various Growth Periods With Spherical Equivalent, Axial Length, and Child's Myopia at 36-Month Visit in GUSTO Participants

Variables	Spherical Equivalent, D			Axial Length, mm			Myopia, Defined as ≤−0.50 D		
	N	*β* (95% CI)*	*P* Value	*N*	*β* (95% CI)†	*P* Value	*N*	OR (95% CI)*	*P* Value
Length: birth	544	0.01 (−0.08, 0.10)	0.82	538	0.08 (0.03, 0.14)	<0.01	544	0.90 (0.63, 1.29)	0.57
Height: 12 mo	512	−0.07 (−0.16, 0.02)	0.15	506	0.21 (0.15, 0.26)	<0.01	512	1.13 (0.77,1.67)	0.54
Height: 24 mo	481	−0.01 (−0.10, 0.09)	0.88	475	0.16 (0.11, 0.22)	<0.01	481	1.07 (0.72, 1.59)	0.74
Height: 36 mo	543	−0.01 (−0.10, 0.08)	0.76	537	0.18 (0.13, 0.24)	<0.01	543	1.11 (0.77, 1.59)	0.59
Weight: birth	544	−0.02 (−0.11, 0.07)	0.71	538	0.12 (0.07, 0.17)	<0.01	544	0.90 (0.63, 1.29)	0.58
BMI: 12 mo	511	0.05 (−0.03, 0.14)	0.22	505	0.04 (−0.02, 0.09)	0.16	511	0.98 (0.67, 1.44)	0.94
BMI: 24 mo	481	0.04 (−0.05, 0.13)	0.34	475	0.05 (−0.01, 0.10)	0.09	481	1.03 (0.69, 1.53)	0.88
BMI: 36 mo	543	0.02 (−0.07, 0.11)	0.63	537	0.08 (0.02, 0.13)	<0.01	543	1.04 (0.72, 1.50)	0.84

* The multivariable models were adjusted for age, sex, ethnicity, maternal education level, and parental myopia.

near work performed by children was stratified by parental myopia categories. No significant trend was observed between near work and number of myopic parents. Thus, we believe that genes may have a greater influence on early-onset myopia in young Asian children.

Near-work and outdoor activities did not have an impact on myopia in our study. Our findings are in agreement with the STARS study that showed no association between near work or outdoor activity with myopia in preschool children aged 6 to 72 months.[17] The lack of association may be due to the lower amount of near work reported among our participants at 2 years old compared to the 2- to 6-year-old preschoolers in Hong Kong. Our participants performed 11.6 hours of near work per week, while the preschoolers in Hong Kong reported 23.7 hours. However, the preschoolers in Hong Kong were slightly older than our participants.[27] Compared to studies in which a protective effect has been demonstrated among children who spent more than 14 hours per week outdoors, children in our study spent an average of 9.8 hours per week outdoors.[15,31] Therefore, they may not have reached the threshold amount required for a similar effect to be observed. Together with the limited variation (SD 1.5 hours) within our subjects, this may explain the negative findings observed (Table 1). As children commence elementary school, they may be exposed to a greater amount of near work. Thus, it is plausible that environmental factors such as near work and outdoor activities may have a larger cumulative effect on myopia when children start attending school. Studies have indicated that among various environmental factors, time spent outdoors is more important than near work.[7,14,15,31] We also examined the effect of age of commencement of preschool and myopia. Multivariate analysis did not reveal any association between age that the child started preschool with SE ($P = 0.18$), AL, ($P = 0.55$) and myopia ($P = 0.78$). Possible explanations for the lack of association may be a small number of myopic children ($n = 35$) and a low number of children attending preschool ($n = 183$).

Some studies have suggested that body stature may be linked to AL due to a shared mechanism between body and eye growth.[32–35] While previous studies have been cross sectional in design, our study had repeated anthropometric measures at birth, 3 weeks, every 3 months from 3 to 18 months, and 24 and 36 months with refraction at 3 years old. We found that a child's stature at any point in time or increased rate of growth in height over several periods was associated with longer AL. However, there was no consistent association between anthropometric measures with myopia and SE. Wong et al.[36] showed that height is positively associated with AL but did not influence refraction in 951 Chinese adults aged 40 to 81 years old. Likewise, most prior studies conducted with measurements of stature and refraction measured at a single point in time did not find significant associations between anthropometric measures and refraction.[18,19,21] The absence of a relationship may be due to a coordinated growth of the components of refraction (mainly AL with corneal and lens powers). During the early infancy stages, the cornea may flatten among subjects with longer AL.[37,38] In the SMS in 1765 children aged 6 years, Ojaimi et al.[18] reported that increase in height was associated with increase in AL and corneal radius, but height was not related to refraction. Lens power decreased substantially in children from approximately 23 D at aged 3 years to 20 D at aged 14 years, compensating for AL growth.[39,40] Our data did not show that BMI was related to the eye measurements, suggesting that obesity in children is not associated with AL or myopia. A recent study suggested that height rather than BMI from birth to 10 years was consistently found to be positively associated with AL but minimally with the development of myopia.[41]

There are several strengths in our study. GUSTO is a birth cohort that tracks growth and other parameters throughout the antenatal period, birth, and the first 3 years of life. All risk factors were collected prospectively. We measured refraction with the use of cycloplegic eye drops in a group of challenging 3-year-old participants to obtain an accurate measurement.

The limitations of our study include loss to follow-up (25%) and refusal of cycloplegic drops (28.5%), which may have led to selection bias. However, this may be minimal, as the analysis in Table 1 did not show differences in findings between those with cycloplegic autorefraction and those without. Our findings that near work and outdoor activities are not important predictors of myopia may be limited by the small proportion of myopic children (6.1%).

In conclusion, our prospective study showed an association between family history of myopia with AL, refraction, and myopia in preschool children aged 3 years. However, we found no evidence of environmental factors influencing early-onset myopia. This study suggests that genetic factors may play a role in the development of early-onset myopia in 3-year-old children. Replication of these findings in other large prospective cohorts of very young children is needed.

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Appendix

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