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Comparison of myopic progression in Finnish and Singaporean children

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ABSTRACT.
Purpose: **To compare 3-year myopic progression between Finnish and Singaporean children.**
Methods: **Myopic progression was compared between 9-year-old (mean age 9.7 ± 0.4 years, n = 92) and 11-year-old (mean age 11.7 ± 0.4 years, n = 144) Finnish (Finnish RCT) children and Singaporean children matched by age and refraction (SCORMMatched, n = 403) and 7- to 8-year-old Singaporean children matched only by refraction (SCORM Young, n = 186). Spherical equivalent (SE) was between −0.50 and −3.00 D. Refraction with cycloplegia was controlled annually for 3 years. Information on parental myopia, mother's education, time spent on near-work and outdoor time was gathered by parental questionnaire.**
Results: **Three-year myopic progression was −2.08 ± 0.96 D and −1.30 ± 0.69 D in the Finnish RCT and Singaporean SCORMMatched 9-year-olds, respectively, and −1.34 ± 0.78 D, and −0.52 ± 0.44 D in the 11-year-olds, respectively ($p < 0.001$ between all groups). Myopic progression was fastest (−2.69 ± 0.89 D) in the SCORM 7-year-olds and similar between the SCORM Matched 9-year-olds and Finnish RCT 11-year-olds ($p = 0.55$). The Finnish RCT and SCORM Matched children showed significant differences in both daily near-work time (1.8 ± 1.0 versus 3.4 ± 1.9 hours per day, $p < 0.001$) and outdoor time (2.6 ± 0.9 versus 0.5 ± 0.4 hours per day, $p < 0.001$). These differences did not, however, explain the differences in myopic progression between the groups. More time spent outdoors was associated with less myopic progression in the Finnish RCT ($r = 0.17$, $p = 0.009$) group only. In the whole materials, greater myopic progression was associated with younger age at baseline ($p < 0.001$), younger age was associated with mother's higher education ($p < 0.001$), and mothers higher education was associated with myopia in both parents ($p < 0.001$).**
Conclusion: **Age at baseline was the most significant factor associated with myopic progression. However, at the same age and with the same initial refraction, the Finnish and Singaporean children showed different myopic progression. This result remains unexplained. Thus, age of myopia onset should be considered when comparing myopic progression between different samples and conducting treatment trials. Parental myopia may be a weak indicator of heredity of myopia.**

Key words: myopia progression – near work – outdoors – age of baseline – Singapore – Finland

The first two authors and the last author contributed equally to this work.

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Introduction

Myopia has reached epidemic levels in many East and South-East Asian countries, including Singapore (Morgan et al. 2012; Wu et al. 2016). The prevalence of myopia in Singaporean schoolchildren has been reported to be 28% in 7-year-olds, 34% in 8-year-olds, 43% in 9-year-olds, 50% in 10-year-olds and 62% in 12-year-olds (Tan 2004). In a sample of secondary school students aged 15–17 years, 74% were myopic (Quek et al. 2004; Tan 2004). These figures are significantly higher than in many European countries.

In the late 20th century, the prevalence of myopia in Finland among 7- to 8-year-old schoolchildren ranged between 0.5% and 1.9% (Laatikainen & Erkkilä 1979; Mäntyjärvi 1983), rising to 16.2% among 12-year-olds

(Pärssinen 1986) and 20–22% among 14- to 15-year-olds (Laatikainen & Erkkilä 1979; Mäntyjärvi 1983).

High education, low outdoor exposure and excessive near-work are the most established lifestyle factors for myopia (Pärssinen 1986; Morgan et al. 2005). The education system and cultural pressure to achieve early academic success in Asia is widely perceived as a significant driver of the current myopia epidemic (Rosner & Belkin 1987; Eong et al. 1993). Starting school at a younger age has been identified as a risk factor for higher myopia prevalence in schoolchildren (Baldev et al. 1990), while younger age at debut leads to faster myopic progression and higher myopia in adulthood (Mäntyjärvi 1985; Chua et al. 2016; Pärssinen & Kauppinen 2019).

At the end of the 20th century, two similar follow-up studies on myopic progression among schoolchildren were conducted. In Finland, 240 myopic schoolchildren with a mean age of 10.9 years (range 8.7–12.8) were recruited during the years 1983–1984 for a randomized clinical trial of myopia treatment (Hemminki & Pärssinen 1987), and myopic progression was followed up annually for 3 years. In Singapore, a prospective cohort study (Singapore Cohort of the Risk Factors for Myopia, SCORM) was initiated in three schools in 1999 and 2001 to identify the genetic and environmental risk factors for myopia among Singaporean schoolchildren (Saw et al. 2002).

The present study compared 3-year myopic progression in schoolchildren in two countries, Finland and Singapore, differing in myopia prevalence and explored potential explanatory factors for similarities and differences in myopic progression.

Methods

Study subjects

Subjects were myopic children from a randomized controlled clinical trial of myopia treatment conducted in Finland (Finnish RCT, Hemminki & Pärssinen 1987) and from the SCORM study conducted in Singapore (Saw et al. 2002).

Finnish children

The Finnish RCT study comprised 240 myopic schoolchildren from the third and fifth grades (119 boys and 121 girls) recruited during the years 1983 to 1984 for a randomized clinical trial on myopia treatment (Hemminki & Pärssinen 1987). Three-year follow-up data were available for 236 children. Ninety-two children were third graders, with a mean age of 9.7 ($\pm$0.36) years and 144 were fifth graders, with a mean age of 11.7 ($\pm$0.4) years. All participants were native Finns, resident in the catchment area of the Central Finland Health Care District. The main inclusion criteria were spherical equivalent (SE) between -0.50 and -3 D, astigmatism $\leq$2 D, no other eye diseases and no previous spectacles for myopia. The children were randomly allocated to three different treatment groups according to the recommended use of spectacles: continuous use, distance use only and bifocals with +1.75 D add. The methodology has been described in detail earlier (Hemminki & Pärssinen 1987). Annual examinations (follow-ups 1, 2 and 3) were conducted for three years. Three-year follow-up data were obtained for 236 children. Mean follow-up time was 3.0 ± 0.2 and 3.0 ± 0.1 years and mean age at the end of the study 12.8 ± 0.5 and 14.7 ± 0.4 years, for children in the 3rd and 5th grades at baseline, respectively (Pärssinen & Lyyra 1993).

Singaporean children

SCORM is a prospective cohort study of children from grades 1–3 recruited from three Singapore schools in 1999 and 2001 (Saw et al. 2002). The methodology has been described in detail previously (Saw et al. 2002; Saw et al. 2005). After exclusions, 1979 (68%) of the original sample of 2913 children participated in SCORM. Exclusion criteria were any serious general or eye diseases, a history of ocular surgery, allergy to eye drops or refusing cycloplegia eye drops. These children were followed up annually for 7 years. The children selected for this report were from the third visit. Figure 1 presents the flow chart of the SCORM study.

Two groups of children were selected from the SCORM sample, that is the SCORM Young and SCORM Matched groups, for comparison with the Finnish RCT children. The SCORM Young were 7- to 8-year-old children matched for SE at baseline with the Finnish RCT children. The SCORM Matched children were matched for age and SE (SE of right eye between -0.50 and -3.00 D) at baseline with the Finnish RCT children.

Ethical approval

In both the Finnish RCT and SCORM studies, ethical approval was obtained from the relevant institutional review board. Informed consents were obtained from parents. Both studies were conducted according to the tenets of the Declaration of Helsinki.

Questionnaire

Socio-demographic and lifestyle information were gathered with a parent-administered questionnaire at baseline in the Finnish RCT and SCORM studies. The items on gender (male/female) and parental myopia (none/either/both) were similar in both studies. Parental myopia was ascertained by questionnaire. Parents were asked if they wore spectacles for poor distant vision (yes or no), and if so the age at which they received their first corrective spectacles. Parents responding ‘yes’ were categorized as myopic. Mother’s education was dichotomized into ‘Lower’ (i.e. no formal education/primary/secondary in SCORM and basic or lower secondary in the Finnish RCT) and ‘Higher’ (i.e. pre-university in SCORM and upper secondary in the Finnish RCT). Lower secondary education in Finland corresponds to primary and secondary education in Singapore and upper secondary in Finland to pre-university in Singapore (Minedu.fi 2012).

In this study, the Finnish RCT parents were asked to estimate to within the nearest half hour (i.e. 0, 0.5,. . ., 3.5, and 4 hour(s) or more, with the last option coded as 4) the time their child spent on homework during weekdays and weekends and holidays, time spent on other near-work, and time spent on sports and outdoor activities (outdoors). The following formula was used to compute the mean daily value: [(mean hours on weekdays $\times$ 5) + (mean hours on weekends and holidays $\times$ 2)]/7. Near work was the sum of the time spent on homework and other near-work.

In SCORM, near work was defined as the time spent on reading, writing, computer work and playing video

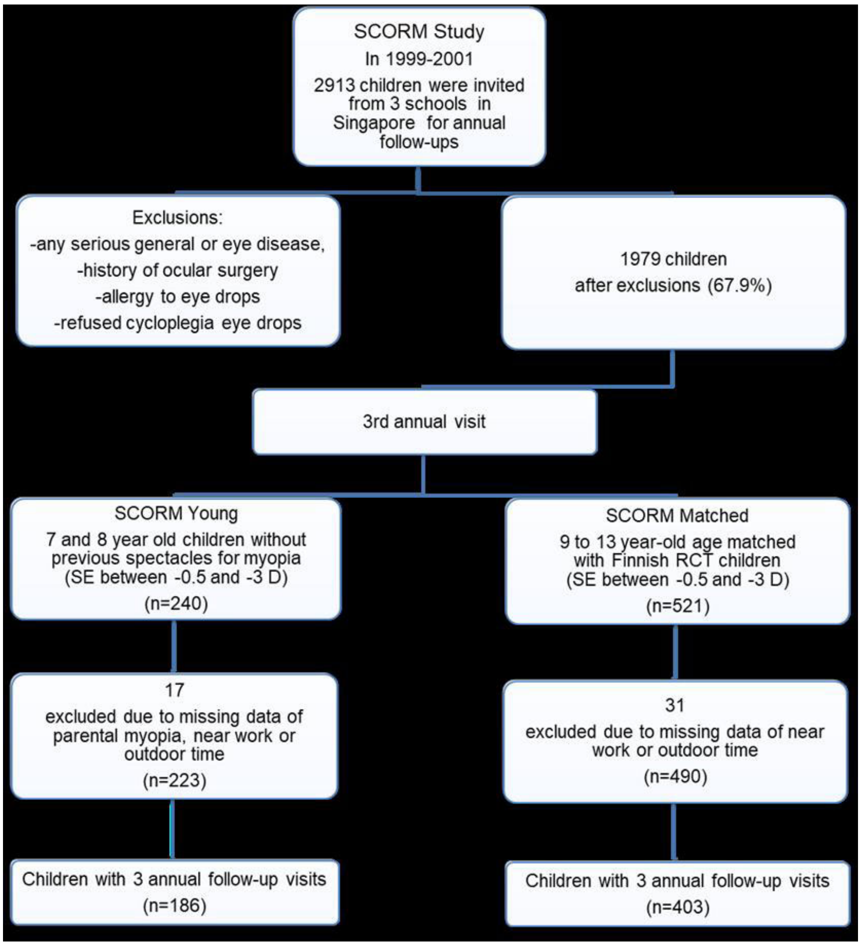

Fig. 1. Flow chart of Singaporean (SCORM) study recruitment.

games outside of school hours and the time spent on homework at home. Parents selected from 5 response options (i.e. 0, 1, 2, 3, ≥4 hour(s) per day) for each of the four near-work activities for weekdays and weekend days separately. To harmonize the SCORM data with the Finnish data, the formula used in the Finnish RCT study was applied to each near-work activity in the SCORM study, where the last category (i.e. ≥4 hours per day, h/d) was recoded as 4 hours.

Clinical measurements

SE at baseline and at the three annual follow-ups was measured with cycloplegia. In the Finnish RCT study, subjective refraction, using the fogging method (O'Brien & Bannon 1948), was performed at baseline and at the three annual follow-ups about 45 min after applying two drops of 1% cyclopentolate hydrochloride (Oftan Syklo Star®) with about 5 min intervals to eyes. Final SE was verified by the red-green duochrome test. All refractions were performed by the same researcher (OP).

In SCORM, all the clinical examinations were conducted by a trained team according to a standard protocol. Cycloplegia was induced with 1 drop of 0.5% proparacaine (Alcon, Texas, USA) followed after a 5-min interval by 3 drops of 1% cyclopentolate hydrochloride (Alcon, Texas, USA). Following an interval of at least 30 min after administration of the last drop of cyclopentolate, a table-mounted auto-keratorefractometer (model RK5, Canon Inc Ltd, Tochigi-ken, Japan) was used to measure participants' refractive error.

Statistical analyses

In the Finnish RCT, as no baseline difference in SE was observed between the right and left eye (paired samples *t*-test: 0.71, $p < 0.001$) and the differences observed between the different treatment groups in myopia progression in the right eye were non-significant (one-way ANOVA, $p > 0.05$), the right eye values were used for analysis. In SCORM, SE in the right and left eye at baseline correlated highly (paired samples *t*-test: *r*: 0.79 for SCORM Matched; 0.76 for SCORM Young, both $p < 0.001$), and thus, the right eye values were used for analysis.

Differences in categorical data between the three study groups were assessed using Pearson's chi-square test and one-way ANOVA for continuous variables. If the chi-square test or one-way ANOVA yielded significant findings (i.e. $p < 0.05$), post hoc tests were performed with Tukey correction to account for multiple pairwise comparisons.

Linear regression with Generalized Estimating Equations (GEE) was used to model myopia SE progression, adjusted for gender, parental myopia, mother's education, time spent on near-work and outdoor time, over 3 years. The auto-regressive 1 correlation matrix was used to analyse the correlation between repeated measurements, and the robust estimates of the standard error option were used to compute the 95% confidence interval. We also investigated whether group (Finnish RCT, SCORM Matched and SCORM Young) was a mediator between time and myopia (SE) with an interaction term between groups and time, where time was defined by the four measurement occasions and treated as a categorical variable. All statistical analyses were performed with STATA ver15 (STATA Corp, Texas, USA).

Results

The SCORM Young children excluded from this study were less myopic (SE = −1.31 D) at baseline than participants (SE = −1.60 D), $p = 0.004$. The non-participant SCORM Matched children's mothers more often had higher education ($p = 0.03$), their parents were more often myopic ($p = 0.004$) and they spent 0.12 h/ longer outdoors ($p = 0.05$) than participants. No other significant differences were observed between the SCORM participants and non-participants.

The ethnicity of most ($n = 465$, 78.9%) of the SCORM children was Chinese; the others were Malay

(n = 80; 13.6%), Indian (n = 39, 6.6%) and Caucasian (n = 5, 0.8%). All the Finnish children were Caucasian. In the SCORM children, baseline SE was slightly more myopic among the Chinese (−1.62 ± 0.69 D) than Indian children (−1.37 ± 0.60 D), p = 0.026 children. No significant differences in baseline SE were observed between the other ethnic groups. When the other ethnic groups were combined and compared with the Chinese group on age at baseline, Chinese children were more often among the younger children (Table 1).

In the SCORM children, myopic progression and risk factors for myopia were compared between the Chinese group and the other ethnic groups combined (Table 2).

Myopic progression was significantly faster and final SE significantly more severe in the Chinese group. Moreover, in both SCORM groups, the Chinese children who were younger at baseline spent more time on near-work than the children of the other ethnicities. In the SCORM Young, but not SCORM Matched group, the Chinese children spent significantly less time outdoors than those of the other ethnicities.

Table 3 shows the baseline characteristics of the SCORM Young, SCORM Matched and Finnish RCT study groups. No significant between-group differences were found in gender or mother's education. The proportion of children with neither parent myopic was lowest, and the proportion with two myopic parents was highest in the SCORM Young group.

The Singaporean children in both groups spent about twice as much time daily on near-work than the Finnish children (p < 0.001, one-way anova). Moreover, mean outdoor time in the Singaporean children was about one-fifth of that in the Finnish children (p < 0.001). The SCORM Young and SCORM Matched groups showed no significant differences in outdoor or near-work.

Between-group comparisons showed that 26% of the Finnish RCT children spent ≤1 h/d on near-work compared to 7% and 4% of the children in the SCORM Matched and SCORM Young groups. The percentages for ≤2 h/d were 62%, 27% and 23%, and for ≥4 h/d 4%, 34% and 31% among the Finnish RCT, SCORM Matched and SCORM Young groups, respectively (one-way anova, p < 0.001 between the Finnish RCT and both SCORM groups in each pairwise comparison). Maximum daily near-work time was 12 and 14 h/d in the SCORM Matched and SCORM Young groups, respectively.

Between-group comparisons of the distributions of outdoor time revealed that 0.4% and 3% of the Finnish RCT children spent ≤0.5 or ≤1 h/d outdoors compared to 68.5% and 89% in the SCORM Matched and 70.9% and 90% in the SCORM Young children (one-way ANOVA, p < 0.001 between the Finnish RCT and both SCORM groups in each pairwise comparison). In the Finnish RCT, 71.2% of children spent ≥2 h/d outdoors compared to 0.8% and 1.3% in the SCORM Young and SCORM Matched groups (One-Way anova, p < 0.001 between the Finnish RCT and both SCORM groups in each pairwise comparison). Maximum daily outdoor time in the Singaporean children was 2.36 h/d, whereas 54 % of the Finnish RCT children spent more than 2.36 h/d outdoors.

Mother's education was significantly higher if both parents were myopic than if neither parent was myopic (Table 4). This association was significant in both the Singaporean (p < 0.001) and Finnish groups

Table 1. Distribution of ethnicity among the Singaporean (SCORM) children by age at baseline.

		Ethnicity				
		Chinese		Other		
	Baseline age, years	N	%	N	%	Pearson Chi-Square, p
SCORM Young	7	89	84.8%	16	15.2%	0.002
	8	66	81.5%	15	18.5%	
SCORM Matched	9	165	82.1%	36	17.9%	
	10	76	75.2%	25	24.8%	
	11	69	68.3%	32	31.7%	

Table 2. Spherical equivalent (SE) at baseline and at end of 3-year follow-up, changes in 3-year myopic progression, and time spent daily on near-work and outdoors among Singaporean SCORM children in Chinese and other ethnic groups combined (Chinese = 465; Other ethnicity: Malay = 80, Indian = 39, and Caucasian = 5).

	Ethnicity					
	SCORM Young (7–8 year-old)			SCORM Matched (9–11 year-old)		
	Chinese	Other ehnicity	t-test, p	Chinese	Other ehnicity	*t*-test, p
N	155	31		310	93	
SE at baseline, D (±SD)	−1.63 (0.70)	−1.46 (0.70)	0.230	−1.62 (0.69)	−1.55 (0.64)	0.388
3-year progression of myopia D (±SD)	−2.58 (0.90)	−2.13 (1.00)	**0.012**	−1.45 (0.75)	−0.87 (0.74)	**0.044**
SE at end of follow-up, D (±SD)	−4.21 (1.05)	−3.59 (1.18)	**0.010**	−2.66 (1.05)	−2.42 (0.97)	**0.038**
Near-work hours, mean daily (±SD	3.56 (1.79)	2.34 (1.21)	**0.001**	3.57 (1.83)	3.01 (2.06)	**0.021**
Outdoors hours, mean daily (±SD)	0.47 (0.38)	0.68 (0.50)	**0.011**	0.52 (0.39)	0.53 (0.43)	0.962

Significant differences bolded.

Table 3. Baseline characteristics of children recruited into SCORM Young, SCORM Matched and Finnish RCT.

	SCORM Young (n = 186)	SCORM Matched (n = 403)	Finnish RCT (n = 236)	p-value
Age at baseline				**<0.001**[Φ]
Mean years (SD)	7.4 (0.5)	9.8 (0.8)	10.3 (0.9)	
Male/Female, N (male %)	94/92 (50.5)	192/211 (47.6)	117/119 (49.5)	0.780
Education of mother				0.427
Lower/Higher, N (%) of lower educated	135/28 (82.8)	310/60 (83.8)	187/47 (79.9)	
Parents' myopia, N (%)				**<0.001**[#]
None	39 (21.1)	159 (39.2)	91 (39.2)	
Either parents	85 (45.9)	166 (41.2)	113 (48.7)	
Both parents	61 (33)	79 (19.6)	28 (12.1)	
Time spent in near-work, hours/day (SD)	3.4 (1.7)	3.4 (1.9)	1.8 (1.0)	**<0.001****
Time spent in outdoor activities, hours/day (SD)	0.5 (0.4)	0.5 (0.4)	2.6 (0.9)	**<0.001****

Significant differences bolded.
Mother education: Lower/Higher = Secondary and below/Pre-university.
One-way ANOVA, $p < 0.001$ in each comparison.
[#] Pairwise post hoc comparison with Tukey. Finnish RCT-SCORM Matched, p = 0.300; Finnish RCT -SCORM Young, $p < 0.001$; SCORM Matched-SCORM Young, $p < 0.001$.
** One-way ANOVA, Finnish RCT-SCORM Matched, $p < 0.001$; Finnish RCT-SCORM Young, $p < 0.001$; SCORM Matched-SCORM Young, p = 0.1.00 and 0.94.

(p = 0.029). Younger age at baseline was associated with two myopic parents in both groups, but the association was significant only for the Singaporean children when analysed separately and for all the children when analysed together.

Myopic progression by age at baseline and country

Baseline SE and changes in SE during the follow-up period are shown by age at baseline in Table 5. At the end of the first year, myopic progression was highest in the youngest, that is 7-year-old SCORM Young children, and lowest in the 11-year-old SCORM Matched children. Comparison of first-year progression between the 9- and 11-year-old children in the SCORM Matched and Finnish RCT groups revealed significantly higher progression in the Finnish RCT ($p < 0.001$, in both age groups). Annual myopic progression gradually decreased during the follow-up in all groups. Total change in myopia at the 3-year follow-up was highest (−2.69 D) in the 7-year-old and lowest in the 11-year-old (ages at baseline) SCORM children (−0.52 D). Comparison of three-year myopic progression between the SCORM Matched and Finnish RCT 9- and 11-year-old children also revealed significantly higher progression in the Finnish RCT children in both age groups ($p < 0.001$).

Figure 2 shows the progression of myopia separately for children of different ages in the different study groups. The slope of myopic progression was steepest in the SCORM Young group. Comparison between the SCORM Matched and Finnish RCT 9- and 11-year-old children revealed that myopic progression was similar in the 9-year-old Singaporean and 11-year-old Finnish children (p = 0.55, *t*-test).

The proportion of children whose myopia remained stable during follow-up (mean myopic progression/year less than −0.25 D) was highest in the SCORM Matched group: 19.9%, 45.5% and 66.3% at baseline age 9, 10 and 11 years, respectively. In the Finnish RCT children, the corresponding proportions were 7.6% and 18.7% in the 9- and 11-year-olds, and in the SCORM Young children 1% and 8.6% in the 7- and 8-year-olds.

Distribution of SE at follow-up end

Figure 3 shows the distributions of SE in the Singaporean children at the 3-year follow-up at ages 10, 12 and 14: the column distribution shows that the younger the age at baseline, the greater the myopic refraction. The prevalence of myopia ≤−3 D was 86.7% and 19.5% among 10-year-olds and 14-year-olds, respectively, and highest SE among 14-year-olds was −4.38 D.

Figure 4 shows the distribution of SE among the Finnish children at ages 12 and 14 years (ages 9 and 11 at

Table 4. Associations between parents' myopia, mother's education and children's age at baseline.

	Singaporean children (SCORM Young and SCORM Matched)			Finnish children (Finnish RCT)			Finnish and Singaporean children combined		
	Parents' myopia			Parents' myopia			Parents' myopia		
Mother's education	None	Both	Chi-Square test, p	None	Both	Chi-Square test, p	None	Both	Chi-Square test, p
Low	69.6%	30.4%	**<0.001**	79.8%	20.2%	**0.029**	72.4%	27.6%	**<0.001**
High	31.9%	68.1%		52.9%	47.1%		37.5%	62.5%	
Children's age at baseline, years									
7	28.1%	71.9%	**<0.001**			0.181	28.1%	71.9%	**<0.001**
8	53.5%	46.5%					53.5%	46.5%	
9	66.1%	33.9%		68.9%	31.1%		66.9%	33.1%	
10	61.8%	38.2%					61.8%	38.2%	
11	72.1%	27.9%		81.1%	18.9%		77.0%	23.0%	

Significant differences bolded.

Table 5. Spherical equivalent (SE) at baseline and changes in SE during follow-up by study group an age.

Age, years	SCORM Young			SCORM Matched	Finnish RCT		SCORM Matched	Finnish RCT	
(*n*)	7 (105)	8 (81)	*t*-test, p	9 (201)	9 (92)	*t*-test, p	11 (101)	11 (144)	*t*-test, p
SE at baseline, D (±SD)	−1.51 (0.71)	−1.71 (0.67)	0.053	−1.58 (0.69)	−1.50 (0.61)	0.301	−1.65 (0.69)	−1.41 (0.56)	**0.004**
SE at I-year follow-up D (±SD)	−2.65 (0.81)	−2.68 (0.85)	0.055	−2.07 (0.79)	−2.34 (0.87)	**0.016**	−1.97 (0.76)	−1.98 (0.67)	0.926
SE at 2-year follow-up D (± SD)	−3.68 (0.97)	−3.48 (0.88)	0.182	−2.59 (0.90)	−3.00 (1.05)	**0.002**	#	−2.36 (0.81)	#
SE at the end of 3-year follow-up D (± SD)	−4.21 (1.07)	−3.99 (1.12)	0.172	−2.88 (0.99)	−3.57 (1.26)	**< 0.001**	−2.17 (0.93)	−2.76 (0.96)	**<0.001**
First year change of SE D (±SD)	−1.14 (0.49)	−0.97 (0.47)	**0.023**	−0.49 (0.36)	−0.84 (0.49)	**< 0.001**	−0.31 (0.34)	−0.56 (0.42)	**<0.001**
3 year change of SE D (±SD)	−2.69 (0.89)	−2.27 (0.94)	**0.002**	−1.30 (0.69)	−2.08 (0.96)	**< 0.001**	−0.52 (0.44)	−1.34 (0.78)	**<0.001**

Significant differences bolded.
[#] Due to missing case data not shown.

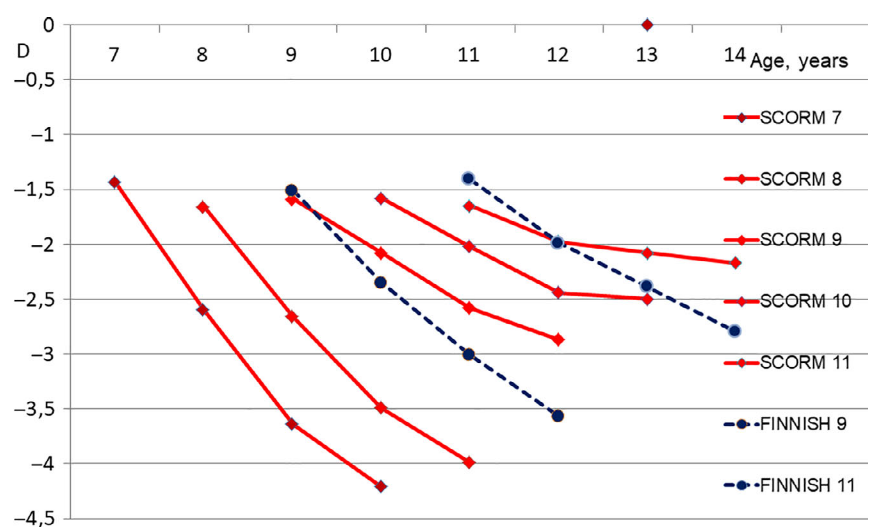

Fig. 2. Myopic progression during the 3-year follow-up in the SCORM and Finnish children by age at baseline.

baseline): the column distribution shows greater myopic refraction in the children aged 9 at baseline when compared with those aged 11 at baseline. The prevalence of myopia ≤−3 D was 70.7% and 37.5% among 12-year-olds and 14-year-olds, respectively, and highest SE among 14-year-olds was −5.38 D.

The proportion of children with high myopia (SE ≤ −5 D) at the follow-up end was associated with age at baseline; differences were observed between the Singaporean and Finnish children. In the Singaporean children at age 7, the prevalence of high myopia three years later was 21%. In the Singaporean and Finnish children aged 9 at baseline, the prevalences were 2% and 14%, respectively (Fisher's exact test, p < 0.001). In the children aged 11 at baseline, 0% of the Singaporean children and 3% of the Finnish children had high myopia (p = 0.117).

Myopic progression by time spent on near-work and outdoors

No significant correlation between near work and myopic progression was found for either study group or age.

In the Finnish children, myopic progression was lower the greater the amount of time spent outdoors (r = 0.17, p = 0.009). The correlation was low but higher in the 9-year-olds (r = 0.39, p < 0.001) than 11-year-olds (r = 0.20, p = 0.019). Similar relationships between myopic progression and time spent outdoors were not found in the Singaporean children (SCORM Young: r = −0.03, p = 0.696; SCORM Matched: r = −0.07, p = 0.185).

Myopic progression by parental myopia

Myopic progression was higher among children with two myopic parents than no myopic parents in both the SCORM and Finnish RCT children (Table 6). However, when analysed by age group, the association was significant only among the 9-year-olds. The myopic progression of children with two myopic parents also decreased with age.

Mother's higher education was associated with parental myopia, and parental myopia was associated with younger child age at baseline (Table 4). Younger baseline age, in turn, showed the most significant association with faster myopic progression. This cascade of associations was present among the younger but not older children at baseline.

Effects of individual adjustment factors on total change

The original study groups contained equal numbers of boys and girls. After exclusions, the final analyses were conducted for 403 boys and 422 girls. Myopic progression was slightly but significantly higher among girls

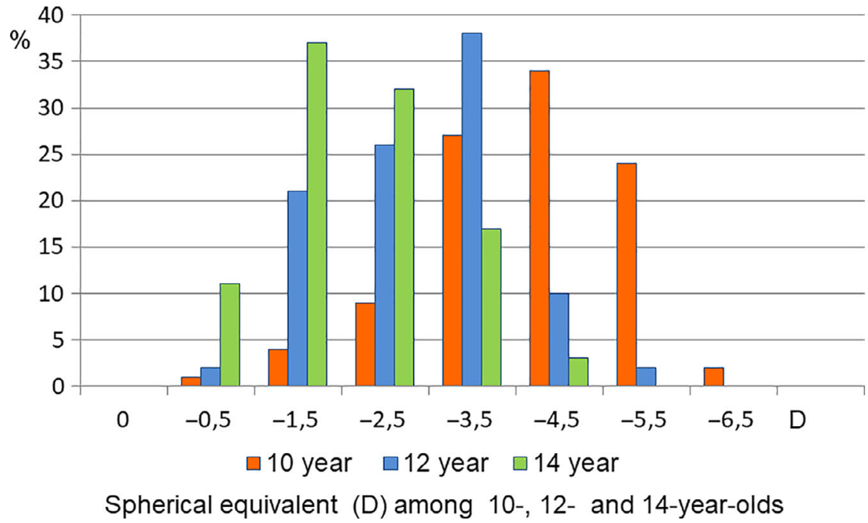

Fig. 3. Distribution of spherical equivalent of Singaporean SCORM Young children (aged 7 at baseline) and SCORM Matched children (aged 9 and 11 at baseline) at ages 10, 12 and 14 years at end of the 3 year follow-up. Grading of SE: 0 to −0.99 D = −0.5 D, −1 to −1.99 = −1.5 D, etc.

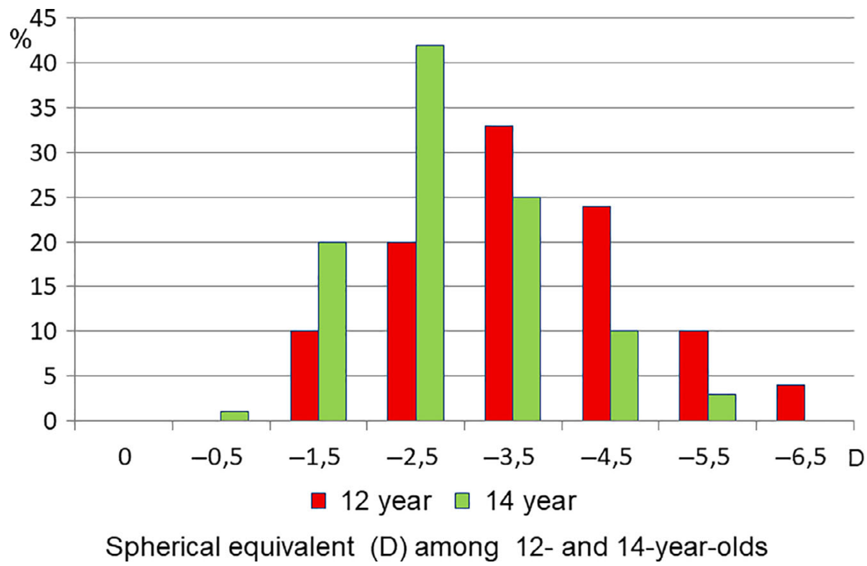

Fig. 4. Distribution of spherical equivalent of 12- and 14-year-old Finnish RCT children (aged 9 and 11 at baseline) at end of the 3 year follow-up. Grading of SE: 0 to −0.99 D = −0.5 D, −1 to −1.99 = −1.5 D, etc.

(−1.63 ± 1.09 D) than boys (−1.41 ± 0.97 D), $p = 0.02$. The influence of different confounding factors was analysed by adjusting the changes in SE by gender, parental myopia, mother's education, and time spent on near-work and outdoor activities (subgroup*time interaction term $p < 0.001$).

Table 7 shows myopic progression adjusted for potential confounders in the different groups. The effect of adjustment on 3-year cumulative myopia progression was −0.01 D in the Finnish RCT, −0.16 D in the SCORM Matched and −0.02 D in the SCORM Young groups. The main factor influencing myopic progression in both the Singaporean and Finnish children was age at baseline.

Discussion

This study investigated similarities and differences in 3-year myopic progression between Singaporean and Finnish schoolchildren. In this study, the Singaporean children spent more time on near-work and less time outdoors. The prevalence of myopia is known to be significantly higher in Singapore than in Finland (Tan 2004; Pärssinen 2012). Several studies have shown an association of higher prevalence of myopia with near-work time (Pärssinen 1986; French et al., 2013a, 2013b; Sun et al. 2018) and less time outdoors (Pärssinen 1986; Rose et al. 2008; Guggenheim et al. 2012; Shah et al. 2017; Xiong et al. 2017). Thus, our primary hypothesis was that myopic progression would not be higher among the Finnish children. However, comparison of the SCORM Matched and Finnish RCT children of the same age at baseline showed the opposite: myopic progression was faster among the Finnish children.

Age at baseline was the most significant factor contributing to the progression of myopia in both the Singaporean and Finnish children. In many previous studies, earlier age of myopia onset, or age of receiving the first spectacles for myopia was a significant predictor of faster myopic progression and higher adulthood myopia (Mäntyjärvi 1985; Pärssinen1986; Saw et al. 2005; Chua et al. 2016; Morgan et al. 2018; Pärssinen & Kauppinen 2019). Because myopic progression varies widely, it is difficult to ascertain the exact time of myopia onset without conducting examinations at short intervals. Therefore, age of receiving the first spectacles has been used to describe the association between age of onset and myopic progression (Midelfart et al. 1992; Iribarren et al. 2009). In Finland, vision screening of all schoolchildren is done at two-yearly intervals, and children with distant vision of ≤0.7 in either eye or who presented with symptoms of poor distant vision between these routine screenings are referred for an eye examination. It can thus be suggested that age of myopia onset, that is the age at which SE changed to ≤−0.5 D, was in most cases less than 2 years prior to the baseline age in this study. The SCORM and Finnish children were matched for SE at baseline.

In this study, comparisons between the SCORM Matched and Finnish RCT children with the same SE at ages 9 and 11 showed, after adjustment for gender, parental myopia, mother's education, time spent on near-work and outdoor activities, that myopic progression was higher in both age groups in the Finnish children. Interestingly the rate of progression between the 9-year-old SCORM children and 11-

Table 6. Myopic progression in dioptres (standard deviation) among Finnish and Singaporean children in different age groups by parents' myopia, no myopic parents (none) or both parents myopic (both).

	Singaporean children (SCORM young and SCORM matched)					Finnish children (Finnish RCT)				
	Parents' myopia					Parents' myopia				
	None		Both			None		Both		
Age at baseline years	N	SE change, D (±SD)	N	SE change, D (±SD)	*t*-test between changes of SE, p	N	SE change, D (±SD)	N	SE change, D (±SD)	*t*-test between changes of SE, p
7 and 8	38	−2.31 (1.10)	43	−2.71 (0.86)	0.057					
9	80	−1.21 (0.60)	41	−1.54 (0.73)	**0.016**	31	−1.70 (0.76)	14	−2.60 (0.97)	**0.004**
10	34	−0.79 (0.77)	21	−0.94 (0.67)	0.497					
11	44	−0.55 (0.73)	17	−0.57 (0.71)	0.916	60	−1.26 (0.71)	14	−1.11 (0.79)	0.508
All ages	196	−1.21 (0.98)	122	−1.85 (1.13)	**< 0.001**	91	−1.41 (0.75)	28	−1.87 (1.16)	**0.016**

Significant differences bolded.

year-old Finnish children was similar. One hypothetical factor which could explain the more rapid myopic progression among the Finnish children than their age-matched Singaporean peers could be the generally much earlier onset of myopia and higher prevalence of myopia among the Singaporean children. It can be speculated that the children who are the first to develop myopic are also those most susceptible to it, while those who develop myopia later are more resistant. Whereas the prevalence of myopia in the Finnish children was only 1–2% at age 7–8 and 16.2% at age 12 (Pärssinen 2012), in the Singaporean children it was 28% at age 7, 34% at age 8, 43% at age 9, 50% at age 10 and 62% at age 12 (Tan 2004). From these percentages, it can be roughly estimated that 90% of the 9-year-old and 85% of the 11-year-old Finnish children were non-myopic compared to 60% and 40% of the Singaporean children. This suggests the possibility of a phase difference in the progression of myopia between the two populations; that is, myopia among those who become myopic first will progress faster. This could be one explanation for the similar myopic progression in the 9-year-old Singaporean and 11-year-old Finnish children.

Significant differences were found between the SCORM Chinese children and those of the other ethnicities (Malay, Indian and Caucasian) at different baseline ages. Among the youngest children at baseline, the proportion of Chinese children was significantly the highest. The other significant differences between these ethnic groups were in time spent on near-work and outdoors. In the 7- to 8-year-old Chinese children, mean near-work time was one hour higher than in the other ethnicities (3.56 versus 2.34 h/d), and in the older SCORM Matched Chinese children, it was about half an hour higher (3.57 versus 3.01 h/d). Several studies have shown an association of myopia incidence with more near-work (Pärssinen 1986; French et al., 2013a, 2013b; Sun et al. 2018) and less time spent outdoors (Pärssinen 1986; Rose et al. 2008; Guggenheim et al. 2012; Shah et al. 2017; Xiong et al. 2017). Thus, it seems reasonable to conclude that the Chinese Singaporean children, with more near-work and less outdoor time, became myopic at younger ages than their age peers in the other ethnic groups. Although myopic progression and myopia at the follow-up end were higher in the Chinese children than those in the other Singaporean ethnic groups, these results are not explained by differences in near-work, outdoor time or ethnicity per se. When the prevalence of myopia was compared between different ethnicities in Singapore and Malaysia, the prevalence of myopia in Singapore Malays, Chinese and Indians was higher than in the same ethnic groups in Malaysia (Saw et al., 2006a, 2006b). Moreover, in both Singapore and Malaysia, the prevalence was higher in the Chinese children than those in the other ethnic groups. Environmental factors were suggested to contribute the differences in myopia prevalence between the same ethnic groups in two neighbouring countries. Differences in myopic progression have also been found among Caucasian children living in different countries. The greater prevalence of myopia among Caucasian children in Northern Ireland than among Caucasian children in Sydney was not explained by risk factors for myopia such as parental myopia, parental education or educational standards (French et al. 2012). One logical explanation for the faster myopic progression in Chinese children found in this study could be earlier onset of myopia

Table 7. Three-year cumulative myopia progression rates among children in the three groups, adjusted for gender, parental myopia, mother's education, time spent on near-work and outdoor activities: group*time interaction term.[#]

Adjusted β (95% CI)	SCORM Young	SCORM Matched	Finland RCT
Baseline	Reference	Reference	Reference
1-year cumulative myopia progression (D)	−1.10 (−1.17, −1.03)	−0.45 (−0.49, −0.41)	−0.67 (−0.74, −0.61)
2-year cumulative myopia progression (D)	−1.95 (−2.07, −1.83)	−0.95 (−1.01, −0.89)	−1.17 (−1.26, −1.08)
3-year cumulative myopia progression (D)	−2.53 (−2.67, −2.39)	−1.17 (−1.26, −1.09)	−1.64 (−1.77, −1.52)

[#] Adjusted for gender, parental myopia, mother education, time spent on near-work and outdoor activities; subgroup*time interaction term ($p < 0.001$). Difference in 3-year cumulative myopia SE (Finland-SCORM (Matched), $p < 0.001$; Finnish RCT-SCORM Young, $p < 0.001$; SCORM Matched-SCORM Young $p < 0.001$).

induced by a higher load of near-work at younger ages. These findings are consistent with previous studies showing that the incidence of myopia is associated with more near-work and that the rate of myopic progression among those already myopic is little influenced by differences in the amount of time spent on near-work or outdoors (Saw et al. 2000; Jordan-Jones et al. 2012).

Even greater differences in near-work and outdoor time than those between the Singaporean ethnic groups of children were observed between the Singaporean and Finnish children in this study. However, time spent on near-work did not explain the difference in myopic progression between the Singaporean and Finnish children or among the Singaporean children.

Studies both in Finland (Pärssinen 1986) and Singapore (Dirani et al. 2009) along with several other studies (Rose et al. 2008; He et al 2015; Guo et al. 2017; Huang et al. 2019; Wu et al. 2020) have found that individuals who spent more time outdoors were less likely to be myopic. In the present study, the considerable differences between the Singaporean and Finnish children in time spent outdoors did not explain the differences between the two populations in myopic progression. However, more time spent outdoors showed a protective influence against myopic progression among the Finnish children, although it was higher among the 9-year-olds than 11-year-olds. One reason for the absence of this association among the Singaporean children could be the low amount of time spent outdoors and the homogeneity of the groups. About 70% of the children in both the SCORM groups spent ≤0.5 h/d outdoors and only about 10% ≥1 h/d, whereas more than 70% of the Finnish children, but only about 1% of the Singaporean children, spent ≥2 h/d outdoors. In a prospective cohort study started in 2010 among schoolchildren in Taiwan, recommendations were 2 h/d outdoor time and a break of 10 min after every 30 min of near-work (Wu et al. 2020). During the follow-up, the trend towards an increase in poor uncorrected distant vision significantly reversed (Wu et al. 2020). The time spent outdoors by the Singaporean children has perhaps been too small to have had a significant influence on myopic progression.

Age at baseline and parental myopia

It remains unclear why earlier onset myopia progresses to higher myopia. This prompts the question, why at a young age, during normal growth, is the eye more susceptible to the additional axial elongation associated with near vision or restricted distant vision? Sonderman (1950) concluded that most scleral growth takes place during the first 6 years, while the posterior pole of the sclera continues to thicken up to around age 14. Sorsby et al. (1961) concluded, based on axial length measurements, that axial length attains its adult dimensions at the same age. In animal experiments, deprivation myopia caused axial elongation and progressed faster in younger animals (Zhi et al. 2010). It would seem reasonable to assume that younger children, whose sclera are still growing, would be more susceptible than older children to environmental influences causing myopia.

An association between parental myopia and child myopia has been found in several studies (Pärssinen 1986; Saw et al 2005; Dirani et al. 2009; French et al., 2013a, 2013b; Cooper & Tkatchenko 2018; Harrington et al. 2019). In our study, when all the children were combined, 70% of those aged 7 at baseline had two myopic parents, whereas this was true for less than 30% of the baseline 11-year-olds. French et al., (2013a, 2013b), in their 5- to 6-year follow-up study among children aged 6 and 12 at baseline, reported a similar finding. Parental myopia was a significant risk factor for incident myopia only in the younger cohort, that is those aged 6 at baseline.

An earlier report on the SCORM study showed that having two myopic parents versus no myopic parents was a risk factor (OR 1.55) for incident myopia (Saw et al., 2006a, 2006b). In this study, having two myopic parents was also associated with more myopic progression. However, when the analyses were performed separately for different age groups, this association remained only for the younger children. The higher myopic progression of −0.40 D among children with two myopic parents in the SCORM Young group was almost significant ($p = 0.057$). In the 9-year-olds in the SCORM Matched and Finnish RCT groups, myopic progression was significantly greater in the children with two myopic parents than no myopic parents. Among the 11-year-olds at baseline, no significant difference in myopic progression with regard to parental myopia was found; this may, however, be due to the small sample size.

Parental myopia has been an established risk factor for myopia for years and has often been considered as evidence for the heredity of myopia (Saw et al. 2001; Cooper & Tkatchenko 2018). Recently, however, large genome-wide association studies have identified 161 independent loci for refractive error that explain 8% of the variance of spherical equivalent in adults and can discriminate myopia from hyperopia to within an accuracy of 0.77 (Tedja et al. 2018).

In this study, if both a child's parents were myopic, their mothers were more often highly educated. Mother's higher education, in turn, was associated with children's younger age at baseline and younger age at baseline associated with greater myopic progression. It is evident that environmental factors affect the risk for myopia in both parents and children, and hence, parents' myopia cannot be regarded solely as an indication of the heredity of myopia.

Conclusion

Small differences in age at baseline were associated with significant differences in three-year myopic progression; however, the influence of age at baseline on myopic progression clearly differs across populations. These factors present significant challenges when comparing studies on myopic progression and conducting multicentre studies and clinical treatment trials.

References

Baldev G, Mangat D, Balram S, Kulshushan C, Ranjit P, Raman P (1990): Myopia in relation to early schooling. In: Weintraub J (ed.). Fourth International Conference on myopia. Singapore: Myopia Int Res Found, Inc 283–289.

Chua SY, Sabanayagam C, Cheung YB et al. (2016): Age of onset of myopia predicts risk of high myopia in later childhood in myopic Singapore children. Ophthalmic Physiol Opt **36**: 388–394.

Cooper J & Tkatchenko AVA (2018): Review of current concepts of the etiology and treatment of myopia. Eye Contact Lens **44**: 231–247.

Dirani M, Tong L, Gazzard G et al. (2009): Outdoor activity and myopia in Singapore teenage children. Br J Ophthalmol **93**: 997–1000.

Eong KA, Tay T & Lim M (1993): Education and myopia in 110,236 young Singaporean males. Singapore Med J **34**: 489–492.

French AN, Morgan IG, Mitchell P & Rose KA (2013a): Risk factors for incident myopia in Australian schoolchildren: the Sydney adolescent vascular and eye study. Ophthalmology **120**: 2100–2108.

French AN, Ashby RS, Morgan IG & Rose KA (2013b): Time outdoors and the prevention of myopia. Exp Eye Res **114**: 58–68.

French A. N., O'Donoghue L., Morgan I. G., Saunders K. J., Mitchell P., Rose K. A. (2012): Comparison of refraction and ocular biometry in European Caucasian children living in Northern Ireland and Sydney, Australia. Invest Ophthalmol Vis Sci **53**: 4021–4031.

Guggenheim JA, Northstone K, McMahon G, Ness AR, Deere K, Mattocks C, Pourcain BS & Williams C (2012): Time outdoors and physical activity as predictors of incident myopia in childhood: a prospective cohort study. Invest Ophthalmol Vis Sci **53**: 2856–2865.

Guo Y, Liu LJ, Tang P, Lv YY, Feng Y, Xu L & Jonas JB (2017): Outdoor activity and myopia progression in 4-year follow-up of Chinese primary school children: The Beijing Children Eye Study. PLoS One **12**: e0175921. https://doi.org/10.1371/journal.pone.0175921. eCollection.

Harrington SC, Stack J. & O'Dwyer V (2019): Risk factors associated with myopia in schoolchildren in Ireland. Br J Ophthalmol **103**: 1803–1809.

He M, Xiang F, Zeng Y et al. (2015): Effect of time spent outdoors at school on the development of myopia among children in China: A randomized clinical trial. JAMA **314**: 1142–1148.

Hemminki E & Pärssinen O (1987): Prevention of myopic progress by glasses. Study design and the first-year results of a randomized trial among schoolchildren. Am J Optomet Phys Opt **64**: 611–616.

Huang PC, Hsiao YC, Tsai CY et al. (2019): Protective behaviours of near work and time outdoors in myopia prevalence and progression in myopic children: a 2-year prospective population study. Br J Ophthalmol. **104**: 956–961. pii: bjophthalmol-2019-314101. doi: https://doi.org/10.1136/bjophthalmol-2019-314101. [Epub ahead of print].

Iribarren R, Cortinez MF & Chiappe JP (2009): Age of first distance prescription and final myopic refractive error. Ophthalmic Epidemiol **16**: 84–89.

Jones-Jordan LA, Sinnott LT, Cotter SA, Kleinstein RN, Manny RE, Mutti DO, Twelker JD & Zadnik K & CS Group (2012): Time outdoors, visual activity, and myopia progression in juvenile-onset myopes. Invest Ophthalmol Vis Sci **53**: 7169–7175.

Laatikainen L & Erkkilä H (1979): Koululaisten silmälöydökset. (Ocular findings in school childeren). Duodecim **95**: 561–569.

Mäntyjärvi M. (1983): Incidence of myopia in a population of Finnish school children. Acta Ophthalmol **61**: 417–423.

Mäntyjärvi MI (1985): Predicting of myopia progression in school children. J Pediatr Ophthalmol Strabismus **22**: 71–75.

Midelfart A, Aamo B, Sjøhaug KA & Dysthe BE (1992): Myopia among medical students in Norway. Acta Ophthalmol (Copenh) **70**: 317–322.

Minedu.fi (2012): Background for Finnish PISA success.

Morgan I & Rose K (2005): How genetic is school myopia? Prog Retinal Eye Res **24**: 1–38.

Morgan IG, Ohno-Matsui K & Saw SM (2012): Myopia. Lancet **379**: 1739–1748.

Morgan IG, French AN, Ashby RS, Guo X, Ding X, He M & Rose KA (2018): The epidemics of myopia: Aetiology and prevention. Prog Retin Eye Res **62**: 134–149.

O'Brien JM & Bannon RE (1948): The fogging method of refraction. A comparative analysis. Am J Ophthalmol **31**: 1453–1459.

Pärssinen O (1986): The wearing of spectacles and occurrence of myopia. Tampere: Acta Universitatis Tamperensis, ser A, Vol **208**, University of Tampere. http://urn.fi/URN:ISBN:978-952-03-1483-5.

Pärssinen O (2012): The increased prevalence of myopia in Finland. Acta Ophthalmol **90**: 497–502.

Pärssinen O & Kauppinen M (2019): Risk factors for high myopia: a 22-year follow-up study from childhood to adulthood. Acta Ophthalmol **97**: 510–518.

Pärssinen O & Lyyra A (1993): Myopia and myopic progression among schoolchildren: a three-year follow-up study. Invest Ophthalmo Vis Sci **34**: 2794–2802.

Quek TP, Chua CG, Chong CS, Chong JH, Hey HW, Lee J, Lim YF & Saw SM (2004): Prevalence of refractive errors in teenage high school students in Singapore. Ophthalmic Physiol Opt **24**: 47–55.

Rose KA, Morgan IG, Ip J, Kifley A, Huynh S, Smith W & Mitchell P (2008): Outdoor activity reduces the prevalence of myopia in children. Ophthalmology **115**: 1279–1285.

Rosner M & Belkin M (1987): Intelligence, education, and myopia in males. Arch Ophthalmol **105**: 1508–1511.

Saw SM, Nieto FJ, Katz J, Schein OD, Levy B & Chew SJ (2000): Factors related to the progression of myopia in Singaporean children. Optom Vis Sci **77**: 549–54.

Saw SM, Nieto FJ, Katz J, Schein OD, Levy B & Chew SJ (2001): Familial clustering and myopia progression in Singapore school children. Ophthal Epidemiol **8**: 227–236.

Saw S-M, Chua W-H, Hong C-Y, Wu H-M, Chan W-Y, Chia K-S, Stone RA & Tan D (2002): Nearwork in early-onset myopia. Invest Ophthalmol Vis Sci **43**: 332.

Saw SM, Tong L, Chua WH, Chia KS, Koh D, Tan DT & Katz J (2005): Incidence and progression of myopia in Singaporean school children. Invest Ophthalmol Vis Sci **46**: 51–57.

Saw SM, Goh PP, Cheng A, Shankar A, Tan DT & Ellwein LB (2006a): Ethnicity-specific prevalences of refractive errors vary in Asian children in neighbouring Malaysia and Singapore. Br J Ophthalmol **90**: 1230–1235.

Saw SM, Shankar A, Tan SB, Taylor H, Tan DT, Stone RA & Wong TY (2006b): A cohort study of incident myopia in Singaporean children. Invest Ophthalmol Vis Sci **47**: 1839–1844.

Shah RL, Huang Y, Guggenheim JA & Williams C (2017): Time outdoors at specific ages during early childhood and the risk of incident myopia. Invest Ophthalmol Vis Sci **58**: 1158–1166.

Sonderman R (1950): Die bedeutung der Bererbung fur die Entwicklung der Myopie. Albrecht Von Graefes Arch Ophthalmol **151**: 200–208.

Sorsby A, Benjamin B, Sheridan M & Stone J, Leary GA (1961): Refraction and its components during the growth of the eye from the age of three. Memo Med Res Counc **301**(Special): 1–67.

Sun JT, An M, Yan XB, Li GH & Wang DB (2018): Prevalence and related factors for myopia in school-aged children in Qingdao. J Ophthalmol. **2018**: 9781987. https://doi.org/10.1155/2018/9781987. eCollection.

Tan DT (2004): The future is near: focus on myopia. Singapore Med J **45**: 451–455.

Tedja MS, Wojciechowski R, Hysi PG et al. (2018): Genome-wide association meta-analysis highlights light-induced signaling as a driver for refractive error. Nat Genet **50**: 834–848.

Wu PC, Huang HM, Yu HJ, Fang PC & Chen CT (2016): Epidemiology of Myopia. Asia Pac J Ophthalmol (Phila) **5**: 386–393.

Wu PC, Chen CT, Chang LC, Niu YZ, Chen ML, Liao LL, Rose K & Morgan IG (2020): Increased time outdoors is followed by reversal of the long-term trend to reduced visual acuity in Taiwan primary school students. Ophthalmology. pii: S0161–6420(20)30139–1. https://doi.org/10.1016/j.ophtha.2020.01.054

Xiong S, Sankaridurg P, Naduvilath T et al. (2017): Time spent in outdoor activities in relation to myopia prevention and control: a meta-analysis and systematic review. Acta Ophthalmol **95**: 551–566.

Zhi ZN, Yang TZ, Xiong SB, Jiang LQ, Pan MZ, Qu J & Zhou XT (2010): Susceptibility of guinea pig eyes to form deprivation myopia and its age-related recovery. Zhonghua Yan Ke Za Zhi **46**: 641–645.

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