Protective Role of Orthokeratology in Reducing Risk of Rapid Axial Elongation: A Reanalysis of Data From the ROMIO and TO-SEE Studies

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Purpose. To determine the relative risk of rapid progression and number needed to treat (NNT) in younger and older children using combined data from the retardation of myopia in orthokeratology (ROMIO) and toric orthokeratology–slowing eye elongation (TO-SEE) studies.

Methods. Data from 136 subjects of two studies, ROMIO and TO-SEE, were retrieved (72 orthokeratology [ortho-k]: 37 ROMIO, 35 TO-SEE; 64 control: 41 ROMIO, 23 TO-SEE) and the myopia control effect on younger (6–8 years) and older (9–12 years) subjects evaluated. The rate of axial elongation was classified as not rapid (axial elongation = <0.36 mm/year) or rapid (axial elongation >0.36 mm/year).

Results. Cumulative frequency curves showed that the younger subjects in the control group had the greatest and most rapid axial elongation at the end of 24 months. In the younger subjects, ortho-k lens wear significantly reduced the risk of rapid progression by 88.8% ($P = 0.002$). The 2-year NNT for the younger ortho-k subgroup was 1.8, suggesting that treating just two younger subjects with ortho-k would prevent one subject from experiencing rapid progression over a 2-year period of treatment. The 2-year NNT for the older ortho-k subgroup was 11.8, which was statistically insignificant ($P = 0.197$).

Conclusions. Orthokeratology significantly reduced risk of rapid progression in younger subjects. Treating just two 6- to 8-year-old subjects with ortho-k instead of single-vision spectacles could prevent one subject from developing rapidly progressing axial elongation during this critical 2-year period.

Keywords: orthokeratology, myopia control, younger children, rapid progression, NNT, relative risk

Myopia, the most frequent cause of distance impairment, is a major concern[1–2] as children who become myopic earlier are more likely to later develop high myopia.[1] Axial elongation, associated with progression of myopia, can lead to adverse mechanical stretching and thinning of the retina, resulting in retinal degenerative changes.[3] For decades, researchers studying myopia have searched for effective ways to slow its progression in children.[4–12] In the last decade, a number of reports have been published on the effectiveness of orthokeratology (ortho-k) for myopia control in children.[9,11,13–18] These studies have been subjected to meta-analysis by two groups of researchers[19,20] who both confirmed the effectiveness of ortho-k for myopia control. However, Si et al.[19] suggested that, since five of the seven studies included in the meta-analysis were from Asia, further work would be required. Two main limitations of meta-analyses are the frequent unavailability of raw data and problems with different methodologies of the studies included in the analysis, which restrict the amount of further statistical analysis that can be performed with the combined data from the studies. However, two of the studies listed in the meta-analyses, retardation of myopia in orthokeratology (ROMIO)[11] and toric orthokeratology–slowing eye elongation (TO-SEE),[17] were prospective cohort studies conducted around the same period of time by the same research team in Hong Kong using the same methodology, with the exception that the former was a randomized study on children with low myopia and low astigmatism, whereas the latter was a nonrandomized study on children with low myopia but moderate to high astigmatism. Raw data from both were available for combined analyses (Table 1). Respectively, the ROMIO[11] and TO-SEE[17] studies reported 46% and 56% slower increases in axial length of children aged 6 to 12 years wearing ortho-k lenses compared to children wearing spectacles. The retardation of myopia in orthokeratology[11] study also reported a significantly lower percentage of younger subjects (age 7–8 years) with rapid axial elongation (>0.36 mm per year [i.e., equivalent myopic progression >1.00 diopter [D] per year]) in the ortho-k group (20%) compared to control subjects wearing single vision spectacles (65%). The toric orthokeratology–slowing eye elongation[17] study reported that the odds of becoming a rapid progressor was 14.9 times greater in subjects wearing single-vision spectacles than those wearing ortho-k lenses, but only eight subjects (ortho-k: $n = 1$; control groups: $n = 7$) in this study demonstrated rapid myopic progression.

The number needed to treat (NNT), an average number of patients needed to be treated to prevent one adverse event or one specified clinical endpoint, is a statistical metric that can

Table 1. Details of ROMIO[11] and TO-SEE[17] Studies

	ROMIO Study	TO-SEE Study
Study design	Randomized	Nonrandomized
Masking	Examiners masked to axial length measurements	
Ethnicity	Chinese	
Age, y	6–10	6–12
Myopia, D	0.50–4.00	0.75–5.00
WTR astigmatism, D	Up to 1.25 (other axes: <0.75)	1.25–3.00
Study group	Menicon Z Night	Menicon Z Night Toric
Control group	Single-vision spectacles	
Data collection	Baseline and every 6 months after start of lens or spectacle wear for 2 years	
Axial length measurement	IOLMaster (Zeiss Humphrey, Dublin, CA, USA)	

WTR, with-the-rule.

help decision making between treatment options. It is treatment-time specific and takes into account both absolute risk and relative treatment effects, allowing the translation of research data into clinical practice.[21] It is a simple way to demonstrate the clinical benefit or impact of a treatment. For example, a 2-year NNT of 100 suggests that 100 subjects would need to be treated for 2 years to prevent one specified (adverse) outcome.

Although the calculated powers to detect a statistically significant difference for both the ROMIO[11] and TO-SEE[17] studies were over 85%, subgroup sample sizes in each study were small. Combining data from these two studies offers the potential to extract further meaningful results with improved statistical power. Specifically, combining these data allows determination of the relative risk (RR) of rapid progression in subjects not using ortho-k treatment. To our knowledge, findings in terms of benefit analysis have not been previously presented for ortho-k.

The purpose of this study was to reanalyze the combined data from the ROMIO and TO-SEE studies to determine the RR of rapid progression in younger and older children, and to determine the NNT, that is, the number of children needed to be fitted with ortho-k to prevent one rapid progressor. Results obtained offer a new perspective on myopia control using ortho-k, specifically on the benefit of this treatment that can be applied in clinical decision making.

Methods

Data from two studies, ROMIO[11] and TO-SEE,[17] were pooled for analysis. Both studies were approved by the Departmental Research Committee of the School of Optometry of The Hong Kong Polytechnic University and written consent was obtained from both subjects and their parents before study participation. Both studies were registered at ClinicalTrials.gov (ROMIO: NCT00962208; TO-SEE: NCT00978692). No significant adverse effect was reported in either study.[11,17]

Treatment of Data

We used commercial software (SPSS 23.0; IBM Corp., Armonk, NY, USA) for statistical analysis. Parametric tests were used for the analysis of refractive sphere and axial length that followed Gaussian distributions, while nonparametric tests were used for the analysis of age and initial cylinder. A linear multiple regression model was utilized to study factors affecting axial elongation. Due to the differences in subject assignments (randomization) in the ROMIO and TO-SEE studies, and moderate to high astigmatism in TO-SEE subjects, one-way analysis of covariance (ANCOVAs) controlled for age, initial sphere, and astigmatism was used to investigate the axial elongation in children with and without ortho-k. Relative risk of rapid progression and NNT were determined for subjects treated with ortho-k and single-vision spectacles.

Results

Data from 136 subjects were retrieved (72 ortho-k: 37 ROMIO, 35 TO-SEE; 64 control: 41 ROMIO, 23 TO-SEE). Table 2 shows the demographic data and axial elongation during the course of the 2-year studies. No significant differences in initial age (Kruskal-Wallis, $P = 0.81$), initial refractive sphere (1-way ANOVA, $F_{3,132} = 1.30$, $P = 0.28$), and initial axial length (1-way ANOVA, $F_{3,132} = 1.30$, $P = 0.59$) were present between subjects from the ROMIO and TO-SEE studies, and between those wearing single-vision spectacles and ortho-k lenses in the two studies. The data from the two studies were pooled and further analyses performed.

Stepwise multiple regression analysis revealed that of the factors investigated, axial elongation was significantly associated with the use of ortho-k (standardized $\beta = -0.48$, $P < 0.001$) and initial age (standardized $\beta = -0.32$, $P < 0.001$), but not with initial refractive sphere, initial refractive cylinder, or initial corneal toricity (part r: −0.04 to 0.09, $P > 0.29$). The regression model was fair in predicting axial elongation based on initial age and the use of ortho-k (adjusted $R^2 = 0.35$) and statistically significant ($F_{2,133} = 35.21$, $P < 0.001$). Axial elongation was negatively associated with age in both groups (control: Pearson $r = 0.44$, $P < 0.001$; ortho-k: Pearson $r = 0.30$, $P = 0.01$).

Table 2. Demographic Data and Axial Elongation of the 136 Subjects That Completed the ROMIO[11] and TO-SEE[17] Studies

	Study	Age, y	Initial Sphere, D	Initial Axial Length, mm	Axial Elongation >2 y, mm
Control	ROMIO, $n = 41$	8.9 ± 1.6	−2.23 ± 0.84	24.40 ± 0.84	0.63 ± 0.26
	TO-SEE, $n = 23$	8.7 ± 1.0	−2.04 ± 1.09	24.18 ± 1.00	0.64 ± 0.31
	P value				0.72*
Ortho-k	ROMIO, $n = 37$	8.9 ± 0.5	−2.05 ± 0.72	24.48 ± 0.71	0.40 ± 0.25
	TO-SEE, $n = 35$	9.0 ± 1.5	−2.46 ± 1.32	24.37 ± 0.88	0.31 ± 0.27
	P value				0.15*
Control	Combined, $n = 64$	8.77 ± 1.27	−2.16 ± 0.93	24.32 ± 0.90	0.63 ± 0.28
Ortho-k	Combined, $n = 72$	8.92 ± 1.22	−2.25 ± 1.07	24.45 ± 0.79	0.35 ± 0.25
	P value	0.805†	0.278‡	0.593‡	<0.001*

* P value from 1-way ANCOVA controlled for age, and initial Rx and initial cylinder.
† P value from Kruskal-Wallis test.
‡ P value from 1-way ANOVA.

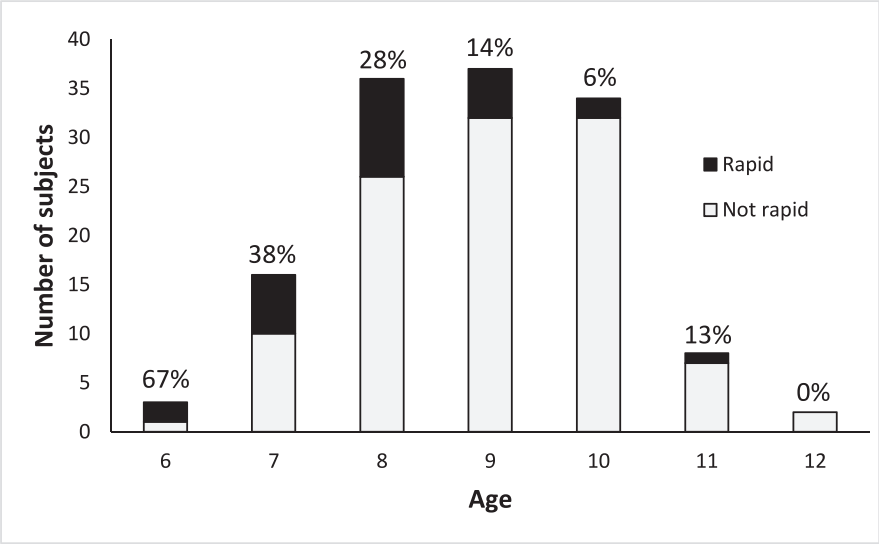

Figure 1. Percentage of subjects with rapid progression (axial elongation >0.36 mm/year; *black*).

Figure 1 shows the overall number and percentage of subjects with rapid progression. The percentage of subjects with rapid progression reduced from 67% at the age of 6 to 28% at the age of 8. The percentage of subjects with rapid progression was rather low (range, 0%–14%) for those aged 9 to 12 years. Therefore, to determine the myopia control effect on younger and older children, the subjects were divided into two age groups: 6 to 8 and 9 to 12 years. The average axial elongations over 2 years were 0.46 ± 0.22 mm and 0.81 ± 0.27 mm, respectively, in the ortho-k and control subjects aged 6 to 8 years and were 0.28 ± 0.26 mm and 0.52 ± 0.22 mm, respectively, in the ortho-k and control subjects aged 9 to 12 years.

Figure 2 shows the cumulative percentage frequencies of subjects with specified axial elongation at the end of 24 months. The graph indicates that ortho-k lens wear led to reduced axial elongation over 2 years of lens wear (curves for

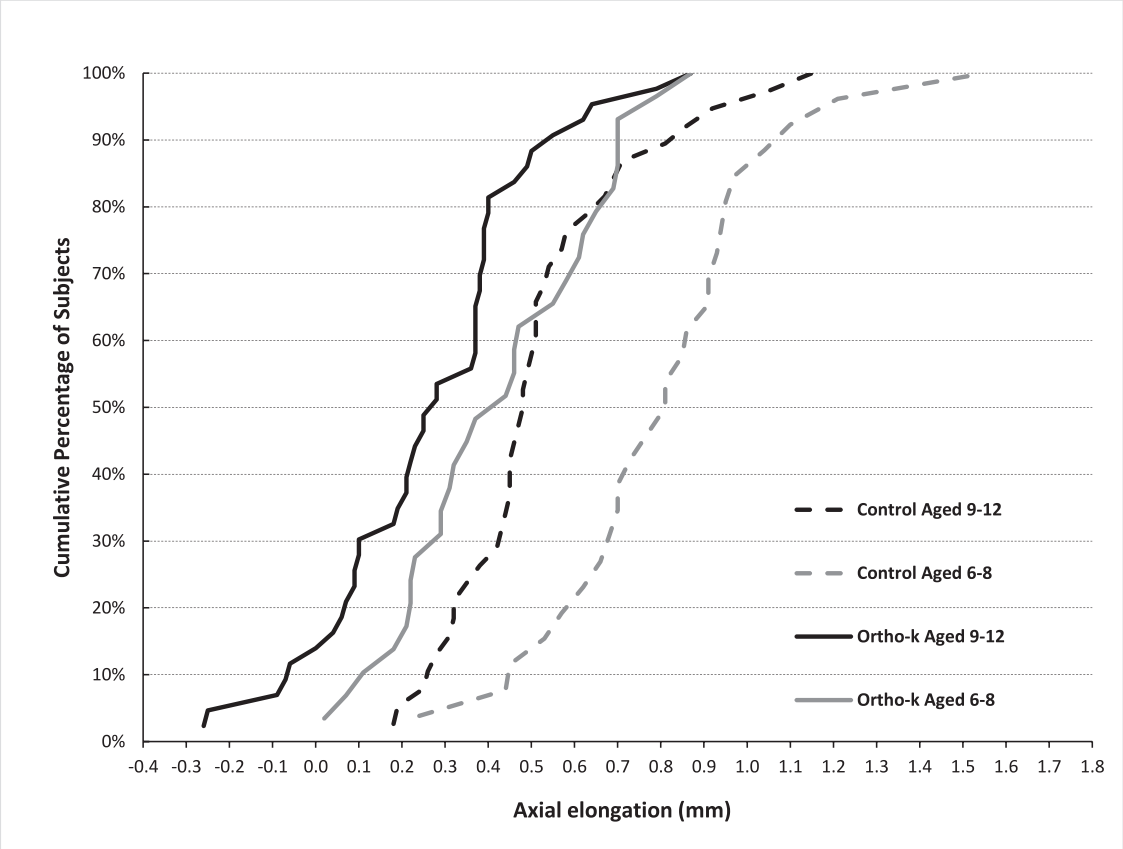

Figure 2. Cumulative percentage frequencies of subjects by age group and axial elongation at the end of 24 months.

Table 3. Relative Risk of Rapid Progression in Relation to the Use of Ortho-k and Initial Age

	Ortho-k	Control	RR (95% CI)	NNT (95% CI)	*P* Value
All					
Rapid	4	21	0.17 (0.06–0.47)	3.67 (2.53–6.65)	*<0.001*
Not rapid	68	43	–	–	–
Aged 6–8 y					
Rapid	2	16	0.11 (0.03–0.44)	1.83 (1.33–2.90)	*0.002*
Not rapid	27	10	–	–	–
Aged 9–12 y					
Rapid	2	5	0.35 (0.07–1.72)	11.76 (4.85–27.67)	0.197
Not rapid	41	33	–	–	–

Italics indicate statistically significant. RR, relative risk; NNT number needed to treat.

ortho-k subjects shifted toward the left for both subgroups compared to curves for control subjects). Older subjects tended to have smaller axial elongation compared to younger subjects. This is true for both ortho-k and control subjects: 50% of subjects in the ortho-k and control groups had axial elongations ranging from 0.27 to 0.86 mm and 0.48 to 1.15 mm, respectively; and interestingly, 14% of older ortho-k subjects displayed a shortening of axial length after 2 years of lens wear. Myopia control effect was more pronounced in the younger ortho-k subjects, with 50% of subjects showing axial elongations of 0.40 to 0.88 mm, compared to 0.81 to 1.55 mm in the younger control subjects. Orthokeratology also increased the percentage of subjects with slow progression (annual axial elongation <0.18 mm (i.e., equivalent myopic progression <0.25 D per year) especially in the younger age group. The percentage of slow progressors was 46% in the older control subjects compared to 56% in the older ortho-k subjects, and 5% in the younger control subjects compared to 25% in the younger ortho-k subjects.

The overall RR of rapid axial elongation was reduced by ortho-k treatment (RR: 0.17; 95% confidence interval [CI]: 0.06–0.47; $P < 0.001$). Considering all subjects, the 2-year NNT was 3.87 (95% CI: 2.5–6.7). In other words, ortho-k can prevent one out of four subjects (aged 6–12 years) from having rapid progression after 2 years of treatment. However, the effect reached statistical significance only for the younger subjects (Table 3). Only 2 of 29 younger subjects in the ortho-k group displayed rapid progression, as compared with 16 of 26 subjects in the control group (RR: 0.11; 95% confidence interval: 0.03–0.44; $P = 0.0018$). This suggested an 88.8% reduction in risk of rapid progression if younger subjects were treated with ortho-k for myopia control. For older subjects, although fewer subjects showed rapid progression compared to the control subgroup, the RR did not reach statistical significance (RR: 0.35; 95% CI: 0.07–1.72, $P = 0.1973$). The 2-year NNT for the younger ortho-k subgroup was 1.8 (95% CI: 1.3–2.9), implying that treating two younger subjects with ortho-k for myopia control would prevent one subject from having rapid progression over a 2-year period of treatment. Although the RR for the subgroup of older ortho-k subjects did not reach statistical significance, the direction of risk remains protective. For this sub-group, the NNT (11.8; 95% CI: 4.85–27.67) was considerably higher. This may be because older subjects tended to have smaller axial length changes compared to the younger subjects (rapid progressors: younger age group = 18/55; older age group = 7/81).

Discussion

Our results confirmed that ortho-k slows axial elongation. It significantly decreased the number of subjects with rapid progression and increased the number of subjects with slow progression over the 2-year treatment period.

Younger subjects showed more rapid axial elongation than older subjects, hence use of ortho-k displayed a more pronounced myopia control effect even though the percentage control was similar in both subgroups. The finding that axial elongation in younger myopic children is more rapid is not new, having been previously reported by several studies.[22–25] In their study, Hyman et al.[25] reported that the baseline age of the children was the "strongest factor independently associated with faster myopic progression." Strong evidence of control of axial elongation, especially in younger children, can justify targeting this age group. Starting ortho-k or other myopia control treatment at age 6 coincides with commencement of primary education, when it is common to implement vision screening[26–30] to ensure that vision problems are addressed early to prevent adverse effects. Children at this age are usually able to accept the required testing procedures. Current knowledge of effectiveness and benefits of ortho-k and other myopia control treatments does question the use of conventional correction with single-vision spectacles or single-vision contact lenses alone for managing early childhood myopia. Practitioners may be prudent to reconsider the routine prescription of such optical aids and take myopia control into consideration, and fully inform parents of the options and the potential benefits and advantages of early implementation.

Most of the previous studies for myopia control, including our work, mainly presented the percentage reduction in axial elongation without actually determining the risk and benefits of the particular treatment. In the current study, although the percentage of reduction in axial elongation was similar in younger and older subjects (around 43%–46%), the RR and NNT of rapid axial elongation with ortho-k were different in the two subgroups. Hence, reporting the overall percentage reduction of myopia or axial elongation alone may not represent adequate information on the effectiveness of any myopia control intervention.

The current study has reported reduced risk and low NNT of rapid axial elongation with ortho-k treatment. The treatment was more effective in reducing rapid axial elongation in younger children; in this subgroup, the risk was reduced by 88.8% with ortho-k treatment. For the older age group, the NNT of rapid progression did not reach statistical significance, but a lower percentage of subjects had rapid axial elongation in the ortho-k group compared to the controls (see Fig. 2). The 2-year NTT metric indicated a substantial benefit of ortho-k treatment for myopia control in younger children by reducing rapid progression in these subjects, as treating just two children for 2 years would prevent one subject from experiencing rapid axial elongation.

It is of interest to note that about 14% of the older ortho-k subjects showed a reduction, instead of an increase in axial length at the end of 2 years of lens wear. None of the younger subjects exhibited this reduction. The cause of this apparent shortening of axial length remains unclear. No other studies have reported prolonged shortening of axial length over the course of treatment, although a shortening of axial length has commonly been observed at the initiation of ortho-k lens wear, attributed at least in part to central corneal thinning[9,11,12,17,18] and choroidal thickening.[31–33] Central corneal thinning reflects the redistribution of corneal tissue and this change usually stabilizes within a few weeks, once the optimal refractive correction has been achieved.[34–35] Compared to reports on the effect of ortho-k on corneal thickness, few studies have investigated changes in choroidal thickness. However, choroidal thickening with ortho-k has been reported in two separate studies.[31,33] One was a short-term study,[33] lasting no more than 4 weeks, and the other was a longer term study,[31] investigating changes 1 to 9 months after lens wear. If the choroid is responding to the change in retinal defocus experienced initially with ortho-k, this adaptation would be expected to end when refractive status correction stabilized (i.e., no uncorrected myopia remains). This explanation is consistent with findings of one of the two above studies that changes in choroidal thickness did not persist beyond the initial stabilization period.[31] However, controlled clinical trials with a larger sample size and of longer duration are warranted to investigate the association between choroidal thickness changes and axial elongation in ortho-k.

As explained above, ROMIO and TO-SEE used the same methodology, with the exception that ROMIO was a randomized control trial whereas TO-SEE allowed self-selection of treatments. Analyses showed that there were no significant differences in the baseline values of pertinent parameters between subjects except for astigmatism, which was shown to have no interaction with axial elongation. The pooled data analyses confirmed previous findings and provided further insight into benefits of ortho-k for myopia control in children. A high prevalence of myopia has until recently been assumed to be a predominantly East Asian problem. Countries, such as China, Singapore, and Japan have voiced concerns about myopia progression in children for many years.[36–41] However, recent studies have revealed that myopia should be considered a worldwide problem.[42–43] Parents who are concerned about myopia progression in their children tend to be more proactive in searching for a treatment for its control and ortho-k is a popular option.[44] A common question asked is the optimal timing for ortho-k treatment for their children. The results of this study suggest that ortho-k treatment should be started in younger myopic children (6–8 years).

It is recognized that results from clinical research are performed under optimal conditions and care in the real-world community may not be as successful due to issues of compliance and practice.[45] Notably, our results are based on analysis of data from a cohort study (TO-SEE) and a randomized control trial (ROMIO) performed by the same group of researchers in Hong Kong, both reporting encouraging outcomes. However, further confirmation should be obtained from studies performed in other settings as cultural factors can affect success of interventions.

In conclusion, ortho-k treatment significantly reduces risk of rapid progression in younger (6–8 years) subjects and is predicted to protect one in two of these subjects from rapid axial elongation. Thus, its use should be seriously considered for young children exhibiting rapid myopia progression.

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References

1. Holden B, Sankaridurg P, Smith E, Aller T, Jong M, He M. Myopia, an underrated global challenge to vision: where the current data takes us on myopia control. *Eye (Lond)*. 2014;28:142–146.
2. Morgan IG, Ohno-Matsui K, Saw SM. Myopia. *Lancet*. 2012;379:1739–1748.
3. Wong TY, Ferreira A, Hughes R, Carter G, Mitchell P. Epidemiology and disease burden of pathologic myopia and myopic choroidal neovascularization: an evidence-based systematic review. *Am J Ophthalmol*. 2014;157:9–25.e12.
4. Grosvenor T, Perrigin D, Perrigin J, Quintero S. Rigid gas-permeable contact lenses for myopia control: effects of discontinuation of lens wear. *Optom Vis Sci*. 1991;68:385–389.
5. Chung KM, Mohidin N, Yeow PT, Tan LL, O'Leary D. Prevalence of visual disorders in Chinese schoolchildren. *Optom Vis Sci*. 1996;73:695–700.
6. Walline JJ, Mutti DO, Jones LA, et al. The contact lens and myopia progression (CLAMP) study: design and baseline data. *Optom Vis Sci*. 2001;78:223–233.
7. Edwards MH, Li RW, Lam CS, Lew JK, Yu BS. The Hong Kong progressive lens myopia control study: study design and main findings. *Invest Ophthalmol Vis Sci*. 2002;43:2852–2858.
8. Gwiazda J, Hyman L, Hussein M, et al. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. *Invest Ophthalmol Vis Sci*. 2003;44:1492–1500.
9. Cho P, Cheung SW, Edwards M. The longitudinal orthokeratology research in children (LORIC) in Hong Kong. A pilot study on refractive changes and myopic control. *Curr Eye Res*. 2005;30:71–80.
10. Tong L, Huang XL, Koh AL, Zhang X, Tan DT, Chua WH. Atropine for the treatment of childhood myopia: effect on myopia progression after cessation of atropine. *Ophthalmology*. 2009;116:572–579.
11. Cho P, Cheung SW. Retardation of myopia in orthokeratology (ROMIO) study: a randomized controlled trial. *Invest Opthalmol Vis Sci*. 2012;53:7077–7085.
12. Swarbrick HA, Alharbi A, Watt K, Lum E, Kang P. Myopia control during orthokeratology lens wear in children using a novel study design. *Ophthalmology*. 2015;122:620–630.
13. Walline JJ, Jones LA, Sinnott LT. Corneal reshaping and myopia progression. *Br J Ophthalmol*. 2009;93:1181–1185.
14. Kakita T, Hiraoka T, Oshika T. Influence of overnight orthokeratology on axial elongation in childhood myopia. *Invest Ophthalmol Vis Sci*. 2011;52:2170–2174.
15. Hiraoka T, Kakita T, Okamoto F, Takahashi H, Oshika T. Long-term effect of overnight orthokeratology on axial length elongation in childhood myopia: a 5-year follow-up study. *Invest Ophthalmol Vis Sci*. 2012;53:3913–3919.
16. Santodomingo-Rubido J, Villa-Collar C, Gilmartin B, Gutierrez-Ortega R. Myopia control with orthokeratology contact lenses

in Spain: refractive and biometric changes. *Invest Ophthalmol Vis Sci*. 2012;53:5060–5065.

17. Chen C, Cheung SW, Cho P. Myopic control using toric orthokeratology (TO-SEE study). *Invest Opthalmol Vis Sci*. 2013;54:6510–6517.
18. Charm J, Cho P. High myopia – partial reduction orthokeratology (HM-PRO) study: A 2-year randomised clinical trial. *Optom Vis Sci*. 2013;90:530–539.
19. Si JK, Tang K, Bi HS, Guo DD, Guo JG, Wang XR. Orthokeratology for myopia control: a meta-analysis. *Optom Vis Sci*. 2015;92:252–257.
20. Sun Y, Xu F, Zhang T, et al. Orthokeratology to control myopia progression: a meta-analysis. *PLoS One*. 2015;10:e0124535.
21. Cook RJ, Sackett DL. The number needed to treat: a clinically useful measure of treatment effect. *BMJ*. 1995;310:452–454.
22. Braun CI, Freidlin V, Sperduto RD, Milton RC, Strahlman ER. The progression of myopia in school age children: data from the Columbia Medical Plan. *Ophthalmic Epidemiol*. 1996;3:13–21.
23. Saw SM, Nieto FJ, Katz J, Schein OD, Levy B, Chew SJ. Factors related to the progression of myopia in Singaporean children. *Optom Vis Sci*. 2000;77:549–554.
24. Saw SM, Chua WH, Gazzard G, Koh D, Tan DT, Stone RA. Eye growth changes in myopic children in Singapore. *Br J Ophthalmol*. 2005;89:1489–1494.
25. Hyman L, Gwiazda J, Hussein M, et al. Relationship of age, sex, and ethnicity with myopia progression and axial elongation in the correction of myopia evaluation trial. *Arch Ophthalmol*. 2005;123:977–9787.
26. Council on School Health. School-based health centers and pediatric practice. *Pediatrics*. 2012;129:387–393.
27. Labour and Welfare Bureau. Hong Kong: The Facts. Available at: http://www.lwb.gov.hk/eng/factsheet/HKFS_rehabilitation.htm. Accessed August 15, 2016.
28. Ministry of Health Singapore. Health Screening for Primary School. Available at: http://www.hpb.gov.sg/HOPPortal/health-article/632. Accessed August 15, 2016.
29. Suram V, Addepalli UK, Krishnaiah S, Kovai V, Khanna RC. Accuracy of vision technicians in screening ocular pathology at rural vision centres of southern India. *Clin Exp Optom*. 2016;99:183–187.
30. Toufeeq A, Oram AJ. School-entry vision screening in the United Kingdom: practical aspects and outcomes. *Ophthalmic Epidemiol*. 2014;21:210–216.
31. Gardner DJ, Walline JJ, Mutti DO. Choroidal thickness and peripheral myopic defocus during orthokeratology. *Optom Vis Sci*. 2015;92:579–588.
32. Swarbrick HA, Alharbi A, Watt K, Lum E, Kang P. Myopia control during orthokeratology lens wear in children using a novel study design. *Ophthalmology*. 2015;122:620–630.
33. Chen Z, Xue F, Zhou J, Qu X, Zhou X. Effects of orthokeratology on choroidal thickness and axial length. *Optom Vis Sci*. 2016;93:1064–1071.
34. Alharbi A, Swarbrick HA. The effects of overnight orthokeratology lens wear on corneal thickness. *Invest Ophthalmol Vis Sci*. 2003;44:2518–2523.
35. Nieto-Bona A, González-Mesa A, Nieto-Bona MP, Villa-Collar C, Lorente-Velazquez A. Short-term effects of overnight orthokeratology on corneal cell morphology and corneal thickness. *Cornea*. 2011;30:646–654.
36. Watanabe S, Yamashita T, Ohba N. A longitudinal study of cycloplegic refraction in a cohort of 350 Japanese schoolchildren. *Ophthalmic Physiol Opt*. 1999;19:22–29.
37. Fan DS, Lam DS, Lam RF, et al. Prevalence, incidence, and progression of myopia of school children in Hong Kong. *Invest Ophthalmol Vis Sci*. 2004;45:1071–1075.
38. Lin LL, Shih YF, Hsiao CK, Chen CJ. Prevalence of myopia in Taiwanese schoolchildren: 1983 to 2000. *Ann Acad Med Singapore*. 2004;33:27–33.
39. Cheng D, Schmid KL, Woo GC. Myopia prevalence in Chinese-Canadian children in an optometric practice. *Optom Vis Sci*. 2007;84:21–32.
40. Lam CS, Lam CH, Cheng SC, Chan LY. Prevalence of myopia among Hong Kong Chinese school children: changes over two decades. *Ophthalmic Physiol Opt*. 2012;32:17–24.
41. You QS, Wu LJ, Duan JL, et al. Prevalence of myopia in school children in greater Beijing: the Beijing Childhood Eye Study. *Acta Ophthalmol*. 2014;92:e398–e406.
42. Williams KM, Bertelsen G, Cumberland P, et al; European Eye Epidemiology (E(3)) Consortium. Increasing prevalence of myopia in europe and the impact of education. *Ophthalmology*. 2015;122:1489–1497.
43. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology*. 2016;123:1036–1042.
44. Cheung P, Lam C, Cho P. Parents' knowledge and perspective of optical methods for myopia control in children. *Optom Vis Sci*. 2014;91:634–641.
45. Haynes B. Can it work? Does it work? Is it worth it? *Br Med J*. 1999;319:652–653.

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