Full title: Long-term efficacy of orthokeratology contact lens wear in controlling the progression of childhood myopia

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ABSTRACT

PURPOSE: The primary outcome of this study is to compare axial length growth of white European myopic children wearing orthokeratology contact lenses (OK) to a control group (CT) over a 7-year period.

METHODS: Subjects 6-12 years of age with myopia -0.75 to -4.00DS and astigmatism ≤1.00DC were prospectively allocated OK or distance single-vision spectacles (SV) correction. Measurements of axial length (Zeiss IOLMaster), corneal topography and cycloplegic refraction were taken at 6-month intervals over a 2-year period. Subjects were invited to return to the clinic approximately 5 years later (i.e. 7 years after the beginning of the study) for assessment of their ocular refractive and biometric components. The CT consisted of 4 SV and 12 subjects who switched from SV to soft contact lens wear after the initial 2-years of SV lens wear. Changes in axial length relative to baseline over a 7-year period were compared between groups.

RESULTS: Fourteen and 16 subjects from the OK and CT groups, respectively were examined 6.7±0.5 years after the beginning of the study. Statistically significant changes in axial length were found over time and between groups (both p<0.001), but not for the time*group interaction (p=0.125). The change in axial length for the OK group was 22% (p=0.328), 42% (p=0.007), 40% (p=0.020), 41% (p=0.013) and 33% (p=0.062) lower than the CT group following 6, 12, 18, 24 and 84 months of lens wear, respectively.

CONCLUSION: A trend towards a reduction in the rate of axial elongation of the order of 33% was found in the OK group in comparison to the CT group following 7-years of lens wear.

Key words: myopia control, orthokeratology, axial length, myopia progression, long-term efficacy
INTRODUCTION
Globally, uncorrected refractive errors represent the second major cause of vision loss\(^1\) of which myopia is the most common and distinctive in that its prevalence has increased substantially in recent decades. To date, it has been estimated that myopia currently affects approximately 30% of the world’s population,\(^2,\)\(^3\) although a significant increase to affect around 50% of the world’s population by 2050 has been forecast.\(^2\) The prevalence of myopia in young adolescents is also increasing and has approached around 25% and up to 98% in industrialized societies of the West and East Asia, respectively.\(^3\) Of particular concern is that relatively low degrees of myopia may be associated with increased risk of ocular complications, such as vitreous and chorioretinal detachment, macular degeneration, and glaucoma all of which can increase the risk of vision loss.\(^4–7\) Furthermore, myopia incurs substantial expenditure such that in the USA, the annual cost for eye examinations and corrections by spectacles and contact lenses has been estimated to be between $2 and $5 billion.\(^8,\)\(^9\) Therefore, finding effective therapies to slow the progression of myopia could potentially benefit millions of individuals and save on substantial healthcare expenditure worldwide.

Several optical treatment options have been used in the past with limited success to eliminate or, at least, reduce myopia progression in children.\(^10–12\) Of these, orthokeratology (OK) contact lens wear appears to be one of the most effective as it has consistently been shown to reduce the axial elongation of the eye by 30 to 50% in comparison with conventional single-vision spectacle (SV) and soft contact lens (SCL).\(^13–18\) Most previous studies have demonstrated reduced rates in axial elongation over 2 years of OK lens wear. A recent meta-analysis study reported that the pooled reduction in axial elongation declined with time, with 55, 51, 51, and 41% obtained after 6, 12, 18, and 24 months of OK lens wear, respectively.\(^19\) However, little is known about the efficacy of OK lens wear in reducing the rate of axial elongation for longer periods of lens wear. Two retrospective studies have shed some light on the latter.\(^20,\)\(^21\) Kwok-Hei Mok and Sin-Ting Chung compared changes in myopia over a 7-year period between 34 children with a mean age at baseline of 9 years wearing OK and 36 children with a mean age at baseline of 10 years wearing SV.\(^20\) Determination
of the final refractive error of the OK lens wearing subjects was conducted by
the washout period method, whereby subjects were refracted after not wearing
the lenses for a period of time until the flatter corneal meridian reverted to its
pre-OK levels.\textsuperscript{20} It took a mean (± standard deviation) of 25.5±1.0 (range 22–
29) days for the central flat corneal curvature to return to pre-OK levels.
Average myopic progression for the OK group (−0.37±0.49D) was significantly
lower than that found for the SV group (−2.06±0.81D) following 7-years of lens
wear.\textsuperscript{20} Downie and Lowe compared the progression rate of manifest refractive
prescription in myopic children under the age of 16 years between 26 OK lens
wearers and 30 age- and refraction-matched SV wearers in 2 yearly intervals
over a period up to 8 years.\textsuperscript{21} The study found that OK wearers showed a
significantly more stable myopic refractive prescription than SV over all of the 2-
year treatment intervals, indicating that OK can reduce the rate of progression
of childhood myopia over the long term.\textsuperscript{21} Furthermore, a subpopulation of OK
lens wearers (64\%) demonstrated an apparent total arrest of manifest myopic
refractive change.\textsuperscript{21} Although the above two studies have provided preliminary
evidence for the long-term efficacy of OK contact lens wear in reducing the
progression of myopia their limitations are retrospective study designs, non-
randomization of subjects to study groups and the use of non-cycloplegic
refractions as primary outcome measures. Furthermore, neither of the studies
measured axial length, the key structural correlate of myopic progression in OK-
treated eyes.\textsuperscript{22} Hiraoka et al. compared changes in axial length between 22 OK
and 21 SV Japanese lens wearers with a mean age at baseline of 10 years
over a period of 5 years.\textsuperscript{23} The study found statistically significant reductions in
the annual increases in axial length in the OK group compared with the SV
group for the first, second, and third years, but not for the fourth and fifth
years.\textsuperscript{23}

We have previously reported the results of the Myopia Control with
Orthokeratology contact lens in Spain (MCOS) study which evaluated
differences in growth of axial length over a 2-year period in white European
children with myopia wearing OK and SV.\textsuperscript{17} We found a statistically significant
difference in axial length elongation relative to baseline between the OK
(0.47±0.18mm) and SV (0.69±0.32mm) groups (p=0.005).\textsuperscript{17} Approximately 5
years after completion of the MCOS study, subjects were contacted by telephone and invited to return to the clinic for evaluation of their ocular refractive and biometric parameters. The purpose of this study is to compare, as the primary outcome measure, differences in growth of axial length over a 7-year period between white European myopic children wearing OK and a control group (CT) wearing SV or SCL. Additionally, refractive and biometric changes in subjects who switched corrections were also evaluated.
METHODS

This study was part of a larger study designed to assess different aspects of OK lens wear specifically prescribed for the control of myopia progression in children.\textsuperscript{17, 24-27} The methods employed in MCOS have been described in detail elsewhere.\textsuperscript{17, 24} In brief, normal, healthy white European subjects 6 to 12 years of age with moderate levels of mean spherical myopia (-0.75 to -4.00D) and astigmatism (≤1.00D) and free of systemic or ocular disease were fitted with Menicon Z Night contact lenses for overnight use (Menicon Co., Ltd, Nagoya, Japan). An OK fit was considered to be successful if the subject showed a CCLRU score regarding anterior eye segment signs ≤ 1 unit, a “bull’s eye” corneal topography pattern and monocular and binocular visual acuities within ±1 line of the best-correct spectacle visual acuity. All subjects underwent ocular examinations including slit-lamp examination, manifest refraction, and corneal topography at baseline and at 6-month intervals over a 2-year period. Follow-up visits were scheduled to fall within 2 hours of awakening in order to measure subjective refraction and visual acuity without the lens on the eye. A decrease in one line of visual acuity accompanied by a change in subjective refraction at any of the follow-up visits was considered clinically significant and was remedied by supplying new contact lenses. Approximately 5 years after completion of the MCOS study, subjects were contacted by telephone and invited to return to the clinic for evaluation of their ocular refractive and biometric parameters. The study was conducted in accordance with the Tenets of the Declaration of Helsinki and approved by the Institutional Ethical Committee Review Board of Novovision Ophthalmology Clinic (Madrid, Spain). Full informed consent and child assent was obtained in writing from the parents/guardians prior to the start of all experimental work and data collection. Patient participation in the study could be discontinued at the examiner’s discretion should significant symptoms or slit-lamp findings occur. Subjects were instructed they could withdraw from the study at any time.

Cycloplegic auto-refraction was performed following the instillation of three drops of cyclopentolate HCl 1% separated 10 min apart in each of the subjects’ eyes using a multidose bottle (Alcon Cusí, Masnou, Barcelona, Spain). Ten minutes after the instillation of the third drop, three auto-refraction
measurements were taken and a mean obtained (Topcon RM 8000B, CA, USA).

Measurements of axial length were taken with the Zeiss IOLMaster (Carl Zeiss Jena GmbH). Three separate measurements of axial length were recorded and a mean obtained.

Corneal topography measurements were performed with the Wavelight Allegro Topolyzer (WaveLight Laser Technologies AG, Erlangen, Germany). The instrument incorporates a high resolution placido-ring corneal topographer which detects 22,000 elevated data points of measurement from 22 ring edges with a claimed accuracy and reproducibility of ± 0.10D according to the manufacturer. The first measurement taken for each eye, which provided an optimum index value according to the manufacturer’s recommendations, was used for the study. The measurement generates a simulated central keratometry reading and the rate of peripheral corneal flattening/steepeening that occurs with displacement from the corneal apex; the latter indicates the degree to which an aspheric surface differs from the spherical form (i.e., the p value). The p value was calculated over a 7-mm chord in accord with the default setting of the instrument.

Statistical analysis
Differences in subjects’ demographics and baseline data between groups were tested using unpaired sample t-tests for all variables, except for the male:female ratio which was tested using a chi-square test. Changes (from baseline) in refractive and biometric data over time and between groups (i.e. OK vs. CT) were tested using a general linear model (GLM) with repeated measures to test the statistical significance of differences in outcome variables (i.e. axial length, spherical and cylindrical refractive components, corneal power and corneal shape) for the between-subject factor of refractive correction (two levels: OK and CT) and for the within-subject factor of time (five levels: 6, 12, 18, 24 and 84 months). The significance of the interaction between OK and CT with respect to time was then tested for all time intervals combined and then separately for each of the five time intervals following post hoc Bonferroni correction. GLM
with repeated measures was also used to test the effect of switching treatments from OK to SCL. Additionally, an unpaired sample t-test was used to test, for each time point, differences between the groups in refractive and biometric variables. Equality of variances and sphericity were tested using the Levene and Mauchly tests respectively to select appropriate p-values. Additionally, simple linear regressions between the change in axial length at 7-years relative to baseline and baseline age, mean spherical equivalent refractive error, axial length, mean central corneal power and corneal shape factor were calculated for the OK and CT groups separately. Differences between groups in the slopes of the regression lines were compared using an analysis of covariance. The strength of association between the different factors is summarized using linear regression equations, $R^2$ squared values and p-values. Data are expressed as mean ± 1 standard error of the mean (SEM). Data from right eyes only were used for analysis. Statistical analyses were performed with IBM SPSS Statistics (IBM Corp., Ver. 22, NY, USA) and graphing with SigmaPlot (Systat software Inc, California, USA). The level of statistical significance was set at 5%.
RESULTS

At the inception of MCOS sixty-nine subjects were examined for eligibility: 8 subjects were not eligible to participate and 31 and 30 children were prospectively allocated to OK and SV, respectively (Figure 1). Twenty-nine and 24 subjects from the OK and SV groups, respectively, thus completed the initial 2 years of the MCOS study. Seven subjects were subsequently lost to follow-up in each group and no further information was able to be collected from these subjects leading to a total of 39 subjects of the original cohort available for review at the 7-year visit. Of these, 14 and 4 remained in their original OK and SV lens wear categories, respectively. In addition, twelve of the 39 subjects switched to standard SCL wear after 2 years of SV lens wear which thus constituted a control group (CT) of 16 subjects (i.e. 4 SV + 12 SCL). Nine subjects switched lens wear category and the effect of which was assessed separately (see subheading below) (Figure 1).

Long-terms effects in the OK and CT groups

The OK and CT groups were followed for 6.9±0.1 and 6.5±0.1 years, respectively; this difference was statistically significant (p=0.001). Subjects reported inserting and removing their OK lenses every night and morning, respectively. None of the subjects from the OK group reported cessation of lens wear for any significant periods of time over the entire 7-year period of OK lens wear. Furthermore, all subjects reported ≥ 0.9 uncorrected decimal visual acuities (equivalent to 0.05 logMAR or >20/25) at the 7-year visit. The incidence, type and timeline of adverse events found over the initial 24 months of the study have been previously reported. At the 84-month visit, all subjects underwent a thorough ophthalmic examination and no remarkable adverse events were found. Furthermore, none of the subjects reported any significant complications in the last 5 years of lens wear. The 12 subjects who switched to standard SCL wear after 2 years of SV lens wear and who became part of the CT group worn SCL for 2.5±0.4 years prior to the 7-years visit. No statistically significant differences between the OK and CT groups were found in any of the baseline demographics and refractive and biometric data (Table 1).
Statistically significant changes were found in axial length both over time and between groups (p<0.001), but not for the time*group interaction (p=0.125) (Figure 2 and Table 2). Changes over time were statistically significant for all pairs of time points (all p≤0.001) (Figure 2 and Table 2). In comparison to the CT group, the change in axial length for the OK group was 22% (p=0.328), 42% (p=0.007), 40% (p=0.020), 41% (p=0.013) and 33% (p=0.062) lower following 6, 12, 18, 24 and 84 months of lens wear, respectively (Figure 2 and Table 2).

Statistically significant differences were also found in the spherical component of the refraction over time, between groups and for the time*group interaction (all p<0.001) (Table 2). Statistically significant differences between time points were found between 6- and 12-, 18-, 24- and 84-months (all p<0.01); between 12- and 84-months (p=0.002); between 18- and 24- and 84-months (both p<0.001); and between 24- and 84-months (p<0.001) (Table 2). Statistically significant differences were found between groups at all the different time points (p<0.001) (Table 2). However, no statistically significant differences were found in the cylindrical component of the refraction over time, between groups or for the time*group interaction (p>0.05) (Table 2).

Statistically significant differences were found in corneal power over time (both p<0.001) and between groups (both p<0.001), but not for the time*group interaction (both p>0.05) for both the flatter and steeper meridians (Table 2). Significant differences were found for pairs of time points between 6-, 12-, 18-, 24- and 84-months for both meridians (all p<0.02) (Table 2). Significant differences were also found between groups in corneal power at all time points for both meridians (all p<0.001) (Table 2). However, no significant differences were found in the corneal shape (i.e. corneal p-value) over time, between groups or for the time*group interaction (all p>0.05) (Table 2).

Univariate linear regression analysis revealed that the older the age at baseline the smaller the axial elongation at 7-years in both study groups, although the relationship was statistically significant for the CT (R²=0.274, p=0.022), but not for the OK group (R²=0.142, p=0.101). The effect of baseline age on axial elongation was, however, similar between groups (p=0.208) (Figure 3 and
Greater corneal powers at baseline were associated with smaller increases in axial length in the OK group ($R^2=0.290$, $p=0.027$), but no significant relationship was found for the CT group ($R^2=0.000$, $p=0.817$) (Figure 4 and Table 3). Furthermore, statistically significant differences were found between groups in the slopes of the regression lines ($p=0.044$) (Figure 4 and Table 3). No significant relationships were found between the change in axial length at 7-years in comparison to baseline and baseline mean spherical equivalent refractive error, axial length and corneal shape for either the OK or CT groups (Table 3). In addition, no statistically significant differences were found between groups in the slopes of the regression lines for either spherical equivalent refractive error, axial length or corneal shape (all $p>0.05$) (Table 3).

The effect of switching treatments

Following 2 years of OK lens wear, eight subjects (4 male and 4 female) switched from OK to SCL $1.7\pm0.5$ years (range 0.2 to 3.9 years) thereafter and wore SCL for the last $3.3\pm0.5$ years (range 1.3 to 5.3 years). A trend was found for increased time of SCL wear to be associated with shorter increases in axial length (Figure 5). The reasons for switching from OK to SCL were (number of subjects): expensive treatment (4), recurrent punctate keratitis (2) and concerns regarding regression (1) and efficacy (1). These subjects had mean ages of $9.3\pm0.4$, $11.4\pm0.4$ and $16.4\pm0.5$ at baseline, following 2 years of OK lens wear and at the 7-years study visit, respectively. On average, axial length increased by $0.57\pm0.06$mm during the initial 2 years of OK lens wear and by $0.80\pm0.16$mm on the subsequent 5 years (Table 4), although there was large between-subject variability (Figure 6). As expected, the increase in axial length following cessation of OK lens wear was associated with an increase in myopia, a steepening of corneal curvature and a more prolate corneal shape (Table 3). In comparison to the CT group (Table 2), these subjects experienced mean reductions in the rate of axial elongation of 47%, 30%, 22% and 19% following 6, 12, 18 and 24 months of OK lens wear, respectively (Tables 2 and 4). However, when these subjects switched from OK to SCL the rate of axial elongation observed at 84 months in comparison to the CT group was -1%, indicating the effect of OK lens wear in reducing the rate of axial elongation is negligible with discontinuation of lens wear (Tables 2 and 4). One male subject
switched from SV to OK lens wear immediately after the initial 2 years of SV lens wear and wore OK lenses for the following 5 years. The reason for changing to OK was to reduce the rate of myopia progression. In this subject, axial length increased by 0.81mm during the initial 2 years of SV lens wear, but only by 0.35mm in the following 5 years of OK lens wear (Table 4).
DISCUSSION

This study assessed the long-term efficacy of OK lens wear in reducing the rate of axial elongation over a period of as long as 7 years in White European subjects. The significant reduction in manifest myopia and the rate of myopia progression found in the OK group after initial lens wear remained throughout the 7-year period and is primarily attributed to the corneal reshaping effect induced by OK contact lens wear and the resultant change in corneal power and shape (Table 2). The CT group, however, showed an average increase in myopia of 2.84D accompanied by negligible changes in corneal power and shape (Table 2).

Of interest is the finding of a trend towards a reduction in the rate of axial elongation of the order of 33% in the OK group in comparison to the CT group following 7-years of lens wear (Figure 2 and Table 2). Interestingly, a study estimated that reducing the rate of myopia progression by 33% would lead to a reduction of 73% in the frequency of high myopia (<-5.00D); such reduction could therefore have important implications in terms of reducing ocular-related morbidity and healthcare costs.

Despite differences in corneal topography and contact lens-induced responses between Caucasian and Japanese ethnicities have been previously reported, our results are similar to those reported by Hiraoka et al. We found OK to reduce the rate of axial elongation by 33% after 7 years of lens wear, whereas Hiraoka et al. found OK to reduce the rate of axial elongation by 31% after 5 years of lens wear. The study of Hiraoka et al. was performed in Japanese subjects using one particular OK contact lens design (i.e. αOrtho-K; Alpha Corp., Nagoya, Japan), whereas the present study was undertaken in White European subjects using a different OK lens design (i.e. Menicon Z Night, Menicon Co., Ltd, Nagoya, Japan). Interestingly, our results also agree with those of Hiraoka et al. in that the benefit of OK in reducing the axial elongation of eye diminishes with longer periods of lens wear.

The reduced efficacy of myopia control with long periods of lens wear found in this study may be attributed to the natural history of myopia progression,
which there is a reduced rate of axial elongation with increased age, thereby making it more difficult to find significant differences between groups in axial length over longer periods of lens wear (Figures 2 and 3, and Table 2). In fact, the increases in axial length over the first 24 months of this study were remarkably similar to those found between 24 and 84 months for both the OK (0.42±0.05 and 0.39±0.04 mm, respectively) and the CT (0.71±0.10 and 0.65±0.11 mm, respectively) groups, clearly indicating a decrease in the rate of axial elongation regardless of the visual correction being worn (Figure 3 and Table 2). It is well established that older age is associated with smaller increases in myopia and axial elongation. Furthermore, it has been previously reported that myopia stabilizes at around 16 years of age. Subjects in this study had mean ages of 10 and 12 years at baseline and following 2 years of OK lens wear, respectively. Therefore, a reduced rate of myopia progression would be expected on these subjects during the subsequent 5 years of data collection.

Greater corneal power was found to be associated with smaller axial elongation in OK wearers (Figure 4). Following OK lens wear, a steeper cornea is likely to provide a smaller treatment zone of central corneal flattening and a wider peripheral ring of increased corneal power. Therefore, it is feasible that a steeper cornea facilitates corneal reshaping and reduction in axial elongation following OK lens wear. The large variability in the increases in axial length found in the 8 subjects who discontinued OK lens wear at 2-years and switched to SCL wear could be attributed to the length of time that SCLs were worn after ceasing OK lens wear (Figure 5), individual differences and differences in the power profile between the different SCLs worn (Figure 6). In any event, the results found on the effect of switching treatments appear to be consistent with those found in the OK and CT groups over the 7-year period in that the efficacy of OK diminishes and resumes with discontinuation and restoration of OK lens wear, respectively.

A limitation of this study is the potential bias introduced by subjects’ self-selection to continue wearing OK, SV or SCL. However, the major limitation
concerns the relatively small sample size employed in this study. The overall power to detect between-subjects differences (i.e. OK vs. CT) in the general linear model employed in our study was $P=0.68$ (IBM SPSS Statistics). However, the power varied at each of the different time points, being lowest at the 6- ($P=0.16$) and 84-month visits ($P=0.47$) and highest at the 12- ($P=0.81$), 18- ($P=0.76$) and 24-month visits ($P=0.73$), indicating that the relatively low statistical power found at the 84-month visit is not only related to the sample size employed but also to the large variability in changes in axial length in both the OK ($0.91 \pm 0.63$ mm) and CT ($1.36 \pm 0.63$ mm) groups. Taking the standard deviation of the change in axial length ($0.63$) and the difference in axial length found between groups at the 84-month visit ($0.45$ mm), a sample size of 32 subjects per group would be needed for a designated statistical power of 0.80 at alpha = 0.05. Despite the above-mentioned limitations, our study offers notable features such as being the first study to assess the efficacy of OK lens wear in White European subjects in reducing the rate of axial elongation over a period of as long as 7 years. In addition, the study measures changes in axial elongation over the entire follow-up period with the IOLMaster, a partial coherence interferometer well known to provide excellent resolution and repeatability.28 Nonetheless, randomized, controlled, clinical trials are warranted to confirm the findings of this study.

In summary, a trend towards a reduction in the rate of axial elongation of the order of 33% was found with long-term OK lens wear in comparison to SV and SCL wearers over a period of 7 years. The reduction observed over time in the efficacy of OK lens wear in slowing the axial elongation of the eye might be partly attributed to axial length (and myopia) stabilization as children approach the teenage years.32 Reducing myopia progression has important implications in terms of reducing ocular-related morbidity and healthcare costs.8, 9
DECLARATION OF INTEREST

The study has been supported in part by Menicon Co., Ltd by providing spectacles or contact lenses and contact lens solutions and by Novovision Ophthalmology Clinic by providing ocular examinations and contact lens fittings and aftercares free of charge to all subjects throughout the study. Jacinto Santodomingo-Rubido and Keiji Sugimoto are full-time employees of Menicon Co., Ltd. The authors alone are responsible for the content and writing of the paper.
REFERENCES


FIGURE LEGENDS

Figure 1. Flow-chart of the subjects recruited for the study. SV, distance singe-
vision spectacles, SCL, soft contact lenses.

Figure 2. Changes (mean ± SD) in axial length (mm) from baseline over time
for the OK (black, solid circles) and CT (white, open circles) groups. Error bars
represent one standard error of the mean. Asterisks indicate statistically
significant differences in the change in axial length between groups at 12-, 18-
and 24-months time intervals (all p≤0.02). OK, orthokeratology; CT, control

Figure 3. Simple linear regressions between the change in axial length at 7
years relative to baseline and age at baseline for the orthokeratology (black,
solid circles and solid line) and control groups (white, open circles and dashed
line).

Figure 4. Simple linear regressions between the change in axial length at 7
years relative to baseline and mean central corneal power at baseline for the
orthokeratology (black, solid circles and solid line) and control groups (white,
on open circles and dashed line).

Figure 5. Simple linear regressions between the change in axial length at 84-
compared with 24-months and the duration of soft contact lens wear.

Figure 6. Changes in axial length (mm) from baseline over time for eight
subjects who switched from OK to SCL after an initial phase of 2 years of OK
lens wear. OK, orthokeratology; SCL, soft contact lens.
TABLE LEGENDS

Table 1. Baseline demographics, refractive and biometric data for both treatment groups. Variables are expressed as mean ± 1SEM. OK, orthokeratology; CT, control.

Table 2. Mean (± SEM) refractive and biometric values for the OK and CT groups who completed the 7-years study at each time interval. OK, orthokeratology; CT, control.

Table 3. Simple linear regressions between the change in axial length at 7-years relative to baseline and the different baseline variables for both the OK and CT groups. The strength of association between the different factors is summarized using linear regression equations, R² values and p-values. OK, orthokeratology; CT, control; MSE, mean spherical equivalent.

Table 4. Mean (± SEM) refractive and biometric values for the 8 subjects who switched from OK to SCL as well as for one single subject who switched from SV to OK at each time interval. OK, orthokeratology; SCL, soft contact lens; SV, single-vision spectacles.
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<th>Orthokeratology</th>
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<th>p-value</th>
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<td>Male/female ratio</td>
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<td>Sphere (D)</td>
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<td>Cylinder (mm)</td>
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<td>Flatter meridian (D)</td>
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<td>Corneal shape factor (p-value)</td>
<td>0.70 ± 0.03</td>
<td>0.70 ± 0.02</td>
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Table 1. Baseline demographics, refractive and biometric data for both treatment groups. Variables are expressed as mean ± SEM.
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<tr>
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<td>-5.00 ± 0.43</td>
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<tr>
<td>Cylinder (D)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Orthokeratology</td>
<td>-0.25 ± 0.09</td>
<td>-0.38 ± 0.09</td>
<td>-0.27 ± 0.10</td>
<td>-0.30 ± 0.10</td>
<td>-0.29 ± 0.13</td>
<td>-0.30 ± 0.10</td>
</tr>
<tr>
<td>Control</td>
<td>-0.30 ± 0.09</td>
<td>-0.25 ± 0.08</td>
<td>-0.30 ± 0.08</td>
<td>-0.30 ± 0.11</td>
<td>-0.37 ± 0.10</td>
<td>-0.59 ± 0.10</td>
</tr>
<tr>
<td><strong>Biometric components</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Axial length (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthokeratology</td>
<td>24.39 ± 0.23</td>
<td>24.52 ± 0.23</td>
<td>24.41 ± 0.23</td>
<td>24.71 ± 0.24</td>
<td>24.81 ± 0.25</td>
<td>25.30 ± 0.31</td>
</tr>
<tr>
<td>Control</td>
<td>24.08 ± 0.27</td>
<td>24.25 ± 0.27</td>
<td>24.46 ± 0.27</td>
<td>24.61 ± 0.26</td>
<td>24.78 ± 0.26</td>
<td>25.43 ± 0.27</td>
</tr>
<tr>
<td>Flatter corneal meridian power (D)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthokeratology</td>
<td>43.18 ± 0.45</td>
<td>41.32 ± 0.46</td>
<td>41.36 ± 0.48</td>
<td>41.10 ± 0.44</td>
<td>41.36 ± 0.49</td>
<td>40.49 ± 0.41</td>
</tr>
<tr>
<td>Control</td>
<td>43.45 ± 0.46</td>
<td>43.51 ± 0.46</td>
<td>43.52 ± 0.46</td>
<td>43.45 ± 0.45</td>
<td>43.47 ± 0.48</td>
<td>42.69 ± 0.42</td>
</tr>
<tr>
<td>Steeper corneal meridian power (D)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthokeratology</td>
<td>43.82 ± 0.41</td>
<td>42.23 ± 0.47</td>
<td>42.12 ± 0.48</td>
<td>41.99 ± 0.43</td>
<td>42.16 ± 0.47</td>
<td>41.35 ± 0.41</td>
</tr>
<tr>
<td>Control</td>
<td>44.11 ± 0.54</td>
<td>44.29 ± 0.51</td>
<td>43.36 ± 0.51</td>
<td>44.31 ± 0.52</td>
<td>44.18 ± 0.53</td>
<td>43.68 ± 0.45</td>
</tr>
<tr>
<td>Corneal shape factor (p-value)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthokeratology</td>
<td>0.70 ± 0.03</td>
<td>0.82 ± 0.05</td>
<td>0.79 ± 0.04</td>
<td>0.82 ± 0.04</td>
<td>0.76 ± 0.05</td>
<td>0.78 ± 0.05</td>
</tr>
<tr>
<td>Control</td>
<td>0.70 ± 0.02</td>
<td>0.70 ± 0.02</td>
<td>0.73 ± 0.02</td>
<td>0.71 ± 0.02</td>
<td>0.74 ± 0.02</td>
<td>0.69 ± 0.03</td>
</tr>
</tbody>
</table>

Table 2. Mean (± SEM) refractive and biometric values for the OK and CT groups who completed the 7-years study at each time interval.
### Table 3.

Simple linear regressions between the change in axial length at 7-years relative to baseline and the different baseline variables for both the OK and CT groups. The strength of association between the different factors is summarized using linear regression equations, $R^2$ values and $p$-values. OK, orthokeratology; CT, control; MSE, mean spherical equivalent.

<table>
<thead>
<tr>
<th></th>
<th>Orthokeratology</th>
<th>Control</th>
<th>Statistical differences between groups in the slopes of the regression lines ($p$-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>$y = -0.165x + 2.620$</td>
<td>$y = -0.220x + 3.469$</td>
<td>$p = 0.208$</td>
</tr>
<tr>
<td></td>
<td>$R^2 = 0.142$, $p = 0.101$</td>
<td>$R^2 = 0.274$, $p = 0.022$</td>
<td></td>
</tr>
<tr>
<td><strong>MSE refractive error (D)</strong></td>
<td>$y = 0.070x + 1.073$</td>
<td>$y = -0.075x + 1.528$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$R^2 = 0.000$, $p = 0.669$</td>
<td>$R^2 = 0.000$, $p = 0.653$</td>
<td></td>
</tr>
<tr>
<td><strong>Axial length (mm)</strong></td>
<td>$y = 0.115x - 1.904$</td>
<td>$y = -0.206x + 6.315$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$R^2 = 0.000$, $p = 0.591$</td>
<td>$R^2 = 0.048$, $p = 0.207$</td>
<td></td>
</tr>
<tr>
<td><strong>Mean central keratometry (D)</strong></td>
<td>$y = -0.235x + 11.131$</td>
<td>$y = -0.021x + 2.282$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$R^2 = 0.290$, $p = 0.027$</td>
<td>$R^2 = 0.000$, $p = 0.817$</td>
<td></td>
</tr>
<tr>
<td><strong>Corneal shape factor (p-value)</strong></td>
<td>$y = -1.541x + 1.982$</td>
<td>$y = -1.868x + 2.659$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>$R^2 = 0.000$, $p = 0.376$</td>
<td>$R^2 = 0.005$, $p = 0.319$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$p = 0.058$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Baseline</td>
<td>6-months</td>
<td>12-months</td>
</tr>
<tr>
<td>--------------------------</td>
<td>----------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
<td><strong>Refractive components</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Sphere (D)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OK to SCL</td>
<td>-2.31 ± 0.38</td>
<td>-0.31 ± 0.06</td>
<td>-0.25 ± 0.13</td>
</tr>
<tr>
<td>SV to OK</td>
<td>-3.75</td>
<td>-4.00</td>
<td>-4.00</td>
</tr>
<tr>
<td>Cylinder (D)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OK to SCL</td>
<td>-0.38 ± 0.08</td>
<td>-0.22 ± 0.07</td>
<td>-0.44 ± 0.11</td>
</tr>
<tr>
<td>SV to OK</td>
<td>-0.75</td>
<td>-0.75</td>
<td>-0.75</td>
</tr>
<tr>
<td><strong>Biometric components</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Axial length (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OK to SCL</td>
<td>24.66 ± 0.30</td>
<td>24.75 ± 0.30</td>
<td>24.90 ± 0.32</td>
</tr>
<tr>
<td>SV to OK</td>
<td>25.00</td>
<td>25.39</td>
<td>25.39</td>
</tr>
<tr>
<td>Flatter corneal meridian power (D)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OK to SCL</td>
<td>42.51 ± 0.75</td>
<td>40.74 ± 0.67</td>
<td>40.84 ± 0.62</td>
</tr>
<tr>
<td>SV to OK</td>
<td>43.30</td>
<td>43.20</td>
<td>43.20</td>
</tr>
<tr>
<td>Steeper corneal meridian power (D)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OK to SCL</td>
<td>43.24 ± 0.63</td>
<td>41.68 ± 0.70</td>
<td>41.69 ± 0.61</td>
</tr>
<tr>
<td>SV to OK</td>
<td>44.00</td>
<td>43.90</td>
<td>43.90</td>
</tr>
<tr>
<td>Corneal shape factor (p-value)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OK to SCL</td>
<td>0.65 ± 0.04</td>
<td>0.87 ± 0.05</td>
<td>0.94 ± 0.02</td>
</tr>
<tr>
<td>SV to OK</td>
<td>0.80</td>
<td>0.82</td>
<td>0.85</td>
</tr>
</tbody>
</table>

Table 4. Mean (± SEM) refractive and biometric values for the 8 subjects who switched from OK to SCL as well as for one single subject who switched from SV to OK at each time interval. OK, orthokeratology; SCL, soft contact lens; SV, single-vision spectacles
69 Children Assessed for eligibility

61 Children Enrolled in the study

31 Children Orthokeratology
- 2 Children Discontinued the study
  - 1 Discomfort
  - 1 Unknown reasons
- 29 Children Orthokeratology
  - 7 Children Discontinued the study
    - 7 Lost to follow-up
- 8 Children Changed lens wear modality
  - 8 Switched to SCL

30 Children Control (SV)
- 6 Children Discontinued the study
  - 4 Lost to follow-up
  - 1 Switched to SCL
  - 1 Switched to...
- 24 Children Control (SV)
- 7 Children Discontinued the study
  - 7 Lost to follow-up

9 Children Changed lens wear modality
- 8 Switched from OK to SCL
- 1 Switched from SV to OK

14 Children Orthokeratology

16 Children Control (4 SV + 12 SCL)