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.[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.[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.[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.[21] Furthermore, a subpopulation of OK lens wearers (64%) demonstrated an apparent total arrest of manifest myopic refractive change.[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.[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.[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.[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.[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).[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.[17, 24-27] The methods employed in MCOS have been described in detail elsewhere.[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

178 measurements were taken and a mean obtained (Topcon RM 8000B, CA,
179 USA).
180
181 Measurements of axial length were taken with the Zeiss *IOLMaster* (Carl Zeiss
182 Jena GmbH).[28] Three separate measurements of axial length were recorded
183 and a mean obtained.
184
185 Corneal topography measurements were performed with the Wavelight Allegro
186 Topolyzer (WaveLight Laser Technologies AG, Erlangen, Germany). The
187 instrument incorporates a high resolution placido-ring corneal topographer
188 which detects 22,000 elevated data points of measurement from 22 ring edges
189 with a claimed accuracy and reproducibility of ± 0.10D according to the
190 manufacturer. The first measurement taken for each eye, which provided an
191 optimum index value according to the manufacturer's recommendations, was
192 used for the study. The measurement generates a simulated central
193 keratometry reading and the rate of peripheral corneal flattening/steepening that
194 occurs with displacement from the corneal apex; the latter indicates the degree
195 to which an aspheric surface differs from the spherical form (i.e., the p value).
196 The p value was calculated over a 7-mm chord in accord with the default setting
197 of the instrument.
198
199 **Statistical analysis**
200 Differences in subjects' demographics and baseline data between groups were
201 tested using unpaired sample t-tests for all variables, except for the male:female
202 ratio which was tested using a chi-square test. Changes (from baseline) in
203 refractive and biometric data over time and between groups (i.e. OK vs. CT)
204 were tested using a general linear model (GLM) with repeated measures to test
205 the statistical significance of differences in outcome variables (i.e. axial length,
206 spherical and cylindrical refractive components, corneal power and corneal
207 shape) for the between-subject factor of refractive correction (two levels: OK
208 and CT) and for the within-subject factor of time (five levels: 6, 12, 18, 24 and
209 84 months). The significance of the interaction between OK and CT with respect
210 to time was then tested for all time intervals combined and then separately for
211 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.[25] 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 $p\leq0.001$) (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 $p\leq0.02$) (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 ($R^2=0.274$, $p=0.022$), but not for the OK group ($R^2=0.142$, $p=0.101$). The effect of baseline age on axial elongation was, however, similar between groups ($p=0.208$) (Figure 3 and

Table 3). 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±0.5 years (range 0.2 to 3.9 years) thereafter and wore SCL for the last 3.3±0.5 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±0.4, 11.4±0.4 and 16.4±0.5 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±0.06mm during the initial 2 years of OK lens wear and by 0.80±0.16mm 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);[29] such reduction could therefore have important implications in terms of reducing ocular-related morbidity[7] and healthcare costs.[8, 9]

Despite differences in corneal topography and contact lens-induced responses between Caucasian and Japanese ethnicities have been previously reported,[30, 31] our results are similar to those reported by Hiraoka et al.[23] 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.[23] 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),[23] 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, in

385 which there is a reduced rate of axial elongation with increased age, thereby
386 making it more difficult to find significant differences between groups in axial
387 length over longer periods of lens wear (Figures 2 and 3, and Table 2). In fact,
388 the increases in axial length over the first 24 months of this study were
389 remarkably similar to those found between 24 and 84 months for both the OK
390 (0.42±0.05 and 0.39±0.04mm, respectively) and the CT (0.71±0.10 and
391 0.65±0.11mm, respectively) groups, clearly indicating a decrease in the rate of
392 axial elongation regardless of the visual correction being worn (Figure 3 and
393 Table 2). It is well established that older age is associated with smaller
394 increases in myopia and axial elongation. Furthermore, it has been previously
395 reported that myopia stabilizes at around 16 years of age.[32] Subjects in this
396 study had mean ages of 10 and 12 years at baseline and following 2 years of
397 OK lens wear, respectively. Therefore, a reduced rate of myopia progression
398 would be expected on these subjects during the subsequent 5 years of data
399 collection.
400
401 Greater corneal power was found to be associated with smaller axial elongation
402 in OK wearers (Figure 4). Following OK lens wear, a steeper cornea is likely to
403 provide a smaller treatment zone of central corneal flattening[33] and a wider
404 peripheral ring of increased corneal power. Therefore, it is feasible that a
405 steeper cornea facilitates corneal reshaping and reduction in axial elongation
406 following OK lens wear.[12, 26]
407
408 The large variability in the increases in axial length found in the 8 subjects who
409 discontinued OK lens wear at 2-years and switched to SCL wear could be
410 attributed to the length of time that SCLs were worn after ceasing OK lens wear
411 (Figure 5), individual differences and differences in the power profile between
412 the different SCLs worn (Figure 6).[34] In any event, the results found on the
413 effect of switching treatments appear to be consistent with those found in the
414 OK and CT groups over the 7-year period in that the efficacy of OK diminishes
415 and resumes with discontinuation and restoration of OK lens wear, respectively.
416
417 A limitation of this study is the potential bias introduced by subjects' self-
418 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=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 ± 0.63 mm) and CT (1.36 ± 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[7] and healthcare costs.[8, 9]

DECLARATION OF INTEREST

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FIGURE LEGENDS

Figure 1. Flow-chart of the subjects recruited for the study. SV, distance single-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 $p \leq 0.02$). 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, 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, R^2 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.

	Orthokeratology	Control	p-value
Age (years)	10.4 ± 0.5	9.6 ± 0.4	0.244
Male/female ratio	8/6	7/9	1.00
Sphere (D)	-2.27 ± 0.31	-2.16 ± 0.26	0.375
Cylinder (mm)	-0.25 ± 0.09	-0.30 ± 0.09	0.876
Axial length (mm)	24.39 ± 0.23	24.08 ± 0.27	0.621
Flatter meridian (D)	43.18 ± 0.45	43.45 ± 0.46	0.665
Steeper meridian (D)	43.82 ± 0.41	44.11 ± 0.54	0.667
Corneal shape factor (p-value)	0.70 ± 0.03	0.70 ± 0.02	0.982

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

	Baseline	6-months	12-months	18-months	24-months	84-months
Refractive components						
Sphere (D)						
Orthokeratology	-2.27 ± 0.31	-0.14 ± 0.07	-0.21 ± 0.07	-0.14 ± 0.07	-0.23 ± 0.06	-0.29 ± 0.10
Control	-2.16 ± 0.26	-2.39 ± 0.29	-2.74 ± 0.30	-3.07 ± 0.30	-3.37 ± 0.32	-5.00 ± 0.43
Cylinder (D)						
Orthokeratology	-0.25 ± 0.09	-0.38 ± 0.09	-0.27 ± 0.10	-0.30 ± 0.10	-0.29 ± 0.13	-0.30 ± 0.10
Control	-0.30 ± 0.09	-0.25 ± 0.08	-0.30 ± 0.08	-0.30 ± 0.11	-0.37 ± 0.10	-0.59 ± 0.10
Biometric components						
Axial length (mm)						
Orthokeratology	24.39 ± 0.23	24.52 ± 0.23	24.41 ± 0.23	24.71 ± 0.24	24.81 ± 0.25	25.30 ± 0.31
Control	24.08 ± 0.27	24.25 ± 0.27	24.46 ± 0.27	24.61 ± 0.26	24.78 ± 0.26	25.43 ± 0.27
Flatter corneal meridian power (D)						
Orthokeratology	43.18 ± 0.45	41.32 ± 0.46	41.36 ± 0.48	41.10 ± 0.44	41.36 ± 0.49	40.49 ± 0.41
Control	43.45 ± 0.46	43.51 ± 0.46	43.52 ± 0.46	43.45 ± 0.45	43.47 ± 0.48	42.69 ± 0.42
Steeper corneal meridian power (D)						
Orthokeratology	43.82 ± 0.41	42.23 ± 0.47	42.12 ± 0.48	41.99 ± 0.43	42.16 ± 0.47	41.35 ± 0.41
Control	44.11 ± 0.54	44.29 ± 0.51	43.36 ± 0.51	44.31 ± 0.52	44.18 ± 0.53	43.68 ± 0.45
Corneal shape factor (p-value)						
Orthokeratology	0.70 ± 0.03	0.82 ± 0.05	0.79 ± 0.04	0.82 ± 0.04	0.76 ± 0.05	0.78 ± 0.05
Control	0.70 ± 0.02	0.70 ± 0.02	0.73 ± 0.02	0.71 ± 0.02	0.74 ± 0.02	0.69 ± 0.03

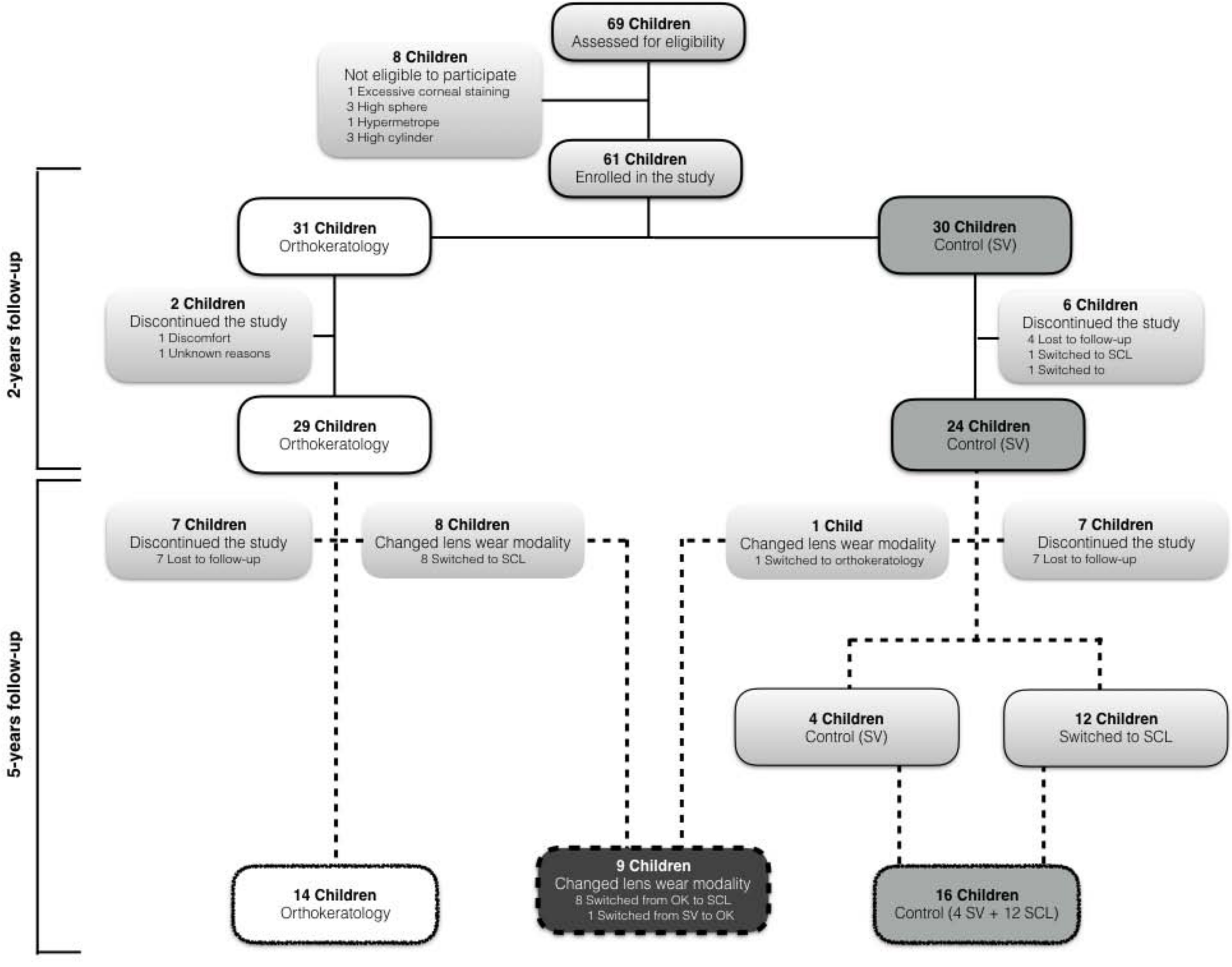
Table 2. Mean (± SEM) refractive and biometric values for the OK and CT groups who completed the 7-years study at each time interval.

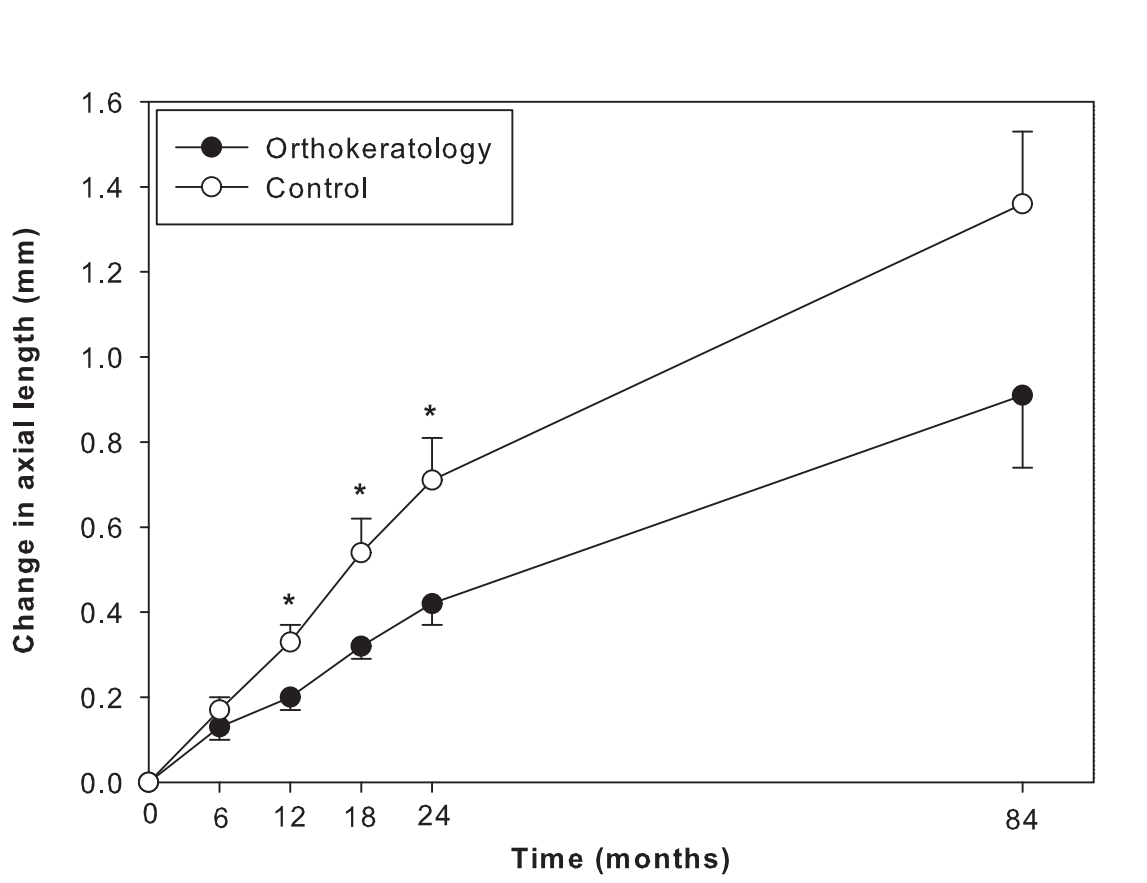
	Orthokeratology	Control	Statistical differences between groups in the slopes of the regression lines (p-value)
Age (years)	y=-0.165x + 2.620 R^2=0.142, p=0.101	**y=-0.220x + 3.469** **R^2=0.274, p=0.022**	p=0.208
MSE refractive error (D)	y=0.070x + 1.073 R^2=0.000, p=0.669	y=-0.075x + 1.528 R^2=0.000, p=0.653	p=0.987
Axial length (mm)	y=0.115x - 1.904 R^2=0.000, p=0.591	y=-0.206x + 6.315 R^2=0.048, p=0.207	p=0.085
Mean central keratometry (D)	**y=-0.235x + 11.131** **R^2=0.290, p=0.027**	y=-0.021x + 2.282 R^2=0.000, p=0.817	p=0.044
Corneal shape factor (p-value)	y=-1.541x + 1.982 R^2=0.000, p=0.376	y=-1.868x + 2.659 R^2=0.005, p=0.319	p=0.058

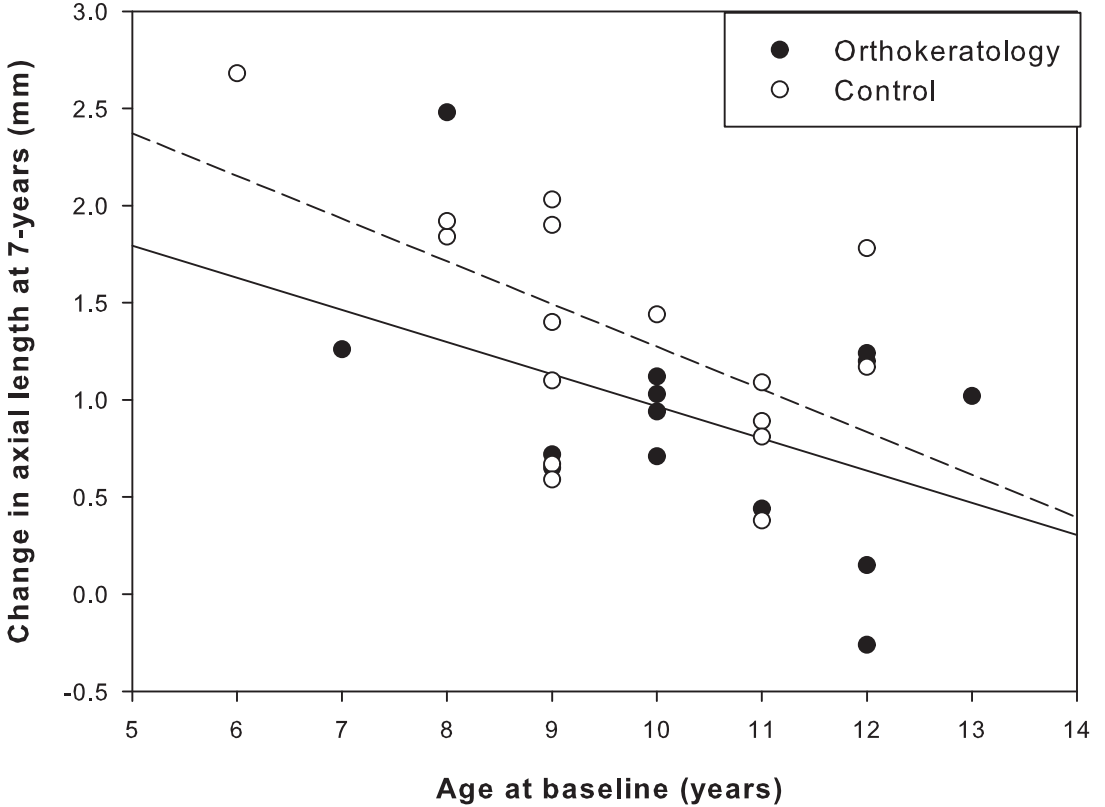
Table 3. Simple linear regressions between the change in axial length at 7-years relative to baseline and the different baseline variables for both the OK and CT groups. The strength of association between the different factors is summarized using linear regression equations, R^2 values and p-values. OK, orthokeratology; CT, control; MSE, mean spherical equivalent

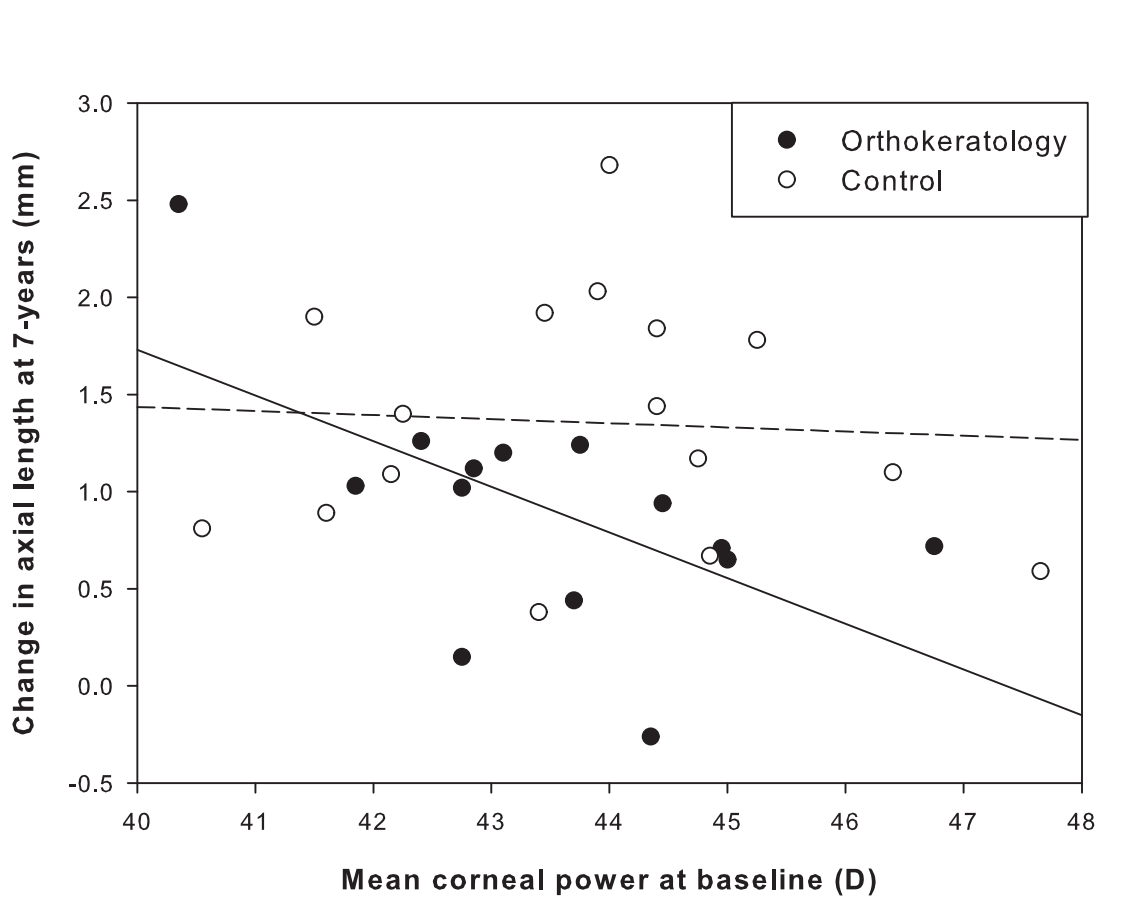
	Baseline	6-months	12-months	18-months	24-months	84-months
Refractive components						
Sphere (D)						
OK to SCL	-2.31 ± 0.38	-0.31 ± 0.06	-0.25 ± 0.13	-0.33 ± 0.08	-0.50 ± 0.12	-4.81 ± 0.62
SV to OK	-3.75	-4.00	-4.00	-4.50	-5.00	-0.25
Cylinder (D)						
OK to SCL	-0.38 ± 0.08	-0.22 ± 0.07	-0.44 ± 0.11	-0.31 ± 0.09	-0.19 ± 0.09	-0.59 ± 0.16
SV to OK	-0.75	-0.75	-0.75	-0.75	-0.50	-0.75
Biometric components						
Axial length (mm)						
OK to SCL	24.66 ± 0.30	24.75 ± 0.30	24.90 ± 0.32	25.06 ± 0.32	25.23 ± 0.32	26.03 ± 0.41
SV to OK	25.00	25.39	25.39	25.72	25.81	26.16
Flatter corneal meridian power (D)						
OK to SCL	42.51 ± 0.75	40.74 ± 0.67	40.84 ± 0.62	40.71 ± 0.74	40.82 ± 0.82	41.54 ± 0.74
SV to OK	43.30	43.20	43.20	43.44	43.44	40.40
Steeper corneal meridian power (D)						
OK to SCL	43.24 ± 0.63	41.68 ± 0.70	41.69 ± 0.61	41.78 ± 0.77	41.76 ± 0.79	42.57 ± 0.67
SV to OK	44.00	43.90	43.90	43.95	44.12	41.5
Corneal shape factor (p-value)						
OK to SCL	0.65 ± 0.04	0.87 ± 0.05	0.94 ± 0.02	0.85 ± 0.05	0.91 ± 0.04	0.68 ± 0.03
SV to OK	0.80	0.82	0.85	0.86	0.85	0.94

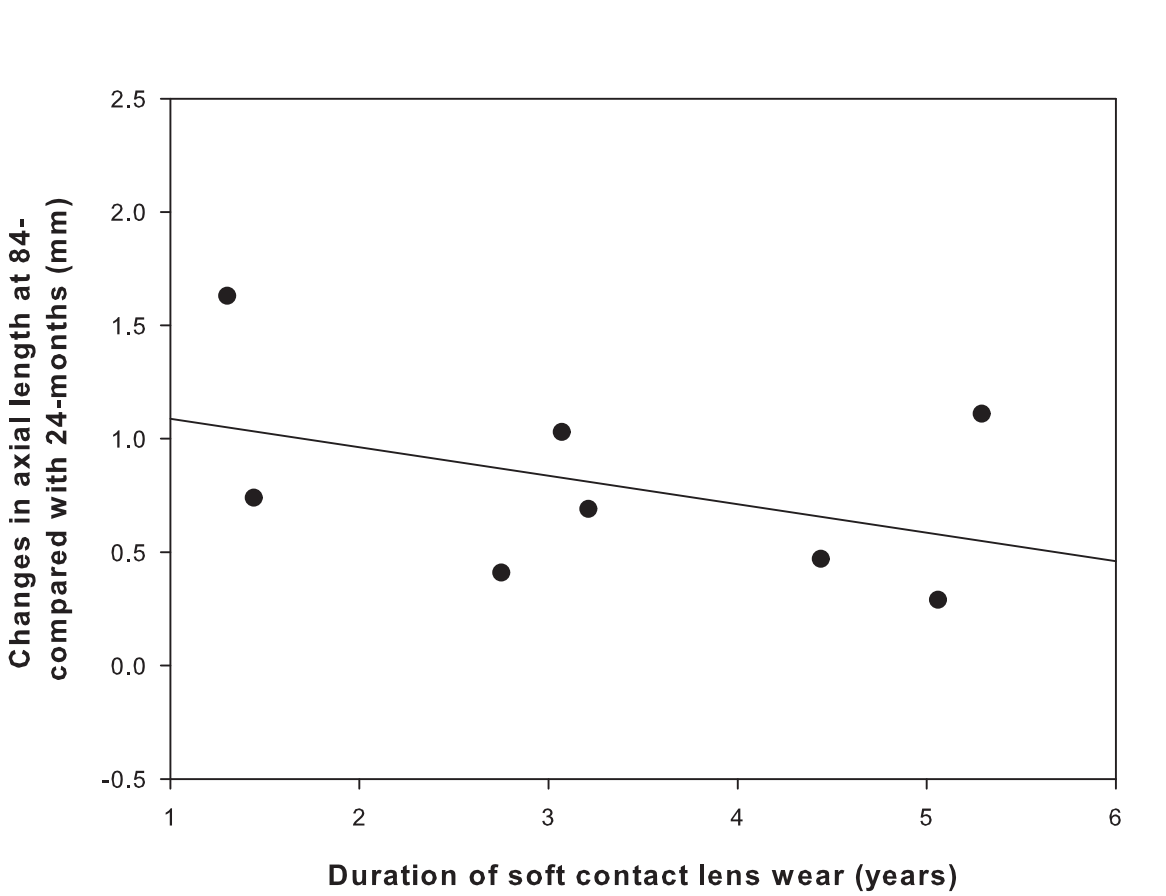
Table 4. Mean (± SEM) refractive and biometric values for the 8 subjects who switched from OK to SCL as well as for one single subject who switched from SV to OK at each time interval. OK, orthokeratology; SCL, soft contact lens; SV, single-vision spectacles

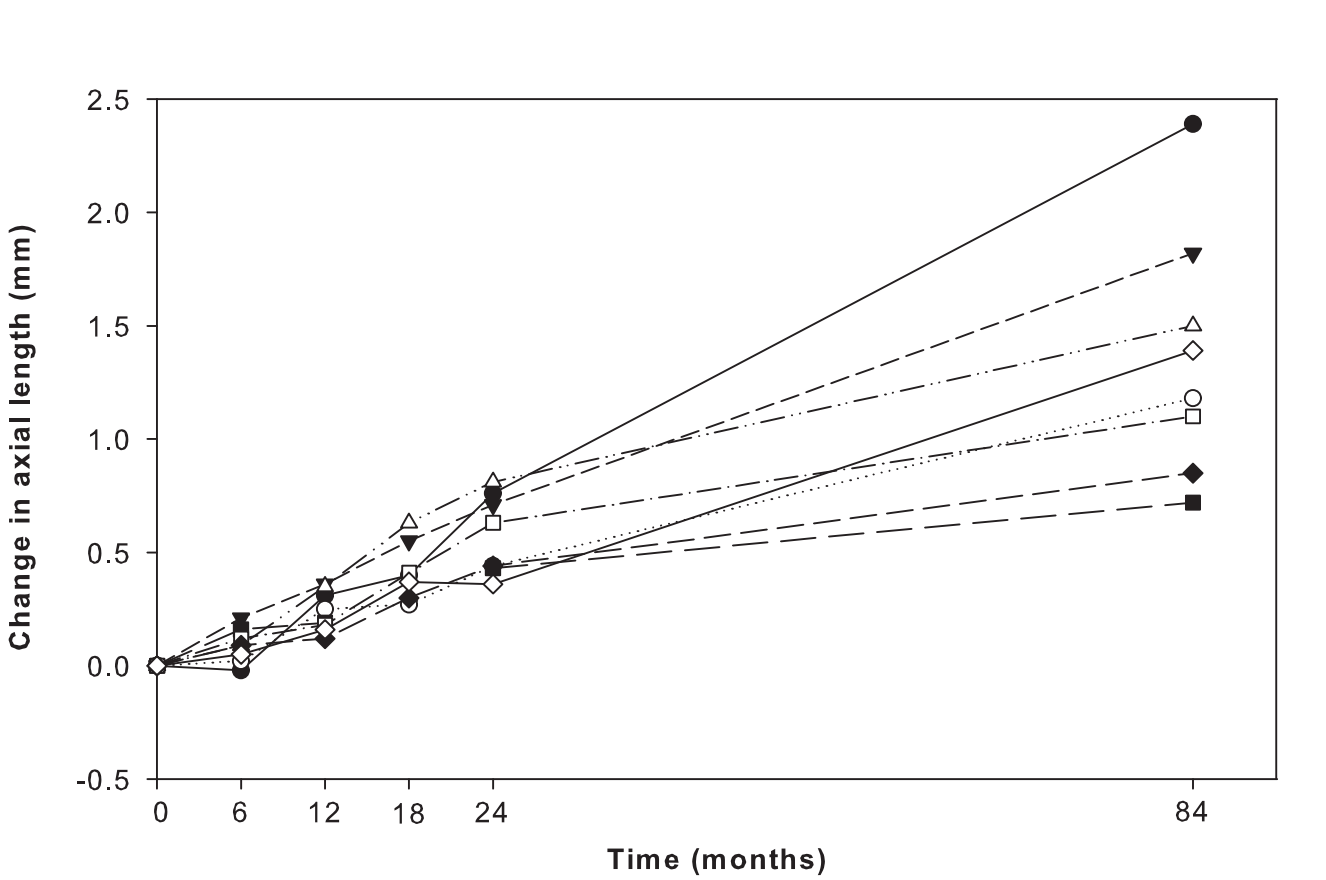

69 Children
Assessed for eligibility
8 Children
Not eligible to participate
1 Excessive corneal staining
3 High sphere
1 Hypermetrope
3 High cylinder
61 Children
Enrolled in the study
2-years follow-up
31 Children
Orthokeratology
30 Children
Control (SV)
2 Children
Discontinued the study
1 Discomfort
1 Unknown reasons
6 Children
Discontinued the study
4 Lost to follow-up
1 Switched to SCL
1 Switched to
29 Children
Orthokeratology
24 Children
Control (SV)
5-years follow-up
7 Children
Discontinued the study
7 Lost to follow-up
8 Children
Changed lens wear modality
8 Switched to SCL
1 Child
Changed lens wear modality
1 Switched to orthokeratology
7 Children
Discontinued the study
7 Lost to follow-up
4 Children
Control (SV)
12 Children
Switched to SCL
14 Children
Orthokeratology
9 Children
Changed lens wear modality
8 Switched from OK to SCL
1 Switched from SV to OK
16 Children
Control (4 SV + 12 SCL)


Orthokeratology
Control
Change in axial length (mm)
Time (months)
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
6
12
18
24
84
*
*
*


Orthokeratology
Control
Change in axial length at 7-years (mm)
Age at baseline (years)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
5
6
7
8
9
10
11
12
13
14


Orthokeratology
Control
Change in axial length at 7-years (mm)
Mean corneal power at baseline (D)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
40
41
42
43
44
45
46
47
48


Changes in axial length at 84-compared with 24-months (mm)
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
1
2
3
4
5
6
Duration of soft contact lens wear (years)


Change in axial length (mm)
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0
6
12
18
24
84
Time (months)