Emmetropia Is Maintained Despite Continued Eye Growth From 16 to 18 Years of Age

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PURPOSE. To examine, in Norwegian adolescents, to what degree emmetropia and low hyperopia were maintained from 16 to 18 years of age, and if this was the case, whether it was associated with continued coordinated ocular growth.

METHODS. Cycloplegic autorefration and ocular biometry, including crystalline lens thickness, were measured in 93 Norwegian adolescents (mean age: 16.7 ± 0.3 years; 63.4% females) and repeated after 2 years. Crystalline lens power was determined by ray tracing over a 1-mm pupil, based on the Gullstrand-Emsley model. Serum vitamin D3 concentration was measured at follow-up.

RESULTS. Emmetropia and low hyperopia (≤−0.50 diopters [D] < spherical equivalent refractive error [SER] < +2.00 D) were present in 91.4% at baseline and 89.2% at follow-up. The emmetropes and low hyperopes who maintained their refractive error exhibited continued ocular axial growth (+0.059 ± 0.070 mm) together with a decrease in crystalline lens power (−0.064 ± 0.291 D) and a deepening of the anterior chamber (+0.028 ± 0.040 mm). Thinning of the crystalline lens was found in 24%. Overall, the negative change in SER was larger in those with the most negative SER at baseline (R2 = 0.178, P < 0.001), and was associated with increases in vitreous chamber depth and in crystalline lens power (R2 = 0.752, P < 0.001), when adjusted for sex. There was no difference in vitamin D3 level between those who exhibited negative versus positive changes in refractive error.

CONCLUSIONS. The results show that emmetropic and low hyperopic eyes were still growing in late adolescence, with refractive errors being maintained through a coordinated decrease in crystalline lens power.

Keywords: emmetropia, refractive errors, ocular growth, ocular biometry, crystalline lens

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and 2016 (n = 246), and all of those who were still students at upper-secondary school in 2018 were invited to participate in a follow-up study (n = 120). Of these 120 participants, 93 (77.5%; 16.7 ± 0.3 years; 63.4% females) gave consent for further participation. There was no difference between this sample (n = 93) and the original sample of 16-year-olds (n = 246) when comparing the frequency of refractive errors (7.5% vs. 11.0% myopia, 57.0% vs. 57.7% hyperopia, χ²(2) = 1.171, P = 0.56), mean SER [+0.49 ± 0.94 D vs. +0.59 ± 1.23 D, Welch t(216.2) = −0.780, P = 0.44], mean ocular axial length [AL; 23.6 ± 0.7 mm vs. 23.4 ± 0.8 mm, t(357) = 1.665, P = 0.10], ethnicity [87.1% vs. 91.1% Norwegian Caucasian, χ²(1) = 1.173, P = 0.28], or sex [63.4% vs. 56.5% females, χ²(1) = 1.337, P = 0.25]. Baseline and follow-up data were collected in March 2016 and over 16 days from January 24 to February 9, 2018, respectively. The majority of participants were Norwegian Caucasians who had grown up in Norway (87.1%). Other ethnicities were Asian (6.5%), African (2.2%), South American (1.1%), and mixed (3.2%; defined as having parents of two different ethnicities). The sample included three participants (3.2%) with a known history of strabismus and five participants (5.4%) who reported having one of the following conditions: factor V Leiden thrombophilia, anti-NMDA (N-methyl-D-aspartate) receptor encephalitis, diabetes, scoliosis, and thalassemia. Removing these from the sample did not affect the results.

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Regional Committee for Medical and Health Research Ethics in Southeast Norway. All participants gave written informed consent after explanation of the nature and possible consequences of the study.

Data Collection

Identical protocols were followed at baseline and follow-up with respect to measurement of cycloplegic ocular biometry and autorefration, as presented previously. For completeness with regard to methods, cycloplegic ocular biometry and autorefraction data were obtained with Zeiss IOLMaster 700 (Carl Zeiss Meditec AG, Jena, Germany; keratometer refractive index 1.3375) and Huvitz autorefractor (HRK-8000A Auto-REF Keratometer; Huvitz Co. Ltd., Gyeonggi-do, Korea) at 13.5-mm vertex distance 15 to 20 minutes after administering 1% cyclopentolate hydrochloride (Minims single dose; Bausch & Lomb UK Ltd., Kingston, England). One drop of cyclopentolate was used if the participant’s irides were blue to green and two drops if they were green to brown. The IOLMaster 700 is known to have high measurement repeatability. Body height was measured to the nearest 0.1 cm, in a standing position without shoes, with the Seca 217 stable stadiometer for mobile height measurement (Seca Deutschland, Hamburg, Germany).

Individual Eye Models

Crystalline lens power (LP; also commonly abbreviated as Pj) was calculated from individual three-surface biconic eye models based on the Gullstrand-Emsley model constructed by ray tracing in Optic Studio v.14.2 (Zemax LLC, Kirkland, WA, USA). The set of models were calculated using a biconic (toric) cornea, with measured corneal curvature in the steepest and flattest meridians along with the corresponding axis, and the measured cycloplegic spherocylindrical refractive error (sphere, cylinder, and axis) at a 13.5-mm vertex distance. The parameters anterior corneal radius of curvatures and axis (CR1, CR2, Axis), anterior chamber depth (ACD), crystalline lens thickness (LT), and AL were taken from the measured biometry data. Per the Gullstrand-Emsley model, the refractive index was set to 1.416 for the crystalline lens and 1.333 for the cornea, aqueous chamber, and vitreous chamber. Front- and back-surface crystalline lens curvatures were optimized through a Zemax merit function utilizing the built-in Damped Least squares algorithm to minimize the root-mean-square wavefront error (ray tracing of a bundle of rays over a 1-mm pupil diameter) and give the best focus at the retina, while forcing the same ratio of crystalline lens surface powers to that of its total equivalent power (58.0% for the front surface, 63.3% for the back surface) as in the Gullstrand-Emsley model (per Bennett and done in the same way as in Li et al.). Zemax files are available online.

Vitamin D₃

Serum vitamin D₃ concentration was measured at follow-up by collecting blood samples by the dried blood spot technique (DBS). The samples were analyzed by Vitas AS (Oslo, Norway), where serum concentrations of 25-hydroxycholecalciferol [25(OH)D₃] were estimated by the LC-MS/MS DBS method with a detection limit of 5 nM, as described elsewhere.

Statistical Analysis

Data were analyzed with the statistical computing software R, version 3.4.0, and data for the right eyes were used in the analysis. SER was estimated as sphere + ½ cylinder. Moderate/high hyperopia was defined as SER ≥ +2.00 D, low hyperopia as +0.50 D ≤ SER < +2.00 D, emmetropia as −0.50 D ≤ SER < +0.50 D, and myopia as SER ≤ −0.50 D. Persistent emmetropes/low hyperopes were defined as those with astigmatism lower than 1.00 diopter cylinder (DC) who maintained emmetropia or low hyperopia throughout the study period. Decline of hyperopia was calculated as the proportion of participants who were not hyperopic at follow-up but were at baseline. Incidence of myopia was calculated as the proportion of myopic participants at follow-up who were not myopic at baseline. Annual decline and incidence rates were found by dividing the proportions by the study period in years.

The χ² test was used to assess differences in prevalence between groups. Mean differences between baseline and follow-up data were examined by paired t-test; between-group differences were examined using 1-way analysis of variance and Student’s or Welch’s two independent sample t-tests for equal or unequal variances, respectively, and Wilcoxon rank sum test for nonnormal data. Kruskal-Wallis and Bonferroni corrected pairwise comparison by Wilcoxon were used to assess differences in SER and ocular biometric parameters between the refractive error groups. Pearson correlation (rP) and multiple linear regressions were used to assess associations between SER and ocular biometric parameters. Significance level was set at α = 0.05.

RESULTS

Changes in Refractive Error

As summarized in Table 1, our sample population of Norwegian adolescents showed relatively stable refractive errors over the study period, with emmetropia and low hyperopia representing 91.4% of participants at baseline (16 years of age) and 89.2% at follow-up (18 years of age). The
Annual decline of hyperopia was 4.7%, and the annual incidence of myopia was 1.2%.

Figure 1 shows the SERs at baseline and follow-up. The changes in SER were, in general, minor (mean ± SD: −0.089 ± 0.206 D; range, −0.67 to +0.40), and only 19% exhibited a negative change larger than 0.25 D. Most (77%) participants maintained their baseline refractive error, as defined by change in SER between −0.25 and +0.25 D over 2 years.

The multiple linear regression models in Table 2 show that those with the most negative SER at baseline had the largest negative changes in SER when adjusted for sex (model A: \( R^2 = 0.129, P < 0.001 \); see also the unadjusted regression line in Fig. 1), and the change in SER was also predicted by baseline AL and CR (model B: \( R^2 = 0.148, P = 0.003 \)) and by baseline AL/CR (model C: \( R^2 = 0.129, P = 0.002 \)). In line with this, change in SER, change in AL, and change in VCD correlated with baseline SER (change in SER: \( r_P = 0.375, P < 0.001 \); change in AL: \( r_P = -0.355, P < 0.001 \); change in VCD: \( r_P = -0.404, P < 0.001 \)).

Changes in Ocular Biometric Parameters in Persistent Emmetropes/Low Hyperopes

Throughout the study period, 83 participants (89.2%) maintained emmetropia or low hyperopia, and 75 of these (80.6% of all) had astigmatism lower than 1.00 DC at both baseline and follow-up. The latter group is, from here onward, termed persistent emmetropes/low hyperopes.

Table 3 summarizes the 2-year changes in SER and ocular biometric parameters in the persistent emmetropes/low hyperopes. This group exhibited an increase in mean LT, ACD, VCD, AL, and AL/CR (\( P < 0.005 \)), a decrease in mean LP (\( P = 0.06 \)), and a negative change in mean SER (\( P = 0.01 \)). There was a slight thinning of mean CCT (\( P < 0.001 \)), but no change in mean CR (\( P = 0.36 \)). The continued elongation of mean AL (+0.059 ± 0.070 mm) equals −0.149 D change in SER (it is assumed that 1-mm increase in AL equals −0.05 D change in SER as estimated from baseline data), mainly compensated for by a decrease in mean LP (−0.064 ± 0.291 D) and deepening of mean ACD (+0.028 ± 0.040 mm). The negative correlation between changes in AL and LP was significant (\( r_P = -0.514, P = 0.006 \)). When compared with the myopes (Table 3), the group of persistent emmetropes/low hyperopes had a smaller increase in mean VCD, AL, and AL/CR (\( P < 0.002 \)), and had a smaller negative change in mean SER (\( P = 0.001 \)), but did not differ in change of mean CCT, CR, ACD, LT, or LP (all \( P > 0.05 \)).

Table 4 summarizes the 2-year changes in SER and ocular biometric parameters for all participants grouped by refractive error at baseline.

LT increased for 76% of the persistent emmetropes/low hyperopes (79% of all emmetropes and hyperopes; range, +0.003 to +0.058 mm), with the remainder exhibiting a decrease in LT (range, −0.001 to −0.065 mm). LT increased for all myopes (range, +0.012 to +0.048 mm). The increase in LT was larger than 0.02 mm for 45% of the persistent emmetropes/low hyperopes and 86% of the myopes.

Associations Between Changes in Refractive Error and Ocular Biometric Parameters

As shown in Table 5, a negative change in SER was associated with increased AL and increased LP in a multiple linear regression model, indicating a 1:1 relationship and the linear regression, respectively, between SER at baseline and follow-up. All below the solid black line exhibited a negative change in SER.

**Figure 1.** Scatterplots of SER at baseline versus 2-year follow-up for (A) all participants and (B) the subgroup of participants who had −1.00 D ≤ SER ≤ +2.00 D (for better visualization of the individual data points within the squared area marked by dotted gray lines in [A]). Crosses and circles represent males and females, respectively. The dashed black lines show the defined limits of myopia (SER ≤ −0.50 D) and hyperopia (SER ≥ +0.50 D), and the solid black line and the dotted red line indicate a 1:1 relationship and the linear regression, respectively, between SER at baseline and follow-up.
regression model in the group of persistent emmetropes/low hyperopes ($R^2 = 0.705, P < 0.001$) and overall ($R^2 = 0.727, P < 0.001$), adjusted for sex. To elucidate the differences in each of the refractive error groups, changes in SER were plotted as a function of changes in AL (Fig. 2A) and changes in LP (Fig. 2B).

There was a clear negative correlation between changes in SER and AL regardless of refractive error (Fig. 2A). hyperopes: $r_P = -0.408, P = 0.002$, emmetropes: $r_P = -0.777, P < 0.001$, myopes: $r_P = -0.604, P = 0.15$. There was also a clear negative correlation between changes in SER and LP in hyperopes (Fig. 2B: $r_P = -0.479, P < 0.001$), but not in emmetropes ($r_P = -0.165, P > 0.05$) or myopes ($r_P = -0.099, P > 0.05$).

The dotted lines in Figure 2 show the calculated change in SER per 1-mm increase in AL (−3.05 D/mm; Fig. 2A), and the change in SER per diopter increase in LP (−1 D per diopter; Fig. 2B). The increase in AL associated with a negative change in SER in hyperopes (open diamonds, dashed line in Fig. 2A) was small compared with myopes and emmetropes. Hyperopes who had a negative change in SER (i.e., a change that brings them nearer to emmetropia) had an increase in LP (dashed line in Fig. 2B nearly overlaps with dotted line). Change in SER did not correlate with change in ACD, change in CR, or change in LT (all $P > 0.05$).

Figure 3 shows change in LP as a function of change in AL for those who had a positive (Fig. 3A) or a negative (Fig. 3B) change in SER. Overall, changes in LP and AL were negatively correlated ($r_P = -0.408, P < 0.001$). However, those with a positive change in SER (change > 0.002 D; Fig. 3A, $n = 35$) had a significantly smaller increase in mean AL (+0.04 ± 0.06 mm vs. +0.09 ± 0.08 mm, $P < 0.001$) and larger decrease in mean LP (−0.20 ± 0.25 D vs. −0.00 ± 0.30 D, $P = 0.001$) than those with a negative change in SER (change < −0.002 D; Fig. 3B, $n = 58$). Those who had a positive change in SER larger than 0.25 D (Fig. 3A, filled symbols, $n = 3$; −0.05 ± 0.05 mm) had a decrease in mean AL, which was opposite and significantly different from those who had a negative change in SER larger than 0.25 D (Fig. 3B, filled symbols, $n = 18$), in which mean AL increased (+0.16 ± 0.08 mm, Wilcoxon $P = 0.002$).

Nine participants (9.7% of all; seven persistent emmetropes/low hyperopes) decreased more than 0.02 mm in AL (≥95% limits of reproducibility of the IOLMaster 700$^{16}$); seven of these had positive changes in SER (two with positive changes in SER larger than 0.25 D).

### Associations of Crystalline Lens Power With Lens Thickness and Ocular Axial Length

The multiple linear regression presented in Table 6 shows that having a strong LP was associated with having a short AL and a thick LT, when adjusted for sex [model A (baseline): $R^2 = 0.645, P < 0.001$; model B (follow-up): $R^2 = 0.646, P < 0.001$]. Figure 4 shows that LP and AL were negatively correlated for emmetropes (baseline $r_P = -0.765$, $P < 0.001$; follow-up $r_P = -0.759$, $P < 0.001$) and hyperopes (baseline $r_P = -0.625$, $P < 0.001$; follow-up $r_P = -0.638$, $P < 0.001$), but not for myopes (baseline and follow-up; $P > 0.05$). LP correlated with LT (baseline $r_P = 0.589$, $P < 0.001$; follow-up $r_P = 0.577$, $P < 0.001$), but there was no correlation between changes in LP and LT ($P > 0.05$). There was neither any correlation between SER and LP or between change in SER and baseline LT or LP.

### Body Height

From baseline to follow-up, body height increased 1.7 ± 1.3 cm (range, −0.7 to 4.1 cm) in males and 0.9 ± 0.8 cm (range, −0.6 to 3.3 cm) in females. Change in height did not correlate

### Table 2. Multiple Linear Regression Models Predicting Changes in SER, Adjusted for Sex

<table>
<thead>
<tr>
<th>Variables</th>
<th>Estimate</th>
<th>CI</th>
<th>P</th>
<th>Variables</th>
<th>Estimate</th>
<th>CI</th>
<th>P</th>
<th>Variables</th>
<th>Estimate</th>
<th>CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>−0.079</td>
<td>−0.15 to −0.01</td>
<td>0.02</td>
<td>Intercept</td>
<td>1.013</td>
<td>−0.46 to 2.49</td>
<td>0.18</td>
<td>Intercept</td>
<td>2.367</td>
<td>0.84 to 3.89</td>
<td>0.003</td>
</tr>
<tr>
<td>Sex, females</td>
<td>−0.082</td>
<td>−0.16 to 0.00</td>
<td>0.05</td>
<td>Sex, females</td>
<td>−0.118</td>
<td>−0.20 to −0.03</td>
<td>0.008</td>
<td>Sex, females</td>
<td>−0.107</td>
<td>−0.19 to −0.02</td>
<td>0.01</td>
</tr>
<tr>
<td>SER baseline</td>
<td>0.084</td>
<td>0.04 to 0.13</td>
<td>&lt;0.001</td>
<td>AL baseline</td>
<td>−0.127</td>
<td>−0.20 to −0.05</td>
<td>0.001</td>
<td>AL/CR baseline</td>
<td>−0.796</td>
<td>−1.50 to −0.29</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Significant $P$ values (<0.05) in bold. adj, adjusted; CI, confidence interval.

### Table 3. Change in SER and Ocular Biometric Parameters for Persistent Emmetropes/Low Hyperopes and for Baseline Myopes. Data Are Presented as Mean ± SD. The Mean Change From Baseline to Follow-Up for the Group of Persistent Emmetropes/Low Hyperopes Was Assessed by Paired Sample $t$-Test and Presented as $P_{change}$. $P_W$ Indicates the Difference Between the Group of Persistent Emmetropes/Low Hyperopes and the Group of Myopes, Assessed by Wilcoxon Rank Sum Test

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Persistent Emmetropes/ Low Hyperopes, $n = 75$</th>
<th>$P_{change}$</th>
<th>Myopes, $n = 7$</th>
<th>$P_W$</th>
</tr>
</thead>
<tbody>
<tr>
<td>SER, D</td>
<td>−0.058 ± 0.195</td>
<td>0.01</td>
<td>−0.358 ± 0.180</td>
<td>0.001</td>
</tr>
<tr>
<td>Sphere, D</td>
<td>−0.040 ± 0.201</td>
<td>0.09</td>
<td>−0.460 ± 0.230</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cyl, DC</td>
<td>−0.035 ± 0.200</td>
<td>0.13</td>
<td>+0.203 ± 0.275</td>
<td>0.02</td>
</tr>
<tr>
<td>CR, mm</td>
<td>+0.002 ± 0.022</td>
<td>0.36</td>
<td>+0.000 ± 0.022</td>
<td>0.95</td>
</tr>
<tr>
<td>CCT, mm</td>
<td>−0.004 ± 0.004</td>
<td>&lt;0.001</td>
<td>−0.003 ± 0.004</td>
<td>0.42</td>
</tr>
<tr>
<td>ACD, mm</td>
<td>+0.028 ± 0.040</td>
<td>&lt;0.001</td>
<td>+0.004 ± 0.021</td>
<td>0.10</td>
</tr>
<tr>
<td>LT, mm</td>
<td>+0.015 ± 0.023</td>
<td>&lt;0.001</td>
<td>+0.029 ± 0.011</td>
<td>0.07</td>
</tr>
<tr>
<td>LP, D</td>
<td>−0.064 ± 0.291</td>
<td>0.06</td>
<td>−0.154 ± 0.264</td>
<td>0.51</td>
</tr>
<tr>
<td>VCD, mm</td>
<td>+0.017 ± 0.071</td>
<td>0.05</td>
<td>+0.145 ± 0.068</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AL, mm</td>
<td>+0.059 ± 0.070</td>
<td>&lt;0.001</td>
<td>+0.178 ± 0.079</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AL/CR</td>
<td>+0.007 ± 0.012</td>
<td>&lt;0.001</td>
<td>+0.023 ± 0.014</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Significant $P$ values (<0.05) in bold. Cyl, cylinder power.
with change in AL, SER, or AL/CR. Mean body height at baseline and follow-up, respectively, were 177.4 ± 5.5 and 179.1 ± 5.8 cm in males and 167.9 ± 5.0 and 168.8 ± 5.0 cm in females.

**Serum Vitamin D₃ Concentration**

Mean s-25(OH)D₃ concentration was 50.9 ± 19.2 nM (range, 16.9–107.3 nM), as measured in 89 of 93 participants at follow-up. Overall, 41.6% had sufficient levels (25.0–125.0 nM), 22.5% were mildly deficient (12.5–24.9 nM), and none were severely deficient (<12.5 nM).²² Those with a negative change in AL or LP. With a negative change in SER (P < 0.05) and with a negative change in AL or LP (P < 0.05). Bonferroni corrected pairwise comparison by Wilcoxon).

### DISCUSSION

This is the first report on longitudinal changes in refractive errors and ocular biometric parameters in a population of adolescents who had low myopia prevalence and were students in a high-performing education system. The main result was that emmetropic and low hyperopic eyes were still exhibiting coordinated ocular growth at 18 years of age. A stable refractive error was maintained through continued ocular axial growth and coordinated decrease in mean LP. Although most participants showed crystalline lens thickening, lens thinning appeared to still take place in some of the 18-year-old emmetropes and low hyperopes. Those with a more negative refractive error at baseline exhibited larger negative changes in refractive error over the 2-year period, and the negative changes were associated with excessive elongation of VCD and increase in LP.

The annual axial length growth in persistent emmetropes/low hyperopes at 18 years of age (median: +0.03 mm, range, -0.05 to +0.16) contradicts the report of Sorsby et al., who suggested ocular axial growth to cease at 13 years of age, and confirms findings reported for a small sample of Danish emmetropes aged 16 to 20 years (n = 16; median: +0.05 mm).²² It is important to note that most participants appeared to have reached full adult height at 18 years of age,²⁵ and no association was found between increases in height and changes in AL from 16 to 18 years of age. The annual percentage change in axial length (0.13%) was lower than reported from 11 to 14 years of age in a study of emmetropic schoolchildren (range, 0.24-0.28% per year).²⁷ Thus, continued coordinated eye growth in late adolescents is at a slower
TABLE 5. Multiple Linear Regression Showing the Association of Changes in SER With Changes in AL and LP, Adjusted for Sex. Model A Is Based on Data From Persistent Emmetropes/Low Hyperopes (n = 75), and Model B Is Based on All Participants (n = 93)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Estimate</th>
<th>2.5%–97.5% CI</th>
<th>P</th>
<th>Estimate</th>
<th>2.5%–97.5% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.048</td>
<td>0.00 to 0.09</td>
<td>0.03</td>
<td>0.050</td>
<td>0.01 to 0.09</td>
<td>0.02</td>
</tr>
<tr>
<td>Sex, females</td>
<td>−0.002</td>
<td>−0.05 to 0.05</td>
<td>0.95</td>
<td>−0.007</td>
<td>−0.05 to 0.04</td>
<td>0.79</td>
</tr>
<tr>
<td>AL change</td>
<td>−2.216</td>
<td>−2.60 to −1.84</td>
<td>&lt;0.001</td>
<td>−2.361</td>
<td>−2.68 to −2.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LP change</td>
<td>−0.413</td>
<td>−0.51 to (−0.32)</td>
<td>&lt;0.001</td>
<td>−0.416</td>
<td>−0.50 to (−0.35)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Significant P values (<0.05) in bold.

TABLE 6. Multiple Linear Regression Showing the Association of LP With AL and LT at Baseline (Model A) and at Follow-Up (Model B), Adjusted for Sex

<table>
<thead>
<tr>
<th>Variables</th>
<th>Estimate</th>
<th>2.5%–97.5% CI</th>
<th>P</th>
<th>Estimate</th>
<th>2.5%–97.5% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>32.562</td>
<td>24.76 to 40.36</td>
<td>&lt;0.001</td>
<td>32.867</td>
<td>25.00 to 40.74</td>
<td>&lt;0.001</td>
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<tr>
<td>Sex, females</td>
<td>0.491</td>
<td>0.10 to 0.88</td>
<td>0.01</td>
<td>0.591</td>
<td>0.19 to 0.99</td>
<td>0.004</td>
</tr>
<tr>
<td>AL</td>
<td>−0.989</td>
<td>−1.25 to −0.72</td>
<td>&lt;0.001</td>
<td>−1.001</td>
<td>−1.27 to −0.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LT</td>
<td>3.881</td>
<td>2.83 to 4.93</td>
<td>&lt;0.001</td>
<td>3.838</td>
<td>2.77 to 4.91</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Significant P values (<0.05) in bold.

FIGURE 3. Relationship between change in LP (D) and change in AL (mm) for those who had a (A) positive change in SER (>0.002 D; n = 35) and (B) negative change in SER (<−0.002 D; n = 58). The black dashed lines show the change in LP per 1-mm increase in AL required to maintain no change in SER (as in Fig. 2), assuming no changes in the other ocular components. Symbols represent the refractive status at follow-up (square: myopes, circle: emmetropes, diamond: hyperopes), and filled symbols represent those with a positive change of more than 0.25 D (in A) and negative change of more than 0.25 D (in B).

FIGURE 4. Relationship between LP (D) and AL (mm) at (A) baseline and (B) follow-up. The symbols represent the refractive error status, and the lines represent the linear regression per refractive error group (red square/solid line: myopes, blue circle/dotted line: emmetropes, black diamond/dashed line: hyperopes).
rate than that observed for children. The continued elongation of AL was mainly compensated for by a decrease in LP and a deepening of the anterior chamber. The latter is known to reduce the effect of LP.28 The annual loss in mean LP (−0.037 ± 0.15 D per year) was the same as that inferred in a cross-sectional study of mainly myopic Chinese adolescents from 14 to 18 years of age (annual decrease −0.038 D).10 The crystalline lens thickened for all myopes; however, 24% of the persistent emmetropes/low hyperopes exhibited negative changes in LP larger than 0.07 mm thinning. Assuming that the repeatability limit for the IOL-Master measurement of LT is ±0.02 mm,10 86% of the myopes increased more than 0.02 mm in lens thickness compared with 45% of the persistent emmetropes/low hyperopes. The lens is known to become thinner throughout childhood, reaching a minimum before reversing direction to become thicker, with earlier reversal time being associated with earlier myopia onset.29 The data presented here confirm that a delay in reversal time being associated with earlier myopia.13 Negative changes in LP were also associated with having a longer eye at baseline, but there were no associations with baseline crystalline LT or LP, contrary to studies in younger children that have reported both a long eye and a thin and weak crystalline lens as risk factors for developing myopia.15,37 The annual incidence of myopia and the negative change in LP (see Table 7) were comparable with reports of Caucasians in Northern Ireland from 12 to 13 through to 18 to 20 years of age,38 but lower than reported for Caucasians and East Asians in Australia from 12 to 17 years of age36 and for slightly older university students in China.25

More than 55% of the participants had lower serum vitamin D3 concentration than the recommended level of ≥50 nM,22 and there was no difference in serum vitamin D3 concentration between those with positive versus negative changes in refractive error. The absence of any apparent correlation with serum vitamin D3, combined with the low myopia frequency seen in this population,12 questions the suggested association between low vitamin D3 levels and increased risk of myopia development.39,40 That myopes had lower vitamin D3 concentration than nonmyopes may be related to the myopes preferring indoor activities, as a consequence of their refractive error. This is in line with Norwegian 16- to 19-year old myopes who reported spending more time indoors in the summer holiday and spending less time doing sports outdoors than nonmyopes.12

A small number of participants (n = 9) decreased in AL beyond the 95% limits of reproducibility of the IOLMaster 700 (±0.02 mm),10 as has been reported for some Northern Irish adolescents.41 This may partly be related to thickening or diurnal variations of the choroid.42 However, shrinkage of AL in response to myopia defocus, beyond what could be explained by measurement errors and thickening of the choroid, has been reported in animals of various species,53 and following atropine treatment in children.12,43,44

Strengths of current study were cycloplegic measures of both biometry and autorefraction, ensuring minimal influence from accommodation, and use of the exact same instruments to measure cycloplegic refractive errors and ocular biometric parameters at both baseline and follow-up, avoiding a possible source of measurement errors. Limitations were related to implementing the Gullstrand-Emsley lens model with a fixed relationship between the crystalline lens surface powers and a fixed equivalent refractive index for the lens rather than gradient indices.56,67 Any possible inaccuracies due to these simplifications are, however, similar to those in research using Bennett’s method for LP calculation,19 and are expected to affect baseline and follow-up data equally. Ocular biometry measures may have been taken at a different time point during the day at follow-up versus baseline, but any diurnal variation throughout the time interval of measurements (8 AM to 4 PM)
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is estimated to be considerably smaller than the changes reported here.\textsuperscript{43} The incidence and reduction rates of myopia and hyperopia, respectively, would need to be confirmed in a larger sample. The reliability and repeatability of Huvitz HRK-8000A is not reported; however, measurements from the Huvitz HRK-7000A are shown to have sufficient test-retest reliability and are in agreement with other autorefractors.\textsuperscript{38}

The results from this longitudinal study of changes in refractive errors and ocular biometric parameters from 16 to 18 years of age in students in a high-performing education system\textsuperscript{12} show continued ocular axial growth in persistent emmetropes/low hyperopes. A stable refractive error was maintained by a coordinated decrease in LP, confirming that lens development may play a pivotal role in protecting against myopia.

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\textbf{References}