Longitudinal analysis of axial length growth in a German cohort of healthy children and adolescents

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Abstract

Purpose: To generate continuous growth curves for axial length (AL) in German children. We hypothesise that percentile curves of AL can be used as a predictive measure of myopia.

Methods: In this longitudinal and cross-sectional LIFE Child Study, children’s non-cycloplegic refraction data was collected using the Zeiss i.Profiler plus while AL was measured using the Haag-Streit Lenstar. Reference growth curves were estimated as a continuous non-parametric function of age.

Results: Data from 4511 visits of 1965 participants (1021 boys and 944 girls) between 3 and 18 years of age were analysed. For all ages and percentiles, the estimated AL was higher in boys than girls. AL differences between boys and girls were most pronounced in the 98th percentile at 3 years of age, being 0.93 mm longer eyes in boys. This difference decreased to 0.21 mm at 18 years of age. While the lower percentiles of AL reach their final value around age 13, the 50th percentile was still increasing by 0.05 mm per year until the end of the observation period. While, in general, children with longer eyes are more likely to develop myopia, this relationship is weaker between the ages of 5 and 8.

Conclusion: The LIFE Child Study data provides European AL data. In both Germany and China, AL has comparable growth rates when the baseline ALs are compared as percentiles. Thus, percentile curves of AL can be used as a predictive measure for the likelihood of developing as well as the progression of myopia.

Introduction

At birth, infants show a wide range of refractive errors, roughly following a Gaussian distribution.1 Up to 6 years of age, the emmetropization process can be observed.2 This is a mechanism to control eye growth in order to become emmetropic or a low hyperope. Beyond the age of 6 years, the trend changes in many populations. Stable refraction is often followed by a myopic shift, which slows down after some years and asymptotes towards a stable myopic refraction.3

At birth, the eye is approximately 17 mm long, and generally grows to about 23 mm in adolescence.4 The elongation is greatest during the first year of life, with decreasing growth rates towards the end of this first year. Jin et al. describe the axial length growth as a logarithmic function, which asymptotes towards the final length. Their final observed length was 24.35 mm at 15 years. At this age, most of the children in their population were myopic.5 These data originate from a cohort of Chinese children of all refractive states. Therefore, their final AL does not represent a common end point of low hyperopia, but axial elongation due to myopia development.6 Hence, the assessment of AL is heavily dependent on the underlying population and the respective prevalent conditions must be taken into

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account, so this final AL cannot necessarily be adapted to other ethnicities.

Hashemi et al. reported that AL is gender-dependent, with longer eyes in boys. Interestingly, the growth rate in their study showed accelerations for boys between 8—10 years and 14—16 years of age, and for girls between 6—7 years and 11—13 years of age. After 14 years, only small changes were observed in either group, and these may be due to myopia development.

The prediction of myopia development and mechanisms to control myopia progression are of increasing scientific interest, mainly due to the increasing prevalence of myopia, especially in east Asia but also in other countries. In combination with the success that has been achieved in slowing myopia progression, for example with atropine eye drops and orthokeratology, a method needs to be developed to predict future myopia progression in the eyes of children.

Axial growth rates are higher in new myopes, but also before myopia onset in children who later go on to become myopic. There is a strong correlation between myopia and axial length, and yet axial length increases disproportionally to myopia at the beginning. Due to the emmetropization processes, excessive elongation of the eye may be compensated by an increased rate of decline of lens power in the early phase. Breslin et al. showed that axial elongation between 6—10 years of age is higher than that between 12—16 years.

While there is data concerning axial elongation in the growing eye with respect to myopia development for Asian populations, there is little data for individuals in central Europe. Tideman et al. used a relatively new approach to predict myopia progression using centile curves. They combined data from three different studies conducted in England and the Netherlands (Generation R Study, Avon Longitudinal Study and Rotterdam Study III) with varying study populations, settings, instruments and methods, as well as different birth years which could result in a different prevalence of myopia. However, AL data were only available for the ages of 6, 9 and 15 years.

Therefore, there is a lack of continuous data showing axial elongation in the growing eye of central Europeans. This would allow the generation of more accurate centile curves for this population. Accordingly, this study aims to develop continuous growth curves showing axial length in German children. We hypothesise that percentile curves of axial length can be used as a predictive measure of myopia.

Methods
Study design
This analysis is part of the LIFE Child Study, which was approved by the Ethical Committee of the Medical Faculty of the University of Leipzig (Reg. No. 264-10-ek) and registered with the trial number NCT02550236. The study design has been described elsewhere. The study site is in Leipzig, Germany.

Participants were invited to present once a year. At each visit, a consent form was signed by the parents and, from the age of 12 years, by the children. Data were analysed from 4511 visits of 1965 participants (1021 boys and 944 girls). Data were collected between 2014 and 2018.

There are ethical restrictions on sharing pseudonymised data sets. The LIFE Child Study collects potentially sensitive information. Publishing data sets is not covered by the informed consent provided by the study participants. Furthermore, the data protection concept of LIFE requests that all (external and internal) researchers interested in accessing data sign a project agreement. Researchers that are interested in accessing and analysing data collected in the LIFE Child Study may contact the data use and access committee (dm@life.uni-leipzig.de).

Measurements
AL was measured with the Lenstar (Haag-Streit, haag-streit.com) and was defined as the distance between the tear film and retinal pigment epithelium. To conduct the measurement, the chin was placed on the chinrest, and the forehead was pressed against a strap. Participants gazed at a fixation light. For each patient, three measurements were obtained for each eye.

Refraction was measured three times in each eye in a darkened room without cycloplegia with the Zeiss i.Profiler plus (Carl Zeiss Vision GmbH, zeiss.com), which is based on a Hartmann-Shack sensor. The room was darkened to maximise pupil size. The refractive error was analysed for a 3 mm pupil and a vertex distance of 12 mm. Myopia was defined as a spherical equivalent <−0.75 D.

Statistical analysis
The World Health Organization (WHO) recommends constructing growth curves as a continuous age-varying distribution described by different parameters dependent on age. Therefore, we applied generalised additive models for location, shape and scale as implemented in the R package GAMLSS (gamlss.com) to create reference curves, which was one of the WHO’s favoured methods for modelling growth curves. We have used the same model to generate centile curves for refraction. To facilitate the comparison with the results by Tideman et al. and Sanz Diez et al., we present the 2nd, 5th, 10th, 25th, 50th, 75th, 90th, 95th and 98th percentiles. To assess the relationship between refractive state as an outcome, eye length and age, we used a logistic regression model with the z-score of the eye length and a
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spline base of age with knots at 25%, 50% and 75% of the data as independent variables.

For AL, the median of all three measurements from the right eye was used for the estimation of the percentile curves. The spherical equivalent (SE) refractive error of the right eye was calculated as sphere + ½ cylinder power using the median result for the three measurements taken with the Zeiss i. Profiler plus.

The eye length growth was calculated from two consecutive measurements of the same proband, which were usually taken annually (equation 1). Measurement pairs less than 6 months or more than 1.5 years apart were excluded, and the AL change was assigned to the mean age of the two visits.

Annual AL change

\[
\text{Annual AL change} = \frac{\text{eye length at 2nd visit} - \text{eye length at 1st visit}}{\text{number of days between 1st and 2nd visit}} \times 365.25 \text{ days}
\]

(1)

Results

Correlation of axial length (AL) with spherical equivalent (SE)

Correlation coefficients for AL with the SE was \(R^2 = 0.32\) and \(R^2 = 0.37\) for boys and girls, respectively, with \(p < 0.0001\) and \(\beta = -0.43\) for boys and \(\beta = -0.44\) for girls. For each dioptre change, AL was on average 0.43 mm/0.44 mm higher. The number of participants, divided into first and follow up visits for each age group, is shown in Table 1. This also shows myopia prevalence, which increases with age.

Table 1. Number of first and follow up visits for each age group and myopia prevalence

| Age group [years] | First visits | Follow up visits | Myopia prevalence | 95% confidence interval |
|-------------------|--------------|------------------|-------------------|------------------------|
| 2.89–2.99         | 4            | 0                | 0%                | 0%–60.24%              |
| 3.00–3.99         | 96           | 2                | 2.08%             | 0.25%–7.32%            |
| 4.00–4.99         | 239          | 36               | 3.04%             | 1.32%–5.91%            |
| 5.00–5.99         | 215          | 145              | 2.56%             | 1.18%–4.80%            |
| 6.00–6.99         | 167          | 191              | 3.16%             | 1.59%–5.59%            |
| 7.00–7.99         | 128          | 223              | 4.65%             | 2.68%–7.44%            |
| 8.00–8.99         | 124          | 218              | 3.90%             | 2.09%–6.58%            |
| 9.00–9.99         | 149          | 217              | 6.91%             | 4.52%–10.03%           |
| 10.00–10.99       | 130          | 219              | 11.11%            | 7.98%–14.93%           |
| 11.00–11.99       | 138          | 223              | 16.08%            | 12.35%–20.41%          |
| 12.00–12.99       | 171          | 204              | 18.68%            | 14.81%–23.07%          |
| 13.00–13.99       | 98           | 236              | 21.69%            | 17.37%–26.51%          |
| 14.00–14.99       | 92           | 209              | 22.79%            | 18.12%–28.02%          |
| 15.00–15.99       | 94           | 185              | 23.60%            | 18.63%–29.15%          |
| 16.00–16.99       | 78           | 135              | 26.42%            | 20.61%–32.89%          |
| 17.00–17.99       | 42           | 103              | 25.87%            | 18.92%–33.86%          |

Annual change in axial length (AL) with age

The mean annual change of the median AL was 0.3 mm per year in 3-year-old children. This decreased to 0.1 mm per year in 13+ year-old children (see Figure 1). The standard error for measurement of eye length was ±0.04 mm. While the 2nd and the 50th percentiles of annual AL change run almost on the same level from 7 years of age onwards for each gender, there are differences in the 98th centile. Here, boys show a higher yearly increase in AL between ages 3 and 9 compared with girls, and the trend changes from age 9 onwards. The 2nd centile is almost 0 for boys of all ages and decreases from 0.1 to 0 between the ages of 3 and 7 for girls. Hence, there are always some children with no change in AL between the two consecutive measurements.

Reference curves for axial length (AL) over age

Separate reference intervals for axial length with respect to age were created for boys and girls. Figure S1 shows the 2nd, 5th, 10th, 25th, 50th, 75th, 90th, 95th and 98th centiles of axial elongation with age from 3 to 18 years. The figure was created based on the method of Sanz Diez et al. to allow easy comparison of the results from each study.

Figure 2 shows the percentile curves of AL for girls and boys on the left side and myopia prevalence as a function of age for each of the presented centiles on the right. The solid lines show the LIFE Child Study results. In comparison, the results of Sanz Diez et al. are shown as dashed lines. In the German cohort, for all ages and all percentiles calculated, AL was higher in boys compared with girls. In our data, the 2nd and 50th percentiles run almost parallel for each gender group. The difference in AL between boys and girls is highest for the 98th centile at 3 years of age, with boys having 0.91 mm longer eyes, although this difference decreases to 0.24 mm at 18 years of age. For both genders and all centiles, the increase in AL is highest between 3 and 11 years of age. In the 2nd centile, there is only marginal eye growth in boys and girls after the age of 13 years (less than 0.05 mm per year) and AL asymptotes towards its final length. For the 50th centile, the eye growth rate in boys and girls is about 0.05 mm per year from the age of 13 years up to the end of the observation period. In the 98th centile, growth rates are highest below the age of 11 years, but remain high up to the end of the observed period with rates of more than 0.1 and 0.15 mm per year for boys and girls, respectively, after 13 years of age.

Prevalence of myopia as a function of axial length (AL) (likelihood to develop myopia)

On the right side of Figure 2, the prevalence of myopia is shown as a function of AL centiles. This graph shows the
likelihood of having or developing myopia for a percentile of AL, as shown in the left hand graph. In the LIFE Child Study at 16 years of age, 2% and 6% of boys and girls, respectively, reached myopic refractive values of more than 0.75 D in the 5th centile. On the other hand, the 95th centile shows that 64% of boys and 59% of girls developed myopia by 16 years of age. Between 3 and 5 years of age, the likelihood of having myopia increases with age, especially above the 50th centile of AL, independent of gender. For the 95th centile, at 3 years of age 5% of males and 4% of females developed myopia, and by age 5 the prevalence has increased to 16% and 8% for boys and girls, respectively. From 5 to 7 years of age, an inverse trend is observed in the boys’ AL centiles, where myopia prevalence decreased compared with the range between 3 and 5 years of age. However, the most pronounced differences are located in the higher centiles. At age 7, 11% of boys are myopic in the 95th centile. For girls, a plateau is reached between ages 5 and 7, with a relatively stable likelihood of being myopic across all centiles. Above 7 years of age, the trend is reversed again and myopia prevalence increases with age for all centiles of AL in both boys and girls. Thus, the increase of myopia prevalence is greater in the higher centiles of axial length. Especially between 8 and 12 years of age, the prevalence increases rapidly with age in the 75th, 90th and 95th centiles for girls, and the 90th and 95th centiles for boys.

Discussion

The decrease in myopia as a function of AL percentiles for boys might be due to the fact that there are relatively few children with myopia in each percentile, due to the low prevalence of myopia at this age. Accordingly, small fluctuations could cause this observation. At a younger age, the measurement error due to findings being obtained without cycloplegia is likely higher than with older children, and could cause fluctuations in responses.22

The relatively stable, reverse trend of myopia prevalence between 5 and 7 years of age could be explained by the findings of Rozema et al. They noted that AL elongation can be observed before myopia onset.12 Between 5 and 8 years of age, the AL was increased in some children, although myopia had not yet developed. After 8 years of age, myopia onset can be measured in most of the children, and therefore, the association between the AL centile and myopia prevalence increased.

Correlation of axial length (AL) with spherical equivalent (SE)

In a cohort from Northern Ireland, McCullough et al. found an annual AL change of 0.12 mm in the 50th centile of AL (0.11 in the 1st centile and 0.15 in the 99th centile) in children between 6 and 16 years of age. However, their AL measurements were not analysed continuously with age, but categorized into four age groups. Therefore, a direct comparison of data is not possible.23 However, their observed annual change is comparable to the annual change in AL of the present investigation in 6 to 16 year old children, which was 0.115 mm per year in the 50th centile, averaged across both genders.
Axial length (AL) in comparison to other studies from Europe and China

In Europe, Tideman et al. were the first to estimate AL centile curves. They presented combined data from three different study cohorts, two of which examined axial length in children. Data on 6- and 9-year old children were collected in the Netherlands, and data on 15-year-old children were collected in the UK. The 50th centiles of our data are very similar to those presented by Tideman et al., as can be seen in Table 2. This underlines that boys have, in general, longer eyes than girls.

As the age-conditional distributions of ALs for 6-, 9- and 15-year-old children are very similar to the data from Tideman et al., our findings are likely to reflect central European populations. Therefore, they complement the results of Tideman et al., as those authors analysed specific time points, but not continuous data covering the entire age span, from 3 to 18 years.

Whereas the LIFE Child Study data is very similar to other findings collected in central Europe, they differ from results obtained in China. The cohort analysed by Sanz Diez et al. from the city of Wuhan included 5 to 16 year old children. At 5 years of age, the differences in mean AL between ethnicities were 0.39 mm in girls and 0.30 mm in boys, as shown in Table 3, which might be due to axial elongation in Chinese preschool children prior to developing myopia. This difference increased up to the age of 16 years, with about a 1.5 mm difference being found in boys and girls. At 5 years of age, the myopia prevalence in the Wuhan cohort was 4.00% and 6.32% for girls and boys, respectively. This increased to 87.93% and 93.44% of 16 year old girls and boys, respectively. At 5 years of age, myopia prevalence in the LIFE Child Study cohort was 4.70% for both genders, which is similar to the results from Sanz Diez et al. This subsequently increased to 28.40% at the age of 18, which is substantially less than the Wuhan cohort.

As AL is linked with refractive error, the longer eyes seen in China are consistent with the higher local prevalence of myopia. However, at the age of 5 years, there is only a small difference in the prevalence of myopia between the LIFE Child Study cohort and the Chinese cohort, and yet a difference in

Figure 2. Left: Continuous centile curves of axial length with respect to age for the LIFE Child Study. Right: Prevalence of myopia as a function of the axial length centiles. Red and blue curves indicate data from girls and boys, respectively. The solid lines show the LIFE Child Study results (Germany) while the dashed lines indicate findings from a cohort in Wuhan, China.© 2021 The Authors. Ophthalmic and Physiological Optics published by John Wiley & Sons Ltd on behalf of College of Optometrists Ophthalmic & Physiological Optics 41 (2021) 532–540
AL can already be observed. This is in line with the findings of Rozema et al. showing that axial elongation can be observed before myopia onset.12 Consequentially, in younger children, the ALs in both ethnicities are likely to be similar, as shown by Lu et al., who examined the AL of a cohort of Chinese children from the Shandong province.17 The respective data was collected from children aged ≥4 years. Table 3 shows increasing differences between ethnicities with age. In general, the Shandong cohort exhibits longer eyes than the LIFE Child Study cohort, but shorter axial lengths than the Wuhan subjects.8 This might be due to the inclusion of children from both rural and urban regions, with the children from rural areas having shorter eyes.17 In a cohort of 3-year-old children in Singapore, consisting of 55% Chinese, 26.1% Malay and 18.9% Indian children, Foo et al. recorded a mean AL of 21.73 mm for both genders,24 whereas in our study population, the mean axial length at 3 years of age was 21.86 mm. These results also support the hypothesis of similar ALs in very young Chinese and German children.

Comparison of the likelihood to develop myopia depending on axial length (AL) in China and Germany

Sanz Diez et al. also published findings on myopia prevalence as a function of AL from the Wuhan cohort.8 Their data presents a continuously increasing prevalence of myopia for each centile of AL up to 12 years of age, as shown by the dashed lines in Figure 2 (right). Thereafter, the prevalence of myopia in girls remained stable for each centile of AL until age 15. However, for boys, a further increase in myopia prevalence could be observed. While our model included age as a continuous explanatory variable, Sanz Diez et al. estimated myopia prevalence for the discrete age groups of 6, 9, 12 and 15 years. Therefore, it cannot be excluded that a weaker relationship between myopia prevalence and AL for a specific age group could be found if the data was analysed accordingly. A dip in the prevalence of myopia (as a function of AL) at 8 years of age may be present in China (as was observed here), but this is not verifiable due to a lack of data.

As the prevalence and the degree of myopia is much higher in China than Germany, the association between higher centiles of AL with myopia will be stronger in China. For both sexes, the 75th centile of AL in China is comparable to the 98th centile in Germany. For example, at 6 years of age, the 75th AL centile in Chinese girls is 23.04 mm, which corresponds approximately to the 98th centile (23.16 mm) in German girls. At the age of 15, the same percentiles correspond to an AL of 25.20 and 25.18 mm in Chinese and German girls, respectively. The same observations are true in boys, that is the 75th centile for boys and girls in Germany is comparable to the 25th centile in the

| Table 2: 2nd, 25th, 50th, 75th and 98th centiles of axial length of children aged 6, 9, 12 and 15 years in China and Europe |
|---|---|---|---|---|---|---|---|
| | Female | | | Male | | |
| | LIFE Child | Tideman et al.9 | Sanz Diez et al.8 | LIFE Child | Tideman et al.9 | Sanz Diez et al.8 |
| | Germany | Europe | China | Germany | Europe | China |
| 6 years | | | | | | |
| 2 | 20.76 | 21.08 | 20.97 | 21.08 | 21.44 | |
| 25 | 21.6 | 22.13 | 22.03 | 22.13 | 22.14 | 22.55 |
| 50 | 22.00 | 22.61 | 22.54 | 22.61 | 22.59 | 22.99 |
| 75 | 22.39 | 23.08 | 23.04 | 23.08 | 23.01 | 23.50 |
| 98 | 23.16 | 23.00 | 23.07 | 24.00 | 25.00 | |
| 9 years | | | | | | |
| 2 | 21.21 | 21.53 | 21.86 | 21.53 | 22.21 | |
| 25 | 22.14 | 22.59 | 23.16 | 22.59 | 22.83 | 23.70 |
| 50 | 22.59 | 23.10 | 23.72 | 23.10 | 23.31 | 24.32 |
| 75 | 23.04 | 23.61 | 24.31 | 23.61 | 23.79 | 24.89 |
| 98 | 23.97 | 24.65 | 25.55 | 24.65 | 25.96 | |
| 12 years | | | | | | |
| 2 | 21.48 | 21.83 | 22.24 | 21.83 | 22.86 | |
| 25 | 22.48 | 22.90 | 23.57 | 22.90 | 24.21 | |
| 50 | 22.99 | 23.44 | 24.16 | 23.44 | 24.83 | |
| 75 | 23.51 | 24.00 | 24.76 | 24.00 | 25.44 | |
| 98 | 24.64 | 25.17 | 26.13 | 25.17 | 26.70 | |
| 15 years | | | | | | |
| 2 | 21.57 | 21.99 | 22.45 | 21.99 | 22.76 | |
| 25 | 22.63 | 23.06 | 23.83 | 23.06 | 23.17 | 24.39 |
| 50 | 23.19 | 23.63 | 24.37 | 23.63 | 23.65 | 25.01 |
| 75 | 23.8 | 24.23 | 25.20 | 24.23 | 24.21 | 25.80 |
| 98 | 25.18 | 25.57 | 27.32 | 25.57 | 27.78 | |

Data from Europe comprise findings from the present study (LIFE child) as well as the results of Tideman et al. (countries: The Netherlands and UK).9 Data from China are from Sanz Diez et al. (Wuhan, China).8
Chinese data. Even though the AL graphs of the two countries are labelled with different centiles, they run approximately parallel at an equivalent level. Although AL increases slightly faster in China than Germany between 6 and 9 years of age, in general, the graphs run almost parallel afterwards for all percentiles.

At the age of 15 years, approximately 64% of German girls in the 98th centile and 68% at the 75th centile in China are myopic (for German boys 73% and Chinese boys 63%). Hence, the link between AL (in absolute numbers) and the likelihood of myopia seems to be very similar in both ethnicities. At the age of 6 years, approximately 11% of German girls at the 98th centile and 3% of Chinese girls at the 75th centile are myopic. This difference in these younger age groups may be because refraction data in China was obtained under cycloplegia whereas cycloplegia was not used in our study. In younger children, this would lead to an overestimation of myopia in Germany.\(^{22}\) When comparing the graphs one must consider that the smoothed curves from the study by Sanz Diez \(et\ al.\)^\(^8\) consist of only three measurement points, whereas the LIFE Child Study delivers more precise curves with continuous data across ages. The 98th German centile and the 75th Chinese can be compared in Table 2. For the lower centiles, which run on the same level, the link between AL and likelihood of myopia was weaker. For example, the 50th centile of AL in China and the 90th centile in Germany run almost on the same level. At this centile, at age 15, 46% of Germany girls (49% boys) are myopic as are 44% of Chinese girls (40% boys). The 25th centile of AL in China and the 75th centile in Germany also run parallel. However, while in China approximately 20% of girls at the 25th AL centile are myopic by age 15, in Germany, the prevalence reaches 32% at the 75th AL percentile for the same age (19% of boys in China and 30% in Germany). Therefore, at this centile with relatively few expected myopic children, the probability of myopia has likely been overestimated in Germany due to the lack of cycloplegia.

**Limitations**

At the higher AL percentiles, and thus likely myopia cases (as a function of AL), the number of children included here is small. Sample sizes varied in each age group, as well as between genders, and that may affect the percentiles and prevalence of myopia. One would also expect a similar development in the likelihood of becoming myopic in girls and boys up to 7 years of age. For these younger age groups it is desirable to gather more data from larger cohorts to improve the curves and the predictive values for the likelihood of myopia.

In addition, we did not use cycloplegia to measure refraction. Rauscher \(et\ al.\) showed that the SE measured with the Zeiss i. Profiler plus was 0.55 D lower without cycloplegia compared with the cycloplegic refraction.\(^{25}\) Thus, it is likely that myopia was overestimated in the present investigation. However, this bias is similar across refractive states, as shown by Rauscher \(et\ al.\). Therefore, it should have no influence on the centile curves of AL with age. The prevalence of myopia for each AL centile as a function of age is likely to have been overestimated compared with a cycloplegic refraction. Additionally, the difference

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**Table 3.** 50th centile of axial length (AL) for children in the LIFE Child Study in Germany and two cohorts in China

| Age (years) | AL Female 50th centile | AL Male 50th centile |
|-------------|------------------------|----------------------|
| Germany | China, Wuhan\(^8\) | China, Shandong\(^17\) | Germany | China, Wuhan\(^8\) | China, Shandong\(^17\) |
| 3 | 21.33 | 21.96 | 21.98 | – | – |
| 4 | 21.55 | 22.17 | 22.02 | 22.41 | 22.71 | 22.52 |
| 5 | 21.78 | 22.56 | 22.25 | 22.61 | 23.03 | 22.65 |
| 6 | 22.00 | 22.84 | 22.39 | 22.80 | 23.31 | 23.04 |
| 7 | 22.21 | 23.40 | 22.83 | 22.96 | 23.88 | 23.28 |
| 8 | 22.41 | 23.73 | 23.04 | 23.10 | 24.26 | 23.61 |
| 9 | 22.75 | 23.92 | 23.29 | 23.23 | 24.44 | 23.88 |
| 10 | 22.88 | 24.15 | 23.54 | 23.34 | 24.69 | 23.97 |
| 11 | 22.99 | 24.16 | 23.69 | 23.44 | 24.82 | 24.14 |
| 12 | 23.07 | 24.29 | 23.81 | 23.53 | 24.81 | 24.37 |
| 13 | 23.14 | 24.44 | 24.17 | 23.59 | 24.96 | 24.69 |
| 14 | 23.19 | 24.50 | 24.36 | 23.63 | 25.15 | 24.63 |
| 15 | 23.25 | 24.73 | 24.57 | 23.67 | 25.19 | 24.76 |
| 16 | 23.29 | – | 24.43 | 23.72 | – | 24.81 |
| 17 | 23.33 | – | 24.27 | 23.77 | – | 24.69 |

The cohort in the city of Wuhan covered the urban region,\(^8\) while the Shandong study included both rural and urban regions.\(^17\)
between cycloplegic and non-cycloplegic refraction is higher in younger children and but reduced in older children.\textsuperscript{22} Therefore, a limitation of our study is the prediction of myopia prevalence in the younger age groups and the lower centiles with few myopia cases. For older ages and higher centiles, predictions of the likelihood of myopia should become more accurate.

While AL is the most important determinant of myopia, it is not the only parameter involved in refractive error development. The principal determinant of myopic maculopathy in adults is not necessarily a refractive error less than \(-5.0\) D, but rather an AL exceeding \(25.3\) mm in women and \(25.9\) mm in men.\textsuperscript{26} In cases with long ALs but no or little myopia, the cornea is flatter. Therefore, to understand the relationship between refractive error and AL, corneal power should also be considered. While analysing this aspect is beyond the scope of this paper, we will consider a complementary paper showing AL curves for different corneal powers. Additionally, while the LIFE Child Study and Sanz Diez et al.\textsuperscript{8} used the Lenstar biometry device, Lu et al.\textsuperscript{17} and Foo et al.\textsuperscript{24} used the IOLMaster to measure AL. In an adult population, there is a measurement difference of approximately \(0.01\) mm between the two devices, with the IOLMaster showing slightly longer AL measurements. However, this measurement difference is clinically insignificant.\textsuperscript{19}

**Conclusion**

In general, AL is longer in boys than girls. This difference is higher for the higher centiles and in younger children. While the lower AL centiles asymptote towards the final AL after 13 years of age, there is a small continuous growth in the 50\textsuperscript{th} centile of 0.05 mm per year from the age of 13 years up to the end of the observation period. In the higher centiles, there is an even higher annual increase in AL for both boys and girls.

Children with longer eyes are more likely to develop myopia. The likelihood of developing myopia increases in general with age. This relationship is weaker between the ages of 5 and 8 years. This might be due to the onset of school myopia, which can be observed as increased AL first, before myopia becomes manifest. Some years after increased elongation of the eye, children start to exhibit myopia. This supports the findings of Rozema et al., who showed that an increase in AL can be observed before the onset of myopia.\textsuperscript{12}

The results of this investigation are very similar to the findings of a previous European study.\textsuperscript{9} However, our data stems from a single cohort and was analysed as continuous data.\textsuperscript{9}

When comparing our data with findings from China, the ALs are similar in children around 3 years of age.\textsuperscript{24} Thereafter, the ALs in China become longer with age compared to those in Germany. If only children with the same AL are compared, then the state of refraction is very similar for each ethnicity at the higher centiles.\textsuperscript{22} It would be of interest to compare the likelihood of developing myopia in different ethnicities for equivalent centiles of AL using the same refractive test methods.

This study supports and implements the application of centile curves of AL as a predictive measure of the likelihood for the development and progression of myopia. Therefore, these data, as the first European dataset over the entire age span of 3–18 years, are highly relevant for the early detection of myopia.

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**Conflict of interest**

S. Wahl and P. Sanz Diez are employees of Carl Zeiss Vision International GmbH; however, none of the authors has any financial or conflicting interests concerning the content of this research, which was conducted following the rules of neutral scientific practice.

**Author contributions**

Carolin Truckenbrod: Conceptualization (equal); Data curation (supporting); Investigation (equal); Methodology (equal); Writing-original draft (lead); Writing-review & editing (lead). Christof Meigen: Conceptualization (equal); Formal analysis (equal); Methodology (equal); Software (equal); Validation (equal); Visualization (equal); Writing-original draft (equal); Writing-review & editing (equal). Manuela Brandt: Data curation (lead); Writing-review & editing (supporting). Mandy Vogel: Methodology (equal); Software (equal); Writing-review & editing (equal). Pablo Sanz Diez: Writing-review & editing (equal). Siegfried Wahl: Supervision (equal); Writing-review & editing (equal). Anne Jurkatat: Investigation (equal); Resources (equal). Wieland Kiess: Funding acquisition (equal); Project administration (equal); Resources (equal); Supervision (equal).

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**Supporting Information**

Additional Supporting Information may be found in the online version of this article:

Figure S1. Left: Continuous centile curves of axial length over age of the LIFE Child study. Right: Prevalence of Myopia as a function of the axial length centiles. The solid lines show the LIFE Child results (Germany) and the dashed lines the results form a cohort in Wuhan, China.12