

BMJ Open Axial length elongation in primary school-age children: a 3-year cohort study in Shanghai

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ABSTRACT

Objective To investigate the axial length (AL) elongation in primary school-age children during 3-year follow-up period and evaluate the associations of AL elongation with spherical equivalent (SE), AL at baseline, body height and weight.

Design A 3-year observational cohort study from 2014 to 2017.

Setting Jinshan Hospital of Fudan University in Shanghai.

Methods A total of 452 children successfully completed their measurements in the 3-year follow-up period. The mean age of those children was 6.9±0.7 years, ranging from 6 to 8 years, and 217 (42.7%) were boys. AL was measured with an ocular biometry system. Refractive error was measured using an auto-refractor without cycloplegia.

Results The mean changes of ALs were 0.27±0.28 mm, 0.52±0.40 mm and 0.89±0.51 mm over 1, 2 and 3 years, respectively. The mean changes of SEs were -0.27±0.80 D, -0.56±1.00 D and -0.95±1.41 D over 1, 2 and 3 years, respectively. Multivariate linear regression analysis revealed that mean change of AL was associated with mean change of SE at all points (all p<0.001). In addition, linear regression analysis revealed that AL elongation in the 3-year follow-up period was associated with AL at baseline (R²=0.009, p=0.045).

Conclusions AL elongation is relatively high in the primary school-age children in Jinshan District, Shanghai. Effect strategies are needed to control AL elongation.

INTRODUCTION

Myopia is becoming a major epidemic problem and has affected a significant proportion of human population, especially school-age children.¹⁻³ It is reported that 4758 million people will suffer from myopia and 938 million people will suffer from high myopia in 2050, approximately accounting for 50% and 10% of the global population, respectively.⁴ The prevalence of myopia in children is especially high for East and South-east Asian, around 80%–90% in children at the age of 17 and 18, whereas 10%–20% of children can have high myopia.⁵ Furthermore, with the decreasing age of myopia onset, children with early-onset myopia will progress for a longer duration and are likely to develop high myopia,⁶ although myopia

Strengths and limitations of this study

- This is a 3-year observational cohort study in Jinshan District, Shanghai, from 2014 to 2017.
- Those children who continuously attended their measurements in the 3-year follow-up period were analysed in the present study.
- This study has a small sample size, thus further studies with larger sample are warranted.

may tend to stabilise at approximately 16 years.⁷

Axial length (AL), one of the ocular anatomic dimensions, is an important variable for the optical quality of the image on the retina of eye.⁸ Excessive AL elongation will lead to developing myopia, which is a major cause of visual impairment such as retinal detachment, myopic macular degeneration and choroidal neovascularisation.⁹⁻¹⁰ Controlling AL elongation of child is crucial to preventing myopia and reducing axial elongation-related myopic complications. However, there are few prospective cohort studies with relatively long follow-up that evaluate AL elongation. Some investigations have reported that the annual AL elongation varies from 0.26 to 0.38 mm in primary school-age children across different regions in China.¹¹⁻¹³ Furthermore, most attention has been paid on the effect of body height and weight on myopia. Cordain *et al*¹¹ have found that myopes are typically taller and heavier. Some associations were found between height and AL in Asian adults and children.¹²⁻¹³ So the relationship of AL elongation with body height and weight in primary school-age children in China still needs more understanding. Such information will help to determine the appropriate time for myopia intervention among Chinese children in the future.

The purpose of this study was to investigate the AL elongation in primary school-age children during 3-year follow-up period, and evaluate the associations of AL elongation with



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sphericalequivalent (SE), AL at baseline, body height and weight.

METHODS

Subjects

This is a 3-year cohort study in Jinshan District, which is located in the southwest of Shanghai, China. One primary school was selected, and children of grades 1 and 2 were included in the study. The exclusion criteria were: a history of severe ocular diseases (eg, cataract, glaucoma) and surgeries; orthokeratology lens correction; failure to cooperate with the examinations. A total of 508 children successfully completed the ocular examinations at baseline; however, 452 (89.0%) children continuously attended their measurements in the 3-year follow-up period, including 414 (81.5%) children without myopia at baseline. Among those children, the mean age was 6.9 ± 0.7 years, ranging from 6 years to 8 years, and 217 (42.7%) were boys.

Written informed consent was obtained from the parents and guardians of all children.

Examination

The annual visit was completed between September 1 and October 30 from 2014 to 2017. According to our previous study,¹⁴ refractive error was measured with an auto-refractor (RK-F1; Canon Corporation, Tokyo, Japan) under non-cycloplegic conditions. The mean value of the three good measurements was then used for analysis. AL was measured with an ocular biometry system (IOL Master; Carl Zeiss Meditec, Oberkochen, Germany). The mean value of the five good measurements was then used for analysis.

Furthermore, body height and weight were recorded for all children. The height was determined to the nearest 0.1 cm in a standardised manner without shoes. The weight was measured to the nearest 0.1 kg without thick clothes.

Statistical analysis

Only children who had completed all the four measurements during the 3-year follow-up period were included in analysis, while those children who lost one or more interviews were not included in analysis. Both eyes of each child were examined, and only data from the right eye was used for analysis. Based on refraction without cycloplegia,¹⁴ myopia was defined as $SE \leq -1.00$ D, and non-myopia was defined as $SE > -1.00$ D.

SPSS V.17.0 software was used for data analysis. One-way analysis of variance with the Bonferroni post-hoc test was used to analyse the differences of covariates and their mean changes among different points. Independent t-test was used to analyse the differences of covariates and their mean changes between genders. Multivariate linear regression analysis was performed to assess the associated factors for AL and its change. Linear regression analysis was performed to assess the relationship between AL

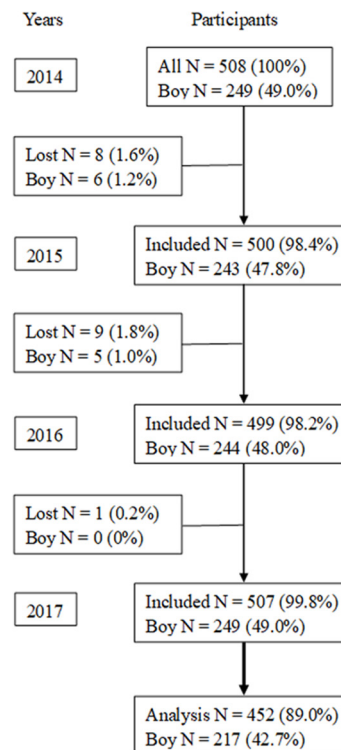


Figure 1 A flowchart illustrating the primary school-age children at each point of the study.

elongation in the 3-year follow-up period and AL at baseline in 2014, SE change in the 3-year follow-up period and SE at baseline in 2014, SE change and AL elongation in the 3-year follow-up period. All p values were two-sided and considered statistically significant when less than 0.05.

Patient and public involvement

The patients were not involved in the design of this study, the development of the research question and outcome measures, the recruitment of subjects and the conduct of the study. Results of the study were disseminated to the parents and guardians of all children in written form. No patient advisers were involved in the design of the study.

RESULTS

The flowchart of the included study population is shown in [figure 1](#). The demographic characteristics of the children included in analysis and those not included in analysis at baseline were shown in [table 1](#). None of the characteristics at baseline differed significantly between the children included in analysis and those not included in analysis (all $p > 0.05$). Significant differences were observed in the enrolled children for analysis between genders in AL ($p < 0.001$), height ($p = 0.003$) and weight ($p < 0.001$), but not for SE ($p = 0.744$).

As shown in [tables 1 and 2](#), the mean ALs were 22.75 ± 0.72 mm, 23.02 ± 0.76 mm, 23.27 ± 0.81 mm and 23.64 ± 0.91 mm at baseline, after 1, 2 and 3 years, respectively. The mean changes of ALs were 0.27 ± 0.28 mm,

Table 1 Demographic characteristics at baseline in 2014

	Children included in analysis			P value*	Children not included in analysis	
	All (n=452)	Boys (n=217)	Girls (n=235)		All (n=56)	P value†
Age	6.9±0.7	6.9±0.7	6.9±0.7	0.978	7.0±0.7	0.408
Axial length (mm)	22.75±0.72	22.98±0.71	22.54±0.65	<0.001	22.69±0.64	0.514
Spherical equivalent (D)	-0.04±0.80	-0.02±0.78	-0.05±0.82	0.744	0.03±1.23	0.567
Height (cm)	123.3±5.8	124.2±5.7	122.6±5.8	0.003	123.0±6.0	0.698
Weight (kg)	26.6±5.7	27.9±6.1	25.4±5.0	<0.001	26.5±5.5	0.408

The mean age was 6.9±0.7 years, ranging from 6 to 8 years in 2014.

*Comparison between boys and girls.

†Comparison between the children included in analysis and not included in analysis.

0.52±0.40 mm and 0.89±0.51 mm over 1, 2 and 3 years, respectively. Boys had longer AL than girls at all points in the 3-year follow-up period (all $p < 0.001$), but no

significant differences in the mean changes of ALs were observed between genders (all $p > 0.05$). The mean SEs were -0.04±0.80 D, -0.31±0.95 D, -0.60±1.18 D and

Table 2 Ocular and body parameters during 3-year follow-up period

	All	Boys	Girls	P value*
Axial length (mm)				
At 1 year	23.02±0.76	23.26±0.76	22.80±0.71	<0.001
At 2 years	23.27±0.81	23.49±0.82	23.07±0.76	<0.001
At 3 years	23.64±0.91	23.84±0.93	23.46±0.86	<0.001
Mean change over 1 year	0.27±0.28	0.27±0.28	0.27±0.29	0.813
Mean change over 2 years	0.52±0.40	0.51±0.39	0.53±0.40	0.495
Mean change over 3 years	0.89±0.51	0.86±0.48	0.92±0.53	0.192
Spherical equivalent (D)				
At 1 year	-0.31±0.95	-0.32±1.02	-0.30±0.88	0.855
At 2 years	-0.60±1.18	-0.58±1.23	-0.61±1.14	0.761
At 3 years	-0.99±1.51	-0.95±1.57	-1.03±1.45	0.590
Mean change over 1 year	-0.27±0.80	-0.30±0.78	-0.26±0.82	0.588
Mean change over 2 years	-0.56±1.00	-0.56±0.95	-0.56±1.06	0.922
Mean change over 3 years	-0.95±1.41	-0.93±1.42	-0.98±1.40	0.695
Height (cm)				
At 1 year	130.1±6.2	130.9±6.2	129.3±6.1	0.009
At 2 years	134.8±6.8	135.5±6.4	134.2±7.1	0.048
At 3 years	141.1±7.3	141.0±6.8	141.2±7.7	0.844
Mean change over 1 year	6.7±1.8	6.7±1.9	6.8±1.6	0.518
Mean change over 2 years	11.5±2.5	11.3±1.9	11.6±2.9	0.125
Mean change over 3 years	17.5±7.4	16.2±9.9	18.6±3.4	0.001
Weight (kg)				
At 1 year	30.0±7.0	31.7±7.6	28.4±5.9	<0.001
At 2 years	33.7±8.0	35.5±8.5	32.1±7.1	<0.001
At 3 years	38.5±9.5	40.6±10.1	36.7±8.4	<0.001
Mean change over 1 year	3.4±2.0	3.8±2.2	3.0±1.6	<0.001
Mean change over 2 years	7.1±3.4	7.6±3.6	6.7±3.2	0.005
Mean change over 3 years	11.8±5.0	12.5±5.6	11.3±4.3	0.009

The mean age was 6.9±0.7 years, ranging from 6 to 8 years in 2014.

*Comparison between boys and girls.

**Table 3** Multivariate logistic regression analysis for potential factors associated with axial length

	2014		2015		2016		2017	
	B	P value	B	P value	B	P value	B	P value
Gender	-0.286	<0.001	-0.279	<0.001	-0.253	<0.001	-0.244	<0.001
Spherical equivalent	-0.158	<0.001	-0.316	<0.001	-0.465	<0.001	-0.562	<0.001
Height	0.307	<0.001	0.263	<0.001	0.215	<0.001	0.226	<0.001
Weight	-0.067	0.267	-0.072	0.249	-0.077	0.156	-0.083	0.112

The mean age was 6.9±0.7 years, ranging from 6 to 8 years in 2014.

-0.99±1.51 D at baseline, after 1, 2 and 3 years, respectively. The mean changes of SEs were -0.27±0.80 D, -0.56±1.00 D and -0.95±1.41 D over 1, 2 and 3 years, respectively. No significant differences in SEs and their mean changes were observed between genders at all points in the 3-year follow-up period (all $p>0.05$). The mean heights were 123.3±5.8 cm, 130.1±6.2 cm, 134.8±6.8 cm and 141.1±7.3 cm at baseline, after 1, 2 and 3 years, respectively. The mean changes of heights were 6.7±1.8 cm, 11.5±2.5 cm and 17.5±7.4 cm over 1, 2 and 3 years, respectively. Boys were taller than girls at baseline, after 1 and 2 years, respectively (all $p<0.05$), except for after 3 years ($p=0.844$). No significant differences in the mean changes of heights over 1 and 2 years were observed between genders (all $p>0.05$), whereas the mean change of height over 3 years was greater in girls than boys ($p=0.001$). The mean weights were 26.6±5.7 kg, 30.0±7.0 kg, 33.7±8.0 kg and 38.5±9.5 kg at baseline, after 1, 2 and 3 years, respectively. The mean changes of weights were 3.4±2.0 kg, 7.1±3.4 kg and 11.8±5.0 kg over 1, 2 and 3 years, respectively. Boys were heavier and had greater mean changes of weights than girls at all points in the 3-year follow-up period (all $p<0.05$). From 2014 to 2017, significant increases were observed among primary school-age children for AL (all $p<0.001$), height (all $p<0.001$), weight (all $p<0.001$), as well as more negative SE (all $p<0.001$) in the group as a whole and when boys and girls were considered separately. Trend was overall similar for mean changes of AL, height, weight and SE.

Multivariate linear regression analysis revealed that mean AL was associated with male gender, mean SE and mean height during each follow-up examination in the 3-year follow-up period (all $p<0.001$), but not associated

with mean weight (all $p>0.05$) (table 3). Furthermore, multivariate linear regression analysis further revealed that mean change of AL was associated with mean change of SE at all points in the 3-year follow-up period (all $p<0.001$), but not associated with gender, mean change of height and mean change of weight (all $p>0.05$) (table 4). In addition, linear regression analysis revealed that AL elongation in the 3-year follow-up period was associated with AL in 2014 ($R^2=0.009$, $p=0.045$; figure 2A); SE change in the 3-year follow-up period was associated with SE in 2014 ($R^2=0.025$, $p=0.001$; figure 2B); SE change in the 3-year follow-up period was associated with AL elongation in the 3-year follow-up period ($R^2=0.347$, $p<0.001$; figure 2C).

The estimated prevalence of myopia from 2014 to 2017 is shown in figure 3. The estimated prevalence of myopia of all children, boys and girls increased from 8.4%, 7.80% and 8.90% in 2014 to 36.7%, 32.70% and 40.40% in 2017, respectively. As shown in table 5, mean AL elongations were significantly greater in myopic children than non-myopic children during 3-year follow-up period (all $p<0.05$).

DISCUSSION

In the present study, AL elongation of approximately 0.30 mm was observed in the primary school-age children in Jinshan District, Shanghai, which agreed with the previous studies. You *et al*¹⁵ found that AL elongation was 0.32 mm/year in Jiading District, Shanghai. In Beijing, another big city of China, mean AL elongation of 0.26 mm was observed in primary school children within the 1-year period.¹⁶ Average eye growth was 0.30 mm/year

Table 4 Multivariate logistic regression analysis for potential factors associated with the change of axial length

	2015–2014*		2016–2014*		2017–2014*	
	B	P value	B	P value	B	P value
Gender	0.012	0.803	0.016	0.722	0.057	0.157
Mean change of spherical equivalent	-0.134	0.004	-0.391	<0.001	-0.565	<0.001
Mean change of height	0.020	0.689	0.059	0.227	-0.001	0.978
Mean change of weight	0.092	0.079	-0.079	0.108	0.049	0.289

The mean age was 6.9±0.7 years, ranging from 6 years to 8 years in 2014.

*Each row displays the association for the change of axial length between the former year and the later year.

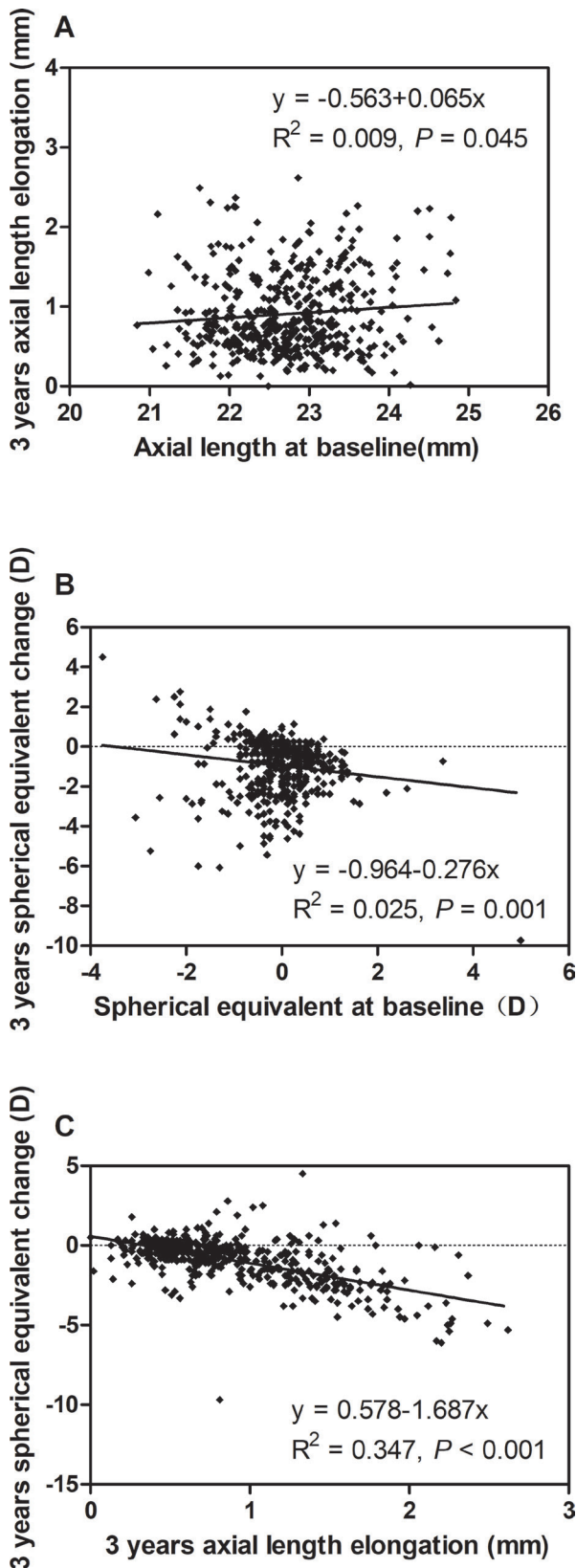


Figure 2 The relationship between AL elongation in the 3-year follow-up period and AL at baseline in 2014, (A) SE change in the 3-year follow-up period and SE at baseline in 2014, (B) SE change and AL elongation in the 3-year follow-up period, (C) using linear regression analysis. The mean age was 6.9 ± 0.7 years, ranging from 6 to 8 years in 2014. AL, axial length; SE, spherical equivalent.

in children aged 7–9 years from Singapore.¹⁷ However, in Baoshan District, another district of Shanghai, AL elongation was 0.38 mm/year.¹⁸ In addition, several studies found that AL elongated slowly in European countries. AL elongation of 0.16 mm/year in British school-aged children of 6–7 years¹⁹ and of 0.21 mm/year in the Netherlands aged from 6 to 9 years²⁰ were less than in the young Chinese children. This discrepancy may be due to ethnic differences.

With the increase in height, and prevalence of myopia, in human populations over recent decades,^{4,21} the question whether these changes may be causally related began to attract attention. In our study, AL significantly correlated with SE and height. In a sample of 565 Chinese twin pairs aged 7–15 years, Zhang *et al.*²² found a significant association between height and AL. In a birth cohort of over the full 10-year period in England, the growth trajectory for height was strongly positively associated with AL at the age of 15 years.²³ However, the mean increase of AL significantly correlated only with the mean change of SE, but not associated with the mean increase of height. Our findings suggested that a taller child tended to have longer AL, which might not be predictive of AL elongation.

Furthermore, AL did not significantly correlate with weight, and the mean increase of AL did not significantly correlate with the mean change of weight as well. This mean weight appeared to have little effect on AL. The results were in agreement with the findings of Roy *et al.*²⁴ and Ojaimi *et al.*²⁵ But Northstone *et al.*²³ found that the pattern of results for weight growth trajectory was strongly positively associated with AL at the age of 15 years. A cross-sectional study of 1498 twins aged between 5 and 80 years in the Australian Twins Eye Study showed that lower birth weight was associated with shorter AL.²⁶ Among Chinese school children aged 7 to 9 years from Singapore, heavier boys had shorter AL, whereas obese girls had longer AL of eyes.¹³ The inconsistent phenomenon suggests that some other factors (eg, diversity in dietary habits in different countries) may be involved in the relationship of body weight and AL.

In the present study, there were no significant differences in the mean change of AL and SE between genders. The finding was in agreement with a meta-analysis,²⁷ which suggested that gender was not a predictor for myopia in Asia. In the COMET children of USA, 3-year axial elongation was similar for boys and girls.²⁸ However, several studies revealed that girls were more prone to myopia than boys,^{29,30} partly because girls might have more indoor near work and less outdoor activities than boys. But the effect of gender on myopia still remains unclear.

We found the increasing estimated prevalence of myopia from 2014 to 2017, and myopic children demonstrated significantly greater mean AL elongations compared with non-myopic children (0.37 mm/year vs 0.22 mm/year), which was consistent with the findings of Tideman *et al.*²⁰ Furthermore, the mean changes of

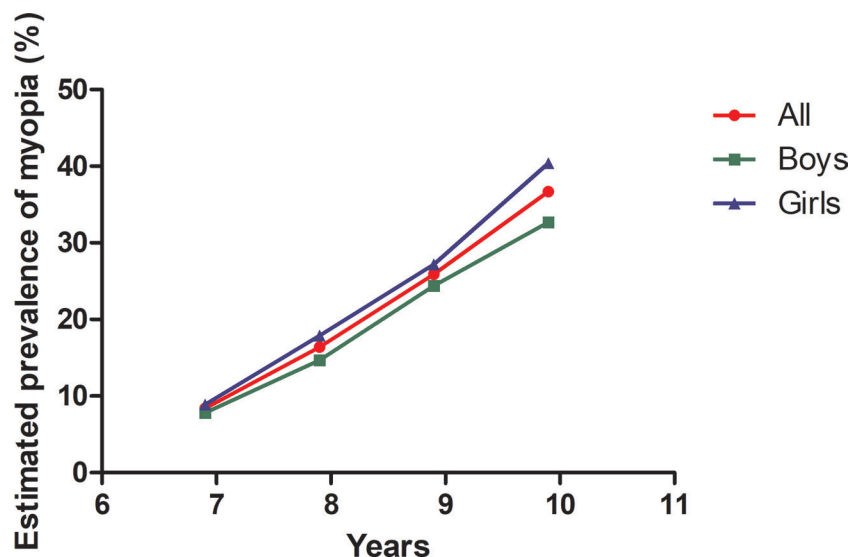


Figure 3 The estimated prevalence of myopia from 2014 to 2017.

ALs were 0.27 ± 0.28 mm, 0.52 ± 0.40 mm and 0.89 ± 0.51 mm over 1, 2 and 3 years, respectively, whereas mean changes of SEs were -0.27 ± 0.80 D, -0.56 ± 1.00 D and -0.95 ± 1.41 D over 1, 2 and 3 years, respectively. In general, 1 mm AL change approximately equates to 2.5 ~ 3D of refractive change. The reason of mismatch between the AL change and SE change may be due to the emmetropisation of the eye during childhood in which compensatory lens changes were influential in modifying SE.³¹

There may be several limitations in this study. First, refractive error was determined by non-cycloplegic auto-refraction, which may result in an overestimation of myopia and underestimation of hyperopia. The difference of approximately -0.50 D was found between cycloplegic and non-cycloplegic refraction among 7–11 years children in our previous study.³² Second, AL elongation was analysed in only one primary school, which could not be representative of the whole of Shanghai. In addition, ocular characteristics (eg, SE, AL, height, weight) at baseline were similar between children for analysis and those not for analysis, suggesting that the sample of this study was relatively representative of the underlying school population.

Table 5 Comparison of axial length elongation between myopic children and non-myopic children during 3-year follow-up period

	2015–2014*	2016–2014*	2017–2014*
Myopic children	0.57 ± 1.22	0.92 ± 1.18	1.13 ± 2.32
Non-myopic children	0.21 ± 1.00	0.38 ± 0.96	0.67 ± 0.97
P	0.001	0.002	0.001

The mean age was 6.9 ± 0.7 years, ranging from 6 to 8 years in 2014.

*Each row displays the association for the change of axial length between the former year and the later year.

In conclusion, the AL elongation of approximately 0.30 mm is relatively high in primary school-age children. AL is associated with male gender, SE and height, whereas the mean increase of AL is associated with the mean change of SE. In addition, AL elongation in the 3-year follow-up period is associated with AL in 2014.

Contributors Concept and design: TL and XZ; analysis and interpretation: TL and BJ; writing the article: TL; critical revision of the article: XZ; final approval of the article: all authors; data collection: TL and BJ; provision of materials, patients or resources: BJ; statistical expertise: BJ and literature research: TL and XZ. All authors have reviewed the manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the Ethics Committee of Jinshan Hospital of Fudan University, Shanghai. All study procedures adhered to the tenets of the Declaration of Helsinki.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. Data are available upon reasonable request.

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