Design and recent results of large-scale cohort epidemiology studies on refractive error in children in Shanghai

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Abstract: Between 2011 and 2013, two large-scale cohort epidemiology studies were launched in Shanghai: the SCALE study, which aimed to provide ocular public health services to cover the entire youth population in Shanghai, and the SCES, which was based on sample surveys and aimed to provide information on the prevalence and incidence of visual impairment and different types of refractive errors. A total of 910,245 children and adolescents were finally enrolled in the SCALE study; three possible methods for monitoring refractive error without mydriasis were tested, and the agreement between the refractive outcomes of three commonly used autorefractors were examined to ensure the accuracy of the results of the SCALE study. A total of 8,627 children were enrolled in the SCES, and the baseline prevalence of different refractive errors, different behaviors associated with 1 year myopic shifts, and the different patterns of 2-year myopia progression between internal migrant and local resident school children have been analyzed. In some subset samples of the SCALE study and the SCES, several refraction components such as choroidal thickness (ChT) and crystalline lens power were also measured, to further elucidate the relationships between the refraction components and myopia as well as the mechanism of myopia incidence and development. The three methods used in Shanghai to prevent and intervene with childhood myopia: increasing outdoor time, low concentration atropine, and use of orthokeratology lens are also addressed in this review.

Keywords: Epidemiology; children; refractive error; myopia

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Introduction

In recent decades, several countries and regions in the world have published data on the prevalence of visual impairment and refractive errors in children, and the prevalence of uncorrected refractive errors and myopia in children in East Asian countries and in many cities in China has proven to be high (1). In Shanghai, the most developed city in eastern China economically, the Shanghai Eye Disease Prevention and Treatment Center (Shanghai Eye Hospital) is the hub of the Shanghai city, district, community three-level eye disease prevention and control network, which was set up in the 1980s and assumed the responsibility for the ocular public health management or the city's children and adolescents. Through annual training from the system, school health teachers and community doctors or general practitioners can learn to conduct eye examination, and screen and diagnose eye diseases, in order to ascertain the visual acuity status of children and adolescents in Shanghai. Based on these examination results, it has been noted that the visual acuity of children and adolescents in Shanghai has been declining in recent decades; therefore, specific eye care services are urgently needed to help curb the occurrence and development of myopia and improve the coverage of refractive error correction for children and adolescents. However, Shanghai has been lacking in data on the prevalence, incidence, and risk factors of refractive errors from large-scale studies in children and adolescents and therefore can neither compare with the data from other countries and other regions in mainland China, nor identify the possible mechanism for the occurrence and development of childhood myopia in Shanghai. During 2011–2013, the Shanghai Eye Disease Prevention and Treatment Center conducted two cohort studies: the Shanghai Child and Adolescent Large-Scale Eye (SCALE) study, which aimed at providing ocular public health services to cover the entire youth population in Shanghai, and the Shanghai Children Eye Study (SCES) based on sample surveys, which aimed to determine the prevalence and incidence of visual impairment and different types of refractive errors. This article briefly describes the design of the SCALE and SCES studies, the current research findings related to refractive errors from these two studies, and our recent studies on intervention in childhood myopia in Shanghai.

The SCALE study

The SCALE study is a prospective, city-wide, school-based study, which aimed to include all children and adolescents aged 4 to 19 years (the number exceeded 1,097,000) in Shanghai and provide insights on the burden of visual impairment and myopia (especially high myopia) in children and adolescents in a metropolitan area of China (2). It is supported by the Shanghai government, and was once listed among the projects of the Shanghai Three-year Action Plan for Public Health Systems Construction (2011–2013). The SCALE study began in 2010, and a total of 910,245 children and adolescents (76% of the enrolled population) from 17 districts of Shanghai underwent examination by the end of 2013. Each participant was required to undergo visual acuity assessment and their parents were required to complete a brief questionnaire to elicit factors associated with refractive errors. Additionally, non-cycloplegic autorefraction and axial length (AL) measurement were performed for the majority of the included population. Each participant was then given an "eye health prescription" based on visual acuity and non-refraction measurement data, and the feedback was sent to the child's parents/carers. Participants who were confirmed or suspected as refractive error patients were asked to undergo further examination, including cycloplegic refraction and a complete eye examination at nearby fixed-point hospitals. The "Refractive Development Archives of Shanghai Children and Adolescents," including the questionnaire, visual acuity, non-cycloplegic autorefraction, AL, and fixed-point hospital examination results were established for the included children. From 2014, a subset of at least 30% of the population enrolled in the SCALE study was followed up and their "Refractive Development Archives" updated annually.

Non-cycloplegic autorefraction was used as the basic examination of SCALE because we found it impossible to conduct refraction under mydriasis in all the children in Shanghai. A large number of Chinese parents did not want their children to undergo cycloplegic autorefraction, mainly because the children did not complain about decreased vision; hence, the parents considered mydriatic examination as unnecessary, particularly since it affected the child's day learning, even though we made every effort to persuade them that their children may still have uncorrected refractive error. This prompted us to find some clues for detecting occult refractive error without mydriasis, and then draw the "eye health prescription." The clues we found are as follows:

Combining uncorrected distance visual acuity (UCDVA) and noncycloplegic autorefraction (NCAR)

A total of 1,639 children aged between 6 and 12 years were included, and their UCDVA and auto-refraction before and after cycloplegia (induced with 1% cyclopentolate drops) were measured. Three screening tests, using UCDVA alone, using NCAR alone, and combining the two measurements, were compared for effectiveness. Receiver operating characteristic (ROC) curves were drawn to obtain the screening thresholds and the corresponding sensitivities and specificities for the three tests. The results showed that the proportion of children being diagnosed with myopia [spherical equivalent refraction (SER) ≤–0.50 D] was 26.11% (428 children). The cut-off for UCDVA was 20/32, with a sensitivity and specificity of 63.6% and 94.0%, respectively. The cut-off for NCAR was SER ≤–0.75 D, with a sensitivity and specificity of 88.6% and 86.1%, respectively. For the combination of the UCDVA and NCAR, the cut-off was UCDVA ≤20/20 and SER ≤–0.75 D, with a sensitivity and specificity of 84.4% and 90.5%, respectively. When the specificity was set at 90%, the sensitivities were 63.55%, 78.50%, and 84.35%, respectively, for UCDVA, NCAR, and the combination test. Based on these data, we concluded that in school-aged children with a high prevalence of myopia, such as in China, combining the UCDVA and NCAR in serial order could improve the screening accuracy compared with using either of the tests alone (3). Later, we conducted another study including 6,825 children aged 4 to 15 years using random cluster sampling. Each participant underwent both non-cycloplegic and cycloplegic autorefraction (induced with 1% cyclopentolate drops) as well as UCDVA and AL measurement. The results showed that compared to cycloplegia, non-cycloplegic refraction resulted in a higher myopic refraction value (paired difference in spherical equivalent: −0.63±0.65 D; 95% CI, −0.612 to −0.65 D), and the differences were greater in younger children and in eyes with greater hyperopic refraction and smaller AL. Combining age and UCDVA data resulted in 77.0% of the eyes being correctly classified as having refractive error; the sensitivity and specificity for myopia classification were 89.3% and 97.6% respectively. Applying the model to only those eyes with UCDVA <20/20 or ≤20/60, the accuracy of the classification could be improved to 80.0% and 97.5% respectively. The conclusion is that although non-cycloplegic refraction alone or combined with age and UCDVA could not get reliable quantitative values of refractive error compared with cycloplegic refraction, it did show acceptable accuracy in qualitatively classifying myopia especially moderate and high myopia, and may be used as an alternative measure when studying the prevalence of visual impairment due to myopia in large scale epidemiological researches and other circumstances that cycloplegia is difficultly accepted or conducted (4).

Combining UCDVA and uncorrected near visual acuity (UCNVA)

A total of 4,416 children aged 6 to 12 years were included in this study. Significant refractive error, including high myopia, high hyperopia, and high astigmatism, was detected with cycloplegic autorefraction in 486 children (11.01%). We found that UCDVA was better than UCNVA in screening for high myopia, while UCNVA was better for detecting high hyperopia and high astigmatism. The series with combined UCDVA and UCNVA data had the biggest area under the ROC curves and the highest Youden index for detecting high hyperopia, myopia, and astigmatism, as well as all significant refractive errors (all P<0.01). Therefore, the series combined test of UCDVA and UCNVA could be applied for large scale screening for significant refractive error (5).

Combining AL/CR ratio and UCDVA

A total of 3,922 children aged 6 to 12 years from 6 primary schools were included. Cycloplegic refraction, AL, corneal radius of curvature (CR), and UCDVA were measured. The correlation coefficients of the SER with the AL/CR ratio, AL, and CR were −0.811, −0.657, and 0.095, respectively. Linear regression showed that every 10.72 D myopic shift was associated with 1 unit increase in the AL/CR ratio. The areas under the ROC curve of the AL/CR ratio, AL, and UCDVA for myopia classification were 0.910, 0.822, and 0.889, respectively. The sensitivities for the AL/CR ratio, AL, UCDVA, and the combination of AL/CR ratio and UCDVA to classify myopia were 72.98%, 50.50%, 71.99%, and 82.96%, respectively, at a specificity of 90%. Therefore, the AL/CR ratio was able to explain the total variance of refraction to a greater extent than AL alone, and combining AL/CR ratio and UCDVA could increase sensitivity without decreasing specificity (6).

We also compared the refractive measurements of three autorefractors used in the SCALE study. A total of 2,072 children and adolescents aged 4 to 18 years from seven schools were enrolled using cluster sampling. Refractive errors were measured using the following three autorefractors (random sequence) under cycloplegic conditions: Topcon KR-8900, Nidek ARK-510A, and Huvitz HRK-7000A. The refraction data, sphere power, cylinder power and axis measurements were converted into SER and Jackson cross-cylinder values (J0 and J45) and compared by repeated-measures analysis of variance (RM-ANOVA) and Bland-Altman 95% limits of agreement (95% LoA). The mean ± SD and 95% LoA of the differences in SER between Topcon and Nidek, Topcon and Huvitz, and Nidek and Huvitz were 0.01±0.24 D (−0.46 to 0.48), −0.06±0.31 D (−0.66 to 0.54), and −0.07±0.26 D (−0.58 to 0.44), and those for the differences in cylinder power were −0.07±0.26 D (−0.57 to 0.44), 0.01±0.32 D (−0.63 to 0.64), and 0.07±0.28 D (−0.48 to 0.62), respectively (RM-ANOVA, P<0.001). This study confirmed a good agreement between three autorefractors in analysis of the prevalence rates of myopia and hyperopia, whereas their agreement was less satisfactory in analysis of the axis and the prevalence of astigmatism. The results facilitate the comparison of data measured with these devices in different studies and the use of three devices in the same study to generate one pool of data, which can be analyzed together (7).

The SCES study

The SCES is a prospective, school-based study, which aims to provide prevalence and incidence of visual impairment and different types of refractive errors in Shanghai, and explore possible risk factors and prediction methods for myopia incidence, providing feasible and effective methods for myopia control and prevention. The SCES study was once named as "Elaborative Shanghai Childhood Ocular Refractive Development Study (E-SCORDS)," it was a cluster-sampled study, which was started in November 2013 and followed up annually, and included 8,627 children from Shanghai. Children underwent visual acuity testing, measurement of AL and CR, slit lamp examination, cycloplegic autorefraction using 1% cyclopentolate, and subjective refraction. A portion of the baseline data, 1- and 2-year cohort studies results are listed below.

Baseline data

During November and December 2013, in 8267 children aged 3 to 10 years, the prevalence of UCDVA, presenting visual acuity, and best-corrected visual acuity in the better eye of ≤20/40 was 19.8%, 15.5%, and 1.7%, respectively. For children whose UCDVA of ≤20/40 in one or both eyes, 93.2% could improve to an acuity of ≥20/32 with refractive correction. Among children whose UCDVA in the better eye of ≤20/40, only 28.7% wore glasses. Prevalence of myopia (cycloplegic spherical equivalent ≤0.5 D in at least one eye) increased from 1.78% in 3-year-old to 52.2% in 10-year-old, while prevalence of hyperopia (cycloplegic spherical equivalent ≥+2.0 D) decreased from 17.8% to 2.6% in the same time frame. After adjusting for age, multivariable logistic analyses showed that attending "high-level" school [odds ratio (OR) =1.42; 95% CI, 1.20–1.68; P<0.001] was significantly associated with a greater prevalence of myopia. We concluded that myopia increased dramatically after 6 years, consistent with a strong environment role for schooling on myopia development (8).

One-year cohort study for related behaviors associated with myopic shifts

Four thousand and eight hundred fourteen primary 1st to 4th grade students aged 6–10 years were included in this study. At 1 year follow-up, the incidence of myopia was 16.0%. Compared to the baseline, the mean changes of AL, AL/CR ratio and SER were 0.32±0.35 mm, 0.032±0.054, and −0.51±0.51 D, respectively. Higher sores in keeping a reasonable distance for reading, writing, or watching TV were a protective factor against myopia, and were negatively associated with the elongation of AL and lower change in myopic refraction after adjusting for confounding factors such as parental myopia, daily near work load, and outdoor activity. Lower scores in selecting an environment with adequate light for visual comfort to read and write was related to the elongation of the AL and increase of AL/CR ratio. Also, better performance in conducting an eye break during continuous near work was negatively associated with the increase of AL/CR ratio and lower change in myopic refraction. Various near work-related behaviors changed as grade levels changed in primary school students, and near work-related behaviors such as keeping an inappropriate eye distance, selecting inadequate lighting environments, and continuous near work without an eye break were predictive factors for myopic shifts. This conclusion provides valuable reference to the school eye health strategy formulation though more studies are required to confirm these findings (9).

Two-year cohort study for different patterns of myopia prevalence and progression between internal migrant and local resident school children

A total of 842 migrant children from 2 migrant schools and 1,081 resident children from 2 local schools were selected randomly. At baseline, children in grades 1 to 4 participated in the study, and among them, children in grades 1 and 2 were followed for 2 years. For children in the 1st and 2nd grades, the prevalence of myopia was similar or even lower in the migrant children compared with the resident children. However, after grade 2, the migrant children showed an accelerated myopia prevalence, resulting in a higher prevalence than that of the resident children by grade 4. During the follow-up, the myopia incidence was similar for grade 1 (28.2%) and grade 2 (26.4%) in the resident children, but was higher for grade 2 children (42.6%) than grade 1 children (32.7%) among the migrants. Correspondingly, increased progression of refractive error and elongation of AL were observed in the migrants from grades 1st to 2nd; however, the progression decreased in resident children as grade level increased. The average time spent on homework increased from grades 2nd to 3rd in parallel with the acceleration of myopia prevalence for migrant children; however, the time spent outdoors did not correspondingly change. We speculated that the acceleration of myopia in migrant children might be a result of a change in their environments, such as intensive education pressure (10). In 2010, there were 36 million migrant children under 18 years old in China.

The refraction components studies in samples from SCALE and SCES

In some subset samples of the SCALE study and the SCES, corneal thickness, anterior chamber depth, lens thickness, and the thickness of retinal layers were also measured, in order to further elucidate the relationships between the refraction components and myopia as well as the mechanism of myopia incidence and development (11-14). The present data suggest that ChT and crystalline lens power are associated with different refractive errors.

ChT and refractive error study

Three cross-sectional studies were conducted. The first study enrolled 144 healthy children aged 6 to 12 years. The second study enrolled 276 children aged 7–13 years. The third enrolled 3,001 children and adolescents aged 6–19 years. The thickness of the choroid, retina, ganglion cell layer, and nerve fiber layer were measured using optical coherence tomography and compared among children with different refractive status. The results showed that ChT, but not retinal thickness, correlated closely with AL and magnitude of refractive error in Chinese children. Subfoveal ChT decreased with age, AL, and a history of preterm delivery, and increased with height. Myopic subjects had a significantly thinner choroid in the subfoveal, parafoveal, and perifoveal sectors, while hyperopic subjects had a thicker choroid in most regions. Choroid thinning is suspected to occur early in myopic progression, before retinal thinning. The AL and magnitude of refractive error were independently related to central foveal ChT. Age was independently and positively correlated with ChT in emmetropes, and mild myopes with SER >–2.00 D, but not in children with SER ≤–2.00 D, suggesting that the protective effect of physiologic choroidal growth with age against rapid AL elongation disappeared and AL elongation became the dominant determinant of ChT among children with myopia worse than –2.00 D (12-14).

Crystalline lens power and myopia

A cross-sectional study including 1992 children and adolescents aged 6–19 years, who underwent ophthalmic examination including AL, cycloplegic refraction, and Pentacam measurements. The crystalline lens power was calculated using Bennett's formula and then compared among children of different age groups, refractive status, and AL. The difference in lens power between myopes and non-myopes was greater in children <10 years old, and relatively smaller between 10 to 14 years, and came to a near plateau in adolescents >14 years. The negative association between lens power and AL was found to be more evident in non-myopes than in myopes, irrespective of age. We found three stages of changes in lens power in children and adolescents aged 6 to 18 years. In addition, the association between lens power and AL differed between the non-myopes and myopes. These findings add to our knowledge about changes in lens power in children and adolescents, suggesting that lesser reduction in lens power might be associated with both, increasing age and increasing AL in myopes (11).

Our recent studies on intervention of children myopia in Shanghai

At present, increased outdoor time, atropine, and orthokeratology lenses may be the most widely used methods for prevention of and intervention in childhood myopia, but none of them is without controversy. In Shanghai, our study group has also tried these 3 means in children.

We began to use orthokeratology lenses for myopia control 20 years ago. Strict inclusion criteria and timely and regular follow-up have been mandated to avoid adverse reactions. Recent studies have shown that orthokeratology lenses have a control effect on children with different degrees of myopia. Among them, moderate myopia exhibits the best control effect (3–6 D). The control effect is least obvious in low-grade myopia (15).

Low concentration atropine, especially 0.01% atropine eye drops, is currently considered to be reliable in the control of myopia, and has fewer side effects (16). In China, there are presently no atropine eye drops available commercially at this concentration. Therefore, 10 years ago, we began to use 1% atropine gel, which can be found in the domestic market, to control myopia with intermittent administration (once a week to once a month). We hope that this mode may reduce the side effects of high concentrations of atropine, while ensuring effective myopia control.

Through our recent meta-analysis of 25 published articles with relevant data, a significant protective effect of outdoor time was found for incident and prevalent myopia. However, dose-response analysis did not find a relationship between time spent outdoors and myopic progression. These results demonstrate that increased time outdoors is effective in preventing the onset of myopia but is, paradoxically, ineffective in slowing progression in eyes that were already myopic (17). Therefore, from 2016, we conducted the first increased outdoor time study for myopia control: 7,200 elementary school students in the 1st and 2nd grades in 24 primary schools were observed for 2 years for incidence of onset and progression of myopia. The students were randomly divided into 3 groups; the first group has 40 minutes of extra outdoor time activity each day, the second group has 80 minutes of extra outdoor time activity each day, and the last group has no extra outdoor time. This study is ongoing and will be completed by the end of 2018.

In summary, the data from the SCALE study and the SCES facilitate our understanding of the onset and progression of myopia in children and adolescents in big cities in China. Several results from these studies, such as the potential to use AL/CR ratio rather than cycloplegic refraction for monitoring refractive error, may help other studies to avoid the need for universal cycloplegia, which is a limiting factor, and potentially lead to more effective prevention. Presently, the SCALE study, the SCES, and the outdoor time study are all ongoing. We look forward to finding more evidence to solve the important, unanswered questions of myopia control in future epidemiological studies.

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Footnote

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References

1. Dolgin E. The myopia boom. Nature 2015;519:276-8.
2. He X, Zhao R, Sankaridurg P, et al. Design and methodology of the Shanghai child and adolescent large-scale eye study (SCALE). Clin Exp Ophthalmol 2017. [Epub ahead of print].
3. Ma Y, He X, Zou H, et al. Myopia screening: combining visual acuity and noncycloplegic autorefraction. Optom Vis Sci 2013;90:1479-85.
4. Sankaridurg P, He X, Naduvilath T, et al. Comparison of non-cycloplegic and cycloplegic autorefraction in categorizing refractive error data in children. Acta Ophthalmol 2017;95:e633-40.
5. Jin P, Zhu J, Zou H, et al. Screening for significant refractive error using a combination of distance visual acuity and near visual acuity. PLoS One 2015;10:e0117399.
6. He X, Zou H, Lu L, et al. Axial length/corneal radius ratio: association with refractive state and role on myopia detection combined with visual acuity in Chinese school children. PLoS One 2015;10:e0111766.
7. Xiong S, Lv M, Zou H, et al. Comparison of Refractive

Measures of Three Autorefractors in Children and Adolescents. Optom Vis Sci 2017;94:894-902.
8. Ma Y, Qu X, Zhu X, et al. Age-specific Prevalence of Visual Impairment and Refractive Error in Children Aged 3-10 Years in Shanghai, China. Invest Ophthalmol Vis Sci 2016;57:6188-96.
9. You X, Wang L, Tan H, et al. Near Work Related Behaviors Associated with Myopic Shifts among Primary School Students in the Jiading District of Shanghai: A School-Based One-Year Cohort Study. PLoS One 2016;11:e0154671.
10. Ma Y, Lin S, Zhu J, et al. Different patterns of myopia prevalence and progression between internal migrant and local resident school children in Shanghai, China: a 2-year cohort study. BMC Ophthalmol 2018;18:53.
11. Xiong S, Zhang B, Hong Y, et al. The Associations of Lens Power With Age and Axial Length in Healthy Chinese Children and Adolescents Aged 6 to 18 Years. Invest Ophthalmol Vis Sci 2017;58:5849-55.
12. Xiong S, He X, Deng J, et al. Choroidal Thickness in 3001 Chinese Children Aged 6 to 19 Years Using Swept-Source OCT. Sci Rep 2017;7:45059.
13. He X, Jin P, Zou H, et al. Choroidal Thickness in Healthy Chinese Children Aged 6 to 12: The Shanghai Children Eye Study. Retina 2017;37:368-75.
14. Jin P, Zou H, Zhu J, et al. Choroidal and Retinal Thickness in Children With Different Refractive Status Measured by Swept-Source Optical Coherence Tomography. Am J Ophthalmol 2016;168:164-76.
15. Zhu MJ, Feng HY, He XG, et al. The control effect of orthokeratology on axial length elongation in Chinese children with myopia. BMC Ophthalmol 2014;14:141.
16. Chia A, Chua WH, Wen L, et al. Atropine for the treatment of childhood myopia: changes after stopping atropine 0.01%, 0.1% and 0.5%. Am J Ophthalmol 2014;157:451-7.e1.
17. Xiong S, Sankaridurg P, Naduvilath T, et al. Time spent in outdoor activities in relation to myopia prevention and control: a meta-analysis and systematic review. Acta Ophthalmol 2017;95:551-66

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