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A Risk Score System for Myopia Symptom Warning*

Dan-dan DU[1], Wen-long XU[2], Li-hua YANG[2, 3], He-xin WANG[4], Chang-mei GU[1], Jia TANG[5], Fang LI[6], Ting XU[2], Shi-qing WU[1], Mei-xia LU[1#]

[1]*Department of Epidemiology and Statistics and the Ministry of Education (MOE) Key Lab of Environment and Health, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China*

[2]*Wuhan Center for Adolescent Poor Vision Prevention & Control, Wuhan 430015, China*

[3]*Wuhan Commission of Experts for the Prevention & Control of Adolescent Poor Vision, Wuhan 430015, China*

[4]*China Innovation and Research and Development Center, Carl Zeiss (Shanghai) Co., Ltd. ZEISS Group, Shanghai 200131, China*

[5]*Wuhan Academy of Educational Science, Wuhan 430030, China*

[6]*Wuhan Centers for Disease Prevention & Control, Wuhan 430015, China*

Summary: Myopia is the leading cause of visual impairments worldwide. Some studies revealed that visual experience in early life affected the final myopia, indicating that environmental factors play an impellent role in the development of myopia. However, risk factors of myopia are still not identified among adolescents in China. A total of 4104 cases of myopia symptom and 3306 emmetropia controls were selected from students in primary and middle schools in Wuhan in 2008. We identified the risk factors associated with myopia symptom by multivariate logistic regression in this cross-sectional study and constructed a risk score system for myopia symptom. The value of the area under the receiver operating characteristic curve (ROC) was 0.735. Furthermore, we followed up 93 students aged 7–9 years for one year and calculated the total points using the score system. We found no significant difference between the final myopia symptom and the results predicted by the total points by pair chi-square test (P>0.05). The score system had a modest ability to estimate the risk factors of myopia symptom. Using this score system, we could identify the students who are at risk of myopia symptom in the future according to their behaviors and environmental factors, and take measures to slow the progress of myopia symptom.

Key words: myopia symptom; adolescents; risk score system

Myopia is a major global public health problem and the leading cause of visual impairment. Many studies showed that the prevalence of myopia tends to increase year by year[1]. Dramatic increases in the prevalence of myopia have been reported in countries such as Singapore, Japan and Korea over the last 50 to 60 years. The prevalence of myopia was reported to be 80% to 90% among high-school graduates, of which high myopia accounted for 10% to 20%[2]. The WHO has defined myopia, ametropia, maculopathy, infection and vitamin deficiency as the main causes of visual impairment and blindness[3]. Although it is commonly believed that the refractive status is largely determined by genes, a growing body of evidence suggests that visual experience in early life affects the growth of the eye and the final refractive status[4].

In recent decades, many studies have been carried out to identify the causes of myopia. The key role of environmental factors is widely accepted[5], though some studies confirmed that genetic factors play a role in the formation of myopia[6]. Further research on the background of a growing prevalence of myopia globally indicates that the impellent role played by environmental factors could not be ignored, especially in East Asian countries[7]. Some studies showed that the primary environmental factors which cause myopia are: prolonged near work and lack of outdoor activities[8, 9].

Clinical researches often focus on true myopia, which would result in irreversible visual impairment. Syndrome surveillance is an useful tool for identifying the threat of potential public health in advance[10]. As an important period in the progression of myopia, myopia symptom is suitable for early visual health surveillance. Thus, environmental factors associated with myopia

Dan-dan DU, E-mail: M201475160@hust.edu.cn
#Corresponding author, E-mail: mlu@hust.edu.cn
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symptom risk could be applicable in surveillance and early warning, which will be benefit to adolescents, especially.

Mathematical models can predict the occurrence of diseases and identify the high-risk groups in advance. They have been widely applied in a series of research studies. The most typical model is the Framingham risk score model. It was designed to estimate the risk of coronary heart disease and has already been implemented in different areas of clinical research. Inspired by the Framingham model, many similar models have been constructed, especially in the area of chronic disease. These include the Framingham model for predicting diabetes mellitus[11], the Stern model for type 2 diabetes mellitus[12], the diabetes prediction model for Asians[13] and the breast cancer forecast model[14]. Indeed, their validations of risk prediction have been well verified. Therefore, we constructed a risk score system to identify groups at high risk for myopia symptom based on the Framingham score model in order to offer early warnings and advice on countermeasures for myopia.

1 SUBJECTS AND METHODS

1.1 Study Data and Ethics Statement

A total of 11 319 subjects were selected from the vision survey of school children in Wuhan in 2008. In the research, a stratified cluster sampling method was adopted. In total, data from 10 schools was collected from the Jiang'an District (downtown area) and Dongxihu District (remote area) in Wuhan. Four primary schools, 4 middle schools and 3 high schools were involved.

The study was approved by the Ethics Committee of Tongji Medical College of Huazhong University of Science and Technology, China, and followed the guidelines of the Declaration of Helsinki. The nature of the study was explained to parents and school students, and written informed consent was obtained from the parents of all participating students.

1.2 Data Collection

A questionnaire aimed to investigate eye behaviors among teenagers was created. The questionnaire was given to all selected students by teachers. The primary school students were asked to fill out the questionnaire with the aid of trained members. The middle school students filled out the questionnaire by themselves. The questionnaire contained items such as near-work activities and the amount of time the respondents spent using their eyes for specific activities. Information on age, gender and address was also collected.

1.3 Methods for Diagnosis of Myopia Symptom

Measurements of uncorrected vision were carried out using the Standard Logarithmic Visual Acuity E Chart by an ophthalmologist. The testing distance between our subjects and the test chart was 5 m. During the process of examination, measures were taken to ensure that the chart was parallel to the eyes of the subjects. The test was started from line 0 log MAR. Once the student identified the optotype correctly, the doctor pointed to the next smaller line. Otherwise, the doctor pointed to the next bigger line. Test time was limited to 5 s per response and all students were supposed to keep their eyes relaxed[15]. After that, we selected 5% of the participants randomly and reexamined their uncorrected vision.

Non-cycloplegic refraction was measured by auto-refractor (TOPCON ACP-8). The DK-10 phoropter was used to test ametropia in each naked eye[16]. Based on the optometry exam results, the spherical equivalent refraction diopters were equal to the spherical refraction diopters plus 1/2 cylindrical refraction diopters. We defined myopia symptom as the spherical equivalent (SE) of refractive error of less than −0.5 diopters (D)[17].

1.4 Multivariate Logistic Regression

Using multivariate logistic regression analysis, the significant variables associated with myopia symtom were identified. All data was analyzed with the Statistical Package for Social Sciences, version 12.0 (SPPS Inc. Chicago, IL, USA).

1.5 Construction of a Risk Model for Myopia Symptom Based on Logistic Regression Analysis

We selected risk factors and determined the value of each category (W_{ij}). As for continuous variables, we assigned points based on their corresponding estimated parameters in multivariate logistic regression analysis, such as coefficient β, ORs and 95% CIs. Each categorical variable was assigned to one point.

The baseline values of reference risk factors (W_{iREF}) were determined by the basic classification of each risk factor. 0 was taken as a benchmark in our score system. The higher the risk, the higher the defined score. The distance β_i (W_{ij}–W_{iREF}) between each category, the benchmark in regression and the constant B were determined. The constant was associated with scores. The risk of myopia symptom was increased 1-fold for every additional year of age. In our model, constant B=1×0.243=0.243. The association between points and the category of each risk factor was determined. $Point_{ij}$ was calculated as follows: $Point_{ij} = \beta_i \times (W_{ij} - W_{iREF})/B$. The final points were rounded to the nearest whole number.

Risk factors were graded, the score of each individual was calculated and the probability of disease on different score levels was estimated [formula 1: $P=1/[1+\exp(-\sum B_iX_i)]$. The total points were calculated in formula 2 ($\sum^{p}_{i=0} B_iX_i \approx B^*$).

1.6 Evaluation of the Accuracy of the Myopia Risk Score System

Using the area under the ROC curve (AUC), we could evaluate the accuracy of the risk score system for myopia symptom[18]. To evaluate the score system, we used the pair chi-square test to compare the final myopia (observed after 1-year follow-up) and the total points (acquired according to the score system) among 93 students whose ages ranged from 7 to 9 years old.

1.7 Data Processing and Statistical Analysis

We used EPI Data 3.1 for data input. All data were double-input and a logical examination was conducted. SPSS 12.0 was used for data analysis. We used multivariate logistic regression to identify risk factors and calculate the odds ratio (OR) and their corresponding 95% CIs and constructed a risk score model in accordance with the Framingham study. We calculated the corresponding prediction probability of each individual using MEDCLAC statistical software.

2 RESULTS

2.1 Multivariate Logistic Regression Results

A total of 11 319 students were sampled in our cross-sectional study. Of the 11 319 students from 10 schools who were eligible to take part in the study, 1892 students (16.72%) were absent from the study, 2017 (17.82%) were hypermetropia, and finally a total of 7410 students (65.47%) were included in our analysis.

Overall, 7410 (4104 with myopia symptom and 3306 with emmetropia) students aged 6–19 years old (mean age: 13 years) were recruited from 20 classes. There were 2148 females and 1956 males among myopia symptom cases and 1437 females and 1809 males among emmetropia controls. The difference in gender between two groups was significant (χ^2=47.235, P<0.001). The mean age of myopia symptom cases and emmetropia controls were 14 and 12 years respectively, with the difference being significant between the two groups (t=35.690, P<0.001). The risk factors associated with myopia symptom were analyzed using multivariate logistic regression analysis and shown in table 1.

The final fitting equation was: logit(P)= –3.762+ $0.243X_1+0.672X_2–0.284X_3+0.607X_{41}+0.292X_{42}+0.235X_5+0.261X_{61}+0.374X_{62}+0.043X_{71}+0.202X_{72}+$

Table 1 Multivariate logistic regression analysis on the factors associated with myopia symptom

Factors	β	S.E.	Wald	P	OR	95% CI	
						Lower bound	Upper bound
Age	0.243	0.010	616.607	<0.001	1.275	1.251	1.300
Urban district							
Remote area	Ref				1.000		
Downtown area	0.672	0.053	157.802	<0.001	1.957	1.763	2.174
Gender							
Female	Ref				1.000		
Male	–0.284	0.054	27.886	<0.001	0.753	0.677	0.836
Reading distance							
≥30 cm	Ref				1.000		
<20 cm	0.607	0.114	28.158	<0.001	1.835	1.467	2.297
20–29 cm	0.292	0.099	8.741	0.003	1.339	1.103	1.624
Average illuminance value in classroom							
≥300 lx	Ref				1.000		
<300 lx	0.235	0.085	7.661	0.006	1.264	1.071	1.493
Break time							
Outside activities	Ref				1.000		
Having a rest	0.261	0.059	19.764	<0.001	1.298	1.157	1.456
Reading inside	0.374	0.092	16.469	<0.001	1.454	1.213	1.742
Time spent on homework							
<2 h	Ref				1.000		
2–3 h	0.043	0.129	0.110	0.740	1.044	0.810	1.345
>3 h	0.202	0.055	13.392	<0.001	1.224	1.098	1.364
Distance for watching TV							
>3 m	Ref				1.000		
<2 m	0.558	0.086	41.924	<0.001	1.748	1.476	2.070
2–3 m	0.318	0.057	30.941	<0.001	1.374	1.228	1.537
Doing eye exercises							
No	Ref				1.000		
Yes	–0.145	0.057	6.483	0.011	0.865	0.773	0.967
Time for outdoor activities							
<1 h	Ref				1.000		
≥1 h	–0.132	0.057	5.457	0.019	0.876	0.784	0.979
Constant	–3.762	0.177	452.691	–	–	–	–

$0.558X_{81}+0.318X_{82}–0.145X_9–0.132X_{10}$ (X_1: age; X_2: urban district; X_3: gender; X_{41}: reading distance <20 cm; X_{42}: reading distance (20–29 cm); X_5: classroom illumination; X_{61}: having a rest during breaks; X_{62}: reading inside classroom during breaks; X_{71}: spending 2–3 h on homework; X_{72}: spending >3 h on homework; X_{81}: distance when watching TV <2 m; X_{82}: distance when watching TV 2-3 m; X_9: doing eye exercises; X_{10}: time for outdoor activities ≥1 h).

Both regular eye exercises and spending more than one hour per day doing outdoor activities revealed a significant protective effect on myopia symptom (OR=0.865, 95% CI=0.773–0.967; OR=0.876, 95% CI=0.784–0.979).

There was a strong negative correlation between myopia symptom and age. The risk increased along with growing age (OR=1.275, 95% CI=1.251–1.300). Compared to students who lived in a remote area, those in the downtown area had a higher risk of myopia symptom (OR=1.957). To improve reading and writing posture, the Ministry of Education in China published a document in 2008, in which the advisable reading distance was one chi (33 cm). So we took students whose reading distance was greater than 30 cm as the reference group. Students whose reading distance was less than 20 cm and those between 20 cm and 29 cm had a 1.835- and 1.339-fold risk of myopia symptom, respectively. The recommendatory classroom illumination is 300 lx. We also investigated classroom lighting conditions. Results showed that poor lighting conditions (average illuminance value <300 lx) in the classroom was also a risk factor for myopia symptom (OR=1.264). We found that different relaxations during break time led to different results. Compared to students who engaged in outdoor activities, those who had a rest or read and wrote in the classroom had an increased risk of myopia symptom (ORs=1.298, 1.454). A significant relationship between myopia symptom and the duration of homework per day was also found. Compared with students who spent less than 2 h on homework, those who spent 2–3 h or over 3 h had a 1.044- and 1.224-fold risk of myopia symptom (OR=1.044, 95% CI=0.810–1.345, and OR=1.224, 95% CI=1.098–1.364, respectively). Students who watched TV at a distance of less than 2 m and 2–3 m had an increased myopia symptom risk when compared with those who watched TV at a distance greater than 3 m (ORs=1.748, 1.374).

2.2 Risk Score System of Myopia Symptom

We constructed a risk score system for myopia symptom based on the Framingham score model. Each level of the risk factor was assigned points (table 2). Among all related factors, age was a continual variable. We transformed age into a categorical variable by classifying our participants into four groups. The age range between 5 and 7 was a critical period for emmetropization, so 6 and 7 years were grouped separately. The W_{ij} of age ranges 8–12 and 13–19 was defined by the average age of each group. The points of ages 6, 7, 8–12 and 13–19 were 0, 1, 4, and 10. Doing eye exercises and spending ≥1 h outdoors were assigned –1 point compared with their corresponding benchmark.

The total number of points was regarded as the test variable and myopia symptom as the status variable. The accuracy of the risk score system for myopia symptom was evaluated according to the area under the ROC curve. The area under the ROC curve was 0.735 (95% CI: 0.725–0.745) and the standard error was 0.006 (P<0.001), suggesting that the score system performed well in estimating the risk of myopia symptom (fig. 1).

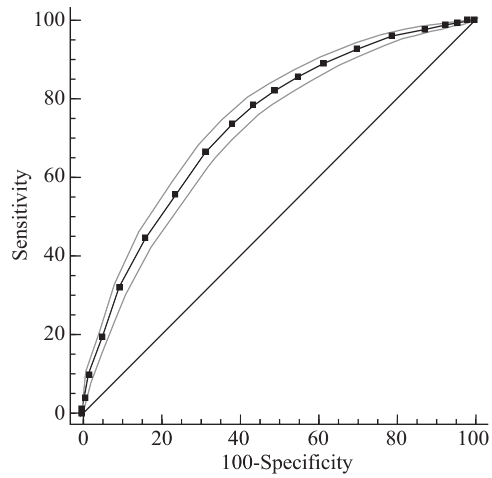

Fig. 1 ROC for total points of risk factors and myopia symptom

2.3 Estimating the Risk of Myopia Symptom

We assigned the factors according to the score system. By adding the scores of each risk factor, we got the total number of points for each student, which ranged from –2 to 21. We calculated the corresponding prediction probability for each individual using MEDCLAC (table 3). We defined the probability of final myopia symptom according to the score. If the score was ≥7, the forecasted probability of myopia symptom was 21.43%, suggesting that the individual has a high risk in developing myopia symptom in the future. Compared with the score lower than 7, the myopia symptom risk of score at 7–11 and higher than 11 were 2.422 and 7.795 (OR=2.422, 95% CI= 2.068–2.836, and OR=7.795, 95% CI=6.752–9.000, respectively) (table 4).

2.4 Testifying the Score System Using Longitudinal Data

We selected a total of 93 students whose age ranged from 7 to 9 years old. Seven-to-nine-year-olds

Table 2 Myopic factors in the score system

Risk factors	Classification	W_{ij}[a]	B[b]	$(W_{ij}{}^{c}–W_{iREF})$	β_i $(W_{ij}–W_{iREF})$	Point[d]
Age[e]						
	6	6=W_{1REF}	0.243	0	0.000	0
	7	7		1	0.243	1
	8–12	10[f]		4	0.972	4
	13–19	16[g]		10	2.430	10
Urban district						
	Remote area	0=W_{2REF}	0.672	0	0.000	0
	Downtown area	1		1	0.672	3
Gender						
	Female	0=W_{3REF}	–0.284	0	0.000	0
	Male	1		1	–0.284	–1
Reading distance						
<20 cm	No	0=W_{4REF}	0.607	0	0.000	0
	Yes	1		1	0.607	3
20–29 cm	No	0=W_{4REF}	0.292	0	0.000	0
	Yes	1		1	0.292	1
Average illuminance value in classroom						
	≥300 lx	0=W_{5REF}	0.235	0	0.000	0
	<300 lx	1		1	0.235	1
Break time						
Having a rest	No	0=W_{6REF}	0.261	0	0.000	0
	Yes	1		1	0.261	1
Reading or writing inside	No	0=W_{6REF}	0.374	0	0.000	0
	Yes	1		1	0.374	1
Homework time						
2–3 h	No	0=W_{7REF}	0.043	0	0.000	0
	Yes	1		1	0.043	0
>3 h	No	0=W_{7REF}	0.202	0	0.000	0
	Yes	1		1	0.202	1
Distance watching TV						
<2 m	No	0=W_{8REF}	0.558	0	0.000	0
	Yes	1		1	0.558	2
2–3 m	No	0=W_{8REF}	0.318	0	0.000	0
	Yes	1		1	0.318	1
Doing eye exercises						
	No	0=W_{9REF}	–0.145	1	0.000	0
	Yes	1		0	–0.145	–1
Time for outside activities ≥1 h						
	No	0=W_{10REF}	–0.132	0	0.000	0
	Yes	1		1	–0.132	–1

Note: [a] Reference standard of factors in each category; [b] Regression coefficient; [c] Factors of each category; [d] Score of factors in each category; [e] The age range between 5 and 7 is a critical period for emmetropization, so children at the age of 6 or 7 years were grouped separately; [f] Age: 8–12; W_{ij}=average of (8,9,10,11,12) =10; [g] Age:13–19, W_{ij}= average of (13,14,15,16,17,18,19) =16; m: meter; h: hour

are in the critical period of visual development. In this period, the development of vision is susceptible to environmental factors. Without effective prevention, children tend to develop myopia.

We used the pair chi-square test to compare the final myopia symptom which was observed after one year of follow-up (from March 2008 to March 2009) and the results predicted by the total points according to the score system; we found no significant difference (χ^2=0.173, P>0.05), which showed that the score system was able to estimate the risk of myopia symptom.

3 DISCUSSION

3.1 Influence Factors of Myopia Symptom among School Students in Wuhan

Epidemiologic studies discovered the important role environmental factors played in the formation and development of myopia[19, 20]. In our study, we used a logistic regression method to identify risk factors for myopia symptom and then devised a risk score system based on the Framingham model. Altogether, ten risk factors (age, urban district, gender, reading distance, illumination, activities during break time, time spent on homework, distance for watching TV, doing eye exercises and time for outdoor activities) were entered into the model. Thus, we could predict myopia symptom by evaluating behaviors and environmental factors, which are relatively easy to measure.

The prevalence of myopia varied between the two genders. Females are more likely to be myopic than males, which was also affirmed in our study. Compared with females, the OR value in males was 0.753 (95% CI: 0.677–0.836). Poor eye habits play an important role in the development of myopia. The first poor habit is short-range reading and writing. In our study, the OR values of reading and writing at a distance of less than 20 cm and between 20 cm and 29 cm were 1.835 and 1.339, respectively, which was consistent with Ip's study[20]. In Ip's study, students whose reading distance was less than 30 cm had 2.5 times greater risk than those whose reading distance was more than 30 cm. The time spent on homework is another risk factor. Ying's study found that there was a significant association between hours of near work and a refractive error in students aged 6 to 12. The multivariate odds ratio for each diopter-hour per week of near work was 1.019 (95% CI: 1.005-1.033)[21]. A recent meta-analysis confirmed that near-work activities increased the prevalence of myopia[22]. In Saw's study, the mean time spent on near work was 3 h in myopic children and 2 h in non-myopic children. This difference was not observed in Saw's study, however[23]. The age of the subjects in Saw's study ranged between 3 and 7 years, while in our study the age range was 6–19 years. You *et al* documented that myopia was associated with dim reading illumination[24]. Based on an animal model of myopia, Smith indicated that the progression of myopia could be slowed down by improving illumination conditions[25]. We also concluded in this study that poor illumination conditions (average illuminance value: <300 lx) are a risk factor for myopia symptom. (OR=1.264, 95% CI: 1.071–1.439).

Table 3 Prediction probability of risk factor scores for myopia symptom

Score	Prediction probability
–2	0.0297
–1	0.0376
0	0.0474
1	0.0597
2	0.0749
3	0.0936
4	0.1163
5	0.1437
6	0.1762
7	0.2143
8	0.2581
9	0.3073
10	0.3612
11	0.4190
12	0.4790
13	0.5397
14	0.5992
15	0.6559
16	0.7085
17	0.7560
18	0.7980
19	0.8344
20	0.8653

A recent randomized clinical trial confirmed that spending a long time on outdoor activities is a protective factor against myopia[26]. Wu's study, which was a prospective, comparative, consecutive, interventional design, also found that time spent outdoors had a significant effect on myopia onset[27]. These studies were consistent with our result. In our study, time spent on outdoor activities greater than 1 h has an OR value of 0.876. Thus, by extending the duration of outdoor activities, we will decrease the incidence of myopia and improve this urgent situation.

There are multiple mechanisms which could explain why increasing outdoor activity time reduces the incidence of myopia. According to an animal model study, the stronger illumination outside may explain the protective effects[25]. Rose's research showed that indoor activities have no effect on myopia, which, to some extent, supported the "illumination theory"[28]. Thus, instead of the sports themselves, the protective effects of outdoor activities are most likely to come from the illumination. However, the biological mechanism is not clear. One possible reason is that outdoor activities can broaden the vision. What is more, lighting stimulates the secretion of dopamine, which can inhibit the eye axis from elongating[29].

It has been decades since the popularization of eye exercises, and their positive effect on protecting eyesight and relieving visual fatigue have already been

Table 4 Different score levels associated with myopia symptom

Factors	β	S.E.	Wald	P	OR	95% CI	
						Lower bound	Upper bound
Score							
–2 to 6	Ref				1.000		
7 to 11	0.885	0.081	120.750	<0.001	2.422	2.068	2.836
12 to 21	2.054	0.073	784.849	<0.001	7.795	6.752	9.000
Constant	–1.179	0.065	327.204	–	–	–	–

affirmed. Ping Zhong's[30] epidemiological studies had testified the effect of eye exercises. We also found that regular eye exercises were a protective factor against myopia symptom (OR=0.865, 95% CI: 0.773–0.967).

3.2 The Accuracy of the Framingham Risk Score Model in Predicting Myopia Symptom

The Framingham Heart study built a multivariable model of predicting coronary heart disease risk, which helps patients to choose the right treatments and change unhealthy behaviors. Moreover, the Framingham Heart study method is widely applied in constructing estimate risk models of other diseases, such as diabetes, high blood pressure, heart failure and kidney disease[31, 32].

In our study, the area under the ROC curve was 0.735 (95% CI: 0.725–0.745), which showed that the score system was able to estimate the risk of myopia symptom. Around the best cutoff point 11, the Youden index was the highest and we could get relatively high sensitivity (73.46%) and specificity (61.98%). Preventive measures should be given when the score is ≥7, including correcting bad eye behaviors, reducing time spent on homework, and keeping reading distance to above 30 cm.

Nevertheless, there were some limitations in our study. One was the lack of cycloplegia. It's widely advisable to apply cycloplegic refraction to measure refractive errors among children. However, with this cohort, it's difficult to carry out cycloplegic refraction in this epidemiological investigation. What's more, we aimed at defining myopia symptom instead of acquiring accurate refraction. Another limitation was that our data was collected by a cross-sectional study. However, we had verified our score system using longitudinal data among 93 students whose age ranged from 7 to 9 years old.

Conflict of Interest Statement

The authors declare no conflict of interest.

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