

Methods and Applications

Targeted Cycloplegia in Refractive Screening of Children and Adolescents: Development and Internal Validation of a Pre-Cycloplegia Risk Prediction Model — 10 PLADs, China, 2020–2024

Ting Li¹; Jingshu Zhang¹; Huijuan Luo¹; Han Yang¹; Wenxin Wang¹; Yifan Wang¹;
Keke Liu^{1,2}; Ran Qin¹; Xin Guo^{2,3,#}

ABSTRACT

Introduction: Cycloplegic refraction is the gold standard for accurate refractive assessment in children and adolescents, but its use is limited by operational complexity and low acceptance. Because effective tools for identifying individuals who require cycloplegia are lacking, this study aimed to develop a risk prediction model for refractive misclassification based on pre-cycloplegia parameters to assist targeted cycloplegic refraction.

Methods: A total of 43,760 children and adolescents aged 5–18 years were enrolled from 10 provincial-level administrative divisions in China using stratified cluster probability-proportional-to-size (PPS) sampling. Pre-cycloplegia data, including individual characteristics, ocular indicators, and lifestyle factors, were collected. Binary logistic regression was used to develop the model, and receiver operating characteristic (ROC) curves were used to determine the optimal cutoff value.

Results: The final model included six core variables and achieved an overall classification accuracy of 79.4% and an area under the ROC curve (AUC) of 0.730. The optimal cutoff score was 18.4. Moderate or low uncorrected visual acuity and abnormal axial length were major risk factors, whereas a higher school stage was protective.

Conclusion: The prediction model demonstrated favorable performance and identified individuals at high risk of refractive misclassification. Individuals with a risk score ≥ 18.4 may be prioritized for cycloplegic refraction.

accurate refractive screening crucial for myopia prevention and control (1). Cycloplegic refraction, which eliminates pseudomyopia by paralyzing accommodation, is regarded as the clinical gold standard (2). Nevertheless, its large-scale application is limited by procedural complexity, potential adverse effects, long examination duration, and low acceptance among children and caregivers. Consequently, non-cycloplegic screening is widely used in large-scale screening programs but carries a high risk of refractive misclassification.

Currently, no evidence-based tool exists to stratify populations into high-risk individuals needing cycloplegia and low-risk individuals for whom non-cycloplegic screening is adequate. This creates a dilemma: overuse of cycloplegia increases the procedural burden, while underuse reduces accuracy. Most existing studies have focused on confirming the advantages of cycloplegia, whereas few have attempted to identify candidates for cycloplegia using pre-cycloplegia indicators (3).

To fill this gap, we developed a risk prediction model for refractive misclassification using pre-cycloplegia individual, ocular, and lifestyle data from a large multicenter sample of children and adolescents. The model aims to determine key risk factors, establish an optimal cutoff score, and provide a practical tool for personalized screening. This strategy balances accuracy and feasibility and supports more efficient refractive screening in clinical and public health practice.

METHODS

This cross-sectional study enrolled 43,760 participants aged 5–18 years from November 2020 to July 2024. Stratified cluster probability-proportional-to-size (PPS) sampling was applied across 10 provincial-level administrative divisions in eastern

Refractive errors are a leading cause of visual impairment in children and adolescents, making

China (Beijing, Zhejiang, Guangdong, and Shandong), central China (Henan, Hunan, and Shanxi), western China (Shaanxi and Chongqing), and northeastern China (Liaoning) to ensure geographic and economic representativeness. Sample regions were selected according to per capita gross domestic product (GDP), and schools and classes were selected proportionally, covering primary, junior, and senior high school students. All students in the selected classes were included in this study. Participants with ineligible refractive data, invalid results because of noncooperation, or incomplete cycloplegic refraction data were excluded. Missing data were handled using complete case analysis. For analyses not involving axial length, the full sample of 43,760 was used; for analyses including axial length as a variable, 43,539 participants with complete axial length records were analyzed. Given the very low missing rate (0.50%) and random distribution of missing cases, no data imputation was performed.

The following pre-cycloplegia data were collected to inform screening decisions. Individual characteristics included sex, school stage (primary, junior high, or senior high school), and economic level (high, middle, or low, classified by regional per capita GDP). Ocular indicators included uncorrected visual acuity [UA, stratified as low (4.0–4.5), moderate (4.6–4.9), or good (5.0–5.2)], axial length (normal or abnormal), and intraocular pressure (normal or abnormal). Lifestyle factors included electronic device use (≤ 1 h/d or > 1 h/d), outdoor activity (< 2 h/d or ≥ 2 h/d), and sleep duration (adequate or inadequate).

All students received four applications of 0.5% tropicamide with one drop administered at 5-min intervals. Cycloplegic refraction was measured three times in each eye using a desktop autorefractor (KR-800; Topcon, Tokyo, Japan), and the mean of the three measurements was used as the refractive value. The adequacy of cycloplegia and pupillary dilation was assessed 30 min after the final application. Right-eye data were used for all statistical analyses. A correct classification was defined as agreement between noncycloplegic and cycloplegic refraction (i.e., both methods classified the participants as myopic or both classified the participants as nonmyopic). Discordant results (false-positive or false-negative classifications) were defined as refractive misclassification. Participants with discordant results were classified as requiring cycloplegia. Standardized protocols and strict multilevel quality-assurance procedures were implemented across all 10 provincial sites throughout

the study period. All autorefractors underwent quarterly calibration and annual intersite consistency testing to control measurement bias. On-site medical and school health staff completed standardized training and competency assessments before data collection, and standardized cycloplegia procedures were enforced uniformly. A three-tier quality control mechanism, including real-time data verification, daily random sample review, and annual cross-site inspection, was adopted to ensure data consistency and reliability. Statistical analyses were conducted using R software (version 4.5.2, R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were expressed as the mean $\pm$ standard deviation (SD) and compared using *t* tests, one-way analysis of variance (ANOVA), or Welch's ANOVA for unequal variances. Categorical variables were reported as frequencies (percentages) and analyzed by the χ^2 test. Forward stepwise binary logistic regression was used to identify independent factors associated with refractive misclassification. Model performance was assessed using receiver operating characteristic (ROC) curves, including the area under the curve (AUC), sensitivity, specificity, and the Youden index; the latter was used to determine the optimal cutoff. A risk-scoring system was established based on standardized regression coefficients. A two-sided $P < 0.05$ was considered statistically significant.

Internal validation was conducted using a random hold-out strategy. The full sample was randomly divided into a training set (70%) for model construction and a test set (30%) for independent performance verification.

Subgroup analyses were conducted to assess model generalizability across geographic regions (eastern, central, western, and northeastern China) and economic strata (high, middle, and low). AUC, sensitivity, specificity, and optimal cutoff were calculated for each subgroup. A sensitivity analysis was conducted by randomly excluding 10% of participants to assess the robustness of the main findings.

RESULTS

Sex, school stage, UA category, axial length, economic level, electronic device use, outdoor activity time, and sleep duration were significantly associated with refractive misclassification (all $P < 0.05$), whereas intraocular pressure was not ($P = 0.363$). Misclassification rates were highest in the moderate UA group (45.0%, 6,460/14,355) and the low UA group

(44.8%, 2,329/5,199) and were substantially higher in the abnormal axial length group (45.8%, 2,250/4,931) than in the normal axial length group (22.2%, 8,587/38,626) (Table 1).

Forward stepwise logistic regression retained six predictors in the final model: school stage, UA category, axial length classification, economic level, electronic device use, and sleep duration (Table 2). The model achieved an overall classification accuracy

of 79.4%, with Cox–Snell $R^2=0.270$ and Nagelkerke $R^2=0.371$.

In subgroup analyses by geographic region, the AUC was 0.752 [95% confidence interval (CI): 0.744, 0.760] in eastern China, 0.728 (95% CI: 0.720, 0.736) in central China, 0.695 (95% CI: 0.678, 0.712) in western China, and 0.639 (95% CI: 0.614, 0.664) in northeastern China. The optimal cutoff scores ranged from 18.2 to 18.6 points across the four regions. When

TABLE 1. Univariate analysis of refractive misclassification among children and adolescents aged 5–18 years in 10 PLADs, China, 2020–2024.

Influencing factor	Sample size	Test statistic	P
Sex			
Male	22,530	Welch's F =38.657	<0.001
Female	21,230		
School stage			
Primary	41,190	Welch's F =839.285	<0.001
Junior	1,585		
Senior	985		
Uncorrected visual acuity			
Low (4.0–4.5)	5,199	Welch's F =8,244.978	<0.001
Moderate (4.6–4.9)	14,355		
Good (5.0–5.2)	24,206		
Axial length			
Normal	38,626	Welch's F =1,133.819	<0.001
Abnormal	4,913		
Economic level			
High	14,417	Welch's F =160.707	<0.001
Middle	22,712		
Low	6,631		
Intraocular pressure			
Normal	40,325	F(ANOVA) =0.829	0.363
Abnormal	3,435		
Electronic device usage			
≤1 h/d	16,090	Welch's F =21.020	<0.001
>1 h/d	27,670		
Outdoor activity time			
<2 h/d	20,739	Welch's F =7.851	<0.001
≥2 h/d	23,021		
Sleep duration			
Adequate	7,946	Welch's F =52.298	<0.001
Inadequate	35,814		

Note: Post hoc comparisons using the LSD test were performed for variables with more than two subgroups. School stage: Primary vs. Junior, $P<0.001$; Primary vs. Senior, $P<0.001$; Junior vs. Senior, $P=0.102$. For uncorrected visual acuity, all pairwise comparisons were $P<0.001$. For economic level, all pairwise comparisons had $P<0.001$.

Abbreviation: LSD=least significant difference; ANOVA=one-way analysis of variance.

TABLE 2. Binary logistic regression analysis of refractive misclassification among children and adolescents.

Variable	B value	Standard error	Wald χ^2	P	OR (95% CI)
School stage	-0.837	0.056	222.44	<0.001	0.43 (0.39, 0.48)
Uncorrected visual acuity (Ref: Good)			9,451.59	<0.001	
Low	1.121	0.070	259.60	<0.001	3.07 (2.68, 3.52)
Moderate	3.459	0.070	2,461.17	<0.001	31.79 (27.73, 36.45)
Axial length (Ref: Normal)	1.314	0.050	682.36	<0.001	3.72 (3.37, 4.11)
Economic level (Ref: Low)			136.58	<0.001	
High	0.135	0.038	12.35	<0.001	1.14 (1.06, 1.23)
Middle	-0.172	0.037	22.15	<0.001	0.84 (0.78, 0.90)
Electronic device usage (Ref: ≤ 1 h/d)	0.049	0.025	3.87	0.049	1.05 (1.00, 1.10)
Sleep duration (Ref: Adequate)	0.133	0.031	18.82	<0.001	1.14 (1.08, 1.21)
Constant	-2.843	0.108	694.77	<0.001	0.06

Abbreviation: OR=odds ratio; CI=confidence interval; SE=standard error; Ref=reference category; Wald χ^2 =Wald chi-square test statistic; B=unstandardized regression coefficient.

stratified by economic level, the AUC was 0.774 (95% CI: 0.766, 0.782) in regions with a high economic level, 0.721 (95% CI: 0.714, 0.729) in regions with a middle economic level, and 0.578 (95% CI: 0.562, 0.594) in regions with a low economic level; the corresponding specificities were 90%, 84%, and 85%, respectively.

After 10% of the participants were randomly excluded in the sensitivity analysis, the model yielded an AUC of 0.729 (95% CI: 0.723, 0.734), with an optimal cutoff of 18.4 points. All six core variables remained in the final model, and the odds ratio (OR) estimates for the key predictors changed by less than 3% relative to those in the primary analysis, indicating that the estimates were not materially altered in this sensitivity analysis.

In the hold-out internal validation, the model achieved an AUC of 0.733 (95% CI: 0.727–0.740) in the training set and 0.721 (95% CI: 0.711–0.731) in the test set. The high consistency of discriminative performance, core predictors and cutoff value between the two sets demonstrated good stability of the model with no obvious overfitting.

A risk-scoring system was constructed using standardized regression coefficients (Table 3). Total risk score=School Stage score + Uncorrected Visual Acuity score + Axial Length score + Economic Level score + Sleep Duration score + Electronic Device Usage score. ROC analysis yielded an AUC of 0.730 (95% CI: 0.725, 0.735; $P<0.001$). At the optimal cutoff of 18.4 points, the Youden index was 0.509, sensitivity was 64.6%, and specificity was 86.3%. This cutoff was used to classify participants as being at high or low risk of refractive misclassification.

DISCUSSION

Using data from 43,760 participants, this study developed a six-variable prediction model for refractive misclassification in children and adolescents, with an AUC of 0.730 and a specificity of 86.3%. This model may help clinicians and public health practitioners identify individuals at high risk of misclassification and support the targeted use of cycloplegic refraction.

Being at a higher school stage was a protective factor (OR=0.43), possibly because older adolescents have more stable refractive status and accommodative function and may cooperate better during examinations (4–5). UA category had the strongest association with misclassification: compared with the good UA group (5.0–5.2), the moderate UA group (4.6–4.9) had 31.79-fold higher odds of misclassification, whereas the low UA group had 3.07-fold higher odds. The elevated predicted risk among primary school children supports consideration of targeted cycloplegia in this age group. Clinically, moderate UA often reflects mild myopia or "pseudomyopia," in which active accommodation under noncycloplegic conditions distorts measurements, making this group prone to false-positive or false-negative classification and therefore an important target for cycloplegic refraction (6). In contrast, the good UA group primarily included emmetropic or mildly hyperopic children and adolescents with stable accommodation, resulting in the lowest misclassification rate and more reliable noncycloplegic screening. Abnormal axial length (OR=3.72) was another important predictor. As an objective ocular measurement associated with myopia

TABLE 3. Risk-score assignments for refractive misclassification in children and adolescents.

Variable	Coded value	Standardized B value	Score
School stage			
Primary	1	-6.29	-6.29
Junior	2	-6.29	-12.58
Senior	3	-6.29	-18.87
Uncorrected visual acuity			
Good	1	0	0
Moderate	2	26.01	26.01
Low	3	8.43	8.43
Axial length			
Normal	1	9.88	0
Abnormal	2	9.88	9.88
Economic level			
Low	1	-1.29	0
Middle	2	-1.29	-1.29
High	3	1.02	1.02
Electronic device usage			
≤1 h/d	1	0.37	0
>1 h/d	2	0.37	0.37
Sleep duration			
Adequate	1	1.00	0
Inadequate	2	1.00	1.00

Abbreviation: B=unstandardized regression coefficient; SE=standard error.

and its progression, axial length may provide useful complementary information during pediatric refractive screening (7). The association between economic level and misclassification was not monotonic: relative to regions with a low economic level, the odds were higher in regions with a high economic level but lower in regions with a middle economic level. Therefore, this finding cannot be explained solely by differences in vision-monitoring systems or awareness and requires further investigation (8). Electronic device use for >1 h/d showed a small association with refractive misclassification ($OR=1.05$). Although electronic device use has been associated with myopia, the mechanism underlying its association with refractive misclassification requires further study (9). Inadequate sleep was also associated with refractive misclassification; however, the mechanism underlying this association requires further study (10). Therefore, a comprehensive assessment of vision-monitoring systems is required to enhance the accuracy and continuity of refractive surveillance in children and adolescents. Although cycloplegia is the gold standard for refractive assessment of children and adolescents, its

complexity restricts its widespread use. This study provides a potentially practical tool to identify candidates who may require cycloplegia, rather than merely verifying its value. From a national public health perspective, this risk-scoring system could potentially be incorporated into routine annual vision screening managed by local CDCs. During school-based screening, school physicians and primary eye care personnel could use the required data to calculate each student's risk score, provided that axial-length measurements are available. The 18.4-point cutoff may support clinical decision-making. Individuals scoring ≥ 18.4 may be prioritized for cycloplegic refraction, especially primary school students with moderate or low UA or abnormal axial length. However, the sensitivity of 64.6% indicates that 35.4% of individuals with refractive misclassification would not be identified at this threshold. Therefore, a score <18.4 should not be used alone to conclude that noncycloplegic screening is sufficiently reliable avoiding unnecessary procedures, lowering workload, reducing discomfort. If prospectively validated, this tiered approach may help allocate limited ophthalmic

personnel, cycloplegic agents, and equipment more efficiently. Reducing unnecessary cycloplegic examinations may also decrease discomfort, including photophobia, blurred near vision, and ocular irritation, and may improve screening adherence. For CDC administrators, the standardized quantitative score may guide targeted resource allocation toward high-risk subgroups, particularly primary school students with poor vision or abnormal axial length, potentially supporting more equitable and efficient myopia-control efforts.

Subgroup analyses showed that the optimal cutoff values were relatively consistent across geographic and economic strata. However, discriminatory performance varied substantially, with AUCs ranging from 0.639 to 0.752 across geographic regions and from 0.578 to 0.774 across economic strata. The sensitivity analysis produced results similar to those of the primary analysis. However, the relatively low AUCs in northeastern China and regions with a low economic level indicate that the model may not perform equally well in all populations. Independent external validation and possible subgroup-specific refinement are therefore needed before nationwide implementation.

This study had several limitations. First, its cross-sectional design precludes causal inference. Future prospective studies are needed to validate the model's long-term predictive performance in children and adolescents. Second, pre-cycloplegia factors such as corneal curvature and accommodative amplitude were not included, which may have limited the accuracy of the model. Third, economic level was defined according to regional GDP rather than individual household economic status. Fourth, the model's discriminatory performance varied substantially across geographic and economic subgroups. Finally, the sensitivity of 64.6% indicates that the selected cutoff would fail to identify some individuals with refractive misclassification. Despite these limitations, the model's relatively high specificity suggests that it may help reduce unnecessary cycloplegia among appropriately identified low-risk individuals; however, it does not ensure that all high-risk individuals will be identified.

In conclusion, this study developed a risk-scoring system for refractive misclassification in children and adolescents. A score ≥ 18.4 may help prioritize individuals for cycloplegic refraction; however, scores < 18.4 should be interpreted together with other clinical information because the model's sensitivity was 64.6%. The model may help prioritize cycloplegic-refraction resources for high-risk groups, including

primary school children, children with UA of 4.6–4.9, and those with abnormal axial length. However, external validation and possible refinement in lower-performing subgroups are required before nationwide implementation. If validated, this approach could balance accuracy and practicality and provide an evidence-based tool for optimizing refractive screening in children and adolescents.

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Corresponding author: Xin Guo, guoxin@chinacdc.cn.

¹ School Health Department, Beijing Center for Disease Prevention and Control, Beijing, China; ² School of Public Health, Capital Medical University, Beijing, China; ³ Preparatory Office for School Health, Chinese Center for Disease Control and Prevention & Chinese Academy of Preventive Medicine, Beijing, China.

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