Repeat Retinomax screening changes positive predictive value

Eugene A. Lowry, BA, a Ryan Lui, b Wayne Enanoria, PhD, a,c Jeremy Keenan, MD, MPH, a,c and Alejandra G. de Alba Campomanes, MD, MPH a

PURPOSE
To quantify changes in autorefraction measurement with repeated readings using the Retinomax autorefractor and to investigate the clinical implications of the results.

METHODS
Children referred from a preschool vision screening program for a failed autorefraction screening test received repeat autorefraction as well as a comprehensive eye examination with cycloplegic retinoscopy at later follow-up. The intraclass correlation coefficient between initial and follow-up autorefraction was calculated to quantify changes in repeated measurements to determine whether the second autorefraction significantly changed the predictive value that a referred child would meet case definition. Cases were defined by AAPOS Vision Screening Committee amblyogenic risk factors under cycloplegic retinoscopy.

RESULTS
Repeat Retinomax autorefraction had an intraclass correlation of 0.70 in the right eye and 0.70 in the left eye for mean sphere. Of 636 children who were referred on their initial screening, 169 (26.5%) passed a repeat screening and this subpopulation had 7 cases (4.1%). Of the 467 (73.5%) who again met referral criteria at repeat screening, 268 (57.4%) met case definition. The difference in case rates between these subgroups was highly significant (Fisher exact test, $P < 0.001$).

CONCLUSIONS
There was clinically significant variability when autorefraction measurements were repeated among those referred from initial screening, allowing further risk stratification. In our study cohort, few children who passed repeat screening required further examination. Significant money and overtreatment risk may potentially be avoided by rescreening children who are initially referred from screening evaluations and only examining those who meet referral criteria after a second screening. (J AAPOS 2014;18:45-49)

The Retinomax autorefractor (Righton, Tokyo, Japan) is an objective vision screener recommended for preschool children. Operating characteristics of this machine have been described previously. The instrument has an infrared camera that takes at least 8 refractive measurements on each eye independently at a working distance of approximately 4 cm. These measurements are then combined to yield an average refractive error with a reliability score for each eye that is determined by the consistency of the individual readings. The average refraction with reliability score is used to make screening decisions and, compared with other screening technologies, has demonstrated a favorable sensitivity and specificity when used by lay vision screeners.

The reliability of the Retinomax in repeat measurements on the same child has not been well characterized to date. One study comparing the mean refractive errors of 299 children with repeat readings found minimal differences between the average population spherical and cylindrical measurements with repeated measurements. The study was limited by comparing population averages with a paired $t$ test and thus underestimating individual variability because positive and negative individual variations neutralize each other at the population level. Individual variability is better assessed with an intraclass correlation coefficient (ICC), which can quantify individual level variability even if the population average remains unchanged. The purpose of this study was to quantify the variability between autorefraction readings performed by lay screeners in preschool children and to calculate the clinical effect of this variability. Specifically, we determined the intraclass correlation coefficient between original and repeat autorefraction. We investigated clinical implications of this variability by determining whether a repeat autorefraction screening significantly changes the probability that a child will meet case definition for amblyogenic risk factors.
Table 1. Cut-off criteria for referral based on noncycloplegic Retinomax screening results and case definition based on AAPOS vision screening committee designated amblyopia risk factors.

<table>
<thead>
<tr>
<th>Refractive Error</th>
<th>Retinomax referral criteria</th>
<th>Amblyopia risk factors ≤48 months of age</th>
<th>Amblyopia risk factors &gt;48 months of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperopia</td>
<td>&gt; 1.25 D</td>
<td>&gt; 4.00 D</td>
<td>&gt; 3.50 D</td>
</tr>
<tr>
<td>Myopia</td>
<td>&gt; 3.25 D</td>
<td>&gt; 3.00 D</td>
<td>&gt; 1.50 D</td>
</tr>
<tr>
<td>Astigmatism</td>
<td>&gt; 1.25 D</td>
<td>&gt; 2.00 D</td>
<td>&gt; 1.50 D</td>
</tr>
<tr>
<td>Anisometropia</td>
<td>H: &gt; 1.25 D</td>
<td>&gt; 2.00 D</td>
<td>&gt; 1.50 D</td>
</tr>
<tr>
<td></td>
<td>M: &gt; 1.75 D</td>
<td>&gt; 2.00 D</td>
<td>&gt; 1.50 D</td>
</tr>
<tr>
<td></td>
<td>A: &gt; 0.75 D</td>
<td>&gt; 2.00 D</td>
<td>&gt; 1.50 D</td>
</tr>
</tbody>
</table>

Subjects and Methods

The medical records of children participating in an autorefration vision screening and eye-care program implemented by Prevent Blindness Northern California, a community nonprofit 501(c)(3) that administers regional preschool vision screening, were retrospectively reviewed. The study received approval from the University of California, San Francisco, Institutional Review Board and was conducted using a database and protocol compliant with the US Health Insurance and Portability and Accountability Act of 1996.

Lay vision screeners performed noncycloplegic in-school autorefraction in low-income urban preschoolers from July 2011 through February 2013 using a Retinomax autorefractor. Targeted preschools were either in the unified school districts, Head Start, or county preschools for low-income children. Children were considered unable to perform the test if a reliability score of ≥ 8 could not be obtained in either eye, as recommended by the manufacturer, and in other studies6; these children were excluded from the current study. Demographic information including age, ethnicity, and sex, were collected at the time of screening.

Children testing worse than any of the prespecified autorefraction thresholds were considered to have failed autorefraction and were referred for follow-up examination at a later date (Table 1). These follow-up examinations were performed in a mobile eye van that visited each school. As part of their follow-up examination, every child underwent repeat noncycloplegic autorefraction with the Retinomax, performed by a different lay screener, as well as a dilated eye examination, including cycloplegic retinoscopy, performed by a licensed optometrist. Preschoolers who were referred from the original school-based autorefraction screening and subsequently received a follow-up comprehensive eye examination on the mobile eye van by March 1, 2013, were included. Children were excluded from the study if they were already known to have eyeglasses, if they had a test reliability score <8 in either initial or repeat screening, or if they were referred for follow-up examination for nonrefractive criteria, such as a failed Hirschberg or cover-uncover test.

The change in repeat Retinomax autorefraction measurements was calculated as the intraclass correlation coefficient of the spherical and cylindrical power between initial and repeat screens. The analysis was stratified on the basis of eye in order to avoid combining nonindependent measurements in the same child.

Table 2. Number of children screened, referred and examined leading to the included study population of 636 children who received repeat screening and examination.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Screened</th>
<th>Referred</th>
<th>Examined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>7614</td>
<td>1303</td>
<td>636</td>
</tr>
<tr>
<td>Age, years, ± SE</td>
<td>4.28 ± 0.01</td>
<td>4.19 ± 0.02</td>
<td>4.32 ± 0.03</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3,720 (49)</td>
<td>564 (43)</td>
<td>285 (45)</td>
</tr>
<tr>
<td>Female</td>
<td>3,771 (50)</td>
<td>700 (54)</td>
<td>351 (55)</td>
</tr>
<tr>
<td>Missing data</td>
<td>123 (2)</td>
<td>39 (3)</td>
<td>0</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>2077 (27)</td>
<td>294 (23)</td>
<td>157 (25)</td>
</tr>
<tr>
<td>African American</td>
<td>1378 (18)</td>
<td>224 (17)</td>
<td>67 (11)</td>
</tr>
<tr>
<td>White</td>
<td>370 (5)</td>
<td>32 (2)</td>
<td>11 (2)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3072 (40)</td>
<td>585 (45)</td>
<td>313 (49)</td>
</tr>
<tr>
<td>Other</td>
<td>437 (6)</td>
<td>48 (4)</td>
<td>17 (3)</td>
</tr>
<tr>
<td>Missing data</td>
<td>280 (4)</td>
<td>120 (9)</td>
<td>71 (11)</td>
</tr>
</tbody>
</table>

Sex, standard error of the mean.

Cases were defined based on amblyopia risk factors as updated by the AAPOS Vision Screening Committee in 2013 (Table 1). We divided the study population into two subpopulations: (1) those who passed repeat screening; and (2) those who again met referral criteria at repeat screening. Case rates between these subpopulations were compared. As cases were defined for an entire individual and not a single eye, all analyses of case rates were performed at the individual level. The Fisher exact test was used to compare the case rates in the two subpopulations. Finally, we examined whether children referred for any specific referral criteria or at different ages were more likely to pass at repeat screening. Wilson binomial confidence intervals were used to calculate 95% confidence intervals for all analyses of dichotomous outcomes.

Results

From July 2011 to March 2013, 7,614 preschool children were successfully screened with the Retinomax autorefractor. An additional 302 children in the potential target population had screening reliability scores <8 (n = 204), already had glasses (n = 62), or were referred for nonrefractive reasons (n = 36). Of those successfully screened with autorefraction, 1,303 met criteria for referral. Of those, 636 received a comprehensive examination, including both repeat noncycloplegic autorefraction as well as a dilated eye examination and were included in this study. The time from original screening day to the day of repeat autorefraction and comprehensive examination averaged 96 days, with a standard deviation of 64 days. The average subject age was 4.3 years, and the racial and ethnic distribution of the children that received follow-up and were included in this study was as follows: 49% Hispanic, 25% Asian, 11% African American, 3% other, 2% white, and 11% unspecified. This distribution generally reflected that of all children screened, although African Americans had disproportionately low follow-up (Table 2).

There was greater variation in sphere than cylinder. Sphere measurements had an intraclass correlation of
0.70 in the right eye (95% CI, 0.65-0.73) and 0.70 in the left eye (95% CI, 0.65-0.73). Cylinder measurements had an intraclass correlation of 0.83 (95% CI, 0.81-0.85) in the right eye and 0.84 (95% CI, 0.82-0.87) in the left eye (Table 3).

Of the 636 children who completed a follow-up examination, 467 (73%) met referral criteria again at repeat screening, whereas 169 (27%) passed the repeat screening. Overall, 275 or 43% (95% CI, 39.3%-47.1%) of children with a follow-up examination met the case definition for amblyogenic risk factors. However, the case rates were significantly different when stratified on the results of the repeat autorefraction. Of those who met referral criteria at repeat autorefraction, 268 of the 467 (57.4%; 95% CI, 50.1%-64.6%) met case definition, whereas only 7 of the 169 who passed the repeat autorefraction (4.1%; 95% CI, 0.0%-8.3%) met case definition ($P < 0.001$, Fisher exact test; Figure 1).

Of 286 children aged ≤48 months of age, 69 (24.1%; 95% CI, 18.8%-29.4%) passed repeat screening, whereas of 350 children >48 months of age, 100 (28.6%; 95% CI, 23.6%-33.5%) passed repeat screening ($P = 0.24$, Fisher exact test). The proportion of children who converted from a referral at first screening to pass at repeat screening for hyperopia was 30% (95% CI, 15%-45%); for myopia, 43% (95% CI, 28%-57%); for astigmatism, 18% (95% CI, 11%-24%); for hyperopic anisometropia, 79% (95% CI, 69%-90%); for myopic anisometropia, 63% (95% CI, 43%-82%); for astigmatic anisometropia, 54% (95% CI, 41%-68%); and for multiple referral indications, 16% (95% CI, 11%-21%).

### Table 3. Spherical and cylindrical power in the first and second non-cycloplegic Retinomax autorefraction of the study population with intraclass correlation coefficients

<table>
<thead>
<tr>
<th>Refractive Error</th>
<th>First screening</th>
<th>Second screening</th>
<th>ICCa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right eye</td>
<td>Left eye</td>
<td>Right eye</td>
</tr>
<tr>
<td>Sphere ± SE</td>
<td>−0.53 ± 0.08</td>
<td>−0.45 ± 0.09</td>
<td>−0.93 ± 0.08</td>
</tr>
<tr>
<td>Cylindrical power ± SE</td>
<td>−1.34 ± 0.04</td>
<td>−1.33 ± 0.04</td>
<td>−1.32 ± 0.04</td>
</tr>
</tbody>
</table>

**ICC**, intraclass correlation coefficient; **SE**, standard error of the mean.
a95% CI in parentheses.

**FIG 1.** Repeat autorefraction and positive predictive value. The prevalence of refractive errors considered to be amblyogenic risk for repeat referrals and repeat passes are shown in the lower and upper pie charts, respectively. Children with refractive errors considered amblyogenic risk factors are shown in black. Only 4.1% of those children who passed the repeat Retinomax met glasses criteria compared with 57.4% of those re-referred on the repeat Retinomax. **ARF**, amblyogenic risk factor.

### Discussion

This study investigated the changes in repeat Retinomax autorefraction screening to determine whether there was any utility in repeat screening of children referred from initial screening. We found that repeated autorefraction results demonstrate little change for cylindrical measurements but considerable variation in repeat readings for spherical measurements. The slight improvements in repeat autorefractions for spherical measurements suggest that repeat autorefractions may have some utility in screening for amblyogenic risk factors.

The differences in case rates stratified by results of the repeat autorefractive screening highlight the variability and importance of repeat screening. These findings support the importance of repeat screening in determining the need for glasses prescription and for amblyogenic risk factors. The results also suggest that repeat screening can help identify children who may benefit from referral for further evaluation or intervention.

While the study findings demonstrate the utility of repeat autorefractive screening, it is important to consider the practical implications and potential limitations. Repeat screening may involve additional costs and inconvenience for both children and their caregivers. Further research could explore strategies to optimize the utility of repeat autorefractive screening while minimizing the burden on participants and healthcare providers.
sphere. The ICC for sphere at 0.70 and 0.70 is considered poor to moderate, whereas the cylinder ICCs of 0.83 and 0.84 are generally considered substantial. \textsuperscript{8-10} These ICC values are lower than many automated measurements, such as Tono-Pen (Reichert Inc, Buffalo, NY) intraocular pressure measurements, which have an ICC of over 0.95 but are consistent with other automated children's vision screening technologies. \textsuperscript{11-13}

The source of variability in repeat screenings is likely multifactorial. Screeners are unlikely to work at exactly the same working distance on serial screening. Because autorefraction is performed on noncycloplegged eyes, children may accommodate. This accommodative effect is known to vary over time in individual patients and may partially explain the difference in repeat autorefraction measurements. \textsuperscript{14} This effect would also explain the higher variability of screening results seen for children referred for anisometropia who generally had higher rates of passing repeat autorefraction. These referrals may be more variable because of the compounding effect of variability in each separate monocular reading. Additionally, different screeners performed the initial and repeat screening. Although lay screeners with equivalent formal training performed both screenings, difference between screeners may have added to variability. Finally, it is important to note that we assessed the repeatability of autorefraction only among children who were referred from the initial screening test, a population that may have more variable measurements.

In our study cohort, children who passed repeat Retinomax screening rarely needed treatment, whereas those who again met referral criteria at repeat screening were likely to have amblyogenic risk factors. The 4\% case prevalence among children who passed repeat screening is lower than that likely to be seen in the general population, which has been estimated in population-based studies to be 15\%-20\%. \textsuperscript{15-17} Furthermore, the population of our study was largely Hispanic and likely to have a higher prevalence of refractive error, making the low case rate more remarkable. \textsuperscript{18} The low prevalence of eye disease in this population suggests that despite referral from the original autorefraction screening, these children are likely to be at average or below average risk of amblyopia and may not require additional intervention. Providing comprehensive examinations to average- or low-risk children remains controversial, given the costs and risks of overtreatment. \textsuperscript{19,20}

If not referred for comprehensive examinations, the 27\% of referred children who passed a repeat Retinomax could also represent a significant financial savings. Reimbursement data from a regional HMO demonstrate the large difference in price between screening and examinations, with a $9 reimbursement for screening and $115 for an eye examination without treatment. \textsuperscript{21} If our data is generalizable to other settings (ie, 25\% of children rescreened with autorefraction not requiring a follow-up examination), then 1 in 4 referred children could be spared a comprehensive eye examination simply by repeat autorefraction. Thus in one scenario, for every 4 repeat autorefraction screening tests ($36 cost), one comprehensive eye examination would be avoided ($115 savings), resulting in approximately $3 of savings for each $1 spent.

The present study has several limitations. Perhaps most importantly, this study was performed only on children who were referred from an initial screening autorefraction, and therefore repeatability metrics apply only to this population. Autorefraction might have higher variability among these children because their initial measurements were more extreme than those not referred. Moreover, because we did not perform comprehensive eye examinations on children who passed the original screening, we cannot report the number who might have passed the first screening but would go on to be referred in a repeat screening and may have clinically significant refractive errors. We could not analyze the repeatability of refraction using power vector analysis since the cylindrical axis was not consistently recorded at the time of the initial autorefraction in this retrospective study. \textsuperscript{22} Eye care providers were not masked to the previous screening results. Furthermore, the demographic information was not complete for all children: these metrics were not critical to programmatic considerations on whether or not to refer and were occasionally left incomplete. However, we can conclude that this study population had a greater representation of minorities and lower income households than the average United States preschool population, which may limit the generalizability of the study results.

In conclusion, this study found that there was significant variation in repeat Retinomax screening results among children who had been previously referred after an initial Retinomax screening. Rescreening referred children may be warranted before providing comprehensive examinations. Children referred from an initial screening who passed repeat screenings were likely to be lower risk than the average screened child and might not benefit from comprehensive eye examinations. Removing these children from the pool of children receiving comprehensive eye examinations has the potential to both reduce costs and avert unnecessary overtreatment.

Acknowledgments

Prevent Blindness Northern California was the 501(c)(3) responsible for the preschool vision screening program analyzed in this study and provided the raw data for this analysis. Allison Milch assisted with data collection. Wing-See Leung, CEO, and April Nakayoshi, Program Director, were the principal collaborators at Prevent Blindness Northern California. They assisted with explaining the screening system processes as implemented by Prevent Blindness Northern California.

References

1. Miller JM, Lessin HR; American Academy of Pediatrics Section on Ophthalmology, Committee on Practice and Ambulatory Medicine, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus, American Association of...


