SECTION EDITOR: LESLIE HYMAN, PhD

Measuring Refraction in Adults in Epidemiological Studies

Elizabeth M. Krantz, MS; Karen J. Cruickshanks, PhD; Barbara E. K. Klein, MD; Ronald Klein, MD; Guan-Hua Huang, PhD; F. Javier Nieto, PhD

Objective: To compare refraction measured before and after pharmacologic cycloplegia.

Methods: This study used preliminary data from the Beaver Dam Offspring Study, which includes adult children of participants in the population-based Epidemiology of Hearing Loss Study of older adults living in Beaver Dam, Wisconsin. Data were available for 5018 eyes of 2529 participants. Refraction was defined by the spherical equivalent (SE), using autorefractor readings. Differences were calculated as the SE after drops were administered minus the SE before drops were administered. Myopia was defined as SE of −1 diopter (D) or less; emmetropia, as SE more than −1 D and less than 1 D; and hyperopia, as SE of 1 D or more.

Results: The mean age was 48 years (range, 22-84 years). The mean difference in SE between measurements before and after cycloplegia was 0.29 D (95% confidence interval, 0.28-0.31). The difference decreased with age and varied by refractive status for participants younger than 50 years, with the largest differences observed among young persons with hyperopic refractive errors. Across all age groups, agreement on classifications of refraction was high (84%-92%).

Conclusions: Overall, clinically inconsequential differences were observed between SEs before and after pharmacologic cycloplegia, suggesting that cycloplegia may not be necessary in epidemiological studies of refraction in adults.

Arch Ophthalmol. 2010;128(1):88-92

In epidemiological studies of presbyopic adults, accommodative effects on refractive error measurement are generally of minimal concern. Accordingly, population-based studies of older adults frequently measure refraction without cycloplegia. However, in younger persons, accommodation can greatly influence refractive error measurement. Studies in children have found that autorefraction estimates without pharmacologic cycloplegia are more myopic than autorefraction estimates obtained after cycloplegia, particularly among children with hyperopia.[1-4] Because of the magnitude of these differences, methods of refraction without cycloplegia are often considered inappropriate for measuring refractive error in children.[2-4] However, there may be subgroups of children where cycloplegia is not critical in epidemiological studies of refraction; the Correction of Myopia Evaluation Trial found minimal differences between refractive error measured with and without cycloplegia for children with myopia.[5]

Because the age-related decline in accommodative ability is a gradual process, it is reasonable that any corresponding effects on the measurement of refraction may also gradually decrease with age. One study of 199 young adults aged 18 to 34 years still found estimates of refraction were more myopic (mean difference of 0.86 diopters [D]) without cycloplegia than with cycloplegia, even when using an autorefractor with a fogging mechanism to minimize accommodation in the absence of cycloplegia.[6] To our knowledge, a large-scale comparison of refractive error measured by autorefraction with and without cycloplegia in a wide age range of adults has not yet been reported. As younger adults are studied, it is important to know the difference in measurement associated with cycloplegia. The purpose of this article was to compare refraction measured by autorefraction without and with cycloplegia in adults.

METHODS

PARTICIPANTS

Initiated in 2005, the Beaver Dam Offspring Study (BOSS) investigates sensory functioning in adult children of participants in the popu-

Author Affiliations: Departments of Ophthalmology and Visual Sciences (Ms Krantz and Drs Cruickshanks, B. E. K. Klein, and R. Klein) and Population Health Sciences (Dr Huang), University of Wisconsin School of Medicine and Public Health, Madison; and Institute of Statistics, National Chiao Tung University, Hsinchu, Taiwan (Drs Huang and Nieto).

lation-based Epidemiology of Hearing Loss Study (EHLS) of older adults living in Beaver Dam, Wisconsin. Details of the EHLS have been published elsewhere.[7] At the 5-year follow-up EHLS examination, participants were asked how many children they had. To identify eligible participants for the BOSS, members of the parent population (EHLS participants) who had reported at least 1 living child were asked for permission to contact their children. Eligible BOSS participants were then the offspring whom EHLS participants gave permission to contact. For this article, we used preliminary data from the BOSS, which included 2529 people (1163 men, 1366 women) aged 22 to 84 years with paired refraction measurements with and without cycloplegia measured on the same day. Most (98%) participants provided paired data for both eyes, whereas 40 people provided measurements for 1 eye only. Therefore, a total of 5018 eyes were available for analysis. The University of Wisconsin–Madison institutional review board approved this study and all participants provided written informed consent.

VISION EXAMINATION

Vision testing in the BOSS included autorefraction, visual acuity tests, contrast sensitivity, amplitude of accommodation, and ocular imaging. Prior to cycloplegia, an autorefractor (WR-5001K; Grand Seiko, Hiroshima, Japan) was used to measure refraction. If there was a refractive error, this correction was used for trial lenses for best-corrected visual acuity and contrast sensitivity testing. After these initial vision tests were completed, 1 drop of tropicamide, 1%, followed by 1 drop of phenylephrine, 2.5% (at least 30 seconds later), was administered to each eye of the participants. Phenylephrine was not given to participants with systolic blood pressure greater than 200 mm Hg or diastolic blood pressure greater than 100 mm Hg. Participants then proceeded to other parts of the examination while their eyes became dilated. Because dilation time can vary across the age range included in the study, examiners were trained to check pupil dilation after 20 minutes and proceed with the ocular examination (imaging and repeat refraction) if the pupils were adequately dilated or continue monitoring until ready. Refraction was again obtained with a Grand Seiko WR-5001K autorefractor.

STATISTICAL METHODS

Refraction was defined by the spherical equivalent (SE), calculated using the sphere (S) and cylinder (C) autorefractor measurements in the following equation: $SE = S + C/2$. For participants who could not identify any letters at a 1-m distance during visual acuity testing, all autorefractor readings for that eye were set to missing. Differences for each eye were calculated by subtracting the SE before drops were administered from the SE after drops were administered. Mean differences were calculated using data from both eyes. Bland-Altman plots[8] were used to assess agreement between the 2 refraction measurements in each eye. Because some of the differences were not normally distributed, the Bland-Altman method of calculating 95% limits of agreement[8] was not used. Instead, the 2.5 and 97.5 percentiles of the differences were calculated to define intervals containing 95% of the sample data using nonparametric methods. For the purposes of this article, these limits will be referred to as 95% limits of agreement, even though the method used to calculate the limits differs from that of Bland and Altman. Since standard errors for the mean difference and interval limits were not calculated, correction for the correlation between eye measurements was not necessary for these initial calculations. However, further analysis using generalized estimating equations used standard errors to provide precision estimates (95% confidence intervals [CIs]) for the estimated mean difference while accounting for the correlation between eyes from the same person.

Myopia was defined as SE of −1 D or less; emmetropia, as SE more than −1 D and less than 1 D; and hyperopia, as SE of 1 D or more. Analyses were stratified by the following age groups: 22 to 39 years, 40 to 49 years, 50 to 59 years, and 60 to 84 years. Within each age group, Bland-Altman analyses were stratified by refractive status (myopia, emmetropia, hyperopia) as defined by the cycloplegic SE. Generalized estimating equations models for each age group included a term for refractive status (as defined by the cycloplegic SE) to give category-specific estimates. Classifications of myopia, emmetropia, and hyperopia based on autorefraction before cycloplegia were compared with classifications based on autorefraction after cycloplegia by calculating the percentage of agreement. Confidence intervals for the percentage of agreement were estimated using generalized estimating equations logistic regression with outcome defined as agreement vs disagreement for each eye. Models were stratified by age group and intercepts were used to estimate 95% CIs for the predicted probability of agreement. All analyses used SAS 9.1 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Among all 5018 eyes, the SE before cycloplegia ranged from −19.13 D to 8.38 D with a mean (SD) of −1.04 (2.48) D. After cycloplegia, the SE ranged from −19.00 D to 7.88 D, with a mean (SD) of −0.75 (2.51) D. Thus, on average, measurements were slightly more hyperopic after cycloplegia than before, with a mean difference of 0.29 D and 95% of the differences between −0.38 D and 1.25 D. Before cycloplegia, 38% of eyes were myopic, 48% were emmetropic, and 14% were hyperopic. After cycloplegia, 36% of eyes were myopic, 43% were emmetropic, and 21% were hyperopic. Thus, classifications were similar with 4405 of 5018 eyes classified the same whether the refraction was before or after cycloplegia (88% agreement; 95% CI, 87%-89%).

For younger persons, differences in SE before and after cycloplegia varied by refractive status, with the smallest differences among eyes with a myopic refractive error and the largest differences among eyes with a hyperopic refractive error (**Figure**, A-F) (**Table 1**). For myopic eyes of 22- to 39-year-old participants, SEs after cycloplegia were on average 0.23 D greater than SEs before cycloplegia. Eyes classified as emmetropic in this age group showed greater differences (mean difference = 0.43 D) and eyes classified as hyperopic displayed the largest discrepancies (mean difference = 1.12 D). Participants aged 40 to 49 years showed a similar pattern, although the differences for eyes with hyperopic refractive errors were not as great as those observed for hyperopic eyes from participants aged 22 to 39 years (Table 1) (Figure, D-F). Corresponding 95% limits of agreement for the differences in these 2 age groups produced narrower intervals for myopic eyes than for hyperopic eyes (Table 1) (Figure, A-F).

Compared with younger age groups, margins between measures of refraction before and after cycloplegia in older participants were both smaller and did not vary greatly by refractive status (Table 1) (Figure, G-H). Cycloplegic SEs from participants aged 50 to 59 years were

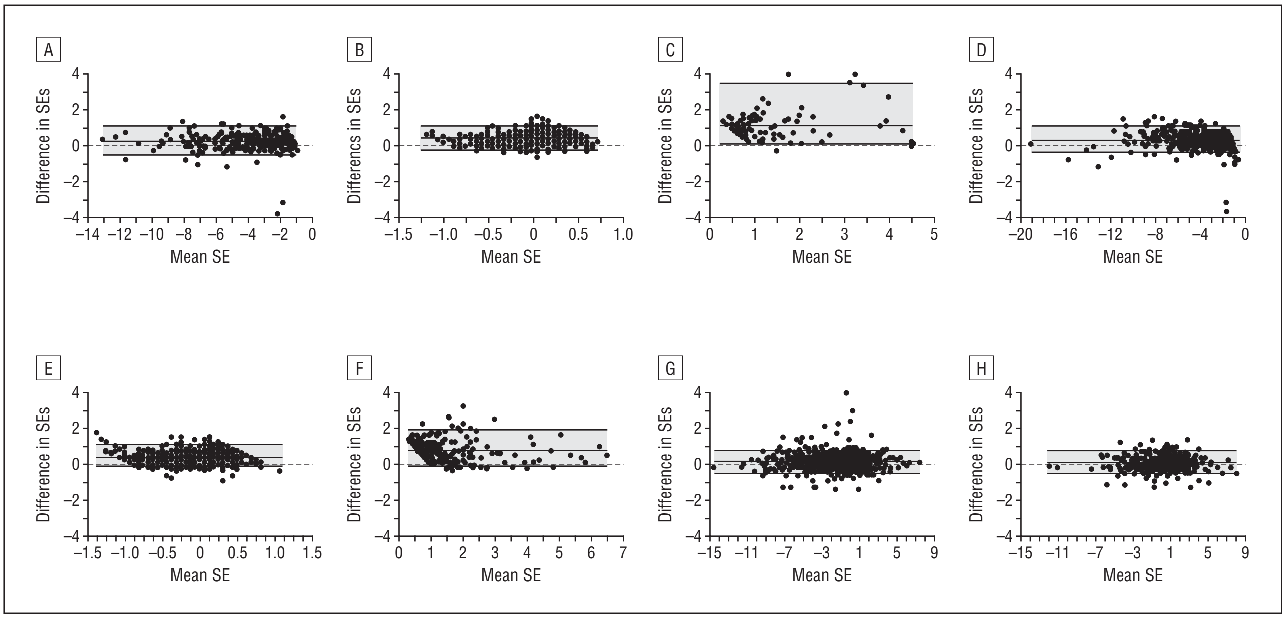

Figure. Bland-Altman plots[8] with the mean spherical equivalent (SE) before and after cycloplegia shown along the x-axis and the difference (SE after cycloplegia−SE before cycloplegia) represented on the y-axis. Horizontal lines represent mean differences as well as 2.5 and 97.5 percentiles used to define 95% limits of agreement (shown in shaded area). A, Ages 22 to 39 years, myopia (n=358 eyes). B, Ages 22 to 39 years, emmetropia (n=394 eyes). C, Ages 22 to 39 years, hyperopia (n=120 eyes). D, Ages 40 to 49 years, myopia (n=708 eyes). E, Ages 40 to 49 years, emmetropia (n=843 eyes). F, Ages 40 to 49 years, hyperopia (n=334 eyes). G, Ages 50 to 59 years, all (n=1573 eyes). H, Ages 60 to 84 years, all (n=688 eyes).

Table 1. Mean Differences and 95% LOA[a]

Age Group, y	Mean Difference[b] (95% LOA), D			
	Myopic Eyes[c]	Emmetropic Eyes[c]	Hyperopic Eyes[c]	All
22-39	0.23 (−0.50 to 1.00)	0.43 (−0.25 to 1.13)	1.12 (0.13 to 3.44)	0.44 (−0.38 to 1.50)
40-49	0.30 (−0.38 to 1.13)	0.39 (−0.13 to 1.13)	0.76 (−0.13 to 1.88)	0.42 (−0.25 to 1.38)
50-59	0.12 (−0.63 to 0.88)	0.15 (−0.38 to 0.63)	0.18 (−0.38 to 0.88)	0.14 (−0.50 to 0.75)
60-84	0.03 (−0.88 to 0.88)	0.10 (−0.50 to 0.75)	0.12 (−0.50 to 0.88)	0.09 (−0.50 to 0.75)

Abbreviations: D, diopters; LOA, limits of agreement; SE, spherical equivalent.
[a]Defined by 2.5 and 97.5 percentiles.
[b]Spherical equivalent after cycloplegia − SE before cycloplegia.
[c]Defined using SE after cycloplegia as follows: myopia, SE of −1 D or less; emmetropia, SE more than −1 D and less than 1 D; hyperopia, SE of 1 D or more.

Table 2. Precision Estimates of Mean Differences Calculated Using Generalized Estimating Equations

Age Group, y	Mean Difference[a] (95% CI), D			
	Myopic Eyes[b]	Emmetropic Eyes[b]	Hyperopic Eyes[b]	All
22-39	0.23 (0.17 to 0.29)	0.43 (0.39 to 0.47)	1.12 (0.95 to 1.28)	0.44 (0.40 to 0.49)
40-49	0.30 (0.26 to 0.33)	0.39 (0.36 to 0.42)	0.76 (0.68 to 0.83)	0.42 (0.39 to 0.44)
50-59	0.12 (0.08 to 0.15)	0.15 (0.13 to 0.18)	0.18 (0.13 to 0.22)	0.14 (0.12 to 0.16)
60-84	0.03 (−0.04 to 0.09)	0.10 (0.06 to 0.14)	0.12 (0.07 to 0.16)	0.09 (0.06 to 0.12)

Abbreviations: CI, confidence interval; D, diopters; LOA, limits of agreement; SE, spherical equivalent.
[a]Spherical equivalent after cycloplegia − SE before cycloplegia.
[b]Defined using cycloplegic SE as follows: myopia, SE of −1 D or less; emmetropia, SE more than −1 D and less than 1 D; hyperopia, SE of 1 D or more.

only an average of 0.14 D greater than SEs without cycloplegia. Differences were also minimal for those aged 60 to 84 years, with a mean difference of 0.09 D. For both of these older age groups, 95% of the differences were between −0.50 D and 0.75 D.

Precision estimates for the mean differences were calculated to describe the variability of the mean difference across numerous samples. The CIs in **Table 2** give a plausible range of the true mean differences for subgroups defined by age and refractive status. Overall, the 95% CI for the mean difference was 0.28 D to 0.31 D. Only 1 of the CIs shown in Table 2 includes zero (myopic eyes in persons aged 60-84 years), indicating that the majority of estimated differences are significantly different from zero.

Table 3. Overall Agreement of Refractive Status Before and After Cycloplegia

Refractive Status Based on SE Before Cycloplegia	No. of Eyes: Refractive Status Based on SE After Cycloplegia: Myopic	Emmetropic	Hyperopic	Total
Ages 22 to 39 y[a]				
Myopic	355	25	0	**380**
Emmetropic	3	369	89	**461**
Hyperopic	0	0	31	**31**
Total	**358**	**394**	**120**	**872**
Ages 40 to 49 y[b]				
Myopic	697	73	0	**770**
Emmetropic	11	769	211	**991**
Hyperopic	0	1	123	**124**
Total	**708**	**843**	**334**	**1885**
Ages 50 to 59 y[c]				
Myopic	578	38	3	**619**
Emmetropic	16	593	58	**667**
Hyperopic	0	18	269	**287**
Total	**594**	**649**	**330**	**1573**
Ages 60 to 84 y[d]				
Myopic	136	10	0	**146**
Emmetropic	7	239	36	**282**
Hyperopic	0	14	246	**260**
Total	**143**	**263**	**282**	**688**

Abbreviations: CI, confidence interval; SE, spherical equivalent.
[a] n=872 Eyes; percentage of agreement=87%; 95% CI, 84%-89%.
[b] n=1885 Eyes; percentage of agreement=84%; 95% CI, 82%-86%.
[c] n=1573 Eyes; percentage of agreement=92%; 95% CI, 90%-93%.
[d] n=688 Eyes; percentage of agreement=90%; 95% CI, 88%-92%.

Overall agreement was high for classifications of myopia, emmetropia, and hyperopia based on refraction with or without cycloplegia for all age groups (**Table 3**). For participants aged 22 to 39 years, 87% of classifications agreed, and for participants aged 40 to 49 years, 84% of classifications agreed. However, this high level of agreement for those younger than 50 years was mostly due to excellent concordance in the myopia classification; of the discrepant cases, most were classified as hyperopic after cycloplegia but were emmetropic before cycloplegia (Table 3). As a result, estimates of the prevalence of hyperopia varied from 4% before cycloplegia to 14% after cycloplegia for those aged 22 to 39 years and from 7% before cycloplegia to 18% after cycloplegia for participants aged 40 to 49 years. Older participants showed slightly greater overall agreement (90%-92%) in refractive error classification, with high consistency in estimates of both the prevalence of myopia and the prevalence of hyperopia (Table 3).

COMMENT

In this study, we found little difference in SE estimates before and after cycloplegia in eyes of adults spanning a wide age range (22-84 years). On average, SEs after cycloplegia were only 0.29 D greater (more hyperopic) than SEs before cycloplegia. However, these differences were not uniform across categories of age and refractive status. For participants 50 years or older, cycloplegia impacted refractive error estimates even less, with mean differences less than 0.15 D. These differences were much smaller than what has been reported among children.[1-4] Minimal differences in this older age group were expected, since many had likely become presbyopic with decreased ability to accommodate.

In participants younger than 50 years, a greater hyperopic shift was noted with cycloplegia, yet the mean differences (0.4 D) were still lower than what has been reported for children[1-4] or adults aged 18 to 34 years.[6] However, the difference between SEs before and after cycloplegia in this age group depended on refractive status, with the largest discrepancies among the hyperopic eyes and the smallest differences among the myopic eyes. Comparisons across studies are limited by differences in the distribution of refractive error as well as differences in definitions for hyperopia and myopia. If we selected young participants (aged 22-39 years; mean, 35 years) with SEs 2 D or greater for comparison with studies done in children, our estimated mean difference between SE before and after cycloplegia (1.62 D) was very similar to what was reported among 12-year-old Australians (1.67 D),[3] but lower than what was reported among 7- to 18-year-old children in China (2.98 D).[2] Among participants in this study aged 40 to 49 years (mean, 45 years), hyperopic eyes with SEs 2 D or greater showed a lower hyperopic shift (0.82 D) compared with the younger BOSS participants.

The Australian study also reported a difference of 1.02 D for 12-year-olds with SEs between 0.5 D and 2.0 D. Using this range of refractive error, our study showed a mean difference of 0.81 D for 22- to 39-year-olds (mean, 36 years) and a difference of 0.66 D for 40- to 49-year-olds (mean, 44 years). Thus, there may be a decline in the effect of accommodation on refractive error estimates as we compare hyperopic eyes of children with hyperopic eyes of younger adults. In contrast to hyperopic eyes of young adults, differences between refraction with and without cycloplegia among myopic eyes of young adults were small, with magnitudes similar to what have been reported among myopic children.[3,5]

Although differences between SEs before and after cycloplegia were statistically significant for most subgroups defined by age and refractive status, the magnitude of the mean differences was generally small. In the context of large-scale epidemiological studies, the magnitude of the mean difference may be more relevant than statistical significance alone. Therefore, in many cases, differences of similar magnitude may not be viewed as clinically significant for research purposes.

Some portion of the differences between refraction before and after drops were administered could have been explained by measurement error in the autorefractor. If the same eye were tested by the same autorefractor under the same conditions on 2 separate occasions, a certain degree of variability in the readings would be expected. Davies et al[9] described repeatability of the Grand Seiko WR-5001K autorefractor readings and found that on repeat testing, approximately 95% of the mean SEs were within 0.50 D of the initial mean SE. That study used a mean value calculated from 6 separate readings during the same session, so there may be greater variability between single measurements. Still, in light of these data, many of the individual differences observed between SEs with and without cycloplegia in those 50 years and older may be due to measurement error. However, the greater individual differences observed among younger participants are unlikely to be entirely due to autorefractor variability.

Classifications of myopia, emmetropia, and hyperopia were similar whether based on refraction measured with or without cycloplegia. For all age groups, 84% or more of classifications agreed. However, for those younger than 50 years, most of the agreement occurred for classification of myopia; the prevalence of hyperopia was underestimated in the absence of cycloplegia.

Clearly, in a clinical setting, cycloplegia may be used to obtain accurate estimates of refractive error in younger patients. However, in epidemiological studies, measurements of refractive error are not generally used for prescribing glasses for distance and instead may be used to provide corrections when measuring visual acuity or to estimate differences between groups of people. The large-scale nature of these studies requires a rapid, safe, relatively inexpensive method of ascertaining refractive error. Cycloplegia adds time to the examination as one waits for the eyes to dilate and bears a very small risk of acute angle-closure glaucoma. When hyperopia or refractive error are not primary end points, or the study is conducted in a setting where the risks of cycloplegia may outweigh the greater accuracy, the error in measuring participants with hyperopia may be acceptable. If investigators are primarily interested in reporting the prevalence of hyperopia among young adults, cycloplegia may be necessary. However, if a study targets older populations, the expected number of young participants with hyperopia is low, or the study is measuring the prevalence of myopia, cycloplegia may not be necessary. Our purpose was to provide the data to enable researchers to make informed decisions appropriate for their studies. We have shown that autorefraction without cycloplegia produces refraction estimates and resulting classifications similar to those obtained under cycloplegia for a broad age range of adults. Focused studies of younger adults, particularly those with hyperopia, may want to consider using cycloplegia when measuring refraction, but for general, large-scale epidemiological studies of adults, cycloplegia may not be essential.

Submitted for Publication: October 14, 2008; final revision received April 20, 2009; accepted April 27, 2009.
Correspondence: Elizabeth M. Krantz, MS, 610 Walnut St, Room 1048, Madison, WI 53726 (krantz@episense.wisc.edu).
Author Contributions: Ms Krantz had full access to all study data and was responsible for the integrity of the data and the accuracy of the analysis.
Financial Disclosure: None.
Funding/Support: This research was supported by National Institutes of Health grant AG021917.
Previous Presentations: Preliminary analysis for this research was presented as a poster at the 2008 Annual Meeting of the Association for Research in Vision and Ophthalmology; April 29, 2008; Fort Lauderdale, Florida. The corresponding abstract was published (Krantz EM, Cruickshanks KJ, Klein BEK, Klein R, Acher CW. Measuring refractive error in adults in epidemiological studies. *Invest Ophthalmol Vis Sci*. 2008;49:ARVO E-Abstract 3133).

REFERENCES

1. Virgili G, Angi M, Molinari A, Casotto V. Cox regression was used to compare the measurement error of two tests vs a gold standard. *J Clin Epidemiol*. 2007;60(4):345-349.
2. Zhao J, Mao J, Luo R, Li F, Pokharel GP, Ellwein LB. Accuracy of noncycloplegic autorefraction in school-age children in China. *Optom Vis Sci*. 2004;81(1):49-55.
3. Fotedar R, Rochtchina E, Morgan I, Wang JJ, Mitchell P, Rose KA. Necessity of cycloplegia for assessing refractive error in 12-year-old children: a population-based study. *Am J Ophthalmol*. 2007;144(2):307-309.
4. el-Defrawy S, Clarke WN, Belec F, Pham B. Evaluation of a hand-held autorefractor in children younger than 6. *J Pediatr Ophthalmol Strabismus*. 1998;35(2):107-109.
5. Gwiazda J, Marsh-Tootle WL, Hyman L, Hussein M, Norton TT; COMET Study Group. Baseline refractive and ocular component measures of children enrolled in the Correction of Myopia Evaluation Trial (COMET). *Invest Ophthalmol Vis Sci*. 2002;43(2):314-321.
6. Jorge J, Queiros A, Gonzalez-Meijome J, Fernandes P, Almeida JB, Parafita MA. The influence of cycloplegia in objective refraction. *Ophthalmic Physiol Opt*. 2005;25(4):340-345.
7. Cruickshanks KJ, Wiley TL, Tweed TS, et al; The Epidemiology of Hearing Loss Study. Prevalence of hearing loss in older adults in Beaver Dam, Wisconsin. *Am J Epidemiol*. 1998;148(9):879-886.
8. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;1(8476):307-310.
9. Davies LN, Mallen EA, Wolffsohn JS, Gilmartin B. Clinical evaluation of the Shin-Nippon NVision K 5001/Grand Seiko WR-5001K Autorefractor. *Optom Vis Sci*. 2003;80(4):320-324.