Amblyopia Risk Factor Prevalence

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ABSTRACT

Purpose: In 2003, the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) published a set of risk factors for amblyopia. The intent was to promote uniformity of reporting and development in screening. Because this prevalence is not yet known, this meta-analysis is an attempt to estimate it.

Methods: Major community preschool eye examination studies were reviewed and AAPOS cut-offs estimated.

Results: The approximate prevalence of anisometropia is 1.2%, hyperopia is 6%, astigmatism is 15%, myopia is 0.6%, strabismus is 2.5%, and visual acuity less than 20/40 is 6%. The mean combined prevalence is 21% ± 2% compared to a prevalence of amblyopia 20/40 and worse of 2.5%.

Conclusions: Knowing risk factor prevalence simplifies validation efforts. Amblyopia screening with a risk factor sensitivity less than 100% is expected and desirable.

INTRODUCTION

With the emergence of commercially available objective screening devices, the Vision Screening Committee of the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) came to consensus as to a group of preschool risk factors for amblyopia in 2000. These risk factors (Table 1) represented refractive error, anatomic features such as strabismus, and visual acuity. These guidelines were published in 2003 to assist industry and investigators to set referral cut-offs and to allow uniform validation comparisons.

Large, cross-sectional studies of deliberate comprehensive eye examinations in preschoolers are complicated and expensive but valuable. Two National Institutes of Health (NIH)-sponsored, related studies are the Multi-Ethnic Pediatric Eye Study (MEPEDS) from Los Angeles and the Baltimore Pediatric Eye Disease Study (BPEDS). Another by Ottar et al. is the initial validation study for the MTI photoscreener. A different, large-scale NIH study, the Vision in Preschoolers Study (VIPS), employed an “enhanced population” because a portion of the children were recruited after having already failed a LEA acuity test in their Headstart programs. None of these has fully complied with the AAPOS 2003 plea for uniform risk factor reporting.

From published data, this is an attempt to glean the AAPOS prevalence data. If the prevalence of risk factors is known, then validating future devices would be simpler and much less expensive; not all “non-referred” subjects would require a
comprehensive eye examination to be able to estimate sensitivity and specificity.

**PATIENTS AND METHODS**

Major pediatric comprehensive eye examination studies were reviewed from publications and from author communication. Data from children between the ages of 2 and 5 years were collected. Specific risk factor prevalence profiles were determined. The type of regression curve that best fit the study with the most data points (Ottar et al.) was a power curve. Unavailable data were then interpolated/extrapolated. Interactions and coexisting risk factors were extracted from data from Ottar et al. and Matta et al. and sorted by amblyopia propensity.

In other words, the prevalence of certain risk factors such as strabismus, reduced visual acuity, media opacity, and ptosis were calculated by averaging the estimates from each study, weighting them according to the number of subjects in the study. For the refractive error risk factors, the estimated prevalence was extracted for a particular amblyopia risk factor according to that study's specifically reported (non-AAPOS) diopter levels. Power regression was then used to attempt to impute a prevalence for the risk factor at the AAPOS-specified threshold. The imputed prevalence estimates for each study were combined into a single overall estimate using a weighted (number of subjects) average. The final step combines the imputed prevalence for each factor into a prevalence of one or more of the amblyogenic factors based on the interaction between coincident factors from one of the contributing studies (Ottar et al.).

The prevalence of children not passing American Academy of Pediatrics visual acuity levels is highly dependent on age-related cooperation; it has been specifically reported from Los Angeles and Australia. The interaction between photoscreening risk factors and acuity referrals is not yet available from the large population studies and the vision screen comparison; The prevalence at AAPOS cutoffs was then estimated and combined.

**RESULTS**

Interpolated prevalence data for individual amblyopia risk factors were extracted (Figures 1-2). Weighted average cut-off levels of prevalence are given in Table 1.

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**TABLE 1**

**Estimating Prevalence of AAPOS Amblyopia Risk Factors**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>AAPOS¹</th>
<th>Ottar et al.⁴</th>
<th>MEPEDS²</th>
<th>BPEDS³</th>
<th>VIPS⁵</th>
<th>Australia⁶</th>
<th>Prevalence</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 2 to 5 yrs</td>
<td>–</td>
<td>949</td>
<td>4359</td>
<td>1756</td>
<td>2588</td>
<td>1738</td>
<td>Each</td>
<td>Combined</td>
</tr>
<tr>
<td>Media opacity</td>
<td>&gt; 1 mm</td>
<td>0.10%</td>
<td>–</td>
<td>–</td>
<td>0.3%</td>
<td>–</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Strabismus</td>
<td>Manifest</td>
<td>0.31%</td>
<td>2.5%</td>
<td>1.3%</td>
<td>–</td>
<td>–</td>
<td>2.0%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Anisometropia</td>
<td>&gt; 1.5 D</td>
<td>0.9%</td>
<td>1.6%</td>
<td>1.5%</td>
<td>2.3%</td>
<td>–</td>
<td>1.2%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Hyperopia</td>
<td>≥ 3.5 D</td>
<td>6%</td>
<td>6%</td>
<td>6%</td>
<td>8%</td>
<td>–</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>Astigmatism</td>
<td>≥ 1.5 D</td>
<td>8%</td>
<td>11%</td>
<td>9.2%</td>
<td>10%</td>
<td>–</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>Astigmatism oblique⁷</td>
<td>≥ 1.0 D</td>
<td>–</td>
<td>5%</td>
<td>8%</td>
<td>–</td>
<td>–</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>Myopia</td>
<td>≥ 3.0 D</td>
<td>.4%</td>
<td>1.1%</td>
<td>0.6%</td>
<td>.8%</td>
<td>–</td>
<td>0.5%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Ptosis</td>
<td>1 mm MRD</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.1%</td>
<td>–</td>
<td>.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Acuity</td>
<td>20/40</td>
<td>5.8%–7.2%</td>
<td>–</td>
<td>–</td>
<td>5.1%</td>
<td>6%</td>
<td>3.0%</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>31%</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>No. combined</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>7,064</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

¹AAPOS = American Association for Pediatric Ophthalmology and Strabismus; MEPEDS = Multi-Ethnic Pediatric Eye Study; BPEDS = Baltimore Pediatric Eye Disease Study; VIPS = Vision in Preschoolers Study; D = diopters; MRD = marginal reflex distance.

²Estimated AAPOS amblyopia risk factor prevalence taken from large population studies that did not report AAPOS diopter levels (Ottar et al., MEPEDS, BPEDS, and Australia) compared to enhanced-population vision screen study, VIPS. Percent values are interpolated by fitting a power curve to reported, non-AAPOS diopter levels. Prevalence column is a weighted average by cohort number for each, individual amblyopia risk factor not accounting for a patient potentially having more than one such risk factor. Adjusted column reduces the total prevalence of anatomic and acuity by one-quarter due to ranked interactive risk factors from two available anatomic studies and one-half reduction due to acuity.

³AAPOS defines oblique astigmatism as more than 10 degrees from vertical or horizontal, whereas MEPEDS and BPEDS use a definition of more than 15 degrees.
The prevalence at AAPOS consensus thresholds for risk factors is anisometropia 1.2% ± 2%, hyperopia 6% ± 1%, astigmatism with-the-rule plus against-the-rule (15°) 9% ± 1%, astigmatism oblique 6% ± 1%, and myopia 0.5% ± .01% for a refractive total of 23% ± 2%. The prevalence of strabismus is 2.0% ± .3%. The prevalence of acuity failure 20/40 or two inter-eye lines is 6% ± 1%. The prevalence of ocular media opacity is approximately 0.2% ± 1% and ptosis is 0.3% ± 1%. This yields a total of individual AAPOS risk factors of 31% ± 2%. Accounting for interacting risk factors reduces the refractive components plus the strabismic component to 16% ± 2%. Assuming a 50% interaction with acuity and combining the other rarer risk factors\(^9,10\) yields 21% ± 2% prevalence for threshold values of AAPOS risk factors.
DISCUSSION

This meta-analysis study would not be needed if the major comprehensive examination studies had reported consistent with the previously published AAPOS guidelines. The AAPOS amblyopia risk factors are more common than some have thought.

Perhaps this high prevalence of risk factors is a surprise because we quote an amblyopia prevalence of approximately 2.5%. A careful Australian study defining amblyopia as a two-line difference plus risk factors estimated an amblyopia prevalence of 1.9%. Amblyopia is conservatively defined using 20/40 and two inter-eye lines as a threshold to improve the power of studies. There actually may be a prevalence of amblyopia of 5% to 6% if we included a much more liberal definition of amblyopia: one inter-eye line difference and visual acuity of 20/25 or worse. The prevalence of amblyopia stratified by corrected visual acuity can be estimated by the Pediatric Eye Disease Investigator Group Amblyopia Treatment Study (PEDIG ATS) enrollment data for unilateral and bilateral cases (Figure 3). In the original Ottar et al. study, a prevalence of similar-to-AAPOS risk factors was estimated at 20.2%.

The first phase of the VIPS employed an enhanced study population; a proportion of enrollees had already been screened with LEA symbols. The intersection of the VIPS prevalence and non-enhanced populations might reveal at which level of a given risk factor, amblyopia, or visual acuity deficits occur. If so, we find excellent agreement between the VIPS and the AAPOS consensus cutoffs for myopia and astigmatism, slightly lower for hyperopia, and an intersection for anisometropia of 1.0 diopter rather than the conservative “greater than 1.5 diopters” from AAPOS consensus. Moving the anisometropia threshold back to 1.0 diopter would more than triple the prevalence, a fact forewarned by the original Ottar et al. study.

This analysis has certain strengths and weaknesses. The contributing studies of more than 10,000 preschool children deliberately sought non-enhanced, cross-sectional data and used carefully controlled, cycloplegic comprehensive examinations. There appeared to be a high level of agreement on the figures for risk factor prevalence between population studies. Some studies provided only 2 diopters, point prevalence for a given risk factor limiting the confidence in the power-curve interpolation, or extrapolation. The estimates of risk factor prevalence interaction came from relatively smaller studies including one on nasolacrimal duct patients. An upper limit of non-interaction (positive predictive value 0% for acuity versus 73% photoscreening) was given by the careful pediatric office-based study by Salcido et al.; the current study estimated the acuity/anatomic risk factor interaction at 50%. The use of power curve to address a small portion of the overall prevalence distribution for these risk factors is not the only mathematic model, but it fit Ottar et al.’s data nicely. AAPOS defines oblique astigmatism as greater than 10 degrees from vertical or horizontal, and MPEDS and BPEDS as greater than 15 degrees. The 2003 AAPOS report addressed preschoolers at an age when acuity testing is possible (3 to 4 years old) and data from comprehensive cycloplegic examinations of refractive error and strabismus covered a wider age range. Finally, although MEPEDS and BPEDS attempt to find difference in prevalence between ethnic groups, the AAPOS risk factor guidelines were designed for preschoolers of all races and this meta-analysis attempts to “lump” rather than to “split” estimates based on race (Figure 1).

The relatively high prevalence of AAPOS 2003 amblyopia risk factors has several implications. A “perfect” screen that refers only children with amblyopia would have a sensitivity for risk factors of only 12%. On the other hand, a different technique that refers only AAPOS risk factor children (100% sensitive) has a false-positive rate for amblyopia of 88%. The positive predictive value of a completely random (poor) screening technique would be 21%. Although it may sound favorable to the naïve consumer to have 100% sensitivity, efficient screening programs should be willing to accept a methodology that is substantially less than 100% sensitive for AAPOS risk factors.

This study is an attempt to glean AAPOS amblyopia risk factor prevalence from more than 9,000 preschoolers having had careful comprehensive eye examinations. Additional specific, short publications by MEPEDS, BPEDS, and VIPS demonstrating AAPOS levels of amblyopia risk factors would still be helpful in further illuminating the information obtained from these studies.

Roughly 1 preschooler in 40 has amblyopia worse than 20/40, whereas approximately 1 in 5 has AAPOS amblyopia risk factors. The prevalence of
risk factors is higher than some had expected. How should we account for 20% prevalence of risk factors, but only 2.5% prevalence of substantial amblyopia? Clearly many children with supra-threshold risk factors such as hyperopia and astigmatism are capable of resolving adequate image quality through robust accommodation so they do not suffer amblyopia worse than 20/40. There also may be many children with a subtle level of amblyopia milder than the “20/40 or 2 inter-eye lines” definition favored by several population studies. Contrary to a cursory naïve impression, we do not want screening to be 100% sensitive for AAPOS risk factors in light of American Academy of Pediatrics guidelines that espouse a series of age-appropriate objective and sensory tests rather than a single, age-based screening during a child’s first decade.

With recent research, there are reasons to modify the 2003 AAPOS Amblyopia Risk Factor Guidelines. A special task force of the Vision Screening Committee for AAPOS headed by Sean Donahue has convened and proposed new levels of amblyopia risk factors to better address estimated prevalence of risk factors, patient age, and the causes of actual amblyopia in March 2012.

REFERENCES