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Screening for Visual Impairment in Children Ages 1–5 Years: Systematic Review to Update the 2004 U.S. Preventive Services Task Force Recommendation

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Structured Abstract

Background: Impaired visual acuity is common in preschool-aged children. Screening for impaired visual acuity in primary care settings could identify children with vision problems at a critical period of visual development and lead to interventions to improve vision, function, and quality of life.

Purpose: To assess the effects of screening for impaired visual acuity in primary care settings in preschool-aged (1 to 5 years) children.

Data Sources: We searched Ovid MEDLINE from 1950 to July 2009, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews through the third quarter of 2009. We supplemented electronic searches with reviews of reference lists of relevant articles and solicited additional citations from experts.

Study Selection: We selected randomized trials and controlled observational studies that directly evaluated screening for impaired visual acuity in preschool-aged children. To evaluate indirect evidence on screening, we also included studies on the diagnostic accuracy of screening tests for impaired visual acuity used in primary care settings, and randomized trials and controlled observational studies that reported clinical outcomes associated with treatments for impaired visual acuity due to refractive error, amblyopia, or amblyogenic risk factors (visual acuity, quality of life, functional capacity [including school performance], or adverse events).

Data Extraction: One investigator abstracted data and a second investigator checked data abstraction for accuracy. Two investigators independently assessed study quality using methods developed by the U.S. Preventive Services Task Force.

Data Synthesis: No randomized trial evaluated outcomes of preschool vision screening compared with no screening. One large, fair-quality randomized trial nested within a population-based cohort study found that repeat orthoptist screening from ages 8 to 37 months was associated with reduced likelihood of amblyopia at age 7.5 years compared with one-time orthoptist screening at age 37 months on one of two definitions of amblyopia. A large, prospective cohort study from this population found that one-time orthoptist screening at age 37 months was associated with no significant difference in risk for amblyopia at age 7.5 years compared with no screening. No study evaluated school performance or other functional outcomes.

No screening test was consistently associated with both high (>90 percent) sensitivity and specificity. In the largest study to directly compare the diagnostic accuracy of different screening tests, differences in likelihood ratio estimates and diagnostic odds ratios for 10 different screening tests were generally small, with the exception of the Random Dot E stereoacuity test, which was associated with a lower diagnostic odds ratio. Diagnostic accuracy of preschool vision tests did not clearly differ in children stratified by age, though testability was generally lower in children ages 1 to 3 years, with the potential exception of the MTI photoscreener.

Three fair- or good-quality trials of preschool-aged children with amblyopia or unilateral refractive error found that treatment (patching and/or eyeglasses) resulted in small (<1 line on the Snellen eye chart) improvements in visual acuity in the amblyopic or worse eye compared with no treatment after 5 weeks to 1 year of follow-up. One trial found larger benefits in the subgroup of children with worse baseline visual impairment. No trial evaluated effects of treatment on school performance or other measures of function. Evidence on whether age has an impact on effectiveness of treatment is mixed. Amblyopia treatments were associated with reversible visual acuity loss in the nonamblyogenic eye in some studies. Evidence on adverse psychosocial effects and effects of suboptimal compliance with amblyopia treatments is limited.

Limitations: We excluded nonEnglish-language studies, could not evaluate for publication bias because of the small numbers of trials, included studies of screening in community-based settings, and did not construct outcomes tables.

Conclusions: Direct evidence on effectiveness of preschool vision screening for improving visual acuity or other clinical outcomes remains limited and does not adequately address whether screening is more effective than no screening. In terms of indirect evidence, a number of screening tests appear to have utility for identification of preschool-aged children with vision problems, and treatments for amblyopia or unilateral refractive error (with or without amblyopia) are associated with mild improvements in visual acuity compared with no treatment. Additional studies are needed to better understand effects of screening compared with no screening, to clarify the risk for potential unintended harms from screening (such as use of unnecessary treatments), and to define the optimal time at which to initiate screening during the preschool years.

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CHAPTER 1. INTRODUCTION

Scope and Purpose

In the United States, common visual problems in young children include refractive error, strabismus, and amblyopia.[1] Vision impairment related to these conditions can reduce quality of life, function, and school performance.[2] In addition, amblyopia and strabismus can affect normal visual development at a critical period of visual development, resulting in irreversible vision loss. Identification of vision problems prior to school entry could help identify children who might benefit from early interventions to correct or improve vision.

The U.S. Preventive Services Task Force (USPSTF) issued an updated recommendation on screening for visual impairment in preschool-aged children in 2004.[3] Since 2004, additional evidence on screening programs and various screening modalities has become available. In 2009, the USPSTF commissioned a new evidence review in order to update its recommendation. The purpose of this report is to systematically evaluate the current evidence on screening for vision problems in preschool-aged children.

Condition Definition

The most common causes of vision impairment in children are: 1) amblyopia and its associated ("amblyogenic") risk factors, 2) strabismus not associated with amblyopia, and 3) refractive error not associated with amblyopia. Amblyopia is a disorder characterized by abnormal processing of visual images in the brain during a critical period of vision development, resulting in a functional reduction of visual acuity.[4] It is associated with conditions that interfere with normal binocular vision, such as strabismus (ocular misalignment), anisometropia (a difference in refractive power between the two eyes), bilateral refractive error, and media opacity (such as cataracts) or other blockage of the visual pathway (such as ptosis or eyelid drooping). Vision impairment associated with amblyopia is not immediately correctable with use of refractive lenses. Standardized definitions for amblyogenic risk factors are available and have been widely adopted (**Table 1**).[5] Strabismus is the most common risk factor for amblyopia, but can inhibit development of normal binocular vision even in the absence of amblyopia.[6]

Refractive error is commonly due to myopia (nearsightedness), hyperopia (farsightedness), and astigmatism. Unlike vision impairment associated with amblyopia, simple refractive error is correctable with use of appropriate lenses, and is not thought to affect normal visual development. Mild hyperopia is normal in young children, who usually achieve normal (20/20) adult visual acuity between the ages of 3 to 7 years.

Prevalence and Burden of Disease

1 to 5 percent of U.S. preschool-aged children have vision impairment.[7] A population-based study of over 6,000 children in Los Angeles County found amblyopia present in 2.6 percent of Hispanic/Latino children and 1.5 percent of black children.[8] Strabismus was present in about 2.5 percent of both ethnic groups. Among over 360,000 preschool-aged children who underwent photoscreening in 15 different programs in the United States, amblyogenic risk factors were identified in 2 percent.[9] European studies of screening in community- and preschool-based settings also reported a prevalence of about 2 percent for amblyogenic risk factors.[10-12] A population-based study of 1,504 white and black children ages 6 to 71 months in Baltimore, Maryland, found that 1.5 percent had decreased bilateral visual acuity and another 1.7 percent wore glasses at presentation.[13] The prevalence of myopia $\geq$1.00 D was 0.7 percent in white children and 5.5 percent in black children, and the prevalence of hyperopia $\geq$3.00 D was 8.9 percent and 4.4 percent, respectively.[14] The prevalence of myopia increases as children enter adolescence and can affect up to 25 percent of adults.[15]

In children, vision impairment can affect school performance and other functions, such as ability to safely participate in sports. Strabismus, the most common contributing factor to amblyopia, can also result in loss of stereopsis, leading to impaired depth perception, as well as teasing and other psychosocial consequences. Although amblyopia is often considered a disease of childhood, it is the most common cause of monocular visual loss in adults ages 20 to 70 years.[16] One risk of amblyopia is that vision loss in the nonamblyopic eye can result in severe vision impairment or blindness. One study estimated at least a 1.2 percent lifetime risk for vision loss for an individual with amblyopia.[17] Long-term functional effects of unilateral vision loss related to amblyopia are not well characterized. A study of a 1958 British birth cohort found no differences at ages 33 or 41 years in educational, health, or social outcomes among 8,432 adults with normal vision and 429 adults with amblyopia.[18]

Etiology and Natural History

Amblyopia is usually unilateral, but bilateral amblyopia can also occur. In addition to decreased visual acuity, amblyopia affects other aspects of vision development, including fusion and stereopsis, which are necessary to form clear three-dimensional images. Amblyopia is associated with conditions that cause misuse or disuse of the eye (such as strabismus), asymmetric refractive error (anisometropia), and conditions associated with visual image deprivation (such as cataracts or ptosis). Although deprivation amblyopia is generally associated with the most severe vision loss, it is also the least common type.[19] Regardless of the cause of amblyopia, the decreased visual acuity is not immediately reversible with simple refractive correction. Left untreated, amblyopia is unlikely to resolve spontaneously.[7, 20] In one study of 18 children ages 4 to 6 years who were poorly adherent with amblyopia treatment, visual acuity improved in only one child after 1 year, stayed about the same in one half, and worsened in the other half.[20] A traditional justification for preschool screening is that amblyopia becomes irreversible if not treated by the time the child reaches the ages of 6 to 10 years.[21, 22] However, a recent trial found

amblyopia treatments may be effective through ages 12 to 17 years, particularly in previously untreated children.[23, 24]

Unlike visual loss associated with amblyopia, simple refractive error is immediately correctable with eyeglasses. The three major types of refractive error are myopia (nearsightedness), hyperopia (farsightedness), and astigmatism (blurred vision at any distance because the radius of curvature of one meridian of the eye is different than that of the orthogonal meridian). These conditions are referred to as refractive error because light is not bent or "refracted" properly, resulting in images that are not accurately focused on the retina. Nearly 20 percent of children develop a refractive error that requires the use of eyeglasses before late adolescence. Some degree of hyperopia is normal in infants and young children and does not need to be treated unless it is severe or causing symptoms, since children have the ability to compensate for hyperopia through enhanced accommodation of the lens.

Risk Factors

Risk factors for amblyopia include prematurity or low birth weight, deprivation of visual stimuli in early infancy up to age 6 years, familial history, and presence of strabismus or uncorrected refractive error (particularly severe asymmetric refractive error).[4, 7, 25] A large (n=7,825) longitudinal study of British school-aged children found that maternal smoking during the first trimester of pregnancy and socioeconomic status were significantly associated with development of amblyopia.[26] Standardized definitions for amblyogenic risk factors are shown in **Table 1**. Risk factors for simple refractive error include prematurity and family history.

Rationale for Screening/Screening Strategies

Amblyopia occurs when amblyogenic risk factors are present or occur in early childhood.[6] Normal vision cannot develop if the images seen by the two eyes are unequally clear, unclear in both eyes, or disparate due to misalignment. If amblyogenic risk factors develop after the ages of 6 to 8 years, amblyopia usually does not occur, as visual maturation has already occurred.[27] Conversely, if amblyopia is treated too late, the visual pathways do not develop properly and visual loss may become permanent. Amblyopia is therefore considered to be a developmental disorder that is most effectively treated during an early, sensitive period. This understanding has been one of the key justifications for preschool vision screening. The other main justification for preschool vision screening is that it provides an opportunity to correct any vision problems before children enter school, potentially promoting school performance during an important period of social and functional development.

Interventions/Treatments

Treatment for simple refractive error is correction with eyeglasses. When amblyopia or amblyogenic risk factors are present, treatment involves correction of the underlying

amblyogenic risk factor if a structural abnormality (such as a cataract or ptosis) is present. When there is no clear structural abnormality, the standard approach in patients with some degree of reversible refractive error is to apply eyeglasses, which can improve or in some cases resolve amblyopia.[28-31] If amblyogenic risk factors or amblyopia persists, the next step is to reduce or eliminate the visual suppressive effect of the nonamblyopic eye through patching (occlusion) or use of atropine drops (which causes visual blurring due to loss of accommodation). After cessation of amblyopia treatment, surgery may be performed for refractory strabismus. Recent randomized trials have investigated the comparative effectiveness of more intensive versus less intensive amblyopia treatments, as well as patching versus atropine. Areas of uncertainty include the optimal time at which to initiate therapy and the optimal duration of treatment. This review will focus on patching and atropine, by far the most common amblyopia treatments.

Current Clinical Practice

Preschool vision screening is frequently offered in primary care and community-based settings. Measurement of visual acuity, commonly reported in Snellen or logarithmic minimum angle of resolutions (logMAR) scales (**Table 2**), along with assessments of strabismus and stereoacuity, are typical components of screening. Some areas of variability in screening practices include when to start screening, who performs screening, how often to screen, and which specific screening tests to use.[32] Recommended visual acuity tests vary according to age (**Table 3**). In a national survey of U.S. pediatricians, only one third reported visual acuity screening in children age 3 years, compared with about 70 percent in children ages 4 or 5 years.[36] Visual acuity testing with charts, such as HOTV or Lea symbols, and ocular alignment testing with the cover-uncover test are the most commonly used screening tests in primary care settings, though stereoacuity testing rates remain low. "Crowded" visual acuity tests (optotypes presented in a line or with crowding bars) are more sensitive for detecting amblyopia than "uncrowded" tests (single isolated optotypes) and are generally recommended in children able to cooperate with the test.[37] Newer screening methods, including photoscreeners and autorefractors, have been proposed as potential replacements or supplements to traditional screening methods. Photoscreeners take optical images to evaluate ocular alignment and refractive error, based on the appearance of the fundus and corneal light reflexes. Autorefractors utilize automated optical methods to determine the refractive error of an eye. Potential advantages of photoscreeners and autorefractors are that they may reduce testing time, increase objectivity of screening, and enhance testability rates in younger children, who may be poorly cooperative with traditional tests. In a national survey, however, fewer than 10 percent of pediatricians reported using photoscreeners or autorefractors,[36] though photoscreeners have been adopted in some mass community-based screening programs.[38] Potential disadvantages of photoscreeners and autorefractors are the relatively high initial costs associated with the instruments, and the need with some photoscreeners for external interpretation of screening results. Children who fail a preschool vision screening test are typically referred for a full ophthalmological exam to confirm presence of vision problems, and further treatment once the visual acuity problem has been confirmed.

Recommendations of Other Groups

The American Academy of Family Practice, the American Academy of Pediatrics, the American Academy of Ophthalmology, and the American Association for Pediatric Ophthalmology and Strabismus recommend preschool vision screening. All recommend measurement of monocular distance visual acuity and testing for ocular misalignment, though the age at which to initiate screening and the specific tests recommended vary among groups (**Table 4**).

Previous USPSTF Recommendation

In 2004, the USPSTF recommended screening to detect amblyopia, strabismus, and defects in visual acuity in children younger than age 5 years ("B recommendation").[3] It found no direct evidence that screening leads to improved visual acuity compared with no screening, but found evidence that early detection and treatment of amblyopia and amblyogenic risk factors can improve visual acuity. The USPSTF found insufficient evidence to determine optimal screening tests, optimal screening frequency, or technical proficiency required of the screening clinician.

CHAPTER 2. METHODS

Using the methods of the USPSTF that are fully detailed in **Appendix A** and with the input of members of the USPSTF, we developed an analytic framework and Key Questions (KQs) (**Figure 1**) to guide our literature search and review. The KQs for this update are:

KQ1. Is vision screening in children ages 1–5 years associated with improved health outcomes?

1a. Does effectiveness of vision screening in children ages 1–5 years vary in different age groups?

KQ2. What is the accuracy and reliability of risk factor assessment for identifying children ages 1–5 years at increased risk for vision impairment?

KQ3. What is the accuracy of screening tests for vision impairment in children ages 1–5 years?

3a. Does accuracy of screening tests for vision impairment vary in different age groups in children ages 1–5 years?

KQ4. What are the harms of vision screening in children ages 1–5 years?

KQ5. What is the effectiveness of treatment for vision impairment in children ages 1–5 years?

KQ6. What are the harms of treatment in children ages 1–5 years at increased risk for vision impairment or vision disorders?

Search Strategies

We searched Ovid MEDLINE from 1950 to July 2009, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews through the third quarter of 2009 (**Appendix A1**). We also reviewed reference lists of relevant articles and queried experts in the field for additional citations.

Study Selection

We selected studies based on predefined inclusion and exclusion criteria developed for each KQ (**Appendix A2**). We defined the target population as children ages 1–5 years evaluated in primary care or community-based settings without known impaired visual acuity or obvious symptoms of impaired visual acuity. We also included studies of vision screening in eye specialty settings, but evaluated their applicability to primary care settings. Although the term "vision impairment" is broad, diseases covered in this review are amblyopia, amblyogenic risk factors (**Table 1**), strabismus, and simple refractive error. For screening tests, we included visual acuity tests, tests for ocular misalignment, stereoacuity tests, photoscreeners, and autorefractors.

We excluded visual acuity testing with cycloplegia and retinoscopy, as well as other tests not commonly used in primary care. For treatments, which are typically provided in eye specialty settings, we focused on risk reduction interventions, including correction of refractive error and penalization of the nonamblyopic eye (with patching or atropine). Outcomes of interest were visual acuity, risk for amblyopia, vision-related function, school performance, and adverse events related to screening or treatment (such as anxiety, labeling, or other psychosocial effects; false-positive rates; unnecessary treatments; and any negative effects on vision). We excluded children with severe congenital conditions or developmental delays, retinopathy of prematurity, glaucoma, congenital cataracts, and high myopia, as these were considered to be outside the scope of preschool vision screening in primary care. This review was limited to published studies available in the English language.

Two reviewers evaluated each study at the title/abstract and full-text article stages to determine eligibility for inclusion. The flow of studies from initial identification of titles and abstracts to final inclusion or exclusion is diagrammed in **Appendix A3**. Studies that were excluded after review of the full-text articles and reasons for exclusion are listed in **Appendix A4**.

Data Abstraction and Quality Rating

We abstracted details about the study population, study design, data analysis, length of follow-up, results, and quality (**Appendix B**). We converted visual acuity measurements from Snellen to logMAR scales using published conversion charts.[32] One author abstracted data and another author verified data abstraction for accuracy. Two authors independently rated the internal validity of each study as "good," "fair," or "poor" based on predefined criteria developed by the USPSTF (**Appendix A5**).[43, 44] For diagnostic accuracy studies, we used the "diagti" procedure in Stata 10.0 (StataCorp, College Station, TX) to calculate sensitivities, specificities, and likelihood ratios. For studies where the reference standard was only performed in a random sample of negative screens, we corrected for verification bias when estimating sensitivity and specificity using the method of Begg and Greenes.[45] In this review, the positive likelihood ratio (PLR) is the odds of a visual condition among subjects with the risk factor *present* compared with those without the risk factor.[46] The negative likelihood ratio (NLR) is the odds of a visual condition among subjects *without* the risk factor compared with those with the risk factor present. We classified PLRs >10 and NLRs $\leq$0.1 as "large/strong," PLRs >5 and $\leq$10 and NLRs >0.1 and $\leq$0.2 as "moderate," PLRs >2 and $\leq$5 and NLRs >0.2 and $\leq$0.5 as "small/weak," and PLRs >1 and $\leq$5 and NLRs >0.5 and $\leq$1 as "very small/very weak."[47]

For all studies we evaluated applicability to populations likely to be encountered in primary care screening settings. Factors we considered when assessing applicability included whether children were recruited from primary care settings, the prevalence of visual conditions, and the severity of visual conditions. Discrepancies in quality ratings were resolved by discussion and consensus.

Data Synthesis

We assessed the overall strength of the body of evidence for each KQ ("good," "fair," or "poor") or part of a KQ using methods developed by the USPSTF, based on the number, quality, and size of studies, consistency of results between studies, and directness of evidence.[43] We did not attempt to quantitatively pool results of studies of diagnostic test accuracy due to marked differences among studies in populations, how screening cutoffs were defined, and target conditions, as well as substantial between-study heterogeneity in results. In addition, there were too few randomized trials of specific treatment comparisons to perform meta-analysis.

External Review

We distributed a draft of the report for review by external experts not affiliated with the USPSTF (**Appendix A6**) and revised the report based on their comments.

CHAPTER 3. RESULTS

Key Question 1. Is Vision Screening in Children Ages 1–5 Years Associated With Improved Health Outcomes?

Summary

No randomized trial evaluated outcomes of preschool vision screening compared with no screening. One large, fair-quality randomized trial nested within a population-based cohort study found that intensive, periodic orthoptist screening from ages 8 to 37 months was associated with reduced likelihood of amblyopia at age 7.5 years compared with one-time orthoptist screening at age 37 months. Intensive orthoptist screening also reduced the likelihood of residual amblyopia among treated children for one of two predefined definitions for amblyopia. A large prospective cohort study from this population found that one-time orthoptist screening at age 37 months was associated with no significant difference in risk for amblyopia at age 7.5 years compared with no screening. Three retrospective cohort studies found that preschool screening was associated with improved school-age vision outcomes compared with no screening, but each had important methodological shortcomings. No study evaluated school performance or other functional outcomes.

Evidence

We identified no randomized trials of vision screening compared with no screening in children ages 1–5 years. A fair-quality, nested randomized trial from the Avon Longitudinal Study of Parents and Children (ALSPAC) population-based cohort compared intensive orthoptist screening before age 3 years (at 8, 12, 18, 25, 31, and 37 months) versus one-time orthoptist screening at age 37 months in 3,490 children born in southwest England (**Table 5**, **Appendixes B1** and **B2**).[48, 49] The major methodological shortcoming of this trial was high loss to follow-up (nearly half of the children did not attend the final examination at age 7.5 years). Screening examinations by the orthoptist consisted of a clinical examination, age-specific visual acuity testing, and cover-uncover testing. All children were offered screening for reduced visual acuity by a school nurse at school entry (at ages 4–5 years). Children with positive screening findings were referred to the hospital eye service for further evaluation and treatment. Amblyopia was defined in two different ways (**Table 5**).

At age 7.5 years, prevalence of amblyopia was about 1 percent lower in the intensive screening group compared with the control group for both definitions of amblyopia, but the difference was statistically significant for only one definition (amblyopia A: 1.45 percent vs. 2.66 percent; relative risk [RR], 0.55 [95% CI, 0.29–1.04]; amblyopia B: 0.63 percent vs. 1.81 percent; RR, 0.35 [95% CI, 0.15–0.86]).[49] Residual amblyopia despite patching treatment was more likely in the control group, but estimates were imprecise and only statistically significant for one of the two amblyopia definitions (amblyopia A: odds ratio [OR], 1.56 [95% CI, 0.62–3.92]; amblyopia B: OR, 4.11 [95% CI, 1.04–16.29]). Visual acuity at age 7.5 years in the (worse) amblyopic eye in patched children was better in the intensive screening group than in the one-time screening

group, by an average of about 1 line on the Snellen eye chart (0.15 logMAR [95% CI, 0.08–0.22] vs. 0.26 logMAR [95% CI, 0.17–0.35]; p<0.001).

A large (n=6,081), fair-quality prospective cohort study from ALSPAC evaluated outcomes of orthoptist screening at age 3 years in one health district versus no preschool screening in two other health districts (**Table 6**, **Appendix B1**).[50] Like the ALSPAC randomized trial, a large proportion of children in the cohort did not have examination results at age 7.5 years available, though the exact proportion was not reported. There was no difference in amblyopia at age 7.5 years between children who did or did not receive preschool vision screening based on any of three prestated definitions (**Table 6**) of amblyopia (amblyopia A: adjusted OR, 0.63 [95% CI, 0.32–1.23]; amblyopia B: adjusted OR, 0.72 [95% CI, 0.43–1.60]; amblyopia C: adjusted OR, 0.65 [95% CI, 0.38–1.10]). Trends toward better amblyopia outcomes in the screened group were even more attenuated when the analysis was based on whether children were offered screening or not, rather than on whether they received screening or not (about two third of the children invited to screening participated).

Three poor-quality retrospective cohort studies found that preschool vision screening was associated with lower likelihood of school-age vision impairment compared with no preschool vision screening (**Table 6**, **Appendix B1**).[51-53] Compared with no screening, one study found that a complete ophthalmologic exam at ages 1 to 2.5 years was associated with lower risk for amblyopia after ages 5.5 to 7 years (amblyopia: RR, 0.39 [95% CI, 0.17–0.87]; amblyopia with visual acuity worse than 20/60: RR, 0.07 [95% CI, 0.01–0.57]).[51] One study found that visual acuity testing by a school nurse 6 to 12 months prior to school entry was associated with lower risk for at least mild vision impairment upon school entry (RR, 0.68 [95% CI, 0.52–0.89]);[52] and one study found that visual acuity testing by a school nurse at age 4 years was associated with lower risk for newly diagnosed vision disorder, amblyopia, or strabismus at age 7 years (RR, 0.15 [95% CI, 0.08–0.31]).[53] Besides use of a retrospective design, major methodological shortcomings in these studies were failure to adjust for potential confounders and varying duration of follow-up within the same study. No study evaluated school performance or other functional outcomes.

Key Question 1a. Does Effectiveness of Vision Screening in Children Ages 1–5 Years Vary in Different Age Groups?

Summary

No randomized trial compared outcomes of preschool vision screening in different age groups. In one randomized trial, screening was initiated earlier in one group (age 8 months) compared with the control group (age 37 months), but it is not possible to determine whether differences in outcomes should be attributed to the earlier age at which screening was started or to the increased frequency of screening that also took place. One poor-quality retrospective cohort study found no difference between screening at ages 2 to 4 years versus screening prior to age 2 years in risk for at least mild vision impairment, but estimates were imprecise and based on a very small sample of children screened. One retrospective cohort study found that the rate of

false-positive screening examinations was about twice as high in children screened at age 1.5 years compared with those screened at age 3.5 years, but did not address other clinical outcomes.

Evidence

No randomized trial directly evaluated effectiveness of screening at different age groups in preschool-aged children. The ALSPAC randomized trial initiated screening earlier (at age 8 months) in an intensive screening group compared with a one-time screening group (at age 37 months), but it is not possible to determine if differences in outcomes should be attributed to the age at which screening was started or the enhanced frequency of screening in the intensive screening group (**Table 5**, **Appendixes B1** and **B2**).[48, 49] One poor-quality retrospective cohort study of Alaskan children found no significant difference in risk for at least mild vision impairment (visual acuity worse than 20/40) between screening at ages 2 to 4 years and screening prior to age 2 years after 2 to 10 years of follow-up, but estimates were imprecise (RR, 3.10 [95% CI, 0.72–13]) (**Table 7**).[54] In addition, this study only reported outcomes for 94 children from over a total of 10,000 screened by the age of 4 years, and did not adjust for potential confounders. One retrospective cohort study found that the rate of false-positives was about twice as high (25 percent vs. 13 percent) in children screened at age 1.5 years compared with those screened at age 3.5 years (screening included the cover-uncover test, a stereoacuity test, photorefraction, plus visual acuity testing in children age 3.5 years), but did not address other clinical outcomes.[55]

Key Question 2. What is the Accuracy and Reliability of Risk Factor Assessment for Identifying Children Ages 1–5 Years at Increased Risk for Vision Impairment?

Summary

No study evaluated the accuracy or reliability of using demographic or clinical features to identify children at higher risk for vision impairment prior to screening, and no study evaluated outcomes of targeted versus universal preschool vision screening.

Evidence

Targeted screening of higher-risk children could be more efficient at identifying those with vision impairment compared with strategies that screen all children, but could also result in more missed diagnoses. No study evaluated the accuracy or reliability of using demographic or clinical features to identify patients at higher risk for vision impairment prior to screening, and no study evaluated yield or outcomes of targeted versus universal preschool vision screening.

Key Question 3. What is the Accuracy of Screening Tests for Vision Impairment in Children Ages 1–5 Years?

Summary

Thirty-one studies evaluated the diagnostic accuracy of various preschool vision screening tests. Four studies evaluated visual acuity tests (Lea symbols and HOTV tests), three evaluated stereoacuity tests (Random Dot E and Randot Stereo Smile II tests), one evaluated the cover-uncover test, four evaluated some combination of clinical examination screening tests, 12 evaluated autorefractors, and 15 evaluated photoscreeners. Diagnostic accuracy estimates for all of these screening tests suggest utility for identification of children at higher risk for amblyogenic risk factors or specific visual conditions, though no test was consistently associated with both high (>90 percent) sensitivity and specificity. In the largest study to directly compare the diagnostic accuracy of different individual screening tests, the Vision in Preschoolers (VIP) study, [56] differences in likelihood ratio estimates among the various tests were generally small, with overlapping confidence intervals. Studies that evaluated combinations of clinical tests (visual acuity, stereoacuity, and ocular alignment) generally reported stronger likelihood ratios than studies that evaluated individual tests.

Evidence

We identified 31 studies on accuracy of various preschool vision screening tests compared with a reference standard[10-12, 57-85] (**Appendixes B3** and **B4**). Cycloplegic refraction was included in the reference standard examination in all but five studies.[10-12, 66, 68] No study was rated good quality. All studies had at least one methodological shortcoming, though the degree to which studies met quality criteria was variable. Four studies were rated overall as poor quality due to one or more serious methodological shortcomings,[12, 63, 66, 73] and the other 23 studies were rated as fair quality. The most frequent shortcomings were exclusion of or failure to include noncompliant children or those with uninterpretable screening tests (10 of 26 studies met this criterion), failure to describe random or consecutive enrollment of subjects (11 studies met this criterion), high or unclear rate of screening failures (12 studies met this criterion), and failure to enroll a representative spectrum of subjects (14 studies met this criterion).

Nineteen studies evaluated children recruited from pediatric ophthalmology clinics.[58, 59, 62-64, 66-70, 72, 73, 76, 77, 79, 80, 83-85] In these studies, the median prevalence of amblyogenic risk factors was 48 percent (range, 6 to 81 percent),[58, 59, 62, 66, 67, 69, 70, 72, 73, 76, 77, 79, 80, 84] and the prevalence of other target vision conditions (variously defined) ranged from 3 to 55 percent.[64, 68, 83, 85] In eight studies of children recruited from primary care, community, or school settings, the median prevalence of amblyogenic risk factors was 12 percent (range, 2 to 20 percent) in five studies[11, 57, 65, 71, 78] and the prevalence of amblyopia was 2 percent in three studies.[10, 12, 60] Two studies evaluated Native American preschool-aged children enrolled in Head Start with a high prevalence of astigmatism and refractive error.[74, 75] The large (n=2,588) VIP study preferentially enrolled children from Head Start with at least one of four target conditions (amblyopia, amblyogenic risk factors, reduced visual acuity, or strabismus) on a screening evaluation (prevalence of amblyopia: 3 percent; prevalence of any of the target conditions: 29 percent).[82, 86]

In addition to its large sample, the VIP study is uniquely informative because it directly compared the diagnostic accuracy of 10 different screening tests (noncycloplegic retinoscopy was also evaluated, but is not included in this review).[82, 86] One issue in the methodological design of the VIP study is that abnormal screening results were not predefined for most screening tests. Rather, after data had been collected, sensitivities for different screening tests were calculated based on cutoffs necessary to achieve specificities of 0.90 or 0.94. An advantage of this approach is that it may facilitate comparisons of diagnostic accuracy across different screening tests since the specificities are roughly equal. A potential disadvantage is that screening cutoffs were determined on a post-hoc basis, which could overestimate accuracy. The main results of the VIP study may not be directly compared with the results of most other studies since it evaluated diagnostic accuracy for a broader range of target conditions, rather than just amblyopia and/or amblyogenic risk factors.

Visual acuity screening. Four fair-quality studies evaluated visual acuity testing with crowded Lea symbols in preschool-aged children (**Table 8**, **Appendixes B3** and **B4**).[59, 74, 75, 82] In the VIP study, an abnormal screening result on the Lea symbols test moderately increased the likelihood of detecting any of the four target visual conditions (PLR, 6.1 [95% CI, 4.8–7.6]), and a normal screening result weakly decreased the likelihood (NLR, 0.42 [95% CI, 0.38–0.50]) when screening thresholds were set to achieve specificities of 0.90.[82] Results were similar when screening cutoffs were revised to achieve specificities of 0.94 (PLR, 8.2 [95% CI, 6.1–11]; NLR, 0.54 [95% CI, 0.49–0.60]).[86] A smaller (n=149) study of children recruited from a pediatric ophthalmology clinic reported moderate to strong PLRs (5.7 [95% CI, 3.8–8.6] and 12 [95% CI, 5.8–24]) and NLRs (0.05 [95% CI, 0.01–0.36] and 0.23 [95% CI, 0.11–0.51]) for amblyogenic risk factors, depending on the cutoff used to define an abnormal screening result.[59] Two other studies evaluated Native American children. One study found that abnormal Lea symbols screening results very weakly increased the likelihood of significant refractive error in preschoolers with astigmatism (PLR, 1.6 [95% CI, 1.4–1.9]),[74] and another study found that abnormal Lea symbols screening results very weakly increased the likelihood of astigmatism (PLR, 1.9 [95% CI, 1.6–2.2]) in a population with high astigmatism prevalence (48 percent).[75]

Few studies directly compared the diagnostic accuracy of different tests of visual acuity. In the VIP study, HOTV and Lea symbols visual acuity testing were associated with similar accuracy (HOTV: PLR for any visual condition, 4.9 [95% CI, 3.9–6.1]; NLR, 0.52 [95% CI, 0.46–0.58]) (**Table 8**, **Appendixes B3** and **B4**).[86] A large (n=5,232), fair-quality Taiwanese study reported similar accuracy for distance and near visual acuity screening, but did not specify which visual acuity tests were evaluated (**Table 8**, **Appendixes B3** and **B4**).[60]

Stereoacuity screening. In three fair-quality studies of the Random Dot E test, the median PLR was 4.2 (range, 3.6–11.4) and the median NLR was 0.65 (range, 0.15–0.81) (**Table 8**, **Appendixes B3** and **B4**).[60, 68, 82] Some of the variability among studies could be due to differences in the target conditions evaluated. The PLR was strongest (11.4) and the NLR weakest (0.81) in a large Chinese study that focused on identification of amblyopia. The other two studies focused on identification of a broader group of visual conditions, including amblyogenic risk factors and simple refractive error (PLR, 4.2 and 3.6; NLR, 0.65 and 0.15).[68, 82]

The VIP study was the only study to directly compare the accuracy of two different stereoacuity tests. It found similar results for the Random Dot E and Randot Stereo Smile II tests (PLR, 4.2 [95% CI, 3.3–5.3] and 4.9 [95% CI, 3.9–6.1], respectively; NLR, 0.65 [95% CI, 0.59–0.71] and

0.62 [95% CI, 0.56–0.67], respectively) when screening cutoffs were set to achieve specificities of 0.90.[82] Results were slightly worse for the Random Dot E stereoacuity test when screening cutoffs were set to achieve specificities of 0.94 (PLR, 2.7 [95% CI, 2.0–3.7] and NLR, 0.85 [95% CI, 0.80–0.90]), but similar for the Randot Stereo Smile II test.[86]

Cover-uncover test. The VIP study found heterotropia on the cover-uncover test moderately useful for identifying children with any visual condition (PLR, 7.9 [95% CI, 4.6–14]), but a normal result had a likelihood ratio just slightly less than 1 (NLR, 0.86 [95% CI, 0.82–0.90]) (**Table 8**, **Appendixes B3** and **B4**).[82] No other study evaluated the diagnostic accuracy of the cover-uncover test.

Autorefractors. Twelve studies (11 fair-quality[10, 57, 64, 65, 69, 73-75, 79, 82, 85] and one poor-quality[66]) evaluated autorefractors (**Table 9**, **Appendixes B3** and **B4**). Four fair-quality studies evaluated the Retinomax autorefractor.[10, 74, 75, 82] In two studies, the median PLR was 3.4 (range, 1.9–6.1) and the median NLR was 0.38 (range, 0.35–0.41).[10, 82] This included the VIP study, with a PLR of 6.1 (95% CI, 5.2–7.0) and NLR of 0.41 (95% CI, 0.37–0.45) for identifying any of four target visual conditions, based on screening cutoffs set to achieve a specificity of 0.90.[82] Results were similar when screening cutoffs were revised to achieve a specificity of 0.94 (PLR, 8.7 [95% CI, 7.2–10] and NLR, 0.51 [95% CI, 0.47–0.55]).[86] A second, fair-quality study found that the Retinomax was associated with weak likelihood ratios (PLR, 1.9 [95% CI, 1.4–2.6] and NLR, 0.35 [95% CI, 0.10–1.2]), but the reference standard was suboptimal (did not necessarily include cycloplegic refraction) and differed according to the results of a repeat screening examination.[10] Two fair-quality studies in Native American populations found moderate to strong PLRs and strong NLRs for identification of significant refractive error in preschoolers with astigmatism (PLR, 6.7 [95% CI, 4.5–9.8] and NLR, 0.11 [95% CI, 0.05–0.22])[74] or for identification of astigmatism in a high-prevalence (48 percent) population (PLR, 18 [95% CI, 10–34] and NLR, 0.08 [95% CI, 0.04–0.13]).[75]

Three fair-quality studies found that abnormal results on the SureSight autorefractor, based on the manufacturer's referral criteria, very weakly to weakly increased the likelihood of the target visual condition (median PLR, 2.2 [range, 1.6 to 2.2]), though normal results strongly to moderately decreased the likelihood (median NLR, 0.24 [range, 0.09 to 0.29]).[69, 79, 82] In the VIP study, PLRs improved when definitions for a positive screening examination were modified to attain a specificity of 0.90 or 0.94 (6.3 [95% CI, 5.2–7.7][82] and 8.6 [95% CI, 6.6–11],[86] respectively), with a relatively small decrease in NLRs (0.41 [95% CI, 0.36–0.47] and 0.52 [95% CI, 0.47–0.58], respectively). However, in another study, in lieu of manufacturer's referral criteria, neither application of the VIP study's 90 percent or 94 percent specificity referral criteria improved diagnostic accuracy (PLR, 2.2 [95% CI, 1.4–3.4] and NLR, 0.32 [95% CI, 0.18–0.56]; and PLR, 2.2 [95% CI, 1.3–3.5] and NLR, 0.47 [95% CI, 0.31–0.77], respectively).[79]

Six studies of the PlusOptix (previously the Power Refractor) autorefractor showed wide variability in diagnostic accuracy estimates.[57, 64-66, 73, 82] One study[66] was rated poor quality and the remainder were rated fair quality. In five studies that evaluated diagnostic accuracy for detection of amblyogenic risk factors (two studies[65, 82] also included nonamblyogenic refractive error), the median PLR was 5.4 (range, 3.0–230) and the median NLR was 0.17 (range, 0.04–0.56).[57, 65, 66, 73, 82] In the VIP study, similar results were obtained based on a screening cutoff to achieve a specificity of 0.90 (PLR, 5.4 [95% CI, 4.4–6.6] and NLR, 0.51 [95% CI, 0.46–0.57])[82] and when screening cutoffs were modified to achieve a specificity of 0.94.[86] Excluding the poor-

quality study[66] did not reduce variability in likelihood ratio estimates. One fair-quality study was an outlier, with a PLR of 230 (95% CI, 14 to 3,680).[64] Specificity was 100 percent (252/252) in this study, but children with negative screening results did not undergo cycloplegic refraction unless they also failed an orthoptist examination (visual acuity, cover-uncover, extraocular movements, prism, and stereoacuity tests). One study reported an improved PLR (from 3.0 to 8.4) when the manufacturer's referral criteria were modified to enhance specificity.[73]

The TopCon autorefractor was evaluated in one fair-quality study of children recruited from pediatric ophthalmology clinics.[85] It found strong PLRs for impaired visual acuity, anisometropia, and astigmatism (range, 10.0 to 14.8) but weak NLRs (range, 0.28 to 0.55).

Only the VIP study directly compared the diagnostic accuracy of different autorefractors.[82, 86] It found slightly stronger likelihood ratios for the Retinomax and SureSight autorefractors compared with the Power Refractor when the manufacturer's referral criteria for the SureSight instrument were replaced with criteria to achieve a specificity of 0.90 or 0.94.

Photoscreeners. 15 studies (13 fair-quality[58, 62, 67, 70-72, 75, 77-79, 81, 83, 84] and two poor-quality[63, 76]) evaluated the diagnostic accuracy of photoscreeners (**Table 10**, **Appendixes B3** and **B4**). Eight studies evaluated the Medical Technologies, Inc. (MTI) photoscreener.[58, 63, 75, 78, 79, 81, 83, 84] In seven studies, the median PLR was 6.2 (range, 2.4–8.7) and the median NLR was 0.26 (range, 0.06–0.67) for identification of amblyogenic risk factors.[58, 63, 75, 78, 79, 81, 83, 84] Estimates from the VIP study fell within the observed range (PLR, 6.2 [95% CI, 2.7–8.1] and NLR, 0.67 [95% CI, 0.62–0.72]), even though the VIP study also evaluated nonamblyopic refractive error and primarily enrolled black (48 percent) or Hispanic (22 percent) children, in whom photoscreening images are typically more difficult to read because they have darker eyes.[82, 88] Excluding the poor-quality study[63] did not reduce the variability in likelihood ratios, nor did stratification of studies according to whether they evaluated pediatric ophthalmology populations or nonspecialty populations. There was also no clear correlation between prevalence of detected conditions and likelihood ratio estimates. One study of Native American children found that the MTI photoscreener was associated with a PLR of 2.3 (95% CI, 1.8–2.9) and a NLR of 0.48 (95% CI, 0.38–0.60) for identification of astigmatism (prevalence, 48 percent).[75]

The VIP study and one other fair-quality study of the iScreen photoscreener reported moderate PLRs (6.2 [95% CI, 4.7–8.1][82] and 8.6 [95% CI, 5.4–14],[72] respectively). The NLR was very weak in the VIP study (0.67 [95% CI, 0.62–0.7]; prevalence of any visual condition, 29 percent),[82] but strong in the other study (0.09 [95% CI, 0.06–0.13]; prevalence of amblyogenic risk factors, 64 percent).[72]

Two fair-quality studies of the Visiscreen 100 photoscreener reported weak to strong PLRs (PLR, 14 [95% CI, 6.3–32]; prevalence of any visual condition, 12 percent;[62] PLR, 3.5 [95% CI, 1.7–7.0]; prevalence of any visual condition, 60 percent),[77] though NLRs were similar at 0.16 and 0.12. Three fair-quality studies found that noncommercial Otago-type photoscreeners (constructed by the study investigators) were associated with widely variable PLRs (median, 16 [range, 2.3 to 110]) and NLRs (median, 0.18 [range, 0.06 to 0.54]) for identification of amblyogenic risk factors.[70, 71, 76] One Chinese study (prevalence of amblyogenic risk factors, 56 percent) found that a computer-photoscreener was associated with strong likelihood ratios (PLR, 9.5; NLR, 0.06 [95% CI not calculable]).[67]

Three studies directly compared the diagnostic accuracy of different photoscreeners.[63, 70, 82] The VIP study reported identical diagnostic accuracy for the MTI and iScreen photoscreeners.[82] One study found an Otago-type photoscreener to be more accurate than an off-axis-type photoscreener, but both were noncommercial photoscreeners constructed by the investigators.[70] The third study found nearly identical diagnostic accuracy for the Fortune Optical VRB-100 and MTI photoscreeners, but was rated poor quality, in part because it used a case-control design.[63]

Combinations of screening tests. Four fair-quality studies[11, 61, 71, 80] and one poor-quality study[12] evaluated the diagnostic accuracy of screening visual acuity, stereoacuity, and ocular alignment in combination, though the specific tests evaluated in the studies varied (**Table 8**, **Appendixes B3** and **B4**). The median PLR was 14 (range, 4.8–17) and the median NLR was 0.28 (range, 0.03–0.91). In four of the five studies, PLRs were strong (11 to 17), though NLRs varied substantially (range, 0.10 to 0.91).[11, 12, 71, 80] In the fifth study, the PLR was weaker (4.8 [95% CI, 2.8–8.4]), with an NLR of 0.39 (95% CI, 0.20–0.75).[61] Reasons for the lower PLR in this study are unclear, as all four studies evaluated similar clinical examination components (visual acuity testing, stereoacuity testing, and external visual inspection) in lower-prevalence populations.

None of the above studies compared different combinations of screening tests or multiple tests compared with single tests. The VIP study found that addition of a test of ocular misalignment (unilateral cover testing, Stereo Smile II test, or MTI photoscreener) to a test of visual acuity or refractive error (Retinomax or SureSight autorefractor and crowded Lea symbols or HOTV tests) increased sensitivity for detection of strabismus by 6 to 31 percent compared with using the test of visual acuity or refractive error alone at a specificity of 90 percent, with little effect on sensitivity for other target conditions.[89] Results were most consistent for the cover-uncover test (15 to 25 percent increase in sensitivity). One other study found that addition of crowded Lea symbols visual acuity testing to the Retinomax autorefractor did not improve diagnostic accuracy for astigmatism in a high-prevalence Native American population, compared with the Retinomax alone.[74]

Direct comparisons of different types of screening tests. Few studies directly compared the accuracy of different types of preschool vision screening tests. The VIP study directly compared diagnostic accuracy of 10 preschool vision screening tests included in this review.[82] With screening cutoffs set to achieve specificities of 0.90, it found that the Random Dot E stereoacuity test, Stereo Smile II test, iScreen photoscreener, and MTI photoscreener had lower sensitivity compared with the Lea symbols or HOTV visual acuity tests, Retinomax autorefractor, SureSight autorefractor, and Power Refractor for detecting any visual condition, but differences in likelihood ratio estimates were generally small (**Table 11**, **Appendixes B3** and **B4**). For example, PLRs for the Random Dot E stereoacuity test and the MTI photoscreener were 4.2 (95% CI, 3.3–5.3) and 6.2 (95% CI, 4.7–8.1) with NLRs of 0.65 (95% CI, 0.59–0.71) and 0.67 (95% CI, 0.62–0.72), respectively, compared with PLRs of 6.1 (95% CI, 4.8–7.6) and 6.1 (95% CI, 5.2–7.0) with NLRs of 0.43 (95% CI, 0.38–0.50) and 0.41 (95% CI, 0.37–0.45) for the Lea symbols visual acuity test and the Retinomax autorefractor, respectively. The cover-uncover test was associated with markedly lower sensitivity but higher specificity than the other tests, resulting in a higher PLR (7.9 [95% CI, 4.6–14]) and a very weak NLR (0.86 [95% CI, 0.82–0.92]). In contrast to the VIP study, a small (n=100) fair-quality study of children recruited from a pediatric ophthalmology clinic (amblyopia prevalence, 58 percent) found that the MTI

photoscreener (PLR, 8.0 [95% CI, 3.5–18]; NLR, 0.06 [95% CI, 0.02–018]; DOR, 140 [95% CI, 26–840]) performed better than the SureSight autorefractor (PLR range, 1.6 to 24; NLR range, 0.06 to 0.51; DOR range, 4.6 to 17), regardless of which referral criteria were used to define abnormal SureSight screening results, though estimates were relatively imprecise.[79]

Other evidence on comparative accuracy of different types of preschool vision screening is limited. One fair-quality study found that an Otago-type photoscreener was substantially more accurate than a combination of visual acuity and stereoacuity testing, but its applicability is limited because it evaluated a noncommercial device constructed by the study investigators.[71] Two fair-quality studies compared preschool vision screening tests in Native American preschool-aged children.[74, 75] One study found that the Retinomax autorefractor (PLR, 6.7 [95% CI, 4.5–9.8] and NLR, 0.11 [95% CI, 0.05–0.22]) was substantially more accurate than Lea symbols visual acuity testing (PLR, 1.6 [95% CI, 1.4–1.9] and NLR, 0.21 [95% CI, 0.10–0.43]) for identification of significant refractive error in children with astigmatism.[74] The other study found that the Retinomax autorefractor (PLR, 18 [95% CI, 10–34] and NLR, 0.08 [95% CI, 0.04–13]) was substantially more accurate than the MTI photoscreener (PLR, 2.4; NLR, 0.5 [95% CI not calculable]) for identification of astigmatism in high-prevalence (48 percent) children.[75]

Key Question 3a. Does Accuracy of Screening Tests for Vision Impairment Vary in Different Age Groups in Children Ages 1–5 Years?

Summary

Evidence on the comparative accuracy of preschool vision tests in different age groups among children ages 1 to 5 years is limited. Four studies found no clear differences in the diagnostic accuracy of various screening tests in preschool-aged children stratified according to age. Testability using common visual acuity tests, stereoacuity tests, photoscreening, and autorefractors generally exceeds 80 to 90 percent in children age 3 years, with small increases in testability rates through age 5 years. Four studies found substantially lower testability with the Random Dot E stereoacuity test, Lea symbols visual acuity test, and the SureSight autorefractor in children ages 1 to 3 years, compared with those ages 4 to 5 years. One large study of statewide screening with the MTI photoscreener by lay examiners found that testability was already 94 percent at age 1 year.

Evidence

Evidence on the comparative accuracy of screening tests for vision impairment in different age groups among children ages 1 to 5 years is limited (**Table 12**, **Appendixes B3** and **B4)**.[61, 69, 72, 83] Four studies found no clear differences in the diagnostic accuracy of various screening tests in preschool-aged children stratified according to age, though estimates were relatively imprecise. One study compared the accuracy of the SureSight autorefractor between children younger than 3 years and children ages 3 to 5 years;[69] one compared the accuracy of the iScreen photoscreener between children ages 3 years or younger and children ages 4 to 6 years;[72] and a third compared

the accuracy of the MTI photoscreener in preschool-aged children stratified into age quartiles.[83] A fourth study found no clear differences in the diagnostic accuracy of a battery of screening tests (Lea symbols test, Frisby stereoacuity test, and external visual inspection) between children younger than 41 months compared with those ages 41 months or older.[61]

Testability rates may provide additional information about the relative utility of screening tests in preschool-aged children at different ages. In general, testability was relatively high in children age 3 years, though small increases occurred through age 5 years in some studies for some screening tests. In the VIP study, Random Dot E testability was 86 percent in 3-year-olds and 93 percent in 5-year-olds,[90] and HOTV and Lea symbols testability was over 95 percent at all ages between 3 and 5 years.[91] Overall testability was nearly 100 percent for the Retinomax autorefractor, MTI photoscreener, Power Refractor II autorefractor, and the SureSight photoscreener.[82] Most (93 percent) of the 3-year-olds in the VIP study were ages 42 to 47 months, so the applicability of these results to younger 3-year-olds is uncertain. Other smaller (n=777 and n=478) studies reported 85 to 92 percent testability for both HOTV and Lea symbols visual acuity testing in 3-year-olds compared with 97 to 100 percent in 4- or 5-year-olds.[92, 93] In a study (n=1,052) that compared the MTI photoscreener with traditional screening (HOTV visual acuity testing, Random Dot E test, and cover-uncover test), testability rates for photoscreening were 77 percent in 3-year-olds and 87 percent in 4-year-olds compared with 85 percent and 94 percent, respectively, for traditional screening.[94]

Few large studies compared testability among children ages 1 to 3 years compared with those ages 3 to 5 years. In the available studies, testability of the most common vision screening tests was generally lower among younger preschool-aged children. One study (n=268) found that Random Dot E testability increased from 65 percent among 2-year-olds to 100 percent in 6-year-olds;[80] another study (n=3,132) found that Random Dot E testability increased from 33 percent among children ages 30 to 36 months to 73 percent among children ages 37 to 48 months, and 96 percent among those ages 49 to 60 months.[95] Another study (n=385) found that Lea symbols testability increased from 56 percent among children ages 31 to 36 months to 76 percent among children older than 36 months.[96] Similarly, a fourth study (n=173) found that testability with the SureSight autorefractor increased from 49 percent among those younger than 3 years to 84 percent among those ages 3 years and older ($p<0.001$).[69] On the other hand, a large (n=15,059) study of photoscreening in the state of Tennessee found that MTI photoscreener testability (administered by lay volunteers) was 94 percent among 1-year-olds, compared with 96 to 98 percent among those ages 2 to 5 years.[38]

Key Question 4. What Are the Harms of Vision Screening in Children Ages 1–5 Years?

Summary

Evidence on harms of preschool vision screening is limited. Although preschool vision screening is associated with potential psychosocial harms related to treatment, one large cohort study found a 50 percent *reduction* in odds of being bullied at age 7.5 years among children offered screening

compared with those who were not offered screening. We identified no other studies on the psychosocial effects of screening.

In populations in which the prevalence of visual conditions is less than 10 percent, six of seven studies that performed the reference standard in all screened children (or a random subset) reported false-positive rates greater than 70 percent. One large study of a statewide preschool photoscreening program found that 20 percent of children with positive screening results who did not meet criteria for amblyopia (false-positives) were prescribed glasses. In about a quarter of cases, corrective lenses were prescribed even though the refractive error was clinically insignificant. No study evaluated the effects of unnecessary corrective lenses or treatment for amblyopia on long-term vision or functional outcomes.

Evidence

Potential harms of preschool vision screening include psychosocial effects, such as labeling and anxiety, unnecessary referrals due to false-positive screening tests, or unnecessary use of corrective lenses or treatments to prevent amblyopia, with potential effects on long-term vision or function. Only one study evaluated potential psychosocial effects of screening. In the large ALSPAC population-based cohort, children offered screening at age 37 months reported a 50 percent *decreased* odds of being bullied at age 7.5 years, compared with those who were not offered screening.[97] Benefits were observed among children who received patching treatment (adjusted OR, 0.39 [95% CI, 0.16 to 0.92]), but not among those treated with eyeglasses. We identified no other controlled studies on psychosocial effects of screening.

False-positive rates (1-positive predictive value) varied depending on the prevalence of the target condition in the population evaluated (**Table 13**). In populations with a prevalence of visual conditions less than 10 percent, six of seven studies that performed the reference standard in all children reported false-positive rates greater than 70 percent.[10-12, 60, 68, 80] The screening tests evaluated included the Retinomax autorefractor,[10] Random Dot E test,[68] and various combinations of clinical screening tests.[11, 12, 60, 80] The seventh study reported a false positive rate of 23 percent for a noncommercial Otago-type photoscreener and 46 percent for a combination of clinical screening tests.[71] In studies with a prevalence of target visual conditions of at least 20 percent, false-positive rates ranged from 5 to 39 percent.[58, 66, 67, 72, 77-79, 83, 84] In the VIP study (prevalence of any visual condition, 29 percent), false-positive rates ranged from 23 to 36 percent for 11 screening tests when screening cutoffs were set to achieve a specificity of 0.90.[82]

One study from a statewide preschool photoscreening program in Tennessee (n=102,508) found that 20 percent (174/890) of children with false-positive screening results were prescribed glasses.[98] About 25 percent of these children had clinically insignificant refractive error (as defined by anisometropia $\leq$0.75 D, hypermetropia $\leq$2.00 D, myopia $\leq$0.75 D, and astigmatism $\leq$0.75 D). The remainder had higher magnitude refractive error, though they did not meet standard criteria for amblyogenic risk factors and in many cases the clinical significance of the refractive error was unclear. No study evaluated effects of unnecessary corrective lenses on long-term vision or functional outcomes. We also identified no studies on rates of unnecessary treatment for amblyopia or amblyogenic risk factors following evaluation in a preschool vision screening program.

Key Question 5. What is the Effectiveness of Treatment for Vision Impairment in Children Ages 1–5 Years?

Summary

In children with unilateral refractive error, one good-quality trial found that patching plus eyeglasses and eyeglasses alone were more effective than no treatment by an average of about 1 line on the Snellen eye chart after 1 year. Effects were larger (1 to 2 lines of visual acuity improvement) in the subgroup of children with worse baseline visual impairment. One fair- and one good-quality trial found that patching resulted in a statistically significant but small (<1 line on the Snellen eye chart) average improvement in visual acuity in children with amblyopia after 5 to 12 weeks of follow-up who were pretreated with eyeglasses if needed for refractive error. Because all three trials evaluated older (ages 4 to 5 years) preschool-aged children, their applicability to younger children is uncertain. No trial evaluated effects of treatment compared with no treatment on school performance or other measures of function. Five fair- or good-quality trials found no differences in visual acuity improvement in the amblyopic eye between shorter and longer daily patching regimens (two trials), different atropine regimens (two trials), or between patching and atropine (one trial).

Evidence on whether age affects outcomes related to treatment is somewhat mixed. Two trials found no interaction between age and amblyopia treatment effects among preschoolers ages 3 to 7 years and one other trial found that delaying treatment for 1 year was associated with similar outcomes compared with immediate treatment in children ages 3 to 5 years. A trial of patching versus atropine found no interaction between age and visual acuity outcomes in preschoolers ages 3 to 7 years through 2 years of follow-up, but at age 10 years, age <5 years at study entry was associated with significantly increased likelihood of amblyopic eye visual acuity of 20/25 or better (57 vs. 38 percent; p=0.004). One other trial found that younger preschoolers (age 3 years) required fewer hours per day of patching to reach significant improvements in visual acuity compared with older preschool-aged children (ages 4 to 8 years).

Evidence

Evidence from controlled trials. Two good-[99, 100] and one fair-quality[101] randomized trials compared effects on visual acuity of patching versus no patching in older (mean age range, 4 to 5 years) preschoolers (**Table 14**, **Appendixes B5** and **B6**). Two of the trials enrolled children with amblyopia and pretreated those with refractive error using eyeglasses prior to allocation to patching or no patching.[100, 101] The third trial compared patching plus eyeglasses or eyeglasses alone with no treatment in children with unilateral refractive error (with or without amblyopia).[99] All trials found that patching was associated with greater improvements in visual acuity compared with no patching, though differences between treated and untreated children were small (less than or about 1 line of visual acuity), and visual acuity improved regardless of patching status. We did not pool results due to differences in baseline visual acuity in the amblyopic eye, inclusion criteria, use of pretreatment eyeglasses, and length of follow-up (range, 5 weeks to 1 year). No trial evaluated school performance or other functional outcomes.

Patching plus eyeglasses versus eyeglasses alone versus no treatment. One good-quality trial compared eyeglasses and patching, eyeglasses alone, and no treatment on visual acuity after 1 year in older (mean age, 4.3 to 5 years) preschool-aged children (n=177) with unilateral refractive error.[99] All participants had unilateral refractive error based on two Snellen visual acuity tests (typically crowded, though uncrowded tests were used in some younger patients), but did not necessarily have amblyopia (the proportion with amblyopia was not reported). Seventy-two percent of participants had anisometropia. Mean logMAR visual acuity was about 0.36 (approximate Snellen equivalent, 20/45). The intensity of patching (hours per day) was not reported.

Both treatment groups experienced statistically significant but small improvements in best-corrected visual acuity after 1 year compared with no treatment (mean difference vs. no treatment, 0.11 logMAR [95% CI, 0.05–0.17] for eyeglasses plus patching; 0.08 logMAR [95% CI, 0.02–0.15] for eyeglasses alone). The average improvement from baseline in logMAR visual acuity was about 0.17 for eyeglasses plus patching, 0.13 for eyeglasses alone, and 0.06 for no treatment. There was no difference between groups in stereoacuity testing.[106] The improvement in visual acuity varied in a preplanned subgroup analysis according to the severity of baseline visual impairment. In children with moderate (0.48 logMAR or worse) baseline refractive error, patching plus eyeglasses was associated with a larger difference compared with no treatment (0.27 logMAR [95% CI, 0.14 to 0.39]). The difference between eyeglasses alone and no treatment was also larger in this subgroup, but did not reach statistical significance (mean, 0.11 logMAR [95% CI, -0.03 to 0.24]). In children with mild (0.18 to 0.30 logMAR) baseline refractive error, average improvements were small in all three groups (mean, 0.19 to 0.24 logMAR), with trivial differences between the treatment and no treatment groups (mean, 0.04 to 0.05 logMAR).

Patching versus no patching in children pretreated with eyeglasses (if necessary). One good-quality trial by the Pediatric Eye Disease Investigator Group (PEDIG) compared eye patching of the nonamblyopic eye (n=87) with no treatment (n=93) in older preschoolers (mean age, 5.3 years) with amblyopia.[100] Most children had no prior amblyopia treatment (89 percent) and most (86 percent) required refractive correction at baseline. Baseline visual impairment in the amblyopic eye was classified as moderate (20/40 to 20/100) in 78 percent of children and severe (20/125 to 20/400) in 17 percent. The study utilized a run-in phase, during which all enrollees wore updated eyeglass prescriptions, until visual acuity in the amblyopic eye stopped improving.[107] Following this run-in period, children entered the treatment phase if they still had at least 2 lines of intraocular visual acuity difference between the amblyopic and nonamblyopic eyes. Children were randomly assigned to either 2 hours of continuous patching per day, including 1 hour of near activities, or no treatment. Both groups wore eyeglasses throughout the trial if required for refractive correction. Investigator-assessed adherence to treatment was good or excellent in 90 percent of patients.

Following 5 weeks of treatment, the mean logMAR visual acuity score in the amblyopic eye was 0.44 (standard deviation [SD], 0.22) in the patching group, compared with 0.51 (SD, 0.28) in the no-treatment group (adjusted mean difference, 0.07 [95% CI, 0.02 to 0.12]; p=0.006), or a difference of less than 1 line on a standard visual acuity chart (Snellen equivalent, 20/50 vs. 20/63). These results reflect a mean change from baseline of 0.12 logMAR in the amblyopic eye in the patching group, compared with a mean change from baseline of 0.04 logMAR in the no-treatment group. The proportion of patients who experienced an improvement of ≥2 lines of

visual acuity was 45 percent in the patching group, compared with 23 percent in the no-treatment group (p=0.003). Results were similar in subgroups of children with moderate (visual acuity in amblyopic eye, 20/40 to 20/100) or severe (20/125 to 20/400) baseline amblyopia.

A smaller fair-quality trial (n=60) compared compliance rates between regimens of 3 and 6 hours per day of eye patching of the nonamblyopic eye in older (mean age, 4.6 years) preschoolers with amblyopia, but also included a no-treatment arm and evaluated visual acuity change as a secondary outcome.[101] All children with refractive error (92 percent of enrollees) received 6 weeks of treatment with corrective lenses prior to allocation to patching or no patching. The mean refractive error in the amblyopic eye was 0.64 logMAR at baseline. Change in logMAR after 12 weeks of patching was 0.29, 0.34, and 0.24 in the 3-hour, 6-hour, and no-treatment group, respectively (p=0.11).

Comparisons of different treatment regimens. Two trials (n=189 and n=97) found similar effects when comparing less with more intense patching regimens in older (mean age, 5 years) preschool-aged children with amblyopia (mean visual acuity in amblyopic eye, 0.45 logMAR).[102, 103] One good-quality PEDIG trial compared patching regimens of 2 versus 6 hours per day[102] and one fair-quality trial compared patching regimens of 6 versus 12 hours per day.[103] Mean logMAR changes in visual acuity from baseline were similar in all groups in both trials at around 0.25. The trial that randomly assigned children to 6 versus 12 hours per day of patching was limited in its ability to evaluate the effects of the intended regimens, as actual patch times averaged 4.2 hours per day (range, 3.7 to 4.7 hours) in the 6-hour/day group, compared with 6.2 hours per day (range, 5.1 to 7.3 hours) in the 12-hour/day group (p=0.06).[103]

Two good-quality PEDIG trials that enrolled similar patient populations (mean age, 5 years; mean visual acuity in amblyopic eye, 0.47 logMAR) found no clear differences in regimens involving atropine penalization of the nonamblyopic eye.[104, 108] In these trials, atropine daily use, weekend use only, and weekend use only plus use of a plano lens in the nonamblyopic eye resulted in clinically significant increases in visual acuity in the amblyopic eye (mean improvement, 0.23 to 0.28 logMAR), with no significant differences in efficacy between compared regimens.

Another good-quality PEDIG trial found no difference between patching and atropine in children ages 3 to 7 years at study entry with moderate amblyopia (visual acuity, 20/40 to 20/100).[105] It found similar improvements in visual acuity after 6 months of treatment (2.8 vs. 3.2 lines of mean visual acuity improvement; between group difference, 0.03 logMAR)[105] as well as at 2 year follow-up (mean between group difference, 0.01 logMAR).[109] Treatment after 6 months was at the discretion of the investigator. Mean visual acuity in the amblyopic eye on the Snellen chart was 20/32 in both groups compared with 20/63 at baseline. Follow-up at age 10 years in a subgroup of 45 percent (188/419) of the children originally enrolled in the trial also showed no difference between groups, with visual acuity improvement in the amblyopic eye largely maintained.[110] At age 10 years, 46 percent of children had visual acuity of 20/25 or better in the amblyopic eye.

Effects of age on treatment outcomes. In children ages 3 years and older, most trials found no association between age at study entry and visual outcomes associated with treatments for amblyopia or unilateral refractive error. No treatment trial enrolled children younger than age 3 years. The PEDIG trial of patching versus no patching found no significant interaction between

age at study entry (range, 3 to 7 years [40 percent <5 years]) and visual outcomes (p=0.14) in children with amblyopia after 5 weeks of treatment.[100] A second trial found that delaying use of eyeglasses or patching for 1 year was not associated with worse visual outcomes after 6 additional months of follow-up compared with immediate treatment in children ages 3 to 5 years.[99]

Three trials that compared different treatment regimens also evaluated effects of age on visual outcomes.[102, 103, 111] One trial found no interaction between age at study entry (range, 3 to 7 years [40 percent <5 years]) and visual outcomes associated with different patching durations after 4 months of treatment (p=0.76).[102] The second trial found no interaction between age at study entry (range, 3 to 7 years [40 percent <5 years]) and visual outcomes associated with atropine or patching after 6 months of treatment (p=0.84)[111] or at 2 year follow-up, with treatments after 6 months at the discretion of investigators (p=0.91).[109] However, when a subgroup of 169 out of 419 children in this trial were evaluated at age 10 years, age <5 years at study entry was associated with slightly better visual acuity. Mean visual acuity in the amblyopic eye was 0.14 logMAR in patients younger than age 5 years at study entry, compared with 0.20 logMAR in patients older than age 5 years at study entry (p<0.001). A significantly higher proportion of patients younger than age 5 years at study entry also had amblyopic eye vision of at least 20/25 at age 10 years compared with patients enrolled at an older age (57 vs. 38 percent; RR, 1.2 [95% CI, 1.1 to 2.1]; p=0.01).[110] The third trial (age range, 3 to 8 years) found that children younger than age 4 years experienced similar visual outcomes with <3 hours/day, 3 to 6 hours/day, and >6 hours/day of patching (p=0.54), but older preschoolers (older than age 4 years) experienced significantly greater improvement in visual acuity with 3 to 6 hours/day of patching compared with <3 hours/day (p=0.03).[103]

Key Question 6. What Are the Harms of Treatment for Children Ages 1–5 Years at Increased Risk for Vision Impairment or Vision Disorders?

Summary

Evidence from five good-quality trials suggests that some amblyopia treatments are associated with increased risk for short-term (reversible) visual acuity loss in the nonamblyopic eye. One trial found that patching was associated with increased risk for ≥2 lines of visual acuity loss compared with atropine (9 vs. 1.4 percent; p<0.001), and one trial found that atropine plus a plano lens was associated with increased risk for ≥1 line of visual acuity loss compared with atropine alone (17 vs. 4 percent; p=0.005). In both trials, visual acuity in the nonamblyopic eye subsequently returned to baseline in almost all children. Three other trials found no difference in risk for visual acuity loss in the nonamblyopic eye between patching versus no patching or in direct comparisons of different patching or atropine regimens.

Evidence on adverse psychosocial effects of amblyopia treatments is limited. One fair-quality follow-up study from a randomized trial found that children were more upset by patching plus eyeglasses compared with eyeglasses alone, and one good-quality trial found that patching was associated with worse emotional well-being compared with atropine.

No trial evaluated the effects of amblyopia treatment compliance on clinical outcomes. In trials that used dose occlusion monitors to measure compliance, the number of actual patching hours per day were about 50 percent of the hours prescribed. One trial found that an educational intervention increased compliance with the prescribed regimen.

Evidence

Loss of visual acuity in the nonamblyopic eye. Five good-quality PEDIG trials evaluated loss of visual acuity in the nonamblyopic eye following amblyopia treatments (**Appendix B5**).[100, 102, 104, 105, 108] One trial found no increased risk for ≥2 lines of visual acuity loss in the nonamblyopic with patching (2/85 [2.4 percent]) compared with no patching (6/88 [6.8 percent]; RR, 1.0 [95% CI, 0.98 to 1.1]; p=0.16) after 5 weeks of treatment.[100] Two other trials found no difference in risk for ≥2 lines of visual acuity loss in the nonamblyopic eye after 4 months with 2-hour (7 percent) versus 6-hour (9 percent) patching regimens (p=0.59)[102] or daily (3 percent) versus weekend (2 percent) atropine regimens (p=0.99).[104]

One trial found that patching was associated with higher risk for ≥2 lines visual acuity loss in the nonamblyopic eye at 6 month follow-up compared with atropine (17/194 [8.8 percent] vs. 3/208 [1.4 percent], respectively; RR, 0.93 [95% CI, 0.88 to 0.97]; p=0.001).[105] Nineteen of the 20 children with visual acuity loss in the nonamblyopic eye recovered vision to 20/20 or at least equal to baseline at 2 years, with no between-group differences in mean visual acuity.[109] One trial found that atropine plus a plano lens was associated with greater risk for ≥1 line of visual acuity loss in the nonamblyopic eye compared with atropine alone at 18 weeks (17 percent [15/88] vs. 4 percent [3/84], respectively; RR, 0.86 [95% CI, 0.78 to 0.95]; p=0.004).[108] Nearly all (17/18) children with decreased visual acuity loss in the nonamblyopic eye at 18 weeks subsequently returned to baseline or better; the exception was one child with 20/25 visual acuity (20/20 at baseline).

Psychological effects. Evidence from randomized trials on the psychological effects of amblyopia treatment in preschool-aged children is limited to two studies.[105, 112] One fair-quality study evaluated children and parents involved in a randomized trial[99] through 2 years following study entry.[112] An important limitation of this study is that follow-up (a questionnaire) was poor (78/177 [44 percent] of initially enrolled patients). Based on mean Rutter scores, there was no significant difference in emotional well-being among 4-year-olds who received glasses (n=46; mean score, 11.6 [SD, 5.3]) and/or patching (n=46; mean score, 11.0 [SD, 5.9]) versus the no-treatment group (n=51; mean score, 11.8 [SD, 5.5]; p=0.60).[112] Based on the results of a questionnaire developed by the study's authors, children randomly assigned to eyeglasses alone were less likely to be upset compared with those randomly assigned to patching plus eyeglasses (age 4 years: 29 vs. 85 percent; p=0.03; age 5 years: 26 vs. 62 percent; p=0.01). Parents of 4-year-olds were also significantly more upset by patching plus eyeglasses than eyeglasses alone (p=0.01), but parents of 5-year-olds showed no differences in feelings between the two regimens (p=0.80). The clinical significance of these results is difficult to interpret because the questionnaire has not been well validated.

One trial of atropine versus patching evaluated parent and child responses to treatment using the Amblyopia Treatment Index (ATI).[113] The ATI is a validated, 18-item questionnaire (each question is scored from 1 to 5 points) that is divided into three subscales: adverse effects of treatment, lack of treatment compliance, and social stigma.[114] Both patching (n=186) and

atropine (n=178) were associated with ATI scores showing decreased emotional well-being (patching: 2.52 [SD, 0.63] vs. atropine: 2.02 [SD, 0.63]; p<0.001), as well as significantly higher (worse) mean scores relative to atropine on all three subscales (**Appendix B5**). Neither age (p=0.56) at treatment nor baseline severity of amblyopia (p=0.38) were significant predictors of ATI scores.[113]

Some observational studies have reported psychological distress and stigmatization associated with amblyopia treatment, particularly patching,[115, 116] though others have found no such correlation.[117]

Compliance. Low levels of compliance with patching for amblyopia could limit effectiveness of treatments.[118-121] However, no trial evaluated effects of compliance on effectiveness of treatment.

Three randomized trials used occlusion dose monitors to test levels of compliance with patching treatment.[101, 103, 122] Two fair-quality trials of different patching regimens found that numbers of hours of patching per day were substantially lower than (by about half) prescribed numbers of hours per day, with greater compliance in those prescribed fewer hours of patching.[101, 103] A third trial found that an educational intervention aimed to increase compliance in children was associated with better compliance (78 vs. 57 percent; RR, 1.4 [95% CI, 1.2 to 1.6]; p<0.0001).[122]

The good-quality PEDIG trial of 2 hours/day versus 6 hours/day of patching included investigator-assessed adherence to treatment as an outcome, based on daily calendar recordings by parents (rather than occlusion dose monitors).[102] Adherence to treatment was judged to be poor in 3 percent of patients in the 2 hour/day group and 11 percent in the 6 hour/day group. However, it was not possible to accurately estimate actual number of hours per day of patching.

CHAPTER 4. DISCUSSION

Summary of Review Findings

Results of this evidence synthesis, organized by KQ, are summarized in **Table 15**. Vision impairment and amblyopia or amblyogenic risk factors are relatively common in preschool-aged children ages 1 to 5 years. As in the previous USPSTF review,[123] direct evidence on health outcomes of preschool vision screening remains limited. On the other hand, more evidence is now available on the accuracy and comparative accuracy of common vision screening tests in preschool-aged children, and more evidence is available to understand the effectiveness and comparative effectiveness of various treatment regimens for amblyopia and unilateral refractive error (with or without amblyopia).

The only available randomized trial of preschool vision screening compared more intensive with less intensive screening, rather than screening versus no screening.[49] Although it found that repeated preschool screening reduced the prevalence of subsequent (school-age) amblyopia by about 1 percent compared with one-time screening, the difference was only statistically significant for one of two definitions of amblyopia used in the trial. One fair-quality prospective cohort study found no significant difference between one-time screening at age 37 months compared with no screening in risk for amblyopia at age 7.5 years,[50] but did find a 50 percent reduction in odds of being bullied,[97] perhaps related to earlier completion of patching regimens. Retrospective cohort studies that found preschool vision screening to be more effective than no screening are of limited usefulness because of important methodological shortcomings.[51-53]

More evidence is now available on the accuracy of various preschool vision screening tests. There is good evidence that commonly used visual acuity tests, stereoacuity tests, cover-uncover tests, autorefractors, and photoscreeners are useful for screening, though differences among studies in the populations evaluated, screening tests evaluated, screening thresholds applied, and target conditions sought make it difficult to reach strong conclusions about how they compare with one another. In the largest study to directly compare many screening tests (the VIP study), differences in likelihood ratio estimates were generally too small to clearly distinguish superior from inferior tests.[82] In addition to diagnostic accuracy, other factors that may affect the choice of screening tests include testability rates at the age being screened, convenience, costs, and how well different tests perform in combination.[11, 61, 71, 80, 89] Studies[11, 61, 71, 80] that evaluated combinations of clinical tests (visual acuity, stereoacuity, and ocular alignment) generally reported stronger likelihood ratios than studies that evaluated individual tests. Screening tests were generally associated with a high rate of false-positives in low-prevalence populations[10-12, 60, 68, 80] which could result in unnecessary prescription of eyeglasses.[98]

There is good evidence that there are effective treatments for visual impairment in preschool-aged children. Although benefits of patching compared with no patching average 1 line or less of visual acuity, some trials pretreated all children with eyeglasses, and benefits appear larger (1 to 2 lines) in children with more severe baseline vision impairment.[99-101] All of the trials enrolled children ages 3 years or older, so applicability to younger preschool-aged children is uncertain. Factors that may affect interpretation of the magnitude of treatment benefits are that the visual impairment associated with amblyopia can become irreversible, is not correctable with

refraction, and potentially affects function over the lifespan of a child. Although patching and atropine appear to be similarly effective treatments for amblyopia,[105] patching may be associated with more short-term (but usually reversible) visual acuity loss in the nonamblyopic eye compared with atropine,[105] as well as more psychological distress,[112] since it is a more visible treatment.

Evidence on when to initiate preschool screening remains limited. One randomized trial initiated screening at different ages, but effects of age could not be separated from effects of repeated versus one-time screening.[49] Other studies indicate a lower rate of false-positive screening results in children screened at age 3.5 years compared with those screened at age 1.5 years,[55] but there was no clear association between age at which treatment was started and effectiveness among preschool-aged children ages 3 years and older.[99, 100, 102, 103, 109-111]

Our conclusions regarding effectiveness of treatments for amblyopia are generally in accordance with Cochrane reviews on treatments for strabismic amblyopia[124] and unilateral refractive amblyopia,[125] even though the Cochrane reviews included studies of therapies not included in our review, as well as older (school-age) children and children with severe amblyopia, who are unlikely to be identified by screening alone.

Limitations

Our evidence review has some potential limitations. First, we excluded nonEnglish-language studies, which could introduce language bias. However, we identified no relevant nonEnglish-language studies in our literature searches. Second, there were too few studies to assess for publication bias. Third, a number of studies evaluated diagnostic accuracy of screening tests or screening programs in community-based settings and eye specialty clinics, which could limit their applicability to primary care settings. Finally, we did not attempt to construct outcomes tables, because the best evidence on screening versus no screening (a large prospective cohort study from the ALSPAC investigators[49]) found no benefits.

Emerging Issues

A number of trials by the PEDIG investigators on therapies for amblyopia, long-term follow-up of amblyopia treatments, and treatment of refractory amblyopia are currently under way or in the follow-up or analysis phase (for more information, go to http://pedig.jaeb.org/Studies.aspx).

Future Research

We identified several important gaps in the evidence on preschool screening for impaired visual acuity. There are no randomized trials showing that preschool vision screening is effective for improving visual or other clinical outcomes compared with no screening, and the only prospective cohort study found no clear benefit from screening.[50] Well-designed studies are

needed to identify optimal methods for vision screening, to understand when to begin screening (e.g., before age 3 years or after age 3 years), to define appropriate screening intervals, and to develop effective strategies for linking preschool-aged children with vision impairment to appropriate care, while avoiding unnecessary use of eyeglasses and other treatments. More studies are also needed to understand optimal amblyopia treatment regimens and to identify optimal combinations of screening tests. At this time, most evidence suggests that less intensive interventions are as effective as more intensive interventions, but minimum effective treatments are not clearly established. Finally, almost all of the trials have focused on effects of preschool vision screening and treatment on visual acuity outcomes. Trials that also address function are needed to clarify how preschool vision screening may affect school performance and other aspects of child development.

Conclusions

Direct evidence on effectiveness of preschool vision screening for improving visual acuity or other clinical outcomes remains very limited and does not adequately address the question of whether screening is more effective than no screening. However, good evidence on diagnostic accuracy and treatments suggest that preschool vision screening could lead to increased detection of visual impairment and greater improvement in visual outcomes than if children were never screened. Additional studies are needed to better understand effects of screening compared with no screening, to clarify the risk for potential unintended harms from screening (such as use of unnecessary treatments), and to define optimal time at which to initiate screening during the preschool years.

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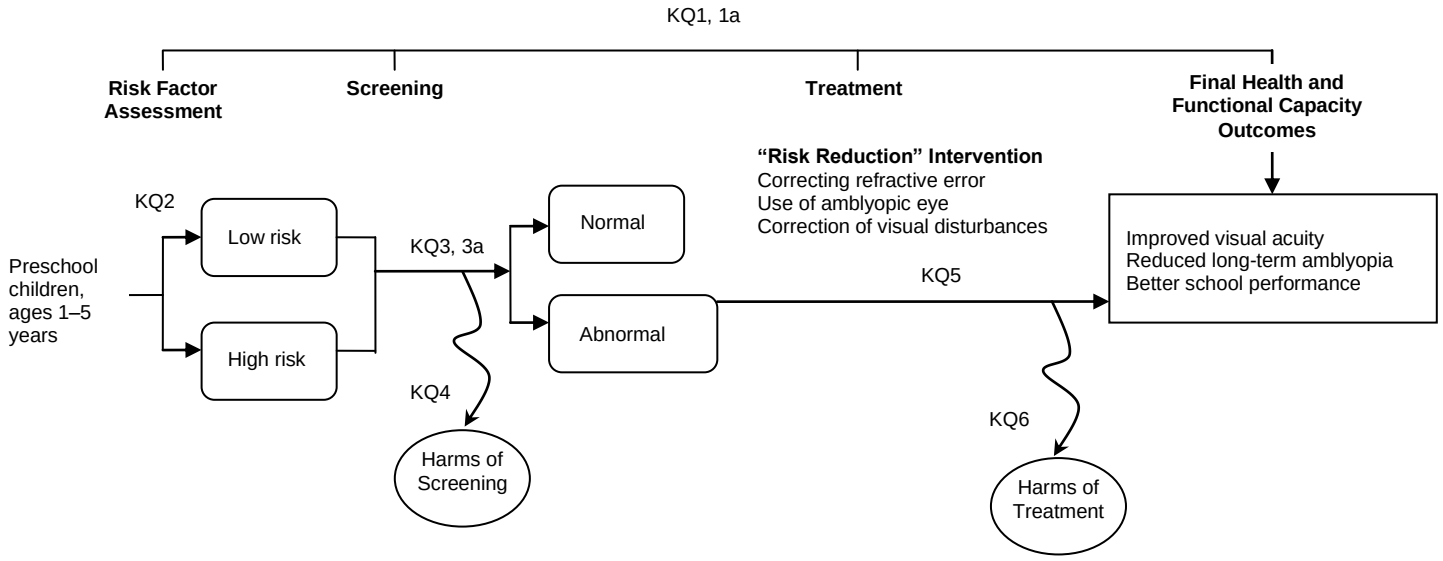
Figure 1. Analytic Framework and Key Questions



Key Questions:

1. Is vision screening in children ages 1–5 years associated with improved health outcomes?

   1a. Does effectiveness of vision screening in children ages 1–5 years vary in different age groups?

2. What is the accuracy and reliability of risk factor assessment for identifying children ages 1–5 years at increased risk for vision impairment?

3. What is the accuracy of screening tests for vision impairment in children ages 1–5 years?

   3a. Does accuracy of screening tests for vision impairment in children ages 1–5 years vary in different age groups?

4. What are the harms of vision screening in children ages 1–5 years?

5. What is the effectiveness of treatment for vision impairment in children ages 1–5 years?

6. What are the harms of treatment for children ages 1–5 years at increased risk for vision impairment or vision disorders?

Table 1. Amblyogenic Risk Factors

Amblyogenic risk factors
• Anisometropia (spherical or cylindrical) > 1.50
• Any manifest strabismus
• Hyperopia > 3.50 D in any meridian
• Any media opacity > 1 mm in size
• Astigmatism > 1.5 D at 90˚ or 180˚ in oblique axis (>10˚ eccentric to 90˚ or 180˚)
• Ptosis ≤ 1 mm margin reflex distance (the distance from the corneal light reflex to the upper lid margin; a standard objective measurement of ptosis)
• Visual acuity per age-appropriate standards

Abbreviations: D=diopter; mm=millimeter.

Source: Donahue et al, 2003.[5] Used with permission.

Table 2. Measurements of Visual Acuity

Snellen			
Feet	**Meters**	**Decimal**	**LogMAR**
20/20	6/6	1.00	0.00
20/30	6/9	0.67	-0.18
20/40	6/12	0.50	-0.30
20/60	6/18	0.33	-0.48
20/80	6/24	0.25	-0.60
20/100	6/30	0.20	-0.70
20/160	6/48	0.13	-0.90
20/200	6/60	0.10	-1.00

Note: Visual Impairment is 20/50 or worse; legal blindness is 20/200 or worse.

Abbreviation: LogMAR=logarithmic minimum angle of resolution.

Source: Holliday, 2004[32]

Table 3. Visual Acuity Tests

Test	Description	Applicable Ages
Allen Cards	Test involving 4 flash cards containing 7 schematic figures. The figures are identified from various distances.	2 to 4 years
HOTV	Test involving identification of the letters “H,” “O,” “T,” and “V.” The letters decrease in size from the top to the bottom of the chart.	Older than 4 years
LEA Symbols	Test involving matching symbols on cards to symbols on the wall. The symbols decrease in size from the top to the bottom of the chart.	2 to 4 years
Snellen Eye Chart	Test involving a chart with 11 lines of letters. The first line consists of one very large letter, and each row below has increasing numbers of letters that decrease in size.	Older than 4 years
Tumbling E	Test involving the letter “E” presented with the arms pointing in different directions. The letters decrease in size from the top to the bottom of the chart.	Older than 4 years

Source: American Academy of Pediatrics, 2003[33]; Prevent Blindness America, 2005[35]

Table 4. Recommendations From Other Organizations

Organization	Year	Screening recommendations	Recommended screening age	Comments
American Academy of Family Physicians (AAFP)[39]	Accessed Web site in 2009	Recommends screening to detect amblyopia, strabismus, and defects in visual acuity in children younger than age 5 years.	Younger than 5 years	
American Academy of Ophthalmology (AAO)[40]	Revised and approved in 2007, original 1991	Joint Policy Statement with AAPOS. Recommends timely screening for the early detection and treatment of eye and vision problems in children. This includes the institution of rigorous vision screening during the preschool years. Early detection of treatable eye disease in infancy and childhood can have far-reaching implications for vision and, in some cases, for general health.	Preschool-aged years	
American Academy of Pediatrics (AAP)[33, 34]	Reaffirmed in 2007, original 2003	**Distance visual acuity** *Tests:* Snellen letters, Snellen numbers, Tumbling E, HOTV, Picture tests (e.g., Allen figures, LEA symbols) *Referral criteria:* Fewer than 4 of 6 correct on 20-ft line, with either eye tested at 10 ft monocularly (i.e., less than 10/20 or 20/40) OR 2-line difference between eyes, even within the passing range (i.e., 10/12.5 and 10/20 or 20/25 and 20/40)	3–6+ years	1. Tests are listed in decreasing order of cognitive difficulty; the highest test that the child is capable of performing should be used. In general, the tumbling E or the HOTV test should be used for children ages 3–5 years and Snellen letters or numbers for children ages 6 years and older. 2. Testing distance of 10 ft is recommended for all visual acuity tests. 3. A line of figures is preferred over single figures. 4. The nontested eye should be covered by an occluder held by the examiner or by an adhesive occluder patch applied to eye; the examiner must ensure that it is not possible to peek with the nontested eye.
		Ocular alignment *Tests:* Cross-cover test at 10 ft (3 m), Random Dot E test at 40 cm, simultaneous red reflex test (Bruckner test) *Referral criteria:* Any asymmetry of pupil color, size, or brightness		Direct ophthalmoscope used to view both red reflexes simultaneously in a darkened room from 2 to 3 feet away; detects asymmetric refractive error as well.
		Ocular media clarity (e.g., cataracts, tumors) *Tests:* Red reflex *Referral criteria:* White pupil, dark spots, absent reflex		Direct ophthalmoscope, darkened room. View eyes separately at 12 to 18 inches; white reflex indicates possible retinoblastoma.
	Reaffirmed in 2008, original 2002	**Photoscreening** All children should be screened for risk factors associated with amblyopia. Guidelines are suggested for the use of photoscreening to detect amblyopia and strabismus in children of various age groups.	Earliest possible age	AAP favors additional research on the efficacy and cost-effectiveness of photoscreening as a vision screening tool.

Table 4. Recommendations From Other Organizations

Organization	Year	Screening recommendations	Recommended screening age	Comments
American Association for Pediatric Ophthalmology and Strabismus (AAPOS)[40]	Revised and approved in 2007, original 1991	Joint Policy Statement with AAO (same as above).	Preschool-aged years	
American Optometric Association (AOA)[41]	Reviewed in 2007, original 1994	A comprehensive eye examination at age 3 years continues to be the most effective approach to prevention or early detection of eye and vision problems in the preschool-aged child.	3 years	
Canadian Task Force on Preventive Health Care (CTFPHC)[42]	1994	There is fair evidence to recommend visual acuity testing, as systematic screening for visual deficits has been found to decrease prevalence later.	Preschool-aged years	

Table 5. Randomized Controlled Trials of Preschool Vision Screening

Study, year, study design	Number of treatment and control subjects	Subject age, sex, diagnosis	Country and setting	Screening intervention	Results	Quality score
Williams et al, 2002[49] and 2003[50] Randomized controlled trial	# approached and eligible: NR # enrolled: 3,490 (2,029 intensive screening, 1,490 one-time screening) # analyzed at 7.5 years: 1,929	Age: Initially tested at ages 8–37 months and followed to age 7.5 years Sex: 48% female (of those at final outcome assessment) Diagnosis: Baseline amblyopia or amblyogenic risk factors NR	United Kingdom Hospital eye services clinic	*Screening at 8, 12, 18, 25, 31, and 37 months* Cover-uncover test; Cardiff cards at 8 and 12 months; Cardiff and Kays pictures test at 18, 25, and 31 months; Kays picture test and HOTV test at 37 months; noncycloplegic autorefraction (performed at all visits, but only used for referral at 37 months) *Screening at 37 months* Cover-uncover test; Kays picture test and HOTV test; noncycloplegic autorefraction	*Screening at 8, 12, 18, 25, 31, and 37 months vs. screening at 37 months only* Amblyopia A at 7.5 years: 1.4% (16/1088) vs. 2.7% (22/826); RR, 0.55 (95% CI, 0.29–1.04) Amblyopia B at 7.5 years: 0.6% (69/1088) vs. 1.8% (15/876); RR, 0.35 (95% CI, 0.15–0.86) Residual amblyopia A among children treated with occlusion: 25% (10/40) vs. 8% (3/40); OR, 1.56 (95% CI, 0.62–3.92) Residual amblyopia B among children treated with occlusion: OR, 4.11 (95% CI, 1.04–16.29) Mean visual acuity in worse eye after patching treatment (adjusted for confounding variables): 0.15 (95% CI, 0.083–0.22) vs. 0.26 (0.17–0.35); p<0.001 Amblyopia A: interocular difference in acuity ≥0.2 logMAR (2 lines on chart) Amblyopia B: interocular difference in acuity ≥0.3 log MAR	Fair

Abbreviations: NR=not reported; CI=confidence interval; LogMAR=logarithmic minimum angle of resolution; OR=odds ratio; RR=relative risk.

Table 6. Controlled Observational Studies of Preschool Vision Screening

Study, year, study design	Number of treatment and control subjects	Subject age, sex, diagnosis	Country and setting	Screening intervention	Results	Quality score
Eibschitz-Tsimhoni et al, 2000[51] Retrospective cohort study	# approached and eligible: 988 in "screening city"; 782 in "nonscreening" city # enrolled: 1,590 (808 were screened at ages 1 to 2.5 years; 782 were not) Loss to follow-up: NR	Age: 8 years Sex: NR Diagnosis: 1% vs. 2.6% amblyopia	Israel Preschool screening	Ophthalmologic exam by orthoptist or ophthalmologist, including Hirschberg corneal reflex text, monocular fixation and following test, ductions and versions exam, cover-uncover test, alternative cover test, and retinoscopy without cycloplegia	*Screening at 1 to 2.5 years vs. no screening at 1 to 2.5 years* Amblyopia at 8 years: 1.0% (8/808) vs. 2.6% (20/782); RR, 0.39 (95% CI, 0.17–0.87) Amblyopia with visual acuity worse than 20/60 at 8 years: 0.1% (1/808) vs. 1.7% (13/782); RR, 0.07 (95% CI, 0.01–0.57)	Poor
Feldman et al, 1980[52] Retrospective cohort study	# approached and eligible: NR # enrolled: 1,508 (745 were screened 6 to 12 months prior to school entry; 763 were not) Loss to follow-up: NR	Age: Mean, 6 years Sex: NR Diagnosis: 13% had at least mild (visual acuity of 20/40 or worse) best-corrected vision impairment	Canada Preschool and school screening	Illiterate E visual acuity test, administered by school nurse	*Screening at 6 to 12 months prior to school entry vs. no screening prior to school entry* Relative risk for at least mild vision impairment upon school entry: 10% (78/763) vs. 15% (112/745); RR, 0.68 (95% CI, 0.52–0.89)	Poor
Kohler et al, 1978[53] Retrospective cohort study	# approached and eligible: NR # enrolled: 2,178 (619 were screened at age 4 years; 1,519 were not) Loss to follow-up: NR	Age: 7 years Sex: NR Diagnosis: 49% had vision disorders classified as requiring treatment, functional amblyopia, or strabismus	Sweden Preschool and school screening	Linear E-chart, administered by school nurse	*Screening at 4 years vs. no screening at 4 years* Relative risk for newly diagnosed vision disorder, amblyopia, or strabismus at 7 years: 5% (29/619) vs. 0.7% (11/1519); RR, 0.15 (95% CI, 0.08–0.31)	Poor

Table 6. Controlled Observational Studies of Preschool Vision Screening

Study, year, study design	Number of treatment and control subjects	Subject age, sex, diagnosis	Country and setting	Screening intervention	Results	Quality score
Williams et al, 2003[50] Prospective cohort study	# approached and eligible: 8,042 (1,917 excluded due to inclusion in quasi-randomized trial; 44 excluded due to developmental delay or organic eye disease) # enrolled: 6,081 (1,516 were screened at age 37 months; 4,565 were not) Loss to follow-up: NR	Age: Cohort tested at 7.5 years; screening offered at 37 months Sex: 49% female Diagnosis: Baseline amblyopia or amblyogenic risk factors NR	United Kingdom Hospital eye services clinic	Kay's pictures or Sheridan Gardiner singles visual acuity test, cover-uncover test, and 20 diopter prism or stereopsis test (or both)	*Screening at 37 months vs. no screening* Amblyopia A at 7.5 years: 1.1% (11/1019) vs. 2.0% (100/5062); adjusted OR, 0.63 (95% CI, 0.32–1.23) Amblyopia B at 7.5 years: 0.7% (7/1019) vs. 1.3% (65/5062); adjusted OR, 0.72 (95% CI, 0.32–1.60) Amblyopia C at 7.5 years: 1.9% (19/1019) vs. 3.4% (171/5062); adjusted OR, 0.65 (95% CI, 0.38–1.10) Mean visual acuity in worse eye after patching treatment (adjusted for confounding variables): 0.14 (95% CI, 0.11–0.18) (n=25) vs. 0.22 (95% CI, 0.20–0.23) (n=166); p<0.0001 Amblyopia A: interocular difference in acuity $\geq$0.2 logMAR (2 lines on chart) Amblyopia B: visual acuity in amblyopic eye 0.3 logMAR or worse (6/12 or worse) Amblyopia C: visual acuity in amblyopic eye 0.18 logMAR or worse (6/9 or worse)	Fair

Abbreviations: NR=not reported; CI=confidence interval; LogMAR=logarithmic minimum angle of resolution; OR=odds ratio; RR=relative risk.

Table 7. Controlled Observational Studies of Vision Screening in Different Preschool Age Groups

Study, year, study design	Number of treatment and control subjects	Subject age, sex, diagnosis	Country and setting	Screening intervention	Results	Quality score
Kirk et al, 2008[54] Retrospective cohort study	# approached and eligible: 10,620 screened # enrolled: 94 (58 screened between ages 2 and 4 years; 36 screened prior to age 2 years) Loss to follow-up: NR	Age: mean, 10.2 years Sex: NR Diagnosis: All referred for an abnormal screening examination	United States Preschool screening	Photoscreener, Inc. (previously MTI Photoscreener), administered by community lay screener	*Screening between 2 and 4 years vs. screening prior to 2 years* Relative risk for at least mild vision impairment (visual acuity 20/40 or worse) at follow-up: 17% (10/58) vs. 6% (2/36); RR, 3.10 (95% CI, 0.72–13.4)	Poor

Abbreviations: NR=not reported; CI=confidence interval; MTI=Medical Technologies, Inc.; RR=relative risk.

Table 8. Diagnostic Accuracy of Visual Acuity Tests, Stereoacuity Tests, Strabismus Tests, and Combinations of Clinical Tests

Study, year	Screening test (reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Quality score
Visual Acuity Tests						
Bertuzzi et al, 2006[59]	LEA symbols visual acuity test (comprehensive eye examination with cycloplegic refraction)	A: 0.96 (0.78–1.0) B: 0.78 (0.56–0.92)	A: 0.83 (0.75–0.90) B: 0.93 (0.87–0.97)	A: 5.7 (3.8–8.6) B: 12 (5.8–24)	A: 0.05 (0.01–0.36) B: 0.23 (0.11–0.51)	Fair
Miller et al, 1999[74]	LEA symbols visual acuity test (cycloplegic refraction and retinoscopy)	0.91 (0.82–0.96)	0.44 (0.37–0.52)	1.6 (1.4–1.9)	0.21 (0.10–0.43)	Fair
Miller et al, 2001[75]	LEA symbols visual acuity test (cycloplegic refraction)	0.93 (0.87–0.97)	0.51 (0.44–0.57)	1.9 (1.6–2.2)	0.14 (0.08–0.27)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[82]	Crowded linear LEA symbols visual acuity test A: 10/32 for age 3 years, 10/20 for ages 4 and 5 years B: 10/32 for age 3 years, 10/25 for age 4 years, 10/20 for age 5 years* (comprehensive eye examination with cycloplegic refraction)	Any condition A: 0.61 (0.56–0.66) B: 0.49 (0.44–0.54) "Very important to detect and treat early" conditions A: 0.77 (0.69–0.84) B: 0.65 (0.56–0.73)	Any condition A: 0.90 (0.88–0.92) B: 0.94 (0.92–0.96)	Any condition A: 6.1 (4.8–7.6) B: 8.2 (6.1–11)	Any condition A: 0.43 (0.38–0.50) B: 0.54 (0.49–0.60)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[82]	Crowded linear HOTV visual acuity test A: 10/25 for ages 3 and 4 years, 10/20 for age 5 years B: 10/32 for ages 3 and 4 years, 10/25 for age 5 years* (comprehensive eye examination with cycloplegic refraction)	Any condition A: 0.54 (0.49–0.59) B: 0.36 (0.31–0.41) "Very important to detect and treat early" conditions A: 0.72 (0.64–0.79) B: 0.48 (0.40–0.57)	Any condition A: 0.89 (0.87–0.91) B: 0.93 (0.91–0.95)	Any condition A: 4.9 (3.9–6.1) B: 5.1 (3.8–6.8)	Any condition A: 0.52 (0.46–0.58) B: 0.69 (0.63–0.74)	Fair
Chang et al, 2007[60]	A1: Distance visual acuity worse than 0.5 at age 3 years, 0.6 at age 4 years, 0.7 at age 5 years, and 0.8 at age 6 years A2: Distance visual acuity worse than 0.7 at age 3 years, 0.8 at age 4 years, 0.9 at age 5 years, and 1.0 at age 6 years B: Near visual acuity worse than 0.7 at age 3 years, 0.8 at age 4 years, 0.9 at age 5 years, and 1.0 at age 6 years (comprehensive eye examination with cycloplegic refraction)	A1: 0.75† A2: 0.84† B: 0.49†	A1: 0.91† A2: 0.69† B: 0.92†	A1: 8.1† A2: 2.7† B: 6.4†	A1: 0.28† A2: 0.24† B: 0.55†	Fair

Table 8. Diagnostic Accuracy of Visual Acuity Tests, Stereoacuity Tests, Strabismus Tests, and Combinations of Clinical Tests

Study, year	Screening test (reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Quality score
Chang et al, 2007[60]	NTU random dot stereogram (comprehensive eye examination with cycloplegic refraction)	0.20†	0.98†	11.4†	0.81†	Fair
Hope et al, 1990[68]	Random dot E stereogram (comprehensive eye examination with cycloplegic refraction for abnormal random dot E stereogram, visual acuity test, or near cover test; otherwise visual acuity screening or near cover test)	0.89 (0.52–1.0)	0.76 (0.68–0.82)	3.6 (2.5–5.2)	0.15 (0.02–0.94)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[82]	Random dot E stereoacuity test A: Nonstereo card for age 3 years, stereo card at 50 cm for age 4 years, stereo card at 100 cm for age 5 years B: Nonstereo card for ages 3 and 4 years, stereo card at 50 cm for age 5 years (comprehensive eye examination with cycloplegic refraction)	Any condition A: 0.42 (0.37–0.47) B: 0.22 (0.18–0.27) "Very important to detect and treat early" conditions A: 0.59 (0.50–0.67) B: 0.30 (0.22–0.38)	Any condition A: 0.90 (0.88–0.92) B: 0.92 (0.90–0.94)	Any condition A: 4.2 (3.3–5.3) B: 2.7 (2.0–3.7)	Any condition A: 0.65 (0.59–0.71) B: 0.85 (0.80–0.90)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[82]	Stereo smile II stereoacuity test A: 240-arc sec card for ages 3 and 4 years, 120-arc sec card for age 5 years B: 480-arc sec card for ages 3 and 4 years, 240-arc sec card for age 5 years[†] (comprehensive eye examination with cycloplegic refraction)	Any condition A: 0.44 (0.39–0.49) B: 0.33 (0.28–0.38) "Very important to detect and treat early" conditions A: 0.72 (0.65–0.79) B: 0.57 (0.50–0.64)	Any condition A: 0.91 (0.89–0.93) B: 0.94 (0.92–0.95)	Any condition A: 4.9 (3.9–6.1) B: 5.5 (4.2–7.3)	Any condition A: 0.62 (0.56–0.67) B: 0.71 (0.66–0.76)	Fair
Cover-Uncover Test						
Vision in Preschoolers Study Group (Phase I), 2004[82]	Cover-uncover test (comprehensive eye examination with cycloplegic refraction)	Any condition 0.16 (0.12–0.20) "Very important to detect and treat early" conditions 0.24 (0.17–0.32)	Any condition 0.98 (0.97–0.99)	Any condition 7.9 (4.6–14)	Any condition 0.86 (0.82–0.90)	Fair

Table 8. Diagnostic Accuracy of Visual Acuity Tests, Stereoacuity Tests, Strabismus Tests, and Combinations of Clinical Tests

Study, year	Screening test (reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Quality score
Combined Clinical Examination Screening Tests						
Barry et al, 2003[11]	Visual inspection, cover-uncover test, eye motility and head posture exam, LEA symbols visual acuity test (second orthoptic examination using more stringent criteria, followed by ophthalmological examination for abnormal, missing, or inconsistent results)	0.91 (0.71–0.99)	0.94 (0.92–0.95)	15 (11–19)	0.10 (0.03–0.36)	Fair
Chui et al, 2004[61]	LEA symbols visual acuity test, Frisby stereoacuity test, and external visual inspection (comprehensive eye examination with cycloplegic refraction)	0.67 (0.41–0.87) <41 months: 0.75 (0.43–0.94) ≥41 months: 0.50 (0.12–0.88)	0.86 (0.79–0.92) <41 months: 0.90 (0.52–0.82) ≥41 months: 0.95 (0.88–0.99)	4.8 (2.8–8.4) <41 months: 2.4 (1.4–4.1) ≥41 months: 10 (3.0–36)	0.39 (0.20–0.75) <41 months: 0.37 (0.13–1.0) >41 months: 0.53 (0.24–1.2)	Fair
Kennedy et al, 1995[71]	Snellen E or Stycar graded balls visual acuity test and Titmus stereotest (comprehensive eye examination without cycloplegic refraction)	0.09 (0.04–0.20) ‡	1.0 (0.99–1.0) ‡	17 (5.5–54) ‡	0.91 (0.84–0.99)‡	Fair
Newman et al, 1999[12]	Sheridan-Gardiner visual acuity; cover-uncover test; ocular movements and convergence; prism test; TNO screening plate; Snellen visual acuity (comprehensive eye examination)	1.0 (0.78–1.0)	0.93 (0.91–0.95)	14 (10–19)	0.03 (0.002–0.51)	Poor
Shallo-Hoffmann et al, 2004[80]	LEA symbol and HOTV charts and Random dot E stereoacuity test (comprehensive eye examination with cycloplegic refraction)	0.73 (0.13–0.98) §	0.94 (0.90–0.96) §	12 (4.7–28) §	0.28 (0.03–2.4)§	Fair

*Determined by cutoff to achieve specificity of 0.95.
† Raw data not provided, unable to calculate confidence intervals.
‡Adjusted for verification bias, based on a 20% sample of negative screens.
§ Adjusted for verification bias, based on a 25% sample of negative screens.

Abbreviations: CI=confidence interval; cm=centimeters.

Table 9. Diagnostic Accuracy of Autorefractors

Study, year	Screening test (reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Quality score
Retinomax Autorefractors						
Barry et al, 2001[10]	Retinomax autorefractor (Second orthoptic examination [LEA single symbol test, cover-uncover test, eye motility, and abnormal head posture] followed by ophthalmological examination for abnormal, missing, or inconsistent results)	0.80 (0.44–0.98)	0.58 (0.53–0.62)	1.9 (1.4–2.6)	0.35 (0.10–1.2)	Fair
Miller et al, 1999[74]	Retinomax K-Plus autorefractor (Cycloplegic refraction and retinoscopy)	0.91 (0.82–0.96)	0.86 (0.80–0.91)	6.7 (4.5–9.8)	0.11 (0.05–0.22)	Fair
Miller et al, 2001[75]	Retinomax K-Plus autorefractor (Cycloplegic refraction)	0.93 (0.88–0.96)	0.95 (0.91–0.98)	18.0 (10.0–34.0)	0.08 (0.04–0.13)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[82]	Retinomax autorefractor (Comprehensive eye examination with cycloplegic refraction)	Any condition A: 0.64 (0.60–0.67) B: 0.52 (0.48–0.56)‡ "Very important to detect and treat early" conditions A: 0.87 (0.84–0.91) B: 0.81 (0.77–0.85)‡	Any condition A: 0.90 (0.88–0.91) B: 0.94 (0.93–0.95)‡	Any condition A: 6.1 (5.2–7.0) B: 8.7 (7.2–10)‡	Any condition A: 0.41 (0.37–0.45) B: 0.51 (0.47–0.55)‡	Fair
SureSight Autorefractors						
Kemper et al, 2005[69]	SureSight autorefractor (Comprehensive eye examination with cycloplegic refraction)	Overall: 0.85 (0.69–0.95) Age <3 years (n=80): 0.80 (0.44–0.97) Age 3–5 years (n=90): 0.88 (0.68–0.97)	Overall: 0.52 (0.40–0.63) Age <3 years: 0.41 (0.24–0.61) Age 3–5 years: 0.58 (0.42–0.71)	Overall: 1.8* Age <3 years: 1.4* Age 3–5 years: 2.1*	Overall: 0.29* Age <3 years: 0.49* Age 3–5 years: 0.21*	Fair
Rogers et al, 2008[79]	SureSight autorefractor Comprehensive eye examination with cycloplegic refraction	A (manufacturer criteria): 0.97 (0.88–1.0) B (VIP 90% specificity criteria): 0.79 (0.67–0.89) C (VIP 94% specificity criteria): 0.67 (0.54–0.79) D (Rowatt et al criteria): 0.62 (0.48–0.74)	A: 0.38 (0.24–0.54) B: 0.64 (0.48–0.78) C: 0.69 (0.53–0.82) D: 0.74 (0.58–0.86)	A: 1.6 (1.2–2.0) B: 2.2 (1.4–3.4) C: 2.2 (1.3–3.5) D: 2.4 (1.4–4.1)	A: 0.09 (0.02–0.37) B: 0.32 (0.18–0.56) C: 0.47 (0.31–0.72) D: 0.51 (0.35–0.75)	Fair

Table 9. Diagnostic Accuracy of Autorefractors

Study, year	Screening test (reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Quality score
Vision in Preschoolers Study Group (Phase I), 2004[82]	SureSight autorefractor (Comprehensive eye examination with cycloplegic refraction)	Any condition A1 (manufacturer criteria): 0.85 (0.81–0.88) A2 (VIP criteria): 0.63 (0.59–0.65) B (VIP criteria): 0.51 (0.46–0.56)‡ "Very important to detect and treat early" conditions A1: 0.96 (0.93–0.99) A2: 0.81 (0.75–0.87) B: 0.75 (0.69–0.81)‡	Any condition A1: 0.62 (0.59–0.65) A2: 0.90 (0.88–0.92) B: 0.94 (0.92–0.95)‡	Any condition A1: 2.2 (2.0–2.4) A2: 6.3 (5.2–7.7) B: 8.6 (6.6–11)‡	Any condition A1: 0.24 (0.19–0.30) A2: 0.41 (0.36–0.47) B: 0.52 (0.47–0.58)‡	Fair
Plusoptix Autorefractors						
Arthur et al, 2008[57]	Plusoptix/Power Refractor autorefractor (Comprehensive eye examination with cycloplegic refraction)	0.83 (0.67–0.93)	0.95 (0.92–0.98)	18 (10–33)	0.17 (0.08–0.36)	Fair
Dahlmann-Noor et al, 2009a[64]	Plusoptix/Power Refractor autorefractor (Comprehensive eye examination with cycloplegic refraction)	Myopia: 0.88 (0.30–1.0) Hyperopia: 0.20 (0.10–0.35) Astigmatism: 0.75 (0.36–0.96) Anisometropia: 0.50 (0.31–0.69)	Myopia: 0.96 (0.89–0.99) Hyperopia: 0.99 (0.92–1.0) Astigmatism: 0.93 (0.86–0.97) Anisometropia: 0.87 (0.77–0.93)	Myopia: 21 (7.8–55) Hyperopia: 26 (1.6–450) Astigmatism: 11 (4.7–24) Anisometropia: 3.7 (1.9–7.1)	Myopia: 0.13 (0.01–1.7) Hyperopia: 0.81 (0.70–0.94) Astigmatism: 0.27 (0.08–0.89) Anisometropia: 0.58 (0.40–0.84)	Fair
Dahlmann-Noor et al, 2009b[65]	Plusoptix/Power Refractor autorefractor (Orthoptist screening with distance acuity testing, cover test, extraocular movements, prism test, and Lang stereotest; comprehensive eye examination with cycloplegic refraction for abnormal autorefractor or orthoptist screening results)	0.45 (0.29–0.62)	1.0 (0.98–1.0)	230 (14–3680)	0.56 (0.42–0.74)	Fair
Ehrt et al, 2007[66]	Plusoptix/Power Refractor autorefractor (Comprehensive eye examination with cycloplegic refraction)	0.71 (0.59–0.82)	0.78 (0.68–0.86)	3.2 (2.2–4.9)	0.37 (0.25–0.54)	Poor

Table 9. Diagnostic Accuracy of Autorefractors

Study, year	Screening test (reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Quality score
Matta et al, 2008[73]	Plusoptix/Power Refractor autorefractor (Comprehensive eye examination with cycloplegic refraction)	A (manufacturer criteria): 0.98 (0.85–1.0) B (revised criteria): 0.98 (0.85–1.0)	A: 0.68 (0.51–0.81) B: 0.88 (0.74–0.96)	A: 3.0 (1.9–4.7) B: 8.4 (3.7–19)	A: 0.04 (0.01–0.26) B: 0.03 (0.00–0.20)	Fair
Other Autorefractors						
Vision in Preschoolers Study Group (Phase I), 2004[82]	Power Refractor autorefractor (now called the Plusoptix) (Comprehensive eye examination with cycloplegic refraction)	Any condition A: 0.54 (0.49–0.59) B: 0.36 (0.31–0.41)‡ "Very important to detect and treat early" conditions A: 0.72 (0.65–0.79) B: 0.56 (0.48–0.63)‡	Any condition A: 0.90 (0.88–0.92) B: 0.94 (0.92–0.95)‡	Any condition A: 5.4 (4.4–6.6) B: 6.0 (4.6–7.9)‡	Any condition A: 0.51 (0.46–0.57) B: 0.68 (0.63–0.73)‡	Fair
Williams et al, 2000[85]	Topcon PR2000 autorefractor (Comprehensive eye examination with cycloplegic refraction)	Spherical error: 0.50 (0.33–0.67)† Anisometropia: 0.74 (0.52–0.90)† Astigmatism: 0.47 (0.28–0.66)†	Spherical error: 0.95 (0.90–0.98)† Anisometropia: 0.95 (0.91–0.98)† Astigmatism: 0.96 (0.92–0.99)†	Spherical error: 9.6 (4.5–20)† Anisometropia: 15 (7.5–32)† Astigmatism: 12 (5.2–30)†	Spherical error: 0.53 (0.38–0.73)† Anisometropia: 0.27 (0.14–0.55)† Astigmatism: 0.55 (0.40–0.78)†	Fair

*Unable to calculate confidence intervals, raw data not provided.
†Results based on cutoffs to obtain specificity of at least 95%.
‡Results based on cutoffs to obtain specificity of 94%.

Abbreviations: CI=confidence interval

Table 10. Diagnostic Accuracy of Photoscreeners

Study, year	Screening test (Reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Quality score
MTI Photoscreener						
Berry et al, 2001[58]	MTI photoscreener (Comprehensive eye examination with cycloplegic refraction)	0.83 (0.61–0.95)	0.68 (0.48–0.84)	2.6 (1.4–4.5)	0.26 (0.10–0.65)	Fair
Cooper et al, 1999[63]	MTI photoscreener (Comprehensive eye examination with cycloplegic refraction)	Reader 1: 0.56 (0.42–0.70) Reader 2: 0.68 (0.54–0.80)	Reader 1: 0.80 (0.65–0.90) Reader 2: 0.86 (0.70–0.95)	Reader 1: 2.8 (1.5–5.2) Reader 2: 4.9 (2.1–11)	Reader 1: 0.55 (0.39–0.77) Reader 2: 0.37 (0.25–0.56)	Poor
Miller et al, 2001[75]	MTI photoscreener (Cycloplegic refraction)	0.66 (0.59–0.73)*	0.71 (0.64–0.78)*	2.3 (1.8–2.9)*	0.48 (0.38–0.60)*	Fair
Ottar et al, 1995[78] and Donahue et al, 2002[87]	MTI photoscreener (Comprehensive eye examination with cycloplegic refraction)	Any amblyogenic risk factor: 0.82 (0.76–0.87) Higher magnitude amblyogenic risk factor: 0.50 (0.39–0.61)	Any amblyogenic risk factor: 0.91 (0.88–0.93) Higher magnitude amblyogenic risk factor: 0.98 (0.97–0.99)	Any amblyogenic risk factor: 8.7 (6.9–11) Higher magnitude amblyogenic risk factor: 33 (18–58)	Any amblyogenic risk factor: 0.20 (0.15–0.27) Higher magnitude amblyogenic risk factor: 0.51 (0.41–0.63)	Fair
Rogers et al, 2008[79]	MTI photoscreener (Comprehensive eye examination with cycloplegic refraction)	0.95 (0.86–0.99)	0.88 (0.74–0.96)	8.0 (3.5–18)	0.06 (0.02–0.18)	Fair
Tong et al, 2000[83]	MTI Photoscreener (Comprehensive eye examination with cycloplegic refraction)	All photographs: 0.56 (0.50–0.62) Informative subset of 313 photographs: 0.65 (0.59–0.71)	All photographs: 0.91 (0.84–0.96) Informative subset of 313 photographs: 0.87 (0.76–0.94)	All photographs: 6.4 (3.4–12) Informative subset of 313 photographs: 4.9 (2.6–9.1)	All photographs: 0.48 (0.42–0.56) Informative subset of 313 photographs: 0.40 (0.33–0.47)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[82]	MTI photoscreener (Comprehensive eye examination with cycloplegic refraction)	Any condition: 0.37 (0.32–0.42) "Very important to detect and treat early" conditions: 0.55 (0.48–0.63) Amblyopia: 0.64 (0.54–0.74) Reduced visual acuity: 0.24 (0.16–0.31) Strabismus: 0.65 (0.53–0.76) Refractive error: 0.42 (0.37–0.48)	Any condition 0.94 (0.92–0.95)	Any condition 6.2 (4.7–8.1)	Any condition 0.67 (0.62–0.72)	Fair

Table 10. Diagnostic Accuracy of Photoscreeners

Study, year	Screening test (Reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Quality score
Weinand et al, 1998[84]	MTI photoscreener (Comprehensive eye examination with cycloplegic refraction)	Pediatrician interpreter: 0.94 (0.86–0.98) Orthoptist interpreter: 0.80 (0.69–0.88) Ophthalmologist 1 interpreter: 0.72 (0.61–0.82) Ophthalmologist 2 interpreter: 0.86 (0.76–0.92)	Pediatrician interpreter: 0.42 (0.20–0.66) Orthoptist interpreter: 0.74 (0.49–0.91) Ophthalmologist 1 interpreter: 0.74 (0.49–0.91) Ophthalmologist 2 interpreter: 0.58 (0.34–0.80)	Pediatrician interpreter: 1.6 (1.1–2.4) Orthoptist interpreter: 3.0 (1.4–6.5) Ophthalmologist 1 interpreter: 2.8 (1.3–5.9) Ophthalmologist 2 interpreter: 2.0 (1.2–3.5)	Pediatrician interpreter: 0.14 (0.05–0.39) Orthoptist interpreter: 0.28 (0.17–0.46) Ophthalmologist 1 interpreter: 0.38 (0.24–0.58) Ophthalmologist 2 interpreter: 0.25 (0.13–0.48)	Fair
iScreen Photoscreener						
Kennedy et al, 2000[72]	iScreen photoscreener (Comprehensive eye examination with cycloplegic refraction [in patients <age 4 years])	0.92 (0.88–0.95)	0.89 (0.83–0.94)	8.6 (5.4–14)	0.09 (0.06–0.13)	Fair
Vision in Preschoolers Study Group (phase I), 2004[82]	iScreen photoscreener (Comprehensive eye examination with cycloplegic refraction)	Any condition: 0.37 (0.32–0.42) "Very important to detect and treat early" conditions: 0.57 (0.50–0.64) Amblyopia: 0.63 (0.52–0.72) Reduced visual acuity: 0.27 (0.20–0.36) Strabismus: 0.50 (0.38–0.62) Refractive error: 0.43 (0.38–0.49)	Any condition 0.94 (0.92–0.95)	Any condition 6.2 (4.7–8.1)	Any condition 0.67 (0.62–0.72)	Fair
Otago-Type Photoscreener						
Kennedy et al, 1989[70]	Otago-type photoscreener; non-commercial (Comprehensive eye examination with cycloplegic refraction)	Any condition: 0.94 (0.87–0.98) Strabismus: 0.91 (0.81–1.01) Refractive error: 0.89 (0.74–1.03) Strabismus + refractive error: 0.98 (0.93–1.02)	Any condition 0.94 (0.89–0.98)	Any condition 16 (8.2–32)	Any condition 0.06 (0.03–0.14)	Fair
Kennedy et al, 1995[71]	Otago-type photoscreener; non-commercial (Comprehensive eye examination without cycloplegic refraction)	0.46 (0.22–0.72)†	1.0 (0.99–1.0)†	110 (38–310)†	0.54 (0.33–0.89)†	Fair

Table 10. Diagnostic Accuracy of Photoscreeners

Study, year	Screening test (Reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Quality score
Molteno et al, 1993[76]	Otago-type photoscreener; non-commercial (History, inspection, cover test, examination of ocular media and fundoscopy through undilated pupils; cycloplegic refraction, dilated fundoscopy, and orthoptic examination with any abnormalities)	0.89 (0.86–0.91)	0.61 (0.55–0.66)	2.3 (2.0–2.6)	0.18 (0.14–0.22)	Poor
Visiscreen Photoscreener						
Cogen et al, 1992[62]	Visiscreen 100 photoscreener (Comprehensive eye examination with cycloplegic refraction "when possible")	0.85 (0.55–0.98)	0.94 (0.87–0.98)	14 (6.3–32)	0.16 (0.05–0.59)	Fair
Morgan et al, 1987[77]	Visiscreen 100 photoscreener (Comprehensive eye examination with cycloplegic refraction)	0.91 (0.76–0.98)	0.74 (0.52–0.90)	3.5 (1.7–7.0)	0.12 (0.04–0.36)	Fair
Other Photoscreeners						
Cooper et al, 1999[63]	Fortune Optical VRB-100 photoscreener (Comprehensive eye examination with cycloplegic refraction)	Reader 1: 0.60 (0.47–0.73) Reader 2: 0.69 (0.54–0.80)	Reader 1: 0.76 (0.60–0.87) Reader 2: 0.86 (0.72–0.95)	Reader 1: 2.5 (1.4–4.3) Reader 2: 4.9 (2.3–10)	Reader 1: 0.52 (0.37–0.75) Reader 2: 0.37 (0.24–0.55)	Poor
Guo et al, 2000[67]	Computer-photorefractor (Comprehensive eye examination with cycloplegic refraction)	0.95 (0.90–0.98)	0.90 (0.84–0.95)	9.6 (5.7–16)	0.06 (0.03–0.11)	Fair
Kennedy et al, 1989[70]	Off-axis-type photoscreener; non-commercial (Comprehensive eye examination with cycloplegic refraction)	Any condition: 0.85 (0.76–0.91) Strabismus: 0.73 (0.58–0.88) Refractive error: 0.89 (0.74–1.03) Strabismus + refractive error: 0.91 (0.82–0.99)	Any condition 0.87 (0.80–0.92)	Any condition 6.5 (4.2–10)	Any condition 0.18 (0.11–0.28)	Fair

*Calculations based on n=379, median sensitivity and specificity.
†Extrapolated from 20% sample of negative screens.

Table 11. Diagnostic Accuracy of Preschool Vision Screening Tests

Test	Target condition	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
VISUAL ACUITY TESTS					
Crowded Lea Symbols Visual Acuity Test (4 studies)					
VIP, 2004[82]	Amblyogenic risk factors or significant nonamblyogenic refractive error	0.61 (0.56–0.66)*	0.90 (0.88–0.92)*	6.1 (4.8–7.6)*	0.43 (0.38–0.50)*
Bertuzzi et al, 2006[59]	Amblyogenic risk factors	0.96 (0.78–1.0)†	0.83 (0.75–0.90)†	5.7 (3.8–8.6)†	0.05 (0.01–0.36)†
			Median (range)	**5.9 (5.7–6.1)**	**0.15 (0.05–0.43)**
Miller et al, 1999[74]	Significant refractive error	0.91 (0.82–0.96)‡	0.44 (0.37–0.52)‡	1.6 (1.4–1.9)‡	0.21 (0.10–0.43)‡
Miller et al, 2001[75]	Astigmatism	0.93 (0.87–0.97)‡	0.51 (0.44–0.57)‡	1.9 (1.6–2.2)‡	0.14 (0.08–0.27)‡
Crowded HOTV Visual Acuity Test (1 study)					
VIP, 2004[82]	Amblyogenic risk factors or significant nonamblyogenic refractive error	0.54 (0.49–0.59)*	0.89 (0.87–0.91)*	4.9 (3.9–6.1)*	0.52 (0.46–0.58)*
STEREOACUITY TESTS					
Random Dot E Stereogram (3 studies)					
Chang et al, 2007[60]	Amblyopia	0.20§	0.98§	11.4§	0.81§
VIP, 2004[82]	Amblyogenic risk factors or significant nonamblyogenic refractive error	0.42 (0.37–0.47)*	0.90 (0.88–0.92)*	4.2 (3.3–5.3)*	0.65 (0.59–0.71)*
Hope et al, 1990[68]	Refractive error or strabismus	0.89 (0.52–1.0)	0.76 (0.68–0.82)	3.6 (2.5–5.2)	0.15 (0.02–0.94)
			Median (range)	**4.2 (3.6–11.4)**	**0.65 (0.15–0.81)**
Stereo Smile II Test (1 study)					
VIP, 2004[82]	Amblyogenic risk factors or significant nonamblyogenic refractive error	0.44 (0.39–0.49)*	0.91 (0.89–0.93)*	4.9 (3.9–6.1)*	0.62 (0.56–0.67)*
OCULAR ALIGNMENT TESTS					
Cover-Uncover Test (1 study)					
VIP, 2004[82]	Amblyogenic risk factors or significant nonamblyogenic refractive error	0.16 (0.12–0.29)	0.98 (0.97–0.99)	7.9 (4.6–14.0)	0.73 (0.15–0.85)
COMBINED CLINICAL TESTS (5 STUDIES)					
Kennedy et al, 1995[71]	Amblyogenic risk factors	0.09 (0.04–0.20)	1.0 (0.99–1.0)	17 (5.5–54)	0.91 (0.84–0.99)
Barry et al, 2003[11]	Amblyopia or amblyogenic risk factors	0.91 (0.71–0.99)	0.94 (0.92–0.95)	15 (11–19)	0.10 (0.03–0.36)
Newman et al, 1999[12]	Amblyopia	1.0 (0.78–1.0)	0.93 (0.91–0.95)	14 (10–19)	0.03 (0.002–0.51)
Shallo-Hoffman et al, 2004[80]	Amblyogenic risk factors	0.73 (0.13–0.98)	0.94 (0.90–0.96)	12 (4.7–28)	0.28 (0.03–2.4)
Chui et al, 2004[61]	Amblyogenic risk factors	0.67 (0.41–0.87)	0.86 (0.79–0.92)	4.8 (2.8–8.4)	0.39 (0.20–0.75)
			Median (range)	**14 (4.8–17)**	**0.28 (0.03–0.91)**

Table 11. Diagnostic Accuracy of Preschool Vision Screening Tests

Test	Target condition	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
AUTOREFRACTORS					
Retinomax (4 studies)					
VIP, 2004[82]	Amblyogenic risk factors or significant nonamblyogenic refractive error	0.64 (0.60–0.67)*	0.90 (0.88–0.91)*	6.1 (5.2–7.0)*	0.41 (0.37–0.45)*
Barry et al, 2001[10]	Amblyopia			1.9 (1.4–2.6)	0.35 (0.10–1.2)
			Median (range)	**3.4 (1.9–6.1)**	**0.38 (0.35–0.41)**
Miller et al, 1999[74]	Significant refractive error	0.91 (0.82–0.96)‡	0.86 (0.80–0.91)‡	6.7 (4.5–9.8)‡	0.11 (0.05–0.22)‡
Miller et al, 2001[75]	Astigmatism	0.93 (0.88–0.96)‡	0.95 (0.91–0.98)‡	18 (10–34)‡	0.08 (0.04–0.13)‡
Suresight (3 studies)					
VIP, 2004[82]	Amblyogenic risk factors or significant nonamblyogenic refractive error	0.85 (0.81–0.88)‖ 0.63 (0.59–0.65)*‡	0.62 (0.59–0.65)‖ 0.90 (0.88–0.92)*‡	2.2 (2.0–2.4)‖ 6.3 (5.2–7.4)*‡	0.24 (0.19–0.30)‖ 0.41 (0.36–0.47)*‡
Kemper et al, 2005[69]	Amblyogenic risk factors	0.85 (0.69–0.95)	0.52 (0.40–0.63)	1.8§	0.29§
Rogers et al, 2008[79]	Amblyogenic risk factors	0.97 (0.88–1.0)‖ 0.79 (0.67–0.89)‡¶	0.38 (0.24–0.54)‖ 0.64 (0.48–0.78)‡¶	1.6 (1.2–2.0)‖ 2.2 (1.4–3.4)‡¶	0.09 (0.02–0.37)‖ 0.32 (0.18–0.52)‡¶
			Median (range)	**1.8 (1.6–2.2)**‖	**0.24 (0.09–0.29)**‖
Topcon PR 2000 (1 study)					
Williams et al, 2000[85]	Spherical error >3.75 D Anisometropia Astigmatism	0.50 (0.33–0.67) 0.74 (0.52–0.90) 0.47 (0.28–0.66)	0.95 (0.90–0.98) 0.95 (0.91–0.98) 0.96 (0.92–0.99)	9.6 (4.5–20) 15 (7.5–32) 12 (5.2–30)	0.53 (0.38–0.73) 0.27 (0.14–0.55) 0.55 (0.40–0.78)
Plusoptix/Power Refractor (6 studies)					
Dahlmann-Noor et al, 2009b[64]	Decreased visual acuity, strabismus, and ptosis	0.45 (0.29–0.62)	1.0 (0.98–1.0)	230 (14–3680)	0.56 (0.42–0.74)
Arthur et al, 2009[57]	Amblyogenic risk factors	0.83 (0.67–0.93)	0.95 (0.92–0.98)	18 (10–33)	0.17 (0.08–0.36)
VIP, 2004[82]	Amblyogenic risk factors or significant nonamblyogenic refractive error	0.54 (0.49–0.59)*	0.90 (0.88–0.92)*	5.4 (4.4–6.6)*	0.51 (0.46–0.57)*
Ehrt et al, 2007[66]	Amblyogenic risk factors	0.71 (0.59–0.82)	0.78 (0.68–0.86)	3.2 (2.2–4.9)	0.37 (0.25–0.54)
Matta et al, 2008[73]	Amblyogenic risk factors	0.98 (0.85–1.0) 0.98 (0.85–1.0)	0.68 (0.51–0.81) 0.88 (0.74–0.96)	3.0 (1.9–4.7)‖ 8.4 (3.7–19)*‡	0.04 (0.01–0.26)‖ 0.03 (0.00–0.20)*‡
			Median (range)	**5.4 (3.0–230)**	**0.17 (0.04–0.56)**
Dahlmann-Noor et al, 2009a[64]	Myopia Hyperopia Astigmatism Anistometropia	0.88 (0.30–1.0) 0.20 (0.10–0.35) 0.75 (0.36–0.96) 0.50 (0.31–0.69)	0.96 (0.89–0.99) 0.99 (0.92–1.0) 0.93 (0.86–0.97) 0.87 (0.77–0.93)	21 (7.8–55) 26 (1.6–450) 11 (4.7–24) 3.7 (1.9–7.1)	0.13 (0.01–1.7) 0.81 (0.70–0.94) 0.27 (0.08–0.89) 0.58 (0.40–0.84)
PHOTOSCREENERS					
MTI Photoscreener (8 studies)					
Ottar et al, 1995[78] and Donahue et al, 2002[87]	Amblyogenic risk factors	0.82 (0.76–0.87)	0.91 (0.88–0.93)	8.7 (6.9–11)	0.20 (0.15–0.27)
Rogers et al, 2008[79]	Amblyogenic risk factors	0.95 (0.86–0.99)	0.88 (0.74–0.96)	8.0 (3.5–18)	0.06 (0.02–0.18)

Table 11. Diagnostic Accuracy of Preschool Vision Screening Tests

Test	Target condition	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
Tong et al, 2000[83]	Amblyogenic risk factors	0.56 (0.50–0.62)	0.91 (0.84–0.96)	6.4 (3.4–12)	0.48 (0.42–0.56)
VIP, 2004[82]	Amblyogenic risk factors or significant nonamblyogenic refractive error	0.37 (0.32–0.42)	0.94 (0.92–0.95)	6.2 (4.7–8.1)	0.67 (0.62–0.72)
Cooper et al,1999[63]	Amblyopia	0.62 (range, 0.56–0.68)#	0.83 (range, 0.80–0.86)#	3.7 (range, 2.8–4.9)#	0.45 (range, 0.37–0.55)#
Berry et al, 2001[58]	Amblyogenic risk factors	0.83 (0.61–0.95)	0.68 (0.48–0.84)	2.6 (1.4–4.5)	0.26 (0.10–0.65)
Weinand et al, 1998[84]	Amblyogenic risk factors	0.83 (range, 0.72–0.94)#	0.66 (range, 0.42–0.74)#	2.4 (range, 1.6–3.0)#	0.26 (range, 0.14–0.38)#
			Median (range)	**6.2 (2.4–8.7)**	**0.26 (0.06–0.67)**
Miller et al, 2001[75]	Significant refractive error	0.66 (0.59–0.73)*	0.71 (0.64–0.78)*	2.3 (1.8–2.9)*	0.48 (0.38–0.60)*
Ottar et al, 1995[78] and Donahue et al, 2002[87]	Higher magnitude amblyogenic risk factors	0.50 (0.39–0.61)	0.98 (0.97–0.99)	33 (18–58)	0.51 (0.41–0.63)
iScreen Photoscreener (2 studies)					
Kennedy et al, 2000[72]	Amblyogenic risk factors	0.92 (0.88–0.95)	0.89 (0.83–0.94)	8.6 (5.4–14)	0.09 (0.06–0.13)
VIP, 2004[82]	Amblyogenic risk factors or significant nonamblyogenic refractive error	0.37 (0.32–0.42)	0.94 (0.92–0.95)	6.2 (4.7–8.1)	0.67 (0.62–0.72)
			Median (range)	**7.3 (6.2–8.6)**	**0.25 (0.09–0.67)**
Visiscreen 100 Photoscreener (2 studies)					
Cogen et al, 1992[62]	Amblyogenic risk factors	0.85 (0.55–0.98)	0.94 (0.87–0.98)	14 (6.3–32)	0.16 (0.05–0.59)
Morgan et al, 1987[77]	Amblyogenic risk factors	0.91 (0.76–0.98)	0.74 (0.52–0.90)	3.5 (1.7–7.0)	0.12 (0.04–0.36)
			Median (range)	**7.0 (3.5–14)**	**0.14 (0.12–0.16)**
Fortune Optical VRB-100 Photoscreener (1 study)					
Cooper et al, 1999[63]	Amblyopia	0.64 (range, 0.60–0.69)#	0.81 (range, 0.76–0.86)#	3.5 (range, 2.5–4.9)#	0.44 (range, 0.37–0.52)#
Computer Photoscreener (1 study)					
Guo et al, 2000[67]	Amblyogenic risk factors	0.95 (0.90–0.98)	0.90 (0.84–0.95)	9.6 (5.7–16)	0.06 (0.03–0.11)
Otago (Noncommercial) Photoscreener (3 studies)					
Kennedy et al, 1995[71]	Amblyogenic risk factors	0.46 (0.22–0.72)	1.0 (0.99–1.0)	110 (38–310)	0.54 (0.33–0.89)
Kennedy et al, 1989[70]	Amblyogenic risk factors	0.94 (0.87–0.98)	0.94 (0.89–0.98)	16 (8.2–32)	0.06 (0.03–0.14)
Molteno et al, 1993[76]	Amblyogenic risk factors	0.89 (0.86–0.91)	0.61 (0.55–0.66)	2.3 (2.0–2.6)	0.18 (0.14–0.22)
			Median (range)	**16 (2.3–110)**	**0.18 (0.06–0.54)**

*Based on 90% specificity.
†Based on 0.80 acuity score cutoff.
#Based on median results from multiple readers.
‡Excluded from calculation of median.
§ Confidence intervals not calculable.
‖Based on manufacturer's referral criteria.
¶Based on VIP 90% specificity criteria.

Table 12. Diagnostic Accuracy of Screening Tests Stratified By Age

Study, year	Screening test	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)
Chui et al, 2004[61]	LEA symbols visual acuity test, Frisby stereoacuity test, and external visual inspection	Overall: 0.67 (0.41–0.87) Age <41 months: 0.75 (0.43–0.94) Age ≥41 months: 0.50 (0.12–0.88)	Overall: 0.86 (0.79–0.92) Age <41 months: 0.90 (0.52–0.82) Age ≥41 months: 0.95 (0.88–0.99)	Overall: 4.8 (2.8–8.4) Age <41 months: 2.4 (1.4–4.1) Age ≥41 months: 10 (3.0–36)
Kemper et al, 2005[69]	SureSight autorefractor	Overall: 0.85 (0.69–0.95) Age <3 years (n=80): 0.80 (0.44–0.97) Age 3–5 years (n=90): 0.88 (0.68–0.97)	Overall: 0.52 (0.40–0.63) Age <3 years: 0.41 (0.24–0.61) Age 3–5 years: 0.58 (0.42–0.71)	Overall: 1.8 Age <3 years: 1.4 Age 3–5 years: 2.1
Kennedy et al, 2000[72]	iScreen photoscreener	Overall: 0.92 (0.88–0.95) Age ≤3 years: 1.0 Age 4–6 years: 0.92	Overall: 0.89 (0.83–0.94) Age ≤3 years: 0.97 Age 4–6 years: 0.95	Overall: 8.6 (5.4–14) Age ≤3 years: 33 Age 4–6 years: 18
Tong et al, 2000[83]	MTI photoscreener	*All photographs; informative subset of 313 photographs* Any condition: 56% (159/284); 65% (159/245) Strabismus: 77% (131/170) Refractive error: 68% (123/181)	*All photographs; informative subset of 313 photographs* Any condition: 91% (94/103); 87% (59/68)	Informative subset of 313 photographs: 5.0
Chui et al, 2004[61]	Overall: 0.39 (0.20–0.75) Age <41 months: 0.37 (0.13–1.0) Age >41 months: 0.53 (0.24–1.2)	Overall: 0.41 (0.24–0.61) Age <41 months: 0.41 (0.21–0.64) Age ≥41 months: 0.43 (0.10–0.82)	Overall: 0.95 (0.89–0.98) Age <41 months: 0.90 (0.74–0.98) Age ≥41 months: 0.96 (0.90–0.99)	Overall: 12 (3.6–45) Age <41 months: 6.5 (1.3–42) Age ≥41 months: 20 (1.8–180)
Kemper et al, 2005[69]	Overall: 0.29 Age <3 years: 0.49 Age 3–5 years: 0.21	Not calculable	Not calculable	Overall: 6.2 Age <3 years: 2.9 Age 3–5 years: 10
Kennedy et al, 2000[72]	Overall: 0.09 (0.06–0.13) Age ≤3 years: not calculable Age 4–6 years: 0.08	Overall: 0.94 (0.90–0.96) Age ≤3 years: 0.97 Age 4–6 years: 0.97	Overall: 0.86 (0.80–0.91)	Overall: 100 (48–210) Age ≤3 years: not calculable Age 4–6 years: 220
Tong et al, 2000[83]	Informative subset of 313 photographs: 0.40	A: 0.95 (0.90–0.98) B: 0.95 (0.90–0.98)	A: 0.43 (0.36–0.50) B: 0.41 (0.33–0.49)	A: 13 (6.3–31) B: 12 (5.6–29)

Table 13. Positive Predictive Values of Screening Tests

Study, year	Screening test	Age of enrollees	N	Proportion with condition	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Barry et al, 2001[10]	Retinomax autorefractor	3 years	404	Amblyopia: 2.5% (10/404)	0.05 (0.02–0.09)	0.99 (0.97–1.0)
Barry et al, 2003[11]	Visual inspection, cover-uncover test, eye motility and head posture exam, Lea symbols visual acuity test	3 years	1180	Amblyopia or amblyogenic risk factors: 2.3% (26/1114)	0.25 (0.16–0.36)	1.0 (0.99–1.0)
Berry et al, 2001[58]	MTI photoscreener	Preschool (subgroup)	51	Amblyogenic risk factors: 45% (23/51)	0.68 (0.48–0.84)	0.83 (0.61–0.95)
Bertuzzi et al, 2006[59]	LEA symbols visual acuity test	38 to 54 months	149	Amblyogenic risk factors: 16% (23/143)	A: 0.52 (0.36–0.68) B: 0.69 (0.48–0.86)	A: 0.99 (0.95–1.0) B: 0.96 (0.90–0.99)
Chang et al, 2007[60]	A: Distance visual acuity B: Near visual acuity C: NTU random dot stereogram	Preschool	5232	Amblyopia: 2.20% (115/5232)	A1: 0.12* A2: 0.04* B: 0.13* C: 0.17*	A1: 0.995* A2: 0.996* B: 0.988* C: 0.986*
Chui et al, 2004[61]	LEA symbols visual acuity test, Frisby stereoacuity test, and external visual inspection	35 to 58 months	178 (141 completed evaluation)	Amblyogenic risk factors: 13% (18/141)	Overall: 0.41 (0.24–0.61) Age <41 months: 0.41 (0.21–0.64) Age ≥41 months: 0.43 (0.10–0.82)	Overall: 0.95 (0.89–0.98) Age <41 months: 0.90 (0.74–0.98) Age ≥41 months: 0.96 (0.90–0.99)
Cogen et al, 1992[62]	Visiscreen 100 photoscreener	6 months to 6 years	127	Any visual condition: 12% (13/113) Refractive error: 5% (6/113) Strabismus: 4% (5/113) Refractive error + strabismus: 1% (1/113) Media opacity: 1% (1/113)	0.65 (0.38–0.86)	0.98 (0.93–1.0)
Cooper et al, 1999[63]	A: Fortune Optical VRB-100 photoscreener B: MTI photoscreener	12 to 44 months	105	61 cases (amblyopia), 44 controls	A (reader 1): 0.76 (0.61–0.87) A (reader 2): 0.86 (0.72–0.95) B (reader 1): 0.78 (0.62–0.89) B (reader 2): 0.88 (0.74–0.96)	A (reader 1): 0.60 (0.46–0.72) A (reader 2): 0.69 (0.54–0.80) B (reader 1): 0.59 (0.46–0.72) B (reader 2): 0.65 (0.50–0.78)
Ehrt et al, 2007[66]	Vision Screener video refractor	0 to 7 years	161	Amblyogenic risk factors: 43% (70/161)	0.71 (0.59–0.82)	0.78 (0.68–0.86)
Guo et al, 2000[67]	A: Computer-photorefractor B: Noncycloplegic retinoscopy	9 to 50 months	300	Amblyogenic risk factors: 56% (168/300)	A: 0.92 (0.87–0.96) B: 0.85 (0.79–0.90)	A: 0.93 (0.87–0.97) B: 0.82 (0.74–0.88)

Table 13. Positive Predictive Values of Screening Tests

Study, year	Screening test	Age of enrollees	N	Proportion with condition	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Hope et al, 1990[68]	Random dot E stereogram	3 to 4 years	176	Refractive error or strabismus: 5% (9/168) Refractive error: 5% (9/168) Strabismus: 0.6% (1/168)	0.17 (0.08–0.31)	0.99 (0.96–1.0)
Kennedy et al, 1989[70]	A: Otago-type photoscreener (noncommercial) B: Off-axis-type photoscreener (noncommercial)	6 years or younger	236	Any amblyogenic risk factor: 42% (98/236) Strabismus only: 14% (33/236) Strabismus + refractive error or anisometropia: 18% (42/236) Refractive error or anisometropia: 8% (18/236) Anisocoria or lid tumor: 2% (5/236)	Any condition A: 0.92 (0.85–0.96) B: 0.82 (0.73–0.89)	Any condition A: 0.96 (0.91–0.98) B: 0.89 (0.82–0.94)
Kennedy et al, 1995[71]	A: Otago-type photoscreener (noncommercial) B: Snellen E or Stycar graded balls visual acuity test and Titmus stereotest	Not reported	264	Any visual condition: 8% (21/264) Strabismus: 1.1% (3/264) Refractive error: 4.2% (11/264) Strabismus and refractive error: 0.8% (2/264) Structural: 0.4% (1/264)	A: 0.77 (0.60–0.95) B: 0.54 (0.28–0.81)	A: 0.98 (0.91–1.00) B: 0.94 (0.91–0.97)
Kennedy et al, 2000[72]	iScreen photoscreener	45% 6 years or younger	449	Amblyogenic risk factors: 64% (273/423)	Overall: 0.94 (0.90–0.96) Age ≤3 years: 0.97 Age 4–6 years: 0.97	0.86 (0.80–0.91)
Miller et al, 1999[74]	A: LEA symbols visual acuity test B: Retinomax K-Plus autorefractor	3 to 5 years	245	Significant refractive error: 31% (76/245); all had astigmatism	A: 0.42 (0.35–0.50) B: 0.75 (0.65–0.83)	A: 0.92 (0.83–0.96) B: 0.95 (0.901–0.98)
Miller et al, 2001[75]	A: LEA symbols visual acuity test B: MTI photoscreener C: Nidek KM-500 Keratometry screener D: Retinomax K-Plus autorefractor	3 to 5 years	379	Astigmatism ≥1.00 D: 48% (182/379)	A: 0.48 (0.41–0.54) B: 0.68 (0.60–0.75)† C: 0.79 (0.73–0.84) D: 0.94 (0.90–0.97)	A: 0.93 (0.88–0.97) B: 0.70 (0.63–0.76)† C: 0.94 (0.90–0.97) D: 0.94 (0.89–0.96)
Morgan et al, 1987[77]	Visiscreen 100 photoscreener	3 months to 8 years	63	Any visual condition: 60% (34/57)	0.84 (0.68–0.94)	0.85 (0.62–0.97)

Table 13. Positive Predictive Values of Screening Tests

Study, year	Screening test	Age of enrollees	N	Proportion with condition	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Newman et al, 1999[12]	Sheridan-Gardiner visual acuity; cover-uncover test; ocular movements and convergence; prism test; TNO screening plate; Snellen visual acuity	3.5 years and at 5–6 years	Cohort of 936; data reported on 597	Amblyopia: 2.5% (15/597)	0.27 (0.16–0.41)	1.0 (0.99–1.0)
Ottar et al, 1995[78] and Donahue et al, 2002[87]	MTI photoscreener	6 to 59 months	949	Amblyogenic risk factors: 20% (192/949)	A: 0.69 (0.62–0.75) B: 0.77 (0.64–0.87)‡	A: 0.95 (0.93–0.97) B: 0.95 (0.93–0.96)‡
Rogers et al, 2008[79]	MTI photoscreener SureSight autorefractor	1 to 6 years	100	Clinically significant amblyopia: 58% (58/100)	A: 0.68 (0.57–0.78) B: 0.75 (0.63–0.86) C: 0.75 (0.61–0.86) D: 0.77 (0.62–0.88) E: 0.92 (0.82–0.97)	A: 0.89 (0.65–0.99) B: 0.69 (0.52–0.83) C: 0.60 (0.45–0.74) D: 0.58 (0.44–0.72) E: 0.92 (0.80–0.98)
Shallo-Hoffmann et al, 2004[80]	LEA symbol and HOTV charts, and random dot E stereoacuity test	2 to 6 years	269	Any vision condition: 6% (5/81)	0.24 (0.08–0.47)	1.00 (0.94–1.0) (adjusted)
Tong et al, 2000[83]	MTI photoscreener	<4 years	387	Strabismus: 49% (190/387) Refractive error: 55% (211/387)	*All photographs; informative subset of 313 photographs* Any condition: 0.95 (0.90–0.98); 0.95 (0.90–0.98)	*All photographs; informative subset of 313 photographs* Any condition: 0.43 (0.36–0.50); 0.41 (0.33–0.49)
Vision in Preschoolers Study Group (Phase I)[82]	Crowded linear LEA symbols visual acuity test	3, 4, or 5 years	3121	Any vision condition: 29% (755/2588) "Very important to detect and treat early" conditions: 5.4% (135/2588) Amblyopia: 2.9% (75/2588) Reduced visual acuity: 5.1% (132/2588) Strabismus: 1.9% (48/2588) Refractive error: 9.3% (240/2588)	Any condition A: 0.73 (0.67–0.78) B: 0.78 (0.72–0.83)	Any condition A: 0.84 (0.82–0.86) B: 0.81 (0.78–0.83)

Table 13. Positive Predictive Values of Screening Tests

Study, year	Screening test	Age of enrollees	N	Proportion with condition	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Vision in Preschoolers Study Group (Phase I)[82]	Crowded linear HOTV visual acuity test	3, 4, or 5 years	3121	Any vision condition: 29% (755/2588) "Very important to detect and treat early" conditions: 5.4% (135/2588) Amblyopia: 2.9% (75/2588) Reduced visual acuity: 5.1% (132/2588) Strabismus: 1.9% (48/2588) Refractive error: 9.3% (240/2588)	Any condition A: 0.68 (0.62–0.74) B: 0.69 (0.62–0.76)	Any condition A: 0.82 (0.79–0.84) B: 0.77 (0.74–0.80)
	Random dot E stereoacuity test				Any condition A: 0.64 (0.58–0.71) B: 0.54 (0.46–0.63)	Any condition A: 0.78 (0.75–0.81) B: 0.80 (0.78–0.83)
	Stereo smile II stereoacuity test				Any condition A: 0.66 (0.60–0.72) B: 0.68 (0.62–0.75)	Any condition A: 0.73 (0.70–0.76) B: 0.78 (0.76–0.80)
	Retinomax autorefractor				Any condition A: 0.71 (0.68–0.75) B: 0.78 (0.74–0.82)	Any condition A: 0.86 (0.84–0.87) B: 0.83 (0.81–0.84)
	SureSight autorefractor				Any condition A1: 0.47 (0.43–0.51) A2: 0.71 (0.66–0.76) B: 0.77 (0.72–0.82)	Any condition A1: 0.91 (0.89–0.93) A2: 0.86 (0.84–0.88) B: 0.83 (0.81–0.85)
	iScreen photoscreener				Any condition 0.71 (0.64–0.77)	Any condition 0.79 (0.77–0.81)
	MTI photoscreener				Any condition 0.71 (0.64–0.77)	Any condition 0.79 (0.77–0.81)
	Power Refractor II				Any condition A: 0.68 (0.65–0.73) B: 0.70 (0.64–0.76)	Any condition A: 0.83 (0.81–0.85) B: 0.79 (0.76–0.81)
	Cover-uncover test				Any condition 0.78 (0.66–0.86)	Any condition 0.73 (0.70–0.76)

Table 13. Positive Predictive Values of Screening Tests

Study, year	Screening test	Age of enrollees	N	Proportion with condition	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Weinand et al, 1998[84]	MTI photoscreener	6 to 48 months	112	Any abnormality: 81% (83/102) Refractive error: 41% (41/102) Strabismus w/out refractive error: 7% (7/102) Strabismus w/refractive error: 21% (21/102) Organic anomaly: 13% (13/102)	A (Pediatrician interpreter): 0.88 (0.79–0.94) B (Orthoptist interpreter): 0.93 (0.84–0.98) C (Ophthalmologist 1 interpreter): 0.92 (0.83–0.98) D (Ophthalmologist 2 interpreter): 0.90 (0.81–0.96)	A (Pediatrician interpreter): 0.62 (0.32–0.86) B (Orthoptist interpreter): 0.45 (0.27–0.64) C (Ophthalmologist 1 interpreter): 0.38 (0.22–0.55) D (Ophthalmologist 2 interpreter): 0.48 (0.27–0.69)
Williams et al, 2000[85]	Topcon PR2000 autorefractor	12.5 to 68.7 months	222	A: Spherical error >3.75 D: 19% (36/189) B: Anisometropia >1.25 D: 12% (23/189) C: Astigmatism >1.25 D: 16% (30/189)	A: 0.69 (0.48–0.86) B: 0.68 (0.46–0.85) C: 0.70 (0.46–0.88)	A: 0.89 (0.83–0.93) B: 0.96 (0.92–0.99) C: 0.91 (0.85–0.94)

*Raw data not provided; unable to calculate confidence intervals.
† Calculation based on n=379, median sensitivity and specificity.
‡ Based on reported sensitivity and specificity, does not match values reported in article.

Table 14. Randomized Controlled Trials of Amblyopia Treatments

Author, year	Population	Follow-up	Intervention: Mean change in visual acuity from baseline	Quality score
Patching + eyeglasses vs. eyeglasses alone vs. no treatment				
Clarke et al, 2003[99]	n=177 Mean age: 4.0 years Mean visual acuity in amblyopic eye: 0.36 logMAR (Snellen equivalent, 20/45)	1 year	Patching (hrs/day not reported) + eyeglasses: 0.18 Mean difference vs. no treatment: 0.109 (95% CI, 0.005 to 0.17) Eyeglasses only: 0.13 Mean difference vs. no treatment: 0.085 (95% CI, 0.02 to 0.15) No treatment: 0.06; p=0.001 (ANOVA) **Results stratified according to baseline severity** *Mild acuity loss at baseline* Patching + eyeglasses: 0.23 Mean difference vs. no treatment: 0.04 (95% CI, -0.06 to 0.13) Eyeglasses only: 0.24 Mean difference vs. no treatment: 0.05 (95% CI, -0.03 to 0.13) No treatment: 0.19; p=0.38 (ANOVA) *Moderate acuity loss at baseline* Patching + eyeglasses: 0.52 Mean difference vs. no treatment: 0.27 (95% CI, 0.14 to 0.39) Eyeglasses only: 0.35; Mean difference vs. no treatment: 0.11 (95% CI, -0.03 to 0.24) No treatment: 0.25; p<0.001 (ANOVA)	Good
Patching vs. no patching, all children pretreated with eyeglasses if indicated				
Awan et al, 2005[101]	n=60 Mean age: 4.6 years Mean visual acuity in amblyopic eye: 0.64 logMAR (Snellen equivalent, 20/90) 55/60 (92%) received eyeglasses for correction of refractive error	12 weeks	3-hr patching: 0.29 (p=0.32 vs. no treatment) 6-hr patching: 0.34 (p=0.09 vs. no treatment) No treatment: 0.24 (p=0.11 vs. both treatments)	Fair
PEDIG, 2006[100]	n=180 Mean age: 5.3 years Mean visual acuity in amblyopic eye: 0.55 logMAR (Snellen equivalent, 20/70) 155/180 (86%) received eyeglasses for correction of refractive error	5 weeks	2-hr patching: 0.12 No treatment: 0.04 Mean between-group difference: 0.07 (95% CI, 0.02 to 0.12); p=0.006	Good

Table 14. Randomized Controlled Trials of Amblyopia Treatments

Author, year	Population	Follow-up	Intervention: Mean change in visual acuity from baseline	Quality score
Occlusion regimens				
PEDIG, 2003[102]	n=189 Mean age: 5.2 years Mean visual acuity in amblyopic eye: 0.48 logMAR (Snellen equivalent, 20/63)	4 months	2-hr patching: 0.24 6-hr patching: 0.24 Mean between-group difference: 0.001 (95% CI, 0.040 to 0.042); p=0.9	Good
Stewart et al, 2007[103]	n=97 Mean age: 5.6 years Mean visual acuity in amblyopic eye: 0.44 logMAR (Snellen equivalent, 20/70)	mean 9 weeks (range, 5–26 weeks)	6-hr patching: 0.26 12-hr patching: 0.24 Mean between-group difference: 0.02 (95% CI, 0.0 to 0.04); p=0.64	Fair
Atropine regimens				
PEDIG, 2004[104]	n=168 Mean age: 5.3 years Mean visual acuity in amblyopic eye: 0.46 logMAR (Snellen equivalent, 20/60)	4 months	Daily atropine: 0.23 Weekend atropine: 0.25 Mean between-group difference: 0.02 (95% CI, -0.21 to 0.09); p=0.52	Good
Patching vs. atropine				
PEDIG, 2002[105]	n=419 Mean age: 5.3 years Mean visual acuity in amblyopic eye: 0.53 logMAR (Snellen equivalent, 20/65)	Initial trial: 6 months; voluntary follow-up through 10 years	*6-month results (mean age: 5.2 years)* Patching: 0.25 Atropine: 0.21 Mean between-group difference: 0.04 (95% CI, 0.005 to 0.064) *2-year results (mean age: 7.2 years)* Follow-up of patients in original study: 363/419 (86.6%) Patching: 0.16 Atropine: 0.17 Mean between-group difference: 0.01 (95% CI, -0.04 to 0.02); p=0.57 *5-yr results (mean age: 10.3 years)* Follow-up of patients in original study: 176/419 (42.0%) Patching 0.19 Atropine 0.16 Mean between-group difference: 0.03 (95% CI, -0.02 to 0.07); p=0.2	Good

Abbreviations: ANOVA=analysis of variance between groups; CI=confidence interval; hr=hour; logMAR = logarithmic minimum angle of resolution; OR=odds ratio; PEDIG=Pediatric Eye Disease Investigator Group; RR=relative risk; vs.=versus.

Table 15. Summary of Evidence

Number of studies, quality score	Limitations	Consistency	Primary care applicability	Summary of findings
KQ 1. Is vision screening in children ages 1–5 years associated with improved health outcomes?				
Screening vs. no screening: 4 cohort studies Intensive periodic vs. one-time screening: 1 RCT *Fair to poor quality*	No study evaluated school performance or other functional outcomes besides vision outcomes. 3 of the 4 cohort studies were retrospective and had important methodological shortcomings. The 1 prospective cohort study compared one-time screening to no screening.	Not applicable (not enough studies addressing the same question to judge consistency)	High	No randomized trial evaluated outcomes of preschool vision screening compared to no screening. One large, fair-quality randomized trial nested within a population-based cohort study found that intensive, periodic orthoptist screening from ages 8 to 37 months was associated with reduced likelihood of amblyopia at age 7.5 years compared to one-time orthoptist screening at age 37 months by about 1%, but the difference was only statistically significant for one of two definitions of amblyopia. A large prospective cohort study from this population found that one-time orthoptist screening at age 37 months was associated with no significant difference in risk for amblyopia at age 7.5 years compared to no screening, using any of three prestated definitions for amblyopia. Three retrospective cohort studies found that preschool screening was associated with improved school-age vision outcomes compared to no screening.
KQ 1a. Does effectiveness of vision screening in children ages 1–5 years vary in different age groups?				
Earlier vs. later screening: 1 RCT, 1 cohort study *Poor quality*	In the RCT, it was not possible to determine whether differences in outcomes should be attributed to the earlier age at which screening was started or to the increased frequency of screening that also took place. In the retrospective cohort study, estimates were imprecise and based on a very small sample of children screened.	Not applicable	High	No randomized trial directly compared outcomes of preschool vision screening in different age groups. In one randomized trial, screening was initiated earlier in one group (age 8 months) compared to the control group (age 37 months), but the earlier group also received periodic screening. One poor-quality retrospective cohort study found no difference between screening at ages 2–4 years versus screening prior to 2 years in risk for at least mild vision impairment.
KQ 2. What is the accuracy and reliability of risk factor assessment for identifying children ages 1–5 years at increased risk for vision impairment?				
No studies	No studies	Not applicable (no studies)	No studies	No study evaluated the accuracy or reliability of risk factor assessment in preschool vision screening, and no study evaluated outcomes of targeted versus universal preschool vision screening.

Table 15. Summary of Evidence

Number of studies, quality score	Limitations	Consistency	Primary care applicability	Summary of findings
KQ 3. What is the accuracy of screening tests for vision impairment in children ages 1–5 years?				
31 diagnostic accuracy studies *Good quality*	Estimates of the diagnostic accuracy of different types of screening tests as well as specific screening tests within the different categories varied substantially across studies, making it difficult to judge comparative diagnostic utility with certainty.	Some inconsistency in diagnostic accuracy estimates	Moderate (mostly specialty or enriched populations with high prevalence)	31 studies evaluated the diagnostic accuracy of various preschool vision screening tests. Four studies evaluated visual acuity tests (LEA symbols and HOTV tests), three evaluated stereoacuity tests (Random dot E stereogram and Stereo Smile II), one evaluated the cover-uncover test, four evaluated some combination of clinical examination screening tests, 12 evaluated autorefractors, and 15 evaluated photoscreeners. Diagnostic accuracy estimates for all of these screening tests suggest utility for identification of children at higher risk for amblyogenic risk factors or specific visual conditions. Differences between studies in the populations evaluated, screening tests evaluated, screening thresholds applied, and target conditions sought make it difficult to reach strong conclusions about how they compare with one another. Studies that evaluated combinations of clinical tests (visual acuity, stereoacuity, and ocular alignment) generally showed superior likelihood ratios compared to studies of individual tests. In the largest study to directly compare the diagnostic accuracy of different individual screening tests (the Vision in Preschoolers [VIP] Study), differences in likelihood ratio estimates between the various tests evaluated were generally small, with overlapping confidence intervals.
KQ 3a. Does accuracy of screening tests for vision impairment in children ages 1–5 years vary in different age groups?				
4 studies *Fair quality*	Limited numbers of studies with some inconsistency.	Some inconsistency	Moderate (mostly specialty or enriched populations with high prevalence)	Evidence on the comparative accuracy of preschool vision tests in different age groups among children ages 1 to 5 years is limited. Four studies found no clear differences in the diagnostic accuracy of various screening tests in preschool-aged children stratified according to age. Testability using common visual acuity tests, stereoacuity tests, photoscreening, and autorefractors generally exceeds 80% to 90% in children ages 3 years and older, with small increases in testability through age 5 years. Four studies found substantially lower testability with the Random dot E stereotest, Lea symbols visual acuity testing, and the SureSight autorefractor in preschool-aged children ages 1–3 years, compared to those ages 3–5 years. One large study of statewide screening with the MTI photoscreener found testability was 94% at age 1 year.

Table 15. Summary of Evidence

Number of studies, quality score	Limitations	Consistency	Primary care applicability	Summary of findings
KQ 4. What are the harms of vision screening in children ages 1–5 years?				
Psychosocial: 1 large cohort study False-positives: 7 studies *Poor quality*	Sparse evidence, except for positive predictive values.	Not applicable (not enough studies addressing the same question to judge consistency)	High	Evidence on harms of preschool vision screening is limited. Although preschool vision screening is associated with potential psychosocial harms related to treatment, one large cohort study found a 50% reduction in odds of being bullied at age 7.5 years among children offered screening compared to those who were not. In populations with a prevalence of visual conditions less than 10%, six of seven studies reported false-positive rates greater than 70%. One large study of a statewide preschool photoscreening program found that 20% of children with positive screens who did not meet criteria for amblyopia or amblyogenic risk factors (false-positives) were prescribed glasses. No study evaluated effects of unnecessary corrective lenses or treatment for amblyopia on long-term vision or functional outcomes.
KQ 5. What is the effectiveness of treatment for vision impairment in children ages 1–5 years?				
Treatment vs. no treatment: 1 RCT Patching treatment vs. no treatment (>85% received eyeglasses): 2 RCTs Comparisons of treatment: 5 RCTs *Fair quality*	All trials evaluated older (ages ≥3 years) preschool-aged children. No trial evaluated effects of treatment compared to no treatment on school performance or other measures of function besides vision outcomes.	Consistent	High	In children with unilateral refractive error, one good-quality trial found that patching plus eyeglasses and eyeglasses alone were more effective than no treatment by an average of about 1 line on the Snellen eye chart after 1 year. Effects were larger (1 to 2 lines of visual acuity improvement) in the subgroup of children with worse baseline visual impairment. One fair- and one good-quality trial found that patching resulted in a statistically significant but small (<1 line on the Snellen eye chart) average improvement in visual acuity in children with amblyopia who were pretreated with eyeglasses if needed after 5 to 12 weeks of follow-up. Five fair- or good-quality trials found no differences in visual acuity improvement in the amblyopic eye between shorter and longer daily patching regimens (2 trials), different atropine regimens (2 trials), or between patching and atropine (1 trial). Three trials found no interaction between age and amblyopia treatment effects among preschoolers ages 3 to 7 years, and one trial found that delaying treatment for 1 year was associated with similar outcomes compared to immediate treatment in children ages 3 to 5 years. One trial found that younger preschoolers (age 3 years) required fewer hours per day of patching to experience optimal improvements in visual acuity compared to older preschool-aged children (ages 4–8 years).

Table 15. Summary of Evidence

Number of studies, quality score	Limitations	Consistency	Primary care applicability	Summary of findings
KQ 6. What are the harms of treatment for children ages 1–5 years at increased risk for vision impairment or vision disorders?				
Nonamblyopic eye visual acuity loss: 5 RCTs *Fair quality* Adverse psychosocial effects: 2 RCTs *Poor quality*	Sparse evidence on adverse psychosocial effects or effects of compliance on clinical outcomes.	Consistent	High	Although one short-term (5 weeks) trial found that patching versus no patching was not associated with an increased risk for visual acuity loss in the nonamblyopic eye, one trial found that patching was associated with an increased risk for ≥2 lines of visual acuity loss compared to atropine (9% vs. 1.4%; p<0.001) and one trial found that atropine plus a plano lens was associated with an increased risk for ≥1 line of visual acuity loss compared to atropine alone (17% vs. 4%; p=0.005). In both trials, visual acuity in the nonamblyopic eye subsequently returned to baseline in almost all children. Two other trials found no difference in risk for visual acuity loss in the nonamblyopic eye in direct comparisons of different patching or atropine regimens. Evidence on adverse psychosocial effects of amblyopia treatments is limited. One fair-quality follow-up study from a randomized trial found that children were more upset by patching plus eyeglasses compared to eyeglasses alone, and one good-quality trial found that patching was associated with worse emotional well-being compared to atropine.

Abbreviations: MTI=Medical Technologies, Inc.; RCT=randomized controlled study; vs=versus.

Appendix A1. Literature Search Strategies

Overall Searches

Database: EBM Reviews – Cochrane Central Register of Controlled Trials

1 amblyopia.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
2 strabismus.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
3 refractive error.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
4 1 or 2 or 3
5 4 and (child$ or pediatri$ or preschool).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
6 limit 5 to yr="2003 - 2008"

Database: EBM Reviews – Cochrane Database of Systematic Reviews

1 amblyopia.mp. [mp=title, short title, abstract, full text, keywords, caption text]
2 strabismus.mp. [mp=title, short title, abstract, full text, keywords, caption text]
3 refractive error.mp. [mp=title, short title, abstract, full text, keywords, caption text]
4 1 or 2 or 3
5 4 and (child$ or pediatri$ or preschool).mp. [mp=title, short title, abstract, full text, keywords, caption text]

Risk Search

Database: Ovid MEDLINE

1 exp Amblyopia/
2 exp Refractive Errors/
3 exp Vision Disorders/
4 or/1-3
5 limit 4 to ("newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)")
6 exp Risk/ or exp Risk Factors/
7 5 and 6
8 limit 7 to yr="1999 - 2008"
9 Case Reports/
10 8 not 9

Screening Search

Database: Ovid MEDLINE

1 vision tests/ or refraction, ocular/ or vision screening/
2 limit 1 to ("newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)")
3 limit 2 to yr="1999 - 2008"
4 limit 3 to humans
5 limit 4 to English language
6 limit 4 to abstracts
7 5 or 6
8 Case Reports/
9 7 not 8
10 English abstract.mp.
11 9 not 10

Treatment Search

Database: Ovid MEDLINE

1 exp Amblyopia/dt, pc, th [Drug Therapy, Prevention & Control, Therapy]
2 exp Refractive Errors/dt, th, pc [Drug Therapy, Therapy, Prevention & Control]
3 1 or 2
4 limit 3 to ("newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)")
5 limit 4 to English language
6 limit 4 to abstracts
7 5 or 6
8 limit 7 to yr="1999 - 2008"

OVERALL

Ages:

Include: Children ages 1–5 years
Exclude: Newborns and children younger than age 1 year, children ages 6 years or older

Diseases:

Include: Amblyopia, amblyogenic risk factors, refractive error
Exclude: Children with severe congenital conditions or developmental delay, retinopathy of prematurity, glaucoma, congenital cataract, pathologic myopia

Language/publication status:

Include: Full-text (i.e., not available only as a conference abstract) journal article published in English

Settings:

Include: Studies performed in primary care, community-based, and school settings
Exclude: Countries with populations not similar to the United States

Study designs:

Exclude: Systematic reviews

KEY QUESTIONS 1 (Screening and Outcomes) and 1a (Variation in Age Groups)

Interventions/diagnostic tests:

Include: Studies of screening tests used or available in primary care settings (e.g., visual acuity tests, tests of stereopsis, tests for strabismus, photoscreeners, autorefractors)
Exclude: Studies of screening tests not used or available in primary care settings (e.g., contrast sensitivity testing, fundoscopic examination, visual acuity testing with cyclopegia) or not intended to detect amblyopia, amblyogenic risk factors, or refractive error (e.g., white reflex screening)

Outcomes:

Include: Improved visual acuity, reduced long-term amblyopia, school performance, function, quality of life

Study designs:

Include: Randomized controlled trials and controlled observational studies

KEY QUESTION 2 (Accuracy/Reliability of Risk Factor Assessment)

Outcomes:

Include: Studies on accuracy or yield of risk factor assessment for targeted screening, or clinical outcomes associated with use of targeted versus universal screening

Appendix A2. Inclusion and Exclusion Criteria for Key Questions

Study designs:

Include: Randomized controlled trials and controlled observational studies

KEY QUESTIONS 3 (Accuracy of Screening Tests) and 3a (Variation in Age Groups)

Diagnostic tests:

Include: Studies of screening tests used or available in primary care settings (e.g., visual acuity tests, tests of stereopsis, tests for strabismus, photoscreeners, autorefractors)
Exclude: Studies of screening tests not used or available in primary care settings (e.g., contrast sensitivity testing, fundoscopic examination, visual acuity testing with cyclopegia) or not intended to detect amblyopia, amblyogenic risk factors, or refractive error (e.g., white reflex screening)

Outcomes:

Include: Sensitivity, specificity, positive and negative predictive values, likelihood ratios, diagnostic odds ratios (or able to calculate such outcomes from data provided)

Study designs:

Include: Studies on diagnostic accuracy of a screening question or diagnostic test compared to a credible reference standard (i.e., cycloplegic refraction)
Exclude: Studies that do not attempt to perform the reference standard in all patients or a random sample

KEY QUESTION 4 (Harms of Screening)

Interventions/diagnostic tests:

Include: Studies of screening tests used or available in primary care settings (e.g., visual acuity tests, tests of stereopsis, tests for strabismus, photoscreeners, autorefractors)
Exclude: Studies of screening tests not used or available in primary care settings (e.g., contrast sensitivity testing, fundoscopic examination, visual acuity testing with cyclopegia) or not intended to detect amblyopia, amblyogenic risk factors, or refractive error (e.g., white reflex screening)

Outcomes:

Include: Harms, including psychological distress, labeling, anxiety, other psychological effects, false-positives, adverse effects on vision in nonimpaired eye

Study designs:

Include: Randomized controlled trials and controlled observational studies

KEY QUESTION 5 (Effectiveness of Treatment)

Interventions/treatments:

Include: Correction of refractive error (eyeglasses), patching, and atropine

Outcomes:

Include: Improved visual acuity, reduced long-term amblyopia, school performance, function, quality of life

Study designs:

Include: Randomized controlled trials

KEY QUESTION 6 (Harms of Treatment)

Interventions/treatments:

Include: Correction of refractive error and penalization of the nonamblyogenic eye (patching, atropine)

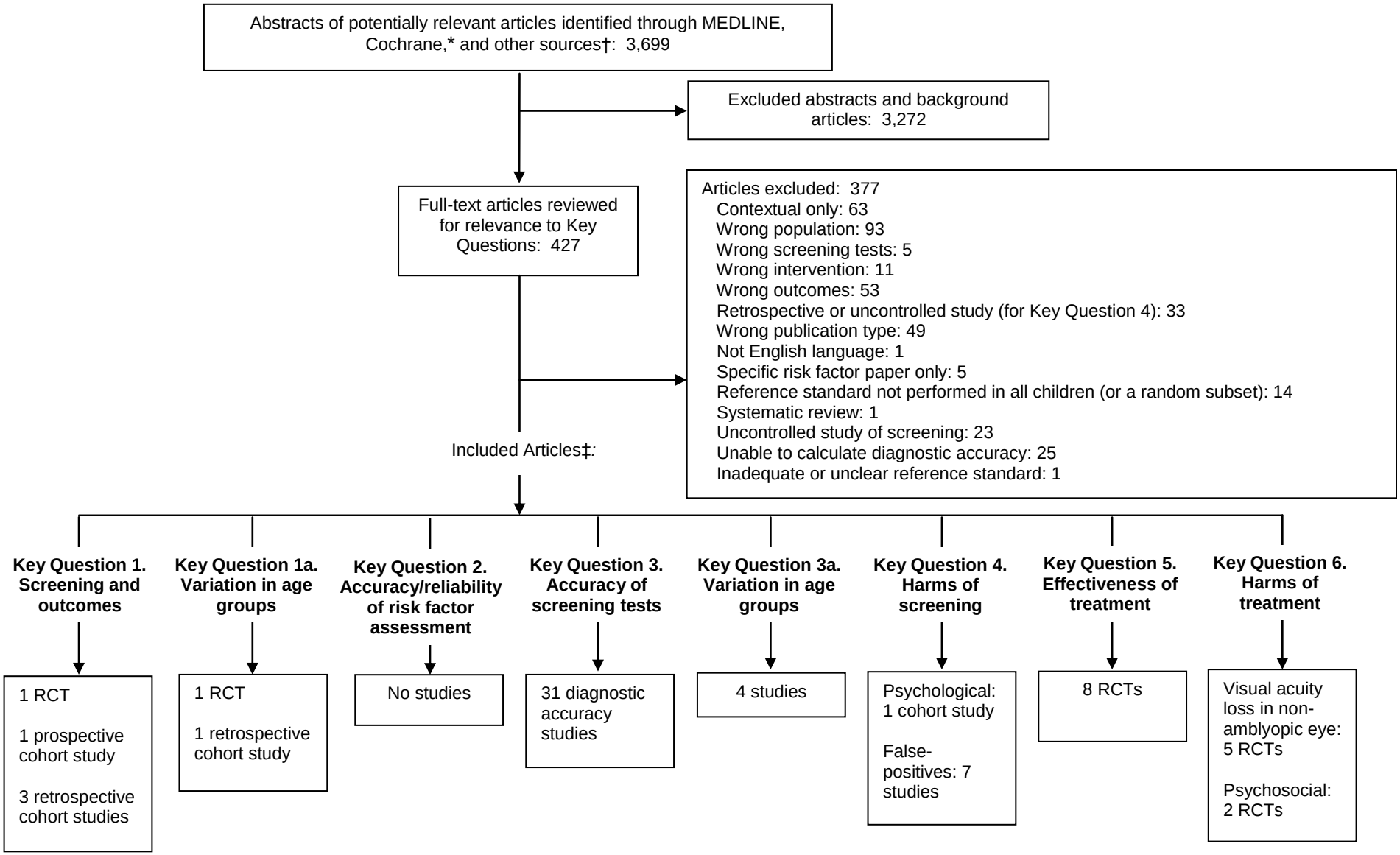
Outcomes:

Include: Harms, including psychological distress, labeling, anxiety, other psychological effects, false-positives, adverse effects on vision in nonimpaired eye

Study designs:

Include: Randomized controlled trials and controlled observational studies

Appendix A3. Literature Flow Diagram



*Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.
†Other sources include reference lists and suggestions by peer reviewers.
‡Some articles are included for more than one Key Question.

Abbreviation: RCT=randomized controlled trial.

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Diagnostic Accuracy Studies

Criteria:

- Screening test relevant, available for primary care, adequately described
- Study uses a credible reference standard, performed regardless of test results
- Reference standard interpreted independently of screening test
- Handles indeterminate results in a reasonable manner
- Spectrum of patients included in study
- Sample size
- Administration of reliable screening test
- Random or consecutive selection of patients[44]
- Screening cutoff predetermined[44]
- All patients undergo the reference standard[44]

Definition of ratings based on above criteria:

Good: Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; assesses reliability of test; has few or handles indeterminate results in a reasonable manner; includes a large number (>100) of broad-spectrum patients with and without disease; study attempts to enroll a random or consecutive sample of patients who meet inclusion criteria[44]; screening cutoffs are prestated.[44]

Fair: Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; includes a moderate sample size (50 to 100 subjects) and a "medium" spectrum of patients (i.e., applicable to most screening settings).

Poor: Has important limitations, such as: uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size of very narrowly selected spectrum of patients.

Randomized Controlled Trials (RCTs) and Cohort Studies

Criteria:

- Initial assembly of comparable groups: RCTs—adequate randomization, including concealment and whether potential confounders were distributed equally among groups; cohort studies—consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, cross-over, adherence, contamination)
- Important differential loss to follow-up or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- Important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies, or intention-to-treat analysis for RCTs; for cluster RCTs, correction for correlation coefficient

Definition of ratings based on above criteria:

Good: Meets all criteria: comparable groups are assembled initially and maintained throughout the study (follow-up at least 80%); reliable and valid measurement instruments are used and applied equally to groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention to confounders in analysis.

Fair: Studies will be graded "fair" if any or all of the following problems occur, without the important limitations noted in the "poor" category below: generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred in follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for.

Poor: Studies will be graded "poor" if any of the following major limitations exists: groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention.

Case Control Studies

Criteria:

- Accurate ascertainment of cases
- Nonbiased selection of cases/controls with exclusion criteria applied equally to both
- Response rate
- Diagnostic testing procedures applied equally to each group
- Measurement of exposure accurate and applied equally to each group
- Appropriate attention to potential confounding variable

Definition of ratings based on criteria above:

Good: Appropriate ascertainment of cases and nonbiased selection of case and control participants; exclusion criteria applied equally to cases and controls; response rate equal to or greater than 80%; diagnostic procedures and measurements accurate and applied equally to cases and controls; and appropriate attention to confounding variables.

Fair: Recent, relevant, without major apparent selection or diagnostic work-up bias but with response rate less than 80% or attention to some but not all important confounding variables.

Poor: Major selection or diagnostic work-up biases, response rates less than 50%, or inattention to confounding variables.

Appendix A6. Expert Reviewers of the Draft Report

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Appendix B1. Screening Evidence Table

Study, year	Purpose of study	Study design	Inclusion criteria	Exclusion criteria	Number of subjects
Eibshitz-Timboni et al, 2000[51]	Evaluate association between screening at ages 1 to 2.5 years and prevalence of amblyopia at age 8 years	Retrospective cohort	Children screened between ages 1 and 2.5 years in one Israeli city, compared to children not screened in another city	NR	# approached and eligible: 988 # enrolled: 1590 (808 had screening at ages 1 to 2.5 years; 782 did not)
Feldman et al, 1980[52]	Evaluate association between screening 6 to 12 months prior to school entry and presence of visual impairment upon school entry	Retrospective cohort	Children screened before entry into kindergarten in one Ontario county compared to children screened at entry in another county; samples matched on SES status according to distribution in the counties	NR	# approached and eligible: NR # enrolled: 1508 (745 had screening 6 to 12 months prior to school entry; 763 did not)
Kirk et al, 2008[54]	Evaluate association between screening prior to age 2 years and presence of visual impairment at least 2 years later	Retrospective cohort	Children screened prior to age 48 months with at least 2-year follow-up data	NR	# approached and eligible: 10620 screened # enrolled: 94 (58 screened prior to age 2 years; 36 not)
Kohler et al, 1978[53]	Evaluate association between screening at age 4 years and risk for visual disorders at age 7 years	Retrospective cohort	Children born between 1963 and 1965 and screened at age 7 years	NR	# approached and eligible: NR # enrolled: 2178 (619 screened at age 4 years; 1519 not)

Study, year	Subject age, sex, diagnosis	Country and setting	Sponsor	Outcomes	Screening intervention
Eibshitz-Timboni et al, 2000[51]	Age: 8 years Sex: NR Diagnosis: 1% vs. 2.6% amblyopia	Israel Preschool screening	Technion-Israel Institute of Technology	Presence of amblyopia at age 8 years	Ophthalmologic exam by an ophthalmologist or orthoptist, including Hirschberg corneal reflex text, monocular fixation and following test, ductions and versions examination, cover-uncover test, alternative cover test, and retinoscopy without cycloplegia
Feldman et al, 1980[52]	Age: mean, 6 years Sex: NR Diagnosis: 13% had at least mild (visual acuity of 20/40 or worse) best-corrected vision impairment	Canada Preschool and school screening	Ontario Ministry of Health	Risk for vision impairment at school entry screening	Illiterate E visual acuity test, administered by school nurse
Kirk et al, 2008[54]	Age: mean, 10.2 years Sex: NR Diagnosis: All referred for an abnormal screening examination	U.S. Preschool screening	Vision screening technology received from a number of vendors (no direct author payments)	Risk for vision impairment at follow-up of at least 2 years in children ages ≥6 years	The Photoscreener, Inc. (previously the MTI Photoscreener), administered by community lay screener

Appendix B1. Screening Evidence Table

Kohler et al, 1978[53]	Age: 7 years Sex: NR Diagnosis: 49% had vision disorders classified as requiring treatment, functional amblyopia, or strabismus	Sweden Preschool and school screening	H. Hierta's and A. Pilt's foundations		Risk for newly diagnosed vision disorder requiring treatment, amblyopia, or strabismus at age 7 years	Linear E-chart, administered by school nurse

Study, year	Results	Follow-up	Loss to follow-up	Compliance to treatment	Adverse events	Quality score
Eibshitz-Timboni et al, 2000[51]	*Screening at 1 to 2.5 years vs. no screening* Amblyopia at age 8 years: 1.0% (8/808) vs. 2.6% (20/782); RR, 0.39 (95% CI, 0.17–0.87) Amblyopia with visual acuity worse than 20/60 at age 8 years: 0.1% (1/808) vs. 1.7% (13/782); RR, 0.07 (95% CI, 0.01–0.57)	5.5–7 years	NR	82% (180 out of 988) of children underwent screening at ages 1 to 2.5 years	NA	Poor
Feldman et al, 1980[52]	*Screening 6 to 12 months prior to school entry vs. no screening* Relative risk for at least mild vision impairment upon school entry: 10% (78/763) vs. 15% (112/745); RR, 0.68 (95% CI, 0.52–0.89)	6–12 months	NR	NA	NA	Poor
Kirk et al, 2008[54]	*Screening at 2 to 4 years vs. screening prior to 2 years* Relative risk for at least mild vision impairment at age >6 years: 17% (10/58) vs. 6% (2/36); RR, 3.10 (95% CI, 0.72–13.4)	2–10 years	NR	NA	NA	Poor
Kohler et al, 1978[53]	*Screening at 4 years vs. no screening* Relative risk for newly diagnosed vision disorder, amblyopia, or strabismus at age 7 years: 5% (29/619) vs. 0.7% (11/1519); RR, 0.15 (95% CI, 0.08–0.31)	3 years	NR	NA	NA	Poor

Study, year	Purpose of study	Study design	Inclusion criteria	Exclusion criteria	Number of subjects
Williams et al, 2002[49] and Williams et al, 2003[50]	Evaluate screening at ages 8, 12, 18, 25, 31, and 37 months vs. screening at age 37 months only on visual outcomes at age 7.5 years	Randomized trial	Children born in southwest England during the last six months of the ALSPAC study period	Children born in the first 15 months of the cohort or whose parents declined to continue with the study or had more than one participating child	# approached and eligible: NR # enrolled: 3490 (2029 had intensive screening; 1490 had one-time screening)

Appendix B1. Screening Evidence Table

Study, year	Subject age, sex, diagnosis	Country and setting	Sponsor	Outcomes	Screening intervention
Williams et al, 2002[49] and Williams et al, 2003[50]	Age: 8 to 37 months (followed to 7.5 years) Sex: 48% female (of those who attended final assessment) Diagnosis: baseline amblyopia or amblyogenic risk factors NR	United Kingdom Hospital eye services clinic	Medical Research Council, R&D Directorate, National Health Service Executive South West, National Eye Research Centre	Prevalence of amblyopia at age 7.5 years; prevalence of residual amblyopia 7.5 years after patching treatment; visual acuity in worse eye after patching treatment Amblyopia A: interocular difference in acuity ≥0.2 logMAR (2 chart lines) Amblyopia B: interocular difference in acuity ≥0.3 logMAR	Screening at 8, 12, 18, 25, 31, and 37 months: cover testing; Cardiff cards at 8 and 12 months, Cardiff and Kays pictures test at 18, 25, and 31 months, Kays picture test and HOTV test at 37 months; noncyclo-plegic autorefraction (performed at all visits, but only used for referral at 37 months) Screening at 37 months: Cover testing, Kays picture test and HOTV test, noncycloplegic autorefraction

Study, year	Results	Follow-up	Loss to follow-up	Compliance to treatment	Adverse events	Quality score
Williams et al, 2002[49] and Williams et al, 2003[50]	*Screening at 8, 12, 18, 25, 31, and 37 months vs. screening at 37 months only* Amblyopia A at age 7.5 years: 1.4% (16/1088) vs. 2.7% (22/826); RR, 0.55 (95% CI, 0.29–1.04) Amblyopia B at age 7.5 years: 0.6% (69/1088) vs. 1.8% (15/876); RR, 0.35 (95% CI, 0.15–0.86) Residual amblyopia A at age 7.5 years among children treated with occlusion: 25% (10/40) vs. 8% (3/40); OR, 1.56 (95% CI, 0.62–3.92) Residual amblyopia B at age 7.5 years among children treated with occlusion: OR, 4.11 (95% CI, 1.04–16.29) Mean visual acuity in worse eye after patching treatment (adjusted for confounding variables): 0.15 (95% CI, 0.083–0.22) vs. 0.26 (95% CI, 0.17–0.35); p<0.001	4.5 years	45% (1561 out of 3490) attended final exam	NA	NA	Fair

Appendix B1. Screening Evidence Table

Study, year	Purpose of study	Study design	Inclusion criteria	Exclusion criteria	Number of subjects
Williams et al, 2003[50]	Evaluate screening at age 37 months vs. screening at school entry (ages 4–5 years) on visual outcomes at age 7.5 years	Prospective cohort study	Children born in southwest England enrolled in the ALSPAC study who had a screening examination at age 7.5 years	Enrolled in a separately reported quasi-randomized trial (Williams et al, 2002[51])	# approached and eligible: 8042 evaluated for inclusion # enrolled: 6081 (1516 were screened at 37 months; 4565 were not)

Study, year	Subject age, sex, diagnosis	Country and setting	Sponsor	Outcomes	Screening intervention
Williams et al, 2003[50]	Age: 7.5 years (screening at 37 months) Sex: 49% female Diagnosis: Baseline amblyopia or amblyogenic risk factors NR	United Kingdom Hospital eye services clinic	Medical Research Council, the Wellcome Trust, UK Department of Health, Department of the Environment, DfEE, National Institutes of Health, "a variety of medical research charities and commercial companies," R&D Directorate, NHS Executive South West	Prevalence of amblyopia at age 7.5 years; prevalence of residual amblyopia 7.5 years after patching treatment; visual acuity in worse eye after patching treatment Amblyopia A: interocular difference in acuity ≥0.2 logMAR (2 chart lines) Amblyopia B: visual acuity in amblyopic eye 0.3 logMAR or worse (6/12 or worse) Amblyopia C: visual acuity in amblyopic eye 0.18 logMAR or worse (6/9 or worse)	Screening at 37 months: Kay pictures or Sheridan Gardiner singles visual acuity test, cover test, and 20 diopter prism or test of stereopsis (or both) No screening at 37 months

Study, year	Results	Follow-up	Loss to follow-up	Compliance to treatment	Adverse events	Quality score
Williams et al, 2003[50]	*Received screening at 37 months vs. no screening* Amblyopia A at 7.5 years: 1.1% (11/1019) vs. 2.0% (100/5062), adjusted OR, 0.63 (95% CI, 0.32–1.23) Amblyopia B at 7.5 years: 0.7% (7/1019) vs. 1.3% (65/5062), adjusted OR, 0.72 (95% CI, 0.32–1.60) Amblyopia C at 7.5 years: 1.9% (19/1019) vs. 3.4% (171/5062), adjusted OR, 0.65 (95% CI, 0.38–1.10) Mean visual acuity in worse eye after patching treatment: 0.14 (95% CI, 0.11–0.18) (n=25) vs. 0.22 (95% CI, 0.20–0.23) (n=166); p<0.0001 *Offered screening at 37 months vs. not offered* Amblyopia A at 7.5 years: 1.4% (21/1516) vs. 2.0% (100/5062); p=0.14 Amblyopia B at 7.5 years: 1.2% (18/1516) vs. 1.3% (65/5062); p=0.59 Amblyopia C at 7.5 years: 2.4% (36/1516) vs. 3.4% (171/5062); p=0.08 Mean visual acuity in worse eye after patching treatment: 0.18 (SD, 0.22) vs. 0.22 (SD, 0.23); p=0.22	4.5 years	NR	NA	NA	Fair

Appendix B1. Screening Evidence Table

Abbreviations: NR=not reported; NA=not assessed; SES=socioeconomic status; #=number; CI=confidence interval; RR=relative risk; OR= odds ratio; SD=standard deviation.

Appendix B2. Screening Quality Ratings

Randomized Controlled Trial

Study, year	Random assignment	Allocation concealed	Groups similar at baseline	Eligibility criteria specified	Blinding of outcome assessors or data analysts	Intention-to-treat analysis	Reporting of attrition, contamination	Differential loss to follow-up or overall high loss to follow-up	Appropriate analysis, including cluster correlation	Funding source	External validity	Quality score
Williams et al, 2002[49] and Williams et al, 2003[50]	No	Yes	Yes	Yes	Can't tell	No	No	Yes	Not applicable	Medical Research Council; R&D Directorate; National Health Service Executive South West; National Eye Research Centre	High	Fair

Appendix B3. Diagnostic Accuracy Evidence Table

Study, year	Screening test	Reference standard	Type of study	Setting	Screener	Age of enrollees	N
Arthur et al, 2009[57]	Plusoptix autorefractor (previously called the Power Refractor)	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Kindergarten Canada	Dental assistant	4-5 years	307
Barry et al, 2001[10]	Retinomax autorefractor	Second orthoptic exam (Lea single symbol test, cover/uncover test, eye motility, and abnormal head posture), followed by ophthalmological exam for abnormal, missing, or inconsistent results	Cross-sectional	Kindergarten Germany	Orthoptist	3 years	404
Barry et al, 2003[11]	Visual inspection, cover-uncover test, eye motility and head posture exam, Lea single symbol visual acuity test	Second orthoptic exam (Lea single symbol test, cover/uncover test, eye motility, and abnormal head posture) using more stringent criteria, followed by ophthalmological exam for abnormal, missing, or inconsistent results	Cohort	Kindergarten Germany	Orthoptist	3 years	1180
Berry et al, 2001[58]	MTI Photoscreener	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic; United States	Not described	Preschool (subgroup)	51

Study, year	Proportion with condition	Definition of a positive screening exam	Definition of a case	Subjects
Arthur et al, 2009[57]	Amblyogenic risk factors: 13% (36/275)	Anisometropia >1 D, astigmatism >1.25 D, myopia >3 D, hyperopia >3.5 D, anisocoria >1 mm, abnormal alignment	Anisometropia >1 D Astigmatism >1.25 D Myopia >3 D Hyperopia >3.5 D Anisocoria >1 mm Strabismus	Age: 4-5 years Female: Not reported
Barry et al, 2001[10]	Amblyopia: 2.5% (10/404)	Acuity outside -1 D to +3 D, cylindric power >1.5 D, or anisometropia >1 D	Any newly administered patching therapy, or any newly administered patching therapy (visual acuity $\leq$0.4 (20/50) in either eye, or difference of visual acuity between eyes $\geq$2 log steps)	Age: 3 years Female: Not reported
Barry et al, 2003[11]	Amblyopia or amblyogenic risk factors: 2.3% (26/1114)	Anatomic abnormality, manifest strabismus or unstable re-fusion upon uncovering, anomalies of eye motility and head posture, visual acuity worse than 10/25 or >1 line difference between eyes and visual acuity in worse eye 10/20 to 10/17	Newly administered spectacle therapy if the corrected visual acuity $\leq$020/50 in either eye, or difference of visual acuity of >2 logarithmic lines (except for myopia); any newly administered patching therapy in presence of risk factors like monolateral strabismus or high refractive error ($\geq$1.5 D, or astigmatism $\geq$3 D)	Age: 3 years Female: Not reported
Berry et al, 2001[58]	Amblyogenic risk factors: 45% (23/51)	Presence of abnormal red reflex, asymmetric corneal light reflection, opacity, or crescent	Myopia $\geq$1.00 D, hyperopia $\geq$2.75 D, astigmatism >1.50 D, anisometropia >1.50 D, >1 mm difference in pupil size, any strabismus, any media opacity, any ptsosis, any fundus abnormality	Age: Not reported Female: Not reported

Appendix B3. Diagnostic Accuracy Evidence Table

Study, year	Proportion unexaminable by screening test	Analysis of screening failures	Proportion who underwent reference standard and included in analyses	Sensitivity (95% CI)	Specificity (95% CI)
Arthur et al, 2009[57]	0.3% (1/307)	Excluded	90% (275/306)	0.83 (0.67-0.93)	0.95 (0.92-0.98)
Barry et al, 2001[10]	Not reported	Not described	95% (404/427)	0.80 (0.44-0.98)	0.58 (0.53-0.62)
Barry et al, 2003[11]	11% (133/1180)	Excluded from analysis	83% (975/1180)	0.91 (0.71-0.99)	0.94 (0.92-0.95)
Berry et al, 2001[58]	Not reported	Not described	100% (51/51)	0.83 (0.61-0.95)	0.68 (0.48-0.84)

Study, year	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality score
Arthur et al, 2009[57]	18 (10-33)	0.17 (0.08-0.36)	0.73 (0.57-0.85)	0.97 (0.94-0.99)	Fair
Barry et al, 2001[10]	1.9 (1.4-2.6)	0.35 (0.1-1.2)	0.05 (0.02-0.09)	0.99 (0.97-1.0)	Fair
Barry et al, 2003[11]	15 (11-19)	0.10 (0.03-0.36)	0.25 (0.16-0.36)	1.0 (0.99-1.0)	Fair
Berry et al, 2001[58]	2.6 (1.4-4.5)	0.26 (0.10-0.65)	0.68 (0.48-0.84)	0.83 (0.61-0.95)	Fair

Study, year	Screening test	Reference standard	Type of study	Setting	Screener	Age of enrollees	N
Bertuzzi et al, 2006[59]	Crowded Lea Symbols visual acuity chart	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic Italy	Not described	38 to 54 months	149
Chang et al, 2007[60]	A: Distance visual acuity (test not reported) B: Near visual acuity (test not reported) C: NTU random dot stereogram	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Public health service stations Taiwan	Nurse	Preschool	5232
Chui et al, 2004[61]	Crowded Lea Symbols visual acuity chart, Frisby stereoacuity test, and external visual inspection	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Not described Canada	Nurse	35 to 58 months	178 (141 completed gold standard evaluation)

Study, year	Proportion with condition	Definition of a positive screening exam	Definition of a case	Subjects
Bertuzzi et al, 2006[59]	Amblyogenic risk factors: 16% (23/143)	Various cutoffs evaluated; results shown for: A: Acuity (decimal score) 0.80 B: Acuity (decimal score) 0.63	Bilateral myopia ≥3 D Unilateral myopia >1.5 D. Bilateral hyperopia ≥3 D Unilateral hyperopia ≥1 D Uni/bilateral astigmatism >1.5 D Lack of media transparency. Any retinal or optic nerve abnormality Strabismus	Age: 38 to 54 months Female: Not reported
Chang et al, 2007[60]	Amblyopia: 2.20% (115/5232)	A1: Distance visual acuity worse than 0.5 at age 3 years, 0.6 at age 4 years, 0.7 at age 5 years, and 0.8 at age 6 years. A2: Distance visual acuity worse than 0.7 at age 3 years, 0.8 at age 4 years, 0.9 at age 5 years, and 1.0 at age 6 years. B: Near visual acuity worse than 0.7 at age 3 years, 0.8 at age 4 years, 0.9 at age 5 years, and 1.0 at age 6 years. C: Stereoacuity worse than 300 sec-arc	Best corrected distance visual acuity worse than 1.0	Age: 76% 3 to 5 years, 24% 6 years Female: 48%

Appendix B3. Diagnostic Accuracy Evidence Table

Chui et al, 2004[61]	Amblyogenic risk factors: 13% (18/141)	Visual acuity 6/12-2 or worse in one or both eyes, difference in visual acuity of two lines or more between eyes, stereoacuity worse than 600" on Frisby or worse than 400" on Titmus, presence of constant or intermittent tropia, monofixation syndrome, myopia >-0.75 D, hyperopia >+3.50 D, astigmatism ≥+1.50 D, anisometropia ≥1.00 D, any other anomaly or inability to complete gold standard exam	Lea Symbols visual acuity of 6/12-2 or worse in one or both eyes Difference in visual acuity of ≥2 lines between eyes Stereoacuity worse than 600" on Frisby or worse than 400" on Titmus Constant or intermittent tropia, monofixation syndrome Myopia ≥-0.75 D Hyperopia ≥3.50 D Astigmatism ≥1.50 D Anisometropia ≥1.00 D Any other abnormality warranting follow-up Unable to complete gold-standard exam	Age: 35 to 58 months Female: Not reported

Study, year	Proportion unexaminable by screening test	Analysis of screening failures	Proportion who underwent reference standard and included in analyses	Sensitivity (95% CI)	Specificity (95% CI)
Bertuzzi et al, 2006[59]	4% (6/149) (7% in those 38-42 months, 3% in those 43-48 months, and 0% in those 49-54 months)	Excluded from analysis	96% (143/149)	A: 0.96 (0.78-1.0) B: 0.78 (0.56-0.92)	A: 0.83 (0.75-0.90) B: 0.93 (0.87-0.97)
Chang et al, 2007[60]	A: 5% (239/5232) B: Not reported C: 3% (174/5232)	Not described	Not described	A1: 0.75* A2: 0.84* B: 0.49* C: 0.20*	A1: 0.91* A2: 0.69* B: 0.92* C: 0.98*
Chui et al, 2004[61]	Not reported	Considered positive screens	79% (141/179)	0.67 (0.41-0.87) <41 months: 0.75 (0.43-0.94) ≥41 months: 0.50 (0.12-0.88)	0.86 (0.79-0.92) <41 months: 0.90 (0.52-0.82) ≥41 months: 0.95 (0.88-0.99)

Study, year	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality score
Bertuzzi et al, 2006[59]	A: 5.7 (3.8-8.6) B: 12 (5.8-24)	A: 0.05 (0.01-0.36) B: 0.23 (0.11-0.51)	A: 0.52 (0.36-0.68) B: 0.69 (0.48-0.86)	A: 0.99 (0.95-1.0) B: 0.96 (0.90-0.99)	Fair
Chang et al, 2007[60]	A1: 8.1* A2: 2.7* B: 6.4* C: 11.4*	A1: 0.28* A2: 0.24* B: 0.55* C: 0.81*	A1: 0.12* A2: 0.04* B: 0.13* C: 0.17*	A1: 1.0* A2: 1.0* B: 0.99* C: 0.99*	Fair
Chui et al, 2004[61]	4.8 (2.8-8.4) <41 months: 2.4 (1.4-4.1) ≥41 months: 10 (3.0-36)	0.39 (0.20-0.75) <41 months: 0.37 (0.13-1.0) >41 months: 0.53 (0.24-1.2)	0.41 (0.24-0.61) <41 months: 0.41 (0.21-0.64) ≥41 months: 0.43 (0.10-0.82)	0.95 (0.89-0.98) <41 months: 0.90 (0.74-0.98) ≥41 months: 0.96 (0.90-0.99)	Fair

Study, year	Screening test	Reference standard	Type of study	Setting	Screener	Age of enrollees	N
Cogen et al, 1992[62]	Visiscreen 100 photoscreener	Comprehensive eye exam with cycloplegic refraction ("when possible")	Cross-sectional	Pediatric ophthalmology clinic. United States	Technician	6 months to 6 years	127
Cooper et al, 1999[63]	A: Fortune Optical VRB-100 photoscreener B: MTI photoscreener	Comprehensive eye exam with cycloplegic refraction	Case-control	Pediatric ophthalmology clinic Australia	Technician	12 to 44 months	105
Dahlmann-Noor et al, 2009a[64]	Plusoptix autorefractor (previously called the Power Refractor)	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United Kingdom	Ophthalmologist, orthoptist, or ophthalmic nurse	4 to 7 years	126

Appendix B3. Diagnostic Accuracy Evidence Table

Dahlmann-Noor et al, 2009b[65]	Plusoptix autorefractor (previously called the Power Refractor)	Orthoptist screening with distance acuity testing, cover test, extraocular movements, prism test, and Lang stereotest; comprehensive eye exam with cycloplegic refraction for abnormal autorefractor or orthoptist screening results	Cross-sectional	Preschool/kindergarten United Kingdom	Ophthalmologist or orthoptist	4 to 7 years	288
Ehrt et al, 2007[66]	Power Refractor autorefractor (now called the Plusoptix)	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic Germany	Orthoptist or pediatric ophthalmologist	0 to 7 years	161
Guo et al, 2000[67]	A: Computer-photorefractor B: Non-cycloplegic retinoscopy	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic China	Not described	9 to 50 months	300

Study, year	Proportion with condition	Definition of a positive screening exam	Definition of a case	Subjects
Cogen et al, 1992[62]	Any visual condition: 12% (13/113) Refractive error: 5% (6/113) Strabismus: 4% (5/113) Refractive error + strabismus: 1% (1/113) Media opacity: 1% (1/113)	Presence of abnormal red reflex, asymmetric corneal light reflection, opacity, or crescent	Hyperopia >4 D Myopia >5 D Astigmatism >2 D Anisometropia >1 D Strabismus Media opacity	Age: 6 months to 6 years Female: Not reported
Cooper et al, 1999[63]	61 cases (amblyopia), 44 controls	Presence of abnormal red reflex, asymmetric corneal light reflection, opacity, or crescent	Hyperopia >3.5 D Anisometropia >1 D Myopia >2 D Astigmatism >2 D Any media opacity or fundus abnormality affecting vision Manifest strabismus	Age: 12 to 44 months Female: Not reported
Dahlmann-Noor et al, 2009a[64]	A: Myopia: 3% (3/108) B: Hypermetropia: 39% (42/108) C: Astigmatism: 12% (13/108) D: Anisometropia: 24% (28/117)	Not reported	Myopia >1 D Hyperopia >3 D Anisometropia >1 D Astigmatism >1.5 D	Age: Mean 5.5 years Female: 49%
Dahlmann-Noor et al, 2009b[65]	Reduced vision in one or both eyes, manifest strabismus, or ptosis: 12% (36/288)	Spherical component <-1.0 D or >+3.0 D, cylinder power >1.5 D, anisometropia of spherical component or of cylinder power >1.0 D	Hyperopia >3.0 D Myopia >1.0 D Strabismus Ptosis	Age: 4 to 7 years (mean 5.6) Female: 52%
Ehrt et al, 2007[66]	Amblyogenic risk factors: 43% (70/161)	Hyperopia ≥3.0 D, myopia ≤2.0 D, astigmatism ≥1.0 D, anisometropia ≥1 D	Hyperopia ≥3 D Myopia ≥2 D Astigmatism ≥1 D Anisometropia ≥1 D	Age: 0 to 7 years (89% 0 to 5 years, 35% 56/161 3 to 5 years)
Guo et al, 2000[67]	Amblyogenic risk factors: 56% (168/300)	Presence of abnormal red reflex, asymmetric corneal light reflection, opacity, or crescent	Myopia ≥1.50 D Hyperopia ≥2.75 D Astigmatism ≥1.75 D Anisometropia v2.00 D Media opacity ≥1.5 mm Strabismus ≥5 °	Age: 9 to 50 months, mean 28 months Female: 49%

Appendix B3. Diagnostic Accuracy Evidence Table

Study, year	Proportion unexaminable by screening test	Analysis of screening failures	Proportion who underwent reference standard and included in analyses	Sensitivity (95% CI)	Specificity (95% CI)
Cogen et al, 1992[62]	11% (14/127)	Excluded from analysis	89% (113/127)	0.85 (0.55-0.98)	0.94 (0.87-0.98)
Cooper et al, 1999[63]	Reader 1: 3% (3/105) Reader 2: 8% (8/105)	Excluded from analysis	Unclear, results reported for 85% to 98% (89 to 103 of 105) patients	A (reader 1): 0.60 (0.47-0.73) A (reader 2): 0.69(0.54-0.80) B (reader 1): 0.56 (0.42 -0.70) B (reader 2): 0.68 (0.54-0.80)	A (reader 1): 0.76 (0.60-0.87) A (reader 2): 0.86 (0.72-0.95) B (reader 1): 0.80 (0.65-0.90) B (reader 2): 0.86 (0.70-0.95)
Dahlmann-Noor et al, 2009a[64]	14% (18/126)	Excluded from analysis	100% (108/108)	A: 0.88 (0.30-1.0) B: 0.20 (0.10-0.35) C: 0.75 (0.36-0.96) D: 0.50 (0.31-0.69)	A: 0.96 (0.89-0.99) B: 0.99 (0.92-1.0) C: 0.93 (0.86-0.97) D: 0.87 (0.77-0.93)
Dahlmann-Noor et al, 2009b[65]	100% (288/288)	Not applicable	100% (288/288)	0.45 (0.29-0.62)	1.0 (0.98-1.0)
Ehrt et al, 2007[66]	43% (70/161)	Considered positive screens	100% (161/161)	0.71 (0.59-0.82)	0.78 (0.68-0.86)
Guo et al, 2000[67]	Not reported	Not described	100% (300/300)	A: 0.95 (0.90-0.98) B: 0.86 (0.80-0.91)	A: 0.90 (0.84-0.95) B: 0.81 (0.73-0.87)

Study, year	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality score
Cogen et al, 1992[62]	14 (6.3-32)	0.16 (0.05-0.59)	0.65 (0.38-0.86)	0.98 (0.93-1.0)	Fair
Cooper et al, 1999[63]	A (reader 1): 2.5 (1.4-4.3) A (reader 2): 4.9 (2.3-10) B (reader 1): 2.8 (1.5-5.2) B (reader 2): 4.9 (2.1-11)	A (reader 1): 0.52 (0.37-0.75) A (reader 2): 0.37 (0.24-0.55) B (reader 1): 0.55 (0.39-0.77) B (reader 2): 0.37 (0.25-0.56)	A (reader 1): 0.76 (0.61-0.87) A (reader 2): 0.86 (0.72-0.95) B (reader 1): 0.78 (0.62-0.89) B (reader 2): 0.88 (0.74-0.96)	A (reader 1): 0.60 (0.46-0.72) A (reader 2): 0.69 (0.54-0.80) B (reader 1): 0.59 (0.46-0.72) B (reader 2): 0.65 (0.50-0.78)	Poor
Dahlmann-Noor et al, 2009a[64]	A: 21 (7.8-55) B: 26 (1.6-450) C: 11 (4.7-24) D: 3.7 (1.9-7.1)	A: 0.13 (0.01-1.7) B: 0.81 (0.70-0.94) C: 0.27 (0.08-0.89) D: 0.58 (0.40-0.84)	A: 0.44 (0.14-0.78) B: 0.94 (0.57-1.0) C: 0.46 (0.20-0.74) D: 0.54 (0.34-0.73)	A: 1.0 (0.95-1.0) B: 0.66 (0.56-0.75) C: 0.98 (0.92-1.0) D: 0.85 (0.75-0.91)	Fair
Dahlmann-Noor et al, 2009b[65]	230 (14-3680)	0.56 (0.42-0.74)	0.97 (0.73-1.0)	0.92 (0.89-0.95)	Fair
Ehrt et al, 2007[66]	3.2 (2.2-4.9)	0.37 (0.25-0.54)	0.71 (0.59-0.82)	0.78 (0.68-0.86)	Poor
Guo et al, 2000[67]	A: 9.6 (5.7-16) B: 4.5 (3.2-6.5)	A: 0.06 (0.03-0.11) B: 0.18 (0.12-0.26)	A: 0.92 (0.87-0.96) B: 0.85 (0.79-0.90)	A: 0.93 (0.87-0.97) B: 0.82 (0.74-0.88)	Fair

Study, year	Screening test	Reference standard	Type of study	Setting	Screener	Age of enrollees	N
Hope et al, 1990[68]	Random dot E stereogram	Comprehensive eye exam with cycloplegic refraction for visual acuity worse than 4/4 with the LMT or worse than 6/6 for Kaye picture cards in children who failed random dot E stereogram, visual acuity screen, or near cover test; otherwise visual acuity screen or near cover test used as reference standard	Cross-sectional	Pediatric ophthalmology clinic New Zealand	Not described	3 to 4 years	176

Appendix B3. Diagnostic Accuracy Evidence Table

Kemper et al, 2005[69]	SureSight autorefractor	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United States	Orthoptist or pediatric ophthalmologist	0 to 5 years	170
Kennedy et al, 1989[70]	A: Otago-type photoscreener (non-commercial) B: Off-axis-type photoscreener (non-commercial)	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic Canada	Technician	6 years or less	236

Study, year	Proportion with condition	Definition of a positive screening exam	Definition of a case	Subjects
Hope et al, 1990[68]	Refractive error or strabismus: 5% (9/168) Refractive error: 5% (9/168) Strabismus: 0.6% (1/168)	Unable to correctly identify the E at least four times in succession at 1 m	Visual acuity 6/12 or worse in either eye Manifest strabismus	Age: 3 to 4 years Female: Not reported
Kemper et al, 2005[69]	Amblyopia: 17% (29/170) Refractive error: 26% (45/170) Strabismus: 18% (30/170) Any visual impairment: 36% (62/170)	SureSight manufacturer referral criteria (hyperopia >2.00 D, myopia >1.00 D, cylinder >1.00 D, or difference >1.00 D)	Anisometropia >1.5 D Hyperopia >3.50 D Myopia >3.00 D Media opacity >1 mm Astigmatism >1.5 D at 90° or 180° or >1.0 D in oblique axis Ptosis ≤1 mm margin reflex distance Visual acuity per age-appropriate standards Manifest strabismus	Age: 0 to 5 years (53% 3 to 5 years) Female: Not reported
Kennedy et al, 1989[70]	Any amblyogenic risk factor: 42% (98/236) Strabismus only: 14% (33/236) Strabismus + refractive error or anisometropia: 18% (42/236) Refractive error or anisometropia: 8% (18/236) Anisocoria or lid tumor: 2% (5/236)	Presence of abnormal red reflex, asymmetric corneal light reflection, opacity, or crescent	Refractive error >3.00 D Astigmatism >2.00 D Corneal or lens opacity Fundus abnormality Strabismus	Age: 0 to 6 years (65% 2 to 6 years) Female: 48%

Study, year	Proportion unexaminable by screening test	Analysis of screening failures	Proportion who underwent reference standard and included in analyses	Sensitivity (95% CI)	Specificity (95% CI)
Hope et al, 1990[68]	5% (8/176)	Excluded from analysis	95% (168/176)	0.89 (0.52-1.0)	0.76 (0.68-0.82)
Kemper et al, 2005[69]	32% (55/170)	Not described, appear to have been excluded	100% (170/170)	Overall: 0.85 (0.69-0.95) <3 years old (n=80): 0.80 (0.44-0.97) 3-5 years old (n=90): 0.88 (0.68-0.97)	Overall: 0.52 (0.40-0.63) <3 years old: 0.41 (0.24-0.61) 3-5 years old: 0.58 (0.42-0.71)
Kennedy et al, 1989[70]	Not reported	Not described	100% (236/236)	Any condition A: 0.94 (0.87-0.98) B: 0.85 (0.76-0.91) Strabismus A: 0.91 (0.81-1.00) B: 0.73 (0.58-0.88) Refractive error A: 0.89 (0.74-1.00) B: 0.89 (0.74-1.00) Strabismus + refractive error A: 0.98 (0.93-1.00) B: 0.91 (0.82-0.99)	Any condition A: 0.94 (0.89-0.98) B: 0.87 (0.80-0.92)

Appendix B3. Diagnostic Accuracy Evidence Table

Study, year	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality score
Hope et al, 1990[68]	3.6 (2.5-5.2)	0.15 (0.02-0.94)	0.17 (0.08-0.31)	0.99 (0.96-1.0)	Fair
Kemper et al, 2005[69]	Overall: 1.8 <3 years old: 1.4 3-5 years old: 2.1	Overall: 0.29 <3 years old: 0.49 3-5 years old: 0.21	Not calculable	Not calculable	Fair
Kennedy et al, 1989[70]	Any condition A: 16 (8.2-32) B: 6.5 (4.2-10)	Any condition A: 0.06 (0.03-0.14) B: 0.18 (0.11-0.28)	Any condition A: 0.92 (0.85-0.96) B: 0.82 (0.73-0.89)	Any condition A: 0.96 (0.91-0.98) B: 0.89 (0.82-0.94)	Fair

Study, year	Screening test	Reference standard	Type of study	Setting	Screener	Age of enrollees	N
Kennedy et al, 1995[71]	A: Otago-type photoscreener (non-commercial) B: Snellen E or Stycar graded balls visual acuity test and Titmus stereotest	Comprehensive eye exam without cycloplegic refraction	Cross-sectional	Kindergarten Canada	Health care aide	Not reported	264
Kennedy et al, 2000[72]	iScreen photoscreener	Comprehensive eye exam with cycloplegic refraction (in patients younger than 4 years old)	Cross-sectional	Pediatric ophthalmology clinic Canada	Technician	45% 6 years or younger	449
Matta et al, 2008[73]	Plusoptix autorefractor (previously called the Photo Refractor)	Comprehensive eye exam with cycloplegic refraction	Cross-sectional or retrospective	Pediatric ophthalmology clinic United States	Not stated	1 to 5 years (data obtained for this subgroup)	80
Miller et al, 1999[74]	A: Crowded Lea Symbols visual acuity chart B: Retinomax K-plus autorefractor	Cycloplegic refraction and retinoscopy	Cross-sectional	Head Start program United States (Native American population)	Head Start staff	3 to 5 years	245

Study, year	Proportion with condition	Definition of a positive screening exam	Definition of a case	Subjects
Kennedy et al, 1995[71]	Any visual condition: 8% (21/264) Strabismus: 1.1% (3/264) Refractive error: 4.2% (11/264) Strabismus and refractive error: 0.8% (2/264) Structural: 0.4% (1/264)	A: Presence of abnormal red reflex, asymmetric corneal light reflection, opacity, or crescent B: Vision less than 20/40 in either eye, or stereoacuity less than 80 seconds of arc	Visual acuity worse than 20/30 Constant tropia present Refractive error >± 3.00 D in either eye with ± 2 D astigmatism Corneal, lens or fundus abnormality	Age: Not reported Female: Not reported
Kennedy et al, 2000[72]	Amblyogenic risk factors: 64% (273/423)	Presence of abnormal red reflex, asymmetric corneal light reflection, opacity, or crescent	Tropia, intermittent or otherwise Refractive error >3.50 D in both eyes Myopia >0.50 D Anisometropia >2.00 D Astigmatism >2.00 D Corneal or lens opacity Fundus abnormality	Age: Median 7 years Female: Not reported
Matta et al, 2008[73]	Amblyogenic risk factors: 50% (40/80)	A: Manufacturer's referral criteria: Anisometropia ≥1.0 D, astigmatism ≥0.75 D, myopia ≥2.0 D for 1-2 years and ≥1.0 D for 3-5 years, hyperopia ≥1.0 D, anisocoria ≥1 mm B: Revised referral criteria: Anisometropia ≥1.25 D, astigmatism ≥1.0 D, myopia ≥2.0 D for 1-2 years and ≥1.0 D for 3-5 years, hyperopia ≥1.25 D, anisocoria ≥1 mm	Anisometropia >1.5 D Any manifest strabismus Hyperopia >3.50 D Myopia >3.00 D Media opacity >1 mm Astigmatism >1.5 D Ptosis <-1 mm margin reflex distance Visual acuity: per age-appropriate std	Age: Range 6 months to 192 months (72% 1-5 years)

Appendix B3. Diagnostic Accuracy Evidence Table

Miller et al, 1999[74]	Significant refractive error: 31% (76/245); all had astigmatism	Age 2-4: Myopia >2.50 D, hyperopia >4.00 D, astigmatism >2.00 D, anisometropia >1.50 D Age 4-7: Myopoia >1.50 D, hyperopia >4.00 D, astigmatism >1.50 D, anisometropia >1.50 D	For ages <2, 2-4, and 4-7 years, respectively. Myopia: >4.00 D, >2.50 D, or >1.50 D. Hyperopia: >5.00 D, >4.00 D, or >1.50 D. Astigmatism: >2.50 D, >2.00 D, or >1.50 D. Anisometropia: >1.50 D (all age groups)	Age: 36% 3 years old, 57% 4 years old, 7% 5 years old. Female: Not reported	

Study, year	Proportion unexaminable by screening test	Analysis of screening failures	Proportion who underwent reference standard and included in analyses	Sensitivity (95% CI)	Specificity (95% CI)
Kennedy et al, 1995[71]	Not reported	Not described	100% (13/13 or 22/22) of positive screens, 20% random sample (241 or 242 of 1232 or 1223) of negative screens	A: 0.46 (0.22-0.72)† B: 0.09 (0.04-0.20)†	A: 1.0 (0.99-1.0)† B: 1.0 (0.99-1.0)†
Kennedy et al, 2000[72]	6% (26/449)	Excluded from analysis	94% (423/449)	0.92 (0.88-0.95) ≤3 years 1.0 4-6 years 0.92	0.89 (0.83-0.94) ≤3 years 0.97 4-6 years 0.95
Matta et al, 2008[73]	Not reported	Not described	100% (109/109)	A: 0.98 (0.85-1.0) B: 0.98 (0.85-1.0)	A: 0.68 (0.51-0.81) B: 0.88 (0.74-0.96)
Miller et al, 1999[74]	4% (10/245)	Not described	100% (245/245)	A: 0.91 (0.82-0.96) B: 0.91 (0.82-0.96)	A: 0.44 (0.37-0.52) B: 0.86 (0.80-0.91)

Study, year	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality score
Kennedy et al, 1995[71]	A: 110 (38-310)† B: 17 (5.5-54)†	A: 0.54 (0.33-0.89)† B: 0.91 (0.84-0.99)†	A: 0.77 (0.60-0.95) B: 0.54 (0.28-0.81)	A: 0.98 (0.91-1.00) B: 0.94 (0.91-0.97)	Fair Age not reported.
Kennedy et al, 2000[72]	8.6 (5.4-14) ≤3 years 33 4-6 years 18	0.09 (0.06-0.13) ≤3 years not calculable 4-6 years 0.08	0.94 (0.90-0.96) ≤3 years 0.97 4-6 years 0.97	0.86 (0.80-0.91)	Fair Most patients ≥7 years; unable to calculate confidence intervals for ≤6 years, though point estimates provided.
Matta et al, 2008[73]	A: 3.0 (1.9-4.7) B: 8.4 (3.7-19)	A: 0.04 (0.01-0.26) B: 0.03 (0.00-0.20)	A: 0.75 (0.61-0.86) B: 0.89 (0.75-0.96)	A: 0.96 (0.80-1.0) B: 0.97 (0.85-1.0)	Fair
Miller et al, 1999[74]	A: 1.6 (1.4-1.9) B: 6.7 (4.5-9.8)	A: 0.21 (0.10-0.43) B: 0.11 (0.05-0.22)	A: 0.42 (0.35-0.50) B: 0.75 (0.65-0.83)	A: 0.92 (0.83-0.96) B: 0.95 (0.901-0.98)	Fair

Study, year	Screening test	Reference standard	Type of study	Setting	N
Miller et al, 2001[75]	A: Crowded Lea Symbols visual acuity chart B: MTI Photoscreener C: Nidek KM-500 Keratometry Screener D: Retinomax K-Plus Autorefractor	Cycloplegic refraction	Cross-sectional	Head Start program United States (Native American population)	379
Molteno et al, 1993[76]	Otago-type photoscreener	History, inspection, cover test, exam of ocular media and fundoscopy through undilated pupils; cycloplegic refraction, dilated fundoscopy, and orthoptic exam with any abnormalities	Cross-sectional	Pediatric ophthalmology clinic New Zealand	1000
Morgan et al, 1987[77]	Visiscreen 100 photoscreener	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United States	63

Appendix B3. Diagnostic Accuracy Evidence Table

Study, year	Proportion with condition	Definition of a positive screening exam	Definition of a case	Subjects
Miller et al, 2001[75]	Astigmatism ≥1.00 D: 48% (182/379)	A: Visual acuity worse than 20/40. B: Presence of abnormal red reflex, asymmetric corneal light reflection, opacity, or crescent. C: Astigmatism ≥2.25 D in either eye D: Astigmatism ≥1.50 D in either eye	Astigmatism ≥2.00 D for children <48 months of age and ≥1.50 D for children ≥48 months of age	Age: 36-63 months Female: 53%
Molteno et al, 1993[76]	Visual acuity worse than 20/20, heterophoria, or anisometropia ≥0.5 D sphere or >1.0 D cylinder: 34% (340/1000)	Yellow or white fundal reflex, deviation of papillary light reflex, inequality of pupil size, any other visible defect	Corrected visual acuity worse than 20/20 in the worse eye Heterophoria, either marked with good binocular vision or moderate with some defect of binocular vision and including intermittent squint with well developed binocular vision Anisometropia ≥0.5 D	Age: Not reported ("infants and children") Female: Not reported
Morgan et al, 1987[77]	Any visual condition: 60% (34/57)	Media opacity Crescent Asymmetric corneal reflex	Hyperopia ≥2.50 D Myopia ≥1 D Anisometropia >1 D Astigmatism >2 D	Age 3 months to 8 years (mean not reported) Female: Not reported

Study, year	Proportion unexaminable by screening test	Analysis of screening failures	Proportion who underwent reference standard and included in analyses	Sensitivity (95% CI)	Specificity (95% CI)
Miller et al, 2001[75]	A: 8% (30/376) B: 6% (24/369)‡ C: 0.3% (1/379) D: 0.5% (2/379)	Unable to complete screening considered positive screen; uninterpretable photographs considered positive screen	100% (379/379)	A: 0.93 (0.87-0.97) B: 0.66 (0.59-0.73)§ C: 0.95 (0.91-0.98) D: 0.93 (0.88-0.96)	A: 0.51 (0.44-0.57) B: 0.71 (0.64-0.78)§ C: 0.77 (0.71-0.83) D: 0.95 (0.91-0.98)
Molteno et al, 1993[76]	Not reported	Not described	100% (1000/1000)	0.89 (0.86-0.91)	0.61 (0.55-0.66)
Morgan et al, 1987[77]	10% (6/63)	Excluded from analysis	90% (57/63)	0.91 (0.76-0.98)	0.74 (0.52-0.90)

Study, year	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality score
Miller et al, 2001[75]	A: 1.9 (1.6-2.2) B: 2.3 (1.8-2.9)§ C: 4.1 (3.2-5.4) D: 18 (10-34)	A: 0.14 (0.08-0.27) B: 0.48 (0.38-0.60)§ C: 0.06 (0.03-0.12) D: 0.08 (0.04-0.13)	A: 0.48 (0.41-0.54) B: 0.68 (0.60-0.75)§ C: 0.79 (0.73-0.84) D: 0.94 (0.90-0.97)	A: 0.93 (0.88-0.97) B: 0.70 (0.63-0.76)§ C: 0.94 (0.90-0.97) D: 0.94 (0.89-0.96)	Fair
Molteno et al, 1993[76]	2.3 (2.0-2.6)	0.18 (0.14-0.22)	0.82 (0.78-0.84)	0.74 (0.69-0.79)	Poor
Morgan et al, 1987[77]	3.5 (1.7-7.0)	0.12 (0.04-0.36)	0.84 (0.68-0.94)	0.85 (0.62-0.97)	Fair

Study, year	Screening test	Reference standard	Type of study	Setting	Screener	Age of enrollees	N
Newman et al, 1999[12]	Sheridan-Gardiner visual acuity; cover-uncover test; ocular movements and convergence; prism test; TNO screening plate; Snellen visual acuity	Comprehensive eye exam	Retrospective cohort	"Community setting" United Kingdom	Orthoptist	3.5 years and at 5-6 years	Cohort of 936 children; data reported on 597
Ottar et al, 1995[78] and Donahue et al, 2002[87]	MTI photoscreener	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Public health and pediatric clinics United States	Orthoptist or pediatrician	6 to 59 months	949

Appendix B3. Diagnostic Accuracy Evidence Table

Study, year	Proportion with condition	Definition of a positive screening exam	Definition of a case	Subjects
Newman et al, 1999[12]	Amblyopia: 2.5% (15/597)	Visual acuity 6/6 or worse Manifest strabismus Decompensating heterophoria Abnormality of ocular movements Abnormal response to 20 base out prism test Negative response to TNO screening plate stereotest Any other ocular abnormality	Best corrected Snellen line acuity of 6/12 or worse in either eye and/or an interocular difference of two Snellen lines or more	Age: 3.5 years at initial screen, 5-6 years at re-screen Female: Not reported
Ottar et al, 1995[78] and Donahue et al, 2002[87]	Amblyogenic risk factors: 20% (192/949); higher-magnitude amblyogenic risk factors: 9% (88/939)	A: Media opacity Strabismus Myopic crescent ≥1 mm Hyperopic crescent ≥2.5 mm Astigmatism ≥2 mm Difference between horizontal and vertical photographs of same eye B: Media opacity >1 mm Strabismus Myopic crescent ≥2.5 mm (4 mm pupillary diameter), ≥4.5 mm (6 mm pupillary diameter), or ≥6.5 mm (8mm pupillary diameter) Hyperopic crescent ≥2.5 mm, ≥4.5 mm, or ≥6.5 mm Astigmatism >1.5 mm, >2.0 mm, or >2.5 mm Anisometropia (no crescent in fellow eye): Crescent ≥2.0 mm, ≥3.5 mm, or ≥4 mm Anisometropia (crescent in fellow eye): Crescent ≥1 mm in fellow eye and 1 mm difference between eyes, ≤2.5 mm in fellow eye and 2 mm difference between eyes or ≥3 mm in fellow eye and 1 mm difference between eyes, or ≤3.5 mm in fellow eye and 2 mm difference between eyes or ≥4 mm crescent in fellow eye and 1 mm difference between eyes	A: Myopia >1.00 D Hyperopia >2.75 D Astigmatism >1.00 D Anisometropia >1.50 D Any media opacity Any strabismus Any abnormality of posterior pole B: Myopia >3.00 D Hyperopia >3.50 D Astigmatism >1.50 D Anisometropia >1.00 D	Age: Mean 29 months Female: Not reported

Study, year	Proportion unexaminable by screening test	Analysis of screening failures	Proportion who underwent reference standard and included in analyses	Sensitivity (95% CI)	Specificity (95% CI)
Newman et al, 1999[12]	Not reported; screening results available for 82% (772/936) of children in cohort	Not described	64% (597/936)	1.0 (0.78-1.0)	0.93 (0.91-0.95)
Ottar et al, 1995[78] and Donahue et al, 2002[87]	2.5% (25/1004) small pupil diameter, poor mydriasis, or poor cooperation	Excluded from analysis	98% (985/1004)	A: 0.82 (0.76-0.87) B: 0.50 (0.39-0.61)	A: 0.91 (0.88-0.93) B: 0.98 (0.97-0.99)

Study, year	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality score
Newman et al, 1999[12]	14 (10-19)	0.03 (0.002-0.51)	0.27 (0.16-0.41)	1.0 (0.99-1.0)	Poor
Ottar et al, 1995[78] and Donahue et al, 2002[87]	A: 8.7 (6.9-11) B: 33 (18-58)	A: 0.20 (0.15-0.27) B: 0.51 (0.41-0.63)	A: 0.69 (0.62-0.75) B: 0.77 (0.64-0.87)‖	A: 0.95 (0.93-0.97) B: 0.95 (0.93-0.96)‖	Fair

Study, year	Screening test	Reference standard	Type of study	Setting	Screener	Age of enrollees	N
Rogers et al, 2008[79]	MTI photoscreener SureSight autorefractor	Comprehensive eye exam with cycloplegic refraction	Randomized controlled trial	Pediatric ophthalmology clinic United States	Trained layperson	1 to 6 years	100

Appendix B3. Diagnostic Accuracy Evidence Table

Shallo-Hoffmann et al, 2004[80]	Crowded Lea Symbol and HOTV visual acuity charts, and Random Dot E stereoacuity test	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United States (mostly attendees at Caribbean-American preschool and children of indigent Spanish-speaking farm workers)	Not described	2 to 6 years	269
Tong et al, 2000[83]	MTI Photoscreener	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United States	Not described	<4 years old	387

Study, year	Proportion with condition	Definition of a positive screening exam	Definition of a case	Subjects
Rogers et al, 2008[79]	Clinically significant amblyopia: 58% (58/100)	A: SureSight manufacturer referral criteria (hyperopia >2.00 D, myopia >1.00 D, cylinder >1.00 D, or difference >1.00 D) B: SureSight 90% VIP specificity referral criteria (≥4.00, ≥1.00, ≥1.50, or ≥3.00) C: SureSight 94% VIP specificity referral criteria (≥4.25, ≥1.00, ≥1.75, ≥3.50) D: SureSight Rowatt et al referral criteria (≥4.25, ≥1.00, ≥2.20, ≥3.00) E: MTI "gold standard" referral criteria (≥3.50, >3.00, >1.50, >1.00)	Anisometropia >1.5 D Hyperopia >3.50 D Myopia >3.00 D Media opacity >1 mm Astigmatism >1.5 D at 90 or 180° or >1.0 D in oblique axis Ptosis ≤1 mm margin reflex distance Visual acuity per age-appropriate standards Manifest strabismus	Age: 1 to 6 years (82 ≤5 years) Female: 55%
Shallo-Hoffmann et al, 2004[80]	Any vision condition: 6% (5/81)	Required to pass threshold for one visual acuity test (Lea Symbol chart: correct identification of 4 of 5 symbols on the passing line for their age; HOTV chart: all or one less than all of the optotypes on the passing live for their age) and stereoacuity test (Random Dot E test: 4 out of 5 correct responses)	2-3 years Isometropia: Myopia ≥3.00 D, hyperopia ≥4.50 D, hyperopia with esotropia >1.50 D, astigmatism >2.00 D Anisometropia: Myopia ≥2.00 D, hyperopia ≥1.50 D, astigmatism ≥2.00 D 3-5 years Isometropia: Myopia ≥3.00 D, hyperopia ≥3.50 D, hyperopia with esotropia >1.00 D, astigmatism >1.50 D Anisometropia: Myopia ≥2.00 D, hyperopia ≥1.00 D, astigmatism ≥1.50 D Any age Intermittent or constant strabismus Two-line difference in monocular visual acuities in association with monocular strabismus or amblyogenic refractive error Any pathology	Age: 2 to 5 years Female: Not reported
Tong et al, 2000[83]	Strabismus: 49% (190/387) Refractive error: 55% (211/387)	Abnormal external exam, media opacity, strabismus, or refractive error (hyperopia ≥2.0 D, myopia ≥2.0 D, anisometropia ≥2.0 D, astigmatism ≥2.0 D)	Not described	Age: 1 to 47 months (44% 2 to 3 years)

Study, year	Proportion unexaminable by screening test	Analysis of screening failures	Proportion who underwent reference standard and included in analyses	Sensitivity (95% CI)	Specificity (95% CI)
Rogers et al, 2008[79]	SureSight: 24% (24/100); 20% (9/45) among children 4 to 6 years old MTI: 4% (4/100); 0% (0/45) among children 4 to 6 years old	Considered positive screens	100% (100/100)	A: 0.97 (0.88-1.0) B: 0.79 (0.67-0.89) C: 0.67 (0.54-0.79) D: 0.62 (0.48-0.74) E: 0.95 (0.86-0.99)	A: 0.38 (0.24-0.54) B: 0.64 (0.48-0.78) C: 0.69 (0.53-0.82) D: 0.74 (0.58-0.86) E: 0.88 (0.74-0.96)

Appendix B3. Diagnostic Accuracy Evidence Table

Shallo-Hoffmann et al, 2004[80]	HOTV: 19% (25/134) Lea: 5% (10/134) Random Dot E: 7% (20/268)	Considered positive screens	100% (21/21) of positive screens, 24% (60/248) of negative screens	0.73 (0.13-0.98)¶	0.94 (0.90-0.96)¶
Tong et al, 2000[83]	19% (74/387)	Classified as positive or negative screens, but unclear how this was done	100% (387/387)	A (all photographs): 0.56 (0.50-0.62) B (informative subset of 313 photographs): 0.65 (0.59-0.71)	A: 0.91 (0.84-0.96) B: 0.87 (0.76-0.94)

Study, year	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality score
Rogers et al, 2008[79]	A: 1.6 (1.2-2.0) B: 2.2 (1.4-3.4) C: 2.2 (1.3-3.5) D: 2.4 (1.4-4.1) E: 8.0 (3.5-18)	A: 0.09 (0.02-0.37) B: 0.32 (0.18-0.56) C: 0.47 (0.31-0.72) D: 0.51 (0.35-0.75) E: 0.06 (0.02-0.18)	A: 0.68 (0.57-0.78) B: 0.75 (0.63-0.86) C: 0.75 (0.61-0.86) D: 0.77 (0.62-0.88) E: 0.92 (0.82-0.97)	A: 0.89 (0.65-0.99) B: 0.69 (0.52-0.83) C: 0.60 (0.45-0.74) D: 0.58 (0.44-0.72) E: 0.92 (0.80-0.98)	Fair
Shallo-Hoffmann et al, 2004[80]	12 (4.7-28)¶	0.28 (0.03-2.4)¶	0.24 (0.08-0.47)	1.00 (0.94-1.0)	Fair 25% sample (every 4th patient) of negative screens underwent reference standard
Tong et al, 2000[83]	A: 6.4 (3.4-12) B: 4.9 (2.6-9.1)	A: 0.48 (0.42-0.56) B: 0.40 (0.33-0.47)	A: 0.95 (0.90-0.98) B: 0.95 (0.90-0.98)	A: 0.43 (0.36-0.50) B: 0.41 (0.33-0.49)	Fair

Study, year	Screening test	Reference standard	Type of study	Setting	Screener	Age of enrollees	N
Vision in Preschoolers Study Group (Phase I), 2004[82]	Crowded Linear Lea Symbols visual acuity test	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Customized Head Start screening vans	Licensed eye professionals	3, 4, or 5 years old	3121

Study, year	Proportion with condition	Definition of a positive screening exam	Definition of a case	Subjects
Vision in Preschoolers Study Group (Phase I), 2004[82]	Any condition (amblyopia, reduced visual acuity, strabismus, or significant refractive error): 29% (755/2588) "Very important to detect and treat early" conditions: 5.4% (135/2588) Amblyopia: 2.9% (75/2588) Reduced visual acuity: 5.1% (132/2588) Strabismus: 1.9% (48/2588) Significant refractive error: 9.3% (240/2588)	A: 10/32 for age 3 years, 10/20 for age 4 or 5 years B: 10/32 for age 3 years, 10/25 for age 4 years, 10/20 for age 5 years#	Amblyopia: ≥2 line interocular difference in visual acuity and unilateral amblyogenic factor; or visual acuity worse than 20/50 (3 years old) or 20/40 (4-5 years old) in one eye, worse than 20/40 (20/30) in contralateral eye, and bilateral amblyogenic factor Reduced visual acuity: Worse than 20/50 (20/40) in one eye, worse than 20/40 (20/30) in contralateral eye, and no bilateral amblyogenic factor; or worse than 20/50 (20/40) in one eye or ≥2-line difference between eyes (except 20/16 and 20/25), and no unilateral amblyogenic factor Strabismus Significant refractive error: Astigmatism >1.50 D, hyperopia >3.25 D, myopia >2.00 D, anisometropia (interocular difference >1.00 D for hyperopia, >3.00 for myopia, >1.50 D for astigmatism, anisometropia (defined) "Very important to detect and treat early" conditions: amblyopia presumed unilateral and worse eye visual acuity ≤20/64 or suspected bilateral; constant strabismus; anisetropia with interocular difference >2 D of hyperopia, >3 D of astigmatism, or >6 D of myopia; hyperopia ≥5.0 D; astigmatism ≥2.5 D; myopia ≥6.0 D	Age: 36 to 71 months (20% 3 years, 53% 4 years, 27% 5 years)

Appendix B3. Diagnostic Accuracy Evidence Table

Study, year	Proportion unexaminable by screening test	Analysis of screening failures	Proportion who underwent reference standard and included in analyses	Sensitivity (95% CI)	Specificity (95% CI)
Vision in Preschoolers Study Group (Phase I), 2004[82]	0.5% (6/1142)	Excluded from analysis	83% (2588/3121) of enrolled patients	Any condition A: 0.61 (0.56-0.66) B: 0.49 (0.44-0.54) "Very important to detect and treat early" conditions A: 0.77 (0.70-0.84) B: 0.65 (0.57-0.73) Amblyopia A: 0.76 (0.66-0.86) B: 0.65 (0.55-0.76) Reduced visual acuity A: 0.58 (0.50-0.67) B: 0.48 (0.39-0.56) Strabismus A: 0.56 (0.42-0.71) B: 0.48 (0.34-0.62) Refractive error A: 0.70 (0.64-0.76) B: 0.40 (0.34-0.46)	Any condition A: 0.90 (0.88-0.92) B: 0.94 (0.92-0.96)

Study, year	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality score
Vision in Preschoolers Study Group (Phase I), 2004[82]	Any condition A: 6.1 (4.8-7.6) B: 8.2 (6.1-11)	Any condition A: 0.43 (0.38-0.50) B: 0.54 (0.49-0.60)	Any condition A: 0.73 (0.67-0.78) B: 0.78 (0.72-0.83)	Any condition A: 0.84 (0.82-0.86) B: 0.81 (0.78-0.83)	Fair

Other screening tests from the Vision in Preschoolers Study Group[82] are abstracted in the following abbreviated table.

Study, year	Screening test	Definition of a positive screening exam	Proportion unexaminable by screening	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)
Vision in Preschoolers Study Group (Phase I), 2004[82]	Crowded Linear HOTV visual acuity test	A: 10/25 for age 3 or 4, 10/20 for age 5 years B: 10/32 for age 3 or 4, 10/25 for age 5 years#	0.6% (7/1141)	Any condition A: 0.54 (0.49-0.59) B: 0.36 (0.31-0.41) "Very important to detect and treat early" conditions A: 0.72 (0.64-0.79) B: 0.48 (0.40-0.57)	Any condition A: 0.89 (0.87-0.91) B: 0.93 (0.91-0.95)	Any condition A: 4.9 (3.9-6.1) B: 5.1 (3.8-6.8)
	Random Dot E stereo-acuity test	A: Nonstereo card for age 3, stereo card at 50 cm for age 4, stereo card at 100 cm for age 5 B: Nonstereo card for age 3 or 4, stereo card at 50 cm for age 5	9.7% (111/1142)	Any condition A: 0.42 (0.37-0.47) B: 0.22 (0.18-0.27) "Very important to detect and treat early" conditions A: 0.59 (0.50-0.67) B: 0.30 (0.22-0.38)	Any condition A: 0.90 (0.88-0.92) B: 0.92 (0.90-0.94)	Any condition A: 4.2 (3.3-5.3) B: 2.7 (2.0-3.7)
	Stereo Smile II stereo-acuity test	A: 240-arc sec card for age 3 or 4, 120-arc sec card for age 5 B: 480-arc sec card for age 3 or 4, 240-arc sec card for age 5	1.9% (27/1446)	Any condition A: 0.44 (0.39-0.49) B: 0.33 (0.28-0.38) "Very important to detect and treat early" conditions A: 0.72 (0.65-0.79) B: 0.57 (0.50-0.64)	Any condition A: 0.91 (0.89-0.93) B: 0.94 (0.92-0.95)	Any condition A: 4.9 (3.9-6.1) B: 5.5 (4.2-7.3)

Appendix B3. Diagnostic Accuracy Evidence Table

Study, year	Screening test	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Vision in Preschoolers Study Group (Phase I), 2004[82]	Crowded Linear HOTV visual acuity test	Any condition A: 0.52 (0.46-0.58) B: 0.69 (0.63-0.74)	Any condition A: 0.68 (0.62-0.74) B: 0.69 (0.62-0.76)	Any condition A: 0.82 (0.79-0.84) B: 0.77 (0.74-0.80)
	Random Dot E stereoacuity test	Any condition A: 0.65 (0.59-0.71) B: 0.85 (0.80-0.90)	Any condition A: 0.64 (0.58-0.71) B: 0.54 (0.46-0.63)	Any condition A: 0.78 (0.75-0.81) B: 0.80 (0.78-0.83)
	Stereo Smile II stereoacuity test	Any condition A: 0.62 (0.56-0.67) B: 0.71 (0.66-0.76)	Any condition A: 0.66 (0.60-0.72) B: 0.68 (0.62-0.75)	Any condition A: 0.73 (0.70-0.76) B: 0.78 (0.76-0.80)

Study, year	Screening test	Definition of a positive screening exam	Proportion unexaminable by screening test	Sensitivity (95% CI)	Specificity (95% CI)
Vision in Preschoolers Study Group (Phase I), 2004[82]	Retinomax autorefractor	A: Hyperopia ≥1.50 D, myopia ≥2.75 D, astigmatism ≥1.50 D, anisometropia ≥2.00 D (year 1) or ≥1.75 D (year 2) B: Hyperopia ≥1.75 D (year 1) or ≥2.50 (year 2), myopia ≥2.75 D, astigmatism ≥2.00 D (year 1) or ≥1.75 D (year 2), anisometropia ≥2.75 D (year 1) or ≥2.50 D (year 2)#	0.5% (6/1142)	Any condition A: 0.64 (0.60-0.67) B: 0.52 (0.48-0.56) "Very important to detect and treat early" conditions A: 0.87 (0.84-0.91 B: 0.81 (0.77-0.85)	Any condition A: 0.90 (0.88-0.91) B: 0.94 (0.93-0.95)
	SureSight autorefractor	A1: Manufacturer criteria: Hyperopia ≥2.00 D, myopia >1.00 D, astigmatism >1.00 D, anisometropia >1.00 D SE A2: VIP Study criteria: Hyperopia ≥4.00 D, myopia ≥1.00 D, astigmatism ≥1.50 D, anisometropia ≥3.00 D B: VIP Study criteria: Hyperopia ≥4.25 D, myopia ≥1.00 D, astigmatism ≥1.75 D, anisometropia ≥3.50 D#	0.3% (8/2577)	Any condition A1: 0.85 (0.81-0.88) A2: 0.63 (0.59-0.65) B: 0.51 (0.46-0.56) "Very important to detect and treat early" conditions A1: 0.96 (0.93-0.99) A2: 0.81 (0.75-0.87) B: 0.75 (0.69-0.81)	Any condition A1: 0.62 (0.59-0.65) A2: 0.90 (0.88-0.92) B: 0.94 (0.92-0.95)
	iScreen photoscreener	As specified by manufacturer or interpreter of iPower photoscreener	0.1% (2/1439)	Any condition 0.37 (0.32-0.42) "Very important to detect and treat early" conditions 0.57 (0.50-0.64)	Any condition 0.94 (0.92-0.95)

Study, year	Screening test	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Vision in Preschoolers Study Group (Phase I), 2004[82]	Retinomax autorefractor	Any condition A: 6.1 (5.2-7.0) B: 8.7 (7.2-10)	Any condition A: 0.41 (0.37-0.45) B: 0.51 (0.47-0.55)	Any condition A: 0.71 (0.68-0.75) B: 0.78 (0.74-0.82)	Any condition A: 0.86 (0.84-0.87) B: 0.83 (0.81-0.84)
	SureSight autorefractor	Any condition A1: 2.2 (2.0-2.4) A2: 6.3 (5.2-7.7) B: 8.6 (6.6-11)	Any condition A1: 0.24 (0.19-0.30) A2: 0.41 (0.36-0.47) B: 0.52 (0.47-0.58)	Any condition A1: 0.47 (0.43--0.51) A2: 0.71 (0.66-0.76) B: 0.77 (0.72-0.82)	Any condition A1: 0.91 (0.89-0.93) A2: 0.86 (0.84-0.88) B: 0.83 (0.81-0.85)
	iScreen photoscreener	Any condition 6.2 (4.7-8.1)	Any condition 0.67 (0.62-0.72)	Any condition 0.71 (0.64-0.77)	Any condition 0.79 (0.77-0.81)

Appendix B3. Diagnostic Accuracy Evidence Table

Study, year	Screening test	Definition of a positive screening exam	Proportion unexaminable by screening test	Sensitivity (95% CI)	Specificity (95% CI)
Vision in Preschoolers Study Group (Phase I), 2004[82]	MTI photoscreener	As specified by manufacturer or interpreter of MTI photoscreener	0% (0/1444)	Any condition 0.37 (0.32-0.42) "Very important to detect and treat early" conditions 0.55 (0.48-0.63)	Any condition 0.94 (0.92-0.95)
	Power Refractor II	A: Hyperopia ≥3.50 D, myopia ≥3.00 D, astigmatism ≥2.00 D, anisometropia ≥1.50 D B: Hyperopia ≥5.00 D, myopia ≥3.75 D, astigmatism ≥2.25 D, anisometropia ≥2.75 D#	1.5% (22/1438)	Any condition A: 0.54 (0.49-0.59) B: 0.36 (0.31-0.41) "Very important to detect and treat early" conditions A: 0.72 (0.65-0.79) B: 0.56 (0.48-0.63)	Any condition A: 0.90 (0.88-0.92) B: 0.94 (0.92-0.95)
	Cover-uncover test	Heterotropia	2.1% (24/1141)	Any condition: 0.16 (0.12-0.20) "Very important to detect and treat early" conditions: 0.24 (0.17-0.31)	Any condition 0.98 (0.97-0.99)

Study, year	Screening test	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Vision in Preschoolers Study Group (Phase I), 2004[82]	MTI photoscreener	Any condition 6.2 (4.7-8.1)	Any condition 0.67 (0.62-0.72)	Any condition 0.71 (0.64-0.77)	Any condition 0.79 (0.77-0.81)
	Power Refractor II	Any condition A: 5.4 (4.4-6.6) B: 6.0 (4.6-7.9)	Any condition A: 0.51 (0.46-0.57) B: 0.68 (0.63-0.73)	Any condition A: 0.68 (0.65-0.73) B: 0.70 (0.64-0.76)	Any condition A: 0.83 (0.81-0.85) B: 0.79 (0.76-0.81)
	Cover-uncover test	Any condition 7.9 (4.6-14)	Any condition 0.86 (0.82-0.90)	Any condition 0.78 (0.66-0.86)	Any condition 0.73 (0.70-0.76)

Study, year	Screening test	Reference standard	Type of study	Setting	Screener	Age of enrollees	N
Weinand et al, 1998[84]	MTI photoscreener	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic	Not described	6 to 48 months	112
Williams et al, 2000[85]	Topcon PR2000 autorefractor	Comprehensive eye exam with cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United Kingdom	Orthoptist	12.5 to 68.7 months	222

Study, year	Proportion with condition	Definition of a positive screening exam	Definition of a case	Subjects
Weinand et al, 1998[84]	Any abnormality: 81% (83/102) Refractive error: 41% (41/102) Strabismus without refractive error: 7% (7/102) Strabismus with refractive error: 21% (21/102) Organic anomaly: 13% (13/102)	Crescent at least half the pupil diameter, asymmetry of light reflexes, or organic abnormalities	Refractive error ≥2 D Manifest strabismus Any organic anomaly	Age: 6 to 48 months Female: Not reported
Williams et al, 2000[85]	A: Spherical error >3.75 D: 19% (36/189) B: Anisometropia >1.25 D: 12% (23/189) C: Astigmatism >1.25 D: 16% (30/189)	Various cutoffs evaluated, cutoffs not pre-defined	Spherical error >3.75 D Anisometropia >1.25 D Astigmatism >1.25 D	Age: Median 48 months Female: Not reported

Appendix B3. Diagnostic Accuracy Evidence Table

Study, year	Proportion unexaminable by screening test	Analysis of screening failures	Proportion who underwent reference standard and included in analyses	Sensitivity (95% CI)	Specificity (95% CI)
Weinand et al, 1998[84]	9% (10/112)	Not described	91% (102/112)	A (Pediatrician interpreter): 0.94 (0.86-0.98) B (Orthoptist interpreter): 0.80 (0.69-0.88) C (Ophthalmologist 1 interpreter): 0.72 (0.61-0.82) D (Ophthalmologist 2 interpreter): 0.86 (0.76-0.92)	A (Pediatrician interpreter): 0.42 (0.20-0.66) B (Orthoptist interpreter): 0.74 (0.49-0.91) C (Ophthalmologist 1 interpreter): 0.74 (0.49-0.91) D (Ophthalmologist 2 interpreter): 0.58 (0.34-0.80)
Williams et al, 2000[85]	15% (33/222)	Excluded from analysis	85% (189/222)	A: 0.50 (0.33-0.67) ** B: 0.74 (0.52-0.90) ** C: 0.47 (0.28-0.66) **	A: 0.95 (0.90-0.98) ** B: 0.95 (0.91-0.98) ** C: 0.96 (0.92-0.99) **

Study, year	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Quality score
Weinand et al, 1998[84]	A (Pediatrician interpreter): 1.6 (1.1-2.4) B (Orthoptist interpreter): 3.0 (1.4-6.5) C (Ophthalmologist 1 interpreter): 2.8 (1.3-5.9) D (Ophthalmologist 2 interpreter): 2.0 (1.2-3.5)	A (Pediatrician interpreter): 0.14 (0.05-0.39) B (Orthoptist interpreter): 0.28 (0.17-0.46) C (Ophthalmologist 1 interpreter): 0.38 (0.24-0.58) D (Ophthalmologist 2 interpreter): 0.25 (0.13-0.48)	A (Pediatrician interpreter): 0.88 (0.79-0.94) B (Orthoptist interpreter): 0.93 (0.84-0.98) C (Ophthalmologist 1 interpreter): 0.92 (0.83-0.98) D (Ophthalmologist 2 interpreter): 0.90 (0.81-0.96)	A (Pediatrician interpreter): 0.62 (0.32-0.86) B (Orthoptist interpreter): 0.45 (0.27-0.64) C (Ophthalmologist 1 interpreter): 0.38 (0.22-0.55) D (Ophthalmologist 2 interpreter): 0.48 (0.27-0.69)	Fair
Williams et al, 2000[85]	A: 9.6 (4.5-20) B: 15 (7.5-32) C: 12 (5.2-30)	A: 0.53 (0.38-0.73) B: 0.27 (0.14-0.55) C: 0.55 (0.40-0.78)	A: 0.69 (0.48-0.86) B: 0.68 (0.46-0.85) C: 0.70 (0.46-0.88)	A: 0.89 (0.83-0.93) B: 0.96 (0.92-0.99) C: 0.91 (0.85-0.94)	Fair

*Raw data not provided, unable to calculate confidence intervals.
†Corrected for verification bias based on a 20% sample of negative screens.
‡Interpretable by at least 6 of 11 reviewers.
§Calculation based on n=379, median sensitivity and specificity.
‖Based on reported sensitivity and specificity, does not match values reported in article.
¶Corrected for verification bias based on a 25% sample of negative screens.
#Determined by cutoff to achieve specificity of 0.95.
**Results based on cutoffs to obtain specificity at least 95%.

Abbreviations: CI=confidence interval; RCT=randomized controlled trial.

Appendix B4. Diagnostic Accuracy Quality Ratings

Study, year	Representative spectrum	Random or consecutive sample	Screening test adequately described	Screening cutoffs predefined	Credible reference standard	Reference standard applied to all screened	Same reference standard applied to all	Reference standard and screening examination interpreted independently	High rate of uninterpretable results or non-compliance with screening test	Analysis includes patients with uninterpretable results or noncompliance	Quality Score
Arthur et al, 2009[57]	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	No	NA	Fair
Barry et al, 2001[10]	Yes	Yes	Yes	Yes	Can't tell	No	No	Can't tell	Can't tell	Can't tell	Fair
Barry et al, 2003[11]	Yes	Yes	Yes	Yes	Can't tell	No	No	Yes	Yes	No	Fair
Berry et al, 2001[58]	No	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Fair
Bertuzzi et al, 2006[59]	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Can't tell	No	No	Fair
Chang et al, 2007[60]	Yes	Can't tell	No	Yes	Yes	Yes	Yes	Can't tell	No	Can't tell	Fair
Chui et al, 2004[61]	Yes	Can't tell	Yes	Yes	Yes	No	Yes	Yes	Can't tell	Yes	Fair
Cogen et al, 1992[62]	Yes	Can't tell	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Fair
Cooper et al, 1999[63]	No	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Poor
Dahlmann-Noor et al, 2009a[64]	No	Can't tell	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Fair
Dahlmann-Noor et al, 2009b[65]	Yes	Can't tell	Yes	Yes	Can't tell	Yes	No	Can't tell	No	NA	Fair
Ehrt et al, 2007[66]	No	Can't tell	Yes	Yes	Can't tell	Can't tell	No	Can't tell	Yes	Yes	Poor
Guo et al, 2000[67]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Fair
Hope et al, 1990[68]	Yes	Can't tell	Yes	Yes	Yes	Yes	No	Can't tell	No	No	Fair
Kemper et al, 2005[69]	No	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Fair
Kennedy et al, 1989[70]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	NA	Fair
Kennedy et al, 1995[71]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't tell	No	NA	Fair
Kennedy et al, 2000[72]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Fair
Matta et al, 2008[73]	No	Can't tell	Yes	Yes	Yes	Yes	Yes	Can't tell	Can't tell	Can't tell	Fair
Miller et al, 1999[74]	No (High prevalence population)	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Fair

Appendix B4. Diagnostic Accuracy Quality Ratings

Study, year	Representative spectrum	Random or consecutive sample	Screening test adequately described	Screening cutoffs predefined	Credible reference standard	Reference standard applied to all screened	Same reference standard applied to all	Reference standard and screening examination interpreted independently	High rate of uninterpretable results or non-compliance with screening test	Analysis includes patients with uninterpretable results or noncompliance	Quality Score
Miller et al, 2001[75]	No (High prevalence population)	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Fair
Molteno et al, 1993[76]	No	Can't tell	Yes	Yes	No	Yes	No	Can't tell	Can't tell	Can't tell	Poor
Morgan et al, 1987[77]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Fair
Newman et al, 1999[12]	Yes	Yes	Yes	Yes	Can't tell	No	Yes	Can't tell	Can't tell	Can't tell	Poor
Ottar et al, 1995[78]	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Can't tell	No	Yes	Fair
Rogers et al, 2008[79]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Shallo-Hoffmann et al, 2004[80]	Yes	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Tong et al, 2000[83]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Fair
VIP, 2004[82]	No	Can't tell	Yes	No	Yes	Yes	Yes	Yes	No	No	Fair
Weinand et al, 1998[84]	No	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Fair
Williams et al, 2000[85]	Yes	Can't tell	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Fair

Appendix B5. Treatment Evidence Table

Author, year	Purpose of study	Study design	Inclusion criteria	Exclusion criteria	# screened/ eligible/enrolled	Subject age, sex, diagnosis	Country & setting	Sponsor
Treatment vs. no treatment								
Clarke et al, 2003[99]	To test efficacy of treatment for unilateral visual loss detected by preschool vision screening and extent to which effectiveness varies with initial severity	RCT	Ages 3-5 years; presence of 6/6 (20/20) vision in one eye and 6/9 (20/30) to 6/36 (2/120) in the other following two screening tests	Ocular abnormalities other than amblyopia	490/254/177	Mean age: 4.0 years Proportion of patients with anisometropia: 127/177 (72%) Baseline visual acuity, amblyopic eye*: 58/177 (33%) 0.18; 52/177 (29%) 0.30; 42/177 (24%) 0.48; 12/177 (7%) 0.60; 13/177 (7%) 0.78; mean 0.36	UK 8 clinical sites	National Health Service Research & Development
Patching treatment vs. no treatment (>85% received eyeglasses)								
Awan et al, 2005[101]	To investigate compliance with patching therapy and dose-effect relationship in occlusion therapy for amblyopia	RCT	Ages ≤8 years; ability to perform a vision test with Glasgow acuity cards; 2 lines of difference in visual acuity on Snellen eye chart	Unable to reliably comply with visual acuity test; >2 lines interocular difference; previous occlusion; no strabismus	77/70/60	Mean age: 4.6 years Mean visual acuity, amblyopic eye: 0.64 Mean visual acuity, sound eye: 0.02 Strabismus: 27/60 (45%) Mixed amblyopia: 25/60 (42%) Proportion of patients requiring refractive correction at baseline: 55/60 (92%)	UK 1 clinical site	National Eye Research Centre; Ulverscroft Foundation

Author, year, title	Measures	Intervention Type	Results	Duration of follow-up	Loss to follow-up	Adverse events	Quality score
Treatment vs. no treatment							
Clarke et al, 2003[99]	BCVA in amblyopic eye after 1 year; follow-up at 1.5 years	Patching + eyeglasses (n=59) vs. eyeglasses only (n=59) vs. no treatment (n=59) for 52 weeks, after which the no-treatment group received eyeglass prescriptions	*Mean BCVA* Patching + eyeglasses: 0.193 (SD, 0.12) Eyeglasses only: 0.216 (SD, 0.17) No treatment: 0.301 (SD, 0.20); p=0.001 *Mean BCVA according to baseline severity* Mild acuity loss at baseline Patching + eyeglasses (n=33): 0.18 (SD, 0.11) Eyeglasses only (n=35): 0.16 (SD, 0.14) No treatment (n=33): 0.22 (SD, 0.17); p=0.11 Moderate acuity loss at baseline Patching + eyeglasses (n=21): 0.22 (SD, 0.13) Eyeglasses only (n=20): 0.31 (SD, 0.17) No treatment (n=22): 0.42 (SD, 0.19) *Mean change in BCVA following 52 weeks of treatment, according to baseline severity* Mild acuity loss at baseline Patching + eyeglasses (n=31): 0.23 (SD, 0.17) Eyeglasses only (n=31): 0.24 (SD, 0.14) No treatment (n=30): 0.19 (SD, 0.17) Moderate acuity loss at baseline Patching + eyeglasses (n=20): 0.52 (SD, 0.19) Eyeglasses only (n=18): 0.35 (SD, 0.20) No treatment (n=21): 0.25 (SD, 0.21)	1.5 years (78 weeks)	At 54 weeks: 13/177 (7.3%) At 78 weeks: 23/177 (13.0%)	*Proportion of patients w/loss of visual acuity in amblyopic eye, according to baseline severity* Mild acuity loss at baseline Patching + eyeglasses: 3/31 (9.7%) Eyeglasses only: 2/31 (6.5%) No treatment: 4/30 (13.3%) Moderate acuity loss at baseline Patching + eyeglasses: 3/20 (15.0%) Eyeglasses only: 2/18 (11.1%) No treatment:5/21 (23.8%)	Good

Appendix B5. Treatment Evidence Table

Author, year, title	Measures	Intervention Type	Results	Duration of follow-up	Loss to follow-up	Adverse events	Quality score
Patching treatment vs. no treatment (>85% received eyeglasses)							
Awan et al, 2005[101]	Primary outcome: mean compliance Other outcomes: improvement in visual acuity following 12 weeks of treatment	3 hours patching/day (n=20) vs. 6 hours patching/day (n=20) vs. no treatment for 12 weeks	*Mean change in visual acuity* 3-hr patching: 0.29 (SD,0.14) 6-hr patching: 0.34 (SD, 0.19) No treatment: 0.24 (SD, 0.17) *Snellen equivalent (lines of improvement)* 3-hr patching: 1.9 (SD, 1.0) 6-hr patching: 2.3 (SD, 1.2) No treatment: 1.6 (SD, 0.12)	12 weeks	8/60 (13%)	*Compliance* 3-hr patching: 57.5% 6-hr patching: 41.2% *Mean time patching* 3-hr patching: 1 hour 43 minutes 6-hr patching: 2 hours 33 minutes	Fair

Author, year, title	Purpose of study	Study design	Inclusion criteria	Exclusion criteria
Pediatric Eye Disease Investigator Group, 2006[100]	To compare 2 hrs of daily patching (combined with 1 hr of concurrent near visual activities) with a control group of eyeglass wear alone (if needed) for treatment of moderate to severe amblyopia in children ages 3 to 7 years	RCT	Age 3-7 years at enrollment; able to have visual acuity determined using the Amblyopia Treatment Study single-surround HOTV protocol; visual acuity in the amblyopic eye of 20/40 to 20/400; visual acuity in the sound eye of 20/40; interocular acuity difference ≥0.3 logMAR (3 lines); completed eyeglass phase or already in optimal correction at least 16 weeks or eyeglasses not needed; amblyopia associated with strabismus, anisometropia, or both meeting the following criteria: ● Strabismic amblyopia: amblyopia in the presence of a heterotropia at distance and/or near fixation, or a history of strabismus surgery (or botulinum), or a documented history of strabismus ● Anisometropic amblyopia: amblyopia in the presence of a 0.50-D difference between eyes in spherical equivalent and/or 1.50-D difference between eyes in astigmatism in any meridian ● Combined mechanism amblyopia: amblyopia in the presence of 1) a heterotropia at distance and/or near fixation, or a history of strabismus surgery (or botulinum), or a documented history of strabismus, and 2) a 1.00-D difference between eyes in spherical equivalent or 1.50-D difference between eyes in astigmatism in any meridian	Amblyopia treatment (other than eyeglasses) in the past month or 1 month of amblyopia treatment in the past 6 months; current vision therapy or orthoptics; ocular cause for reduced visual acuity; myopia more than a spherical equivalent of 6.00 D; prior intraocular or refractive surgery; known skin reactions to patch or bandage adhesives
Occlusion regimens				
Pediatric Eye Disease Investigator Group, 2003[102]	To compare 2 hrs vs. 6 hrs of daily patching as treatment for moderate amblyopia in children ages <7 years	RCT	Age <7 years; able to measure visual acuity using the Amblyopia Treatment Study visual acuity testing protocol with the Electronic Visual Acuity Tester 8; visual acuity in the amblyopic eye 20/40 and 20/80; visual acuity in the sound eye 20/40; intereye acuity difference ≥3 logMAR; if amblyopia was previously treated, no patching treatment within 6 months of enrollment and no other amblyopia treatment of any type (other than eyeglasses) within 1 month of enrollment (any treatment more than 6 month prior to enrollment was acceptable); refractive error corrected for at least 4 weeks; amblyopia associated with strabismus, refractive error/anisometropia, or both meeting the following criteria: ● Strabismic amblyopia: amblyopia 1) in the presence of either a heterotropia at distance and/or near fixation or a history of strabismus surgery (or botulinum), and 2) in the absence of refractive error meeting the criteria below for combined-mechanism amblyopia ● Refractive/anisometropic: amblyopia in the presence of anisometropia ≥0.5 D of spherical equivalent or ≥1.50 D difference in astigmatism in any meridian, with no measurable heterotropia at distance or near fixation, that persisted after at least 4 weeks of eyeglass correction ● Combined-mechanism (strabismic and anisometropic): amblyopia 1) in the presence of either a heterotropia at distance and/or near fixation or a history of strabismus surgery (or botulinum), and 2) anisometropia ≥1.00 D. spherical equivalent or ≥1.50 D difference in astigmatism in any meridian that persisted after at least 4 weeks of eyeglass correction.	Presence of an ocular cause for reduced visual acuity; myopia with a spherical equivalent of -6.00 D; prior intraocular surgery; known skin reaction to patch or bandage adhesive

Appendix B5. Treatment Evidence Table

Author, year, title	# screened/ eligible/ enrolled	Subject age, sex, diagnosis	Country & setting	Sponsor	Measures	Intervention Type
Pediatric Eye Disease Investigator Group, 2006[100]	NR/NR/180	Mean age: 5.3 years Sex: 49.4% female Ethnicity: 81% white; 6% black; 9% Hispanic/ Latino; 1% Asian; 3% mixed race; <1% unknown History: 89% no prior amblyopia treatment; 8% prior patching; <1% prior atropine; 2% prior patching and atropine Diagnosis: 23% strabismus; 47% anisometropia; 30% strabismus and anisometropia Mean visual acuity, amblyopic eye: 0.55 (SD, 0.23); Snellen equivalent, 20/80 Mean visual acuity, sound eye: 0.03 (SD, 0.11); Snellen equivalent, 20/20 Mean refractive error, amblyopic eye: 4.92 (SD, 2.13) Mean refractive error, sound eye: 2.72 (SD, 1.93) Proportion of patients requiring refractive correction at baseline: 155/180 (86%)	U.S. 46 clinical sites	National Eye Institute	BCVA in amblyopic eye after 5 weeks of treatment	16 week run-in for patients who required use of eyeglasses followed by randomization to patching (n=87) or control (n=93) groups for 5 weeks (with continued use of eyeglasses if needed, regardless of randomization group) Patching regimen: 2 continuous hrs per day, with at least 1 hr of near activities (requiring hand-eye coordination) during patching
Occlusion regimens						
Pediatric Eye Disease Investigator Group, 2003[102]	NR/NR/189	Mean age: 5.2 years Sex: 44% female Ethnicity: 85% white; 4% African-American; 6% Hispanic;1% Asian-American; 2% mixed race; 2% other Diagnosis: strabismus 40%; anisometropia 33%; strabismus and anisometropia 27% Mean visual acuity, amblyopic eye: 0.48 (SD, 0.10) Mean visual acuity, sound eye: 0.07 (SD, 0.10) Mean refractive error, amblyopic eye: 4.12 (SD, 3.00) Mean refractive error, sound eye: 3.07 (SD, 2.35)	U.S. 35 ophthalmology clinics	National Eye Institute	Visual acuity in amblyopic eye at 4 months	Sound eye occlusion, 2 hours/day (n=95) vs. 6 hours/day (n=94) for 4 months

Author, year, title	Results	Duration of follow-up	Loss to follow-up	Adverse events	Quality score
Pediatric Eye Disease Investigator Group, 2006[100]	Mean change in visual acuity from baseline: patching 1.1 lines vs. control 0.5 lines (adjusted mean difference, 0.07 [95% CI, 0.02–0.12]; p=0.006) Proportion of patients with ≥2 lines of improvement in visual acuity: patching 38/85 (44.7%) vs. control 18/88 (20.5%)	5 weeks	7/180 (3.9%)	Withdrawals at 5 weeks: patching 2/87 (2.3%) vs. control 5/93 (5.4%) Withdrawals due to AEs not reported Proportion of patients with loss of ≥2 lines of visual acuity, amblyopic eye: patching 4/85 (4.7%) vs. control 8/88 (9.0%) Proportion of patients with loss of ≥2 lines of visual acuity, sound eye: patching 2/85 (2.4%) vs. control 6/88 (6.8%); p=0.28	Good
Occlusion regimens					
Pediatric Eye Disease Investigator Group, 2003[102]	Mean improvement in visual acuity: 2.40 lines (SD, 1.34) 2- hr/day patching vs. 2.40 lines (SD, 1.63) 6-hr/day patching (mean between-group difference, 0.001 [95% CI, -0.040 to 0.042]) Physician-rated adherence, 2-hr/day patching vs. 6-hr/day patching: Excellent: 58% vs. 37% Fair:14% vs. 15% Poor: 3% vs. 11%	4 months	8/189 (4.2%)	Loss of ≥2 lines of visual acuity: 6/89 (7%) 2-hr/day patching vs. 8/92 (9%) 6-hr/day patching; p=0.59 Intermittent exotropia: 1/89 (1%) 2-hr/day patching vs. 1/92 (1%) 6-hr/day patching Small-angle strabismus: 2/89 (2%) 2-hr/day patching vs. 1/92 (1%) 6-hr/day patching	Good

Appendix B5. Treatment Evidence Table

Author, year, title	Purpose of study	Study design	Inclusion criteria	Exclusion criteria	# screened/ eligible/enrolled
Stewart et al, 2007[103]	To compare visual outcome in response to 2 prescribed rates of occlusion: 6 hrs/day vs. 12 hrs/day	RCT (not blinded)	Age 3-8 years with anisometropia and/or strabismus; a significant difference (at least 0.1 logMAR) in intraocular acuity; no occlusion therapy; no ocular pathology or learning difficulties	NR	NR/122/97 (refractive adaptation phase); 80 (occlusion phase)
Atropine regimens					
Pediatric Eye Disease Investigator Group, 2004[104]	To compare daily atropine as prescribed treatments for moderate amblyopia in children ages < 7 years	RCT	Age < 7 years; able to measure visual acuity using ATS visual acuity testing protocol on EVA Tester; visual acuity in amblyopic eye ≤20/40 and ≥20/80; visual acuity in sound eye ≥20/40; intereye acuity difference ≥3 logMAR lines; no amblyopia treatment (other than eyeglasses) in month before enrollment and no more than 1 month of amblyopia treatment in 6 months before enrollment (any treatment more than 6 months before enrollment acceptable); refractive error corrected for at least 4 wks; amblyopia associated with strabismus, refractive error/anisometropia, or both meeting the following criteria: ● Strabismic amblyopia: amblyopia 1) in the presence of either heterotropia at distance and/or near fixation or a history of strabismus surgery (or botulinum) and 2) in the absence of refractive error, meeting criteria below for combined mechanism amblyopia ● Refractive/anisometropic: amblyopia in the presence of anisometropia of ≥0.50 D of SE or ≥1.50-D difference in astigmatism in any meridian, with no measurable heterotropia at distance or near fixation, which persisted after at least 4 wks of eyeglass correction ● Combined mechanism: amblyopia 1) in the presence of either heterotropia at distance and/or near fixation or a history of strabismus surgery (or botulinum) and 2) anisometropia of ≥1.00-D SE or ≥1.50-D difference in astigmatism in any meridian, which persisted after at least 4 wks of eyeglass correction	Ocular cause for reduced visual acuity; myopia >SE -6.00 D in amblyopic eye; myopia > SE -0.50 D in sound eye; bifocal glasses; Down syndrome; prior intraocular surgery; known allergic reaction to atropine	NR/NR/168

Author, year, title	Subject age, sex, diagnosis	Country & setting	Sponsor	Measures	Intervention Type	Results
Stewart et al, 2007[103]	Mean age: 5.6 years Sex: NR Anisometropia: 42/97 (43%) Strabismus: 21/97 (22%) Mixed anisometropia + strabismus: 34/97 (35%) Mean visual acuity, amblyopic eye: 0.55 logMAR (SD, 0.28)	UK; 2 ophthalmology clinics	Fight for Sight UK	Visual acuity following 18 wks of refractive adaptation followed by up to 26 wks of occlusion (mean duration of occlusion, 9 wks); objectively monitored rate of occlusion	18 wks refractive adaptation w/eyeglasses, followed by occlusion 6 hrs/day (n=40) or 12 hrs/day (n=40) until visual acuity no longer improved (up to 26 wks; mean duration, 9 wks)	Mean change in visual acuity: 0.26 (95% CI, 0.21–0.31) 6-hr/day vs. 0.24 (95% CI, 0.19–0.29) 12-hr/day Mean daily occlusion: 4.2 hr/day (95% CI, 3.7–4.7) 6-hr/day group vs. 6.2 hr/day (95% CI, 5.1–7.3) 12-hr/day group; p=0.06
Atropine regimens						
Pediatric Eye Disease Investigator Group, 2004[104]	Mean age: 5.3 years; Sex: 39% female Ethnicity: 79% white; 4% black; 12% Hispanic; 2% Asian; 1% American Indian/Alaskan Native; 1% mixed race; 2% unknown/not reported Strabismus: 33%; Anisometropia: 41% Strabismus + anisometropia: 23% Mean distance visual acuity, amblyopic eye: 0.46 (SD, 0.10) Mean distance visual acuity, sound eye: 0.05 (SD, 0.10) Mean refractive error, amblyopic eye: 4.22 (SD, 2.37) Mean refractive error, sound eye: 3.03 (SD, 2.16)	US; 30 clinical sites	National Eye Institute	Visual acuity in amblyopic eye after 4 months of treatment	1% atropine sulfate daily (n=83) vs. weekends only (n=85) for 4 months	Mean change in visual acuity at 4 months: daily group 2.3 lines vs. weekend group 2.3 lines (mean between-group difference, 0.00 [95% CI, -0.04 to 0.04]) Increase of ≥2 lines of visual acuity at 4 months (completers): daily use 56/77 (72.7%) vs. weekend use 60/83 (72.3%)

Appendix B5. Treatment Evidence Table

Author, year, title	Duration of follow-up	Loss to follow-up	Adverse events	Quality score
Stewart et al, 2007[103]	Up to 26 weeks	0/80 (occlusion group)	NR	Fair
Atropine regimens				
Pediatric Eye Disease Investigator Group, 2004[104]	4 months; 26 daily and 32 weekend patients continued treatment beyond study endpoint (up to 26 weeks; mean 10 additional weeks)	8/168 (4.8%)	Withdrawals due to AEs: 4/83 (4.8%) daily group vs. 0/84 (0%) weekend group Loss of ≥2 lines of visual acuity, sound eye: 2/77 (2.6%) daily use vs. 2/83 (2.4%) weekend use; p=0.99	Good

Author, year, title	Purpose of study	Study design	Inclusion criteria	Exclusion criteria	# screened/ eligible/ enrolled	Subject age, sex, diagnosis
Patching versus atropine						
Pediatric Eye Disease Investigator Group, 2002[105]† *Additional publications*: Pediatric Eye Disease Investigator Group, 2005[109] 2008[110] 2003[113] 2003[126]	To compare patching and atropine as treatments for moderate amblyopia in children age <7 years	RCT	Age <7 years; able to measure visual acuity using ATS visual acuity testing protocol; visual acuity in amblyopic eye 20/40 and 20/100; visual acuity in sound eye 20/40; intereye acuity difference 3 lines; no more than 2 months of amblyopia therapy in past 2 years (any treatment more than 2 years ago acceptable); refractive error corrected for at least 4 wks; amblyopia associated with strabismus, refractive error/anisometropia or both meeting the following criteria: ● Strabismic amblyopia: amblyopia 1) in presence of either heterotropia at distance and/or near fixation or history of strabismus surgery (or botulinum) and 2) in the absence of refractive error, meeting criteria below for combined-mechanism amblyopia. ● Refractive/anisometropic: amblyopia in presence of anisometropia 0.5-D spherical equivalent or 1.50-D difference in astigmatism in any meridian, with no measurable heterotropia at distance or near fixation, that persisted after at least 4 wks of eyeglass correction. ● Combined-mechanism: amblyopia in the presence of 1) either heterotropia at distance and/or near fixation or history of strabismus surgery (or botulinum), and 2) anisometropia 1.00-D spherical equivalent or 1.50-D difference in astigmatism in any meridian that persisted after at least 4 wks of eyeglass correction.	Presence of ocular cause for reduced visual acuity; prior intraocular surgery; myopia (spherical equivalent of ≥ -0.50 D) in either eye; Down syndrome; known skin reaction to patch or bandage adhesive, or allergy to atropine or other cycloplegics	NR/NR/419	Mean age: 5.3 years Sex: 47% female Ethnicity: 83% white; 5% black; 6% Hispanic; 2% Asian; 2% mixed; 2% other 74% no prior amblyopia treatment; 20% prior patching; 2% prior atropine use; 0.2% prior patching + atropine use; 5% other prior treatment (including eyeglass occluder and fogging) Cause of amblyopia: 38% strabismus; 37% amblyopia; 24% strabismus + anisometropia Mean visual acuity, amblyopic eye: 0.53 (SD, 0.13) Mean visual acuity, sound eye: 0.09 (SD, 0.11) Mean intereye acuity difference: 4.4 lines (SD, 1.3) Mean refractive error, amblyopic eye: 4.46 (SD, 2.13) Mean refractive error, sound eye: 2.82 (SD, 2.00)

Appendix B5. Treatment Evidence Table

Author, year, title	Country & setting	Sponsor	Measures	Intervention Type	Results
Patching vs. atropine					
Pediatric Eye Disease Investigator Group, 2002[105] † *Additional publications*: Pediatric Eye Disease Investigator Group, 2005[109] 2008[110] 2003[113] 2003[126]	US; 47 clinical sites	National Eye Institute	Visual acuity after 6 months	Patching (n=215) vs. 1% atropine sulfate (n=204) 1 drop/day for 6 months Patching regimen: min 6 hr/day to max all waking hr/day; treatment maintained with minimal patching as long as reverse amblyopia did not develop; patching time could be reduced (but had to be at least 7 hrs/week) provided that visual acuity in amblyopic eye remained at least 1 or more lines of visual acuity worse than the sound eye; if visual acuity between two eyes became equal, patching was discontinued; if criteria for successful treatment not met by 16 wks, patching time increased to 12 (or more) hrs/day if not previously at that level Atropine regimen: Daily atropine use, with encouraged use of sunglasses and hats when in sunlight; if visual acuity in amblyopic eye met criteria for successful treatment, use of atropine could be reduced to 2x/wk; if visual acuity in both eyes became the same, atropine use could be discontinued; hyperopic patients (sound eye) had na eyeglass lens reduction if amblyopic eye visual acuity was not improved following 16 wks of treatment; if allergic to atropine, patients were switched to 5% topical homatropine	<u>6-month results: mean age 5.2 years</u> Mean change in visual acuity from baseline, amblyopic eye: patching 3.16 lines (SD, 1.6) vs. atropine 2.84 lines (SD, 1.6) Patients with ≥3 lines of improvement from baseline: patching 146/208 (70.1%) vs. atropine 116/194 (59.8%) Patients with treatment success (visual acuity 20/30 or better or ≥3 lines of improvement from baseline): patching 164/208 (78.8%) vs. atropine 144/194 (74.2%) (95% CI, -4.0 to 13.0) <u>2-year results: mean age 7.2 years</u> Follow-up of 363/419 (86.6%) enrolled patients; mean change in visual acuity from baseline, amblyopic eye: patching 3.7 lines (SD, 1.7) vs. atropine 3.6 lines (SD, 1.8) <u>5-year results: mean age 10.3 years</u> 176/419 (42.0%) of patients in original study; mean visual acuity, amblyopic eye: patching 0.19 (SD, 0.14) vs. atropine 0.16 (SD, 0.16) Mean visual acuity, sound eye: -0.03 Mean visual acuity in amblyopic eye: patients <5 years at randomization 0.14 (20/25 or 2 lines; n=68/169) vs. patients >5 years at randomization 0.20 (20/32; n=101/169); p=<0.001 Visual acuity 20/25 or better at age 10 years: patients <5 years at randomization 57% vs. patients >5 years at randomization 38%; p=0.004 Proportion of patients with visual acuity 20/25 or better, amblyopic eye: patching 42% vs. atropine 49%; p=0.74

Author, year, title	Duration of follow-up	Loss to follow-up	Adverse events	Quality score	Comments
Patching vs. atropine					
Pediatric Eye Disease Investigator Group, 2002[105]† *Additional publications*: Pediatric Eye Disease Investigator Group, 2005[109] 2008[110] 2003[113] 2003[126]	Initial trial: 6 months; voluntary follow-up to age 10 years	RCT: 17/419 (4.1%)	<u>6-month results</u> Withdrawals: patching 7/215 (3.3%) vs. atropine 10/204 (4.9%); withdrawals due to AEs not reported Loss of 1 line of visual acuity, sound eye: patching 14/208 (6.7%) vs. atropine 30/194 (15.5%) Loss of ≥2 lines of visual acuity, sound eye: patching 3/208 (1.4%) vs. atropine 17/194 (8.8%); p<0.001 Loss of visual acuity requiring treatment: 0/208 (0%) patching vs. 1/194 (0.5%) atropine Skin irritation in patching group: 98/208 (47%) Any ocular AE in atropine group: 50/194 (26%) Amblyopia Treatment Index Score, mean overall score: patching 2.52 (SD, 0.63) vs. atropine 2.02 (SD, 0.63); p<0.001 Mean Adverse Effects subscale score: patching 2.35 (SD, 0.69) vs. atropine 2.11 (SD, 0.72); p=0.002 Mean Lack of Treatment Compliance subscale score: patching 2.46 (SD, 0.96) vs. atropine 1.99 (SD, 0.83); p<0.001 Mean Social Stigma subscale score: patching 3.09 (SD, 0.81) vs. 1.84 (SD, 0.74; p<0.001 <u>2-year results</u> Mean visual acuity, sound eye: patching -0.02 (SD, 0.08) vs. atropine -0.01 (0.10); p=0.27 Recovery of loss of visual acuity in patients with previous loss of ≥2 lines of visual acuity (to 20/20 or equal): patching 3/3 (100%) vs. atropine 16/17 (94.1%)	Good	At 10 yrs follow-up, patients <5 yrs at randomization had significantly better amblyopic eye visual acuity than patients >5 yrs at randomization regardless of initial cause of amblyopia. Mean visual acuity at 10-yr follow-up: age <5 yrs 0.14 logMAR (68/154) vs. age >5 yrs 0.20 logMAR (101/265); p<0.001

Appendix B5. Treatment Evidence Table

*Converted from Snellen metric measures.
†Included in previous version of report; results of long-term follow-up subsequently published in 2005 and 2008.

Abbreviations: AE=adverse effects; BCVA=best corrected visual acuity; CI=confidence interval, D=diopter; NR=not reported, RCT=randomized controlled study, SD=standard deviation; SE= spherical equivalent.

Appendix B6. Treatment Quality Ratings

Study, year	Random assignment	Allocation concealed	Groups similar at baseline	Eligibility criteria specified	Blinding	Blinding outcome assessors or data analysts	Intention-to-treat analysis	Reporting of attrition, contamination	Differential loss to follow-up, overall high loss to follow-up, or incomplete follow-up	Funding source	External validity	Quality score
Awan et al, 2005[101]	Can't tell	Yes	Yes	Yes	Patients: No Providers: No	No	Yes	Yes	No	National Eye Research Center; Ulverscroft Foundation	Mean age: 4.6 years Mean visual acuity amblyopic eye: 0.64; mean visual acuity sound eye: 0.02 Strabismus: 27/60 (45%) Mixed amblyopia: 25/60 (42%)	Fair
Clarke et al, 2003[99]	Yes	Yes	Yes	Yes	Patients: No Providers: No	Yes	Yes	Yes	No	National Health Service Research and Development	Mean age: 4.0 years Proportion w/anisometropia: 127/177 (72%) Baseline visual acuity amblyopic eye*: 58/177 (33%) 0.18; 52/177 (29%) 0.30; 42/177 (24%) 0.48; 12/177 (7%) 0.60; 13/177 (7%) 0.78	Good
Pediatric Eye Disease Invest-igator Group, 2006[100]	Yes	Can't tell	Yes	Yes	Patients: No Providers: No	Yes	Yes	Yes	No	National Eye Institute	Mean age 5.3 years 49.4% female; 81% white; 6% black; 9% Hispanic/Latino; 1% Asian; 3% mixed race; <1% other 89% no prior amblyopia treatment; 8% prior patching; <1% prior atropine; 2% prior patching + atropine 23% strabismus; 47% anisometropia; 30% strabismus + anisometropia Mean visual acuity amblyopic eye: 0.55 (SD 0.23); Snellen equivalent 20/80; mean visual acuity sound eye: 0.03 (SD 0.11); Snellen equivalent 20/20; mean refractive error amblyopic eye: 4.92 (SD 2.13); mean refractive error sound eye: 2.72 (SD 1.93)	Good
Pediatric Eye Disease Investi-gator Group, 2003[102]	Yes	Can't tell	Yes	Yes	Patients: No Providers: No	Yes	Yes	Yes	No	National Eye Institute	Mean age: 5.2 years 44% female; 85% white; 4% black; 6% Hispanic;1% Asian; 2% mixed race; 2% other Strabismus 40%; anisometropia 33%; Strabismus + anisometropia 27% Mean visual acuity sound eye: 0.07 (SD 0.10); mean visual acuity amblyopic eye: 0.48 (SD 0.10); mean refractive error sound eye: 3.07 (SD 2.35); mean refractive error amblyopic eye: 4.12 (SD 3.00)	Good

Appendix B6. Treatment Quality Ratings

Study, year	Random assignment	Allocation concealed	Groups similar at baseline	Eligibility criteria specified	Blinding	Blinding outcome assessors or data analysts	Intention-to-treat analysis	Reporting of attrition, contamination	Differential loss to follow-up, overall high loss to follow-up, or incomplete follow-up	Funding source	External validity	Quality score
Stewart et al, 2007[103]	Yes	Can't tell	Yes	Yes	Patients: No Providers: No	Can't tell	Yes	Yes	No	Fight for Sight UK	Mean age: 5.6 years Sex: NR Anisometropia 42/97 (43%); strabismus 21/97 (22%); mixed anisometropia + strabismus 34/97 (35%)	Fair
Pediatric Eye Disease Investi-gator Group, 2004[104]	Yes	Can't tell	Yes	Yes	Patients: No Providers: No	Yes	Yes	Yes	No	National Eye Institute	Mean age: 5.3 years 39% female; 79% white; 4% black; 12% Hispanic; 2% Asian; 1% American Indian/Alaskan Native; 1% mixed race; 2% unknown Strabismus 33%; anisometropia 41%; strabismus + anisometropia 23% Mean distance visual acuity amblyopic eye 0.46 (SD 0.10); mean distance visual acuity sound eye 0.05 (SD 0.10); mean refractive error amblyopic eye 4.22 (SD 2.37); mean refractive error sound eye 3.03 (SD 2.16)	Good
Pediatric Eye Disease Investi-gator Group, 2002[105]	Yes	Can't tell	Yes	Yes	Patients: No Providers: No	Yes	Yes	Yes	No	National Eye Institute	Mean age: 5.3 years 47% female; 83% white; 5% black; 6% Hispanic; 2% Asian; 2% mixed; 2% other 74% no prior amblyopia treatment; 20% prior patching; 2% prior atropine; 0.2% prior patching + atropine; 5% other prior treatment (eyeglass occluder and fogging) Cause of amblyopia: 38% strabismus; 37% amblyopia; 24% strabismus + anisometropia Mean visual acuity amblyopic eye: 0.53 (SD 0.13); mean visual acuity sound eye: 0.09 (SD 0.11); mean intereye acuity difference (lines): 4.4 (SD 1.3); mean refractive error amblyopic eye: 4.46 (SD 2.13); mean refractive error sound eye: 2.82 (SD 2.00)	Good

*Converted from Snellen metric measures.