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Vision Screening in Children Ages 6 Months to 5 Years: A Systematic Review for the U.S. Preventive Services Task Force

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Prepared by:
RTI International–University of North Carolina Evidence-based Practice Center
Research Triangle Park, NC

Investigators:
Daniel E. Jonas, MD, MPH
Halle R. Amick, MSPH
Ina F. Wallace, PhD
Cynthia Feltner, MD, MPH
Emily B. Vander Schaaf, MD, MPH
Callie L. Brown, MD, MPH
Claire Baker

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Structured Abstract

Purpose: To systematically review the evidence on screening for and treatment of amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years.

Data Sources: PubMed/MEDLINE, the Cochrane Library, Cumulative Index of Nursing and Allied Health Literature, and trial registries through June 2016; reference lists of included articles and existing systematic reviews; outside experts; reviewers; and surveillance of the literature through June 7, 2017.

Study Selection: Two investigators independently selected English-language studies using a priori criteria. Eligible studies included randomized, controlled trials (RCTs) or prospective cohort studies with a concurrent control group that evaluated screening in children without known impaired visual acuity or obvious symptoms of impaired visual acuity; studies evaluating accuracy of screening tests compared with cycloplegic refraction or a comprehensive eye examination; RCTs of treatment compared with inactive controls; and controlled cohort or case-control studies assessing harms of screening or treatment.

Data Extraction: One investigator extracted data and a second checked accuracy. Two reviewers independently rated quality for all included studies using predefined criteria.

Data Synthesis: We included 40 studies; 34 evaluated test accuracy. No RCTs compared screening with no screening. One prospective cohort study (N=6,081) from the population-based Avon Longitudinal Study of Parents and Children (ALSPAC) compared screening at age 37 months with no screening among children who were routinely screened at ages 4 to 5 years (in both groups) and found no statistically significant difference for amblyopia prevalence at age 7.5 years for three different definitions of amblyopia (adjusted odds ratio, 0.63 [95% confidence interval (CI), 0.32 to 1.23] for interocular difference in acuity ≥0.2 logarithm of the minimum angle of resolution [logMAR], 0.72 [95% CI, 0.32 to 1.60] for interocular difference in acuity ≥0.3 logMAR, and 0.65 [95% CI, 0.38 to 1.10] for visual acuity in amblyopic eye 0.18 logMAR or worse). One RCT (N=3,490) from ALSPAC found about a 1 percent lower prevalence of amblyopia at age 7.5 years for intensive screening (at ages 8, 12, 18, 25, 31, and 37 months) compared with screening at age 37 months, although the difference was only statistically significant for one of two definitions of amblyopia (interocular difference in acuity ≥0.2 logMAR, 1.5% vs. 2.7%; relative risk, 0.55 [95% CI, 0.29 to 1.04]; interocular difference in acuity ≥0.3 logMAR, 0.6% vs. 1.8%; relative risk, 0.35 [95% CI, 0.15 to 0.86]).

Estimates for screening tests suggest utility for identifying children at higher risk for amblyopia risk factors or other visual conditions. Positive likelihood ratios were in the moderate range (5 to 10) for most studies, indicating that an abnormal result moderately increased the likelihood of target conditions. Most studies that evaluated combinations of clinical tests found high (>10) positive likelihood ratios. The largest study to directly compare multiple tests found similar accuracy across screening tests. Low testability rates may limit tests in children younger than age 3 years, especially clinical tests (e.g., visual and stereoacuity tests), but some data suggest that photoscreeners have high testability rates for younger children.

RCTs of treatment show that: 1) patching improves visual acuity of the amblyopic eye by an average of less than 1 line on the Snellen chart after 5 to 12 weeks among children with amblyopia risk factors pretreated with glasses, and more children treated with patching than with no patching experienced improvement of 2 or more lines (45% vs. 21%; p=0.003); 2) patching plus glasses improves visual acuity by about 1 line after 1 year (0.11 logMAR [95% CI, 0.05 to 0.17]) among children with amblyopia risk factors not pretreated with glasses; 3) glasses alone improve visual acuity by less than 1 line after 1 year (0.08 logMAR [95% CI, 0.02 to 0.15]) among children with amblyopia risk factors; and 4) the magnitude of improvement for patching plus glasses or glasses alone was greater among children with worse baseline visual acuity.

Few studies addressed potential adverse effects of screening. One prospective cohort study (N=4,473) from the ALSPAC project assessed school-age bullying by age 8 years among the subgroup of patched children; those screened in preschool had lower rates of bullying compared with those not screened in preschool. Screening tests are associated with high false-positive rates in low-prevalence populations; studies with a lower prevalence (<10%) of vision abnormalities showed much higher rates of false-positive results (usually >75%), while studies with a high prevalence had lower false-positive rates (usually <35%).

Limitations: No included studies evaluated school performance, functioning, or quality of life. The main limitation of the ALSPAC studies was high overall attrition (approximately 50%). Common methodological limitations of test accuracy studies included high (or not reported) rates of uninterpretable results or noncompliance with tests, unclear handling of uninterpretable results or noncompliance in analyses, lack of a representative spectrum of participants, and lack of a random or consecutive sample. Studies of test accuracy were most commonly conducted in Head Start programs, schools, the community, or ophthalmology clinics; primary care clinics were rarely involved. Applicability of findings to primary care settings is therefore less certain.

Conclusions: Studies that directly evaluated the effectiveness of screening were limited (because of study designs, attrition, imprecision, and quality) and do not establish whether vision screening in preschool-age children is better than no screening. Indirect evidence supports 1) the utility of multiple screening tests for identifying preschool-age children at higher risk for amblyopia risk factors or other visual conditions (most studies found that abnormal results moderately increased the likelihood of target conditions), and 2) the effectiveness of some treatments for improving visual acuity outcomes, although improvements were small, on average. Evidence on adverse effects of screening indicated a reduction in bullying and high false-positive rates in low-prevalence populations.

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Chapter 1. Introduction

Scope and Purpose

This report was conducted for the U.S. Preventive Services Task Force (USPSTF) to update its 2011 recommendation on the topic of screening for amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years. The purpose of this report is to systematically evaluate the current evidence on vision screening and treatment for populations and settings relevant to primary care in the United States. In this report, we summarize the evidence on the benefits and harms of vision screening and treatment and the characteristics of screening tests.

Condition Definition

The most common causes of vision problems in children are amblyopia and its associated risk factors (**Table 1**), nonamblyopic strabismus, and nonamblyopic refractive error.[1-4] Amblyopia is a neurodevelopmental disorder that arises from abnormal processing of visual images that leads to a functional reduction of visual acuity.[5] Amblyopia is usually unilateral but can occur in both eyes at once. It results from conditions that interfere with normal binocular vision. Specific conditions associated with amblyopia are anisometropia (a difference in refractive power between the eyes, in which one foveal image is more blurred than the other), strabismus (ocular misalignment, in which each eye does not have the same image on the fovea), and deprivation (caused by the blockage of the visual pathway, often due to cataracts, ptosis, or refractive error due to myopia, hyperopia, and/or astigmatism).[6-10] **Appendix A** provides definitions for these conditions and other relevant terms used in this report. Strabismic and anisometropic amblyopia can coexist. Strabismus can also inhibit development of normal binocular vision in the absence of amblyopia.[11]

Refractive errors in children are due to myopia (nearsighted), hyperopia (farsighted), and/or astigmatism. For young children, mild hyperopia is normal; normal adult visual acuity (20/20) is typically achieved between the ages of 5 to 7 years.[12, 13]

Prevalence and Burden

Recent population-based studies of U.S. children younger than age 6 years estimate that the prevalence of amblyopia, strabismus, and anisometropia ranges from 1 to 6 percent.[4, 14-16] Amblyopia risk factors were identified in 5 percent of preschool-age children from 16 photoscreening programs (>400,000 total participants) in the United States.[17] In children younger than age 3 years, strabismus appears to be the most common cause of amblyopia; in children ages 3 to 6 years, strabismus and anisometropia contribute equally.[18] About 4 percent of children younger than age 6 years have myopia, up to 20 percent have hyperopia, and 5 to 10 percent have astigmatism.[19-21]

Vision abnormalities in young children could diminish school performance, function, and quality

of life, although the long-term functional effects of vision abnormalities are somewhat uncertain. A study of a 1958 British birth cohort that compared adults with normal vision (N=8,432) and adults with amblyopia (N=429) found no differences in educational, health, or social outcomes at ages in the 30s and 40s. Nevertheless, amblyopia is perhaps the most common cause of monocular visual loss in adults.[22] The lifetime risk of vision loss for persons with amblyopia has been estimated at around 1.2 percent or higher; amblyopia may significantly increase the risk of severe visual impairment or blindness in the event of vision loss in the nonamblyopic eye.[23, 24] Strabismus can result in loss of stereopsis (i.e., depth perception) and psychosocial consequences (e.g., from bullying or from diminished self-esteem).

Risk Factors and Natural History

Risk factors for amblyopia, strabismus, and refractive error include positive family history in a first-degree relative, prematurity or low birth weight, low levels of caregiver education, and maternal substance abuse and/or smoking during pregnancy.[25-30] Younger age is associated with higher rates of astigmatism[28] and myopia (within the population ages 6 months to 6 years).[29, 31] Additional risk factors for amblyopia include deprivation of visual stimuli in infancy and early childhood and lack of health insurance.[25, 32, 33]

It is highly unlikely that untreated amblyopia will resolve spontaneously.[32, 34] Although amblyopia is treatable, efficacy decreases as children age, and visual loss can become irreversible.[35-37] Visual impairments left untreated can lead to both short- and long-term physical and psychological problems, including physical and verbal bullying,[38, 39] depression and anxiety,[39] poor visuomotor skills,[40, 41] low self-esteem,[42] problems at school and work,[39, 43] and accidents and injuries.[44]

Rationale for Screening/Screening Strategies

There are generally two rationales for screening for amblyopia, its risk factors, and refractive error in preschool-age children. First, preschool vision screening allows detection and treatment of vision abnormalities during a critical developmental stage. Amblyopia is thought to be most effectively treated early because the visual pathways will not develop appropriately otherwise, and vision loss may become permanent. Normal vision development requires that images seen by both eyes are equally clear and aligned. Amblyopia is caused by risk factors present in early childhood.[11] It usually does not occur when amblyopia risk factors develop later (i.e., school age, after age 6 years) because the visual system has already developed.[45] Second, preschool vision screening allows detection and treatment of vision abnormalities before school entry, allowing for optimal school performance and development and potentially minimizing psychosocial consequences.

A variety of screening tools are available to evaluate ocular alignment, visual acuity, and stereoacuity (**Table 2**). Ocular alignment testing (i.e., strabismus testing) evaluates for alignment-related amblyopia etiologies. Visual acuity testing screens for refractive error and visual deficits associated with amblyopia, such as cataracts. Tests of stereoacuity assess depth

perception, the absence of which may suggest underlying amblyopia. These screening tools can be used in isolation or together to evaluate children's vision.

Photoscreening devices use optical images (photographs) of the eye's red reflex to identify risk factors in both eyes simultaneously. Most photoscreeners can estimate refractive error, media opacity, and ocular alignment.[46] Interpretation of the image is subjective and based on pre-established pass/fail criteria; older devices require a trained interpreter, but newer machines often include computerized interpretation or relay information to a central reading system. Image acquisition takes a few seconds and captures both eyes at once, making them especially useful for preverbal or developmentally delayed children and children who are unable to tolerate longer examinations.[46]

Autorefractors are computerized instruments that provide objective refractive status by measuring how light changes as it enters and reflects off the back of the eye. For patients with reduced visual acuity, it determines the lens power required to accurately focus light on the retina. Advantages of autorefractors include ease and time of use, ready availability, and patient tolerance. Handheld autorefractors require only a few seconds of a child's attention, potentially increasing testability rates versus traditional tabletop models, especially among young children.[47] A disadvantage of autorefraction is that it typically measures one eye at a time, limiting its ability to detect strabismus without refractive error.[46]

Treatment Approaches

A mainstay of treatment is correction of refractive error, either with eyeglasses or contact lenses. If anisometropic amblyopia persists after a trial of refractive correction, occlusion therapy is the preferred management.[37, 48, 49] Occlusion therapy consists of covering the nonamblyogenic eye with a traditional eye patch, atropine 1 percent eye drops to blur near vision, or optical penalization (placing a Bangerter occlusion foil over eyeglass lens).[50, 51] Poor visual acuity not related to amblyopia is often due to refractive error, which includes myopia, hyperopia, and/or astigmatism. Refractive error can be easily and immediately treated with corrective lenses, either eyeglasses or contact lenses, in children as young as 1 week old.[51]

Vision therapy (i.e., using eye exercises) is used by some practitioners to treat a variety of eye conditions.[52, 53] It has been used alone or in combination with occlusion and/or correction of refractive error.[54] Vision therapy can consist of near-vision tasks (such as tracing or threading beads), binocular therapy, ocular motility training, accommodative therapy, and fixation training.[55] It may involve the use of lenses, prisms, filters, occluders, specialized instruments, and computer programs, and typically lasts for at least several months.[52]

Surgical interventions may be required for some causes of amblyopia. Refractory strabismus due to poor ocular alignment can be treated with surgery; the length or location of the extraocular muscles is adjusted to improve the alignment of the eye (but this does not necessarily improve amblyopia or visual acuity).[51] If occlusive pathology is present, this must also be corrected surgically, such as with cataract removal or ptosis correction, in which the levator muscle is tightened, causing the eyelid to elevate so it is symmetric with the other eyelid and allowing a

full field of vision.

Current Clinical Practice in the United States

Preschool vision screening is routinely offered in primary care settings. However, estimates of preschool vision screening rates vary by age, location, and other population characteristics. Rates of screening at age 3 years are generally around 40 percent,[56-59] though an analysis of Alabama well-child visits found that only 12 percent of 3-year-olds were screened for vision problems.[60] Rates of screening generally increase with the child's age. In a survey of pediatricians, 84 percent reported beginning screening before age 5 years (34% began at age 3 years), and 3 percent began screening at 6 months.[61] These rates appear to remain relatively unchanged since older surveys of pediatricians and family physicians.[59, 62] Caregiver reports of screening rates are roughly similar in the 2009–2010 Medical Expenditure Panel Survey.[63] In the same data, rates of screening varied by race/ethnicity and family income. Hispanic children were less likely than non-Hispanic children to have reported vision screening; children whose families earned 200 percent or more above the federal poverty level were more likely to have reported vision screening than those whose families had lower incomes.[63] In 2010, the U.S. Department of Health and Human Services reported that 60 percent of children covered by Medicaid in nine states did not receive a vision screening.[64]

Typical components of screening include tests of ocular alignment, visual acuity, and stereoacuity. Measures of visual acuity are generally reported as Snellen (e.g., 20/20, 20/25, 20/30, 20/40, and 20/50) or logarithm of the minimum angle of resolution (logMAR) scales (e.g., 0.00, 0.09, 0.18, 0.30, and 0.40, respectively). In the United States, primary care practices vary in the specific screening tests used, who performs the screening, and screening frequency.[50] The most commonly used screening tests in primary care settings are visual acuity testing with charts (e.g., LEA Symbols, HOTV) and ocular alignment testing with the cover-uncover test.[65]

Few recent estimates exist for the use of autorefractors and photoscreeners in clinical practice. In two surveys, fewer than 10 percent of pediatricians reported using autorefraction and/or photoscreening.[59, 61] However, at a single multispecialty group practice, the introduction of a photoscreener increased the rate of screening among 3-year-olds from 10 to 80 percent.[66] Use has likely increased in recent years because major clinical practice guidelines now recommend photoscreening and handheld autorefraction as alternatives to other forms of screening for children age 6 months or older; some mass community-based screening programs have implemented their use.[63] Children who fail vision screening tests are typically referred for a complete ophthalmological examination.

Several guidelines have been issued related to screening children for amblyopia, its risk factors, and refractive error (**Appendix A**). Briefly, the American Academy of Family Physicians recommends vision screening for all children at least once between the ages of 3 and 5 years to detect the presence of amblyopia or its risk factors; it concluded that the current evidence is insufficient to assess the balance of benefits and harms of vision screening for children younger than age 3 years. In a joint statement, the American Academy of Pediatrics, the American Association for Pediatric Ophthalmology and Strabismus, the American Academy of

Ophthalmology, and the American Academy of Certified Orthoptists recommend that vision screening should be performed at an early age and at regular intervals with age-appropriate, valid methods. For children ages 6 months to 3 years, they recommend overall vision assessment with physical examination tests (fixation and follow response, red reflex test, external inspection via direct observation, pupil examination using a flashlight), with the addition of instrument-based vision screening (autorefraction, photoscreening), when available, for children ages 1 to 3 years. They recommend that visual acuity screening may be attempted at age 3 years using HOTV or LEA Symbols. For children ages 4 to 5 years, they recommend visual acuity screening using HOTV or LEA Symbols, cross cover test, and red reflex test. The Canadian Task Force on Preventive Health Care states that there is fair evidence to include testing of visual acuity in the periodic health examination of preschool-age children.

Previous USPSTF Recommendation

In 2011 the USPSTF recommended that all children be screened to detect amblyopia or its risk factors at least once between the ages of 3 to 5 years (B recommendation). The USPSTF concluded that the evidence was insufficient to assess the balance of benefits and harms of vision screening for children younger than age 3 years (I statement).

Chapter 2. Methods

Key Questions and Analytic Framework

The Evidence-based Practice Center investigators, USPSTF members, and Agency for Healthcare Research and Quality (AHRQ) Medical Officers developed the scope and Key Questions (KQs). **Figure 1** shows the analytic framework and KQs that guided the review. The KQs for this review were:

1. Does screening for amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years reduce long-term amblyopia or improve visual acuity, school performance, functioning, and/or quality of life?
   a. Does the effectiveness of screening in children ages 6 months to 5 years vary among different age groups?
2. What is the accuracy and reliability of screening tests for amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years?
   a. Does the accuracy or reliability of screening tests for amblyopia, its risk factors, and refractive error vary among different age groups?
3. What are the harms of screening for amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years?

4a. Does treatment of amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years improve visual acuity?

4b. Does treatment of amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years reduce long-term amblyopia or improve school performance, functioning, and/or quality of life?

5. What are the harms of treatment of amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years?

Data Sources and Searches

We searched PubMed/MEDLINE, the Cumulative Index to Nursing and Allied Health Literature, and the Cochrane Library for English-language articles published from January 2009 through June 2016, with surveillance of the literature through June 7, 2017. We used Medical Subject Headings as search terms when available and keywords when appropriate, focusing on terms to describe relevant populations, tests, interventions, outcomes, and study designs. We relied primarily on the 2011 systematic review for the USPSTF[67-69] to identify potentially relevant studies published before 2009 (we reassessed all articles included in that systematic review using our eligibility criteria). We conducted targeted searches for unpublished literature by searching ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform. Complete search terms and limits are listed in **Appendix B**. To supplement electronic searches, we reviewed the reference lists of pertinent review articles and studies that met our inclusion criteria and added all previously unidentified relevant articles. We reviewed all literature suggested by peer reviewers or public comment respondents and incorporated eligible studies into the final review.

Study Selection

We developed inclusion and exclusion criteria for populations, interventions, comparators, outcomes, timing, settings, and study designs with input from the USPSTF (**Appendix B**). We included English-language studies of children ages 6 months to 5 years conducted in countries categorized as "very high" on the United Nations Human Development Index. We excluded studies of children with eye injury/trauma, severe congenital conditions or developmental delays, retinopathy of prematurity, glaucoma, congenital cataract, neurodevelopmental disorders, systemic conditions associated with ocular abnormalities, or pathologic myopia. We excluded studies that were not available as full-text articles (e.g., conference abstracts, posters).

For KQs 1 through 3 (benefits, accuracy, and harms of screening), we required studies to enroll children without known impaired visual acuity or obvious symptoms of impaired visual acuity. For KQs 4 and 5 (benefits and harms of treatment), we included children with amblyopia, amblyopia risk factors, and/or refractive error. Studies performed in primary care, community-based, and school settings were eligible for all KQs. For KQs 2 through 5, studies performed in specialty settings (e.g., ophthalmology or optometry practices) were also eligible.

For KQs 1 through 3 (benefits, accuracy, and harms of screening), we included studies of screening tests used or available in primary care, including visual acuity tests (e.g., autorefraction; picture identification tests, such as Allen test cards or LEA symbols; HOTV chart; Snellen chart; tumbling E chart), stereoacuity tests (e.g., contour stereotests, such as the Frisby, Random Dot E, Stereo Smile, and Titmus Fly tests; Moving Dynamic Random Dot Stereosize test), and ocular alignment tests (e.g., photoscreening, corneal light reflex test, cover-uncover test, red reflex test). We excluded studies of screening tests not used or available in primary care settings (e.g., contrast sensitivity test, funduscopic examination, visual acuity test with cycloplegia) or not intended to detect amblyopia, amblyopia risk factors, or refractive error (e.g., white reflex test). For KQs 1 and 3 (benefits and harms of screening), we required studies to compare screened with nonscreened groups or earlier (at a younger age) versus later screening (at an older age). For KQ 2 (accuracy of screening), we required studies to compare the screening test with an evaluation that included cycloplegic refraction and/or a comprehensive eye examination. We excluded studies with no comparison group or nonconcordant historical controls.

For KQs 4 and 5 (benefits and harms of treatment), studies that evaluated correction of refractive error (eyeglasses), penalization of the nonamblyopic eye (eye patch, atropine), and vision therapy (eye exercises) were eligible. We required studies to compare the treatment with no treatment, sham, or inactive control. We excluded studies with no comparison group, nonconcordant historical controls, or comparative studies of various interventions (i.e., head-to-head studies without an additional comparison group).

We required studies for KQs 1 and 4 (benefits of screening and treatment) to report at least one of the following outcomes: long-term amblyopia, visual acuity, school performance, functioning, or quality of life. Eligible outcomes for KQ 2 were sensitivity; specificity; positive and negative predictive values; likelihood ratios; diagnostic odds ratios (ORs); and measures of reliability, including reproducibility, interrater reliability, and testability (ability of children to cooperate

with the test). For KQs 3 and 5 (harms of screening and treatment), studies must have reported a harm, such as psychological distress, labeling, anxiety, other psychological effects, false-positive results, or adverse effects on vision in the nonimpaired eye.

For KQ 1, we included randomized, controlled trials (RCTs) and prospective cohort studies with an eligible comparator. For KQ 2 (screening accuracy), we included cross-sectional studies, cohort studies, or trials focused on assessment of diagnostic accuracy. We excluded studies that did not attempt to perform the reference standard in all participants or in a random sample of participants. For KQs 3 and 5 (harms), we included RCTs, controlled cohort studies, and case-control studies. For KQ 4 (benefits of treatment), only RCTs were eligible.

Quality Assessment and Data Abstraction

For each included study, one investigator extracted pertinent information about the methods, populations, interventions, comparators, outcomes, timing, settings, and study designs. A second team member reviewed all data extractions for completeness and accuracy. To provide a consistent metric for visual acuity outcome measures, results were converted to logMAR measurements using established conversion charts.[70]

We assessed the quality of studies as good, fair, or poor using predefined criteria developed by the USPSTF and adapted for this topic (**Appendix B**).[71] Two independent reviewers assigned quality ratings for each study. Disagreements were resolved by discussion with an experienced team member. We included only studies rated as good or fair quality.

Data Synthesis and Analysis

We qualitatively synthesized findings for each KQ by summarizing the characteristics and results of included studies in tabular and narrative format. We did not attempt to quantitatively pool results of studies of test accuracy because of the considerable clinical and methodological heterogeneity, specifically as a result of the variety of screening cutoff definitions, target condition definitions, enrolled populations, and results. We did not attempt quantitative synthesis of treatment studies because there were too few trials making similar comparisons.

For KQ 2 (accuracy), we calculated sensitivity, specificity, likelihood ratios, and predictive values when sufficient data were reported by articles. When qualitatively evaluating likelihood ratios, we considered positive likelihood ratios (PLRs) to indicate a minimal (1–2), small (2–5), moderate (5–10), or large (>10) increase in the risk of the condition of interest (e.g., amblyopia or its risk factors). We considered negative likelihood ratios (NLRs) to indicate a minimal (0.5–1), small (0.2–0.5), moderate (0.1–0.2), or large (<0.1) decrease in the risk of the condition of interest. Likelihood ratios below 0.1 or above 10 are typically thought to provide strong evidence for ruling out (NLR <0.1) or ruling in (PLR >10) diagnoses.[72, 73]

We assessed the overall strength of the body of evidence for each KQ as high, moderate, low, or insufficient using methods developed for the USPSTF (based on methods of the Evidence-based

Practice Center program[68, 69]), based on the overall quality of studies, consistency of results between studies, precision of findings, and risk of reporting bias. We also assessed the applicability of the findings to U.S. primary care populations and settings.

Expert Review and Public Comment

This draft report was reviewed by content experts, USPSTF members, and AHRQ Medical Officers and was revised based on comments. It was also posted for public comment and revised based on public comments.

USPSTF Involvement

This review was funded by AHRQ. AHRQ staff and USPSTF members participated in developing the scope of the work and reviewed draft manuscripts, but the authors are solely responsible for the content.

Chapter 3. Results

Literature Search

We identified 2,182 unique records and further assessed 366 full-text articles for eligibility (**Figure 2**). We excluded 320 articles for various reasons detailed in **Appendix C** and included 40 published studies (described in 46 articles) of good or fair quality. Of all the included studies, two addressed the effectiveness of screening (KQ 1), 34 evaluated diagnostic test accuracy (KQ 2), 17 provided information on the harms of screening (KQ 3), three reported benefits of treatment (KQ 4), and three reported harms of treatment (KQ 5). The sum of studies (when adding the numbers included for each KQ) exceeds 40 because some studies were included for more than one KQ. Details of quality assessments of included studies and studies excluded because of poor quality are provided in **Appendix D**.

Results by KQ

KQ 1. Direct Evidence That Screening Improves Health Outcomes

We identified no eligible RCTs comparing vision screening with no screening. We included two fair-quality studies, one RCT[74, 75] and one prospective cohort study,[76] enrolling children from the population-based Avon Longitudinal Study of Parents and Children (ALSPAC) project. ALSPAC is a geographically defined birth cohort study enrolling 14,000 children (85% of those eligible) born in Southwest England between April 1991 and December 1992.[74] The RCT compared earlier, intensive screening (before age 3 years) with later, one-time screening. The cohort study compared screening at age 3 years (specifically, at age 37 months) with no preschool screening. The included studies reported prevalence of amblyopia at age 7.5 years. Neither study evaluated school performance, functioning, or quality of life outcomes. The major methodological shortcoming in both studies was high attrition; in the RCT, 55 percent of children randomized did not attend the final examination at age 7.5 years and were excluded from analyses.[76] Similarly, about half of children in the cohort did not have examination results available at age 7.5 years and were excluded from analyses.[76] In addition, the method of randomization in the RCT was not adequate; children were randomized to the intervention or control group according to the last digit of the mother's day of birth.[74, 75]

The RCT (N=3,490) was nested within the ALSPAC cohort and compared intensive orthoptist visual screening before age 3 years (at 8, 12, 18, 25, 31, and 37 months) with one-time orthoptist screening at age 37 months (**Table 3**).[74, 75] Eligible participants were those born in the last 6 months of the ALSPAC cohort whose parents agreed to attend regular clinic examinations; about half were female and 5 percent were nonwhite.[74] Baseline data for amblyopia or amblyopia risk factors were not reported. The intervention screening examination by the orthoptist consisted of a clinical examination, age-specific visual acuity testing, and the cover-uncover test. Children with positive results on the visual acuity or cover-uncover test in either group were referred to the hospital eye service for further evaluation and treatment. In addition, children in both groups

were offered what was considered usual care in terms of surveillance for visual problems: 1) examination at age 8 months and 18 months by a health visitor (taking history, observing visual behavior, and using a cover-uncover test), with referrals if a problem was suspected,[74] and 2) visual screening at school entry (ages 4 to 5 years) by a school nurse.[75]

The trial reported that the prevalence of amblyopia at 7.5 years was approximately 1 percent lower in the intensive screening group than in the control group, but the difference was only statistically significant for one of their two definitions of amblyopia (**Table 3**) (amblyopia A: 1.5% vs. 2.7%; relative risk [RR], 0.55 [95% confidence interval (CI), 0.29 to 1.04]; amblyopia B: 0.6% vs. 1.8%; RR, 0.35 [95% CI, 0.15 to 0.86]).[75] Among children who received patching treatment (n=40 in each group), presence of residual amblyopia at age 7.5 years was more likely in the one-time screening group than in the intensive-screening group, but the difference was only statistically significant for one of the two definitions of amblyopia, and estimates were imprecise (amblyopia A: OR, 1.56 [95% CI, 0.62 to 3.92]; amblyopia B: OR, 4.11 [95% CI, 1.04 to 16.29]).[75] Also, among children who received patching treatment, visual acuity at age 7.5 years in the worse eye was better in the intensive-screening group than in the one-time screening group (0.15 logMAR [95% CI, 0.08 to 0.22] vs. 0.26 logMAR [95% CI, 0.17 to 0.35]; $p<0.001$).[75]

The prospective cohort study (N=6,081 completers) compared orthoptist screening at age 3 years in one health district with no preschool screening in two other health districts (**Table 3**).[76] Eligible participants were those who attended the examination at age 7.5 years and were not enrolled in the ALSPAC RCT; about half were female, and race/ethnicity was not described.[76] One of the three health districts in the ALSPAC study area offered preschool orthoptic vision screening and the other two did not. Screening examination by the orthoptist consisted of a monocular vision test, a cover-uncover test, and an assessment of binocularity; positive findings on any part of the examination resulted in referral to the hospital eye service for further evaluation. All children in the study area were offered vision screening at school entry (ages 4 to 5 years).[76]

Among participants who attended the examination at age 7.5 years and were not part of the ALSPAC RCT, there were no statistically significant differences between groups (those who did vs. did not receive preschool vision screening) in amblyopia at age 7.5 years, based on any of the studies' three definitions of amblyopia (**Table 3**) (amblyopia A: adjusted OR, 0.63 [95% CI, 0.32 to 1.23]; amblyopia B: adjusted OR, 0.72 [95% CI, 0.32 to 1.60]; amblyopia C: adjusted OR, 0.65 [95% CI, 0.38 to 1.10]).[76] Trends toward better amblyopia outcomes in the screened group were more attenuated when the analysis was based on a comparison of whether children were offered screening rather than whether they received screening (about two-thirds of the children invited to screening participated).[76]

KQ 2. Accuracy and Reliability of Screening Tests

We included 34 fair-quality studies (described in 38 articles) that evaluated the accuracy of one or more vision screening tests (**Appendix Tables E1–11**).[65, 77-113] The studies evaluated a variety of test types, including visual acuity tests (LEA Symbols or HOTV, 6 studies), stereoacuity tests (Stereo Smile II or Random Dot E, 4 studies), ocular alignment tests (cover-uncover test, 1 study), a combination of clinical tests (4 studies), autorefractors (16 studies), photoscreeners (11

studies), and retinal birefringence scanning (1 study) (**Table 4**). Screening was administered by a variety of personnel across studies, including orthoptists, orthoptists and pediatricians, orthoptists and ophthalmologists, licensed eye professionals, nurses, trained laypersons, Head Start staff, research staff, and technicians, and was sometimes not reported. Sample sizes ranged from 63[99] to 4,040.[94, 111] Nineteen studies were conducted in the United States, five in Canada, seven in Europe, and three in either Australia or New Zealand (**Appendix Table E2**).

The age of participants in most studies was 3 years or older (e.g., 3 to 4, 3 to 5, 4 to 5, or 3 to 7 years). About a third of the studies included participants younger than age 3 years,[77, 83, 89, 90, 95, 96, 99, 100, 102, 103, 105, 109-111] and some reported including children as young as age 6 months.[83, 90, 96, 100, 109] The included studies reported accuracy of tests for a variety of target conditions, ranging from very specific (e.g., astigmatism, myopia, anisometropia) to broad (e.g., amblyopia risk factors) (**Table 4**).

Less than half of the included studies (14 studies) recruited participants from ophthalmology clinics.[81, 83, 84, 87, 90, 91, 93, 96, 99, 102, 103, 105, 109, 110] Most (17 studies) recruited from community, Head Start, or school settings;[65, 77-80, 85, 86, 88, 92, 94, 95, 97, 98, 104, 106-108, 111] one study was conducted in a private pediatric primary care clinic,[89] one was conducted partly in a primary care setting (in public health and pediatric clinics),[100] and one did not report the setting.[82] The prevalence of target conditions was generally much higher in samples from ophthalmology clinics than in those from primary care, community, Head Start, or school settings (>70% of studies from ophthalmology clinics reported prevalence ≥36% [range, 36% to 81%], whereas all of the studies from primary care, community, Head Start, or school settings reported prevalence ≤36% [range, 1% to 36%]).

The largest studies used data from phases 1 and/or 2 of the Vision In Preschoolers (VIP) study group (≤4,040 participants) and reported prevalence of any target conditions from 21 to 36 percent. The VIP study enrolled children from Head Start and oversampled children with amblyopia, amblyopia risk factors, reduced visual acuity, or strabismus identified on a screening evaluation.[65, 88, 94, 104, 106-108, 111] Phase 1 of the VIP study enrolled 3- to 5-year-old children in Head Start who were selected to overrepresent children with vision problems and compared the accuracy of 11 screening tests.[65] Tests were conducted in specially equipped vans that provided a standard environment with minimal distractions. Phase 2 compared the performance of nurse versus lay screeners and focused on four of the 11 screeners (based on findings of phase 1); specifically, Retinomax autorefractor, SureSight Vision Screener, crowded linear LEA Symbols visual acuity test at 10 feet, and the Stereo Smile II test.[108] Unlike many of the other included studies that focused on just amblyopia and/or amblyopia risk factors, the VIP study evaluated accuracy for a broader range of conditions, including significant nonamblyogenic refractive error.

The included studies were all rated fair quality (**Appendix Table D3**). The most common methodological shortcomings were a high rate (or not reporting the rate) of uninterpretable results or noncompliance with screening test or reference standard (14 studies [41%]), not reporting whether children with uninterpretable results or noncompliance were included in analyses (16 studies [47%]), lack of a representative spectrum of patients (19 studies [56%]), and lack of description of enrolling a random or consecutive sample (22 studies [65%]).

Publications from phases 1 and 2 of the VIP study were assessed as fair quality. Key methodological limitations included not enrolling a representative spectrum of patients and not predefining screening cutoffs (rather than predefining cutoffs, sensitivity for each test was calculated based on the cutoff needed to yield specificity of 0.90 or 0.94). Although this approach allows for clear comparison of sensitivity across tests (because the specificity is essentially fixed), it may introduce bias and may overestimate accuracy, because cutoffs were defined post hoc. The applicability of the VIP study may be limited because it did not enroll a representative spectrum, study subjects may have experienced fatigue from the volume of tests (children underwent 6 to 8 procedures, many more than are typically used in routine clinical screening), and testing was conducted by highly skilled personnel in a controlled environment (in phase 1).

Visual Acuity Tests

Six fair-quality studies evaluated visual acuity tests (LEA Symbols or HOTV, 6 studies) (**Table 4; Appendix E**).[65, 81, 97, 98, 107, 108] All six assessed LEA Symbols and two[65, 107] also assessed HOTV.

Three publications from the VIP study group (6,019 total participants) evaluated the accuracy of LEA Symbols for detecting amblyopia risk factors or significant nonamblyogenic refractive error.[65, 107, 108] When screening test cutoffs were set to achieve specificity of 90 percent, phase 1 of the VIP study found that an abnormal result moderately increased the likelihood of amblyopia risk factors or significant nonamblyogenic refractive error both overall (PLR, 6.1 [95% CI, 4.8 to 7.6])[65] and for those in the 3-, 4-, and 5-year-old age groups (PLR range, 5.95 to 7.39).[107] It found that a normal result indicated a small decrease in the likelihood both overall (NLR, 0.43 95% CI, 0.38 to 0.50) and for those in the 3-, 4-, and 5-year-old age groups (NLR range, 0.39 to 0.47]).[65, 107] In phase 2, when using nurse and lay screeners, the VIP study found that an abnormal result indicated a small increase in the likelihood of amblyopia risk factors or significant nonamblyogenic refractive error (PLRs, 4.9 [95% CI, 4.0 to 6.0] and 3.7 [95% CI, 3.0 to 4.7], respectively), and that a normal result indicated a minimal decrease in the likelihood (NLRs, 0.57 [95% CI, 0.52 to 0.62] and 0.70 [95% CI, 0.65 to 0.76], respectively).

The other three studies (773 total participants) that evaluated LEA Symbols each reported test characteristics for detecting different target conditions; one each for amblyopia risk factors, significant refractive error, and astigmatism. Briefly, one study (N=149) from a pediatric ophthalmology setting found that an abnormal result moderately increased the likelihood of amblyopia risk factors (PLR, 5.7 [95% CI, 3.8 to 8.6]) and a normal result indicated a large decrease in the likelihood (NLR, 0.05 [95% CI, 0.01 to 0.36]).[81] The other two evaluated Native American children in Head Start and found that an abnormal result minimally increased the likelihood of either significant refractive error (among those with astigmatism)[97] or astigmatism[98] and a normal result indicated a small[97] or moderate[98] decrease in the likelihood, respectively (**Table 4**).

Two publications from the VIP study group (3,121 total participants) evaluated the accuracy of HOTV visual acuity tests for detecting amblyopia risk factors or significant nonamblyogenic refractive error.[65, 107] Both evaluated participants from phase 1 and found that an abnormal result

indicated a small to moderate increase in the likelihood of amblyopia risk factors or significant nonamblyogenic refractive error when screening test cutoffs were set to achieve specificity of 90 percent (overall PLR, 4.9 [95% CI, 3.9 to 6.1];[65] PLR range, 3.76 to 6.83 for the 3-, 4-, and 5-year-old age groups[107]). They found that normal results indicated a minimal to small decrease in the likelihood (**Table 4**).

Stereoacuity Tests

Four fair-quality studies (7,801 total participants) evaluated stereoacuity tests, either the Stereo Smile II, the Randot Preschool Stereoacuity, or Random Dot E (**Table 4**).[65, 77, 87, 108] These included evaluations of phase 1 and 2 of the VIP study and the Sydney Paediatric Eye Disease Study. Most of the studies found that abnormal results indicated a small increase in the likelihood of target conditions (PLR range, 3.6 to 4.9 in most studies) (**Table 4**) and normal results indicated either a minimal[65, 108] decrease in the likelihood of amblyopia risk factors or significant nonamblyogenic refractive error, or a moderate[87] decrease in the likelihood of refractive error or strabismus.

Ocular Alignment Tests

Phase 1 of the VIP study (N=3,121) was the only study that evaluated an ocular alignment test, the cover-uncover test (**Table 4**).[65] It found that abnormal results indicated a moderate increase in the likelihood of amblyopia risk factors or significant nonamblyogenic refractive error (PLR, 7.9 [95% CI, 4.6 to 14.0]) and normal results indicated a minimal decrease in the likelihood.

Combinations of Clinical Tests

Four fair-quality studies (1,854 total participants) evaluated a combination of clinical tests, including visual acuity tests, stereoacuity tests, and ocular alignment tests (**Table 4; Appendix Table E1**).[80, 82, 92, 103] The specific tests evaluated varied somewhat across studies (**Appendix Table E1**). Three of the four studies found that abnormal results indicated a large increase in the likelihood of amblyopia or its risk factors (PLR range, 12 to 17).[80, 92, 103] The largest of these three studies (N=1,180) was set in kindergartens in Germany and evaluated 3-year-olds, with screening conducted by an orthoptist.[80] The one study that found a smaller PLR (4.8 [95% CI, 2.8 to 8.4]) was the smallest (N=141) of the four studies; screening was conducted by nurses and the study setting was not reported.[82] The four studies found more variability for NLRs, with results ranging from minimal[92] to small[82, 103] to moderate[80] NLRs (range, 0.10 to 0.91) (**Table 4**).

Autorefractors

Sixteen fair-quality studies (16,712 observations) evaluated autorefractors (**Table 4; Appendix E**).[65, 78, 79, 84, 85, 89, 90, 94, 96-98, 102, 106, 108, 110, 111] Eight evaluated Retinomax,[65, 79, 94, 97, 98, 106, 108, 111] seven evaluated SureSight,[65, 89, 90, 94, 102, 108, 111] five evaluated Plusoptix/Power Refractor,[65, 78, 84, 85, 96] one evaluated the Topcon PR 2000,[110] and one evaluated the Palm to Automatic Refractometer.[106] Overall, most studies found moderate PLRs and small NLRs, although some found large PLRs and NLRs.

Autorefractor screening was administered by a variety of personnel across studies, including orthoptists, ophthalmologists, licensed eye professionals, nurses, trained laypersons, research staff, and Head Start staff, and was sometimes not reported. Sample sizes ranged from 80[96] to 4,040.[94, 111] Eleven studies were conducted in the United States, one in Canada, and four in Europe (**Appendix Table E2**). The age of participants in most studies was 3 years or older (e.g., 3 to 5, 4 to 5 years). Five studies included participants younger than age 3 years,[89, 90, 96, 102, 110] and two of those included children as young as age 6 months.[90, 96] The included studies reported accuracy of tests for a variety of target conditions, ranging from very specific (e.g., astigmatism, myopia, anisometropia) to broad (e.g., amblyopia risk factors) (**Table 4**). Most (10 studies) recruited from Head Start or school settings.[65, 78, 79, 85, 94, 97, 98, 106, 108, 111] Five of the studies recruited participants from ophthalmology clinics,[84, 90, 96, 102, 110] and one took place in a pediatric primary care clinic.[89]

Retinomax

Of the eight studies that evaluated Retinomax,[65, 79, 94, 97, 98, 106, 108, 111] most found that abnormal results indicated a moderate increase in the likelihood of target conditions (i.e., moderate PLRs) and a normal result indicated a small decrease in the likelihood (i.e., small PLRs) (**Table 4**). For example, when screening test cutoffs were set to achieve specificity of 90 percent, phase 1 of the VIP study found that an abnormal result moderately increased the likelihood of amblyopia risk factors or significant nonamblyogenic refractive error (PLR, 6.1 [95% CI, 5.2 to 7.0]) and a normal result indicated a small decrease in the likelihood (NLR, 0.41 [95% CI, 0.37 to 0.45]).[65]

Some studies found slightly higher or lower likelihood ratios. One study that evaluated 3- to 5-year-old Native American children in Head Start (N=379) found a large PLR for astigmatism,[98] and one study of 3-year-olds in kindergartens in Germany (N=404) found a minimal PLR for amblyopia.[79] Two studies that evaluated 3- to 5-year-old Native American children in Head Start found that a normal result indicated a moderate to large decrease in the likelihood of either significant refractive error (among those with astigmatism)[97] or astigmatism among a high-prevalence (48%) population.[98]

SureSight

Of the seven studies that evaluated the SureSight autorefractor,[65, 89, 90, 94, 102, 108, 111] four were from the VIP study group and evaluated the accuracy for detecting amblyopia risk factors or significant nonamblyogenic refractive error.[65, 94, 108, 111] When screening test cutoffs were set to achieve specificity of 90 percent, phase 1 of the VIP study found that an abnormal result moderately increased the likelihood of amblyopia risk factors or significant nonamblyogenic refractive error (PLR, 6.3 [95% CI, 5.2 to 7.4]) and a normal result indicated a small decrease in the likelihood (NLR, 0.41 [95% CI, 0.36 to 0.47]).[65] In phase 2, when using nurse and lay screeners, the VIP study found similar results.[108] In contrast, when screening test cutoffs were set based on the manufacturer's referral criteria, the VIP study found a small PLR (2.2 [95% CI, 2.0 to 2.4]). Similarly, two other U.S.-based studies that recruited from ophthalmology settings (270 total participants) reported small PLRs for the likelihood of amblyopia risk factors when using the manufacturer's referral criteria.[90, 102]

One study with 102 participants ages 2 to 6 years conducted in a private pediatric primary care practice in the United States reported that an abnormal result moderately increased the likelihood of amblyopia or strabismus (PLR, 7.9 [95% CI, 4.7 to 13.4]) and a normal result indicated a large decrease in the likelihood (NLR, 0.0).[89] Screening with SureSight detected the only participant with amblyopia or strabismus (sensitivity, 100%); the study found a specificity of 87 percent (95% CI, 79% to 93%).

Plusoptix

All five of the studies that evaluated the Plusoptix autorefractor (previously known as the Power Refractor) reported moderate to large PLRs for some of the target conditions they assessed (**Table 4**).[65, 78, 84, 85, 96] When screening test cutoffs were set to achieve specificity of 90 percent, phase 1 of the VIP study found that an abnormal result moderately increased the likelihood of amblyopia risk factors or significant nonamblyogenic refractive error (PLR, 5.4 [95% CI, 4.4 to 6.6]) and a normal result indicated a minimal decrease in the likelihood (NLR, 0.51 [95% CI, 0.46 to 0.57]).[65] Another study reported similarly that an abnormal result moderately increased the likelihood of ambylogenic risk factors (PLR, 8.4 [95% CI, 3.7 to 19]) when referral criteria were modified to enhance specificity.[96] Three of the five studies reported large PLRs for amblyopia risk factors; myopia, hyperopia, and astigmatism; or decreased visual acuity, strabismus, and ptosis.[78, 84, 85]

Topcon PR 2000

The only included study (N=222) that evaluated the Topcon PR 2000 recruited children from ophthalmology clinics in the United Kingdom and reported moderate to large PLRs and small to minimal NLRs for spherical error, anisometropia, and astigmatism (**Table 4**).[110]

Palm to Automatic Refractometer

The only included study (N=190) that evaluated the Palm to Automatic Refractometer was the pilot portion of phase 2 of the VIP study.[106] It reported a moderate PLR for a combination of four target conditions (amblyopia, strabismus, refractive error, and reduced visual acuity) and a small NLR when screening was conducted by one trained and certified non–eye-care professional screener (**Table 4**).

Photoscreeners

Eleven fair-quality studies (12 publications, 6,187 observations) evaluated photoscreeners (**Table 4; Appendix E**).[65, 83, 91-93, 98-102, 105, 109] Six studies (7 publications) evaluated the MTI photoscreener,[65, 98, 100-102, 105, 109] two evaluated the iScreen photoscreener,[65, 93] two evaluated the VisiScreen 100 photoscreener,[83, 99] and two evaluated an Otago photoscreener.[91, 92] Overall, most studies found moderate PLRs and small NLRs, although some found larger or smaller likelihood ratios.

Photoscreening was administered by a variety of personnel across studies, including orthoptists and pediatricians,[100, 101] licensed eye professionals,[65] trained laypersons,[102] and technicians,[83, 91-

[93] and was sometimes not reported.[105, 109] Sample sizes ranged from 63[99] to 3,121.[65] Seven studies were conducted in the United States and three in Canada, and one country was not reported (**Appendix Table E2**). Most studies allowed for inclusion of children younger than age 3 years. The included studies reported accuracy of tests for a variety of target conditions, ranging from very specific (e.g., astigmatism, strabismus) to broad (e.g., amblyopia risk factors) (**Table 4**). Most (7 studies) recruited from ophthalmology clinics, with fewer recruiting from primary care, community, Head Start, or school settings.[65, 92, 98, 100]

MTI Photoscreener

Of the six studies (7 publications) that evaluated the MTI photoscreener,[65, 98, 100-102, 105, 109] most (including phase 1 of the VIP study) found that abnormal results indicated a moderate increase in the likelihood (i.e., moderate PLRs) of amblyopia risk factors or a composite of amblyopia risk factors or significant nonamblyogenic refractive error (**Table 4**).[65, 100-102, 105] One study also reported a large PLR for detecting higher-magnitude amblyopia risk factors (PLR, 33 [95% CI, 18 to 58]).[100, 101] Two other studies found small PLRs for 3- to 5-year-old Native American children in Head Start (N=379) for astigmatism[98] or 6- to 48-month-old children (N=112) in an ophthalmology clinic for amblyopia risk factors.[109] Most of the included studies found small to minimal NLRs (**Table 4**),[65, 98, 100, 101, 105, 109] although one study of 100 children ages 1 to 6 years screened by a trained layperson in ophthalmology clinics found a large NLR for amblyopia risk factors (0.06 [95% CI, 0.02 to 0.18]).[102]

iScreen Photoscreener

Both of the included studies that evaluated the iScreen photoscreener found moderate PLRs (**Table 4**).[65, 93] However, NLRs differed. Phase 1 of the VIP study found that normal results indicated a minimal decrease in the likelihood of amblyopia risk factors or significant nonamblyogenic refractive error (NLR, 0.67 [95% CI, 0.62 to 0.72]),[65] whereas a Canadian study of more than 400 children (prevalence of amblyopia risk factors, 64%) screened by a technician in ophthalmology clinics found a large NLR for amblyopia risk factors (0.09 [95% CI, 0.06 to 0.13]).[93]

VisiScreen 100 Photoscreener

The two included studies of the VisiScreen 100 photoscreener found very different PLRs but similar NLRs (**Table 4**).[83, 99] Both were conducted in the United States in ophthalmology settings and targeted amblyopia risk factors. One found a large PLR (14 [95% CI, 6.3 to 32]) and moderate NLR (0.16 [95% CI, 0.05 to 0.59]) among 127 children ages 6 months to 6 years who were screened by a technician.[83] The other found a small PLR (3.5 [95% CI, 1.7 to 7.0]) and moderate NLR (0.12 [95% CI, 0.04 to 0.36]) among 63 children ages 3 months to 8 years.[99]

Otago Photoscreener

The two included studies of Otago-type photoscreeners (noncommercial; developed by the study investigators) both found large PLRs for amblyopia risk factors but very different NLRs (**Table 4**).[91, 92] Both were conducted in Canada with screening by a technician, but one (N=236) was

conducted in an ophthalmology clinic[91] and one (N=264) in a school setting (kindergarten).[92] The former found a large NLR (0.06 [95% CI, 0.03 to 0.14]),[91] whereas the latter found a minimal NLR (0.54 [95% CI, 0.33 to 0.89]).[92]

Retinal Birefringence Scanning

One study with 102 participants ages 2 to 6 years conducted in a private pediatric primary care practice in the United States evaluated the Pediatric Vision Scanner. It reported that an abnormal result indicated a large increase in the likelihood of amblyopia or strabismus (PLR, 10.4 [95% CI, 5.6 to 19.4]) and a normal result indicated a large decrease in the likelihood (NLR, 0.0).[89] Screening with the Pediatric Vision Scanner detected the only participant with amblyopia or strabismus (sensitivity, 100%); the study found a specificity of 90 percent (95% CI, 83% to 96%).

Direct Comparisons of Different Screening Tests

Few of the included studies directly compared different tests. The best evidence directly comparing various tests comes from the VIP study investigators. As described above, phase 1 of the VIP study compared 11 screening tests among 3- to 5-year-old children in Head Start.[65] Tests were conducted in specially equipped vans that provided a standard environment with minimal distractions. Phase 2 compared the performance of nurse versus lay screeners and focused on the best four screening tests (based on findings of phase 1): Retinomax autorefractor, SureSight Vision Screener, LEA Symbols, and the Stereo Smile II test.[108] When screening test cutoffs were set to achieve specificity of 90 percent, phase 1 of the VIP study reported higher sensitivities for LEA Symbols or HOTV visual acuity tests, Retinomax autorefractor, SureSight autorefractor, and Power Refractor for detecting any visual condition than for the Random Dot E stereoacuity test, Stereo Smile II test, iScreen photoscreener, and MTI photoscreener (**Appendix Table E8**). Nevertheless, likelihood ratios were similar, and PLRs generally fell within the moderate range, with NLRs in the small to minimal range. Confidence intervals generally overlapped.

KQ 2a. Does Accuracy Vary by Age?

We included five studies that evaluated whether accuracy varies by age (results are summarized in **Appendix Table E7**).[82, 90, 93, 105, 107] All five evaluated different screening tests, including visual acuity tests (LEA Symbols and HOTV),[107] a combination of clinical tests (LEA Symbols visual acuity test, Frisby stereoacuity test, and external visual inspection),[82] the SureSight autorefractor,[90] the iScreen photoscreener,[93] or the MTI photoscreener.[105] All five assessed different age stratifications/comparisons. As described above (under "Visual Acuity Tests"), the VIP study group reported similar PLRs and NLRs among children in the 3-, 4-, and 5-year-old age groups for LEA Symbols and HOTV visual acuity tests for detecting amblyopia risk factors or significant nonamblyogenic refractive error.[107] The study that evaluated a combination of clinical tests (N=141 evaluated) compared children age 41 months or older with those younger than age 41 months.[82] The study of the SureSight autorefractor compared children ages 3 to 5 years with those younger than age 3 years.[90] The study of the iScreen photoscreener compared children ages 4 to 6 years with those age 3 years or younger.[93] The study of the MTI photoscreener compared children by quartiles of age.[105] Overall, data were relatively limited and

estimates were somewhat imprecise, but studies did not find any clear differences in accuracy of tests when results were stratified according to age.

Testability

The ability of children to complete various screening tests (i.e., testability) provides additional information about how the utility of tests may vary by age. Testability information was reported by many of the included studies, although few of those reported data stratified by age or for children younger than age 3 years. **Appendix Table E8** summarizes the proportion of children who were reported to be unexaminable in each study. Overall, testability exceeded 90 percent in the majority of studies, and few studies reported testability rates less than 80 percent for any tests, but all studies that reported rates less than 80 percent included children younger than age 3 years.[77, 90, 95, 102] Further, some studies demonstrated that testability rates improved somewhat as children age from 2 to 5 or 6 years[95, 103] or from 3 to 5 years,[65, 81, 113] and others found that testability was better for children ages 4 to 6 years than for the overall sample of participants ages 1 to 6 years[102] or for those age 3 years or older than for those younger than age 3 years.[90]

Several studies addressed variation in testability of visual acuity and stereoacuity by age. The Sydney Paediatric Eye Disease Study (N=1,170) found that testability rates were 10 percent for visual testing with HOTV at ages 24 to less than 30 months, and steadily improved to 80 percent by ages 36 to less than 42 months and to 95 percent by ages 48 to less than 54 months among Australian children.[95] The VIP study found testability rates greater than 95 percent for LEA Symbols and HOTV at ages 3, 4, and 5 years, but found higher rates of testability for 5-year-olds than for 3-year-olds for Random Dot E (95% vs. 86%).[65, 112, 113] A smaller study (N=149) from ophthalmology clinics in Italy found that testability with LEA Symbols improved from 93 percent in children ages 38 to 42 months up to 100 percent in those ages 49 to 54 months.[81] A study from U.S. ophthalmology clinics (N=269) reported an increase in Random Dot E testability from 65 to 100 percent from ages 2 to 6 years.[103]

For autorefractors and photoscreeners, the VIP study found testability rates near 100 percent.[65] Applicability to younger children is uncertain because the VIP study did not include children younger than age 3 years. Further, the vast majority (93%) of the 3-year-olds in the study were at least age 42 months. Two smaller studies from U.S. ophthalmology clinics reported better testability for older preschool-age children than for younger ones. The first study (N=100) found that testability with both the SureSight autorefractor and the MTI photoscreener was perhaps slightly better for children ages 4 to 6 years than for the overall sample of participants ages 1 to 6 years (80% vs. 76% and 100% vs. 96%, respectively).[102] The other study (N=170) reported that testability with the SureSight autorefractor was worse for children younger than age 3 years than for those age 3 years or older (49% vs. 84%; $p<0.001$).[90]

The study with 102 participants ages 2 to 6 years conducted in a private pediatric primary care practice in the United States reported testability rates of 93 percent (95/102) and 94 percent (96/102) with the Pediatric Vision Scanner and the SureSight autorefractor, respectively.[89] All but one of the children unable to perform a test were age 2 or 3 years. Among 2-year-olds, 17 percent (5/29) were unable to be tested with the Pediatric Vision Scanner, and 14 percent (4/29) were unable to be tested with the SureSight autorefractor.

KQ 3. Harms of Screening

We included one controlled study that evaluated potential psychosocial effects[114] and used 16 studies of test accuracy described in KQ 2 to calculate false-positive rates (1 minus positive predictive value).

The one controlled study used the ALSPAC population-based cohort (N=4,473) to assess bullying.[114] It prospectively compared children who had been offered state-provided preschool screening for amblyopia (at age 37 months) with those who had not. The study aimed to test the theory that preschool screening might reduce bullying. In theory, although patching treatment and wearing glasses may increase the risk of being bullied, preschool screening may result in greater likelihood that any needed patching treatment is concluded before school starts, thus avoiding potential psychosocial effects. The outcome measure was bullying victimization by age 8 years assessed with a structured standard interview; children were asked whether they had repeatedly (≥4 times per month) been the victims of bullying.

The study showed a reduction in school-age bullying among patched children screened in preschool. Children offered screening had a lower likelihood of being bullied compared with those not screened earlier (25.7% vs. 47.1%; p=0.033; adjusted OR, 0.39 [95% CI, 0.16 to 0.92], adjusted for sex, paternal socioeconomic class, highest level of maternal education, and type of housing). These effects were seen in children who were patched and not in those who were only prescribed glasses. The authors suggest that the findings indicate that earlier screening can potentially reduce psychosocial harms.

The most frequently assessed potential harms of screening were false-positive results (that would lead to unnecessary referrals). In general, studies with a lower prevalence (<10%) of vision abnormalities showed much higher false-positive rates (usually >75%), while studies with a high prevalence had lower false-positive rates (usually <35%) (**Figure 3**).

In seven studies with vision disorder prevalence more similar to the general population (1% to 8%), false-positive rates were generally high. Six of the seven studies found false-positive rates between 62 and 99 percent;[77, 79, 80, 87, 89, 103] rates ranged from 23 to 99 percent when considering all seven studies.[77, 79, 80, 87, 89, 92, 103] The one study (N=270) that reported a lower false-positive rate was unlike the other studies in that it sampled a subset (rather than all) of children with normal screening results; participants were children who screened positive (n=29) plus a random sample of those who did not (n=241).[92] It found false-positive rates of 46 and 23 percent for a manual approach to screening (Snellen E or Stycar-graded balls visual acuity tests and Titmus stereotest) and for an Otago-type photoscreener, respectively. The seven studies with low prevalence of vision disorders evaluated the performance of the Retinomax autorefractor,[79] Random Dot E,[77, 87] Stereo Smile II test,[77] Otago-type photoscreener,[91] Pediatric Vision Scanner,[89] SureSight autorefractor,[89] or a combination of manual screening tools.[80, 92, 103]

In contrast, in nine studies with a higher prevalence (20% to 81%), false-positive rates were generally lower. Seven of these nine studies had false-positive rates less than 32 percent,[93, 99, 100, 102, 105, 107, 109] and rates ranged from 3 to 65 percent.[65, 93, 99, 100, 102, 105-107, 109] These studies evaluated the iScreen photoscreener,[65, 93] VisiScreen 100 photoscreener,[99] MTI photoscreener,[65,

[100, 102, 105, 109] SureSight autorefractor,[65, 102] LEA Symbols,[65, 107] HOTV,[65, 107] Random Dot E,[65] cover-uncover test,[65] noncycloplegic retinoscopy,[65] Retinomax autorefractor,[65, 106] Stereo Smile II test,[65] Power Refractor II,[65] Palm-Automatic Refractometer,[106] and SureSight Vision Screener.[65, 102]

KQ 4. Benefits of Treatment of Amblyopia, Its Risk Factors, and Refractive Error

We included one fair- and two good-quality trials that evaluated benefits of treatment (**Table 5**).[115-117] All three trials were included in the previous review.[67] All trials evaluated patching for amblyopia or amblyopic risk factors. Two of the included trials compared patching with no patching (children were pretreated with eyeglasses if indicated in both groups),[116, 117] and one compared patching plus eyeglasses versus eyeglasses alone versus no treatment.[115] One trial included a run-in phase, during which all participants wore updated eyeglass prescriptions until visual acuity in the amblyopic eye stopped improving;[116] another trial treated children with refractive error with 6 weeks of corrective lenses prior to allocation.[117] None of the included studies evaluated atropine or vision therapy. Sample sizes ranged from 60[117] to 180.[116] The trials enrolled preschoolers with a mean age ranging from 4 to 5.2 years. All three studies included children based on visual acuity criteria. Only one of the three trials (the one that compared patching plus eyeglasses vs. eyeglasses alone vs. no treatment) enrolled screen-detected children.[115] Duration of treatment (and followup) was different in each trial: 5 weeks (1 year),[116] 12 weeks (12 weeks),[117] and 1 year (1.5 years).[115] All included trials were conducted in the United States[116] or the United Kingdom.[115, 117] Most of the trials reported different outcome measures. Of the three studies, two measured best corrected visual acuity[115, 116] and one measured improvement in visual acuity as a secondary outcome.[117] We did not pool results primarily because of differences in populations (e.g., eligibility criteria, baseline visual acuity), outcome measures, comparisons, and duration of followup. Overall, the trials indicate that treatment of amblyopia or its risk factors results in small improvements in visual acuity, on average.

Patching Versus No Patching

Two of the three trials compared patching with no patching (**Table 5**).[116, 117] First, one good-quality trial from the Pediatric Eye Disease Investigator Group[116] randomized 180 children whose baseline mean logMAR acuity was 0.56 (approximate Snellen equivalent of 20/75). After adjusting for baseline acuity, children treated with 2 hours per day of patching had better visual acuity in the amblyopic eye (mean logMAR visual acuity, 0.44 [equivalent Snellen, 20/50]) than those in the no-patching group (mean logMAR acuity, 0.51 [Snellen equivalent, 20/63]) at the end of the 5-week trial (adjusted mean difference in logMAR, 0.07 [95% CI, 0.02 to 0.12]). Visual acuity in the amblyopic eye had improved by an average of 1.1 lines in the patching group and 0.5 lines in the no-patching group (a difference of <1 line on a standard visual acuity chart). The investigators also found a difference of 0.10 (95% CI, 0.05 to 0.14) between treatment groups in mean best logMAR acuity (achieved at any visit) adjusted for baseline acuity at followup (including visits from week 5 through at least week 17). The proportion of children who experienced an improvement of at least 2 lines on the visual acuity chart was greater in the patching group than in the no-patching group (45% vs. 21%; p=0.003).

The second trial randomized 60 children with strabismic or mixed amblyopia to 3 hours of patching per day, 6 hours of patching per day, or no patching.[117] The mean baseline logMAR acuity in the amblyopic eye was 0.63, 0.69, and 0.59 (approximate Snellen equivalents of 20/85, 20/100, and 20/80) in the three treatment groups, respectively. The trial focused primarily on assessing compliance but also reported visual acuity among secondary outcomes. It reported no statistically significant differences between groups in mean visual acuity improvement after 12 weeks (0.29 vs. 0.34 vs. 0.24, respectively; p=0.11; approximate Snellen equivalents of 1.9, 2.3, and 1.6 lines, respectively). However, the effect estimates trended in favor of the patching groups, compliance was suboptimal (participants wore patching for 58% of the prescribed time in the 3-hour group [mean, 103 minutes] and for 41% in the 6-hour group [mean, 153 minutes]), and the study was underpowered to find a small difference between groups.

Patching Plus Eyeglasses Versus Eyeglasses Alone Versus No Treatment

One good-quality trial compared patching plus glasses, glasses alone, and no treatment among preschoolers (N=177) with unilateral refractive error.[115] The mean baseline logMAR acuity in the amblyopic eye for these 177 children was 0.36 (approximate Snellen equivalent, 20/45). The hours per day of patching were not reported. The trial found that both treatment conditions resulted in better visual acuity at 1 year compared with no treatment (mean difference in best corrected visual acuity between patching plus eyeglasses and no treatment, 0.11 logMAR [95% CI, 0.05 to 0.17]; mean difference between glasses alone and no treatment, 0.08 [95% CI, 0.02 to 0.15]). The differences between groups in acuity were not significant at 6 months posttrial, after all groups had received treatment (after the 1-year followup visit, children in the no-treatment and glasses-only groups received treatment following the same protocol as those in the combined treatment group).

Atropine

We found no eligible studies that examined atropine.

Vision Therapy

We found no eligible studies that examined vision therapy.

Treatment Differences for Subgroups

Two of the included trials[115, 116] examined treatment outcomes for subgroups defined by baseline visual acuity. First, the good-quality trial from the Pediatric Eye Disease Investigator Group (N=180) assessed subgroups with either moderate (20/40 to 20/100) or severe (20/125 to 20/400) amblyopia at baseline.[116] Findings for these subgroups were similar to the overall trial results for the primary outcome, visual acuity in the amblyopic eye. Second, the good-quality trial that compared patching plus eyeglasses, eyeglasses alone, and no treatment among preschoolers (N=177) assessed subgroups defined by baseline visual acuity abnormality.[115] The authors assessed children with mild (0.18 to 0.30 logMAR) and moderate or worse (≥0.48 logMAR) refractive error at baseline and examined differences between treatment groups. For children with moderate refractive error at baseline, patching plus eyeglasses resulted in much greater

improvement than no treatment at 1 year (0.27 logMAR [95% CI, 0.14 to 0.39]) compared with improvement for all participants (0.11 logMAR [95% CI, 0.05 to 0.17]); the difference between eyeglasses alone and no treatment did not reach statistical significance, but the estimate of effect was also larger in this subgroup (0.11 logMAR [95% CI, -0.03 to 0.24]) than for all participants (0.08 logMAR [95% CI, 0.02 to 0.15]). For children with mild refractive error at baseline, neither patching plus eyeglasses nor glasses alone was significantly different than no treatment at the end of the trial (between-group differences were negligible [0.04 to 0.05 logMAR]; improvements were small in all three groups [from 0.19 to 0.24 logMAR]).

KQ 4b. Long-Term Amblyopia, School Performance, Functioning, and Quality of Life

We found no eligible studies that examined these outcomes.

KQ 5. Harms of Treatment of Amblyopia, Its Risk Factors, and Refractive Error

We included one fair- and two good-quality trials (described in four articles) that evaluated harms of treatment (**Table 5**).[115-118] Two of the included trials compared patching with no patching (children were pretreated with eyeglasses if indicated),[116, 117] and one compared patching plus eyeglasses versus eyeglasses alone versus no treatment.[115] None of the included studies evaluated atropine. Sample sizes ranged from 60[117] to 180.[116] All three enrolled preschoolers with a mean age ranging from 4 to 5.3 years. Duration of treatment (and followup) varied from 5 weeks (1 year)[116] to 12 weeks (12 weeks)[117] to 1 year (1.5 years).[115] A single trial reported each outcome for which we found evidence; none of the included trials reported on similar outcomes. Overall, the trials provide limited evidence but suggest that patching may have some psychological harms.

Harms to the Nonamblyopic Eye

One trial comparing patching (n=87) with no patching (n=93) found that worsening visual acuity (decrease >1 line from baseline) in the nonamblyopic eye was not significantly different between groups at 5 weeks (2.4% vs. 6.8%, respectively; p=0.28).[116] There was also no difference between treatment groups on the Randot Preschool Stereoacuity Test (p=0.6). Among children with no ocular deviation at baseline (n=118), five patients in the patching group and three patients in the no-treatment group had a new small-angle strabismus (1 to 8 PD), and one patient in the no-treatment group had a new strabismus of more than 8 PD.

Loss of Visual Acuity in the Amblyopic Eye

The trial comparing patching plus eyeglasses (n=59), eyeglasses alone (n=59), and no treatment (n=59) found no statistically significant difference between treatment groups at the 1-year followup in proportion of children with worsening of uncorrected visual acuity in the amblyopic eye (change >0.1 logMAR) among those with baseline mild acuity loss (9.7% vs. 6.5% vs. 13.3%; p=0.28) or baseline moderate acuity loss (15.0% vs. 11.1% vs. 23.8%; p=0.13); trends

favored fewer children with loss of visual acuity in the treatment groups than in the no-treatment group.[115]

Psychological Harms

A substudy[118] of the trial[115] that compared patching plus eyeglasses, eyeglasses alone, and no treatment examined the emotional status of children undergoing treatment (144/177 participants completed questionnaires) and found there was no difference between treatment groups with regard to the child being happy, cooperative, or good tempered most or all of the time; teasing by siblings or friends; problems at preschool; or mean Rutter behavior score (a validated scale assessing emotional and behavioral problems in children). Parents completed a questionnaire assessing these items on a 4- or 5-point rating scale at baseline (all participants), 3 months after beginning treatment (participants in active treatment only), and 2 years after recruitment (all participants). However, the study reported that children were more upset by patching plus eyeglasses than by eyeglasses alone; less than a third of children wearing glasses were upset by treatment compared with more than half of children wearing patching and glasses (29% vs. 85% at age 4 years; p=0.03; 26% vs. 62% at age 5 years; p=0.005). Although the study reported some negative effects of glasses or patching for the child (difficulty wearing patch or glasses, upset, coping with treatment) and parent (worry about treatment, upset by treatment, arguments about treatment), it did not compare with psychosocial outcomes for the no-treatment group. Therefore, we are unable to determine how the reported psychosocial harms compared with no treatment.

Other Harms

One trial (N=60) comparing no treatment, patching for 3 hours per day, or patching for 6 hours per day reported that no patients experienced an adverse event, such as inverse amblyopia or patch allergy.[117]

Chapter 4. Discussion

Summary of Evidence

Table 6 provides a summary of findings in this evidence review. This table is organized by KQ and provides a summary of outcomes along with a description of consistency, precision, quality, body of evidence limitations, strength of evidence grade, and applicability.

Benefits and Harms of Screening

For our overarching question (KQ 1), we did not identify any eligible RCTs that directly compared screening with no screening. We graded the strength of evidence as low because of unknown consistency (with a single study making each comparison), imprecision, and quality. The two included studies, one prospective cohort and one RCT, evaluated different comparisons. Both focused on the outcome of amblyopia prevalence at age 7.5 years; neither reported school performance, functioning, or quality of life. The prospective cohort study compared screening (at age 37 months) with no screening and found no statistically significant difference between screened and nonscreened groups for any definition of amblyopia.[76] The RCT compared more intensive screening (at ages 8, 12, 18, 25, 31, and 37 months) with screening at age 37 months and found an approximately 1 percent lower prevalence of amblyopia at age 7.5 years and large relative reductions (RR, 0.55 and 0.35) for intensive screening (at ages 8, 12, 18, 25, 31, and 37 months) than for screening at age 37 months, although the difference was only statistically significant for one of two definitions of amblyopia.[74, 75] The main limitation of both studies was high overall attrition (approximately 50%). The findings are applicable to healthy preschool-age children who receive vision screening at ages 4 to 5 years as part of usual care. Trained orthoptists conducted screening examinations in both studies.

For harms of screening (KQ 3), we found limited evidence. Evidence included one prospective cohort study that showed a reduction in harm (i.e., less school-age bullying by age 8 years) among patched children screened in preschool compared with patched children not screened in preschool.[114] We found no studies reporting other measures of psychosocial distress, labeling, or anxiety. We graded the strength of evidence as low for the bullying outcome (downgraded because of unknown consistency, imprecision, and quality). In theory, although both glasses and patching have been reported to increase the risk of being bullied,[38] preschool screening may allow for treatment before school starts, thus avoiding potential bullying and psychosocial distress. Repeatedly being subjected to bullying is associated with physical and emotional problems and may lead to long-term adverse effects.[119, 120]

Harms of preschool vision screening might include unnecessary referrals due to false-positive results, overdiagnosis, or unnecessary treatment. We calculated false-positive rates using studies of test accuracy and found, similar to the previous review on this topic,[67, 121] that screening tests are associated with high false-positive rates among populations with a low prevalence of vision abnormalities. We graded the strength of evidence for false-positive rates as moderate (downgraded because of fair, as opposed to good, quality of the individual studies and the related

methodological limitations). Calculated rates were reasonably consistent across studies of similar prevalence and were reasonably precise. We found no eligible studies directly examining whether false-positive screening results lead to unnecessary treatments or subsequent long-term vision or functional impairments. A large (N=102,508) retrospective uncontrolled study from a statewide photoscreening program in Tennessee that did not meet eligibility criteria (because it lacked a control group) found that 19.5 percent (174/890) of children with false-positive screening results were prescribed glasses.[122]

Accuracy and Reliability of Screening Tests

Estimates for all tests suggest utility for identifying children at higher risk for amblyopia risk factors or other visual conditions. PLRs were in the moderate range (5 to 10) for most studies, although some studies found lower or higher PLRs, and most studies that evaluated combinations of clinical tests found high (>10) PLRs. The VIP study, the largest study to directly compare multiple tests, generally found similar accuracy across tests. We graded the strength of evidence for studies of test accuracy as low, because of imprecision and considering our quality assessments of the individual studies. Common methodological limitations of studies included high (or not reported) rates of uninterpretable results or noncompliance with tests, not reporting whether uninterpretable results or noncompliance were included in analyses, lack of a representative spectrum, and lack of a random or consecutive sample.

Findings are applicable to a variety of settings and screening personnel. Studies were conducted in Head Start, school, community, primary care, and ophthalmology settings, although only two studies were conducted completely[89] or partly[100] in primary care settings.[100] Screening was administered by an array of personnel across studies, including pediatricians, eye professionals, nurses, and trained laypersons, indicating that many types of personnel can conduct screening.

We found that accuracy did not clearly differ for preschool-age children in different age groups. However, unlike studies of photoscreeners, most studies of clinical test accuracy did not enroll children younger than age 3 years. Data were relatively limited and estimates were somewhat imprecise, but studies did not find any clear differences in accuracy of tests when results were stratified according to age.

Testability may limit the utility of some screening tests, especially clinical tests, in children younger than age 3 years. Although relatively few of the included studies assessed changes in testability by age, those that did generally found better testability in the older preschool age (3 years or older), and some reported very low testability rates with visual acuity and stereoacuity tests for those younger than age 3 years. In contrast, some data suggest that photoscreeners have high testability rates for children as young as age 1 year (e.g., a statewide photoscreening program administered by a volunteer lay network in Tennessee found that 1-year-olds had testability rates of 94%).[123]

Benefits and Harms of Treatment of Amblyopia, Its Risk Factors, and Refractive Error

Our review found some evidence of moderate strength supporting the effectiveness of some treatments for improving visual acuity outcomes, although improvements were small, on average. We found no studies that evaluated potential effectiveness of treatments for reducing long-term amblyopia or for improving school performance, functioning, or quality of life, and no eligible studies that evaluated atropine or vision therapy. The three included trials all enrolled children age 3 years or older, and applicability to those younger than age 3 years is unclear. The trials varied somewhat in the populations (children with amblyopic risk factors pretreated with glasses or not pretreated with glasses) and interventions/comparisons (two evaluated patching vs. no patching; one compared patching plus glasses vs. glasses alone vs. no treatment). The trial that compared patching plus eyeglasses, eyeglasses alone, and no treatment enrolled screen-detected children, demonstrating the applicability of findings to the main population of interest for this review.[115]

Taken together, the trials provide evidence of moderate strength that: 1) patching improves visual acuity of the amblyopic eye by an average of less than 1 line on the Snellen chart after 5 to 12 weeks compared with no patching among children with amblyopic risk factors pretreated with glasses, 2) patching plus glasses improves visual acuity by about 1 line after 1 year compared with no treatment among children with amblyopic risk factors not pretreated with glasses, and 3) glasses alone improve visual acuity by less than 1 line after 1 year compared with no treatment among children with amblyopic risk factors. Of note, the magnitude of improvement for patching plus glasses or glasses alone was greater among children with worse baseline visual acuity. Few trials reported binary outcomes that may facilitate determination of how many participants achieved a clinically meaningful change, although one trial reported that more children treated with patching than with no patching experienced improvement of at least 2 lines (45% vs. 21%; p=0.003).[116]

For adverse effects of treatment, we found limited evidence, with a single trial reporting each outcome for which we found data. We graded the strength of evidence as low, downgrading because of unknown consistency (with a single study for each outcome) and imprecision. The trials suggest that patching does not worsen visual acuity in the nonamblyopic eye but that it may be associated with some psychological harms, because child or parental upset/worry about treatment was greater with patching than with glasses alone. However, the study reporting the association did not compare this outcome with an untreated group, and it is uncertain whether upset/worry from treatment is greater than what might result from an untreated vision problem.

Minimal Clinically Meaningful Changes in Visual Acuity

Definitions for a clinically important change in visual acuity in young children vary across studies. Recent studies consider a change of 0.2 logMAR (about 2 lines on the Snellen chart) as the minimal clinically important change.[124-128] Others consider smaller changes clinically meaningful, generally between 0.10 logMAR (about 1 line on the Snellen chart) and 0.15 logMAR (between 1 and 2 lines).[115, 129, 130] When assessing whether improvement in visual

acuity represents a clinically meaningful change, practitioners may also consider that visual impairment associated with amblyopia can become permanent and may limit functioning for the lifetime of a child.[23, 131]

Some of the variation in defining a clinically important change is likely associated with the lack of consensus about the minimum perceptible change in acuity. That, largely, is due to varying ranges of test-retest reliability, both within and between the available screening tests.[132, 133] Visual acuity test results may be influenced by factors[134] such as ambient lighting in the testing room, lighting of the test target, design of the test chart, the child's pupil size, and the person administering the test. Test-retest reliability for the most common vision screening tests shows that visual acuity can vary by roughly 0.10 logMAR (1 line) between administrations, independent of any real change in acuity.[127, 129, 130, 135, 136] As a result, large treatment studies have calculated sample size requirements based on the ability to detect a change of at least 0.1 logMAR between treatment groups.[137-140]

Limitations

Our review has some limitations. For studies of test accuracy conducted in ophthalmology settings, details about the study participants were sometimes limited, making it difficult to determine whether participants had known impaired visual acuity or obvious symptoms of impaired visual acuity. Thus, we may have included some studies that would not meet eligibility criteria if additional description of the study populations was available. Next, studies of test accuracy were most commonly conducted in Head Start programs, schools, the community, or ophthalmology clinics; primary care clinics were rarely involved, and applicability of findings to primary care settings is therefore less certain.

We did not include comparative effectiveness (i.e., head-to-head) studies, such as those comparing atropine with patching. The previous review for the USPSTF identified head-to-head trials that compared different patching regimens (e.g., 2- vs. 6-hour per day patching), different atropine regimens (daily vs. weekend atropine), and patching versus atropine.[137, 139-143] The review concluded that the trials found no differences in visual acuity improvement in the amblyopic eye between the treatments.

For studies evaluating adverse effects of treatment, eligible studies were required to have a concurrent control group, and we did not include head-to-head comparative effectiveness studies (e.g., comparing patching with atropine). Because they lack an inactive treatment control group, head-to-head studies do not provide evidence on whether treatment increases the risk of adverse effects compared with no treatment. A previous systematic review for the USPSTF summarized adverse effects from head-to-head trials and found that patching (vs. atropine) and atropine plus a plano lens (vs. atropine alone) were associated with an increased risk of temporary worsening of visual acuity ($\geq$2 lines or $\geq$1 line) in the nonamblyogenic eye in two trials, but visual acuity subsequently returned to baseline in nearly all children.[67] The review noted that two other trials found no difference in risk for visual acuity loss in the nonamblyopic eye when comparing different patching or atropine regimens.[67] Previous head-to-head studies examining atropine have noted that commonly reported adverse effects include light sensitivity, lid/conjunctival irritation,

eye pain/headache, and facial flushing.[137, 141] Skin irritation was also reported as an adverse effect of patching in one study.[137] One head-to-head study of patching and atropine found that both treatments were well tolerated but that patching had worse subscale scores for adverse effects, difficulty with compliance, and social stigma.[137] Another qualitative study of children with amblyopia found that children undergoing treatment often felt self-conscious, embarrassed, and ashamed, and these concerns were predominantly related to glasses or patching.[144] Overall, most of the adverse effects identified in various head-to-head studies were mild and resolved after treatment completion.

Finally, we excluded studies published in languages other than English and those conducted in countries not categorized as "very high" on the Human Development Index, as defined by the United Nations Development Programme.

Future Research Needs

We identified multiple evidence gaps that could be addressed with future research. We found no RCTs evaluating the effectiveness of screening (compared with no screening) and no good-quality RCTs evaluating when to begin screening (e.g., comparing initiation prior to age 3 years with initiation after age 3 years) or assessing various screening intervals. In addition, none of the included trials of screening or treatment assessed effectiveness for improving important health outcomes such as school performance, functioning, or quality of life; all trials focused on visual acuity outcomes. Next, although evidence generally supports the accuracy of screening tests, it does not establish which approach to screening or which combination of screening tests is the best. Finally, we found very little evidence from primary care settings on the accuracy of screening tests.[100]

Conclusion

Studies that directly evaluated the effectiveness of screening were limited (because of study designs, attrition, imprecision, and quality) and do not establish whether vision screening in preschool-age children is better than no screening. All included studies that evaluated the effectiveness of screening or treatment reported visual acuity outcomes; none evaluated school performance, functioning, or quality of life. Indirect evidence supports 1) the accuracy of multiple screening tests for identifying preschool-age children at higher risk for amblyopia risk factors or other visual conditions (most studies found that abnormal results moderately increased the likelihood of target conditions), and 2) the effectiveness of some treatments for improving visual acuity outcomes, although improvements were small, on average. Evidence on potential adverse effects of screening was limited but indicated a reduction in bullying and high false-positive rates in low-prevalence populations.

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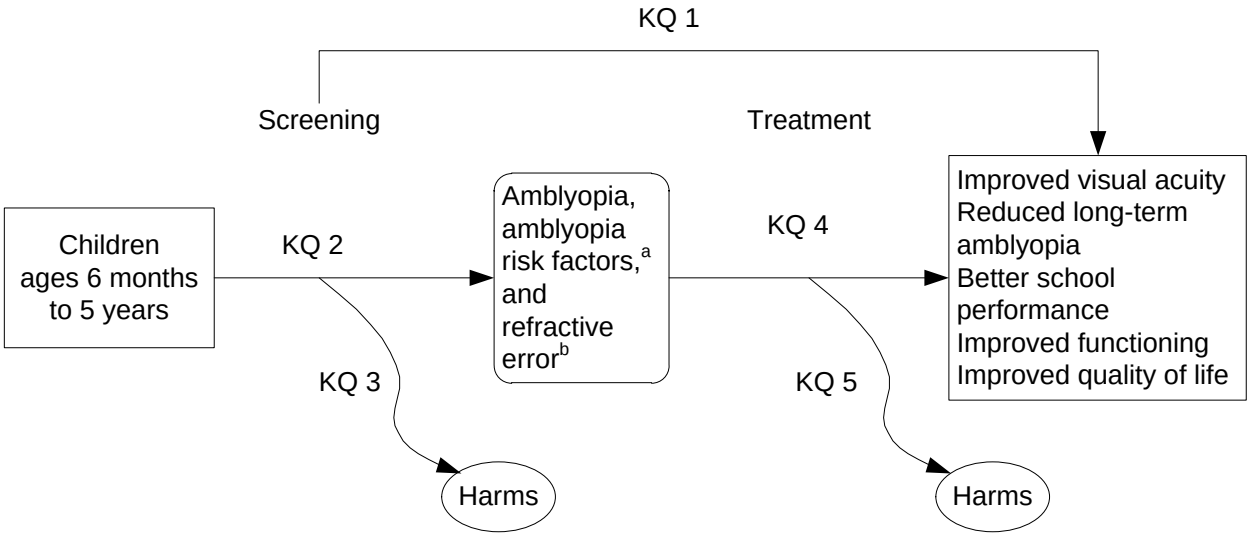
Figure 1. Analytic Framework



Abbreviation: KQ=Key Question.

[a] Amblyopia risk factors include anisometropia, strabismus, hyperopia, any media opacity, astigmatism, and abnormal visual acuity (which includes substantial isoametropic refractive error).
[b] Determination of refractive error will be based on age-appropriate standards.

KQs to Be Systematically Reviewed

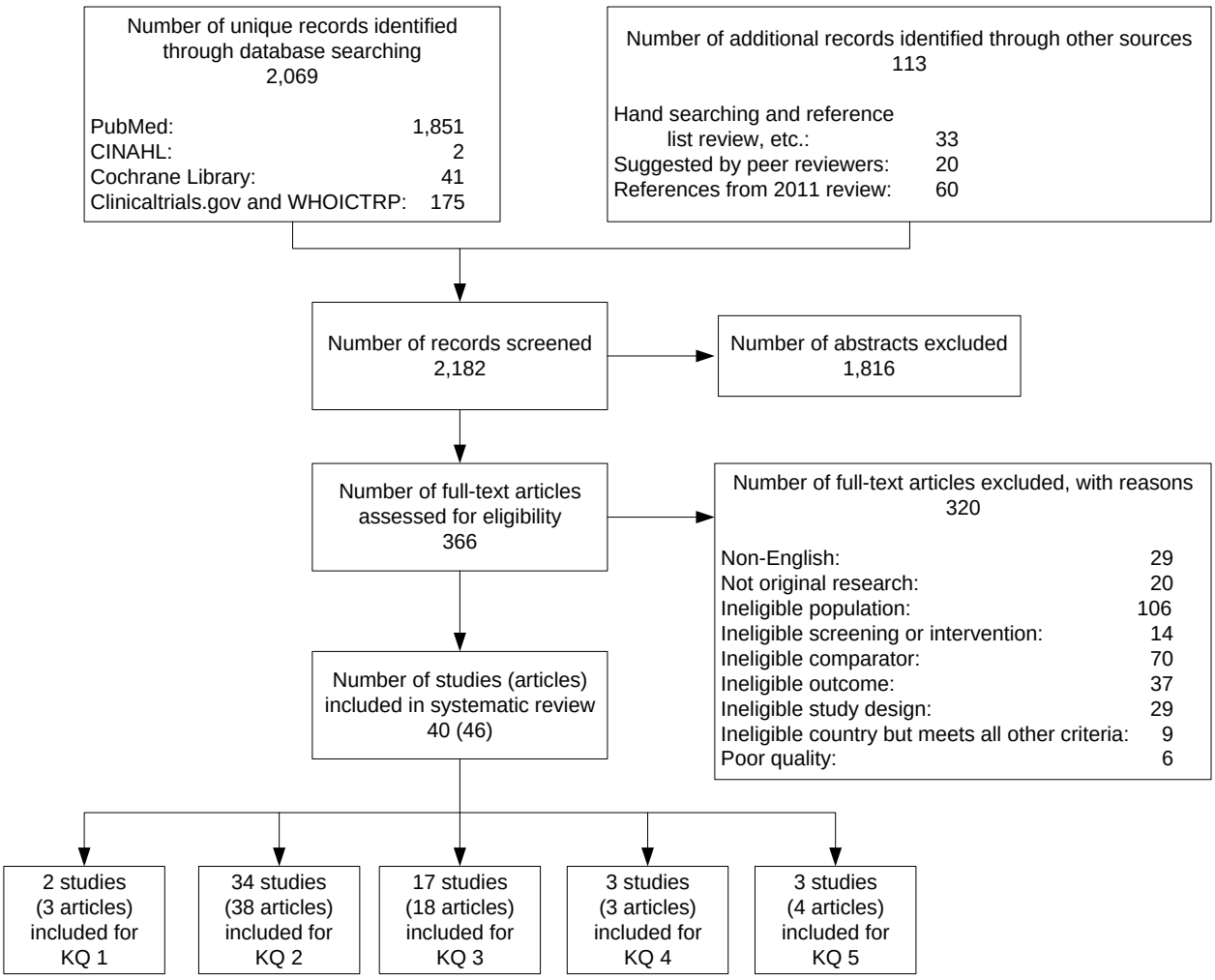
1. Does screening for amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years reduce long-term amblyopia or improve visual acuity, school performance, functioning, and/or quality of life?
    a. Does the effectiveness of screening in children ages 6 months to 5 years vary among different age groups?
2. What are the accuracy and reliability of screening tests for amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years?
    a. Do the accuracy and reliability of screening tests for amblyopia, its risk factors, and refractive error vary among different age groups?
3. What are the harms of screening for amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years?

4a. Does treatment of amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years improve visual acuity?

4b. Does treatment of amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years reduce long-term amblyopia or improve school performance, functioning, and/or quality of life?

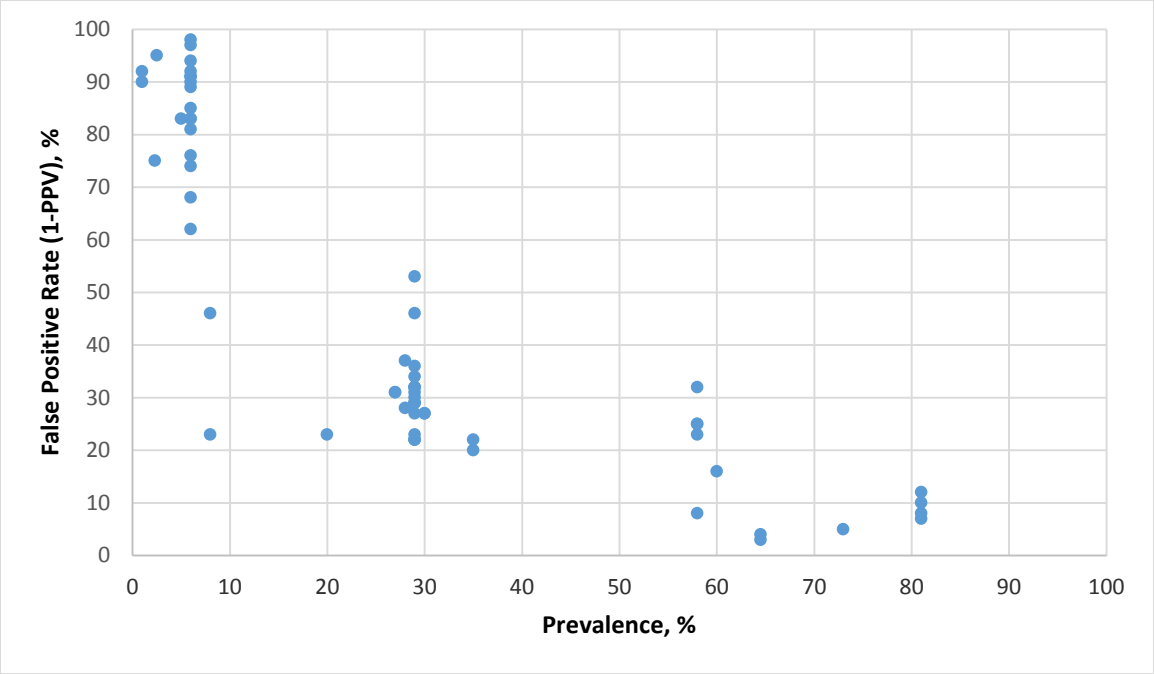
5. What are the harms of treating amblyopia, its risk factors, and refractive error in children ages 6 months to 5 years?

Figure 2. Summary of Evidence Search and Selection Diagram



Note: The sum of the numbers of studies/articles per KQ exceeds the total number of studies/articles because some studies/articles were included in multiple KQs.

Figure 3. Relationship Between Prevalence of Vision Problems and False-Positive Rates in 16 Studies



Abbreviation: PPV=positive predictive value.

Table 1. Risk Factors for Amblyopia[a]

Age, Months	Risk Factor
12 to 30	Astigmatism >2.0 D Hyperopia >4.5 D Anisometropia >2.5 D Myopia >-3.5 D
31 to 48	Astigmatism >2.0 D Hyperopia >4.0 D Anisometropia >2.0 D Myopia >-3.0 D
>48	Astigmatism >1.5 D Hyperopia >3.5 D Anisometropia >1.5 D Myopia >-1.5 D
All ages[b]	Manifest strabismus >8 PD in primary position Media opacity >1 mm

[a] Adapted from Donahue et al, 2013.[145]
[b] Ptosis has been removed from the list because nearly all amblyopia-related ptosis occurs in the setting of superimposed anisometropia.[145]

Abbreviations: D=diopter; PD=prism diopter.

Table 2. Screening Tests for Visual Impairment Used in or Available in Primary Care Settings

Screening Test	Description of Test
Photoscreening	A trained observer evaluates images of corneal light reflexes from a calibrated camera; binocular; also assesses visual acuity
Corneal light reflex test (Hirschberg test)	Symmetric light reflex in both pupils from light held 2 feet away; can also detect cataracts and tumors
Cover-uncover test (cross cover test)	Alignment changes when covering or uncovering a single focusing eye
Simultaneous red reflex test (Bruckner test)	Equal red reflexes when viewed through ophthalmoscope; can also detect cataracts and tumors
Autorefractive screening	Estimates refractive error using an automated device; monocular; does not assess ocular alignment
Picture identification tests (Allen Cards, LEA Symbols)	Figure identification from various distances
HOTV	Identification of letters HOTV; letters gradually decrease in size
Snellen	Letter or number identification; letters or numbers gradually decrease in size
Tumbling E	Identification of the direction of arms of the letter E; letters gradually decrease in size
Contour stereotests (Frisby, Random Dot E, Stereo Smile, Titmus Fly, TNO)	Use of polarized glasses and stereo cards to determine whether a child can correctly identify a 3-dimensional image
Moving Dynamic Random Dot Stereosize test[146]	Computer-generated moving stereotest dots

Table 3. Characteristics and Results of Studies Included for KQ 1

Author, Year Study	Overall N and N Participants in Each Group	Subject Age, Sex	Country and Setting	Screening Intervention vs. Control	Main Results
Williams et al, 2001[74] and 2002[75] RCT	N randomized: 3,490 (2,029 intensive screening,1,490 one-time screening) N analyzed at age 7.5 years: 1,914	Age: Initially tested at age 8–37 months and followed to age 7.5 years Sex: 48% female (of those analyzed)	United Kingdom Orthoptic clinic in community	Screening at ages 8, 12, 18, 25, 31, and 37 months[a] vs. screening at age 37 months[b]	Amblyopia A[c] at age 7.5 years: 1.5% (16/1,088) vs. 2.7% (22/826); RR, 0.55 (95% CI, 0.29 to 1.04) Amblyopia B[d] at age 7.5 years: 0.6% (69/1,088) vs. 1.8% (15/876); RR, 0.35 (95% CI, 0.15 to 0.86) Residual amblyopia A in children treated with occlusion: 25% (10/40) vs. 8% (3/40); OR, 1.56 (95% CI, 0.62 to 3.92) Residual amblyopia B in children treated with occlusion: OR, 4.11 (95% CI, 1.04 to 16.29) Mean visual acuity in worse eye after patching treatment (adjusted for confounding variables): 0.15 (95% CI, 0.083 to 0.22) vs. 0.26 (95% CI, 0.17 to 0.35); p<0.001
Williams et al, 2003[76] Prospective cohort	N eligible: NR N analyzed at age 7.5 years: 6,081 (1,516 were screened at age 37 months, 4,565 were not)	Age: Cohort tested at age 7.5 years; screening offered at age 37 months Sex: 47% female (of those analyzed)	United Kingdom Orthoptic clinic in community	Screening[e] at age 37 months vs. no screening	Amblyopia A[c] at age 7.5 years: 1.1% (11/1,019) vs. 2.0% (100/5,062); adjusted OR[f], 0.63 (95% CI, 0.32 to 1.23) Amblyopia B[d] at age 7.5 years: 0.7% (7/1,019) vs. 1.3% (65/5,062); adjusted OR[f], 0.72 (95% CI, 0.32 to 1.60) Amblyopia C[g] at age 7.5 years: 1.9% (19/1,019) vs. 3.4% (171/5,062); adjusted OR[f], 0.65 (95% CI, 0.38 to 1.10) Mean visual acuity in worse eye after patching treatment (adjusted for confounding variables): 0.14 (95% CI, 0.11 to 0.18) (n=25) vs. 0.22 (95% CI, 0.20 to 0.23) (n=166); p<0.0001

[a] Cover-uncover test; Cardiff cards at ages 8 and 12 months; Cardiff and Kays pictures test at ages 18, 25, and 31 months; Kays picture test and HOTV Crowded Symbols Distance Visual Acuity Test at age 37 months; noncycloplegic autorefraction (performed at all visits but only used for referral at age 37 months).
[b] Cover-uncover test; Kays picture test and HOTV test; noncycloplegic autorefraction.
[c] Amblyopia A=interocular difference in acuity ≥0.2 logMAR (2 lines on chart).
[d] Amblyopia B=interocular difference in acuity ≥0.3 logMAR.
[e] Kays pictures or Sheridan Gardiner singles visual acuity test, cover-uncover test, and 20 diopter prism or stereopsis test (or both).
[f] Adjusted for sex, highest level of maternal education, birth weight, family history of strabismus/amblyopia, and duration of breastfeeding.
[g] Amblyopia C=visual acuity in amblyopic eye 0.18 logMAR or worse (6/9 or worse).

Abbreviations: CI=confidence interval; KQ=key question; logMAR=logarithm of the minimum angle of resolution; N=number; NR=not reported; OR=odds ratio; RCT=randomized, controlled trial; RR=relative risk.

Table 4. Summary of Main Results From Studies of Diagnostic Accuracy of Preschool Vision Screening Tests (KQ 2)

Author, Year	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 (6 studies)					
Bertuzzi et al, 2006[81]	Amblyopia risk factors	0.96 (0.78 to 1.0)	0.83 (0.75 to 0.90)	5.7 (3.8 to 8.6)	0.05 (0.01 to 0.36)
Miller et al, 1999[97]	Significant refractive error	0.91 (0.82 to 0.96)	0.44 (0.37 to 0.52)	1.6 (1.4 to 1.9)	0.21 (0.10 to 0.43)
Miller et al, 2001[98]	Astigmatism	0.93 (0.87 to 0.97)	0.51 (0.44 to 0.57)	1.9 (1.6 to 2.2)	0.14 (0.08 to 0.27)
Schmidt (VIP) et al, 2004[65]	Amblyopia risk factors or significant nonamblyogenic refractive error	0.61 (0.56 to 0.66)[a]	0.90 (0.88 to 0.92)[a]	6.1 (4.8 to 7.6)[a]	0.43 (0.38 to 0.50)[a]
VIP Study Group, 2005[108] Phase II; nurse screener	Amblyopia risk factors or significant nonamblyogenic refractive error	0.49 (0.44 to 0.54)	0.90 (0.88 to 0.92)	4.9 (4.0 to 6.0)	0.57 (0.52 to 0.62)
VIP Study Group, 2005[108] Phase II; lay screener	Amblyopia risk factors or significant nonamblyogenic refractive error	0.37 (0.32 to 0.42)	0.90 (0.88 to 0.92)	3.7 (3.0 to 4.7)	0.70 (0.65 to 0.76)
VIP Study Group, 2010[107] Phase I, year 1	Amblyopia risk factors or significant nonamblyogenic refractive error	Ranged from 0.57 (0.46 to 0.67) to 0.65 (0.54 to 0.75)[c]	Ranged from 0.90 (0.84 to 0.94) to 0.92 (0.87 to 0.95)[c]	Ranged from 5.95 (3.58 to 9.88) to 7.39 (4.57 to 11.93)[c]	Ranged from 0.39 (0.29 to 0.52) to 0.47 (0.37 to 0.60)[c]
Crowded HOTV Visual Acuity Test (2 studies)					
VIP Study Group, 2004[65]	Amblyopia risk factors or significant nonamblyogenic refractive error	0.54 (0.49 to 0.59)[a]	0.89 (0.87 to 0.91)[a]	4.9 (3.9 to 6.1)[a]	0.52 (0.46 to 0.58)[a]
VIP Study Group, 2010[107]	Amblyopia risk factors or significant nonamblyogenic refractive error	Ranged from 0.46 (0.33 to 0.59) to 0.57 (0.46 to 0.67)[c]	Ranged from 0.87 (0.82 to 0.91) to 0.92 (0.87 to 0.95)[c]	Ranged from 3.76 (2.27 to 6.22) to 6.83 (4.21 to 11.10)[c]	Ranged from 0.47 (0.37 to 0.60) to 0.62 (0.49 to 0.79)[c]
Stereoacuity Tests					
Random Dot E Stereogram (2 studies)					
Hope et al, 1990[87]	Refractive error or strabismus	0.89 (0.52 to 1.0)	0.76 (0.68 to 0.82)	3.6 (2.5 to 5.2)	0.15 (0.02 to 0.94)
VIP Study Group, 2004[65]	Amblyopia risk factors or significant nonamblyogenic refractive error	0.42 (0.37 to 0.47)[a]	0.90 (0.88 to 0.92)[a]	4.2 (3.3 to 5.3)[a]	0.65 (0.59 to 0.71)[a]
Randot Preschool Stereoacuity Test (1 study)					
Afsari et al, 2013[77]	Amblyopia	Ranged from 0.24 (0.03 to 0.44) to 0.53 (0.25 to 0.77)[d]	Ranged from 0.93 (0.91 to 0.94) to 0.98 (0.97 to 0.99)[d]	Ranged from 7.57 to 12.00[d]	Ranged from 0.51 to 0.78)[d]
Afsari et al, 2013[77]	Anisometropia	Ranged from 0.09 (-0.03 to 0.20) to 0.35 (0.15 to 0.54)[d]	Ranged from 0.93 (0.91 to 0.94) to 0.98 (0.97 to 0.99)[d]	Ranged from 5.0 to 7.5[d]	Ranged from 0.70 to 0.93[d]
Afsari et al, 2013[77]	Strabismus	Ranged from 0.27 (0.12 to 0.42) to 0.48 (0.31 to 0.66)[d]	Ranged from 0.93 (0.92 to 0.95) to 0.99 (0.98 to 0.99)[d]	Ranged from 6.86 to 27.0[d]	Ranged from 0.56 to 0.74[d]
Stereo Smile II Test (3 studies)					
Afsari et al, 2013[77]	Amblyopia	0.50 (0.01 to 0.99)	Ranged from 0.59 (0.55 to 0.64) to 0.95 (0.93 to 0.97)[e]	Ranged from 1.22 to 10[e]	Ranged from 0.84 to 0.58[e]
Afsari et al, 2013[77]	Anisometropia	Ranged from 0.17 (-4 to 38) to 0.33 (0.07 to 0.60)[e]	Ranged from 0.59 (0.54 to 0.64) to 0.95 (0.93 to 0.97)[e]	Ranged from 0.81 to 3.4[e]	Ranged from 0.87 to 1.14[e]

Table 4. Summary of Main Results From Studies of Diagnostic Accuracy of Preschool Vision Screening Tests (KQ 2)

Author, Year	Target Condition	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Afsari et al, 2013[77]	Strabismus	Ranged from 0.50 (0.22 to 0.78) to 0.83 (0.62 to 1.04)[e]	Ranged from 0.60 (0.56 to 0.65) to 0.96 (0.94 to 0.98)[e]	Ranged from 2.08 to 12.5[e]	Ranged from 0.28 to 0.57[e]
VIP Study Group, 2004[65]	Amblyopia risk factors or significant nonamblyogenic refractive error	0.44 (0.39 to 0.49)[a]	0.91 (0.89 to 0.93)[a]	4.9 (3.9 to 6.1)[a]	0.62 (0.56 to 0.67)[a]
VIP Study Group, 2005[108] Phase II; nurse screener	Amblyopia risk factors or significant nonamblyogenic refractive error	0.45 (0.40 to 0.50)	0.90 (0.88 to 0.92)	4.5 (3.6 to 5.6)	0.61 (0.56 to 0.67)
VIP Study Group, 2005[108] Phase II; lay screener	Amblyopia risk factors or significant nonamblyogenic refractive error	0.40 (0.36 to 0.45)	0.90 (0.88 to 0.92)	4.0 (3.2 to 5.0)	0.67 (0.62 to 0.72)
Ocular Alignment Tests					
Cover-Uncover Test (1 study)					
VIP Study Group, 2004[65]	Amblyopia risk factors or significant nonamblyogenic refractive error	0.16 (0.12 to 0.29)	0.98 (0.97 to 0.99)	7.9 (4.6 to 14.0)	0.73 (0.15 to 0.85)
Combined Clinical Tests (4 Studies)					
Barry et al, 2003[80]	Amblyopia or amblyopia risk factors	0.91 (0.71 to 0.99)	0.94 (0.92 to 0.95)	15 (11 to 19)	0.10 (0.03 to 0.36)
Chui et al, 2004[82]	Amblyopia risk factors	0.67 (0.41 to 0.87)	0.86 (0.79 to 0.92)	4.8 (2.8 to 8.4)	0.39 (0.20 to 0.75)
Kennedy et al, 1995[92]	Amblyopia risk factors	0.09 (0.04 to 0.20)	1.0 (0.99 to 1.0)	17 (5.5 to 54)	0.91 (0.84 to 0.99)
Shallo-Hoffman et al, 2004[103]	Amblyopia risk factors	0.73 (0.13 to 0.98)	0.94 (0.90 to 0.96)	12 (4.7 to 28)	0.28 (0.03 to 2.4)
Autorefractors					
Retinomax (8 studies)					
Barry et al, 2001[79]	Amblyopia			1.9 (1.4 to 2.6)	0.35 (0.10 to 1.2)
Kulp, 2014[94] VIP (Phases 1 and 2)	Any significant refractive error: hyperopia >+3.25 D, myopia >2.00 D, astigmatism >1.50 D, and anisometropia >1.00 D IOD in hyperopia, >3.00 D IOD in myopia, or >1.50 D IOD in astigmatism	0.73 (NR)[f]	0.90 (NR)	NR	NR
Miller et al, 1999[97]	Significant refractive error	0.91 (0.82 to 0.96)	0.86 (0.80 to 0.91)	6.7 (4.5 to 9.8)	0.11 (0.05 to 0.22)
Miller et al, 2001[98]	Astigmatism	0.93 (0.88 to 0.96)	0.95 (0.91 to 0.98)	18 (10 to 34)	0.08 (0.04 to 0.13)
VIP Study Group, 2004[65]	Amblyopia risk factors or significant nonamblyogenic refractive error	0.64 (0.60 to 0.67)[a]	0.90 (0.88 to 0.91)[a]	6.1 (5.2 to 7.0)[a]	0.41 (0.37 to 0.45)[a]
VIP Study Group, 2011[106]	Overall	0.78 (0.67 to 0.88)[g]	0.90 (0.83 to 0.95)	7.58 (4.37 to 13.15)	0.24 (0.15 to 0.38)
VIP Study Group, 2011[106]	Amblyopia	0.88 (0.68 to 0.97)	0.90 (0.83 to 0.95)	8.59 (5.27 to 13.99)	0.14 (0.05 to 0.40)
VIP Study Group, 2011[106]	Strabismus	0.70 (0.35 to 0.93)	0.90 (0.83 to 0.95)	7.04 (3.84 to 12.92)	0.33 (0.13 to 0.86)
VIP Study Group, 2011[106]	Refractive error	0.84 (0.71 to 0.92)	0.90 (0.83 to 0.95)	8.11 (4.78 to 13.74)	0.18 (0.10 to 0.33)
VIP Study Group, 2011[106]	Reduced visual acuity	0.70 (0.35 to 0.93)	0.90 (0.83 to 0.95)	7.04 (3.84 to 12.92)	0.33 (0.13 to 0.86)
VIP Study Group, 2005[108] Phase II; nurse screener	Amblyopia risk factors or significant nonamblyogenic refractive error	0.68 (0.64 to 0.72)	0.90 (0.88 to 0.92)	6.8 (5.6 to 8.3)	0.36 (0.31 to 0.41)
VIP Study Group, 2005[108] Phase II; lay screener	Amblyopia risk factors or significant nonamblyogenic refractive error	0.62 (0.57 to 0.66)	0.90 (0.88 to 0.92)	6.2 (5.1 to 7.6)	0.42 (0.38 to 0.48)

Table 4. Summary of Main Results From Studies of Diagnostic Accuracy of Preschool Vision Screening Tests (KQ 2)

Author, Year	Target Condition	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Ying, 2011[111] VIP (Phases 1 and 2)	Group 1 conditions: presumed unilateral amblyopia, suspected bilateral amblyopia, strabismus, severe anisometropia, hyperopia ≥5.0 D, astigmatism ≥2.5 D, or myopia ≥6.0 D	0.87 (NR)[h]	0.90 (NR)	NR	NR
Suresight (7 studies)					
Jost et al, 2015[89]	Amblyopia or strabismus	1.00 (0.02 to 1.0)	0.87 (0.79 to 0.93)	7.9 (4.7 to 13.4)	0.0
Kemper et al, 2005[90]	Amblyopia risk factors	0.85 (0.69 to 0.95)	0.52 (0.40 to 0.63)	1.8[j]	0.29[j]
Kulp, 2014[94]	Any significant refractive error: hyperopia >+3.25 D, myopia >2.00 D, astigmatism >1.50 D, and anisometropia >1.00 D IOD in hyperopia, >3.00 D IOD in myopia, or >1.50 D IOD in astigmatism.	0.68 (NR)[f]	0.90 (NR)	NR	NR
Rogers et al, 2008[102]	Amblyopia risk factors	0.97 (0.88 to 1.0)[i] 0.79 (0.67 to 0.89)[k]	0.38 (0.24 to 0.54)[i] 0.64 (0.48 to 0.78)[k]	1.6 (1.2 to 2.0)[i] 2.2 (1.4 to 3.4)[k]	0.09 (0.02 to 0.37)[i] 0.32 (0.18 to 0.52)[k]
VIP Study Group, 2004[65]	Amblyopia risk factors or significant nonamblyogenic refractive error	0.85 (0.81 to 0.88)[i] 0.63 (0.59 to 0.65)[a]	0.62 (0.59 to 0.65)[i] 0.90 (0.88 to 0.92)[a]	2.2 (2.0 to 2.4)[i] 6.3 (5.2 to 7.4)[a]	0.24 (0.19 to 0.30)[i] 0.41 (0.36 to 0.47)[a]
VIP Study Group, 2005[108] Phase II; nurse screener	Amblyopia risk factors or significant nonamblyogenic refractive error	0.64 (0.60 to 0.68)	0.90 (0.88 to 0.92)	6.4 (5.3 to 7.8)	0.40 (0.35 to 0.45)
VIP Study Group, 2005[108] Phase II; lay screener	Amblyopia risk factors or significant nonamblyogenic refractive error	0.61 (0.56 to 0.66)	0.90 (0.88 to 0.92)	6.1 (5.0 to 7.5)	0.43 (0.39 to 0.49)
Ying, 2011[111] VIP (Phases 1 and 2)	Group 1 conditions: presumed unilateral amblyopia, suspected bilateral amblyopia, strabismus, severe anisometropia, hyperopia ≥5.0 D, astigmatism ≥2.5 D, or myopia ≥6.0 D	0.82 (NR)[h]	0.90 (NR)	NR	NR
Topcon PR 2000 (1 study)					
Williams et al, 2000[110]	Spherical error >3.75 D Anisometropia Astigmatism	0.50 (0.33 to 0.67) 0.74 (0.52 to 0.90) 0.47 (0.28 to 0.66)	0.95 (0.90 to 0.98) 0.95 (0.91 to 0.98) 0.96 (0.92 to 0.99)	9.6 (4.5 to 20) 15 (7.5 to 32) 12 (5.2 to 30)	0.53 (0.38 to 0.73) 0.27 (0.14 to 0.55) 0.55 (0.40 to 0.78)
Plusoptix/Power Refractor (5 studies)					
Arthur et al, 2009[78]	Amblyopia risk factors	0.83 (0.67 to 0.93)	0.95 (0.92 to 0.98)	18 (10 to 33)	0.17 (0.08 to 0.36)
Dahlmann-Noor et al, 2009[85]	Decreased visual acuity, strabismus, and ptosis	0.45 (0.29 to 0.62)	1.0 (0.98 to 1.0)	230 (14 to 3680)	0.56 (0.42 to 0.74)
Dahlmann-Noor et al, 2009[84]	Myopia	0.88 (0.30 to 1.0)	0.96 (0.89 to 0.99)	21 (7.8 to 55)	0.13 (0.01 to 1.7)
	Hyperopia	0.20 (0.10 to 0.35)	0.99 (0.92 to 1.0)	26 (1.6 to 450)	0.81 (0.70 to 0.94)
	Astigmatism	0.75 (0.36 to 0.96)	0.93 (0.86 to 0.97)	11 (4.7 to 24)	0.27 (0.08 to 0.89)
	Anistometropia	0.50 (0.31 to 0.69)	0.87 (0.77 to 0.93)	3.7 (1.9 to 7.1)	0.58 (0.40 to 0.84)

Table 4. Summary of Main Results From Studies of Diagnostic Accuracy of Preschool Vision Screening Tests (KQ 2)

Author, Year	Target Condition	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Matta et al, 2008[96]	Amblyopia risk factors	0.98 (0.85 to 1.0) 0.98 (0.85 to 1.0)	0.68 (0.51 to 0.81) 0.88 (0.74 to 0.96)	3.0 (1.9 to 4.7)[l] 8.4 (3.7 to 19)[a]	0.04 (0.01 to 0.26)[l] 0.03 (0.00 to 0.20)[a]
VIP Study Group, 2004[65]	Amblyopia risk factors or significant nonamblyogenic refractive error	0.54 (0.49 to 0.59)[a]	0.90 (0.88 to 0.92)[a]	5.4 (4.4 to 6.6)[a]	0.51 (0.46 to 0.57)[a]
Palm-Automatic Refractometer (1 study)					
VIP Study Group, 2011[106] Phase II (Pilot)	Overall	0.74 (0.61 to 0.84)[l]	0.90 (0.83 to 0.95)	7.14 (4.10 to 12.43)	0.29 (0.19 to 0.44)
VIP Study Group, 2011[106] Phase II (Pilot)	Amblyopia	0.75 (0.53 to 0.90)	0.90 (0.83 to 0.95)	7.36 (4.38 to 12.36)	0.28 (0.14 to 0.56)
VIP Study Group, 2011[106] Phase II (Pilot)	Strabismus	0.70 (0.35 to 0.93)	0.90 (0.83 to 0.95)	7.04 (3.84 to 12.92)	0.33 (0.13 to 0.86)
VIP Study Group, 2011[106] Phase II (Pilot)	Refractive error	0.84 (0.71 to 0.92)	0.90 (0.83 to 0.95)	8.11 (4.78 to 13.74)	0.18 (0.10 to 0.33)
VIP Study Group, 2011[106] Phase II (Pilot)	Reduced visual acuity	0.30 (0.06 to 0.65)	0.90 (0.83 to 0.95)	3.02 (1.06 to 8.61)	0.78 (0.52 to 1.17)
Photoscreeners					
MTI Photoscreener (6 studies)					
Miller et al, 2001[110]	Astigmatism	0.66 (0.59 to 0.73)	0.71 (0.64 to 0.78)	2.3 (1.8 to 2.9)	0.48 (0.38 to 0.60)
Ottar et al, 1995[100] and Donahue et al, 2002[101]	Amblyopia risk factors	0.82 (0.76 to 0.87)	0.91 (0.88 to 0.93)	8.7 (6.9 to 11)	0.20 (0.15 to 0.27)
Ottar et al, 1995[100] and Donahue et al, 2002[101]	Higher magnitude amblyopia risk factors	0.50 (0.39 to 0.61)	0.98 (0.97 to 0.99)	33 (18 to 58)	0.51 (0.41 to 0.63)
Rogers et al, 2008[102]	Amblyopia risk factors	0.95 (0.86 to 0.99)	0.88 (0.74 to 0.96)	8.0 (3.5 to 18)	0.06 (0.02 to 0.18)
Tong et al, 2000[105]	Amblyopia risk factors	0.56 (0.50 to 0.62)	0.91 (0.84 to 0.96)	6.4 (3.4 to 12)	0.48 (0.42 to 0.56)
VIP Study Group, 2004[65]	Amblyopia risk factors or significant nonamblyogenic refractive error	0.37 (0.32 to 0.42)	0.94 (0.92 to 0.95)	6.2 (4.7 to 8.1)	0.67 (0.62 to 0.72)
Weinand et al, 1998[109]	Amblyopia risk factors	0.83 (range, 0.72 to 0.94)[m]	0.66 (range, 0.42 to 0.74)[m]	2.4 (range, 1.6 to 3.0)[m]	0.26 (range, 0.14 to 0.38)[m]
iScreen Photoscreener (2 studies)					
Kennedy et al, 2000[93]	Amblyopia risk factors	0.92 (0.88 to 0.95)	0.89 (0.83 to 0.94)	8.6 (5.4 to 14)	0.09 (0.06 to 0.13)
VIP Study Group, 2004[65]	Amblyopia risk factors or significant nonamblyogenic refractive error	0.37 (0.32 to 0.42)	0.94 (0.92 to 0.95)	6.2 (4.7 to 8.1)	0.67 (0.62 to 0.72)
VisiScreen 100 Photoscreener (2 studies)					
Cogen et al, 1992[83]	Amblyopia risk factors	0.85 (0.55 to 0.98)	0.94 (0.87 to 0.98)	14 (6.3 to 32)	0.16 (0.05 to 0.59)
Morgan et al, 1987[99]	Amblyopia risk factors	0.91 (0.76 to 0.98)	0.74 (0.52 to 0.90)	3.5 (1.7 to 7.0)	0.12 (0.04 to 0.36)
Otago (Noncommercial) Photoscreener (2 studies)					
Kennedy et al, 1995[92]	Amblyopia risk factors	0.46 (0.22 to 0.72)	1.0 (0.99 to 1.0)	110 (38 to 310)	0.54 (0.33 to 0.89)
Kennedy et al, 1989[91]	Amblyopia risk factors	0.94 (0.87 to 0.98)	0.94 (0.89 to 0.98)	16 (8.2 to 32)	0.06 (0.03 to 0.14)
Off-Axis-Type Photoscreener (1 study)					
Kennedy et al, 1989[91]	Amblyopia risk factors	0.85 (0.76 to 0.91)	0.87 (0.80 to 0.92)	6.5 (4.2 to 10)	0.18 (0.11 to 0.28)

Table 4. Summary of Main Results From Studies of Diagnostic Accuracy of Preschool Vision Screening Tests (KQ 2)

Author, Year	Target Condition	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Retinal Birefringence Scanning					
Pediatric Vision Scanner (1 study)					
Jost et al, 2016[89]	Amblyopia or strabismus	1.00 (0.02 to 1.0)	0.90 (0.83 to 0.96)	10.4 (5.61 to 19.4)	0.0

[a] Based on 90% specificity.
[b] Based on 0.80 acuity score cutoff.
[c] Results stratified by age: 3, 4 years to young, 4 years to old, and 5 years (see Appendix E Table 7).
[d] Results stratified by levels of disparity: 120, 240, and 480 arcsec (see Appendix E Table 1).
[e] Results stratified by levels of disparity: 200, 400, and 800 arcsec (see Appendix E Table 1).
[f] Data presented are for 90% specificity; data for 94% specificity are in Appendix E Table 4.
[g] For all of the "sensitivity" cells for Ciner et al, 2011[106] in this section: data presented are for 90% specificity; data for 94% specificity are in Appendix E Table 4.
[h] Data presented are for 90% specificity; data for additional levels of specificity and for additional groups of conditions are in Appendix E Table 4.
[i] Based on manufacturer's referral criteria.
[j] Confidence intervals not calculable.
[k] Based on VIP 90% specificity criteria.
[l] For all of the sensitivity data cells: data presented are for 90% specificity; data for additional levels of specificity are in Appendix E Table 4.
[m] Based on median results from multiple readers.

Abbreviations: CI=confidence interval; D=diopter; IOD=interocular difference; KQ=key question; NR=not reported; VIP=Vision in Preschoolers.

Table 5. Characteristics and Results of Randomized Trials That Evaluate Treatment of Amblyopia, Its Risk Factors, and Refractive Error (KQs 4 and 5)

Author, Year Study Name Quality	Sample Size Duration	Age Diagnosis	Country Setting	Intervention(s) vs. Control	Main Results
Awan, Proudlock, and Gottlob, 2005[117] Fair	60 12 weeks	Mean age, 4.6 years (range, up to 8) 45% strabismus 42% mixed amblyopia	U.K. Ophthalmology and orthoptic clinics	Patching 3 hours/day Patching 6 hours/day No treatment for 12 weeks Eyeglasses were prescribed for all who needed them (all groups)	*Mean change (SD) in visual acuity* 3-hour patching: 0.29 (0.14) 6-hour patching: 0.34 (0.19) No treatment: 0.24 (0.17) *Snellen equivalent (lines of improvement)* 3-hour patching: 1.9 (1.0) 6-hour patching: 2.3 (1.2) No treatment: 1.6 (0.12)
Clarke et al, 2003[115] Good	177 1 year of treatment (78 weeks followup)	Mean age, 4 years (range, 3 to 5) 72% anisometropia	U.K. 8 eye clinics	Patching + eyeglasses vs. eyeglasses only vs. no treatment	*Mean (SD) best-corrected visual acuity at 1 year* Patching + eyeglasses: 0.19 (0.12) Eyeglasses only: 0.22 (0.17) No treatment: 0.30 (0.20) Mean difference (95% CI) from no treatment: Patching + eyeglasses: 0.11 (0.05 to 0.17) Eyeglasses only: 0.08 (0.02 to 0.15) *In the subgroup with moderate acuity loss at baseline (n=63):* Mean difference (95% CI) from no treatment: Patching + eyeglasses: 0.27 (0.14 to 0.39) Eyeglasses only: 0.11 (-0.03 to 0.24)
Wallace et al, 2006[116] PEDIG Good	180 5 weeks of treatment (≤52 weeks followup)	Mean age, 5.2 years (range, 3 to 7) 23% strabismus, 47% anisometropia, 30% strabismus and anisometropia	U.S. 46 clinical sites	Patching 2 hours/day (with ≥1 hour of near activities) vs. no patching Continued use of eyeglasses if needed, regardless of randomization group	*Mean change (SD) in lines from baseline in amblyopic eye at 5 weeks* Patching vs. control: 1.1 (1.6) vs. 0.5 (1.7) *Mean (SD) logMAR acuity* Patching vs. control: 0.44 (0.22) vs. 0.51 (0.28) Mean difference (95% CI) in logMAR acuity, adjusted for baseline acuity: 0.07 (0.02 to 0.12) *Mean (SD) improvement in lines in amblyopic eye, best-measured acuity (from 5 to 52 weeks)* Patching vs. control: 2.2 (1.8) vs. 1.3 (1.4) Difference (95% CI) in mean best logMAR acuity, adjusted for baseline acuity: 0.10 (0.05 to 0.14) *Proportion of patients with ≥2 lines of improvement in visual acuity:* Patching vs. control: 38/85 (45%) vs. 18/88 (21%)

Abbreviations: CI=confidence interval; IXT=intermittent exotropia; KQ=key question; logMAR=logarithm of the minimum angle of resolution; PACT=prism and alternate cover test; PD=prism diopters; PEDIG=Pediatric Eye Disease Investigator Group; RCT=randomized, controlled trial; SD=standard deviation; SPCT=simultaneous prism and cover test; U.K.=United Kingdom; U.S.=United States.

Table 6. Summary of Evidence for Vision Screening in Children

KQ	No. of Studies (k), No. of Participants or Observations (n) Study Designs	Summary of Findings by Outcome	Consistency/ Precision	Reporting Bias	Quality	Body of Evidence Limitations	Strength of Evidence	Applicability
1	k=2, n=7,995 analyzed 1 RCT (1,914) 1 prospective cohort (6,081)	*School performance, functioning, or quality of life:* Neither study reported these outcomes *Prevalence of amblyopia at age 7.5 years* *RCT:* Approximately 1% lower for intensive screening (at ages 8, 12, 18, 25, 31, and 37 months) than for screening at age 37 months; difference was statistically significant for 1 of 2 definitions of amblyopia[a] *Cohort:* No statistically significant difference between screened (at age 37 months) and nonscreened groups for any definition of amblyopia[b]	Consistency unknown/ imprecise	Not detected	2 fair	Studies had high overall attrition (approximately 50%) and compared different screening strategies; RCT did not use a valid randomization method	Low	Healthy preschool-age children who received vision screening at ages 4 to 5 years by a school nurse as part of usual care. Trained orthoptists conducted screening exams in both studies.
2	k=34, n=45,588 observations[c] k=6 for VA tests k=4 for stereoacuity tests k=1 for cover-uncover test k=4 for a combination of clinical tests k=16 for autorefractors k=11 for photoscreeners k=1 for retinal birefringence scanning Studies of test accuracy	Estimates for all tests suggest utility for identification of children at higher risk for amblyopia risk factors or other visual conditions, with PLRs most commonly in the moderate range (5 to 10). Evidence suggests that combinations of clinical tests have higher PLRs (>10). The VIP study, the largest study to directly compare multiple tests, generally found similar likelihood ratios across tests. Accuracy did not clearly differ for children stratified according to age.	Mostly consistent/ Imprecise	Not detected	34 fair	Many studies recruited from specialty clinics or enrolled populations with high prevalence; heterogeneity of populations, settings, and target conditions evaluated; common shortcomings included high (or NR) rates of uninterpretable results or noncompliance with tests, not reporting whether uninterpretable results or noncompliance were included in analyses, lacking a representative spectrum, and lacking a random or consecutive sample	Low	Most studies of clinical tests didn't include children younger than age 3 years; however, most studies of photoscreeners and 5 of 16 studies of autorefractors included them. Applicable to a variety of settings and screening personnel, although only one study was conducted completely in a primary care setting and another was described as being conducted partly in primary care.

Table 6. Summary of Evidence for Vision Screening in Children

KQ	No. of Studies (k), No. of Participants or Observations (n) Study Designs	Summary of Findings by Outcome	Consistency/ Precision	Reporting Bias	Quality	Body of Evidence Limitations	Strength of Evidence	Applicability
3	k=17 n=14,196 1 prospective cohort (4,473) 16 observational studies of test accuracy (9,723)	*Likelihood of being bullied:* Lower for patched children offered screening at age 37 months than for those not screened (25.7% vs. 47.1%; p=0.033; adjusted OR, 0.39 [95% CI, 0.16 to 0.92])[d] *False-positive rates (1−PPV):* Studies with a lower prevalence (<10%) of vision abnormalities had higher rates (usually >75%) than studies with higher prevalence (usually <35%)	*Bullying:* NA (consistency unknown) for single study/ imprecise *False-positive rates:* Reasonably consistent (across studies of similar prevalence)/ reasonably precise	Not detected	17 fair	Risk of selection bias and confounding in the cohort study that reported bullying Did not assess psychological effects or other harms of false-positive results	Low for bullying Moderate for false-positive rates Insufficient for other harms	Children being screened for amblyopia or its risk factors
4a	k=2 n=240 RCTs	Patching vs. no patching: *Visual acuity of amblyopic eye*: On average, small (<1 line on Snellen chart) improvement after 5 to 12 weeks; more children experienced improvement of ≥2 lines (45% vs. 21%; p=0.003) in the one study reporting it	Consistent/ precise	Not detected	1 good 1 fair	Compliance with treatment was low in the fair-quality study; the fair-quality study focused on compliance and was underpowered to find a small difference between groups in visual acuity	Moderate for improved visual acuity	Children age 3 years or older with amblyopic risk factors pretreated with glasses
4a	k=1 n=177 RCT	Patching + glasses vs. glasses alone vs. no treatment: *Visual acuity*: On average, improvement of about 1 line on Snellen chart at end of trial (1 year) for patching + glasses vs. no treatment (0.11 logMAR [95% CI, 0.05 to 0.17]) and <1 line for glasses alone; magnitude of improvement was greater for children with worse baseline acuity	NA (single study)/precise	Not detected	Good	Children younger than age 3 years not eligible; mean age, 4 years (range, 3 to 5 years)	Moderate for improved visual acuity[e]	Children age 3 years or older with amblyopic risk factors (unilateral vision impairment)

Table 6. Summary of Evidence for Vision Screening in Children

KQ	No. of Studies (k), No. of Participants or Observations (n) Study Designs	Summary of Findings by Outcome	Consistency/ Precision	Reporting Bias	Quality	Body of Evidence Limitations	Strength of Evidence	Applicability
4a	k=0	Atropine vs. control for any eligible outcome	NA	NA	NA	NA	Insufficient	NA
4b	k=0	Long-term amblyopia and improved school performance, functioning, and/or quality of life	NA	NA	NA	NA	Insufficient	NA
5	k=3 n=417 RCTs	*Worsening visual acuity in the nonamblyopic eye:* Risk not increased with patching vs. no patching at 5 weeks (2.4% vs. 6.8%; p=0.28) *Loss of visual acuity in the amblyopic eye:* No significant difference between patching + glasses, glasses alone, and no treatment at 1 year[f] *Child happiness or behavioral problems:* No difference between patching + glasses, glasses alone, and no treatment *Child/parental upset/worry about treatment:* Greater with patching than with glasses alone	NA (single study reported each outcome)/ imprecise	Not detected	2 good 1 fair	Overall sparse evidence on harms of treatment; no included studies examined atropine; assessment did not compare glasses and patching with the no-treatment group for the psychological harms identified (child difficulty coping, upset, parental worry)	Low	Children receiving treatment for amblyopia or its risk factors with eyeglasses or patching

[a] Amblyopia A: 1.5% vs. 2.7% (RR, 0.55 [95% CI, 0.29 to 1.04]); amblyopia B: 0.6% vs. 1.8% (RR, 0.35 [95% CI, 0.15 to 0.86]).
[b] Amblyopia A: adjusted OR, 0.63 (95% CI, 0.32 to 1.23); amblyopia B: adjusted OR, 0.72 (95% CI, 0.32 to 1.60); amblyopia C: adjusted OR, 0.65 (95% CI, 0.38 to 1.10). All ORs adjusted for sex, highest level of maternal education, birth weight, family history of strabismus/amblyopia, and duration of breastfeeding.
[c] Some study participants contributed multiple observations (e.g., if they were evaluated with multiple tests).
[d] The effects were seen in children who were patched but not those prescribed only glasses.
[e] In our assessment of the strength of evidence, we considered that these findings are generally consistent with those from the patching vs. no-patching studies and that the magnitude of improvement was greater for children with worse baseline acuity.
[f] 9.7% vs. 6.5% vs. 13.3% (p=0.28) for children with mild baseline acuity loss; 15.0% vs. 11.1% vs. 23.8% (p=0.13) for children with moderate baseline acuity loss, respectively, for patching plus eyeglasses, eyeglasses alone, and no treatment.

Abbreviations: CI=confidence interval; k=number of studies; KQ=key question; logMAR=logarithm of the minimum angle of resolution; n=sample size; NA=not applicable; OR=odds ratio; PACT=prism and alternate cover test; PD=prism diopter; PLR=positive likelihood ratio; PPV=positive predictive value; RCT=randomized, controlled trial; RR=relative risk; VA=visual acuity; VIP=Vision in Preschoolers.

Amblyopia: A neurodevelopmental disorder that arises from abnormal processing of visual images during a critical period of vision development, resulting in a functional reduction of visual acuity.

Ametropia: An abnormal refractive condition (such as myopia, hyperopia, or astigmatism) of the eye in which images fail to focus on the retina; also referred to as refractive error.

Anisometropia: A difference in refractive power between the eyes in which one foveal image is more blurred than the other.

Astigmatism: Blurred vision caused by a failure to focus light evenly onto the retina because of deviation from normal spherical curvature.

Cataract: A clouding or loss of transparency of the lens in the eye as a result of tissue breakdown and protein clumping.

Emmetropia: A state in which the eye is relaxed and focused on an object more than 6 meters or 20 feet away. The light rays coming from that object are essentially parallel, and the rays are focused on the retina without effort.

Hyperopia: A condition in which visual images come to a focus behind the retina of the eye and vision is better for distant than near objects.

Isoametropia: Refractive error that is similar in both eyes.

Myopia: A condition in which visual images come to a focus in front of the retina of the eye because of defects in the refractive media or abnormal length of the eyeball, resulting especially in defective vision for distant objects.

Ptosis: Drooping of the upper eyelid due to paralysis, disease, or a congenital condition.

Stereopsis: The perception of depth produced by the reception in the brain of visual stimuli from both eyes in combination; also known as binocular vision.

Strabismus: Ocular misalignment in which each eye does not have the same image on the fovea.

Visual acuity: Sharpness of vision, measured by the ability to discern letters or numbers at a given distance according to a fixed standard.

Appendix A Table 1. Summary of Recommendations From Other Groups

Group, Year	Recommendation(s)
American Academy of Family Physicians (AAFP), 2011[147]	The AAFP recommends vision screening for all children at least once between the ages of 3 and 5 years to detect the presence of amblyopia or its risk factors. The AAFP concludes that the current evidence is insufficient to assess the balance of benefits and harms of vision screening for children <3 years of age.
American Academy of Pediatrics (AAP), American Association for Pediatric Ophthalmology and Strabismus (AAPOS), American Academy of Ophthalmology (AAO), and American Academy of Certified Orthoptists, 2016[148] (joint statement)	Vision screening should be performed at an early age and at regular intervals with age-appropriate, valid methods, ideally within the medical home. Recommended screening components by age are: **Newborn to 6 months:** Fixation and follow response, red reflex (for ocular media clarity), and external inspection via direct observation. **6 months to 1 year of age:** The above (for newborn to 6 months) plus pupil examination using a flashlight. **1 to 3 years:** The above (for 6 months to 1 year) plus instrument-based vision screening (photoscreening, autorefraction) when available. Visual acuity screening may be attempted at age 3 years using HOTV or LEA Symbols. **4 to 5 years of age:** Visual acuity screening using HOTV or LEA Symbols, cross cover test, and red reflex.
American Optometric Association (AOA), 2002[149]	All children should receive regular comprehensive eye examinations (by an eye care specialist) beginning at 6 months of age after an initial eye screening at birth, typically performed by the pediatrician. Eye examinations are then recommended at age 3 years, before entering first grade, and then periodically at 2-year intervals (or more frequently in children who have visual complaints or risk factors for vision impairment).
Canadian Task Force on Preventive Health Care (CTFPHC), 1989[150]	There is fair evidence to include testing of visual acuity in the periodic health examination of preschool children.

Search Strategies

PubMed search, 10/12/2015

Search	Query	Items found
#1	Search amblyopia [Mesh] OR amblyopia OR strabismus [Mesh] OR strabismus OR "Depth Perception"[Mesh] OR stereopsis OR ptosis OR "Refractive Errors "[Mesh] OR "refractive error" OR "refractive errors" OR "Vision Disorders"[Mesh]	147438
#2	Search amblyopia [Mesh] OR amblyopia OR strabismus [Mesh] OR strabismus OR "Depth Perception"[Mesh] OR stereopsis OR ptosis OR "Refractive Errors "[Mesh] OR "refractive error" OR "refractive errors" OR "Vision Disorders"[Mesh] Filters: Infant: 1-23 months	9631
#3	Search amblyopia [Mesh] OR amblyopia OR strabismus [Mesh] OR strabismus OR "Depth Perception"[Mesh] OR stereopsis OR ptosis OR "Refractive Errors "[Mesh] OR "refractive error" OR "refractive errors" OR "Vision Disorders"[Mesh] Filters: Infant: 1-23 months; Preschool Child: 2-5 years	18242
#4	Search (child [tiab] OR children [tiab] OR preschool* [tiab] OR pediatri* [tiab])	1083423
#5	Search (#1 AND #4)	14520
#6	Search (#3 OR #5)	24670
#7	Search (#3 OR #5) Filters: Publication date from 2009/01/01 to 2015/10/12	5520
#8	Search "Vision Tests"[Mesh] OR "Refraction, Ocular"[Mesh] OR "Vision Screening"[Mesh] OR photoscreen* OR autorefract* OR "Visual Acuity "[Mesh] OR cycloplegic refract*)	84019
#9	Search "Amblyopia/drug therapy"[Mesh] OR "Amblyopia/prevention and control"[Mesh] OR "Amblyopia/therapy"[Mesh] OR "Refractive Errors/drug therapy"[Mesh] OR "Refractive Errors/prevention and control"[Mesh] OR "Refractive Errors/therapy"[Mesh] OR “eye exercises” [all fields] OR “vision therapy” [all fields] OR “eye therapy” [all fields] OR “vision exercises” [all fields] OR “fixation training” [all fields] OR “near vision tasks” [all fields] OR “binocular therapy” [all fields] OR Ocular motility disorders/therapy OR “near activities” [all fields] OR “accommodative therapy” [all fields] OR “visual training” [all fields] OR orthoptics [all fields]	24915
#10	Search (#7 AND #8)	1878
#11	Search (#7 AND #9)	1069
#12	Search ((randomized[title/abstract] AND controlled[title/abstract] AND trial[title/abstract]) OR (controlled[title/abstract] AND trial[title/abstract]) OR "controlled clinical trial"[publication type] OR "Randomized Controlled Trial"[Publication Type] OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]))	615199
#13	Search (“Case-Control Studies"[MeSH] OR "Cohort Studies"[MeSH] OR "comparative study"[pt] OR "Epidemiologic Studies"[MeSH] OR "Cross-Over Studies"[MeSH] OR "Follow-Up Studies"[MeSH] OR “observational study” OR “observational studies” OR "cohort"[tw] OR "case control"[tw] OR “prospective cohort” OR “prospective studies”[MeSH] OR (prospective*[All Fields] AND cohort[All Fields] AND (study[All Fields] OR studies[All Fields])) OR "cross-sectional studies"[MeSH Terms] OR “cross-sectional study”[tw])	3378268
#14	Search ("Sensitivity and Specificity"[Mesh] OR "Predictive Value of Tests"[Mesh] OR "ROC Curve"[Mesh] OR "Reproducibility of Results"[Mesh] OR "False Negative Reactions"[Mesh] OR "False Positive Reactions"[Mesh] OR "predictive value"[tw] OR sensitivity[tw] OR specificity[tw] OR accuracy[tw] OR ROC[tw] OR reproducib*[tw] OR "false positive"[tw] OR "false negative"[tw] OR "likelihood ratio"[tw])	1941693
#15	Search (#10 AND #12)	115
#16	Search (#10 AND #13)	1139
#17	Search (#10 AND #14)	313
#18	Search (#15 OR #16 OR #17)	1295
#19	Search (#11 AND #12)	142
#20	Search (#11 AND #13)	589
#21	Search (#19 OR #20)	645
#22	Search (#7 AND #8) Filters: Review	99
#23	Search (#7 AND #8) Filters: Review; Systematic Reviews	123
#24	Search (#7 AND #9) Filters: Review	100
#25	Search (#7 AND #9) Filters: Review; Systematic Reviews	121

Appendix B. Detailed Methods

Cochrane Library, 10/12/2015

ID	Search	Hits
#1	[mh amblyopia] or amblyopia or [mh strabismus] or strabismus or [mh "Depth Perception"] or stereopsis or ptosis or [mh "Refractive Errors"] or "refractive error" or "refractive errors" or [mh "Vision Disorders"]	4054
#2	child or children or preschool* or pediatri*	107944
#3	#1 and #2	1301
#4	[mh "Vision Tests"] or [mh "Refraction, Ocular"] or [mh "Vision Screening"] or photoscreen* or autorefract* or [mh "Visual Acuity"] or cycloplegic refract*	4534
#5	[mh Amblyopia/dt] or [mh Amblyopia/pc] or [mh Amblyopia/th] or [mh "Refractive Errors/dt"] or [mh "Refractive Errors/pc"] or [mh "Refractive Errors/th"] or "eye exercises" or "vision therapy" or "eye therapy" or "vision exercises" or "fixation training" or "near vision tasks" or "binocular therapy" or [mh "Ocular motility disorders"/th] or "near activities" or "accommodative therapy" or "visual training" or orthoptics	338
#6	#3 and #4	432
#7	#3 and #5	172
#8	(randomized and controlled and trial) or (controlled and trial) or "controlled clinical trial":pt or "Randomized Controlled Trial":pt or [mh "Single-Blind Method"] or [mh "Double-Blind Method"] or [mh "Random Allocation"]	625248
#9	[mh "Case-Control Studies"] or [mh "Cohort Studies"] or "comparative study":pt or [mh "Epidemiologic Studies"] or [mh "Cross-Over Studies"] or [mh "Follow-Up Studies"] or "observational study" or "observational studies" or "cohort" or "case control" or "prospective cohort" or [mh "prospective studies"] or (prospective and cohort and (study or studies)) or [mh "cross-sectional studies"] or "cross-sectional study"	257795
#10	[mh "Sensitivity and Specificity"] or [mh "Predictive Value of Tests"] or [mh "ROC Curve"] or [mh "Reproducibility of Results"] or [mh "False Negative Reactions"] or [mh "False Positive Reactions"] or "predictive value" or sensitivity or specificity or accuracy or ROC or reproducib* or "false positive" or "false negative" or "likelihood ratio"	78943
#11	#6 and #8	367
#12	#6 and #9	250
#13	#6 and #10	122
#14	#11 or #12 or #13 Publication Year from 2009 to 2015	120
#15	#7 and #8	157
#16	#7 and #9	103
#17	#15 or #16	159

Cumulative Index to Nursing and Allied Health Literature (CINAHL), 10/13/2015

#	Query	Limiters/Expanders	Results
S15	S13 or S14	Limiters - Published Date: 20090101-20151031; Exclude MEDLINE records Search modes - Boolean/Phrase	0
S14	S5 and S7	Search modes - Boolean/Phrase	0
S13	S5 and S6	Search modes - Boolean/Phrase	0
S12	(S9 OR S10 OR S11)	Limiters - Published Date: 20090101-20151031; Exclude MEDLINE records Search modes - Boolean/Phrase	1
S11	S4 AND S8	Search modes - Boolean/Phrase	1
S10	S4 AND S7	Search modes - Boolean/Phrase	0
S9	S4 AND S6	Search modes - Boolean/Phrase	0
S8	mh "Sensitivity and Specificity" or mh "Predictive Value of Tests" or mh "ROC Curve" or mh "Reproducibility of Results" or mh "False Negative Reactions" or mh "False Positive Reactions" or "predictive value" or sensitivity or specificity or accuracy or ROC or reproducib* or "false positive" or "false negative" or "likelihood ratio"	Search modes - Boolean/Phrase	186,360
S7	PT "comparative study" OR (mh "Case-Control Studies" or mh "Cohort Studies" or mh "Epidemiologic Studies" or mh "Cross-Over Studies" or mh "Follow-Up Studies" or "observational study" or "observational studies" or "prospective cohort" or mh "prospective studies" or (prospective and cohort and (study or studies)) or mh "cross-sectional studies" or "cross-sectional study")	Search modes - Boolean/Phrase	307,379
S6	PT ("controlled clinical trial" or "Randomized Controlled Trial") OR (mh "Single-Blind Method" or mh "Double-Blind Method" or mh "Random Allocation")	Search modes - Boolean/Phrase	53,998
S5	S1 and S3	Limiters - Published Date: 20090101-20151031; Exclude MEDLINE records; Publication Type: Systematic Review; Age Groups: Infant: 1-23 months, Child, Preschool: 2-5 years Search modes - Boolean/Phrase	1
S4	S1 and S2	Limiters - Published Date: 20090101-20151031; Exclude MEDLINE records; Publication Type: Systematic Review; Age Groups: Infant: 1-23 months, Child, Preschool: 2-5 years Search modes - Boolean/Phrase	1
S3	(MH "Amblyopia/DT/PC/TH") or (MH "Refractive Errors/DT/PC/TH") or (MH "Ocular Motility Disorders/TH") or "eye exercises" or "vision therapy" or "eye therapy" or "vision exercises" or "fixation training" or "near vision tasks" or "binocular therapy" or "near activities" or "accommodative therapy" or "visual training" or orthoptics	Search modes - Boolean/Phrase	603
S2	mh "Vision Tests" or mh "Refraction, Ocular" or mh "Vision Screening" or photoscreen* or autorefract* or mh "Visual Acuity" or cycloplegic refract*	Search modes - Boolean/Phrase	7,947
S1	mh amblyopia or mh strabismus or mh "Depth Perception" or stereopsis or ptosis or mh "Refractive Errors" or mh "Vision Disorders"	Limiters - Age Groups: Infant: 1-23 months, Child, Preschool: 2-5 years Search modes - Boolean/Phrase	1,016

Additional Searches, October 20, 2015

ClinicalTrials.gov

Screening, with date and child limits:

(amblyopia OR strabismus OR "Depth Perception" OR stereopsis OR ptosis OR "Refractive Errors" OR "refractive error" OR "Vision Disorders") AND ("Vision Tests" OR "Refraction, Ocular" OR “ocular refraction OR "Vision Screening" OR photoscreen* OR autorefract* OR "Visual Acuity" OR cycloplegic refract*) | Child | received from 01/01/2009 to 10/20/2015

Treatment, with date and child limits:

(amblyopia OR strabismus OR "Depth Perception" OR stereopsis OR ptosis OR "Refractive Errors" OR "refractive error" OR "Vision Disorders") AND (“eye exercises” OR “vision therapy OR “eye therapy” OR “vision exercises” OR “fixation training” OR “near vision tasks” OR “binocular therapy” OR Ocular motility disorders OR “near activities” OR “accommodative therapy” OR “visual training” OR orthoptics) AND INFLECT EXACT "Child" [AGE-GROUP] AND ("01/01/2009" : "10/20/2015" [FIRST-RECEIVED-DATE]

World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) strategy

Screening

Vision Tests OR ocular refraction OR Vision Screening OR photoscreen* OR autorefract* OR Visual Acuity OR cycloplegic refract* (in TITLE)

AND

amblyopia OR strabismus OR Depth Perception OR stereopsis OR ptosis OR Refractive Errors OR refractive error OR Vision Disorders (in CONDITION)

LIMITED TO CHILDREN; RECRUITMENT STATUS-ALL

Treatment

amblyopia OR strabismus OR Depth Perception OR stereopsis OR ptosis OR Refractive Errors OR refractive error OR Vision Disorders (in CONDITION)

AND

(eye exercises OR vision therapy OR eye therapy OR vision exercises OR fixation training OR near vision tasks OR binocular therapy OR Ocular motility disorders OR near activities OR accommodative therapy OR visual training OR orthoptics) (in INTERVENTION)

LIMITED TO CHILDREN; RECRUITMENT STATUS-ALL

Update Search Strategies

PubMed search, 06/07/2016

Search	Query	Items found
#1	Search amblyopia [Mesh] OR amblyopia OR strabismus [Mesh] OR strabismus OR "Depth Perception"[Mesh] OR stereopsis OR ptosis OR "Refractive Errors "[Mesh] OR "refractive error" OR "refractive errors" OR "Vision Disorders"[Mesh]	153313
#2	Search amblyopia [Mesh] OR amblyopia OR strabismus [Mesh] OR strabismus OR "Depth Perception"[Mesh] OR stereopsis OR ptosis OR "Refractive Errors "[Mesh] OR "refractive error" OR "refractive errors" OR "Vision Disorders"[Mesh] Filters: Infant: 1-23 months	9910
#3	Search amblyopia [Mesh] OR amblyopia OR strabismus [Mesh] OR strabismus OR "Depth Perception"[Mesh] OR stereopsis OR ptosis OR "Refractive Errors "[Mesh] OR "refractive error" OR "refractive errors" OR "Vision Disorders"[Mesh] Filters: Infant: 1-23 months; Preschool Child: 2-5 years	18707
#4	Search (child [tiab] OR children [tiab] OR preschool* [tiab] OR pediatri* [tiab])	1122706
#5	Search (#1 AND #4)	15037
#6	Search (#3 OR #5)	25390
#7	Search (#3 OR #5) Filters: Publication date from 2015/04/01	763
#8	Search "Vision Tests"[Mesh] OR "Refraction, Ocular"[Mesh] OR "Vision Screening"[Mesh] OR photoscreen* OR autorefract* OR "Visual Acuity "[Mesh] OR cycloplegic refract*)	87344
#9	Search "Amblyopia/drug therapy"[Mesh] OR "Amblyopia/prevention and control"[Mesh] OR "Amblyopia/therapy"[Mesh] OR "Refractive Errors/drug therapy"[Mesh] OR "Refractive Errors/prevention and control"[Mesh] OR "Refractive Errors/therapy"[Mesh] OR “eye exercises” [all fields] OR “vision therapy” [all fields] OR “eye therapy” [all fields] OR “vision exercises” [all fields] OR “fixation training” [all fields] OR “near vision tasks” [all fields] OR “binocular therapy” [all fields] OR Ocular motility disorders/therapy OR “near activities” [all fields] OR “accommodative therapy” [all fields] OR “visual training” [all fields] OR orthoptics [all fields]	25531
#10	Search (#7 AND #8)	213
#11	Search (#7 AND #9)	115
#12	Search ((randomized[title/abstract] AND controlled[title/abstract] AND trial[title/abstract]) OR (controlled[title/abstract] AND trial[title/abstract]) OR "controlled clinical trial"[publication type] OR "Randomized Controlled Trial"[Publication Type] OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]))	638598
#13	Search (“Case-Control Studies"[MeSH] OR "Cohort Studies"[MeSH] OR "comparative study"[pt] OR "Epidemiologic Studies"[MeSH] OR "Cross-Over Studies"[MeSH] OR "Follow-Up Studies"[MeSH] OR “observational study” OR “observational studies” OR "cohort"[tw] OR "case control"[tw] OR “prospective cohort” OR “prospective studies”[MeSH] OR (prospective*[All Fields] AND cohort[All Fields] AND (study[All Fields] OR studies[All Fields])) OR "cross-sectional studies"[MeSH Terms] OR “cross-sectional study”[tw])	3503813
#14	Search ("Sensitivity and Specificity"[Mesh] OR "Predictive Value of Tests"[Mesh] OR "ROC Curve"[Mesh] OR "Reproducibility of Results"[Mesh] OR "False Negative Reactions"[Mesh] OR "False Positive Reactions"[Mesh] OR "predictive value"[tw] OR sensitivity[tw] OR specificity[tw] OR accuracy[tw] OR ROC[tw] OR reproducib*[tw] OR "false positive"[tw] OR "false negative"[tw] OR "likelihood ratio"[tw])	2020506
#15	Search (#10 AND #12)	14
#16	Search (#10 AND #13)	119
#17	Search (#10 AND #14)	32
#18	Search (#15 OR #16 OR #17)	144
#19	Search (#11 AND #12)	20
#20	Search (#11 AND #13)	60
#21	Search (#19 OR #20)	69
#22	Search (#7 AND #8) Filters: Review	10
#23	Search (#7 AND #8) Filters: Review; Systematic Reviews	12
#24	Search (#7 AND #9) Filters: Review	11
#25	Search (#7 AND #9) Filters: Review; Systematic Reviews	15

Appendix B. Detailed Methods

Cochrane Library, 06/07/2016

ID	Search	Hits
#1	[mh amblyopia] or amblyopia or [mh strabismus] or strabismus or [mh "Depth Perception"] or stereopsis or ptosis or [mh "Refractive Errors"] or "refractive error" or "refractive errors" or [mh "Vision Disorders"]	4375
#2	child or children or preschool* or pediatri*	114634
#3	#1 and #2	1412
#4	[mh "Vision Tests"] or [mh "Refraction, Ocular"] or [mh "Vision Screening"] or photoscreen* or autorefract* or [mh "Visual Acuity"] or cycloplegic refract*	5016
#5	[mh Amblyopia/dt] or [mh Amblyopia/pc] or [mh Amblyopia/th] or [mh "Refractive Errors/dt"] or [mh "Refractive Errors/pc"] or [mh "Refractive Errors/th"] or "eye exercises" or "vision therapy" or "eye therapy" or "vision exercises" or "fixation training" or "near vision tasks" or "binocular therapy" or [mh "Ocular motility disorders"/th] or "near activities" or "accommodative therapy" or "visual training" or orthoptics	369
#6	#3 and #4	471
#7	#3 and #5	186
#8	(randomized and controlled and trial) or (controlled and trial) or "controlled clinical trial":pt or "Randomized Controlled Trial":pt or [mh "Single-Blind Method"] or [mh "Double-Blind Method"] or [mh "Random Allocation"]	673266
#9	[mh "Case-Control Studies"] or [mh "Cohort Studies"] or "comparative study":pt or [mh "Epidemiologic Studies"] or [mh "Cross-Over Studies"] or [mh "Follow-Up Studies"] or "observational study" or "observational studies" or "cohort" or "case control" or "prospective cohort" or [mh "prospective studies"] or (prospective and cohort and (study or studies)) or [mh "cross-sectional studies"] or "cross-sectional study"	279243
#10	[mh "Sensitivity and Specificity"] or [mh "Predictive Value of Tests"] or [mh "ROC Curve"] or [mh "Reproducibility of Results"] or [mh "False Negative Reactions"] or [mh "False Positive Reactions"] or "predictive value" or sensitivity or specificity or accuracy or ROC or reproducib* or "false positive" or "false negative" or "likelihood ratio"	84491
#11	#6 and #8	408
#12	#6 and #9	280
#13	#6 and #10	130
#14	#11 or #12 or #13 Publication Year from 2015 to 2016	17
#15	#7 and #8	170
#16	#7 and #9	113
#17	#15 or #16 Publication Year from 2015 to 2016	8

Appendix B. Detailed Methods

Cumulative Index to Nursing and Allied Health Literature (CINAHL), 06/07/2016

	Query	Limiters/Expanders	Results
S20	S16 or S17 or S18	Limiters - Published Date: 20150401-; Exclude MEDLINE records Search modes - Boolean/Phrase	1
S19	S16 or S17 or S18	Search modes - Boolean/Phrase	26
S18	S15 and S9	Search modes - Boolean/Phrase	7
S17	S15 and S8	Search modes - Boolean/Phrase	19
S16	S15 and S7	Search modes - Boolean/Phrase	3
S15	S1 and S3	Search modes - Boolean/Phrase	123
S14	S10 or S11 or S12	Limiters - Published Date: 20150401-; Exclude MEDLINE records Search modes - Boolean/Phrase	1
S13	S10 or S11 or S12	Search modes - Boolean/Phrase	129
S12	S6 and S9	Search modes - Boolean/Phrase	58
S11	S6 and S8	Search modes - Boolean/Phrase	81
S10	S6 and S7	Search modes - Boolean/Phrase	6
S9	mh "Sensitivity and Specificity" or mh "Predictive Value of Tests" or mh "ROC Curve" or mh "Reproducibility of Results" or mh "False Negative Reactions" or mh "False Positive Reactions" or "predictive value" or sensitivity or specificity or accuracy or ROC or reproducib* or "false positive" or "false negative" or "likelihood ratio"	Search modes - Boolean/Phrase	199,643
S8	PT "comparative study" OR (mh "Case-Control Studies" or mh "Cohort Studies" or mh "Epidemiologic Studies" or mh "Cross-Over Studies" or mh "Follow-Up Studies" or "observational study" or "observational studies" or "prospective cohort" or mh "prospective studies" or (prospective and cohort and (study or studies)) or mh "cross-sectional studies" or "cross-sectional study")	Search modes - Boolean/Phrase	322,154
S7	PT ("controlled clinical trial" or "Randomized Controlled Trial") OR (mh "Single-Blind Method" or mh "Double-Blind Method" or mh "Random Allocation")	Search modes - Boolean/Phrase	56,553
S6	S1 and S2	Search modes - Boolean/Phrase	345
S5	S1 and S3	Limiters - Published Date: 20150401-20161231; Exclude MEDLINE records; Publication Type: Systematic Review; Age Groups: Infant: 1-23 months, Child, Preschool: 2-5 years Search modes - Boolean/Phrase	1
S4	S1 and S2	Limiters - Published Date: 20150401-20161231; Exclude MEDLINE records; Publication Type: Systematic Review; Age Groups: Infant: 1-23 months, Child, Preschool: 2-5 years Search modes - Boolean/Phrase	1
S3	(MH "Amblyopia/DT/PC/TH") or (MH "Refractive Errors/DT/PC/TH") or (MH "Ocular Motility Disorders/TH") or "eye exercises" or "vision therapy" or "eye therapy" or "vision	Search modes - Boolean/Phrase	636

	Query	Limiters/Expanders	Results
	exercises" or "fixation training" or "near vision tasks" or "binocular therapy" or "near activities" or "accommodative therapy" or "visual training" or orthoptics		
S2	mh "Vision Tests" or mh "Refraction, Ocular" or mh "Vision Screening" or photoscreen* or autorefract* or mh "Visual Acuity" or cycloplegic refract*	Search modes - Boolean/Phrase	8,237
S1	mh amblyopia or mh strabismus or mh "Depth Perception" or stereopsis or ptosis or mh "Refractive Errors" or mh "Vision Disorders"	Limiters - Age Groups: Infant: 1-23 months, Child, Preschool: 2-5 years Search modes - Boolean/Phrase	1,040

Appendix B Table 1. Study Eligibility Criteria

	Include	Exclude
Populations	**All KQs:** Children age 6 months to 5 years **KQs 1–3:** Children without known impaired visual acuity or obvious symptoms of impaired visual acuity **KQs 4, 5:** Children with amblyopia, amblyopia risk factors, and/or refractive error	Newborns, children younger than age 6 months, and children age 6 years or older; children with severe congenital conditions or developmental delays, retinopathy of prematurity, glaucoma, congenital cataract, neurodevelopmental disorders, systemic conditions associated with ocular abnormalities, or pathologic myopia
Setting	**All KQs:** Studies performed in primary care, community-based, and school settings; studies conducted in countries categorized as "Very High" on the Human Development Index, as defined by the United Nations Development Programme **KQs 2–5:** Specialty settings (e.g., ophthalmology or optometry practices)	
Screening tests and interventions	**KQs 1–3:** Studies of screening tests used or available in primary care settings, including visual acuity tests (e.g., autorefraction; picture identification tests, such as Allen test cards or LEA symbols; HOTV chart; Snellen chart; tumbling E chart), stereoacuity tests (e.g., contour stereotests, such as the Frisby, Random Dot E, Stereo Smile, and Titmus Fly tests; Moving Dynamic Random Dot Stereosize test), and ocular alignment tests (e.g., photoscreening, corneal light reflex test, cover-uncover test, cross cover test, red reflex test) **KQs 4, 5:** Correction of refractive error (eyeglasses), penalization of the nonamblyopic eye (eye patch, atropine), and vision therapy (eye exercises)	**KQs 1–3:** Studies of screening tests not used or available in primary care settings (e.g., contrast sensitivity test, fundoscopic examination, visual acuity test with cycloplegia) or not intended to detect amblyopia, amblyopia risk factors, or refractive error (e.g., white reflex test) **KQs 4, 5:** Surgical interventions for strabismus or other indications
Comparisons	**KQs 1, 3:** Screened vs. nonscreened groups or earlier (at a younger age) vs. later screening (at an older age) **KQ 2:** Evaluations that include cycloplegic refraction and/or a comprehensive eye examination; for evaluations of reliability (test-retest), the comparison may be the same test administered at different time points or by a different person. **KQs 4, 5:** No treatment or sham or inactive control	No comparison, nonconcordant historical controls, comparative studies of various interventions (i.e., head-to-head studies without an additional eligible comparison group)
Outcomes	**KQs 1, 4:** Reduced long-term amblyopia and improved visual acuity, school performance, functioning, and quality of life **KQ 2:** Sensitivity, specificity, positive and negative predictive values, likelihood ratios, and diagnostic odds ratios (or ability to calculate such outcomes from data provided); measures of reliability, including reproducibility, interrater reliability, and testability (ability of children to cooperate with the test) **KQs 3, 5:** Harms, including psychological distress, labeling, anxiety, other psychological effects, false-positive results, and adverse effects on vision in the nonimpaired eye	Cost-effectiveness or cost-related outcomes **KQ 2:** Studies providing only associations, correlations, or other outcomes
Study designs	**KQ 1:** Randomized, controlled trials and prospective cohort studies with an eligible comparator **KQ 2:** Cross-sectional studies, cohort studies, or trials	Case reports, case series, systematic reviews, and all other study designs not listed as eligible

Appendix B Table 1. Study Eligibility Criteria

	Include	Exclude
	focused on assessment of diagnostic accuracy **KQs 3, 5:** Randomized, controlled trials; controlled cohort studies; case-control studies **KQ 4:** Randomized, controlled trials	**KQ 2:** Studies that do not attempt to perform the reference standard in all participants or a random sample of participants
Language and publication status	English-language, full-text journal articles	Languages other than English, publications available only as a conference abstract

Abbreviation: KQ=Key Question.

Appendix B Table 2. U.S. Preventive Services Task Force Quality Rating Criteria

Criteria for Randomized, Controlled Trials

- Initial assembly of comparable groups: Randomized controlled trials (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, crossovers, adherence, and contamination)
- Important differential loss to followup or overall high loss to followup
- 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 (followup ≥80%); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention is given to confounders in the 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 on whether some (although not major) differences occurred in followup; 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 exist: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied equally among groups (including not masking outcome assessment); and key confounders are given little or no attention.

Sources: U.S. Preventive Services Task Force, Procedure Manual, Appendix VII , Harris et al, 2001[71]

Appendix B Table 2. U.S. Preventive Services Task Force Quality Rating Criteria

Criteria for Studies of Screening Tests

- 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: Although this is one of the criteria listed in the current procedures manual, we did not consider sample size when assessing study quality, because sample size affects precision of the estimate.
- Administration of reliable screening test.

In addition to the criteria listed in the USPSTF procedures manual, we also considered the criteria described in Appendix D (which details quality assessments of individual studies).

Definition of Ratings Based on Above Criteria

Good	Relevant and adequately described study populations for the outcome of interest (i.e., sensitivity, specificity), screening test well described in terms of test procedures followed and threshold used for a "positive" or "negative" test, credible reference standard used for outcome of interest (i.e., sensitivity or specificity), generally interprets reference standard independently of screening test, outcomes clearly reported and valid, handles indeterminate results in a reasonable manner.
Fair	Mostly includes a relevant and adequately described study population for the outcome of interest (i.e., sensitivity, specificity), screening test described although may include some ambiguity about test procedures followed or threshold for a "positive" or "negative" test, credible reference standard mostly used for outcome of interest (i.e., sensitivity or specificity), interpretation of reference standard may or may not be independent of screening test, outcomes mostly clearly reported although may have some ambiguity regarding how indeterminate results were handled.
Poor	Has fatal flaw such as study population not appropriate for outcome of interest (i.e., sensitivity, specificity), screening test improperly administered or not at all described, use of noncredible reference standard, reference and screening test not independently assessed, outcomes not clearly or accurately reported with no information about how indeterminate tests were handled.

Criteria Adapted from: U.S. Preventive Services Task Force, Procedure Manual Appendix VII, Harris et al, 2001.[71]

Appendix C. Excluded Studies

Coding scheme:

- X1 Non-English
- X2 Not original research
- X3 Ineligible population
- X4 Ineligible screening or intervention
- X5 Ineligible comparator
- X6 Ineligible outcome
- X7 Ineligible setting
- X8 Ineligible study design
- X9 Ineligible country
- X10 Poor quality

1. Joint statement--Learning disabilities, dyslexia, and vision. *Pediatrics*. 2009 Aug;124(2):837-44. doi: 10.1542/peds.2009-1445. PMID: 19651597. Exclusion Code: X2.
2. Prevalence and causes of visual impairment in African-American and Hispanic preschool children: the multi-ethnic pediatric eye disease study. *Ophthalmology*. 2009 Oct;116(10):1990-2000.e1. doi: 10.1016/j.ophtha.2009.03.027. PMID: 19592106. Exclusion Code: X6.
3. Interobserver reliability of the prism and alternate cover test in children with esotropia. *Arch Ophthalmol*. 2009 Jan;127(1):59-65. doi: 10.1001/archophthalmol.2008.548. PMID: 19139339. Exclusion Code: X3.
4. Impact of confidence number on accuracy of the SureSight Vision Screener. *Optom Vis Sci*. 2010 Feb;87(2):96-103. doi: 10.1097/OPX.0b013e3181cc8fb9. PMID: 20061987. Exclusion Code: X6.
5. Abrams MS, Duncan CL, McMurtrey R. Development of motor fusion in patients with a history of strabismic amblyopia who are treated part-time with Bangerter foils. *J AAPOS*. 2011 Apr;15(2):127-30. doi: 10.1016/j.jaapos.2010.12.012. PMID: 21470883. Exclusion Code: X5.
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Appendix C. Excluded Studies

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Appendix C. Excluded Studies

104. Han ZH, Qiu M. [Randomized Controlled Clinical Trials for Treatment of Child Amblyopia with Otopoint Pellet-pressure Combined with Chinese Medical Herbs]. *Zhen Ci Yan Jiu*. 2015 Jun;40(3):247-50. PMID: 26237980. Exclusion Code: X1.
105. Handa T, Ishikawa H, Nishimoto H, et al. Effect of motion stimulation without changing binocular disparity on stereopsis in strabismus patients. *Am Orthopt J*. 2010;60:87-94. PMID: 21061889. Exclusion Code: X5.
106. Hardgrave N, Hatley J, Lewerenz D. Comparing LEA numbers low vision book and Feinbloom visual acuity charts. *Optom Vis Sci*. 2012 Nov;89(11):1611-8. doi: 10.1097/OPX.0b013e31826ab10a. PMID: 23026789. Exclusion Code: X3.
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109. Hashemi H, Khabazkhoob M, Asharlous A, et al. Cycloplegic autorefraction versus subjective refraction: the Tehran Eye Study. *Br J Ophthalmol*. 2015 Nov 5doi: 10.1136/bjophthalmol-2015-307871. PMID: 26541436. Exclusion Code: X3.
110. Hatt SR, Leske DA, Liebermann L, et al. Variability of angle of deviation measurements in children with intermittent exotropia. *J AAPOS*. 2012 Apr;16(2):120-4. doi: 10.1016/j.jaapos.2011.11.008. PMID: 22525165. Exclusion Code: X3.
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117. Ingram RM, Lambert TW, Gill LE. Visual outcome in 879 children treated for strabismus: insufficient accommodation and vision deprivation, deficient emmetropisation and anisometropia. *Strabismus*. 2009 Oct-Dec;17(4):148-57. doi: 10.3109/09273970903376010. PMID: 20001509. Exclusion Code: X8.
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119. Jaeb Center for Health R, National Eye I. A Pilot Clinical Trial of Overminus Spectacle Therapy for Intermittent Exotropia. 2015. Exclusion Code: X6.

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120. Jaeb Center for Health R, National Eye I. Observation Versus Occlusion Therapy for Intermittent Exotropia. 2015. Exclusion Code: X6.
121. Jaeb Center for Health R, National Eye I. Hyperopia Treatment Study 1 (HTS1) - Glasses vs Observation. 2018. Exclusion Code: X6.
122. Jefferis JM, Connor AJ, Clarke MP. Amblyopia. *BMJ*. 2015;351:h5811. doi: 10.1136/bmj.h5811. PMID: 26563241. Exclusion Code: X2.
123. Jethani J, Seethapathy G, Purohit J, et al. Measuring normal ocular torsion and its variation by fundus photography in children between 5-15 years of age. *Indian J Ophthalmol*. 2010 Sep-Oct;58(5):417-9. doi: 10.4103/0301-4738.67060. PMID: 20689198. Exclusion Code: X3.
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130. Khan T. Is there a critical period for amblyopia therapy? Results of a study on older anisometropic amblyopes. Journal of Clinical and Diagnostic Research; 2015. p. Nc01-nc4. Exclusion Code: X3.
131. Kirk S, Armitage MD, Dunn S, et al. Calibration and validation of the 2WIN photoscreener compared to the PlusoptiX S12 and the SPOT. *J Pediatr Ophthalmol Strabismus*. 2014 Sep-Oct;51(5):289-92. doi: 10.3928/01913913-20140701-01. PMID: 25000209. Exclusion Code: X3.
132. Kirk VG, Clausen MM, Armitage MD, et al. Preverbal photoscreening for amblyogenic factors and outcomes in amblyopia treatment: early objective screening and visual acuities. *Arch Ophthalmol*. 2008 Apr;126(4):489-92. doi: 10.1001/archopht.126.4.489. PMID: 18413517. Exclusion Code: X8.
133. Kirschen D, Isenberg SJ. The effectiveness of an autorefractor with eye-tracking capability in pediatric patients. *J AAPOS*. 2014 Jun;18(3):217-21. doi: 10.1016/j.jaapos.2013.12.019. PMID: 24924271. Exclusion Code: X3.
134. Koenraads Y, Braun KP, van der Linden DC, et al. Perimetry in young and neurologically impaired children: the Behavioral Visual Field (BEFIE) Screening Test revisited. *JAMA Ophthalmol*. 2015 Mar;133(3):319-25. doi: 10.1001/jamaophthalmol.2014.5257. PMID: 25541916. Exclusion Code: X4.
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137. Koklanis K, Le T, Georgievski Z. The base-to-base induced-tropia prism test for detection of amblyopia: a pilot study. *J AAPOS*. 2010 Dec;14(6):484-7. doi: 10.1016/j.jaapos.2010.08.015. PMID: 21168071. Exclusion Code: X3.
138. Kortum K, Kernt M, Reznicek L. [Significance of ophthalmological imaging in common hereditary retinal diseases]. *Klin Monbl Augenheilkd*. 2013 Mar;230(3):223-31. doi: 10.1055/s-0032-1327906. PMID: 23229225. Exclusion Code: X1.
139. Koslowe KC, Spierer A, Rosner M, et al. Evaluation of accommotrac biofeedback training for myopia control. *Optom Vis Sci*. 1991 May;68(5):338-43. PMID: 1852394. Exclusion Code: X3.
140. Kothari M, Bhaskare A, Mete D, et al. Evaluation of central, steady, maintained fixation grading for predicting inter-eye visual acuity difference to diagnose and treat amblyopia in strabismic patients. *Indian J Ophthalmol*. 2009 Jul-Aug;57(4):281-4. doi: 10.4103/0301-4738.53052. PMID: 19574695. Exclusion Code: X3.
141. Kothari M, Kosumbkar S. Ultra-rapid school vision screening in developing nations using the Bruckner test. *Am Orthopt J*. 2010;60:82-6. PMID: 21061888. Exclusion Code: X3.
142. Krishnacharya PS. Study on accommodation by autorefraction and dynamic refraction in children. *J Optom*. 2014 Oct-Dec;7(4):193-202. doi: 10.1016/j.optom.2014.07.001. PMID: 25130066. Exclusion Code: X6.
143. Kulp M, Mitchell GL, Borsting E, et al. Effectiveness of placebo therapy for maintaining masking in a clinical trial of vergence/accommodative therapy. Invest Ophthalmol Vis Sci; 2009. p. 2560-6. Exclusion Code: X3.
144. Kulp MT. Findings from the Vision In Preschoolers (VIP) Study. *Optom Vis Sci*. 2009 Jun;86(6):619-23. doi: 10.1097/OPX.0b013e3181a59bf5. PMID: 19417714. Exclusion Code: X2.
145. Kulp MT, Foster NC, Holmes JM, et al. Effect of ocular alignment on emmetropization in children <10 years with amblyopia. *Am J Ophthalmol*. 2012 Aug;154(2):297-302.e1. doi: 10.1016/j.ajo.2012.02.035. PMID: 22633344. Exclusion Code: X5.
146. Kumaran A, Htoon HM, Tan D, et al. Analysis of Changes in Refraction and Biometry of Atropine- and Placebo-Treated Eyes. *Invest Ophthalmol Vis Sci*. 2015 Aug;56(9):5650-5. doi: 10.1167/iovs.14-14716. PMID: 26313301. Exclusion Code: X3.
147. Kwon M, Lu ZL, Miller A, et al. Assessing binocular interaction in amblyopia and its clinical feasibility. *PLoS One*. 2014;9(6):e100156. doi: 10.1371/journal.pone.0100156. PMID: 24959842. Exclusion Code: X3.
148. Lai XJ, Alexander J, Ho A, et al. Design and validation of a method for evaluation of interocular interaction. *Optom Vis Sci*. 2012 Feb;89(2):183-96. doi: 10.1097/OPX.0b013e31823ee04a. PMID: 22157978. Exclusion Code: X3.
149. Lai YH, Tseng HY, Hsu HT, et al. Uncorrected visual acuity and noncycloplegic autorefraction predict significant refractive errors in Taiwanese preschool children. *Ophthalmology*. 2013 Feb;120(2):271-6. doi: 10.1016/j.ophtha.2012.08.009. PMID: 23182455. Exclusion Code: X9.
150. Lan W, Zhao F, Li Z, et al. Validation and cost-effectiveness of a home-based screening system for amblyopia. *Ophthalmology*. 2012 Jun;119(6):1265-71. doi: 10.1016/j.ophtha.2011.12.027. PMID: 22365057. Exclusion Code: X9.
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152. Lavezzo MM, Sousa RL, Kanamura MS, et al. [PhotoScreener for preschool children visual screening]. *Arq Bras Oftalmol*. 2010 Jan-Feb;73(1):52-6. PMID: 20464114. Exclusion Code: X1.
153. Leat SJ. To prescribe or not to prescribe? Guidelines for spectacle prescribing in infants and children. *Clin Exp Optom*. 2011 Nov;94(6):514-27. doi: 10.1111/j.1444-0938.2011.00600.x. PMID: 21722183. Exclusion Code: X2.
154. Lee SH, Chang JW. The relationship between higher-order aberrations and amblyopia treatment in hyperopic anisometropic amblyopia. *Korean J Ophthalmol*. 2014 Feb;28(1):66-75. doi: 10.3341/kjo.2014.28.1.66. PMID: 24505201. Exclusion Code: X8.
155. Leon A, Donahue SP, Morrison DG, et al. The age-dependent effect of anisometropia magnitude on anisometropic amblyopia severity. *J AAPOS*. 2008 Apr;12(2):150-6. doi: 10.1016/j.jaapos.2007.10.003. PMID: 18155938. Exclusion Code: X8.
156. Leske DA, Holmes JM, Melia BM, et al. Evaluation of the Intermittent Exotropia Questionnaire using Rasch analysis. *JAMA Ophthalmol*. 2015 Apr;133(4):461-5. doi: 10.1001/jamaophthalmol.2014.5622. PMID: 25634146. Exclusion Code: X3.
157. Li SL, Reynaud A, Hess RF, et al. Dichoptic movie viewing treats childhood amblyopia. *J AAPOS*. 2015 Oct;19(5):401-5. doi: 10.1016/j.jaapos.2015.08.003. PMID: 26486019. Exclusion Code: X5.
158. Lim HT, Chun BY. Comparison of OCT measurements between high myopic and low myopic children. *Optom Vis Sci*. 2013 Dec;90(12):1473-8. doi: 10.1097/opx.0000000000000086. PMID: 24121408. Exclusion Code: X3.
159. Lira RP, Santo IF, Astur GL, et al. Refractive error in school children in Campinas, Brazil. *Arq Bras Oftalmol*. 2014 May-Jun;77(3):203-4. PMID: 25295913. Exclusion Code: X3.
160. Liu XT, Zhang F, Lu F. Evaluation of cycloplegic effectiveness of cyclopentolate and atropine. [Chinese]. Zhonghua Shiyan Yanke Zazhi/Chinese Journal of Experimental Ophthalmology; 2012. p. 353-7. Exclusion Code: X1.
161. Lobanova IV, Leshchenko IA, Markova E, et al. [Impact of the method choice and the extent of correction on the development of visual evoked potentials in children and adolescents with refractive anomalies]. *Vestn Oftalmol*. 2013 Jul-Aug;129(4):44-50, 2-3. PMID: 24137982. Exclusion Code: X1.
162. Longmuir S, Pfeifer W, Coussens T, et al. Usefulness of iris reactivity to light to determine the peak cycloplegia in hyperopic children. *Insight*. 2012 Winter;37(1):12-4, 30. PMID: 22439352. Exclusion Code: X3.
163. Longmuir SQ, Boese EA, Pfeifer W, et al. Practical community photoscreening in very young children. *Pediatrics*. 2013 Mar;131(3):e764-9. doi: 10.1542/peds.2012-1638. PMID: 23400603. Exclusion Code: X8.
164. Longmuir SQ, Pfeifer W, Leon A, et al. Nine-year results of a volunteer lay network photoscreening program of 147 809 children using a photoscreener in Iowa. *Ophthalmology*. 2010 Oct;117(10):1869-75. doi: 10.1016/j.ophtha.2010.03.036. PMID: 20656350. Exclusion Code: X5.
165. Longmuir SQ, Pfeifer W, Shah SS, et al. Validity of a layperson-administered Web-based vision screening test. *J AAPOS*. 2015 Feb;19(1):29-32. doi: 10.1016/j.jaapos.2014.10.021. PMID: 25727583. Exclusion Code: X4.
166. Loudon SE, Rook CA, Nassif DS, et al. Rapid, high-accuracy detection of strabismus and amblyopia using the pediatric vision scanner. *Invest Ophthalmol Vis Sci*. 2011 Jul;52(8):5043-8. doi: 10.1167/iovs.11-7503. PMID: 21642624. Exclusion Code: X3.
167. Lowry EA, Lui R, Enanoria W, et al. Repeat Retinomax screening changes positive predictive value. *J AAPOS*. 2014 Feb;18(1):45-9. doi: 10.1016/j.jaapos.2013.11.004. PMID: 24568982. Exclusion Code: X3.

168. Lowry EA, Wang W, Nyong'o O. Objective vision screening in 3-year-old children at a multispecialty practice. *J AAPOS*. 2015 Feb;19(1):16-20. doi: 10.1016/j.jaapos.2014.09.008. PMID: 25727580. Exclusion Code: X5.
169. Ma DJ, Yang HK, Hwang JM. Reliability and validity of an automated computerized visual acuity and stereoacuity test in children using an interactive video game. *Am J Ophthalmol*. 2013 Jul;156(1):195-201.e1. doi: 10.1016/j.ajo.2013.02.018. PMID: 23582763. Exclusion Code: X3.
170. Ma X, Congdon N, Yi H, et al. Safety of Spectacles for Children's Vision: A Cluster-Randomized Controlled Trial. *Am J Ophthalmol*. 2015 Nov;160(5):897-904. doi: 10.1016/j.ajo.2015.08.013. PMID: 26284747. Exclusion Code: X3.
171. Ma X, Zhou Z, Yi H, et al. Effect of providing free glasses on children's educational outcomes in China: cluster randomized controlled trial. *BMJ*. 2014;349:g5740. doi: 10.1136/bmj.g5740. PMID: 25249453. Exclusion Code: X3.
172. Mansouri B, Singh P, Globa A, et al. Binocular training reduces amblyopic visual acuity impairment. *Strabismus*. 2014 Mar;22(1):1-6. doi: 10.3109/09273972.2013.877945. PMID: 24564723. Exclusion Code: X3.
173. Mathew JA, Shah SA, Simon JW. Varying difficulty of Snellen letters and common errors in amblyopic and fellow eyes. *Arch Ophthalmol*. 2011 Feb;129(2):184-7. doi: 10.1001/archophthalmol.2010.369. PMID: 21320964. Exclusion Code: X3.
174. Matta NS, Arnold RW, Singman EL, et al. Comparison between the plusoptiX and MTI Photoscreeners. *Arch Ophthalmol*. 2009 Dec;127(12):1591-5. doi: 10.1001/archophthalmol.2009.294. PMID: 20008713. Exclusion Code: X3.
175. Matta NS, Arnold RW, Singman EL, et al. Can a photoscreener help us remotely evaluate and manage amblyopia? *Am Orthopt J*. 2011;61:124-7. doi: 10.3368/aoj.61.1.124. PMID: 21856880. Exclusion Code: X3.
176. Matta NS, Singman EL, McCarus C, et al. Screening for amblyogenic risk factors using the PlusoptiX S04 photoscreener on the indigent population of Honduras. *Ophthalmology*. 2010 Sep;117(9):1848-50. doi: 10.1016/j.ophtha.2010.01.038. PMID: 20472292. Exclusion Code: X9.
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178. McCullough SJ, Little JA, Breslin KM, et al. Comparison of refractive error measures by the IRX3 aberrometer and autorefraction. *Optom Vis Sci*. 2014 Oct;91(10):1183-90. doi: 10.1097/opx.0000000000000379. PMID: 25192432. Exclusion Code: X3.
179. McCurry TC, Lawrence LM, Wilson ME, et al. The plusoptiX S08 photoscreener as a vision screening tool for children with autism. *J AAPOS*. 2013 Aug;17(4):374-7. doi: 10.1016/j.jaapos.2013.05.006. PMID: 23928004. Exclusion Code: X3.
180. McGlone L, Hamilton R, McCulloch DL, et al. Visual outcome in infants born to drug-misusing mothers prescribed methadone in pregnancy. *Br J Ophthalmol*. 2014 Feb;98(2):238-45. doi: 10.1136/bjophthalmol-2013-303967. PMID: 24246372. Exclusion Code: X3.
181. Melia BM, Holmes JM, Chandler DL, et al. Classifying stability of misalignment in children with esotropia using simulations. *Arch Ophthalmol*. 2010 Dec;128(12):1555-60. doi: 10.1001/archophthalmol.2010.293. PMID: 21149779. Exclusion Code: X8.
182. Meyer-Rusenberg B, Thill M, Vujancevic S, et al. Conservative management of bilateral persistent pupillary membranes with 18 years of follow-up. *Graefes Arch Clin Exp Ophthalmol*. 2010 Jul;248(7):1053-4. doi: 10.1007/s00417-010-1318-9. PMID: 20182884. Exclusion Code: X8.

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183. Mirzajani A, Heirani M, Jafarzadehpur E, et al. A comparison of the Plusoptix S08 photorefractor to retinoscopy and cycloretinoscopy. *Clin Exp Optom*. 2013 Jul;96(4):394-9. doi: 10.1111/cxo.12063. PMID: 23679982. Exclusion Code: X6.

184. Moghaddam AA, Kargozar A, Zarei-Ghanavati M, et al. Screening for amblyopia risk factors in pre-verbal children using the Plusoptix photoscreener: a cross-sectional population-based study. *Br J Ophthalmol*. 2012 Jan;96(1):83-6. doi: 10.1136/bjo.2010.190405. PMID: 21515564. Exclusion Code: X8.

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186. Mohan K, Sharma A. Long-term treatment results of accommodative esotropia. *J AAPOS*. 2014 Jun;18(3):261-5. doi: 10.1016/j.jaapos.2014.01.018. PMID: 24924281. Exclusion Code: X8.

187. Mohney BG, Cotter SA, Chandler DL, et al. A Randomized Trial Comparing Part-time Patching with Observation for Intermittent Exotropia in Children 12 to 35 Months of Age. *Ophthalmology*. 2015 Aug;122(8):1718-25. doi: 10.1016/j.ophtha.2015.04.025. PMID: 26072346. Exclusion Code: X6.

188. Moll AM, Rao RC, Rotberg LB, et al. The role of the random dot Stereo Butterfly test as an adjunct test for the detection of constant strabismus in vision screening. *J AAPOS*. 2009 Aug;13(4):354-6. doi: 10.1016/j.jaapos.2009.03.008. PMID: 19482495. Exclusion Code: X3.

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190. Moseley MJ, Wallace MP, Stephens DA, et al. Personalized versus standardized dosing strategies for the treatment of childhood amblyopia: study protocol for a randomized controlled trial. *Trials*. 2015;16:189. doi: 10.1186/s13063-015-0711-4. PMID: 25906974. Exclusion Code: X5.

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192. Nathan NR, Donahue SP. Modification of Plusoptix referral criteria to enhance sensitivity and specificity during pediatric vision screening. *J AAPOS*. 2011 Dec;15(6):551-5. doi: 10.1016/j.jaapos.2011.08.008. PMID: 22153399. Exclusion Code: X3.

193. Newman DK, East MM. Preschool vision screening: negative predictive value for amblyopia. *Br J Ophthalmol*. 1999 Jun;83(6):676-9. PMID: 10340974. Exclusion Code: X5.

194. Norgett Y, Siderov J. Crowding in children's visual acuity tests--effect of test design and age. *Optom Vis Sci*. 2011 Aug;88(8):920-7. doi: 10.1097/OPX.0b013e31821bd2d3. PMID: 21532515. Exclusion Code: X5.

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198. Ore L, Garozli HJ, Schwartz N, et al. Factors influencing prevalence of vision and ocular abnormalities among Jewish and Arab Israeli schoolchildren. *Isr Med Assoc J*. 2014 Sep;16(9):553-8. PMID: 25351012. Exclusion Code: X3.
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301. Wallace DK, Lazar EL, Holmes JM, et al. A randomized trial of increasing patching for amblyopia. *Ophthalmology*. 2013 Nov;120(11):2270-7. doi: 10.1016/j.ophtha.2013.04.008. PMID: 23755872. Exclusion Code: X5.
302. Wallace DK, Lazar EL, Melia M, et al. Stereoacuity in children with anisometropic amblyopia. *J AAPOS*. 2011 Oct;15(5):455-61. doi: 10.1016/j.jaapos.2011.06.007. PMID: 22108357. Exclusion Code: X6.
303. Wallace DK, Lazar EL, Repka MX, et al. A randomized trial of adding a plano lens to atropine for amblyopia. *J AAPOS*. 2015 Feb;19(1):42-8. doi: 10.1016/j.jaapos.2014.10.022. PMID: 25727586. Exclusion Code: X4.
304. Walsh LA, Hahn EK, LaRoche GR. The method of treatment cessation and recurrence rate of amblyopia. *Strabismus*. 2009 Sep;17(3):107-16. doi: 10.1080/09273970903126709. PMID: 20804358. Exclusion Code: X5.
305. Wang J, Hatt SR, O'Connor AR, et al. Final version of the Distance Randot Stereotest: normative data, reliability, and validity. *J AAPOS*. 2010 Apr;14(2):142-6. doi: 10.1016/j.jaapos.2009.12.159. PMID: 20199880. Exclusion Code: X3.
306. Wang XM, Ma LX, Wang LH. [Research of cyclopentolate 1% on the effect of cycloplegia for Chinese hyperopic children]. *Zhonghua Yan Ke Za Zhi*. 2011 Nov;47(11):989-94. PMID: 22336064. Exclusion Code: X1.
307. Wu J, Nazemi F, Schofield J, et al. Effectiveness of telescopic magnification in the treatment of amblyopia: a pilot study. *Arch Ophthalmol*. 2010 Mar;128(3):297-302. doi: 10.1001/archophthalmol.2009.400. PMID: 20212198. Exclusion Code: X5.

Appendix C. Excluded Studies

308. Wu L, Zhang GL, Yang YX. [Clinical study on electrical plum-blossom needle for treatment of amblyopia in children]. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2011 Mar;31(3):342-5. PMID: 21485075. Exclusion Code: X1.
309. Wu PC, Yang YH, Fang PC. The long-term results of using low-concentration atropine eye drops for controlling myopia progression in schoolchildren. *J Ocul Pharmacol Ther*. 2011 Oct;27(5):461-6. doi: 10.1089/jop.2011.0027. PMID: 21815829. Exclusion Code: X3.
310. Xie JZ, Tarczy-Hornoch K, Lin J, et al. Color vision deficiency in preschool children: the multi-ethnic pediatric eye disease study. *Ophthalmology*. 2014 Jul;121(7):1469-74. doi: 10.1016/j.ophtha.2014.01.018. PMID: 24702753. Exclusion Code: X4.
311. Yamada T, Hatt SR, Leske DA, et al. Spectacle wear in children reduces parental health-related quality of life. *J AAPOS*. 2011 Feb;15(1):24-8. doi: 10.1016/j.jaapos.2010.11.003. PMID: 21315631. Exclusion Code: X3.
312. Yamada T, Hatt SR, Leske DA, et al. A new computer-based pediatric vision-screening test. *J AAPOS*. 2015 Apr;19(2):157-62. doi: 10.1016/j.jaapos.2015.01.011. PMID: 25892043. Exclusion Code: X3.
313. Yan XR, Jiao WZ, Li ZW, et al. Performance of the Plusoptix A09 photoscreener in detecting amblyopia risk factors in Chinese children attending an eye clinic. *PLoS One*. 2015;10(6):e0126052. doi: 10.1371/journal.pone.0126052. PMID: 26030210. Exclusion Code: X3.
314. Yang HK, Hwang JM. The effect of target size and accommodation on the distant angle of deviation in intermittent exotropia. *Am J Ophthalmol*. 2011 May;151(5):907-13.e1. doi: 10.1016/j.ajo.2010.11.021. PMID: 21333266. Exclusion Code: X3.
315. Yeh ML, Chen HH, Chung YC. One year study on the integrative intervention of acupressure and interactive multimedia for visual health in school children. *Complement Ther Med*. 2012 Dec;20(6):385-92. doi: 10.1016/j.ctim.2012.09.001. PMID: 23131368. Exclusion Code: X3.
316. Yilmaz I, Ozkaya A, Alkin Z, et al. Comparison of the Plusoptix A09 and Retinomax K-Plus 3 with retinoscopy in children. *J Pediatr Ophthalmol Strabismus*. 2015 Jan-Feb;52(1):37-42. doi: 10.3928/01913913-20141230-06. PMID: 25643369. Exclusion Code: X3.
317. Ying GS, Huang J, Maguire MG, et al. Associations of anisometropia with unilateral amblyopia, interocular acuity difference, and stereoacuity in preschoolers. *Ophthalmology*. 2013 Mar;120(3):495-503. doi: 10.1016/j.ophtha.2012.08.014. PMID: 23174398. Exclusion Code: X5.
318. Ying GS, Maguire MG, Cyert LA, et al. Prevalence of vision disorders by racial and ethnic group among children participating in head start. *Ophthalmology*. 2014 Mar;121(3):630-6. doi: 10.1016/j.ophtha.2013.09.036. PMID: 24183422. Exclusion Code: X6.
319. Zhang Y, Huang S, Ye H, et al. [A design of refractometer based on blur circle]. *Zhongguo Yi Liao Qi Xie Za Zhi*. 2011 Mar;35(2):103-7. PMID: 21706792. Exclusion Code: X1.
320. Zinkernagel SM, Mojon DS. Distance doubling visual acuity test: a reliable test for nonorganic visual loss. *Graefes Arch Clin Exp Ophthalmol*. 2009 Jun;247(6):855-8. doi: 10.1007/s00417-008-1019-9. PMID: 19089440. Exclusion Code: X3.

Appendix D Table 1. Quality Assessment for Randomized, Controlled Trial (KQ 1)

Study, Year	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Were outcome measurements equal, valid, and reliable?	Were outcome assessors masked?	Did the study have cross-overs or contamination raising concern for bias?	Differential loss to followup or overall high loss to followup raising concern for bias?	Did the study use acceptable statistical methods?	Quality Rating	Comments
Williams et al, 2001[74] and 2002[75]	No	Yes	Yes	Yes	Yes	NR	No	Yes	Modified ITT, no handling of missing data	Fair	Participants were invited to intervention or control according to the last digit of the mother's day of birth (not random); high overall attrition; of 3,490 children invited, 1,914 attended the final exam at 7.5 years and were included in analyses (55% of those randomized); differential attrition was low (1%); modified ITT (children remained in groups they were invited in to, regardless of whether they attended intervention clinics); no handling of missing data.

Abbreviations: ITT=intention to treat; KQ=Key Question.

Appendix D Table 2. Quality Assessment for Prospective Cohort Study (KQ 1)

First Author, Year	Did the study have differential attrition or overall high attrition raising concern for bias?	Were outcome measurements equal, valid, and reliable?	Were outcome assessors masked?	Was the duration of followup adequate to assess the outcome?	Did the analysis control for baseline differences between groups?	Did the analysis control for potential confounders?	Did the analysis account for differences in treatment received by the groups?	Were the statistical methods used to assess the outcomes appropriate?	Quality Rating	Comments
Williams et al, 2003[76]	Yes; see footnote[a]	Yes	Yes	Yes	Yes	Yes	NA	Yes	Fair	See footnote[a]

[a] High overall attrition. Approximately 14,000 were recruited/enrolled in ALSPAC cohort study; 8,042 attended the final exam at 7.5 years. Of these, 1,917 were in the RCT and excluded and 44 had developmental delays and were excluded, leaving 6,081 analyzed (of those, 1,516 had been offered preschool vision screening and 1,019 had received it).

Abbreviations: ALSPAC=Avon Longitudinal Study of Parents and Children; KQ=Key Question; RCT=randomized controlled trial.

Appendix D Table 3. Quality Assessments: Studies of Test Accuracy and Reliability (KQ 2)

Author, Year	Representative Spectrum[a]	Random or Consecutive Sample	Screening Test Adequately Described	Screening Cutoffs Predefined	Credible Reference Standard	Reference Standard Applied to All Screened or Random Samples[b]	Time Between Test and Reference Short Enough[c]	Reference Standard and Screening Exam Interpreted Independently	High Rate of Uninterpretable Results or Noncompliance with Screening Test	Analysis Includes Patients with Uninterpretable Results or Noncompliance	Quality Score
Adler et al, 2012[151]	Unclear	Yes	Yes	NA	Yes (test-retest)	Yes	Yes	Partially (for less than half of retests)	No	NA	Poor
Afsari et al, 2013[77]	Yes	NR	Yes	No	Yes	Yes	Yes	NR	Yes (35%)	No	Fair
Arthur et al, 2009[78]	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	No	NA	Fair
Barry et al, 2001[79]	Yes	Yes	Yes	Yes	NR	No	Yes	NR	NR	NR	Fair
Barry et al, 2003[80]	Yes	Yes	Yes	Yes	NR	No	Yes	Yes	Yes	No	Fair
Bertuzzi et al, 2006[81]	Yes	NR	Yes	Yes	Yes	Yes	Yes	NR	No	No	Fair
Chui et al, 2004[82]	Yes	NR	Yes	Yes	Yes	No	Yes	Yes	NR	Yes	Fair
Cogen et al, 1992[83]	Yes	NR	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Fair
Cooper et al, 1999[152]	No	NR	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Poor
Dahlmann-Noor et al, 2009[84]	No	NR	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Fair
Dahlmann-Noor et al, 2009[85]	Yes	NR	Yes	Yes	NR	Yes	Yes	NR	No	NA	Fair
Ehrt et al, 2007[153]	No	NR	Yes	Yes	NR	NR	Yes	NR	Yes	Yes	Poor
Harvey et al, 2009[86]	No	NR	Yes	NA	NA (testability)	NA	NA	NA	No	Yes	Fair
Hope et al, 1990[87]	Yes	NR	Yes	Yes	Yes	Yes	Yes	NR	No	No	Fair
Huang et al, 2013[88]	No	Yes (random for those who passed; all those who failed screen)	Yes	No	Yes	Yes	Yes	Yes	No	No	Fair
Jost, 2015 [89]	Yes	Yes	Yes	Yes	Yes	No (but attempted to)	NR	Yes	Yes	Yes (former) No (latter)	Fair

Appendix D Table 3. Quality Assessments: Studies of Test Accuracy and Reliability (KQ 2)

Author, Year	Representative Spectrum[a]	Random or Consecutive Sample	Screening Test Adequately Described	Screening Cutoffs Predefined	Credible Reference Standard	Reference Standard Applied to All Screened or Random Samples[b]	Time Between Test and Reference Short Enough[c]	Reference Standard and Screening Exam Interpreted Independently	High Rate of Uninterpretable Results or Noncompliance with Screening Test	Analysis Includes Patients with Uninterpretable Results or Noncompliance	Quality Score
Kemper et al, 2005[90]	No	Yes	Yes	Yes	Yes	Yes	Yes	NR	NR	NR	Fair
Kennedy et al, 1989[91]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	NA	Fair
Kennedy et al, 1995[92]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NR	No	NA	Fair
Kennedy et al, 2000[93]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Fair
Kulp et al, 2014[94]	No	Yes (random for those who passed; all those who failed screen)	Yes	No	Yes	Yes	Yes	Yes	No	NR	Fair
Leone et al, 2012[95]	Yes	NR	Yes	NA	NA (testability)	NA	NA	NA	Yes, for age 24 to <36 months	Yes	Fair
Matta et al, 2008[96]	No	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR	Fair
Miller et al, 1999[97]	No (High-prevalence population)	NR	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Fair
Miller et al, 2001[98]	No (High-prevalence population)	NR	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Fair
Molteno et al, 1993[154]	No	NR	Yes	Yes	No	Yes	Yes	NR	NR	NR	Poor
Morgan et al, 1987[99]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Fair
Ottar et al, 2002[101]	Yes	NR	Yes	Yes	Yes	Yes	Yes	NR	No	Yes	Fair
Rogers et al, 2008[102]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Schmidt (VIP) et al, 2004[65]; Freedman, 2006[104]	No	NR	Yes	No	Yes	Yes	Yes	Yes	No	No	Fair

Appendix D Table 3. Quality Assessments: Studies of Test Accuracy and Reliability (KQ 2)

Author, Year	Representative Spectrum[a]	Random or Consecutive Sample	Screening Test Adequately Described	Screening Cutoffs Predefined	Credible Reference Standard	Reference Standard Applied to All Screened or Random Samples[b]	Time Between Test and Reference Short Enough[c]	Reference Standard and Screening Exam Interpreted Independently	High Rate of Uninterpretable Results or Noncompliance with Screening Test	Analysis Includes Patients with Uninterpretable Results or Noncompliance	Quality Score
Shallo-Hoffmann et al, 2004[103]	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Fair
Singman et al, 2013[155]	No	Yes	Yes	Yes	Yes	NR	Unclear	NR	Unclear	NR	Poor
Tong et al, 2000[105]	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Fair
VIP, 2011[106]	No	NR	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Fair
VIP, 2010[107]	No	NR	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Fair
VIP, 2005[108]	No	NR	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Fair
Weinand et al, 1998[109]	No	NR	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Fair
Williams et al, 2000[110]	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Fair
Ying et al, 2011[111]	No	NR	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Fair

[a] Was the spectrum of patients representative of the patients who will receive the test in primary care?
[b] Did the whole or a random selection of the sample receive reference test? Did patients receive the same reference diagnostic test regardless of screening test results?
[c] Is the time period between the test and reference test short enough (to be reasonably sure that the condition did not change between the two tests) (no longer than 1 year)?

Abbreviations: VIP=Vision in Preschoolers.

Appendix D Table 4. Quality Assessments for Randomized, Controlled Trials That Evaluate Treatment of Amblyopia, Its Risk Factors, and Refractive Error (KQs 4 and 5)

First Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Was intervention fidelity adequate?	What was reported adherence to the intervention?	What was the overall attrition?	What was the differential attrition?	Did the study have differential attrition or overall high attrition raising concern for bias?
Awan et al, 2005[117]	NR	Yes	Yes	Yes	1 hour, 43 min per day for the 3-hour group; 2 hours, 33 min per day for 6-hour group	13.3%	5%	No
Clarke et al, 2003[115]	Yes	Yes	Yes	Yes	69% of those prescribed glasses wore them most or all the time; 6% would not wear them at all. 25/42 (60%) requiring patching wore it >two-thirds of the required time; 7% would not wear at all	5.1% (at 52 weeks)	0	No
Wallace et al, 2006[116] PEDIG	Yes	NR	Yes	Yes	Patching adherence was excellent (76–100%) for 68%, good (51–75%) for 22%, and fair-poor for 9%	3.9% (at 5 weeks)	3.1%	No

Abbreviations: KQ=Key Question; min=minutes; NR=not reported; PEDIG=Pediatric Eye Disease Investigator Group.

First Author, Year	Did the study have cross-overs or contamination raising concern for bias?	Were outcome measurements equal, valid, and reliable?	Were patients masked?	Were providers masked?	Were outcome assessors masked?	Was the duration of followup adequate to assess the outcome?	What was the method used to handle missing data?	Did the study use acceptable statistical methods?	Quality Rating
Awan et al, 2005[117]	No	Yes	No	No	No	Yes	NR	Yes	Fair
Clarke et al, 2003[115]	No (very few)	Yes	No	No	Yes	Yes	None	Yes	Good
Wallace et al, 2006[116] PEDIG	No	Yes	No	No	Yes	Yes	None	Yes	Good

Abbreviations: ITT=intention to treat; KQ=Key Question; NR=not reported; PEDIG=Pediatric Eye Disease Investigator Group.

Appendix E Table 1. Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests, by Test Type (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
Visual Acuity Tests						
Bertuzzi et al, 2006[81]	LEA Symbols visual acuity test (comprehensive eye exam with cycloplegic refraction)	A: 0.96 (0.78 to 1.0) B: 0.78 (0.56 to 0.92)	A: 0.83 (0.75 to 0.90) B: 0.93 (0.87 to 0.97)	A: 5.7 (3.8 to 8.6) B: 12 (5.8 to 24)	A: 0.05 (0.01 to 0.36) B: 0.23 (0.11 to 0.51)	Fair
Miller et al, 1999[97]	LEA Symbols visual acuity test (cycloplegic refraction and retinoscopy)	0.91 (0.82 to 0.96)	0.44 (0.37 to 0.52)	1.6 (1.4 to 1.9)	0.21 (0.10 to 0.43)	Fair
Miller et al, 2001[98]	LEA Symbols visual acuity test (cycloplegic refraction)	0.93 (0.87 to 0.97)	0.51 (0.44 to 0.57)	1.9 (1.6 to 2.2)	0.14 (0.08 to 0.27)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[65]	Crowded linear LEA Symbols visual acuity test A: 10/32 for age 3 years, 10/20 for age 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 exam with cycloplegic refraction)	Any condition A: 0.61 (0.56 to 0.66) B: 0.49 (0.44 to 0.54) "Very important to detect and treat early" conditions A: 0.77 (0.69 to 0.84) B: 0.65 (0.56 to 0.73)	Any condition A: 0.90 (0.88 to 0.92) B: 0.94 (0.92 to 0.96)	Any condition A: 6.1 (4.8 to 7.6) B: 8.2 (6.1 to 11)	Any condition A: 0.43 (0.38 to 0.50) B: 0.54 (0.49 to 0.60)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[65]	Crowded linear HOTV visual acuity test A: 10/25 for age 3 and 4 years, 10/20 for age 5 years B: 10/32 for age 3 and 4 years, 10/25 for age 5 years* (comprehensive eye exam with cycloplegic refraction)	Any condition A: 0.54 (0.49 to 0.59) B: 0.36 (0.31 to 0.41) "Very important to detect and treat early" conditions A: 0.72 (0.64 to 0.79) B: 0.48 (0.40 to 0.57)	Any condition A: 0.89 (0.87 to 0.91) B: 0.93 (0.91 to 0.95)	Any condition A: 4.9 (3.9 to 6.1) B: 5.1 (3.8 to 6.8)	Any condition A: 0.52 (0.46 to 0.58) B: 0.69 (0.63 to 0.74)	Fair
Stereoacuity Tests						
Afsari et al, 2013[77] Sydney Paediatric Eye Disease Study	Stereoacuity: All: Lang-Stereotest II <30 mo and older that could not do RPST-Stereo Smile Stereoacuity II Test >/30 mo-Randot Preschool Stereoacuity Test (Comprehensive exam [per Multi-ethnic Pediatric Eye Disease Study and Baltimore Pediatric Eye Disease Study protocol] and autorefraction)	SSST-strabismus 120: 83%(62 to 104) 240: 50% (22 to 78) 480: 50% (22 to 78) SSST-anisometropia 120: 33% (7 to 60) 240: 17% (-4 to 38) 480: 17% (-4 to 38) SSST-amblyopia 120: 50% (1 to 99) 240: 50% (1 to 99) 480: 50% (1 to 99) RPST-strabismus 200: 48% (31 to 66) 400: 36% (20 to 53) 800: 27% (12 to 42) RPST-anisometropia	SSST-strabismus 120: 60% (56 to 65) 240: 87% (83 to 90) 480: 96% (94 to 98) SSST-anisometropia 120: 59% (54 to 64) 240: 85% (82 to 89) 480: 95% (93 to 97) SSST-amblyopia 120: 59% (55 to 64) 240: 86% (82 to 89) 480: 95% (93 to 97) RPST-strabismus 200: 93% (92 to 95) 400: 97% (96 to 98) 800: 99% (98 to 99) RPST-anisometropia	SSST-strabismus 120: 2.08 240: 3.85 480: 12.5 SSST-anisometropia 120: 0.81 240: 1.13 480: 3.40 SSST-amblyopia 120: 1.22 240: 3.57 480: 10 RPST-strabismus 200: 6.86 400: 12.00 800: 27.0 RPST-anisometropia	SSST-strabismus 120: 0.28 240: 0.57 480: 0.52 SSST-anisometropia 120: 1.14 240: 0.97 480: 0.87 SSST-amblyopia 120: 0.84 240: 0.58 480: 0.53 RPST-strabismus 200: 0.56 400: 0.66 800: 0.74 RPST-anisometropia	Fair

Appendix E Table 1. Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests, by Test Type (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
		200: 35% (15 to 54) 400: 30% (12 to 49) 800: 9% (-3 to 20) RPST-amblyopia 200: 53% (25 to 77) 400: 47% (23 to 71) 800: 24% (3 to 44)	200: 93% (91 to 94) 400: 96% (95 to 97) 800: 98% (97 to 99) RPST-amblyopia 200: 93% (91 to 94) 400: 96% (95 to 97) 800: 98% (97 to 99)	200: 5.0 400: 7.50 800: 4.50 RPST-amblyopia 200: 7.57 400: 11.75 800: 12.00	200: 0.70 400: 0.73 800: 0.93 RPST-amblyopia 200: 0.51 400: 0.55 800: 0.78	
Hope et al, 1990[87]	Random Dot E stereogram (comprehensive eye exam 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 to 1.0)	0.76 (0.68 to 0.82)	3.6 (2.5 to 5.2)	0.15 (0.02 to 0.94)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[65]	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 age 3 and 4 years, stereo card at 50 cm for age 5 years (comprehensive eye exam with cycloplegic refraction)	Any condition A: 0.42 (0.37 to 0.47) B: 0.22 (0.18 to 0.27) "Very important to detect and treat early" conditions A: 0.59 (0.50 to 0.67) B: 0.30 (0.22 to 0.38)	Any condition A: 0.90 (0.88 to 0.92) B: 0.92 (0.90 to 0.94)	Any condition A: 4.2 (3.3 to 5.3) B: 2.7 (2.0 to 3.7)	Any condition A: 0.65 (0.59 to 0.71) B: 0.85 (0.80 to 0.90)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[65]	Stereo Smile II Stereoacuity Test A: 240-arc sec card for age 3 and 4 years, 120-arc sec card for age 5 years B: 480-arc sec card for age 3 and 4 years, 240-arc sec card for age 5 years[†] (comprehensive eye exam with cycloplegic refraction)	Any condition A: 0.44 (0.39 to 0.49) B: 0.33 (0.28 to 0.38) "Very important to detect and treat early" conditions A: 0.72 (0.65 to 0.79) B: 0.57 (0.50 to 0.64)	Any condition A: 0.91 (0.89 to 0.93) B: 0.94 (0.92 to 0.95)	Any condition A: 4.9 (3.9 to 6.1) B: 5.5 (4.2 to 7.3)	Any condition A: 0.62 (0.56 to 0.67) B: 0.71 (0.66 to 0.76)	Fair
VIP Study Group, 2010[107] Phase I, year 1	A. LEA Symbols B. HOTV Symbols (comprehensive eye exam including monocular threshold visual acuity using electronic visual acuity tester, distance and near cover test, and cycloplegic retinoscopy)	For 90% specificity *To detect >1 condition* *3 years* A: 0.61 (0.47 to 0.73) B: 0.46 (0.33 to 0.59) *4 years-young* A: 0.57 (0.46 to 0.67) B: 0.57 (0.46 to 0.67) *4 years-old* A: 0.65 (0.54 to 0.75) B: 0.57 (0.45 to 0.67) *5 years*	Specificity set at 90% or closest to 90% achievable *To detect >1 condition* *3 years* A: 0.90 (0.84 to 0.94) B: 0.88 (0.82 to 0.93) *4 years-young* A: 0.91 (0.86 to 0.94) B: 0.91 (0.86 to 0.94) *4 years-old* A: 0.90 (0.85 to 0.94)	*>1 Condition* *3 years* A: 5.95 (3.58 to 9.88) B: 3.76 (2.27 to 6.22) *4 years-young* A: 6.21 (3.95 to 9.78) B: 6.21 (3.95 to 9.78) *4 years-old* A: 6.63 (4.29 to 10.25) B: 4.33 (2.92 to 6.41) *5 years* A: 7.39 (4.57 to 11.93)	*>1 Condition* *3 years* A: 0.43 (0.31 to 0.60) B: 0.62 (0.49 to 0.79) *4 years-young* A: 0.47 (0.37 to 0.60) B: 0.47 (0.37 to 0.60) *4 years-old* A: 0.39 (0.29 to 0.52) B: 0.50 (0.39 to 0.64) *5 years* A: 0.43 (0.34 to 0.55)	Fair

Appendix E Table 1. Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests, by Test Type (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
		A: 0.60 (0.51 to 0.70) B: 0.56 (0.46 to 0.65) *To detect a group 1 condition* *3 years* A: 0.83 (0.61 to 0.95) B: 0.57 (0.34 to 0.77) *4 years-young* A: 0.73 (0.56 to 0.86) B: 0.65 (0.47 to 0.80) *4 years-old* A: 0.83 (0.65 to 0.94) B: 0.80 (0.61 to 0.92) *5 years* A: 0.78 (0.63 to 0.88) B: 0.82 (0.68 to 0.91)	B: 0.87 (0.82 to 0.91) *5 years* A: 0.92 (0.87 to 0.95) B: 0.92 (0.87 to 0.95) *To detect a group 1 condition* *3 years* A: 0.90 (0.85 to 0.94) B: 0.88 (0.83 to 0.92) *4 years-young* A: 0.91 (0.87 to 0.94) B: 0.91 (0.87 to 0.94) *4 years-old* A: 0.90 (0.86 to 0.93) B: 0.87 (0.82 to 0.91) *5 years* A: 0.92 (0.88 to 0.95) B: 0.92 (0.88 to 0.95)	B: 6.83 (4.21 to 11.10) *Group 1 Condition* *3 years* A: 8.35 (5.24 to 13.31) B: 4.72 (2.79 to 7.98) *4 years-young* A: 8.00 (5.24 to 12.20) B: 7.11 (4.57 to 11.07) *4 years-old* A: 8.24 (5.57 to 12.19) B: 6.10 (4.27 to 8.72) *5 years* A: 9.52 (6.20 to 14.60) B: 10.02 (6.57 to 15.28)	B: 0.48 (0.39 to 0.59) *Group 1 Condition* *3 years* A: 0.19 (0.08 to 0.47) B: 0.49 (0.31 to 0.79) *4 years-young* A: 0.30 (0.17 to 0.51) B: 0.39 (0.25 to 0.60) *4 years-old* A: 0.19 (0.08 to 0.41) B: 0.23 (0.11 to 0.47) *5 years* A: 0.24 (0.15 to 0.41) B: 0.20 (0.11 to 0.36)	
VIP Study Group, 2005[108] Phase II	Linear LEA Symbols Single LEA Symbols (comprehensive eye exam including monocular distance visual acuity, cover testing, cycloplegic retinoscopy)	By severity *Any condition* *Nurse* A: 0.49 (0.44 to 0.54) B: NA *Lay Screener* A: 0.37 (0.32 to 0.42)[c] B: 0.61 (0.56 to 0.66) *Group1* *Nurse* A: 0.60 (0.53 to 0.67) B: NA *Lay Screener* A: 0.50 (0.42 to 0.58)[c] B: 0.78 (0.72 to 0.83) *Group 2* *Nurse* A: 0.38 (0.30 to 0.47) B: NA *Lay Screener* A: 0.19 (0.12 to 0.27)[c] B: 0.51 (0.42 to 0.59)	By severity *Any condition* *Nurse* A: 0.90 (0.88 to 0.92) B: NA *Lay Screener* A: 0.90 (0.88 to 0.92)[c] B: 0.91 (0.89 to 0.93) *Group1* *Nurse* A: 0.90 (0.88 to 0.92) B: NA *Lay Screener* A: 0.90 (0.88 to 0.92)[c] B: 0.91 (0.89 to 0.93) *Group 2* *Nurse* A: 0.90 (0.88 to 0.92) B: NA *Lay Screener* A: 0.90 (0.88 to 0.92)[c] B: 0.91 (0.89 to 0.93)	By severity *Any condition* *Nurse* A: 4.9 (4.0 to 6.0) B: NA *Lay Screener* A: 3.7 (3.0 to 4.7)[d] B: 6.8 (5.5 to 8.4) *Group1* *Nurse* A: 6.0 (4.8 to 7.4) B: NA *Lay Screener* A: 5.0 (4.0 to 6.4)[d] B: 8.7 (7.0 to 10.7) *Group 2* *Nurse* A: NA B: 3.8 (2.9 to 5.0) *Lay Screener* A: 1.9 (1.3 to 2.9)[d] B: 5.6 (4.4 to 7.3)	By severity *Any condition* *Nurse* A: 0.57 (0.52 to 0.62) B: NA *Lay Screener* A: 0.70 (0.65 to 0.76)[d] B: 0.43 (0.38 to 0.48) *Group1* *Nurse* B: 0.44 (0.38 to 0.53) C: NA *Lay Screener* A: 0.56 (0.48 to 0.65)[d] B: 0.24 (0.19 to 0.31) *Group 2* *Nurse* A: NA B: 0.69 (0.60 to 0.78) *Lay Screener* A: 0.90 (0.82 to 0.98)[d] B: 0.54 (0.46 to 0.64)	Fair

Appendix E Table 1. Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests, by Test Type (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
		Group 3 *Nurse* A: 0.42 (0.32 to 0.52) B: NA *Lay Screener* A: 0.35 (0.25 to 0.45)[c] B: 0.40 (0.31 to 0.50)	*Group 3* *Nurse* A: 0.90 (0.88 to 0.92) B: NA *Lay Screener* A: 0.90 (0.88 to 0.92)[c] B: 0.91 (0.89 to 0.93)	*Group 3* *Nurse* A: 4.2 (3.1 to 5.6) B: NA *Lay Screener* A: 3.5 (2.5 to 4.8)[d] B: 4.4 (3.3 to 6.0)	*Group 3* *Nurse* A: 0.65 (0.55 to 0.76) B: NA *Lay Screener* A: 0.73 (0.63 to 0.84)[d] B: 0.66 (0.57 to 0.77)	
VIP Study Group, 2005[108] Phase II	Stereo Smile II Stereo Smile IIA (comprehensive eye exam including monocular distance visual acuity, cover testing, cycloplegic retinoscopy)	By severity *Any condition* *Nurse* A: 0.45 (0.40 to 0.50) B: NA *Lay Screener* A: 0.40 (0.36 to 0.45) B: 0.47 (0.42 to 0.52)[c] *Group1* *Nurse* A: 0.58 (0.51 to 0.65) B: NA *Lay Screener* A: 0.56 (0.49 to 0.63) B: 0.70 (0.62 to 0.77)[c] *Group 2* *Nurse* A: 0.37 (0.29 to 0.45) B: NA *Lay Screener* A: 0.31 (0.24 to 0.40) B: 0.31 (0.23 to 0.40)[c] *Group 3* *Nurse* A: 0.30 (0.21 to 0.39) B: NA *Lay Screener* A: 0.23 (0.16 to 0.32) B: 0.26 (0.17 to 0.35)[c]	By severity *Any condition* *Nurse* A: 0.90 (0.88 to 0.92) B: NA *Lay Screener* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92)[c] *Group1* *Nurse* A: 0.90 (0.88 to 0.92) B: NA *Lay Screener* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92)[c] *Group 2* *Nurse* A: 0.90 (0.88 to 0.92) B: NA *Lay Screener* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92)[c] *Group 3* *Nurse* A: 0.90 (0.88 to 0.92) B: NA *Lay Screener* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92)[c]	By severity *Any condition* *Nurse* A: 4.5 (3.6 to 5.6) B: NA *Lay Screener* A: 4.0 (3.2 to 5.0) B: 4.7 (3.8 to 5.8)[d] *Group1* *Nurse* A: 5.8 (4.7 to 7.2) B: NA *Lay Screener* A: 5.6 (4.5 to 7.0) B: 7.0 (5.7 to 8.6)[d] *Group 2* *Nurse* A: 3.7 (2.8 to 4.9) B: NA *Lay Screener* A: 3.1 (2.3 to 4.2) B: 3.2 (2.3 to 4.3)[d] *Group 3* *Nurse* A: 3.0 (2.1 to 4.2) B: NA *Lay Screener* A: 2.3 (1.6 to 3.4) B: 2.6 (1.8 to 3.8)[d]	By severity *Any condition* *Nurse* A: 0.61 (0.56 to 0.67) B: NA *Lay Screener* A: 0.67 (0.62 to 0.72) B: 0.59 (0.53 to 0.65)[d] *Group1* *Nurse* A: 0.47 (0.40 to 0.55) B: NA *Lay Screener* A: 0.49 (0.42 to 0.57) B: 0.34 (0.27 to 0.42)[d] *Group 2* *Nurse* A: 0.70 (0.62 to 0.80) B: NA *Lay Screener* A: 0.76 (0.68 to 0.85) B: 0.76 (0.67 to 0.86)[d] *Group 3* *Nurse* A: 0.78 (0.69 to 0.89) B: NA *Lay Screener* A: 0.85 (0.77 to 0.95) B: 0.83 (0.74 to 0.93)[a]	Fair

Appendix E Table 1. Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests, by Test Type (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
Cover-Uncover Test						
Vision in Preschoolers Study Group (Phase I), 2004[65]	Cover-uncover test (comprehensive eye exam with cycloplegic refraction)	Any condition 0.16 (0.12 to 0.20) "Very important to detect and treat early" conditions 0.24 (0.17 to 0.32)	Any condition 0.98 (0.97 to 0.99)	Any condition 7.9 (4.6 to 14)	Any condition 0.86 (0.82 to 0.90)	Fair
Combined Clinical Examination Screening Tests						
Barry et al, 2003[79]	Visual inspection, cover-uncover test, eye motility and head posture exam, LEA Symbols visual acuity test (second orthoptic exam using more stringent criteria, followed by ophthalmological exam for abnormal, missing, or inconsistent results)	0.91 (0.71 to 0.99)	0.94 (0.92 to 0.95)	15 (11 to 19)	0.10 (0.03 to 0.36)	Fair
Chui et al, 2004[82]	LEA Symbols visual acuity test, Frisby stereoacuity test, and external visual inspection (comprehensive eye exam with cycloplegic refraction)	0.67 (0.41 to 0.87) <41 months: 0.75 (0.43 to 0.94) ≥41 months: 0.50 (0.12 to 0.88)	0.86 (0.79 to 0.92) <41 months: 0.90 (0.52 to 0.82) ≥41 months: 0.95 (0.88 to 0.99)	4.8 (2.8 to 8.4) <41 months: 2.4 (1.4 to 4.1) ≥41 months: 10 (3.0 to 36)	0.39 (0.20 to 0.75) <41 months: 0.37 (0.13 to 1.0) >41 months: 0.53 (0.24 to 1.2)	Fair
Kennedy et al, 1995[92]	Snellen E or Stycar-graded balls visual acuity test and Titmus stereotest (comprehensive eye exam without cycloplegic refraction)	0.09 (0.04 to 0.20) ‡	1.0 (0.99 to 1.0) ‡	17 (5.5 to 54) ‡	0.91 (0.84 to 0.99)‡	Fair
Shallo-Hoffmann et al, 2004[103]	LEA Symbols and HOTV chart and Random Dot E stereoacuity test (comprehensive eye exam with cycloplegic refraction)	0.73 (0.13 to 0.98) §	0.94 (0.90 to 0.96) §	12 (4.7 to 28) §	0.28 (0.03 to 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; NA=not available; VIP=Vision in Preschoolers.

Appendix E Table 2. Characteristics of Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Screening Test	Reference Standard	Type of Study	Setting Country	Screener	N
Afsari et al, 2013[77] Sydney Paediatric Eye Disease Study	Lang-Stereotest II (all) Randot Preschool Stereoacuity Test (children 30 months and older) Stereo Smile Stereoacuity II Test (children <30 months and children that could not do RPST)	Comprehensive exam (per Multi-ethnic Pediatric Eye Disease Study and Baltimore Pediatric Eye Disease Study protocol) and autorefraction	Cross-sectional	Clinic; identified subjects from door-to-door census in the Sydney Metropolitan area Australia	Medical doctors and orthoptists trained in the study protocol	1,606
Arthur et al, 2009[78]	Plusoptix autorefractor (previously called the Power Refractor)	Cycloplegic refraction	Cross-sectional	Kindergarten Canada	Dental assistant	307
Barry et al, 2001[79]	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	404
Barry et al, 2003[80]	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	1,180
Bertuzzi et al, 2006[81]	Crowded LEA Symbols visual acuity chart	Cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic Italy	Not described	149
Chui et al, 2004[82]	Crowded LEA Symbols visual acuity chart, Frisby stereoacuity test, and external visual inspection	Cycloplegic refraction	Cross-sectional	Not described Canada	Nurse	178 (141 completed gold standard evaluation)
Cogen et al, 1992[83]	VisiScreen 100 photoscreener	Cycloplegic refraction ("when possible")	Cross-sectional	Pediatric ophthalmology clinic United States	Technician	127

Appendix E Table 2. Characteristics of Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Screening Test	Reference Standard	Type of Study	Setting Country	Screener	N
Dahlmann-Noor et al, 2009a[84]	Plusoptix autorefractor (previously called the Power Refractor)	Cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United Kingdom	Ophthalmologist, orthoptist, or ophthalmic nurse	126
Dahlmann-Noor et al, 2009b[85]	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	288
Harvey et al, 2009[86]	Welch Allyn SureSight®	NA (study of testability)	Cross-sectional	Head Start program, kindergarten/first grade classrooms, from the community; United States (Native American population)	NR	937
Hope et al, 1990[87]	Random Dot E stereogram	Comprehensive eye exam with cycloplegic refraction for visual acuity worse than 4/4 with the letter matching test 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	176
Jost, 2015[89]	A: Pediatric Vision Scanner[a] B: SureSight Autorefractor	Comprehensive eye exam with cycloplegic retinoscopy	Cross-sectional	Pediatric primary care, United States	Research staff	293 enrolled and screened; 102 had reference standard
Kemper et al, 2005[90]	SureSight autorefractor	Cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United States	Orthoptist or pediatric ophthalmologist	170

Appendix E Table 2. Characteristics of Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Screening Test	Reference Standard	Type of Study	Setting Country	Screener	N
Kennedy et al, 1989[91]	A: Otago-type photoscreener (non-commercial) B: Off-axis-type photoscreener (non-commercial)	Cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic Canada	Technician	236
Kennedy et al, 1995[92]	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	264
Kennedy et al, 2000[93]	iScreen photoscreener	Comprehensive eye exam with cycloplegic refraction (in patients younger than 4 years old)	Cross-sectional	Pediatric ophthalmology clinic Canada	Technician	449
Kulp et al, 2014[94] VIP (Phases 1 and 2)	A: Noncycloplegic retinoscopy (used in phase 1, year 1) B: Retinomax autorefractor (used in both phases, both years) C: SureSight Vision Screener (used in phase 1, year 02 and Phase II)	Cycloplegic retinoscopy	Cross-sectional	Enrolled in 5 Head Start clinical centers; phase 1 screened in mobile medical units; Phase II screened in schools United States	Phase 1: eye care professionals Phase II: nurses and lay screeners	4040 (1142 from Phase 1, year 1; 1446 from Phase 1, year 2; 1452 from Phase II)
Leone et al, 2012[95] Sydney Paediatric Eye Disease Study	HOTV letters on electronic visual acuity tester	NA (study of testability)	Cross-sectional	Clinic; identified subjects from door-to-door census in the Sydney Metropolitan area Australia	Medical doctors and orthoptists trained in the study protocol	24 to 59 months: 1,170
Matta et al, 2008[96]	Plusoptix autorefractor (previously called the Photo Refractor)	Cycloplegic refraction	Cross-sectional or retrospective	Pediatric ophthalmology clinic United States	Not stated	80
Miller et al, 1999[97]	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	245

Appendix E Table 2. Characteristics of Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Screening Test	Reference Standard	Type of Study	Setting Country	Screener	N
Miller et al, 2001[98]	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)	NR	379
Morgan et al, 1987[99]	VisiScreen 100 photoscreener	Cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United States	NR	63
Ottar et al, 1995[100] and Donahue et al, 2002[101]	MTI photoscreener	Cycloplegic refraction	Cross- sectional	Public health and pediatric clinics United States	Orthoptist or pediatrician	949
Rogers et al, 2008[102]	MTI photoscreener SureSight autorefractor	Cycloplegic refraction	Randomized controlled trial	Pediatric ophthalmology clinic United States	Trained layperson	100
Shallo-Hoffmann et al, 2004[103]	Crowded LEA Symbol and HOTV visual acuity charts, and Random Dot E stereoacuity test	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	269
Tong et al, 2000[105]	MTI Photoscreener	Cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United States	Not described	387
Schmidt et al, 2004[65] and Freedman et al, 2006[104] VIP Study Phase I	Crowded Linear LEA Symbols visual acuity test	Cycloplegic refraction	Cross-sectional	Customized Head Start screening vans United States	Licensed eye professionals	3,121

Appendix E Table 2. Characteristics of Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Screening Test	Reference Standard	Type of Study	Setting Country	Screener	N
VIP Study Group, 2011[106] Phase II (Pilot)	A. Palm-Automatic Refractometer (Palm A-R) B. Retinomax (autorefractor)	Comprehensive eye exam including cycloplegic retinoscopy, distance and near cover test, and monocular threshold vision acuity using crowded HOTV optotypes	Cross-sectional	PreK Head Start programs Philadelphia, United States	One trained and certified non-eye-care professional screener (other VIP Phase II publications describe use of nurse and lay screeners)	190
VIP Study Group, 2010[107] Phase I, year 1	A. LEA Symbols B. HOTV Symbols	Comprehensive eye examination including monocular threshold visual acuity using electronic visual acuity tester, distance and near cover test, and cycloplegic retinoscopy	Cross-sectional	PreK Head Start programs United States	Optometrist or ophthalmologist	1,142
VIP Study Group, 2005[108] Phase II	A. Retinomax autorefractor B. SureSight C. Linear LEA Symbols D. Single LEA Symbols[b] E. Stereo Smile II F. Stereo Smile II[b]	Comprehensive eye examinations including monocular distance visual acuity, cover testing, cycloplegic retinoscopy	Cross-sectional	Head Start Centers, Screening in Yr 1: Vans (LEA Symbols and Stereoacuity), Yr. 2: Head Start Centers United States	Nurses and lay screeners	Year 1: 1,446 Year 2: 1,452
Weinand et al, 1998[109]	MTI photoscreener	Cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic Germany	Not described	112
Williams et al, 2000[110]	Topcon PR2000 autorefractor	Cycloplegic refraction	Cross-sectional	Pediatric ophthalmology clinic United Kingdom	Orthoptist	222
Ying et al, 2011[111] VIP (Phases I and II)	A: noncyclopegic retinoscopy (only in Phase 1) B: Retinomax C: SureSight	Comprehensive eye examination including monocular threshold visual acuity, cover testing, stereopsis, and cycloplegic retinoscopy	Cross-sectional	PreK Head Start programs United States	Phase 1: eye care professionals Phase II: nurses and lay screeners	4,040

[a] The Pediatric Vision Scanner is not a photoscreener or an autorefractor, it uses a new technology called retinal birefringence scanning.
[b] Lay screeners conducted testing in a VIP van in the 2002 academic year.

Abbreviations: N=sample size; NA=not applicable; RPST=Randot Preschool Stereoacuity Test; VIP=Vision in Preschoolers.

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
Afsari et al, 2013[77] Sydney Paediatric Eye Disease Study	43 of 1,606 had strabismus 35 of 1606 had anisometropia 19 of 1606 had amblyopia	Multiple thresholds given for purposes of normative analysis, not all of which are described here	Strabismus: heterotropia either constant or intermittent Anisometropia: interocular spherical equivalent or anisoastimatism with cylindrical refractive error in any meridian ≥1.00 Amblyopia: interocular difference in visual acuity between the two eyes ≥2 lines, and associated with strabismus, anisometropia or deprivation factor either from history or exam (including cataract, corneal opacities, ptosis, surgical lid closure)	24–72 months NR
Arthur et al, 2009[78]	Amblyopia 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	4 to 5 years Not reported
Barry et al, 2001[79]	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 ≤0.4 (20/50) in either eye, or difference of visual acuity between eyes ≥2 log steps)	3 years Not reported
Barry et al, 2003[80]	Amblyopia or amblyopia risk factors: 2.3% (26/1,114)	Anatomic abnormality, manifest strabismus or unstable refusion 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 ≤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 (≥1.5 D, or astigmatism ≥3 D)	3 years Not reported
Bertuzzi et al, 2006[81]	Amblyopia 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	38 to 54 months Not reported
Chui et al, 2004[82]	Amblyopia 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	35 to 58 months Not reported

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
Cogen et al, 1992[83]	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	6 months to 6 years Not reported
Dahlmann-Noor et al, 2009a[84]	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	Mean 5.5 years 49%
Dahlmann-Noor et al, 2009b[85]	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	4 to 7 years 52%
Hope et al, 1990[87]	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	3 to 4 years Not reported
Jost, 2015[89]	Amblyopia: 1% (1/102) Strabismus: 0	A: Binocularity score $\leq$ 60% B: Refer result per manufacturer's recommendation	Not described	2-6 years
Kemper et al, 2005[90]	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	0 to 5 years (53% 3 to 5 years) Not reported
Kennedy et al, 1989[91]	Any amblyopia 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	0 to 6 years (65% 2 to 6 years) 48%

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
Kennedy et al, 1995[92]	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	Not reported Not reported
Kennedy et al, 2000[93]	Amblyopia 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	Median 7 years Not reported
Kulp et al, 2014[94] VIP (Phases 1 and 2)	Any SRE: ranged from 21% to 26% across groups	Classified as screening pass or fail based on the child's worse eye and using the most positive meridian for hyperopia, most negative meridian for myopia, cylinder for astigmatism, and maximum IOD for anisometropia. Several cutpoints used for each test; see results.	Group 1: hyperopia ≥+5.0 D, myopia ≥6.0 D, astigmatism ≥2.5 D, anisometropia (IOD): >2.0 D hyperopia, >3.0 D astigmatism, or >6.0 D myopia Groups 1 and 2: hyperopia >+3.25 D with IOD in SE of ≥+0.5 D, myopia ≥4.0 D, astigmatism >1.5 D, anisometropia (IOD): >1.0 D hyperopia, >1.5 D astigmatism, or >3.0 D myopia Groups 1, 2, and 3: hyperopia >+3.25 D with IOD in SE of <+0.5 D, myopia >2.0 D, astigmatism and anisometropia NA	3 to 5 years NR
Matta et al, 2008[96]	Amblyopia 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 standard	6 months to 192 months (72% 1–5 years) NR
Miller et al, 1999[97]	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 age <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)	36% 3 years old, 57% 4 years old, 7% 5 to 7 years old Not reported

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
Miller et al, 2001[98]	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	36–63 months 53%
Morgan et al, 1987[99]	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	3 months to 8 years NR
Ottar et al, 1995[100] and Donahue et al, 2002[101]	Amblyopia risk factors: 20% (192/949); higher-magnitude amblyopia 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 (8 mm 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	Mean 29 months NR
Rogers et al, 2008[102]	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 referral criteria (≥4.25, ≥1.00, ≥2.20, ≥3.00) E: MTI "gold standard" referral criteria	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	1 to 6 years (82 ≤5 years) 55%

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
		(≥3.50, >3.00, >1.50, >1.00)		
Shallo-Hoffmann et al, 2004[103]	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	2 to 5 years Not reported
Tong et al, 2000[105]	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	1 to 47 months (44% 2 to 3 years) NR
Schmidt et al, 2004[65] and Freedman et al, 2006[104] VIP Study (Phase I)	Any condition (amblyopia, reduced visual acuity, strabismus, or significant refractive error): 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1% (132/2,588) Strabismus: 1.9% (48/2,588) Significant refractive error: 9.3% (240/2,588)	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 Crowded Linear HOTV: 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 Random Dot E: 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 Stereo Smile II 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	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: stigmatism >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"	36 to 71 months (20% 3 years, 53% 4 years, 27% 5 years) NR

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
		Retinomax: 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)	conditions: amblyopia presumed unilateral and worse eye visual acuity ≤20/64 or suspected bilateral; constant strabismus; anismetropia 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	
Schmidt et al, 2004[65] and Freedman et al, 2006[104] VIP Study (Phase I)		SureSight: 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[c] iScreen and MTI photoscreeners: As specified by manufacturer or interpreter 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[c] Cover-uncover test: Heterotropia		
VIP Study Group, 2011[106]	Amblyopia: 13% (24/181) Strabismus: 6% (10/181) Refractive error: 30% (55/181) Reduced Visual Acuity: 6% (10/181) Any targeted condition: 36% (65/181)	A: Palm-AR Hyperopia (90% specificity): ≥1 D Myopia (90% specificity): ≥3.75 D Astigmatism (90% specificity): ≥2 D Anisometropia (90% specificity): ≥2.5 D Hyperopia (94% specificity): ≥1.5 D Myopia (94% specificity): ≥3.75 D Astigmatism (94% specificity): ≥2 D Anisometropia (94% specificity): ≥2.5 D B: Retinomax Hyperopia (90% specificity): ≥1.25 D	*Group 1 (Very important to detect and treat early):* Amblyopia: Presumed unilateral: ≥3 line interocular difference, a unilateral amblyogenic factor, and worse eye visual acuity ≤20/64; Suspected bilateral: a bilateral amblyogenic factor, worse eye visual acuity <20/50 (3 yr. olds) or <20/40 (4 yr. olds), contralateral eye visual acuity worse than 20/40 (3 yr. olds) or 20/30 (4 yr. olds) Strabismus: constant	3–5 years, Mean: 4.3 years 48% female

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
		Myopia (90% specificity): ≥3.25 D Astigmatism (90% specificity): ≥1.25 D Anisometropia (90% specificity): ≥1.75 D Hyperopia (94% specificity): ≥1.25 D Myopia (94% specificity): ≥3.5 D Astigmatism (94% specificity): ≥2.5 D Anisometropia (94% specificity): ≥1.5 D	Refractive error: Severe anisometropia: interocular difference >2 D hyperopia, >3 D astigmatism, or >6 D myopia; Hyperopia ≥5.0 D; Astigmatism ≥2.5 D; Myopia ≥6.0 D *Group 2 (Important to detect early)* Amblyopia: Suspected unilateral: 2-line interocular difference and unilateral amblyogenic factor; Presumed unilateral: ≥3 line interocular difference, a unilateral amblyogenic factor, and worse eye visual acuity >20/64. Strabismus: intermittent Refractive error: Anisometropia: interocular difference >1 D hyperopia, >1.5 D astigmatism, or >3 D myopia; Hyperopia >3.25 D and <5.0 D and interocular difference in SE ≥0.5 D; Astigmatism >1.5 D and <2.5 D; Myopia ≥4.0 D and <6.0 D *Group 3 (Detection clinically useful)* Unexplained reduced visual acuity; Bilateral: no bilateral amblyogenic factor, worse eye visual acuity <20/50 (3 yr. olds) or <20/40 (4 yr. olds), contralateral eye visual acuity worse than 20/40 (3 yr. olds.) or 20/30 (4 yr. olds); Unilateral: no unilateral amblyogenic factor, worse eye visual acuity <20/50 (3 yr. olds) or <20/40 (4 yr. olds) or ≥2 line difference between eyes (except 20/16 and 20/25) Refractive error: Hyperopia >3.25 D and <5.0 D and interocular difference in SE <0.5 D; Myopia >2.0 D and <4.0 D	
VIP Study Group, 2010[107]	*3 years* ≥1 Condition (Amblyopia, Strabismus, Refractive Error, Reduced visual acuity): 27% (59/215) Group 1 (very important to detect and treat conditions): 11% (23/215) *Young 4 years* ≥1 Condition: 30% (93/311) Group 1:12% (37/311) *Old 4 years*	*3 years* A: 10/25 B: 10/32 *Young 4 years* A: 10/25 B: 10/25 *Old 4 years* A: 10/20 B: 10/20 *5 years* A: 10/20 B: 10/20	Amblyopia: Presumed unilateral: ≥3-line interocular difference, a unilateral amblyogenic factor Suspected unilateral: 2-line interocular difference in visual acuity unilateral amblyogenic factor Suspected bilateral: Worse than 20/50 (3 yr. olds) or 20/40 (4-5 yr. olds) in one eye, worse than 20/40 (3 yr. olds.) or 20/30 (4-5 yr. olds) in contralateral eye, and a bilateral amblyogenic factor Reduced visual acuity:	3–5 years Sex NR

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
	≥1 Condition: 28% (83/297) Group1: 10% (30/297) *5 years* ≥1 Condition: 35% (111/319) Group1: 15% (49/319)		Bilateral: Worse than 20/50 (3 yr. olds) or 20/40 (4-5 yr. olds) in one eye, worse than 20/40 (3 yr. olds) or 20/30(4-5 yr. olds) in contralateral eye, and no bilateral amblyogenic factor Unilateral: Worse than 20/50 (3 yr. olds) or 20/40 (4-5 yr. olds) in one eye or 2-line difference between eyes (except 20/16 and 20/25), and no unilateral amblyogenic factor Strabismus: Any heterotropia in primary gaze Significant refractive error: Astigmatism: >1.50 D between principal meridians Hyperopia: >3.25 D in any meridian Myopia: >2.00 D in any meridian Anisometropia interocular difference >1.00 D for hyperopia, >3.00 for myopia, >1.50 D for astigmatism, antimetropic (one eye hyperopic, one eye myopic) difference >1.0 D and one eye >1.00 D hyperopia, antimetropic difference >3.0 D and one eye >2.0 D myopia	
VIP Study Group, 2005[108]	Year 2 (2003) *Any target condition (amblyopia, strabismus, refractive error, reduced visual acuity)*: 32% (462/1,452) *Group 1 (Very important to detect and treat conditions)*: 14.5% (210/1452)[b] *Group 2 (Important to detect early)*: 9.9% (144/1,452) *Group 3 (Detection clinically useful)*: 4.7% (108/1,452) Year 1 (only Lay Screeners) *Any targeted condition*: 27% (391/1446) *Group 1:* 12% (172/1,446) *Group 2*: 8% (121/1,446) *Group 3:* 7% (98/1,446)	Retinomax Hyperopia Nurse: ≥1.75 D Lay screener: ≥1.5 D Myopia Nurse: ≥3.25 D Lay screener: ≥3.0 D Astigmatism Nurse: ≥1.5 D Lay screener: ≥1.75 D Anisometropia Nurse: ≥2.75 D Lay screener: ≥2.0 D Sure Sight Hyperopia Nurse: ≥4.0 D Lay screener: ≥4.5 D Myopia Nurse: ≥1.0 D Lay screener: ≥1.0 D Astigmatism Nurse: ≥1.75 D	*Amblyopia* Unilateral: 3-line (presumed or 2-line (suspected) interocular acuity difference accompanied by strabismus and/or anisometropia. Bilateral: Reduced visual acuity and an amblyogenic factor in each eye (i.e., astigmatism >2.5 D, hyperopia >5.0 D, or myopia >8.0 D). *Reduced Visual Acuity* 3 yr olds: worse than 20/50 4 yr olds: worse than 20/40	3 to 5 years NR

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
		Lay screener: ≥1.75 D Anisometropia Nurse: ≥2.75 D Lay screener: ≥2.75 D Linear LEA Symbols Age 3 Nurse: 10/32 Lay Screener: 10/25 Age 4 Nurse: 10/25 Lay screener: 10/25 Age 5 Nurse: 10/20 Lay Screener: 10/25		
VIP Study Group, 2005[108]		Single LEA Symbols Age 3 Lay Screener: 5/12.5 Age 4 Lay screener: 5/10 Age 5 Lay Screener: 5/10 Stereo Smile II (2nd year) Age 3 Nurse: 480 arc sec card Lay Screener: 240 arc sec card Age 4 Nurse: 120 arc sec card Lay screener: 120 arc sec card Age 5 Nurse: 120 arc sec card Lay Screener: 120 arc sec card Stereo Smile II (1st year) Age 3 Lay Screener: 240 arc sec card Age 4 Lay screener: 120 arc sec card Age 5 Lay Screener: 120 arc sec card		
Weinand et al, 1998[109]	Any abnormality: 81% (83/102) Refractive error: 41% (41/102) Strabismus without refractive error: 7% (7/102) Strabismus	Crescent at least half the pupil diameter, asymmetry of light reflexes, or organic abnormalities	Refractive error ≥2 D, manifest strabismus, any organic anomaly	6 to 48 months Not reported

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
	with refractive error: 21% (21/102) Organic anomaly: 13% (13/102)			
Williams et al, 2000[110]	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	Median 48 months Not reported
Ying et al, 2011[111] VIP (Phases 1 and 2)	Any VIP-targeted condition: 27% to 32% Group 1 condition: 12% to 15%	Failure criteria dependent upon specificity for any targeted condition and given for each condition: Specificity 0.50 *Hyperopia* A: 2.00 B: 1.50 C: 2.25 *Myopia* A:1.00 B: 2.00 C: 0.50 *Astigmatism* A: 0.50 B: 0.75 C: 0.75 *Anisometropia* A: 1.00 B: 0.75 C: 1.00 Specificity 0.60 *Hyperopia* A: 1.75 B: 0.75 C: 3.25 *Myopia* A: 0.25 B: 2.50 C: 0.75 *Astigmatism* A: 0.75 B: 0.75 C: 0.75	*Group 1 (Very important to detect and treat early)* Amblyopia: Presumed unilateral: ≥3 lines' interocular difference, a unilateral amblyogenic factor, and worse eye visual acuity ≤20/64 Suspected bilateral: a bilateral amblyogenic factor, worse eye visual acuity <20/50 (3 yr. olds) or <20/40 (4–5 yr. olds), contralateral eye visual acuity worse than 20/40 (3 yr. olds) or 20/30 (4–5 yr. olds) Strabismus: constant Refractive error: Severe anisometropia: interocular difference >2 D hyperopia, >3 D astigmatism, or >6 D myopia Hyperopia: ≥5.0 D Astigmatism: ≥2.5 D Myopia: ≥6.0 D *Group 2 (Important to detect early)* Amblyopia: Suspected unilateral: 2-line interocular difference and unilateral amblyogenic factor; Presumed unilateral: ≥3-line interocular difference, a unilateral amblyogenic factor, and worse eye visual acuity >20/64 Strabismus: intermittent Refractive error: Anisometropia: interocular difference >1 D hyperopia, >1.5 D astigmatism, or >3 D myopia Hyperopia: >3.25 D and <5.0 D and interocular difference in SE ≥0.5 D Astigmatism: >1.5 D and <2.5 D	3 to 5 years NR

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
		Anisometropia A: 0.75 B: 2.25 C: 1.75	Myopia ≥4.0 D and <6.0 D	
Ying et al, 2011[111] VIP (Phases 1 and 2)		Specificity 0.70 *Hyperopia* A: 2.00 B: 0.75 C: 2.50 *Myopia* A: 0.25 B: 2.50 C: 0.75 *Astigmatism* A: 1.00 B: 1.00 C: 1.25 *Anisometropia* A: 1.00 B: 2.25 C: 1.25 Specificity 0.80 *Hyperopia* A: 2.50 B: 1.25 C: 3.25 *Myopia* A: 2.00 B: 4.00 C: 0.75 *Astigmatism* A: 1.00 B: 1.00 C: 1.25 *Anisometropia* A: 1.00 B: 1.75 C: 2.25	*Group 3 (Detection clinically useful)* Unexplained reduced visual acuity Bilateral: no bilateral amblyogenic factor, worse eye visual acuity <20/50 (3 yr. olds) or <20/40 (4–5 yr. olds), contralateral eye visual acuity worse than 20/40 (3 yr. olds.) or 20/30 (4–5 yr. olds) Unilateral: no unilateral amblyogenic factor, worse eye visual acuity <20/50 (3 yr. olds) or <20/40 (4–5 yr. olds) or ≥2 line difference between eyes (except 20/16 and 20/25) Refractive error Hyperopia: >3.25 D and <5.0 D and interocular difference in SE <0.5 D Myopia: >2.0 D and <4.0 D	

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
Ying et al, 2011[111] VIP (Phases 1 and 2)		Specificity 0.85 *Hyperopia* A: 2.50 B: 1.00 C: 4.25 *Myopia* A: 1.25 B: 3.75 C: 0.75 *Astigmatism* A: 1.25 B: 1.25 C: 1.25 *Anisometropia* A: 1.00 B: 2.25 C: 3.00 Specificity 0.90 *Hyperopia* A: 2.75 B: 1.75 C: 3.75 *Myopia* A: 2.75 B: 3.75 C: 0.75 *Astigmatism* A: 1.25 B: 1.25 C: 1.75 *Anisometropia* A: 1.50 B: 2.75 C: 2.75		
Ying et al, 2011[111] VIP (Phases 1 and 2)		Specificity 0.95 *Hyperopia* A: 2.50 B: 1.75 C: 5.00 *Myopia* A: 2.00 B: 4.00 C: 1.00		

Appendix E Table 3. Characteristics of Samples in Studies That Report Diagnostic Accuracy of Visual Acuity, Stereoacuity, Strabismus, and Combination Tests (KQ 2)

Author, Year Study Name	Proportion With Condition	Definition of a Positive Screening Exam	Definition of a Case	Age of Enrollees Sex (as % Female)
		Astigmatism A: 2.00 B: 1.75 C: 2.00 *Anisometropia* A: 2.00 B: 2.75 C: 4.00		

[a] Based on 90% specificity.
[b] Based on 0.80 acuity score cutoff.
[c] Based on median results from multiple readers.
‡ Excluded from calculation of median.
[d] Confidence intervals not calculable.
[e] Based on manufacturer's referral criteria.

Abbreviations: D=diopter; IOD=intraocular difference; mm=millimeter; NR=not reported; Palm-AR=Palm-Automatic Refractometer; SRE=significant refractive error; VIP=Vision In Preschoolers; yr.=year.

Appendix E Table 4. Diagnostic Accuracy of Autorefractors (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
Retinomax Autorefractors						
Barry et al, 2001[79]	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)	0.80 (0.44 to 0.98)	0.58 (0.53 to 0.62)	1.9 (1.4 to 2.6)	0.35 (0.10 to 1.2)	Fair
Kulp et al, 2014[94] VIP (Phases 1 and 2)	Retinomax (cycloplegic retinoscopy)	Data reported for multiple cutpoints and multiple set specificites (Table S6 of supplement) *Any SRE*[a] A: 0.96 B: 0.93 C: 0.91 D: 0.86 E: 0.83 F: 0.73 Data also reported separately for myopia, hyperopia, astigmatism, and anisometropia for each cutpoint	A: 0.50 B: 0.60 C: 0.70 D: 0.80 E: 0.85 F: 0.90	NR	NR	Fair
Miller et al, 1999[97]	Retinomax K-Plus autorefractor (cycloplegic refraction and retinoscopy)	0.91 (0.82 to 0.96)	0.86 (0.80 to 0.91)	6.7 (4.5 to 9.8)	0.11 (0.05 to 0.22)	Fair
Miller et al, 2001[98]	Retinomax K-Plus autorefractor (cycloplegic refraction)	0.93 (0.88 to 0.96)	0.95 (0.91 to 0.98)	18.0 (10.0 to 34.0)	0.08 (0.04 to 0.13)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[65]	Retinomax autorefractor (comprehensive eye exam with cycloplegic refraction)	Any condition A: 0.64 (0.60 to 0.67) B: 0.52 (0.48 to 0.56)[b] "Very important to detect and treat early" conditions A: 0.87 (0.84 to 0.91) B: 0.81 (0.77 to 0.85)[b]	Any condition A: 0.90 (0.88 to 0.91) B: 0.94 (0.93 to 0.95)[b]	Any condition A: 6.1 (5.2 to 7.0) B: 8.7 (7.2 to 10)[b]	Any condition A: 0.41 (0.37 to 0.45) B: 0.51 (0.47 to 0.55)[b]	Fair

Appendix E Table 4. Diagnostic Accuracy of Autorefractors (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
VIP Study Group, 2011[106] Phase II (Pilot)	Retinomax autorefractor (comprehensive eye exam with cycloplegic refraction)	For 90% specificity, by severity *Overall* 0.78 (0.67–0.88) *Group 1* 0.93 (0.84–0.94) *Group 2* 0.64 (0.41–0.83) *Group 3* 0.73 (0.45–0.92) Type of Condition *Amblyopia* 0.88 (0.68–0.97) *Strabismus* 0.70 (0.35–0.93) *Refractive Error* 0.84 (0.71–0.92) *Reduced visual acuity* 0.70 (0.35-0.93) For 94% specificity, by severity *Overall* 0.66 (0.53–0.77) *Group 1* 0.82 *Group 2* 0.50 *Group 3* 0.60 Type of Condition *Amblyopia* 0.83 *Strabismus* 0.60 *Refractive Error* 0.75 *Reduced visual acuity* 0.30	Specificity set at 90% or 94% for all sensitivities reported; calculated 95% CIs were (0.83–0.95) and (0.88–0.98), respectively	For 90% specificity, by severity *Overall* 7.58 (4.37–13.15) *Group 1* 9.47 (5.79–15.48) *Group 2* 6.32 (3.61–11.09) *Group 3* 7.16 (4.16–12.34) Type of Condition *Amblyopia* 8.59 (5.27–13.99) *Strabismus* 7.04 (3.84–12.92) *Refractive Error* 8.11 (4.78–13.74) *Reduced visual acuity* 7.04 (3.84–12.92) For 94% specificity, by severity *Overall* 10.96 (5.24–22.95)	For 90% specificity, by severity *Overall* 0.24 (0.15–0.38) *Group 1* 0.08 (0.02–0.30) *Group 2* 0.40 (0.23–0.70) *Group 3* 0.30 (0.13–0.69) Type of Condition *Amblyopia* 0.14 (0.05–0.40) *Strabismus* 0.33 (0.13–0.86) *Refractive Error* 0.18 (0.10–0.33) *Reduced visual acuity* 0.33 (0.13–0.86) For 94% specificity, by severity *Overall* 0.36 (0.26–0.51)	Fair

Appendix E Table 4. Diagnostic Accuracy of Autorefractors (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
VIP Study Group, 2005[108] Phase II	Retinomax autorefractor	By severity, screener tool *Any condition* *Nurse* 0.68 (0.64–0.72) *Lay Screener* 0.62 (0.57–0.66) *Group1* *Nurse* 0.88 (0.83–0.92) *Lay Screener* 0.85 (0.79–0.89) *Group 2* *Nurse* 0.59 (0.51–0.67) *Lay Screener* 0.49 (0.41–0.58) *Group 3* *Nurse* 0.39 (0.30–0.49) *Lay Screener* 0.36 (0.27–0.46)	By severity, screener tool *Any condition* *Nurse* 0.90 (0.88–0.92) *Lay Screener* 0.90 (0.88–0.92) *Group1* *Nurse* 0.90 (0.88–0.92) *Lay Screener* 0.90 (0.88–0.92) *Group 2* *Nurse* 0.90 (0.88–0.92) *Lay Screener* 0.90 (0.88–0.92) *Group 3* *Nurse* 0.90 (0.88–0.92) *Lay Screener* 0.90 (0.88–0.92)	By severity, screener tool *Any condition* *Nurse* 6.8 (5.6–8.3) *Lay Screener* 6.2 (5.1–7.6) *Group1* *Nurse* 8.8 (7.3–10.7) *Lay Screener* 8.5 (7.0–10.3) *Group 2* *Nurse* 5.9 (4.7–7.4) *Lay Screener* 4.9 (3.8–6.3) *Group 3* *Nurse* 3.9 (2.9–5.3) *Lay Screener* 3.6 (2.6–4.9)	By severity, screener tool *Any condition* *Nurse* 0.36 (0.31–0.41) *Lay Screener* 0.42 (0.38–0.48) *Group1* *Nurse* 0.13 (0.09–0.19) *Lay Screener* 0.17 (0.12–0.23) *Group 2* *Nurse* 0.46 (0.37–0.55) *Lay Screener* 0.56 (0.48–0.66) *Group 3* *Nurse* 0.68 (0.58–0.79) *Lay Screener* 0.71 (0.62–0.82)	Fair
Ying et al, 2011[111] VIP (Phases 1 and 2)	Retinomax autorefractor	Sensitivity dependent upon specificity for any targeted condition and given for Group 1 and any targeted condition[c] Specificity 0.50 *Group 1 Conditions* 0.96 *Any Targeted Condition* 0.90 Specificity 0.60 *Group 1 Conditions* 0.96 *Any Targeted Condition* 0.88 Specificity 0.70 *Group 1 Conditions* 0.95 *Any Targeted Condition* 0.83 Specificity 0.80	Fixed at 0.50, 0.60, 0.70, 0.80, 0.85, 0.90, or 0.95	NR	NR	Fair

Appendix E Table 4. Diagnostic Accuracy of Autorefractors (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
		Group 1 Conditions 0.92 *Any Targeted Condition* 0.77 Specificity 0.85 *Group 1 Conditions* 0.91 *Any Targeted Condition* 0.73 Specificity 0.90 *Group 1 Conditions* 0.87 *Any Targeted Condition* 0.68 Specificity 0.95 *Group 1 Conditions* 0.83 *Any Targeted Condition* 0.58				
SureSight Autorefractors						
Jost, 2015[89]	SureSight autorefractor (comprehensive eye exam with cycloplegic retinoscopy)	1.00 (0.02 to 1.0)	0.87 (0.79 to 0.93)	7.9 (4.7 to 13.4)	0.0	Fair
Kemper et al, 2005[90]	SureSight autorefractor (comprehensive eye exam with cycloplegic refraction)	Overall: 0.85 (0.69–0.95) Age <3 years (n=80): 0.80 (0.44–0.97) Age 3 to 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 to 5 years: 0.58 (0.42–0.71)	Overall: 1.8[d] Age <3 years: 1.4[d] Age 3 to 5 years: 2.1[d]	Overall: 0.29[d] Age <3 years: 0.49[d] Age 3 to 5 years: 0.21[d]	Fair
Kulp et al, 2014[94] VIP (Phases 1 and 2)	SureSight Vision Screener used in Phase 1, year 1 (cycloplegic retinoscopy)	Data reported for multiple cutpoints and multiple set specificites (Table S6 of supplement) *Any SRE*[e] A: 0.94 B: 0.91 C: 0.88 D: 0.83 E: 0.77 F: 0.68	A: 0.50 B: 0.60 C: 0.70 D: 0.80 E: 0.85 F: 0.90	NR	NR	Fair

Appendix E Table 4. Diagnostic Accuracy of Autorefractors (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
		Data also reported separately for myopia, hyperopia, astigmatism, and anisometropia for each cutpoint				
Rogers et al, 2008[102]	SureSight autorefractor (comprehensive eye exam 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 (0.4–0.74)	A: 0.38 (0.24 to 0.54) B: 0.64 (0.48 to 0.78) C: 0.69 (0.53 to 0.82) D: 0.74 (0.58 to 0.86)	A: 1.6 (1.2 to 2.0) B: 2.2 (1.4 to 3.4) C: 2.2 (1.3 to 3.5) D: 2.4 (1.4 to 4.1)	A: 0.09 (0.02 to 0.37) B: 0.32 (0.18 to 0.56) C: 0.47 (0.31 to 0.72) D: 0.51 (0.35 to 0.75)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[65]	SureSight autorefractor (comprehensive eye exam 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)[b] "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)[b]	Any condition A1: 0.62 (0.59 to 0.65) A2: 0.90 (0.88 to 0.92) B: 0.94 (0.92 to 0.95)[b]	Any condition A1: 2.2 (2.0 to 2.4) A2: 6.3 (5.2 to 7.7) B: 8.6 (6.6 to 11)[b]	Any condition A1: 0.24 (0.19 to 0.30) A2: 0.41 (0.36 to 0.47) B: 0.52 (0.47 to 0.58)[b]	Fair
VIP Study Group, 2005[108] Phase II	SureSight (comprehensive eye exam including monocular distance visual acuity, cover testing, cycloplegic retinoscopy)	By severity *Any condition* *Nurse* 0.64 (0.60–0.68) *Lay Screener* 0.61 (0.56–0.66) *Group1* *Nurse* 0.83 (0.77-0.88) *Lay Screener* 0.82 (0.76–0.87) *Group 2* *Nurse* 0.57 (0.48-0.65) *Lay Screener* 0.51 (0.42–0.59) *Group 3* *Nurse* 0.34 (0.25–0.44) *Lay Screener* 0.34 (0.25–0.44)	By severity *Any condition* *Nurse* 0.90 (0.88–0.92) *Lay Screener* 0.90 (0.88–0.92) *Group1* *Nurse* 0.90 (0.88–0.92) *Lay Screener* 0.90 (0.88–0.92) *Group 2* *Nurse* 0.90 (0.88–0.92) *Lay Screener* 0.90 (0.88–0.92) *Group 3* *Nurse* 0.90 (0.88–0.92) *Lay Screener* 0.90 (0.88–0.92)	By severity *Any condition* *Nurse* 6.4 (5.3–7.8) *Lay Screener* 6.1 (5.0–7.5) *Group1* *Nurse* 8.3 (6.8–10.1) *Lay Screener* 8.2 (6.7–10.0) *Group 2* *Nurse* 5.7 (4.5–7.2) *Lay Screener* 5.1 (4.0–6.5) *Group 3* *Nurse* 3.4 (2.5–4.7) *Lay Screener* 3.4 (2.5–4.7)	By severity *Any condition* *Nurse* 0.40 (0.35–0.45) *Lay Screener* 0.43 (0.39–0.49) *Group1* *Nurse* 0.19 (0.14–0.26) *Lay Screener* 0.20 (0.15–0.27) *Group 2* *Nurse* 0.48 (0.40–0.58) *Lay Screener* 0.55 (0.46–0.65) *Group 3* *Nurse* 0.73 (0.64–0.84) *Lay Screener* 0.73 (0.64–0.84)	Fair

Appendix E Table 4. Diagnostic Accuracy of Autorefractors (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
Ying et al, 2011[111] VIP (Phases 1 and 2)	SureSight (comprehensive eye exam including monocular threshold visual acuity, cover testing, stereopsis, and cycloplegic retinoscopy)	Sensitivity dependent on specificity for any targeted condition and given for group 1 and any targeted condition[f] Specificity 0.50 *Group 1 Conditions* 0.98 *Any Targeted Condition* 0.91 Specificity 0.60 *Group 1 Conditions* 0.95 *Any Targeted Condition* 0.88 Specificity 0.70 *Group 1 Conditions* 0.95 *Any Targeted Condition* 0.83 Specificity 0.80 *Group 1 Conditions* 0.90 *Any Targeted Condition* 0.77 Specificity 0.85 *Group 1 Conditions* 0.87 *Any Targeted Condition* 0.72 Specificity 0.90 *Group 1 Conditions* 0.82 *Any Targeted Condition* 0.65 Specificity 0.95 *Group 1 Conditions* 0.77 *Any Targeted Condition* 0.55	Fixed at 0.50, 0.60, 0.70, 0.80, 0.85, 0.90, or 0.95	NR	NR	Fair

Appendix E Table 4. Diagnostic Accuracy of Autorefractors (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
Plusoptix Autorefractors						
Arthur et al, 2009[78]	Plusoptix/Power Refractor autorefractor (comprehensive eye exam with cycloplegic refraction)	0.83 (0.67 to 0.93)	0.95 (0.92 to 0.98)	18 (10 to 33)	0.17 (0.08 to 0.36)	Fair
Dahlmann-Noor et al, 2009a[84]	Plusoptix/Power Refractor autorefractor (comprehensive eye exam with cycloplegic refraction)	Myopia: 0.88 (0.30 to 1.0) Hyperopia: 0.20 (0.10 to 0.35) Astigmatism: 0.75 (0.36 to 0.96) Anisometropia: 0.50 (0.31 to 0.69)	Myopia: 0.96 (0.89 to 0.99) Hyperopia: 0.99 (0.92 to 1.0) Astigmatism: 0.93 (0.86 to 0.97) Anisometropia: 0.87 (0.77 to 0.93)	Myopia: 21 (7.8 to 55) Hyperopia: 26 (1.6 to 450) Astigmatism: 11 (4.7 to 24) Anisometropia: 3.7 (1.9 to 7.1)	Myopia: 0.13 (0.01 to 1.7) Hyperopia: 0.81 (0.70 to 0.94) Astigmatism: 0.27 (0.08 to 0.89) Anisometropia: 0.58 (0.40 to 0.84)	Fair
Dahlmann-Noor et al, 2009b[85]	Plusoptix/Power Refractor autorefractor (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)	0.45 (0.29 to 0.62)	1.0 (0.98 to 1.0)	230 (14 to 3680)	0.56 (0.42 to 0.74)	Fair
Matta et al, 2008[96]	Plusoptix/Power Refractor autorefractor (comprehensive eye exam with cycloplegic refraction)	A (manufacturer criteria): 0.98 (0.85 to 1.0) B (revised criteria): 0.98 (0.85 to 1.0)	A: 0.68 (0.51 to 0.81) B: 0.88 (0.74 to 0.96)	A: 3.0 (1.9 to 4.7) B: 8.4 (3.7 to 19)	A: 0.04 (0.01 to 0.26) B: 0.03 (0.00 to 0.20)	Fair
Other Autorefractors						
Vision in Preschoolers Study Group (Phase I), 2004[65]	Power Refractor autorefractor (now called the Plusoptix) (comprehensive eye exam with cycloplegic refraction)	Any condition A: 0.54 (0.49 to 0.59) B: 0.36 (0.31 to 0.41)[b] "Very important to detect and treat early" conditions A: 0.72 (0.65 to 0.79) B: 0.56 (0.48 to 0.63)[b]	Any condition A: 0.90 (0.88 to 0.92) B: 0.94 (0.92 to 0.95)[b]	Any condition A: 5.4 (4.4 to 6.6) B: 6.0 (4.6 to 7.9)[b]	Any condition A: 0.51 (0.46 to 0.57) B: 0.68 (0.63 to 0.73)[b]	Fair

Appendix E Table 4. Diagnostic Accuracy of Autorefractors (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
VIP Study Group, 2011[106] Phase II (Pilot)	Palm-Automatic refractometer (comprehensive eye exam including cycloplegic retinoscopy, distance and near cover test, and monocular threshold vision acuity using crowded HOTV optotypes	For 90% Specificity, by severity *Overall* 0.74 (0.61–0.84) *Group 1* 0.79 (0.59–0.92) *Group 2* 0.77 (0.55–0.92) *Group 3* 0.60 (0.32–0.84) Type of Condition *Amblyopia* 0.75 (0.53–0.90) *Strabismus* 0.70 (0.35–0.93) *Refractive Error* 0.84 (0.71–0.92) *Reduced visual acuity* 0.30 (0.06–0.65) For 94% Specificity, by severity *Overall* 0.66 (0.53–0.77) *Group 1* 0.71 *Group 2* 0.64 *Group 3* 0.60 Type of Condition *Amblyopia* 0.67 *Strabismus* 0.60 *Refractive Error* 0.76 *Reduced visual acuity* 0.30	Specificity set at 90% or 94% for all sensitivities reported; calculated 95% Cis were (0.83–0.95) and (0.88–0.98), respectively.	For 90% Specificity, by severity *Overall* 7.14 (4.10–12.43) *Group 1* 8.01 (4.77–13.45) *Group 2* 7.68 (4.58–12.88) *Group 3* 5.86 (3.18–10.80) Type of Condition *Amblyopia* 7.36 (4.38–12.36) *Strabismus* 7.04 (3.84–12.92) *Refractive Error* 8.11 (4.78–13.74) *Reduced visual acuity* 3.02 (1.06–8.61) For 94% Specificity, by severity *Overall* 10.96 (5.24–22.95)	For 90% Specificity, by severity *Overall* 0.29 (0.19–0.44) *Group 1* 0.24 (0.12–0.48) *Group 2* 0.25 (0.12–0.55) *Group 3* 0.45 (0.24–0.83) Type of Condition *Amblyopia* 0.28 (0.14–0.56) *Strabismus* 0.33 (0.13–0.86) *Refractive Error* 0.18 (0.10–0.33) *Reduced visual acuity* 0.78 (0.52–1.17) For 94% Specificity, by severity *Overall* 0.36 (0.26–0.51)	Fair

Appendix E Table 4. Diagnostic Accuracy of Autorefractors (KQ 2)

Study, Year	Screening Test (Reference Standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
Williams et al, 2000[110]	Topcon PR2000 autorefractor (comprehensive eye examination with cycloplegic refraction)	Spherical error: 0.50 (0.33 to 0.67)[g] Anisometropia: 0.74 (0.52 to 0.90)[g] Astigmatism: 0.47 (0.28 to 0.66)[g]	Spherical error: 0.95 (0.90 to 0.98)[g] Anisometropia: 0.95 (0.91 to 0.98)[g] Astigmatism: 0.96 (0.92 to 0.99)[g]	Spherical error: 9.6 (4.5 to 20)[g] Anisometropia: 15 (7.5 to 32)[g] Astigmatism: 12 (5.2 to 30)[g]	Spherical error: 0.53 (0.38 to 0.73)[g] Anisometropia: 0.27 (0.14 to 0.55)[g] Astigmatism: 0.55 (0.40 to 0.78)[g]	Fair

[a] Data in main paper focused on area under the curve (AUC). For detection of each type of SRE, AUC of each test was high; AUC was better for detecting the most severe levels of SRE than for all Res considered important to detect (AUC 0.97 to 1.00 vs. 0.92 to 0.93). The AUC of each screening test was high for myopia (AUC 0.97 to 0.99). Noncycloplegic retinoscopy and Retinomax performed better than SureSight for hyperopia (AUC 0.92 to 0.99 and 0.90 to 0.98 vs. 0.85 to 0.94, $P \leq 0.02$), Retinomax performed better than NCR for astigmatism greater than 1.50 D (AUC 0.95 vs.0.90, P0.01), and SureSight performed better than Retinomax for anisometropia (AUC 0.85 to 1.00 vs. 0.76 to 0.96, $P \leq 0.07$). Performance was similar for nurse and lay screeners in detecting any SRE (AUC 0.92 to 1.00 vs. 0.92 to 0.99).

[b] Results based on cutoffs to obtain specificity of 94%.

[c] Data in main paper focused on AUC. The AUC for detecting any VIP-targeted condition was 0.83 for NCR, 0.83 (phase I) to 0.88 (phase II) for Retinomax, and 0.86 (phase I) to 0.87 (phase II) for SureSight. The AUC was 0.93 to 0.95 for detecting group 1 (most severe) conditions and did not differ between instruments or screeners or by age of the child.

[d] Unable to calculate confidence intervals, raw data not provided.

[e] Data in main paper focused on AUC. For detection of each type of SRE, AUC of each test was high; AUC was better for detecting the most severe levels of SRE than for all Res considered important to detect (AUC 0.97 to 1.00 vs. 0.92 to 0.93). The AUC of each screening test was high for myopia (AUC 0.97 to 0.99). Noncycloplegic retinoscopy and Retinomax performed better than SureSight for hyperopia (AUC 0.92 to 0.99 and 0.90 to 0.98 vs. 0.85 to 0.94, $P \leq 0.02$), Retinomax performed better than NCR for astigmatism greater than 1.50 D (AUC 0.95 vs.0.90, P0.01), and SureSight performed better than Retinomax for anisometropia (AUC 0.85 to 1.00 vs. 0.76 to 0.96, $P \leq 0.07$). Performance was similar for nurse and lay screeners in detecting any SRE (AUC 0.92 to 1.00 vs. 0.92 to 0.99).

[f] Data in main paper focused on area AUC. The AUC for detecting any VIP-targeted condition was 0.83 for NCR, 0.83 (phase I) to 0.88 (phase II) for Retinomax, and 0.86 (phase I) to 0.87 (phase II) for SureSight. The AUC was 0.93 to 0.95 for detecting group 1 (most severe) conditions and did not differ between instruments or screeners or by age of the child.

[g] Results based on cutoffs to obtain specificity of at least 95%.

Abbreviations: AUC=area under the curve; CI=confidence interval; NCR=noncycloplegic refraction; NR=not reported; SRE=significant refractive error; VIP=Vision In Preschoolers.

Appendix E Table 5. Diagnostic Accuracy of Photoscreeners (KQ 2)

Study, Year	Screening test (Reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
MTI Photoscreener						
Miller et al, 2001[98]	MTI photoscreener (cycloplegic refraction)	0.66 (0.59 to 0.73)[a]	0.71 (0.64 to 0.78)[a]	2.3 (1.8 to 2.9)[a]	0.48 (0.38 to 0.60)[a]	Fair
Ottar et al, 1995[100] and Donahue et al, 2002[101]	MTI photoscreener (comprehensive eye exam with cycloplegic refraction)	Any amblyopia risk factor: 0.82 (0.76 to 0.87) Higher magnitude amblyopia risk factor: 0.50 (0.39 to 0.61)	Any amblyopia risk factor: 0.91 (0.88 to 0.93) Higher magnitude amblyopia risk factor: 0.98 (0.97 to 0.99)	Any amblyopia risk factor: 8.7 (6.9 to 11) Higher magnitude amblyopia risk factor: 33 (18 to 58)	Any amblyopia risk factor: 0.20 (0.15 to 0.27) Higher magnitude amblyopia risk factor: 0.51 (0.41 to 0.63)	Fair
Rogers et al, 2008[102]	MTI photoscreener (comprehensive eye exam with cycloplegic refraction)	0.95 (0.86 to 0.99)	0.88 (0.74 to 0.96)	8.0 (3.5 to 18)	0.06 (0.02 to 0.18)	Fair
Tong et al, 2000[105]	MTI photoscreener (comprehensive eye examination with cycloplegic refraction)	All photographs: 0.56 (0.50 to 0.62) Informative subset of 313 photographs: 0.65 (0.59 to 0.71)	All photographs: 0.91 (0.84 to 0.96) Informative subset of 313 photographs: 0.87 (0.76 to 0.94)	All photographs: 6.4 (3.4 to 12) Informative subset of 313 photographs: 4.9 (2.6 to 9.1)	All photographs: 0.48 (0.42 to 0.56) Informative subset of 313 photographs: 0.40 (0.33 to 0.47)	Fair
Vision in Preschoolers Study Group (Phase I), 2004[65]	MTI photoscreener (comprehensive eye exam with cycloplegic refraction)	Any condition: 0.37 (0.32 to 0.42) "Very important to detect and treat early" conditions: 0.55 (0.48 to 0.63) Amblyopia: 0.64 (0.54 to 0.74) Reduced visual acuity: 0.24 (0.16 to 0.31) Strabismus: 0.65 (0.53 to 0.76) Refractive error: 0.42 (0.37 to 0.48)	Any condition: 0.94 (0.92 to 0.95)	Any condition: 6.2 (4.7 to 8.1)	Any condition: 0.67 (0.62 to 0.72)	Fair
Weinand et al, 1998[109]	MTI photoscreener (comprehensive eye exam with cycloplegic refraction)	Pediatrician interpreter: 0.94 (0.86 to 0.98) Orthoptist interpreter: 0.80 (0.69 to 0.88) Ophthalmologist 1 interpreter: 0.72 (0.61 to 0.82) Ophthalmologist 2 interpreter: 0.86 (0.76 to 0.92)	Pediatrician interpreter: 0.42 (0.20 to 0.66) Orthoptist interpreter: 0.74 (0.49 to 0.91) Ophthalmologist 1 interpreter: 0.74 (0.49 to 0.91) Ophthalmologist 2 interpreter: 0.58 (0.34 to 0.80)	Pediatrician interpreter: 1.6 (1.1 to 2.4) Orthoptist interpreter: 3.0 (1.4 to 6.5) Ophthalmologist 1 interpreter: 2.8 (1.3 to 5.9) Ophthalmologist 2 interpreter: 2.0 (1.2 to 3.5)	Pediatrician interpreter: 0.14 (0.05 to 0.39) Orthoptist interpreter: 0.28 (0.17 to 0.46) Ophthalmologist 1 interpreter: 0.38 (0.24 to 0.58) Ophthalmologist 2 interpreter: 0.25 (0.13 to 0.48)	Fair

Appendix E Table 5. Diagnostic Accuracy of Photoscreeners (KQ 2)

Study, Year	Screening test (Reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
iScreen Photoscreener						
Kennedy et al, 2000[93]	iScreen photoscreener (comprehensive eye exam with cycloplegic refraction [in patients <age 4 years])	0.92 (0.88 to 0.95)	0.89 (0.83 to 0.94)	8.6 (5.4 to 14)	0.09 (0.06 to 0.13)	Fair
Vision in Preschoolers Study Group (phase I), 2004[65]	iScreen photoscreener (comprehensive eye exam with cycloplegic refraction)	Any condition: 0.37 (0.32 to 0.42) "Very important to detect and treat early" conditions: 0.57 (0.50 to 0.64) Amblyopia: 0.63 (0.52 to 0.72) Reduced visual acuity: 0.27 (0.20 to 0.36) Strabismus: 0.50 (0.38 to 0.62) Refractive error: 0.43 (0.38 to 0.49)	Any condition: 0.94 (0.92 to 0.95)	Any condition: 6.2 (4.7 to 8.1)	Any condition: 0.67 (0.62 to 0.72)	Fair
Otago-Type Photoscreener						
Kennedy et al, 1989[91]	Otago-type photoscreener; non-commercial (comprehensive eye exam with cycloplegic refraction)	Any condition: 0.94 (0.87 to 0.98) Strabismus: 0.91 (0.81 to 1.01) Refractive error: 0.89 (0.74 to 1.03) Strabismus + refractive error: 0.98 (0.93 to 1.02)	Any condition: 0.94 (0.89 to 0.98)	Any condition: 16 (8.2 to 32)	Any condition: 0.06 (0.03 to 0.14)	Fair
Kennedy et al, 1995[92]	Otago-type photoscreener; non-commercial (comprehensive eye exam without cycloplegic refraction)	0.46 (0.22 to 0.72)[b]	1.0 (0.99 to 1.0)[b]	110 (38 to 310)[b]	0.54 (0.33 to 0.89)[b]	Fair
VisiScreen Photoscreener						
Cogen et al, 1992[83]	VisiScreen 100 photoscreener (comprehensive eye exam with cycloplegic refraction "when possible")	0.85 (0.55 to 0.98)	0.94 (0.87 to 0.98)	14 (6.3 to 32)	0.16 (0.05 to 0.59)	Fair

Appendix E Table 5. Diagnostic Accuracy of Photoscreeners (KQ 2)

Study, Year	Screening test (Reference standard)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Quality
Morgan et al, 1987[99]	VisiScreen 100 photoscreener (comprehensive eye exam with cycloplegic refraction)	0.91 (0.76 to 0.98)	0.74 (0.52 to 0.90)	3.5 (1.7 to 7.0)	0.12 (0.04 to 0.36)	Fair
Other Photoscreeners						
Kennedy et al, 1989[91]	Off-axis-type photoscreener; non-commercial (comprehensive eye exam with cycloplegic refraction)	Any condition: 0.85 (0.76 to 0.91) Strabismus: 0.73 (0.58 to 0.88) Refractive error: 0.89 (0.74 to 1.03) Strabismus + refractive error: 0.91 (0.82 to 0.99)	Any condition: 0.87 (0.80 to 0.92)	Any condition: 6.5 (4.2 to 10)	Any condition: 0.18 (0.11 to 0.28)	Fair

[a] Calculations based on n=379, median sensitivity and specificity.
[b] Extrapolated from 20% sample of negative screens.

Abbreviations: CI=confidence interval.

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

Study, Year	Screening Test	Age of Enrollees	N	Proportion with Condition	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
Afsari et al, 2013[77] Sydney Paediatric Eye Disease Study	Stereoacuity: All—Lang-Stereotest II <30 mo and older children that could not do RPST - Stereo Smile Stereoacuity II Test >/30 mo to Randot Preschool Stereoacuity Test	24–72 months	1,606	43 of 1,606 had strabismus 35 of 1,606 had anisometropia 19 of 1,606 had amblyopia	SSST-strabismus 120: 5.59 240: 9.84 480: 31.58 SSST-anisometropia 120: 2.26 240: 3.12 480: 9.09 SSST-amblyopia 120: 1.13 240: 3.12 480: 9.09 RPST-strabismus 200: 18.60 400: 25.53 800: 37.50 RPST-anisometropia 200: 9.30 400: 14.89 800: 8.33 RPST-amblyopia 200: 10.47 400: 17.02 800: 16.67	SSST-strabismus 120: 99.21 240: 98.39 480: 98.55 SSST-anisometropia 120: 96.88 240: 97.29 480: 97.57 SSST-amblyopia 120: 99.22 240: 99.46 480: 99.51 RPST-strabismus 200: 98.30 400: 97.97 800: 97.74 RPST-anisometropia 200: 98.50 400: 98.46 800: 98.02 RPST-amblyopia 200: 99.20 400: 99.13% 800: 98.77%
Barry et al, 2001[79]	Retinomax autorefractor	3 years	404	Amblyopia: 2.5% (10/404)	0.05 (0.02 to 0.09)	0.99 (0.97 to 1.0)
Barry et al, 2003[80]	Visual inspection, cover-uncover test, eye motility and head posture exam, LEA Symbols visual acuity test	3 years	1,180	Amblyopia or amblyopia risk factors: 2.3% (26/1114)	0.25 (0.16 to 0.36)	1.0 (0.99 to 1.0)
Bertuzzi et al, 2006[81]	LEA Symbols visual acuity test	38 to 54 months	149	Amblyopia risk factors: 16% (23/143)	A: 0.52 (0.36 to 0.68) B: 0.69 (0.48 to 0.86)	A: 0.99 (0.95 to 1.0) B: 0.96 (0.90 to 0.99)
Chui et al, 2004[82]	LEA Symbols visual acuity test, Frisby stereoacuity test, and external visual inspection	35 to 58 months	178 (141 completed evaluation)	Amblyopia risk factors: 13% (18/141)	Overall: 0.41 (0.24 to 0.61) Age <41 months: 0.41 (0.21 to 0.64) Age ≥41 months: 0.43 (0.10 to 0.82)	Overall: 0.95 (0.89 to 0.98) Age <41 months: 0.90 (0.74 to 0.98) Age ≥41 months: 0.96 (0.90 to 0.99)

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

Study, Year	Screening Test	Age of Enrollees	N	Proportion with Condition	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
Cogen et al, 1992[83]	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 to 0.86)	0.98 (0.93 to 1.0)
Hope et al, 1990[87]	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 to 0.31)	0.99 (0.96 to 1.0)
Jost, 2015[89]	A: Pediatric Vision Scanner B: SureSight Autorefractor	2-6 years	293 enrolled and screened; 102 had reference standard	Amblyopia: 1% (1/102) Strabismus: 0	A: 0.10 (0.00 to 0.44) B: 0.08 (0.002 to 0.36)	A: 1.0 (0.96 to 1.0) B: 1.0 (0.96 to 1.0)
Kennedy et al, 1989[91]	A: Otago-type photoscreener (noncommercial) B: Off-axis-type photoscreener (noncommercial)	6 years or younger	236	Any amblyopia 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 to 0.96) B: 0.82 (0.73 to 0.89)	Any condition A: 0.96 (0.91 to 0.98) B: 0.89 (0.82 to 0.94)
Kennedy et al, 1995[92]	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 to 0.95) B: 0.54 (0.28 to 0.81)	A: 0.98 (0.91 to 1.00) B: 0.94 (0.91 to 0.97)
Kennedy et al, 2000[93]	iScreen photoscreener	45% 6 years or younger	449	Amblyopia risk factors: 64% (273/423)	Overall: 0.94 (0.90 to 0.96) Age ≤3 years: 0.97 Age 4 to 6 years: 0.97	0.86 (0.80 to 0.91)

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

Study, Year	Screening Test	Age of Enrollees	N	Proportion with Condition	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
Miller et al, 1999[97]	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 to 0.50) B: 0.75 (0.65 to 0.83)	A: 0.92 (0.83 to 0.96) B: 0.95 (0.901 to 0.98)
Miller et al, 2001[98]	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 to 0.54) B: 0.68 (0.60 to 0.75)[a] C: 0.79 (0.73 to 0.84) D: 0.94 (0.90 to 0.97)	A: 0.93 (0.88 to 0.97) B: 0.70 (0.63 to 0.76)[a] C: 0.94 (0.90 to 0.97) D: 0.94 (0.89 to 0.96)
Morgan et al, 1987[99]	VisiScreen 100 photoscreener	3 months to 8 years	63	Any visual condition: 60% (34/57)	0.84 (0.68 to 0.94)	0.85 (0.62 to 0.97)
Ottar et al, 1995[100] and Donahue et al, 2002[101]	MTI photoscreener	6 to 59 months	949	Amblyopia risk factors: 20% (192/949)	A: 0.69 (0.62 to 0.75) B: 0.77 (0.64 to 0.87)[b]	A: 0.95 (0.93 to 0.97) B: 0.95 (0.93 to 0.96)[b]
Rogers et al, 2008[102]	MTI photoscreener SureSight autorefractor	1 to 6 years	100	Clinically significant amblyopia: 58% (58/100)	A: 0.68 (0.57 to 0.78) B: 0.75 (0.63 to 0.86) C: 0.75 (0.61 to 0.86) D: 0.77 (0.62 to 0.88) E: 0.92 (0.82 to 0.97)	A: 0.89 (0.65 to 0.99) B: 0.69 (0.52 to 0.83) C: 0.60 (0.45 to 0.74) D: 0.58 (0.44 to 0.72) E: 0.92 (0.80 to 0.98)
Shallo-Hoffmann et al, 2004[103]	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 to 0.47)	1.00 (0.94 to 1.0) (adjusted)
Tong et al, 2000[105]	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 to 0.98); 0.95 (0.90 to 0.98)	All photographs; informative subset of 313 photographs Any condition: 0.43 (0.36 to 0.50); 0.41 (0.33 to 0.49)
Schmidt et al, 2004 (Vision in Preschoolers Study Group) (Phase I)[65]	Crowded linear LEA Symbols visual acuity test	3, 4, or 5 years	3,121	Any vision condition: 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1% (132/2,588) Strabismus: 1.9% (48/2,588) Refractive error: 9.3% (240/2,588)	Any condition A: 0.73 (0.67 to 0.78) B: 0.78 (0.72 to 0.83)	Any condition A: 0.84 (0.82 to 0.86) B: 0.81 (0.78 to 0.83)

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

Study, Year	Screening Test	Age of Enrollees	N	Proportion with Condition	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
Schmidt et al, 2004 (Vision in Preschoolers Study Group) (Phase I)[65]	Crowded linear HOTV visual acuity test	3, 4, or 5 years	3,121	Any vision condition: 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1% (132/2,588) Strabismus: 1.9% (48/2,588) Refractive error: 9.3% (240/2,588)	Any condition A: 0.68 (0.62 to 0.74) B: 0.69 (0.62 to 0.76)	Any condition A: 0.82 (0.79 to 0.84) B: 0.77 (0.74 to 0.80)
Schmidt et al, (Vision in Preschoolers Study Group) (Phase I)[65]	Random Dot E stereoacuity test	3, 4, or 5 years	3,121	Any vision condition: 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1% (132/2,588) Strabismus: 1.9% (48/2,588) Refractive error: 9.3% (240/2,588)	Any condition A: 0.64 (0.58 to 0.71) B: 0.54 (0.46 to 0.63)	Any condition A: 0.78 (0.75 to 0.81) B: 0.80 (0.78 to 0.83)
Schmidt et al, 2004 (Vision in Preschoolers Study Group) (Phase I)[65]	Stereo Smile II Stereoacuity Test	3, 4, or 5 years	3,121	Any vision condition: 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1% (132/2,588) Strabismus: 1.9% (48/2,588) Refractive error: 9.3% (240/2,588)	Any condition A: 0.66 (0.60 to 0.72) B: 0.68 (0.62 to 0.75)	Any condition A: 0.73 (0.70 to 0.76) B: 0.78 (0.76 to 0.80)
Schmidt et al, 2004 (Vision in Preschoolers Study Group) (Phase I)[65]	Retinomax autorefractor	3, 4, or 5 years	3,121	Any vision condition: 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1% (132/2,588) Strabismus: 1.9% (48/2,588)	Any condition A: 0.71 (0.68 to 0.75) B: 0.78 (0.74 to 0.82)	Any condition A: 0.86 (0.84 to 0.87) B: 0.83 (0.81 to 0.84)

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

Study, Year	Screening Test	Age of Enrollees	N	Proportion with Condition	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
				Refractive error: 9.3% (240/2,588)		
Schmidt et al, 2004 (Vision in Preschoolers Study Group) (Phase I)[65]	SureSight autorefractor	3, 4, or 5 years	3,121	Any vision condition: 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1% (132/2,588) Strabismus: 1.9% (48/2,588) Refractive error: 9.3% (240/2,588)	Any condition A1: 0.47 (0.43 to 0.51) A2: 0.71 (0.66 to 0.76) B: 0.77 (0.72 to 0.82)	Any condition A1: 0.91 (0.89 to 0.93) A2: 0.86 (0.84 to 0.88) B: 0.83 (0.81 to 0.85)
Schmidt et al, 2004 (Vision in Preschoolers Study Group) (Phase I)[65]	iScreen photoscreener	3, 4, or 5 years	3,121	Any vision condition: 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1% (132/2,588) Strabismus: 1.9% (48/2,588) Refractive error: 9.3% (240/2,588)	Any condition 0.71 (0.64 to 0.77)	Any condition 0.79 (0.77 to 0.81)
Schmidt et al, 2004 (Vision in Preschoolers Study Group) (Phase I)[65]	MTI photoscreener	3, 4, or 5 years	3,121	Any vision condition: 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1% (132/2,588) Strabismus: 1.9% (48/2,588) Refractive error: 9.3% (240/2,588)	Any condition 0.71 (0.64 to 0.77)	Any condition 0.79 (0.77 to 0.81)
Schmidt et al, 2004 (Vision in Preschoolers Study Group) (Phase I)[65]	Power Refractor II	3, 4, or 5 years	3,121	Any vision condition: 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1%	Any condition A: 0.68 (0.65 to 0.73) B: 0.70 (0.64 to 0.76)	Any condition A: 0.83 (0.81 to 0.85) B: 0.79 (0.76 to 0.81)

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

Study, Year	Screening Test	Age of Enrollees	N	Proportion with Condition	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
				(132/2,588) Strabismus: 1.9% (48/2,588) Refractive error: 9.3% (240/2,588)		
Schmidt et al, 2004 (Vision in Preschoolers Study Group) (Phase I)[65]	Cover-uncover test	3, 4, or 5 years	3,121	Any vision condition: 29% (755/2,588) "Very important to detect and treat early" conditions: 5.4% (135/2,588) Amblyopia: 2.9% (75/2,588) Reduced visual acuity: 5.1% (132/2,588) Strabismus: 1.9% (48/2,588) Refractive error: 9.3% (240/2,588)	Any condition 0.78 (0.66 to 0.86)	Any condition 0.73 (0.70 to 0.76)
VIP Study Group, 2011[106]	Retinomax autorefractor	3 to 5 years	190	Amblyopia: 13% (24/181) Strabismus: 6% (10/181) Refractive error: 30% (55/181) Reduced Visual Acuity: 6% (10/181) Any targeted condition: 36% (65/181)	0.81 (0.69-0.90)	0.88 (0.81-0.93)
VIP Study Group, 2011[106]	Palm-Automatic Refractor	3 to 5 years	190	Amblyopia: 13% (24/181) Strabismus: 6% (10/181) Refractive error: 30% (55/181) Reduced Visual Acuity: 6% (10/181) Any targeted condition: 36% (65/181)	0.80 (0.68-0.89)	0.86 (0.78-0.92)
VIP Study Group, 2010[107]	LEA Symbols	3 to 5 years	1,142	*3 years* ≥1 Condition (Amblyopia, Strabismus, Refractive Error, Reduced visual acuity): 27% (59/215) Group1 (very important to detect and treat conditions): 11% (23/215) *Young 4 years* ≥1 Condition: 30% (93/311) Group1:12% (37/311)	*≥1 Condition* *3 years* 0.69 (0.55-0.81) *4 years-young* 0.73 (0.61-0.82) *4 years-old* 0.72 (0.60-0.82) *5 years* 0.80 (0.70-0.88) *Group 1 Condition* *3 years*	*≥1 Condition* *3 years* 0.86 (0.80-0.91) *4 years-young* 0.83 (0.78-0.88) *4 years-old* 0.87 (0.82-0.91) *5 years* 0.81 (0.76-0.86) *Group 1 Condition* *3 years*

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

Study, Year	Screening Test	Age of Enrollees	N	Proportion with Condition	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
				Old 4 years ≥1 Condition: 28% (83/297) Group1: 10% (30/297) *5 years* ≥1 Condition: 35% (111/319) Group1: 15% (49/319)	0.50 (0.33-0.67) *4 years-young* 0.52 (0.38-0.66) *4 years-old* 0.48 (0.34-0.62) *5 years* 0.63 (0.50-0.75)	0.98 (0.94-0.99) *4 years-young* 0.96 (0.93-0.98) *4 years-old* 0.98 (0.95-0.99) *5 years* 0.96 (0.93-0.98)
VIP Study Group, 2010[107]	HOTV symbols	3 to 5 years	1,142	*3 years* ≥1 Condition (Amblyopia, Strabismus, Refractive Error, Reduced visual acuity): 27% (59/215) Group1 (very important to detect and treat conditions): 11% (23/215) *Young 4 years* ≥1 Condition: 30% (93/311) Group1:12% (37/311) *Old 4 years* ≥1 Condition: 28% (83/297) Group1: 10% (30/297) *5 years* ≥1 Condition: 35% (111/319) Group1: 15% (49/319)	*≥1 Condition* *3 years* 0.59 (0.43-0.73) *4 years-young* 0.73 (0.61-0.82) *4 years-old* 0.63 (0.51-0.74) *5 years* 0.78 (0.68-0.87) *Group 1 Condition* *3 years* 0.36 (0.21-0.54) *4 years-young* 0.49 (0.34-0.64) *4 years-old* 0.41 (0.28-0.54) *5 years* 0.65 (0.51-0.76)	*≥1 Condition* *3 years* 0.81 (0.74-0.87) *4 years-young* 0.83 (0.78-0.88) *4 years-old* 0.84 (0.78-0.88) *5 years* 0.80 (0.74-0.85) *Group 1 Condition* *3 years* 0.94 (0.90-0.97) *4 years-young* 0.95 (0.92-0.97) *4 years-old* 0.97 (0.95-0.99) *5 years* 0.97 (0.93-0.98)
VIP Study Group, 2005[108]	Retinomax	3 to 5 years	Yr 1: 1,446 Yr 2: 1,452	Year 2 (2003) *Any target condition (amblyopia, strabismus, refractive error, reduced visual acuity)*: 32% (462/1,452) *Group1 (Very important to detect and treat conditions)*: 14.5% (210/1,452) *Group 2 (Important to detect early)*: 9.9% (144/1,452) *Group 3 (Detection clinically useful)*: 4.7% (108/1,452) Year 1 (only Lay Screeners) *Any targeted condition*: 27% (391/1,446) *Group 1:* 12% (172/1,446)	By severity, screener tool *Any condition* *Nurse* 0.76 (0.72–0.80) *Lay Screener* 0.74 (0.70–0.79) *Group1* *Nurse* 0.65 (0.59–0.71) *Lay Screener* 0.64 (0.58–0.70) *Group 2* *Nurse* 0.46 (0.39–0.54) *Lay Screener* 0.42 (0.34–0.50) *Group 3*	By severity, screener tool *Any condition* *Nurse* 0.86 (0.83–0.88) *Lay Screener* 0.84 (0.81–0.86) *Group1* *Nurse* 0.97 (0.96–0.98) *Lay Screener* 0.97 (0.95–0.98) *Group 2* *Nurse* 0.94 (0.92–0.95) *Lay Screener* 0.92 (0.91–0.94) *Group 3*

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

Study, Year	Screening Test	Age of Enrollees	N	Proportion with Condition	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
				Group 2: 8% (121/1,446) *Group 3:* 7% (98/1,446)	*Nurse* 0.30 (0.22–0.38) *Lay Screener* 0.28 (0.21–0.37)	*Nurse* 0.93 (0.91–0.95) *Lay Screener* 0.93 (0.91–0.94)
VIP Study Group, 2005[108]	SureSight	3 to 5 years	Yr 1: 1,446 Yr 2: 1,452	Year 2 (2003) *Any target condition (amblyopia, strabismus, refractive error, reduced visual acuity)*: 32% (462/1,452) *Group1 (Very important to detect and treat conditions)*: 14.5% (210/1,452) *Group 2 (Important to detect early)*: 9.9% (144/1,452) *Group 3 (Detection clinically useful)*: 4.7% (108/1,452) Year 1 (only Lay Screeners) *Any targeted condition*: 27% (391/1,446) *Group 1:* 12% (172/1,446) *Group 2*: 8% (121/1,446) *Group 3:* 7% (98/1,446)	By severity, screener tool *Any condition* *Nurse* 0.75 (0.70–0.79) *Lay Screener* 0.74 (0.69–0.78) *Group1* *Nurse* 0.64 (0.58–0.69) *Lay Screener* 0.63 (0.57–0.69) *Group 2* *Nurse* 0.45 (0.38–0.53) *Lay Screener* 0.42 (0.35–0.50) *Group 3* *Nurse* 0.27 (0.20–0.36) *Lay Screener* 0.27 (0.20–0.36)	By severity, screener tool *Any condition* *Nurse* 0.84 (0.82–0.86) *Lay Screener* 0.83 (0.81–0.85) *Group1* *Nurse* 0.96 (0.95–0.97) *Lay Screener* 0.96 (0.94–0.97) *Group 2* *Nurse* 0.93 (0.92–0.95) *Lay Screener* 0.93 (0.91–0.94) *Group 3* *Nurse* 0.93 (0.91–0.94) *Lay Screener* 0.93 (0.91–0.94)
VIP Study Group, 2005[108]	Linear LEA Symbols	3 to 5 years	Yr 1: 1,446 Yr 2: 1,452	Year 2 (2003)[c] *Any target condition (amblyopia, strabismus, refractive error, reduced visual acuity)*: 32% (462/1,452) *Group1 (Very important to detect and treat conditions)*: 14.5% (210/1,452) *Group 2 (Important to detect early)*: 9.9% (144/1,452) *Group 3 (Detection clinically useful)*: 4.7% (108/1,452) Year 1 (only Lay Screeners)[d] *Any targeted condition*: 27% (391/1,446) *Group 1:* 12% (172/1,446)	By severity, screener tool *Any condition* *Nurse* 0.70 (0.64–0.75) *Lay Screener* 0.58 (0.52–0.64) *Group1* *Nurse* 0.56 (0.49–0.63) *Lay Screener* 0.45 (0.38–0.52) *Group 2* *Nurse* NA *Lay Screener* 0.18 (0.12–0.26) *Group 3*	By severity, screener tool *Any condition* *Nurse* 0.79 (0.77–0.81) *Lay Screener* 0.79 (0.77–0.82) *Group1* *Nurse* 0.91 (0.89–0.93) *Lay Screener* 0.92 (0.90–0.93) *Group 2* *Nurse* NA *Lay Screener* 0.91 (0.89–0.92) *Group 3*

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

Study, Year	Screening Test	Age of Enrollees	N	Proportion with Condition	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
				Group 2: 8% (121/1,446) *Group 3:* 7% (98/1,446)	*Nurse* 0.31 (0.24–0.40) *Lay Screener* 0.24 (0.18–0.32)	*Nurse* 0.93 (0.92–0.95) *Lay Screener* 0.94 (0.92–0.95)
VIP Study Group, 2005[108]	Single LEA Symbols	3 to 5 years	Yr 1: 1,446 Yr 2: 1,452	Year 2 (2003)[c] *Any target condition (amblyopia, strabismus, refractive error, reduced visual acuity)*: 32% (462/1,452) *Group1 (Very important to detect and treat conditions)*: 14.5% (210/1,452) *Group 2 (Important to detect early)*: 9.9% (144/1,452) *Group 3 (Detection clinically useful)*: 4.7% (108/1,452) Year 1 (only Lay Screeners)[d] *Any targeted condition*: 27% (391/1,446) *Group 1:* 12% (172/1,446) *Group 2*: 8% (121/1,446) *Group 3:* 7% (98/1,446)	By severity, screener tool *Any condition* *Nurse* NA *Lay Screener* 0.76 (0.71–0.80) *Group1* *Nurse* NA *Lay Screener* 0.65 (0.59–0.71) *Group 2* *Nurse* 0.36 (0.28–0.44) *Lay Screener* 0.45 (0.37–0.53) *Group 3* *Nurse* NA *Lay Screener* 0.33 (0.25–0.41)	By severity, screener tool *Any condition* *Nurse* NA *Lay Screener* 0.83 (0.81–0.86) *Group1* *Nurse* NA *Lay Screener* 0.95 (0.94–0.96) *Group 2* *Nurse* 0.91 (0.89–0.93) *Lay Screener* 0.93 (0.91–0.94) *Group 3* *Nurse* NA *Lay Screener* 0.93 (0.92–0.95)
VIP Study Group, 2005[108]	Stereo Smile	3 to 5 years	Yr 1: 1,446 Yr 2: 1,452	Year 2 (2003)[c] *Any target condition (amblyopia, strabismus, refractive error, reduced visual acuity)*: 32% (462/1,452) *Group1 (Very important to detect and treat conditions)*: 14.5% (210/1,452) *Group 2 (Important to detect early)*: 9.9% (144/1,452) *Group 3 (Detection clinically useful)*: 4.7% (108/1,452) Year 1 (only Lay Screeners)[d] *Any targeted condition*: 27% (391/1,446) *Group 1:* 12% (172/1,446)	By severity, screener tool *Any condition* *Nurse* 0.68 (0.62–0.73) *Lay Screener* 0.65 (0.59–0.71) *Group1* *Nurse* 0.55 (0.48–0.62) *Lay Screener* 0.54 (0.48–0.61) *Group 2* *Nurse* 0.35 (0.27–0.43) *Lay Screener* 0.31 (0.24–0.40) *Group 3*	By severity, screener tool *Any condition* *Nurse* 0.78 (0.75–0.80) *Lay Screener* 0.76 (0.74–0.79) *Group1* *Nurse* 0.91 (0.89–0.93) *Lay Screener* 0.91 (0.89–0.92) *Group 2* *Nurse* 0.91 (0.89–0.92) *Lay Screener* 0.90 (0.88–0.92) *Group 3*

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

Study, Year	Screening Test	Age of Enrollees	N	Proportion with Condition	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
				Group 2: 8% (121/1,446) *Group 3:* 7% (98/1,446)	*Nurse* 0.24 (0.17–0.33) *Lay Screener* 0.20 (0.13–0.28)	*Nurse* 0.92 (0.90–0.94) *Lay Screener* 0.91 (0.90–0.93)
VIP Study Group, 2005[108]	Stereo Smile II	3 to 5 years	Yr 1: 1,446 Yr 2: 1,452	Year 2 (2003)[c] *Any target condition (amblyopia, strabismus, refractive error, reduced visual acuity)*: 32% (462/1,452) *Group1 (Very important to detect and treat conditions)*: 14.5% (210/1,452) *Group 2 (Important to detect early)*: 9.9% (144/1,452) *Group 3 (Detection clinically useful)*: 4.7% (108/1,452) Year 1 (only Lay Screeners)[d] *Any targeted condition*: 27% (391/1,446) *Group 1:* 12% (172/1,446) *Group 2*: 8% (121/1,446) *Group 3:* 7% (98/1,446)	By severity, screener tool *Any condition* *Nurse* NA *Lay Screener* 0.64 (0.58–0.69) *Group1* *Nurse* NA *Lay Screener* 0.53 (0.47–0.60) *Group 2* *Nurse* NA *Lay Screener* 0.27 (0.20–0.35) *Group 3* *Nurse* NA *Lay Screener* 0.19 (0.13–0.27)	By severity, screener tool *Any condition* *Nurse* NA *Lay Screener* 0.82 (0.80–0.84) *Group1* *Nurse* NA *Lay Screener* 0.95 (0.93–0.96) *Group 2* *Nurse* NA *Lay Screener* 0.92 (0.90–0.94) *Group 3* *Nurse* NA *Lay Screener* 0.93 (0.91–0.94)
Weinand et al, 1998[109]	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 to 0.94) B (Orthoptist interpreter): 0.93 (0.84 to 0.98) C (Ophthalmologist 1 interpreter): 0.92 (0.83 to 0.98) D (Ophthalmologist 2 interpreter): 0.90 (0.81 to 0.96)	A (Pediatrician interpreter): 0.62 (0.32 to 0.86) B (Orthoptist interpreter): 0.45 (0.27 to 0.64) C (Ophthalmologist 1 interpreter): 0.38 (0.22 to 0.55) D (Ophthalmologist 2 interpreter): 0.48 (0.27 to 0.69)
Williams et al, 2000[110]	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 to 0.86) B: 0.68 (0.46 to 0.85) C: 0.70 (0.46 to 0.88)	A: 0.89 (0.83 to 0.93) B: 0.96 (0.92 to 0.99) C: 0.91 (0.85 to 0.94)

[a] Calculation based on n=379; unable to calculate confidence intervals.

Appendix E Table 6. Predictive Values of Screening Tests (KQ 2)

[b] Based on reported sensitivity and specificity, does not match values reported in article.
[c] Each child is represented in *only one* of the four groups, corresponding to the child's most severe condition. Within each group, a child may be represented *more than once* if the child had more than one condition within the group
[d] Lay Screeners conducted testing in a VIP van in the 2002 academic year. In the 2002 academic year, 391 children had one or more GSE conditions, 172 had group 1 conditions, 121 had group 2 conditions, 98 had group 3 conditions, and 1055 children had no GSE conditions.

Abbreviations: CI=confidence interval; GSE=gold standard examination; N=number; RCT=randomized controlled trial; yr=year.

Appendix E Table 7. Diagnostic Accuracy of Screening Tests, Stratified by Age (KQ 2)

Study, Year Sample Size	Screening Test Setting	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)
Chui et al, 2004[82] 141	LEA Symbols visual acuity test, Frisby stereoacuity test, and external visual inspection Not reported	Overall: 0.67 (0.41 to 0.87) Age <41 months: 0.75 (0.43 to 0.94) Age ≥41 months: 0.50 (0.12 to 0.88)	Overall: 0.86 (0.79 to 0.92) Age <41 months: 0.90 (0.52 to 0.82) Age ≥41 months: 0.95 (0.88 to 0.99)	Overall: 4.8 (2.8 to 8.4) Age <41 months: 2.4 (1.4 to 4.1) Age ≥41 months: 10 (3.0 to 36)
Kemper et al, 2005[90] 170	SureSight autorefractor Pediatric ophthalmology clinic	Overall: 0.85 (0.69 to 0.95) Age <3 years (n=80): 0.80 (0.44 to 0.97) Age 3 to 5 years (n=90): 0.88 (0.68 to 0.97)	Overall: 0.52 (0.40 to 0.63) Age <3 years: 0.41 (0.24 to 0.61) Age 3 to 5 years: 0.58 (0.42 to 0.71)	Overall: 1.8 Age <3 years: 1.4 Age 3 to 5 years: 2.1
Kennedy et al, 2000[93] 449	iScreen photoscreener Pediatric ophthalmology clinic	Overall: 0.92 (0.88 to 0.95) Age ≤3 years: 1.0 Age 4 to 6 years: 0.92	Overall: 0.89 (0.83 to 0.94) Age ≤3 years: 0.97 Age 4 to 6 years: 0.95	Overall: 8.6 (5.4 to 14) Age ≤3 years: 33 Age 4 to 6 years: 18
Tong et al, 2000[105] 387	MTI photoscreener Pediatric ophthalmology clinic	*All photographs; informative subset of 313 photographs*[a] 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
VIP Study Group, 2010[107] 1,142	LEA Symbols PreK Head Start programs	For 90% specificity *To detect >1 Condition* *3 years* 0.61 (0.47 to 0.73) *4 years-young* 0.57 (0.46 to 0.67) *4 years-old* 0.65 (0.54 to 0.75) *5 years* 0.60 (0.51 to 0.70) *To detect a group 1 condition* *3 years* 0.83 (0.61-0.95) *4 years-young* 0.73 (0.56 to 0.86) *4 years-old* 0.83 (0.65 to 0.94) *5 years* 0.78 (0.63 to 0.88)	Specificity set at 90% or closest to 90% achievable *To detect >1 Condition* *3 years* 0.90 (0.84 to 0.94) *4 years-young* 0.91 (0.86 to 0.94) *4 years to old* 0.90 (0.85 to 0.94) *5 years* 0.92 (0.87 to 0.95) *To detect a group 1 condition* *3 years* 0.90 (0.85 to 0.94) *4 years-young* 0.91 (0.87-0.94) *4 years-old* 0.90 (0.86 to 0.93) *5 years* 0.92 (0.88 to 0.95)	*≥1 Condition* *3 years* 5.95 (3.58 to 9.88) *4 years-young* 6.21 (3.95 to 9.78) *4 years-old* 6.63 (4.29 to 10.25) *5 years* 7.39 (4.57 to 11.93) *Group 1 Condition* *3 years* 8.35 (5.24 to 13.31) *4 years-young* 8.00 (5.24 to 12.20) *4 years-old* 8.24 (5.57 to 12.19) *5 years* 9.52 (6.20 to 14.60)

Appendix E Table 7. Diagnostic Accuracy of Screening Tests, Stratified by Age (KQ 2)

Study, Year Sample Size	Screening Test Setting	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)
VIP Study Group, 2010[107] 1,142	HOTV symbols PreK Head Start programs	For 90% specificity *To detect >1 Condition* *3 years* 0.46 (0.33 to 0.59) *4 years-young* 0.57 (0.46 to 0.67) *4 years-old* 0.57 (0.45 to 0.67) *5 years* 0.56 (0.46 to 0.65) *To detect a group 1 condition* *3 years* 0.57 (0.34 to 0.77) *4 years-young* 0.65 (0.47 to 0.80) *4 years-old* 0.80 (0.61 to 0.92) *5 years* 0.82 (0.68 to 0.91)	Specificity set at 90% or closest to 90% achievable *To detect >1 Condition* *3 years* 0.88 (0.82 to 0.93) *4 years-young* 0.91 (0.86 to 0.94) *4 years-old* 0.87 (0.82 to 0.91) *5 years* 0.92 (0.87 to 0.95) *To detect a group 1 condition* *3 years* 0.88 (0.83 to 0.92) *4 years-young* 0.91 (0.87 to 0.94) *4 years-old* 0.87 (0.82 to 0.91) *5 years* 0.92 (0.88 to 0.95)	*≥1 Condition* *3 years* 3.76 (2.27 to 6.22) *4 years-young* 6.21 (3.95 to 9.78) *4 years-old* 4.33 (2.92 to 6.41) *5 years* 6.83 (4.21 to 11.10) *Group 1 Condition* *3 years* 4.72 (2.79 to 7.98) *4 years-young* 7.11 (4.57 to 11.07) *4 years-old* 6.10 (4.27 to 8.72) *5 years* 10.02 (6.57 to 15.28)

[a] The article reports the following: "The sensitivity and specificity were stratified by age of the child or by date of enrollment in the study. There was no statistically significant difference ($P > 0.05$) between each quartile and the aggregate when sorted by either criterion (data not shown). Thus we can assume that any difficulties in photographing younger children and any changes in the experience of the photographer during this study did not distort the results." The article did not report the age cutoffs that correspond to the quartiles that they compared. For the full sample of participants: range 1 to 47 months; 81% are <36 months; mean age 22 months, median age 21 months.

Abbreviations: CI=confidence interval; n=number.

Appendix E Table 8. Additional Diagnostic Accuracy Study Results (KQ 2)

First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
Afsari et al, 2013[77] Sydney Paediatric Eye Disease Study	35% (855/2,461)	Excluded	All had reference standard	SSST-strabismus 120: 83% (62 to 104) 240: 50% (22 to 78) 480: 50% (22 to 78) SSST-anisometropia 120: 33% (7 to 60) 240: 17% (-4 to 38) 480: 17% (-4 to 38) SSST-amblyopia 120: 50% (1 to 99) 240: 50% (1 to 99) 480: 50% (1 to 99) RPST-strabismus 200: 48% (31 to 66) 400: 36% (20 to 53) 800: 27% (12 to 42) RPST-anisometropia 200: 35% (15 to 54) 400: 30% (12 to 49) 800: 9% (-3 to 20) RPST-amblyopia 200: 53% (25 to 77) 400: 47% (23 to 71) 800: 24% (3 to 44)	SSST-strabismus 120: 60% (56 to 65) 240: 87% (83 to 90) 480: 96% (94 to 98) SSST-anisometropia 120: 59% (54 to 64) 240: 86% (82 to 89) 480: 95% (93 to 97) SSST-amblyopia 120: 59% (55 to 64) 240: 85% (82 to 89) 480: 95% (93 to 97) RPST-strabismus 200: 93% (92 to 95) 400: 97% (96 to 98) 800: 99% (98 to 99) RPST-anisometropia 200: 93% (91 to 94) 400: 96% (95 to 97) 800: 98% (97 to 99) RPST-amblyopia 200: 93% (91 to 94) 400: 96% (95 to 97) 800: 98% (97 to 99)
Arthur et al, 2009[78]	0.3% (1/307)	Excluded	90% (275/306)	0.83 (0.67 to 0.93)	0.95 (0.92 to 0.98)
Barry et al, 2001[79]	NR	NR	95% (404/427)	0.80 (0.44 to 0.98)	0.58 (0.53 to 0.62)
Barry et al, 2003[80]	11% (133/1,180)	Excluded from analysis	83% (975/1,180)	0.91 (0.71 to 0.99)	0.94 (0.92 to 0.95)
Bertuzzi et al, 2006[81]	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 to 1.0) B: 0.78 (0.56 to 0.92)	A: 0.83 (0.75 to 0.90) B: 0.93 (0.87 to 0.97)

Appendix E Table 8. Additional Diagnostic Accuracy Study Results (KQ 2)

First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
Chui et al, 2004[82]	NR	Considered positive screens	79% (141/179)	0.67 (0.41–0.87) <41 months: 0.75 (0.43 to 0.94) ≥41 months: 0.50 (0.12 to 0.88)	0.86 (0.79–0.92) <41 months: 0.90 (0.52 to 0.82) ≥41 months: 0.95 (0.88 to 0.99)
Cogen et al, 1992[83]	11% (14/127)	Excluded from analysis	89% (113/127)	0.85 (0.55 to 0.98)	0.94 (0.87 to 0.98)
Dahlmann-Noor et al, 2009a[84]	14% (18/126)	Excluded from analysis	100% (108/108)	A: 0.88 (0.30 to 1.0) B: 0.20 (0.10 to 0.35) C: 0.75 (0.36 to 0.96) D: 0.50 (0.31 to 0.69)	A: 0.96 (0.89 to 0.99) B: 0.99 (0.92 to 1.0) C: 0.93 (0.86 to 0.97) D: 0.87 (0.77 to 0.93)
Dahlmann-Noor et al, 2009b[85]	0% (0/288)	NA	100% (288/288)	0.45 (0.29 to 0.62)	1.0 (0.98 to 1.0)
Harvey, 2009[86]	4.4% (34/825) were unable to obtain any acceptable measurement; 11.3% (93/825) unable to obtain measurement with confidence ≥6	Excluded those with uninterpretable gold standard	825	NR	NR
Hope et al, 1990[87]	5% (8/176)	Excluded from analysis	95% (168/176)	0.89 (0.52 to 1.0)	0.76 (0.68 to 0.82)
Jost, 2015[89]	A: 7% (7/102) B: 6% (6/102)	Received the reference standard but were excluded from the analysis	A: 93% (95/102) B: 94% (96/102)	A: 1.00 (0.02 to 1.0) B: 1.00 (0.02 to 1.0)	A: 0.90 (0.83 to 0.96) B: 0.87 (0.79 to 0.93)
Kemper et al, 2005[90]	32% (55/170)	Not described, appear to have been excluded	100% (170/170)	Overall: 0.85 (0.69 to 0.95) <3 years old (n=80): 0.80 (0.44 to 0.97) 3–5 years old (n=90): 0.88 (0.68 to 0.97)	Overall: 0.52 (0.40 to 0.63) <3 years old: 0.41 (0.24 to 0.61) 3–5 years old: 0.58 (0.42 to 0.71)
Kennedy et al, 1989[91]	NR	NR	100% (236/236)	Any condition A: 0.94 (0.87 to 0.98) B: 0.85 (0.76 to 0.91) Strabismus A: 0.91 (0.81 to 1.00) B: 0.73 (0.58 to 0.88) Refractive error A: 0.89 (0.74 to 1.00) B: 0.89 (0.74 to 1.00) Strabismus + refractive error A: 0.98 (0.93 to 1.00) B: 0.91 (0.82 to 0.99)	Any condition A: 0.94 (0.89 to 0.98) B: 0.87 (0.80 to 0.92)

Appendix E Table 8. Additional Diagnostic Accuracy Study Results (KQ 2)

First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
Kennedy et al, 1995[92]	NR	NR	100% (13/13 or 22/22) of positive screens, 20% random sample (241 or 242 of 1,232 or 1223) of negative screens	A: 0.46 (0.22 to 0.72)[b] B: 0.09 (0.04 to 0.20)[b]	A: 1.0 (0.99 to 1.0)[b] B: 1.0 (0.99 to 1.0)[b]
Kennedy et al, 2000[93]	6% (26/449)	Excluded from analysis	94% (423/449)	0.92 (0.88 to 0.95) ≤3 years: 1.0 4–6 years: 0.92	0.89 (0.83 to 0.94) ≤3 years: 0.97 4–6 years: 0.95
Kulp et al, 2014[94] VIP (Phases 1 and 2)	NR (but it was 0.5% in the VIP Phase I publication from 2004)	NR	NR	Data reported for multiple cutpoints and multiple set specificities (Table S6 of supplement)[a] *Any SRE* *NCR* A: 0.96 B: 0.94 C: 0.93 D: 0.89 E: 0.85 F: 0.81 *Retinomax* A: 0.96 B: 0.93 C: 0.91 D: 0.86 E: 0.83 F: 0.73 *SureSight* A: 0.94 B: 0.91 C: 0.88 D: 0.83 E: 0.77 F: 0.68 Data also reported separately for myopia, hyperopia, astigmatism, and anisometropia for NCR, Retinomax, and SureSight for each cutpoint	A: 0.50 B: 0.60 C: 0.70 D: 0.80 E: 0.85 F: 0.90

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First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
Leone et al, 2012[95] Sydney Paediatric Eye Disease Study	Visual acuity testing using ATS HOTV: 24 to <30 mo: 90% 30 to <36 mo: 53% 36 to <42 mo: 20% 42 to <48 mo: 7% 48 to <54 mo: 5% 54 to <60 mo: 2% ATS HOTV by age and gender: 24 to <42 mo male: 44% 24 to <42 mo female: 47% 42 to <60 mo male: 92% 42 to <60 mo female: 99% ATS HOTV by age and race 24 to <42 mo European Caucasian: 49% 24 to <42 mo East Asian: 53% 24 to<42 mo Other: 36% 42 to <60 mo European Caucasian: 96% 42 to <60 mo East Asian: 98% 42 to <60 mo Other: 93%	NA	NA	NA	NA
Matta et al, 2008[96]	Not reported	Not described	100% (109/109)	A: 0.98 (0.85 to 1.0) B: 0.98 (0.85 to 1.0)	A: 0.68 (0.51 to 0.81) B: 0.88 (0.74 to 0.96)
Miller et al, 1999[97]	4% (10/245)	Not described	100% (245/245)	A: 0.91 (0.82 to 0.96) B: 0.91 (0.82 to 0.96)	A: 0.44 (0.37 to 0.52) B: 0.86 (0.80 to 0.91)
Miller et al, 2001[98]	A: 8% (30/376) B: 6% (24/369)[b] 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 to 0.97) B: 0.66 (0.59 to 0.73)[c] C: 0.95 (0.91 to 0.98) D: 0.93 (0.88 to 0.96)	A: 0.51 (0.44 to 0.57) B: 0.71 (0.64 to 0.78)[c] C: 0.77 (0.71 to 0.83) D: 0.95 (0.91 to 0.98)
Morgan et al, 1987[99]	10% (6/63)	Excluded from analysis	90% (57/63)	0.91 (0.76 to 0.98)	0.74 (0.52 to 0.90)

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First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
Ottar et al, 1995[100] and Donahue et al, 2002[101]	2.5% (25/1,004) small pupil diameter, poor mydriasis, or poor cooperation	Excluded from analysis	98% (985/1,004)	A: 0.82 (0.76 to 0.87) B: 0.50 (0.39 to 0.61)	A: 0.91 (0.88 to 0.93) B: 0.98 (0.97 to 0.99)
Rogers et al, 2008[102]	SureSight: 24% (24/100); 20% (9/45) in children ages 4–6 years MTI: 4% (4/100); 0% (0/45) in children ages 4–6 years	Considered positive screens	100% (100/100)	A: 0.97 (0.88 to 1.0) B: 0.79 (0.67 to 0.89) C: 0.67 (0.54 to 0.79) D: 0.62 (0.48 to 0.74) E: 0.95 (0.86 to 0.99)	A: 0.38 (0.24 to 0.54) B: 0.64 (0.48 to 0.78) C: 0.69 (0.53 to 0.82) D: 0.74 (0.58 to 0.86) E: 0.88 (0.74 to 0.96)
Shallo-Hoffmann et al, 2004[103]	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 to 0.98)¶	0.94 (0.90 to 0.96)¶
Tong et al, 2000[105]	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 to 0.62) B (informative subset of 313 photographs): 0.65 (0.59 to 0.71)	A: 0.91 (0.84 to 0.96) B: 0.87 (0.76 to 0.94)
Schmidt et al, 2004[65] and Freedman et al, 2006[104] VIP Study (Phase I)	0.5% (6/1142)	Excluded from analysis	83% (2,588/3,121) of enrolled patients	Any condition A: 0.61 (0.56 to 0.66) B: 0.49 (0.44 to 0.54) "Very important to detect and treat early" conditions A: 0.77 (0.70 to 0.84) B: 0.65 (0.57 to 0.73) Amblyopia A: 0.76 (0.66 to 0.86) B: 0.65 (0.55 to 0.76) Reduced visual acuity A: 0.58 (0.50 to 0.67) B: 0.48 (0.39 to 0.56) Strabismus A: 0.56 (0.42 to 0.71) B: 0.48 (0.34 to 0.62) Refractive error A: 0.70 (0.64 to 0.76) B: 0.40 (0.34 to 0.46)	Any condition A: 0.90 (0.88 to 0.92) B: 0.94 (0.92 to 0.96)

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First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
Schmidt et al, 2004[65] and Freedman et al, 2006[104] Crowded Linear HOTV visual acuity test	0.6% (7/1141)	Excluded from analysis	83% (2,588/3,121) of enrolled patients	Any condition A: 0.54 (0.49 to 0.59) B: 0.36 (0.31 to 0.41) "Very important to detect and treat early" conditions A: 0.72 (0.64 to 0.79) B: 0.48 (0.40 to 0.57)	Any condition A: 0.89 (0.87 to 0.91) B: 0.93 (0.91 to 0.95)
Schmidt et al, 2004[65] and Freedman et al, 2006[104] Random Dot E stereoacuity test	9.7% (111/1142)	Excluded from analysis	83% (2,588/3,121) of enrolled patients	Any condition A: 0.42 (0.37 to 0.47) B: 0.22 (0.18 to 0.27) "Very important to detect and treat early" conditions A: 0.59 (0.50 to 0.67) B: 0.30 (0.22 to 0.38)	Any condition A: 0.90 (0.88 to 0.92) B: 0.92 (0.90 to 0.94)
Schmidt et al, 2004[65] and Freedman et al, 2006[104] Stereo Smile II stereoacuity test	1.9% (27/1,446)	Excluded from analysis	83% (2,588/3,121) of enrolled patients	Any condition A: 0.44 (0.39 to 0.49) B: 0.33 (0.28 to 0.38) "Very important to detect and treat early" conditions A: 0.72 (0.65 to 0.79) B: 0.57 (0.50 to 0.64)	Any condition A: 0.91 (0.89 to 0.93) B: 0.94 (0.92 to 0.95)
Schmidt et al, 2004[65] and Freedman et al, 2006[104] Retinomax autorefractor	0.5% (6/1,142)	Excluded from analysis	83% (2,588/3,121) of enrolled patients	Any condition A: 0.64 (0.60 to 0.67) B: 0.52 (0.48 to 0.56) "Very important to detect and treat early" conditions A: 0.87 (0.84 to 0.91 B: 0.81 (0.77 to 0.85)	Any condition A: 0.90 (0.88 to 0.91) B: 0.94 (0.93 to 0.95)

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First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
Schmidt et al, 2004[65] and Freedman et al, 2006[104] SureSight autorefractor	0.3% (8/2,577)	Excluded from analysis	83% (2,588/3,121) of enrolled patients	Any condition A1: 0.85 (0.81 to 0.88) A2: 0.63 (0.59 to 0.65) B: 0.51 (0.46 to 0.56) "Very important to detect and treat early" conditions A1: 0.96 (0.93 to 0.99) A2: 0.81 (0.75 to 0.87) B: 0.75 (0.69 to 0.81)	Any condition A1: 0.62 (0.59 to 0.65) A2: 0.90 (0.88 to 0.92) B: 0.94 (0.92 to 0.95)
Schmidt et al, 2004[65] and Freedman et al, 2006[104] iScreen photoscreener	0.1% (2/1,439)	Excluded from analysis	83% (2,588/3,121) of enrolled patients	Any condition: 0.37 (0.32 to 0.42) "Very important to detect and treat early" conditions: 0.57 (0.50 to 0.64)	Any condition: 0.94 (0.92 to 0.95)
Schmidt et al, 2004[65] and Freedman et al, 2006[104] MTI photoscreener	0% (0/1444)	Excluded from analysis	83% (2,588/3,121) of enrolled patients	Any condition: 0.37 (0.32 to 0.42) "Very important to detect and treat early" conditions: 0.55 (0.48 to 0.63)	Any condition: 0.94 (0.92 to 0.95)
Schmidt et al, 2004[65] and Freedman et al, 2006[104] Power Refractor II	1.5% (22/1,438)	Excluded from analysis	83% (2,588/3,121) of enrolled patients	Any condition A: 0.54 (0.49 to 0.59) B: 0.36 (0.31 to 0.41) "Very important to detect and treat early" conditions A: 0.72 (0.65 to 0.79) B: 0.56 (0.48 to 0.63)	Any condition A: 0.90 (0.88 to 0.92) B: 0.94 (0.92 to 0.95)
Schmidt et al, 2004[65] and Freedman et al, 2006[104] Cover-uncover test	2.1% (24/1,141)	Excluded from analysis	83% (2,588/3,121) of enrolled patients	Any condition: 0.16 (0.12 to 0.20) "Very important to detect and treat early" conditions: 0.24 (0.17 to 0.31)	Any condition: 0.98 (0.97 to 0.99)

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First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
VIP Study Group, 2011[106]	A (Palm-AR): 0.8% (3/380 eyes) B (Retinomax): 0.3% (1/380)	Considered them to be a positive screen	95% (181/190)	For 90% specificity, by severity *Overall* A: 0.74 (0.61 to 0.84) B: 0.78 (0.67 to 0.88) *Group 1* A: 0.79 (0.59 to 0.92) B: 0.93 (0.84 to 0.94) *Group 2* A: 0.77 (0.55 to 0.92) B: 0.64 (0.41 to 0.83) *Group 3* A: 0.60 (0.32 to 0.84) B: 0.73 (0.45 to 0.92) Type of Condition *Amblyopia* A: 0.75 (0.53 to 0.90) B: 0.88 (0.68 to 0.97) *Strabismus* A: 0.70 (0.35 to 0.93) B: 0.70 (0.35 to 0.93) *Refractive Error* A: 0.84 (0.71 to 0.92) B: 0.84 (0.71 to 0.92) *Reduced visual acuity* A: 0.30 (0.06 to 0.65) B: 0.70 (0.35 to 0.93)	Specificity set at 90% or 94% for all sensitivities reported; calculated 95% CIs were (0.83 to 0.95) and (0.88 to 0.98), respectively.
VIP Study Group, 2011[106]		Considered them to be a positive screen	95% (181/190)	For 94% specificity, by severity *Overall* A: 0.66 (0.53 to 0.77) B: 0.66 (0.53 to 0.77) *Group 1* A: 0.71 B: 0.82 *Group 2* A: 0.64 B: 0.50 *Group 3* A: 0.60 B: 0.60 Type of Condition *Amblyopia*	

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First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
				A: 0.67 B: 0.83 *Strabismus* A: 0.60 B: 0.60 *Refractive Error* A: 0.76 B: 0.75 *Reduced visual acuity* A: 0.30 B: 0.30	
VIP Study Group, 2010[107]	A: 0.53% (6/1,253) B: 0.79% (9/1,253)	Considered them to be a positive screen	91% (1,142/1,253)	For 90% specificity *To detect >1 Condition* *3 years* A: 0.61 (0.47 to 0.73) B: 0.46 (0.33 to 0.59) *4 years to young* A: 0.57 (0.46 to 0.67) B: 0.57 (0.46 to 0.67) *4 years to old* A: 0.65 (0.54 to 0.75) B: 0.57 (0.45 to 0.67) *5 years* A: 0.60 (0.51 to 0.70) B: 0.56 (0.46 to 0.65) *To detect a group 1 condition* *3 years* A: 0.83 (0.61 to 0.95) B: 0.57 (0.34 to 0.77) *4 years to young* A: 0.73 (0.56 to 0.86) B: 0.65 (0.47 to 0.80) *4 years to old* A: 0.83 (0.65 to 0.94) B: 0.80 (0.61 to 0.92) *5 years* A: 0.78 (0.63 to 0.88) B: 0.82 (0.68 to 0.91)	Specificity set at 90% or closest to 90% achievable *To detect >1 Condition* *3 years* A: 0.90 (0.84 to 0.94) B: 0.88 (0.82 to 0.93) *4 years to young* A: 0.91 (0.86 to 0.94) B: 0.91 (0.86 to 0.94) *4 years to old* A: 0.90 (0.85 to 0.94) B: 0.87 (0.82 to 0.91) *5 years* A: 0.92 (0.87 to 0.95) B: 0.92 (0.87 to 0.95) *To detect a group 1 condition* *3 years* A: 0.90 (0.85 to 0.94) B: 0.88 (0.83 to 0.92) *4 years to young* A: 0.91 (0.87 to 0.94) B: 0.91 (0.87 to 0.94) *4 years to old* A: 0.90 (0.86 to 0.93) B: 0.87 (0.82 to 0.91) *5 years* A: 0.92 (0.88 to 0.95) B: 0.92 (0.88 to 0.95)

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First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
Ying et al, 2011[111] VIP (Phases 1 and 2)	A: 0.79% (9/1,142) B: 0.35% (19/5,476) C: 1.27% (55/4,341)	Considered them to be a positive screen	NR	Sensitivity dependent on specificity for any targeted condition and given for group 1 and any targeted condition[d] Specificity 0.50 *Group 1 Conditions* A: 0.98 B: 0.96 C: 0.98 *Any Targeted Condition* A: 0.88 B: 0.90 C: 0.91 Specificity 0.60 *Group 1 Conditions* A: 0.96 B: 0.96 C: 0.95 *Any Targeted Condition* A: 0.84 B: 0.88 C: 0.88 Specificity 0.70 *Group 1 Conditions* A: 0.96 B: 0.95 C: 0.95 *Any Targeted Condition* A: 0.81 B: 0.83 C: 0.83	Fixed at 0.50, 0.60, 0.70, 0.80, 0.85, 0.90, or 0.95
Ying et al, 2011[111] VIP (Phases 1 and 2)				Specificity 0.80 *Group 1 Conditions* A: 0.96 B: 0.92 C: 0.90 *Any Targeted Condition* A: 0.76 B: 0.77 C: 0.77 Specificity 0.85	

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				Group 1 Conditions A: 0.92 B: 0.91 C: 0.87 *Any Targeted Condition* A: 0.71 B: 0.73 C: 0.72 Specificity 0.90 *Group 1 Conditions* A: 0.90 B: 0.87 C: 0.82 *Any Targeted Condition* A: 0.64 B: 0.68 C: 0.65 Specificity 0.95 *Group 1 Conditions* A: 0.85 B: 0.83 C: 0.77 *Any Targeted Condition* A: 0.56 B: 0.58 C: 0.55	
VIP Study Group, 2005[108] Phase II	<2%	NR	Year 1: NR Year 2: 94% (1,452/1,541)	By severity, screener tool *Any condition* *Nurse* A: 0.68 (0.64 to 0.72) B: 0.64 (0.60 to 0.68) C: 0.49 (0.44 to 0.54) D: NA E: 0.45 (0.40 to 0.50) F: NA *Lay Screener* A: 0.62 (0.57 to 0.66) B: 0.61 (0.56 to 0.66) C: 0.37 (0.32 to 0.42)[b] D: 0.61 (0.56 to 0.66) E: 0.40 (0.36 to 0.45)	By severity, screener tool *Any condition* *Nurse* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92) C: 0.90 (0.88 to 0.92) D: NA E: 0.90 (0.88 to 0.92) F: NA *Lay Screener* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92) C: 0.90 (0.88 to 0.92)[b] D: 0.91 (0.89 to 0.93) E: 0.90 (0.88 to 0.92)

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First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
				F: 0.47 (0.42 to 0.52)[b]	F: 0.90 (0.88 to 0.92)[b]
				Group1 *Nurse* A: 0.88 (0.83 to 0.92) B: 0.83 (0.77 to 0.88) C: 0.60 (0.53 to 0.67) D: NA E: 0.58 (0.51 to 0.65) F: NA *Lay Screener* A: 0.85 (0.79 to 0.89) B: 0.82 (0.76 to 0.87) C: 0.50 (0.42 to 0.58)[b] D: 0.78 (0.72 to 0.83) E: 0.56 (0.49 to 0.63) F: 0.70 (0.62 to 0.77)[b]	*Group1* *Nurse* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92) C: 0.90 (0.88 to 0.92) D: NA E: 0.90 (0.88 to 0.92) F: NA *Lay Screener* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92) C: 0.90 (0.88 to 0.92)[b] D: 0.91 (0.89 to 0.93) E: 0.90 (0.88 to 0.92) F: 0.90 (0.88 to 0.92)[b]
VIP Study Group, 2005[108] Phase II				*Group 2* *Nurse* A: 0.59 (0.51 to 0.67) B: 0.57 (0.48 to 0.65) C: 0.38 (0.30 to 0.47) D: NA E: 0.37 (0.29 to 0.45) F: NA *Lay Screener* A: 0.49 (0.41 to 0.58) B: 0.51 (0.42 to 0.59) C: 0.19 (0.12 to 0.27)[b] D: 0.51 (0.42 to 0.59) E: 0.31 (0.24 to 0.40) F: 0.31 (0.23 to 0.40)[b] *Group 3* *Nurse* A: 0.39 (0.30 to 0.49) B: 0.34 (0.25 to 0.44) C: 0.42 (0.32 to 0.52) D: NA E: 0.30 (0.21 to 0.39) F: NA	*Group 2* *Nurse* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92) C: 0.90 (0.88 to 0.92) D: NA E: 0.90 (0.88 to 0.92) F: NA *Lay Screener* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92) C: 0.90 (0.88 to 0.92)[b] D: 0.91 (0.89 to 0.93) E: 0.90 (0.88 to 0.92) F: 0.90 (0.88 to 0.92)[b] *Group 3* *Nurse* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92) C: 0.90 (0.88 to 0.92) D: NA E: 0.90 (0.88 to 0.92) F: NA

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				Lay Screener A: 0.36 (0.27 to 0.46) B: 0.34 (0.25 to 0.44) C: 0.35 (0.25 to 0.45)[b] D: 0.40 (0.31 to 0.50) E: 0.23 (0.16 to 0.32) F: 0.26 (0.17 to 0.35)[b]	*Lay Screener* A: 0.90 (0.88 to 0.92) B: 0.90 (0.88 to 0.92) C: 0.90 (0.88 to 0.92)[b] D: 0.91 (0.89 to 0.93) E: 0.90 (0.88 to 0.92) F: 0.90 (0.88 to 0.92)[b]
Weinand et al, 1998[109]	9% (10/112)	Not described	91% (102/112)	A (Pediatrician interpreter): 0.94 (0.86 to 0.98) B (Orthoptist interpreter): 0.80 (0.69 to 0.88) C (Ophthalmologist 1 interpreter): 0.72 (0.61 to 0.82) D (Ophthalmologist 2 interpreter): 0.86 (0.76 to 0.92)	A (Pediatrician interpreter): 0.42 (0.20 to 0.66) B (Orthoptist interpreter): 0.74 (0.49 to 0.91) C (Ophthalmologist 1 interpreter): 0.74 (0.49 to 0.91) D (Ophthalmologist 2 interpreter): 0.58 (0.34 to 0.80)
Williams et al, 2000[110]	15% (33/222)	Excluded from analysis	85% (189/222)	A: 0.50 (0.33 to 0.67)[e] B: 0.74 (0.52 to 0.90)[e] C: 0.47 (0.28 to 0.66)[e]	A: 0.95 (0.90 to 0.98)[e] B: 0.95 (0.91 to 0.98)[e] C: 0.96 (0.92 to 0.99)[e]
Ying et al, 2011[111] VIP (Phases 1 and 2)	A: 0.79% (9/1,142) B: 0.35% (19/5,476) C: 1.27% (55/4,341)	Considered them to be a positive screen	NR	Sensitivity dependent on specificity for any targeted condition and given for group 1 and any targeted condition[f] Specificity 0.50 Group 1 Conditions A: 0.98 B: 0.96 C: 0.98 Any Targeted Condition A: 0.88 B: 0.90 C: 0.91 Specificity 0.60 Group 1 Conditions A: 0.96 B: 0.96 C: 0.95 Any Targeted Condition A: 0.84 B: 0.88 C: 0.88	Fixed at 0.50, 0.60, 0.70, 0.80, 0.85, 0.90, or 0.95

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Ying et al, 2011[111] VIP (Phases 1 and 2)				Specificity 0.70 Group 1 Conditions A: 0.96 B: 0.95 C: 0.95 Any Targeted Condition A: 0.81 B: 0.83 C: 0.83 Specificity 0.80 *Group 1 Conditions* A: 0.96 B: 0.92 C: 0.90 *Any Targeted Condition* A: 0.76 B: 0.77 C: 0.77 Specificity 0.85 *Group 1 Conditions* A: 0.92 B: 0.91 C: 0.87 *Any Targeted Condition* A: 0.71 B: 0.73 C: 0.72 Specificity 0.90 *Group 1 Conditions* A: 0.90 B: 0.87 C: 0.82 *Any Targeted Condition* A: 0.64 B: 0.68 C: 0.65 Specificity 0.95 *Group 1 Conditions* A: 0.85 B: 0.83 C: 0.77	

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First Author, Year Study Name	Proportion Unexaminable by Screening Test	How Did Study Handle Unexaminable Patients and/or Uninterpretable Results?	Proportion Who Underwent Reference Standard and Included in Analyses	Sensitivity (95% CI)	Specificity (95% CI)
				Any Targeted Condition A: 0.56 B: 0.58 C: 0.55	

[a] Data in main paper focused on area under the curve (AUC). For detection of each type of SRE, AUC of each test was high; AUC was better for detecting the most severe levels of SRE than for all Res considered important to detect (AUC 0.97 to 1.00 vs. 0.92 to 0.93). The AUC of each screening test was high for myopia (AUC 0.97 to 0.99). Noncycloplegic retinoscopy and Retinomax performed better than SureSight for hyperopia (AUC 0.92 to 0.99 and 0.90 to 0.98 vs. 0.85 to 0.94, P ≤ 0.02), Retinomax performed better than NCR for astigmatism greater than 1.50 D (AUC 0.95 vs.0.90, P=0.01), and SureSight performed better than Retinomax for anisometropia (AUC 0.85 to 1.00 vs. 0.76 to 0.96, P ≤ 0.07). Performance was similar for nurse and lay screeners in detecting any SRE (AUC 0.92 to 1.00 vs. 0.92 to 0.99).
[b] Interpretable by at least 6 of 11 reviewers.
[c] Calculation based on n=379, median sensitivity and specificity.
[d] Data in main paper focused on AUC. The AUC for detecting any VIP-targeted condition was 0.83 for NCR, 0.83 (phase I) to 0.88 (phase II) for Retinomax, and 0.86 (phase I) to 0.87 (phase II) for SureSight. The AUC was 0.93 to 0.95 for detecting group 1 (most severe) conditions and did not differ between instruments or screeners or by age of the child.
[e] Results based on cutoffs to obtain specificity at least 95%.
[f] Data in main paper focused on AUC. The AUC for detecting any VIP-targeted condition was 0.83 for NCR, 0.83 (phase I) to 0.88 (phase II) for Retinomax, and 0.86 (phase I) to 0.87 (phase II) for SureSight. The AUC was 0.93 to 0.95 for detecting group 1 (most severe) conditions and did not differ between instruments or screeners or by age of the child.

Abbreviations: AUC=area under the curve; CI=confidence interval; mo=month; NA=not applicable; NR=not reported; RPST=Randot Preschool Stereoacuity Test; SSST=Stereo Smile Stereoacuity Test; VIP=Vision In Preschoolers.

Appendix E Table 9. Diagnostic Accuracy Study Results (KQ 2)

Author, Year Study Name	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)	Quality
Afsari et al, 2013[77] Sydney Paediatric Eye Disease Study	SSST-strabismus 120: 2.08 240: 3.85 480: 12.5 SSST-anisometropia 120: 0.81 240: 1.13 480: 3.40 SSST-amblyopia 120: 1.22 240: 3.57 480: 10 RPST-strabismus 200: 6.86 400: 12.00 800: 27.0 RPST-anisometropia 200: 5.0 400: 7.50 800: 4.50 RPST-amblyopia 200: 7.57 400: 11.75 800: 12.00	SSST-strabismus 120: 0.28 240: 0.57 480: 0.52 SSST-anisometropia 120: 1.14 240: 0.97 480: 0.87 SSST-amblyopia 120: 0.84 240: 0.58 480: 0.53 RPST-strabismus 200: 0.56 400: 0.66 800: 0.74 RPST-anisometropia 200: 0.70 400: 0.73 800: 0.93 RPST-amblyopia 200: 0.51 400: 0.55 800: 0.78	SSST-strabismus 120: 5.59 240: 9.84 480: 31.58 SSST-anisometropia 120: 2.26 240: 3.12 480: 9.09 SSST-amblyopia 120: 1.13 240: 3.12 480: 9.09 RPST-strabismus 200: 18.60 400: 25.53 800: 37.50 RPST-anisometropia 200: 9.30 400: 14.89 800: 8.33 RPST-amblyopia 200: 10.47 400: 17.02 800: 16.67	SSST-strabismus 120: 99.21 240: 98.39 480: 98.55 SSST-anisometropia 120: 96.88 240: 97.29 480: 97.57 SSST-amblyopia 120: 99.22 240: 99.46 480: 99.51 RPST-strabismus 200: 98.30 400: 97.97 800: 97.74 RPST-anisometropia 200: 98.50 400: 98.46 800: 98.02 RPST-amblyopia 200: 99.20 400: 99.13% 800: 98.77%	
Arthur et al, 2009[78]	18 (10 to 33)	0.17 (0.08 to 0.36)	0.73 (0.57 to 0.85)	0.97 (0.94 to 0.99)	Fair
Barry et al, 2001[79]	1.9 (1.4 to 2.6)	0.35 (0.1 to 1.2)	0.05 (0.02 to 0.09)	0.99 (0.97 to 1.0)	Fair
Barry et al, 2003[80]	15 (11 to 19)	0.10 (0.03 to 0.36)	0.25 (0.16 to 0.36)	1.0 (0.99 to 1.0)	Fair
Bertuzzi et al, 2006[81]	A: 5.7 (3.8 to 8.6) B: 12 (5.8 to 24)	A: 0.05 (0.01 to 0.36) B: 0.23 (0.11 to 0.51)	A: 0.52 (0.36 to 0.68) B: 0.69 (0.48 to 0.86)	A: 0.99 (0.95 to 1.0) B: 0.96 (0.90 to 0.99)	Fair
Chui et al, 2004[82]	4.8 (2.8 to 8.4) <41 months: 2.4 (1.4 to 4.1) ≥41 months: 10 (3.0 to 36)	0.39 (0.20 to 0.75) <41 months: 0.37 (0.13 to 1.0) >41 months: 0.53 (0.24 to 1.2)	0.41 (0.24 to 0.61) <41 months: 0.41 (0.21 to 0.64) ≥41 months: 0.43 (0.10 to 0.82)	0.95 (0.89 to 0.98) <41 months: 0.90 (0.74 to 0.98) ≥41 months: 0.96 (0.90 to 0.99)	Fair
Cogen et al, 1992[83]	14 (6.3 to 32)	0.16 (0.05 to 0.59)	0.65 (0.38 to 0.86)	0.98 (0.93 to 1.0)	Fair
Dahlmann-Noor et al, 2009[84]	A: 21 (7.8 to 55) B: 26 (1.6 to 450) C: 11 (4.7 to 24) D: 3.7 (1.9 to 7.1)	A: 0.13 (0.01 to 1.7) B: 0.81 (0.70 to 0.94) C: 0.27 (0.08 to 0.89) D: 0.58 (0.40 to 0.84)	A: 0.44 (0.14 to 0.78) B: 0.94 (0.57 to 1.0) C: 0.46 (0.20 to 0.74) D: 0.54 (0.34 to 0.73)	A: 1.0 (0.95 to 1.0) B: 0.66 (0.56 to 0.75) C: 0.98 (0.92 to 1.0) D: 0.85 (0.75 to 0.91)	Fair
Dahlmann-Noor et al, 2009[85]	230 (14 to 3,680)	0.56 (0.42 to 0.74)	0.97 (0.73 to 1.0)	0.92 (0.89 to 0.95)	Fair
Hope et al, 1990[87]	3.6 (2.5 to 5.2)	0.15 (0.02 to 0.94)	0.17 (0.08 to 0.31)	0.99 (0.96 to 1.0)	Fair
Jost, 2015[89]	A: 10.4 (5.61 to 19.4) B: 7.9 (4.7 to 13.4)	A: 0.0 B: 0.0	A: 0.10 (0.00 to 0.44) B: 0.08 (0.002 to 0.36)	A: 1.0 (0.96 to 1.0) B: 1.0 (0.96 to 1.0)	Fair

Appendix E Table 9. Diagnostic Accuracy Study Results (KQ 2)

Author, Year Study Name	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)	Quality
Kemper et al, 2005[90]	Overall: 1.8 <3 years old: 1.4 3 to 5 years old: 2.1	Overall: 0.29 <3 years old: 0.49 3 to 5 years old: 0.21	Not calculable	Not calculable	Fair
Kennedy et al, 1989[91]	Any condition A: 16 (8.2 to 32) B: 6.5 (4.2 to 10)	Any condition A: 0.06 (0.03 to 0.14) B: 0.18 (0.11 to 0.28)	Any condition A: 0.92 (0.85 to 0.96) B: 0.82 (0.73 to 0.89)	Any condition A: 0.96 (0.91 to 0.98) B: 0.89 (0.82 to 0.94)	Fair
Kennedy et al, 1995[92]	A: 110 (38 to 310)[a] B: 17 (5.5 to 54)[a]	A: 0.54 (0.33 to 0.89)[a] B: 0.91 (0.84 to 0.99)[a]	A: 0.77 (0.60 to 0.95) B: 0.54 (0.28 to 0.81)	A: 0.98 (0.91 to 1.00) B: 0.94 (0.91 to 0.97)	Fair
Kennedy et al, 2000[93]	8.6 (5.4 to 14) ≤3 years 33 4 to 6 years 18	0.09 (0.06 to 0.13) ≤3 years not calculable 4 to 6 years 0.08	0.94 (0.90 to 0.96) ≤3 years 0.97 4 to 6 years 0.97	0.86 (0.80 to 0.91)	Fair
Kulp et al, 2014[94] VIP (Phases 1 and 2)	NR	NR	NR	NR	Fair
Matta et al, 2008[96]	A: 3.0 (1.9 to 4.7) B: 8.4 (3.7 to 19)	A: 0.04 (0.01 to 0.26) B: 0.03 (0.00 to 0.20)	A: 0.75 (0.61 to 0.86) B: 0.89 (0.75 to 0.96)	A: 0.96 (0.80 to 1.0) B: 0.97 (0.85 to 1.0)	Fair
Miller et al, 1999[97]	A: 1.6 (1.4 to 1.9) B: 6.7 (4.5 to 9.8)	A: 0.21 (0.10 to 0.43) B: 0.11 (0.05 to 0.22)	A: 0.42 (0.35 to 0.50) B: 0.75 (0.65 to 0.83)	A: 0.92 (0.83 to 0.96) B: 0.95 (0.901 to 0.98)	Fair
Miller et al, 2001[98]	A: 1.9 (1.6 to 2.2) B: 2.3 (1.8 to 2.9) C: 4.1 (3.2 to 5.4) D: 18 (10 to 34)	A: 0.14 (0.08 to 0.27) B: 0.48 (0.38 to 0.60)[b] C: 0.06 (0.03 to 0.12) D: 0.08 (0.04 to 0.13)	A: 0.48 (0.41 to 0.54) B: 0.68 (0.60 to 0.75)[b] C: 0.79 (0.73 to 0.84) D: 0.94 (0.90 to 0.97)	A: 0.93 (0.88 to 0.97) B: 0.70 (0.63 to 0.76)[b] C: 0.94 (0.90 to 0.97) D: 0.94 (0.89 to 0.96)	Fair
Morgan et al, 1987[99]	3.5 (1.7 to 7.0)	0.12 (0.04 to 0.36)	0.84 (0.68 to 0.94)	0.85 (0.62 to 0.97)	Fair
Ottar et al, 1995[100]; Donahue et al, 2002[101]	A: 8.7 (6.9 to 11)	A: 0.20 (0.15 to 0.27)	A: 0.69 (0.62 to 0.75)	A: 0.95 (0.93 to 0.97)	Fair
Rogers et al, 2008[102]	A: 1.6 (1.2 to 2.0) B: 2.2 (1.4 to 3.4) C: 2.2 (1.3 to 3.5) D: 2.4 (1.4 to 4.1) E: 8.0 (3.5 to 18)	A: 0.09 (0.02 to 0.37) B: 0.32 (0.18 to 0.56) C: 0.47 (0.31 to 0.72) D: 0.51 (0.35 to 0.75) E: 0.06 (0.02 to 0.18)	A: 0.68 (0.57 to 0.78) B: 0.75 (0.63 to 0.86) C: 0.75 (0.61 to 0.86) D: 0.77 (0.62 to 0.88) E: 0.92 (0.82 to 0.97)	A: 0.89 (0.65 to 0.99) B: 0.69 (0.52 to 0.83) C: 0.60 (0.45 to 0.74) D: 0.58 (0.44 to 0.72) E: 0.92 (0.80 to 0.98)	Fair
Shallo-Hoffmann et al, 2004[103]	12 (4.7 to 28)[c]	0.28 (0.03 to 2.4)[c]	0.24 (0.08 to 0.47)	1.00 (0.94 to 1.0)	Fair
Tong et al, 2000[105]	A: 6.4 (3.4 to 12) B: 4.9 (2.6 to 9.1)	A: 0.48 (0.42 to 0.56) B: 0.40 (0.33 to 0.47)	A: 0.95 (0.90 to 0.98) B: 0.95 (0.90 to 0.98)	A: 0.43 (0.36 to 0.50) B: 0.41 (0.33 to 0.49)	Fair
Schmidt et al, 2004[65]; Freedman et al, 2006[104] VIP Study (Phase I)	Any condition A: 6.1 (4.8 to 7.6) B: 8.2 (6.1 to 11)	Any condition A: 0.43 (0.38 to 0. B: 0.54 (0.49 to 0.	Any condition 50) A: 0.73 (0.67 to 0.78) 60) B: 0.78 (0.72 to 0.83)	Any condition A: 0.84 (0.82 to 0.86) B: 0.81 (0.78 to 0.83)	Fair
Schmidt et al, 2004[65]; Freedman et al, 2006[104] VIP Study (Phase I) Crowded Linear HOTV visual acuity test	Any condition A: 4.9 (3.9 to 6.1) B: 5.1 (3.8 to 6.8)	Any condition A: 0.52 (0.46 to 0.58) B: 0.69 (0.63 to 0.74)	Any condition A: 0.68 (0.62 to 0.74) B: 0.69 (0.62 to 0.76)	Any condition A: 0.82 (0.79 to 0.84) B: 0.77 (0.74 to 0.80)	Fair

Appendix E Table 9. Diagnostic Accuracy Study Results (KQ 2)

Author, Year Study Name	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)	Quality
Schmidt et al, 2004[65]; Freedman et al, 2006[104] VIP Study (Phase I) Random Dot E stereoacuity test	Any condition A: 4.2 (3.3 to 5.3) B: 2.7 (2.0 to 3.7)	Any condition A: 0.65 (0.59 to 0.71) B: 0.85 (0.80 to 0.90)	Any condition A: 0.64 (0.58 to 0.71) B: 0.54 (0.46 to 0.63)	Any condition A: 0.78 (0.75 to 0.81) B: 0.80 (0.78 to 0.83)	Fair
Schmidt et al, 2004[65]; Freedman et al, 2006[104] VIP Study (Phase I) Stereo Smile II stereoacuity test	Any condition A: 4.9 (3.9 to 6.1) B: 5.5 (4.2 to 7.3)	Any condition A: 0.62 (0.56 to 0.67) B: 0.71 (0.66 to 0.76)	Any condition A: 0.66 (0.60 to 0.72) B: 0.68 (0.62 to 0.75)	Any condition A: 0.73 (0.70 to 0.76) B: 0.78 (0.76 to 0.80)	Fair
Schmidt et al, 2004[65]; Freedman et al, 2006[104] VIP Study (Phase I) Retinomax autorefractor	Any condition A: 6.1 (5.2 to 7.0) B: 8.7 (7.2 to 10)	Any condition A: 0.41 (0.37 to 0.45) B: 0.51 (0.47 to 0.55)	Any condition A: 0.71 (0.68 to 0.75) B: 0.78 (0.74 to 0.82)	Any condition A: 0.86 (0.84 to 0.87) B: 0.83 (0.81 to 0.84)	Fair
Schmidt et al, 2004[65]; Freedman et al, 2006[104] VIP Study (Phase I) SureSight autorefractor	Any condition A1: 2.2 (2.0 to 2.4) A2: 6.3 (5.2 to 7.7) B: 8.6 (6.6 to 11)	Any condition A1: 0.24 (0.19 to 0.30) A2: 0.41 (0.36 to 0.47) B: 0.52 (0.47 to 0.58)	Any condition A1: 0.47 (0.43 to to 0.51) A2: 0.71 (0.66 to 0.76) B: 0.77 (0.72 to 0.82)	Any condition A1: 0.91 (0.89 to 0.93) A2: 0.86 (0.84 to 0.88) B: 0.83 (0.81 to 0.85)	Fair
VIP Study Group (Phase I), 2004[108] iScreen photoscreener	Any condition 6.2 (4.7 to 8.1)	Any condition 0.67 (0.62 to 0.72)	Any condition 0.71 (0.64 to 0.77)	Any condition 0.79 (0.77 to 0.81)	Fair
Schmidt et al, 2004[65]; Freedman et al, 2006[104] VIP Study (Phase I) MTI photoscreener	Any condition 6.2 (4.7 to 8.1)	Any condition 0.67 (0.62 to 0.72)	Any condition 0.71 (0.64 to 0.77)	Any condition 0.79 (0.77 to 0.81)	Fair
Schmidt et al, 2004[65]; Freedman et al, 2006[104] VIP Study (Phase I) Power Refractor II	Any condition A: 5.4 (4.4 to 6.6) B: 6.0 (4.6 to 7.9)	Any condition A: 0.51 (0.46 to 0.57) B: 0.68 (0.63 to 0.73)	Any condition A: 0.68 (0.65 to 0.73) B: 0.70 (0.64 to 0.76)	Any condition A: 0.83 (0.81 to 0.85) B: 0.79 (0.76 to 0.81)	Fair
Schmidt et al, 2004[65]; Freedman et al, 2006[104] VIP Study (Phase I) Cover-uncover test	Any condition 7.9 (4.6 to 14)	Any condition 0.86 (0.82 to 0.90)	Any condition 0.78 (0.66 to 0.86)	Any condition 0.73 (0.70 to 0.76)	Fair

Appendix E Table 9. Diagnostic Accuracy Study Results (KQ 2)

Author, Year Study Name	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)	Quality
VIP Study Group, 2011[106]	For 90% specificity, by severity *Overall* A: 7.14 (4.10 to 12.43) B: 7.58 (4.37 to 13.15) *Group 1* A: 8.01 (4.77 to 13.45) B: 9.47 (5.79 to 15.48) *Group 2* A: 7.68 (4.58 to 12.88) B: 6.32 (3.61 to 11.09) *Group 3* A: 5.86 (3.18 to 10.80) B: 7.16 (4.16 to 12.34) Type of Condition *Amblyopia* A: 7.36 (4.38 to 12.36) B: 8.59 (5.27 to 13.99) *Strabismus* A: 7.04 (3.84 to 12.92) B: 7.04 (3.84 to 12.92) *Refractive Error* A: 8.11 (4.78 to 13.74) B: 8.11 (4.78 to 13.74) *Reduced visual acuity* A: 3.02 (1.06 to 8.61) B: 7.04 ((3.84 to 12.92) For 94% Specificity, by severity *Overall* A: 10.96 (5.24 to 22.95) B: 10.96 (5.24 to 22.95)	For 90% specificity, by severity *Overall* A: 0.29 (0.19 to 0.44) B: 0.24 (0.15 to 0.38) *Group 1* A: 0.24 (0.12 to 0.48) B: 0.08 (0.02 to 0.30) *Group 2* A: 0.25 (0.12 to 0.55) B: 0.40 (0.23 to 0.70) *Group 3* A: 0.45 (0.24 to 0.83) B: 0.30 (0.13 to 0.69) Type of Condition *Amblyopia* A: 0.28 (0.14 to 0.56) B: 0.14 (0.05 to 0.40) *Strabismus* A: 0.33 (0.13 to 0.86) B: 0.33 (0.13 to 0.86) *Refractive Error* A: 0.18 (0.10 to 0.33) B: 0.18 (0.10 to 0.33) *Reduced visual acuity* A: 0.78 (0.52 to 1.17) B: 0.33 (0.13 to 0.86) For 94% Specificity, by severity *Overall* A: 0.36 (0.26 to 0.51) B: 0.36 (0.26 to 0.51)	For 90% specificity, by severity *Overall* A: 0.80 (0.68 to 0.89) B: 0.81 (0.69 to 0.90) *Group 1* A: 0.59 (0.42 to 0.75) B: 0.63 (0.47 to 0.78) *Group 2* A: 0.52 (0.34 to 0.69) B: 0.47 (0.28 to 0.66) *Group 3* A: 0.35 (0.17 to 0.56) B: 0.39 (0.22 to 0.59) Type of Condition *Amblyopia* A: 0.53 (0.35 to 0.70) B: 0.57 (0.39 to 0.73) *Strabismus* A: 0.29 (0.13 to 0.51) B: 0.29 (0.13 to 0.51) *Refractive Error* A: 0.78 (0.65 to 0.88) B: 0.78 (0.65 to 0.88) *Reduced visual acuity* A: 0.15 (0.3 to 0.38) B: 0.29 (0.13 to 0.51) For 94% Specificity, by severity *Overall* A: 0.86 (0.73 to 0.94) B: 0.86 (0.73 to 0.94)	For 90% specificity, by severity *Overall* A: 0.86 (0.78 to 0.92) B: 0.88 (0.81 to 0.93) *Group 1* A: 0.96 (0.91 to 0.98) B: 0.99 (0.95 to 1.00) *Group 2* A: 0.97 (0.93 to 0.99) B: 0.95 (0.90 to 0.98) *Group 3* A: 0.96 (0.92 to 0.99) B: 0.97 (0.93 to 0.99) Type of Condition *Amblyopia* A: 0.96 (0.91 to 0.98) B: 0.98 (9.94 to 1.00) *Strabismus* A: 0.98 (0.95 to 1.00) B: 0.98 (0.95 to 1.00) *Refractive Error* A: 0.93 (0.86 to 0.97) B: 0.93 (0.86 to 0.97) *Reduced visual acuity* A: 0.96 (0.91 to 0.98) B: 0.98 (0.95 to 1.00) For 94% Specificity, by severity *Overall* A: 0.83 (0.76 to 0.89) B: 0.83 (0.76 to 0.89)	Fair
VIP Study Group, 2010[107]	*≥1 Condition* *3 years* A: 5.95 (3.58 to 9.88) B: 3.76 (2.27 to 6.22) *4 years to young* A: 6.21 (3.95 to 9.78) B: 6.21 (3.95 to 9.78) *4 years to old* A: 6.63 (4.29 to 10.25) B: 4.33 (2.92 to 6.41) *5 years* A: 7.39 (4.57 to 11.93)	*≥1 Condition* *3 years* A: 0.43 (0.31 to 0.60) B: 0.62 (0.49 to 0.79) *4 years to young* A: 0.47 (0.37 to 0.60) B: 0.47 (0.37 to 0.60) *4 years to old* A: 0.39 (0.29 to 0.52) B: 0.50 (0.39 to 0.64) *5 years* A: 0.43 (0.34 to 0.55)	*≥1 Condition* *3 years* A: 0.69 (0.55 to 0.81) B: 0.59 (0.43 to 0.73) *4 years to young* A: 0.73 (0.61 to 0.82) B: 0.73 (0.61 to 0.82) *4 years to old* A: 0.72 (0.60 to 0.82) B: 0.63 (0.51 to 0.74) *5 years* A: 0.80 (0.70 to 0.88)	*≥1 Condition* *3 years* A: 0.86 (0.80 to 0.91) B: 0.81 (0.74 to 0.87) *4 years to young* A: 0.83 (0.78 to 0.88) B: 0.83 (0.78 to 0.88) *4 years to old* A: 0.87 (0.82 to 0.91) B: 0.84 (0.78 to 0.88) *5 years* A: 0.81 (0.76 to 0.86)	Fair

Appendix E Table 9. Diagnostic Accuracy Study Results (KQ 2)

Author, Year Study Name	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)	Quality
	B: 6.83 (4.21 to 11.10) *Group 1 Condition* *3 years* A: 8.35 (5.24 to 13.31) B: 4.72 (2.79 to 7.98) *4 years to young* A: 8.00 (5.24 to 12.20) B: 7.11 (4.57 to 11.07) *4 years to old* A: 8.24 (5.57 to 12.19) B: 6.10 (4.27 to 8.72) *5 years* A: 9.52 (6.20 to 14.60) B: 10.02 (6.57 to 15.28)	B: 0.48 (0.39 to 0.59) *Group 1 Condition* *3 years* A: 0.19 (0.08 to 0.47) B: 0.49 (0.31 to 0.79) *4 years to young* A: 0.30 (0.17 to 0.51) B: 0.39 (0.25 to 0.60) *4 years to old* A: 0.19 (0.08 to 0.41) B: 0.23 (0.11 to 0.47) *5 years* A: 0.24 (0.15 to 0.41) B: 0.20 (0.11 to 0.36)	B: 0.78 (0.68 to 0.87) *Group 1 Condition* *3 years* A: 0.50 (0.33 to 0.67) B: 0.36 (0.21 to 0.54) *4 years to young* A: 0.52 (0.38 to 0.66) B: 0.49 (0.34 to 0.64) *4 years to old* A: 0.48 (0.34 to 0.62) B: 0.41 (0.28 to 0.54) *5 years* A: 0.63 (0.50 to 0.75) B: 0.65 (0.51 to 0.76)	B: 0.80 (0.74 to 0.85) *Group 1 Condition* *3 years* A: 0.98 (0.94 to 0.99) B: 0.94 (0.90 to 0.97) *4 years to young* A: 0.96 (0.93 to 0.98) B: 0.95 (0.92 to 0.97) *4 years to old* A: 0.98 (0.95 to 0.99) B: 0.97 (0.95 to 0.99) *5 years* A: 0.96 (0.93 to 0.98) B: 0.97 (0.93 to 0.98)	
VIP Study Group, 2005[108] Phase II	By severity, screener tool *Any condition* *Nurse* A: 6.8 (5.6 to 8.3) B: 6.4 (5.3 to 7.8) C: 4.9 (4.0 to 6.0) D: NA E: 4.5 (3.6 to 5.6) F: NA *Lay Screener* A: 6.2 (5.1 to 7.6) B: 6.1 (5.0 to 7.5) C: 3.7 (3.0 to 4.7) D: 6.8 (5.5 to 8.4) E: 4.0 (3.2 to 5.0) F: 4.7 (3.8 to 5.8) *Group1* *Nurse* A: 8.8 (7.3 to 10.7) B: 8.3 (6.8 to 10.1) C: 6.0 (4.8 to 7.4) D: NA E: 5.8 (4.7 to 7.2) F: NA *Lay Screener* A: 8.5 (7.0 to 10.3) B: 8.2 (6.7 to 10.0) C: 5.0 (4.0 to 6.4) D: 8.7 (7.0 to 10.7)	By severity, screener tool *Any condition* *Nurse* A: 0.36 (0.31 to 0.41) B: 0.40 (0.35 to 0.45) C: 0.57 (0.52 to 0.62) D: NA E: 0.61 (0.56 to 0.67) F: NA *Lay Screener* A: 0.42 (0.38 to 0.48) B: 0.43 (0.39 to 0.49) C: 0.70 (0.65 to 0.76) D: 0.43 (0.38 to 0.48) E: 0.67 (0.62 to 0.72) F: 0.59 (0.53 to 0.65) *Group1* *Nurse* A: 0.13 (0.09 to 0.19) B: 0.19 (0.14 to 0.26) C: 0.44 (0.38 to 0.53) D: NA E: 0.47 (0.40 to 0.55) F: NA *Lay Screener* A: 0.17 (0.12 to 0.23) B: 0.20 (0.15 to 0.27) C: 0.56 (0.48 to 0.65) D: 0.24 (0.19 to 0.31)	By severity, screener tool *Any condition* *Nurse* A: 0.76 (0.72 to 0.80) B: 0.75 (0.70 to 0.79) C:0.70 (0.64 to 0.75) D: NA E: 0.68 (0.62 to 0.73) F: NA *Lay Screener* A: 0.74 (0.70 to 0.79) B: 0.74 (0.69 to 0.78) C: 0.58 (0.52 to 0.64) D: 0.76 (0.71 to 0.80) E: 0.65 (0.59 to 0.71) F: 0.64 (0.58 to 0.69) *Group1* *Nurse* A: 0.65 (0.59 to 0.71) B: 0.64 (0.58 to 0.69) C: 0.56 (0.49 to 0.63) D: NA E: 0.55 (0.48 to 0.62) F: NA *Lay Screener* A: 0.64 (0.58 to 0.70) B: 0.63 (0.57 to 0.69) C: 0.45 (0.38 to 0.52) D: 0.65 (0.59 to 0.71)	By severity, screener tool *Any condition* *Nurse* A: 0.86 (0.83 to 0.88) B: 0.84 (0.82 to 0.86) C: 0.79 (0.77 to 0.81) D: NA E: 0.78 (0.75 to 0.80) F: NA *Lay Screener* A: 0.84 (0.81 to 0.86) B: 0.83 (0.81 to 0.85) C: 0.79 (0.77 to 0.82) D: 0.83 (0.81 to 0.86) E: 0.76 (0.74 to 0.79) F: 0.82 (0.80 to 0.84) *Group1* *Nurse* A: 0.97 (0.96 to 0.98) B: 0.96 (0.95 to 0.97) C: 0.91 (0.89 to 0.93) D: NA E: 0.91 (0.89 to 0.93) F: NA *Lay Screener* A: 0.97 (0.95 to 0.98) B: 0.96 (0.94 to 0.97) C: 0.92 (0.90 to 0.93) D: 0.95 (0.94 to 0.96)	Fair

Appendix E Table 9. Diagnostic Accuracy Study Results (KQ 2)

Author, Year Study Name	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)	Quality
	E: 5.6 (4.5 to 7.0) F: 7.0 (5.7 to 8.6)	E: 0.49 (0.42 to 0.57) F: 0.34 (0.27 to 0.42)	E: 0.54 (0.48 to 0.61) F: 0.53 (0.47 to 0.60)	E: 0.91 (0.89 to 0.92) F: 0.95 (0.93 to 0.96)	
VIP Study Group, 2005[108] Phase II	*Group 2* *Nurse* A: 5.9 (4.7 to 7.4) B: 5.7 (4.5 to 7.2) C: NA D: 3.8 (2.9 to 5.0) E: 3.7 (2.8 to 4.9) F: NA *Lay Screener* A: 4.9 (3.8 to 6.3) B: 5.1 (4.0 to 6.5) C: 1.9 (1.3 to 2.9) D: 5.6 (4.4 to 7.3) E: 3.1 (2.3 to 4.2) F: 3.2 (2.3 to 4.3) *Group 3* *Nurse* A: 3.9 (2.9 to 5.3) B: 3.4 (2.5 to 4.7) C: 4.2 (3.1 to 5.6) D: NA E: 3.0 (2.1 to 4.2) F: NA *Lay Screener* A: 3.6 (2.6 to 4.9) B: 3.4 (2.5 to 4.7) C: 3.5 (2.5 to 4.8) D: 4.4 (3.3 to 6.0) E: 2.3 (1.6 to 3.4) F: 2.6 (1.8 to 3.8)	*Group 2* *Nurse* A: 0.46 (0.37 to 0.55) B: 0.48 (0.40 to 0.58) C: NA D: 0.69 (0.60 to 0.78) E: 0.70 (0.62 to 0.80) F: NA *Lay Screener* A: 0.56 (0.48 to 0.66) B: 0.55 (0.46 to 0.65) C: 0.90 (0.82 to 0.98) D: 0.54 (0.46 to 0.64) E: 0.76 (0.68 to 0.85) F: 0.76 (0.67 to 0.86) *Group 3* *Nurse* A: 0.68 (0.58 to 0.79) B: 0.73 (0.64 to 0.84) C: 0.65 (0.55 to 0.76) D: NA E: 0.78 (0.69 to 0.89) F: NA *Lay Screener* A: 0.71 (0.62 to 0.82) B: 0.73 (0.64 to 0.84) C: 0.73 (0.63 to 0.84) D: 0.66 (0.57 to 0.77) E: 0.85 (0.77 to 0.95) F: 0.83 (0.74 to 0.93)	*Group 2* *Nurse* A: 0.46 (0.39 to 0.54) B: 0.45 (0.38 to 0.53) C: NA D: 0.36 (0.28 to 0.44) E: 0.35 (0.27 to 0.43) F: NA *Lay Screener* A: 0.42 (0.34 to 0.50) B: 0.42 (0.35 to 0.50) C: 0.18 (0.12 to 0.26) D: 0.45 (0.37 to 0.53) E: 0.31 (0.24 to 0.40) F: 0.27 (0.20 to 0.35) *Group 3* *Nurse* A: 0.30 (0.22 to 0.38) B: 0.27 (0.20 to 0.36) C: 0.31 (0.24 to 0.40) D: NA E: 0.24 (0.17 to 0.33) F: NA *Lay Screener* A: 0.28 (0.21 to 0.37) B: 0.27 (0.20 to 0.36) C: 0.24 (0.18 to 0.32) D: 0.33 (0.25 to 0.41) E: 0.20 (0.13 to 0.28) F: 0.19 (0.13 to 0.27)	*Group 2* *Nurse* A: 0.94 (0.92 to 0.95) B: 0.93 (0.92 to 0.95) C: NA D: 0.91 (0.89 to 0.93) E: 0.91 (0.89 to 0.92) F: NA *Lay Screener* A: 0.92 (0.91 to 0.94) B: 0.93 (0.91 to 0.94) C: 0.91 (0.89 to 0.92) D: 0.93 (0.91 to 0.94) E: 0.90 (0.88 to 0.92) F: 0.92 (0.90 to 0.94) *Group 3* *Nurse* A: 0.93 (0.91 to 0.95) B: 0.93 (0.91 to 0.94) C: 0.93 (0.92 to 0.95) D: NA E: 0.92 (0.90 to 0.94) F: NA *Lay Screener* A: 0.93 (0.91 to 0.94) B: 0.93 (0.91 to 0.94) C: 0.94 (0.92 to 0.95) D: 0.93 (0.92 to 0.95) E: 0.91 (0.90 to 0.93) F: 0.93 (0.91 to 0.94)	Fair
Weinand et al, 1998[109]	A (Pediatrician interpreter) 1.6 (1.1 to 2.4) B (Orthoptist interpreter): 3.0 (1.4 to 6.5) C (Ophthalmologist 1 interpreter 2.8 (1.3 to 5.9) D (Ophthalmologist 2 interpreter 2.0 (1.2 to 3.5)	A (pediatrician interpreter): 0.14 (0.05 to 0.39) B (Orthoptist interpreter): 0.28 (0.17 to 0.46) C (Ophthalmologist 1 interpreter): 0.38 (0.24 to 0.58) D (Ophthalmologist 2 interpreter): 0.25 (0.13 to 0.48)	A (pediatrician interpreter): 0.88 (0.79 to 0.94) B (Orthoptist interpreter): 0.93 (0.84 to 0.98) C (Ophthalmologist 1 interpreter): 0.92 (0.83 to 0.98) D (Ophthalmologist 2 interpreter): 0.90 (0.81 to 0.96)	A (pediatrician interpreter): 0.62 (0.32 to 0.86) B (Orthoptist interpreter): 0.45 (0.27 to 0.64) C (Ophthalmologist 1 interpreter): 0.38 (0.22 to 0.55) D (Ophthalmologist 2 interpreter): 0.48 (0.27 to 0.69)	Fair

Appendix E Table 9. Diagnostic Accuracy Study Results (KQ 2)

Author, Year Study Name	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)	Quality
Williams et al, 2000[110]	A: 9.6 (4.5 to 20) B: 15 (7.5 to 32) C: 12 (5.2 to 30)	A: 0.53 (0.38 to 0 B: 0.27 (0.14 to 0 C: 0.55 (0.40 to 0	A: 0.69 (0.48 to 0.86) B: 0.68 (0.46 to 0.85) C: 0.70 (0.46 to 0.88)	A: 0.89 (0.83 to 0.93) B: 0.96 (0.92 to 0.99) C: 0.91 (0.85 to 0.94)	Fair
Ying et al, 2011[111] VIP (Phases 1 and 2)	NR	NR	NR	NR	Fair

[a] Extrapolated from sample of negative screens.
[b] Calculation based on n=379, median sensitivity and specificity.
[c] 25% sample (every 4th patient) of negative screens underwent reference standard

Abbreviations: CI=confidence interval; NR=not reported; RCT=randomized controlled trial; RPST=Randot Preschool Stereoacuity Test; SSST=Stereo Smile Stereoacuity Test.

Appendix E Table 10. Characteristics of Studies That Report Reliability (KQ 2)

First Author, Year Study Name	Screening Test	Type of Study	Setting Country	If Test-Retest, Indicate Time Between Tests	If Interrater, List N of Raters and Any Differences Between Raters	N
Huang et al, 2013[88] Vision In Preschoolers Phase II	Retinomax	Cross-sectional	Schools (Head Start) United States	Not applicable	Lay screeners: 16 Nurse screeners: 15 All received the same training and supervision	1,452 total; 1,433 (2,849 eyes) analyzed
Huang et al, 2013[88] Vision In Preschoolers Phase II	SureSight	Cross-sectional	Schools (Head Start) United States	Not applicable	Lay screeners: 16 Nurse screeners: 15 All received the same training and supervision	1,452 total; 1,404 (2,729 eyes) analyzed

Abbreviations: N=number.

Appendix E Table 11. Results of Studies That Report Reliability (KQ 2)

First Author, Year Study Name Screening Test	Test-Retest Reliability	Interrater Reliability	Comments or Other Measures of Reliability
Huang et al, 2013[88] VIP Phase II Retinomax; overall sample	NR	Mean (SD) [95% limits of agreement] of difference (Lay to nurse) Sphere: -0.04 (0.81) [-1.63 to 1.54] Cylinder: 0.00 (0.26) [-0.52 to 0.51] Spherical equivalent: -0.04 (0.82) [-1.65 to 1.56]	NA
Huang et al, 2013[88] VIP Phase II Retinomax; by age	NR	Mean (95% limits of agreement) of difference (Lay to nurse) *3 years old (N=722)* Sphere: -0.08 (-1.78 to 1.61) Cylinder: 0.01 (-0.47 to 0.50) Spherical equivalent: -0.08 (-1.80 to 1.64) *4 years old (N=1569)* Sphere: -0.03 (-1.58 to 1.53) Cylinder: 0.01 (-0.53 to 0.54) Spherical equivalent: -0.02 (-1.60 to 1.55) *5 years old (N=558)* Sphere: -0.03 (-1.54 to 1.48) Cylinder: -0.04 (-0.52 to 0.43) Spherical equivalent: -0.05 (-1.58 to 1.48)	NA
Huang et al, 2013[88] VIP Phase II Retinomax; by presence of SRE	NR	Mean (95% limits of agreement) of difference (Lay to nurse) *Yes, SRE present (N=737)* Sphere: -0.04 (-1.93 to 1.84) Cylinder: 0.04 (-0.57 to 0.66) Spherical equivalent: -0.02 (-1.93 to 1.89) *No, SRE not present (N=2112)* Sphere: -0.04 (-1.51 to 1.42) Cylinder: -0.02 (-0.48 to 0.45) Spherical equivalent: -0.05 (-1.54 to 1.44)	NA

Appendix E Table 11. Results of Studies That Report Reliability (KQ 2)

First Author, Year Study Name Screening Test	Test-Retest Reliability	Interrater Reliability	Comments or Other Measures of Reliability
Huang et al, 2013[88] VIP Phase II Retinomax; by spherical equivalent from gold standard exams	NR	Mean (95% limits of agreement) of difference (Lay to nurse) *≤ -0.5 D (N=125)* Sphere: 0.11 (-1.90 to 2.11) Cylinder: 0.06 (-0.77 to 0.90) Spherical equivalent: 0.14 (-1.90 to 2.17) *>-0.5, ≤ 1 D (N=1104)* Sphere: -0.03 (-1.46 to 1.40) Cylinder: -0.01 (-0.56 to 0.53) Spherical equivalent: -0.04 (-1.49 to 1.41) *>1, ≤ 2 D (N=1057)* Sphere: -0.04 (-1.65 to 1.57) Cylinder: 0.00 (-0.51 to 0.51) Spherical equivalent: -0.04 (-1.67 to 1.59) *>2 D (N=563)* Sphere: -0.10 (-2.25 to 2.05) Cylinder: 0.01 (-0.54 to 0.55) Spherical equivalent: -0.10 (-2.28 to 2.09)	NA
Huang et al, 2013[88] VIP Phase II SureSight; overall sample	NR	Mean (SD) [95% limits of agreement] of difference (Lay to nurse) Sphere: 0.05 (0.78) [-1.48 to 1.58] Cylinder: 0.01 (0.30) [-0.58 to 0.60] Spherical equivalent: 0.06 (0.77) [-1.45 to 1.57]	NA
Huang et al, 2013[88] VIP Phase II SureSight; by age	NR	Mean (95% limits of agreement) of difference (Lay to nurse) *3 years old (N=697)* Sphere: 0.07 (-1.57 to 1.71) Cylinder: 0.03 (-0.55 to 0.61) Spherical equivalent: 0.08 (-1.54 to 1.70) *4 years old (N=1503)* Sphere: 0.05 (-1.47 to 1.57) Cylinder: 0.005 (-0.62 to 0.63) Spherical equivalent: 0.05 (-1.45 to 1.55) *5 years old (N=529)* Sphere: 0.04 (-1.36 to 1.44) Cylinder: 0.004 (-0.52 to 0.52) Spherical equivalent: 0.04 (-1.34 to 1.42)	NA

Appendix E Table 11. Results of Studies That Report Reliability (KQ 2)

First Author, Year Study Name Screening Test	Test-Retest Reliability	Interrater Reliability	Comments or Other Measures of Reliability
Huang et al, 2013[88] VIP Phase II SureSight; by presence of SRE	NR	Mean (95% limits of agreement) of difference (Lay to nurse) *Yes, SRE present (N=641)* Sphere: 0.05 (-1.51 to 1.61) Cylinder: 0.01 (-0.67 to 0.70) Spherical equivalent: 0.05 (-1.51 to 1.61) *No, SRE not present (N=2,088)* Sphere: 0.05 (-1.46 to 1.57) Cylinder: 0.01 (-0.55 to 0.57) Spherical equivalent: 0.06 (-1.43 to 1.55)	NA
Huang et al, 2013[88] VIP Phase II SureSight; by spherical equivalent from gold standard exams	NR	Mean (95% limits of agreement) of difference (Lay to nurse) *≤ -0.5 D (N=108)* Sphere: -0.16 (-1.62 to 1.29) Cylinder: 0.02 (-0.91 to 0.95) Spherical equivalent: -0.15 (-1.79 to 1.49) *>-0.5, ≤ 1 D (N=1,073)* Sphere: 0.06 (-1.37 to 1.49) Cylinder: 0.02 (-0.60 to 0.63) Spherical equivalent: 0.07 (-1.32 to 1.45) *>1, ≤ 2 D (N=1,036)* Sphere: 0.05 (-1.67 to 1.76) Cylinder: 0.01 (-0.61 to 0.63) Spherical equivalent: 0.05 (-1.64 to 1.74) *>2 D (N=512)* Sphere: 0.10 (-1.73 to 1.94) Cylinder: -0.01 (-0.63 to 0.61) Spherical equivalent: 0.10 (-1.72 to 1.92)	NA

Abbreviations: D=diopter; NA=not applicable; NR=not reported; SD=standard deviation; SRE=significant refractive error; VIP=Vision In Preschoolers.

Appendix E Table 12. Characteristics of Randomized, Controlled Trials That Evaluate Treatment of Amblyopia, Its Risk Factors, and Refractive Error (KQs 4 and 5)

Author, Year Study Name	Purpose of Study	Inclusion Criteria	Exclusion Criteria	# Screened/ Eligible/ Enrolled	Age Sex Diagnosis
Awan et al, 2005[117]	To investigate compliance with patching therapy and dose-effect relationship in occlusion therapy for amblyopia	Age ≤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%)
Clarke et al, 2003[115]	To test efficacy of treatment for unilateral visual loss detected by preschool vision screening and extent to which effectiveness varies with initial severity	Age 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 Sex: NR Proportion of patients with anisometropia: 127/177 (72%) Baseline visual acuity, amblyopic eye[a]: 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
Wallace et al, 2006[116] PEDIG	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 age 3 to 7 years	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	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	NR/ NR/ 180	Mean age: 5.2 years Sex: 44% 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)

Appendix E Table 12. Characteristics of Randomized, Controlled Trials That Evaluate Treatment of Amblyopia, Its Risk Factors, and Refractive Error (KQs 4 and 5)

Author, Year Study Name	Purpose of Study	Inclusion Criteria	Exclusion Criteria	# Screened/ Eligible/ Enrolled	Age Sex Diagnosis
		difference between eyes in astigmatism in any meridian			Proportion of patients requiring refractive correction at baseline: 155/180 (86%)

Abbreviations: D=diopter; IXT=intermittent exotropia; NR=not reported; PACT=prism and alternate cover test; PD=prism diopters; PEDIG=Pediatric Eye Disease Investigator Group; RCT=randomized controlled trial; SD=standard deviation.

Appendix E Table 13. Characteristics of Randomized, Controlled Trials That Evaluate Treatment of Amblyopia, Its Risk Factors, and Refractive Error (KQ 4s and 5)

Author, Year Study Name	Country Setting	Measures	Duration	Quality
Clarke et al, 2003[115]	U.K. 8 clinical sites	Best corrected visual acuity in amblyopic eye after 1 year; followup at 1.5 years	54 weeks treatment; 78 weeks followup	Good
Wallace et al, 2006[116] PEDIG	U.S. 46 clinical sites	Best corrected visual acuity in amblyopic eye after 5 weeks of treatment	5 weeks treatment; up to 52 weeks followup	Good
Awan et al, 2005[117]	U.K. 1 clinical site	Primary outcome: mean compliance Other outcomes: improvement in visual acuity following 12 weeks of treatment	12 weeks	Fair

Abbreviations: KQ=Key Question; PACT=prism and alternate cover test; PEDIG=Pediatric Eye Disease Investigator Group; SPCT=simultaneous prism and cover test; U.K.=United Kingdom; U.S.=United States.

Appendix E Table 14. Results of Randomized, Controlled Trials That Evaluate Treatment of Amblyopia, Its Risk Factors, and Refractive Error (KQ 4)

Author, Year Study Name	Intervention (N) Comparison (N)	Results
Awan et al, 2005[117]	3 hours patching/day (n=20) 6 hours patching/day (n=20) No treatment for 12 weeks Glasses were prescribed for all who needed them.	*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)
Clarke et al, 2003[115]	Patching + eyeglasses (n=59) Eyeglasses only (n=59) No treatment (n=59) for 52 weeks, after which the no-treatment group received eyeglass prescriptions All patients evaluated during the 1 year followup period and were prescribed patching as needed	*Mean (SD) best corrected visual acuity at end of trial* Patching + eyeglasses (n=54): 0.193 (0.12) Eyeglasses only (n=55): 0.216 (0.17) No treatment (n=55): 0.301 (0.20); p=0.001 Mean difference (95% CI) from no treatment: Patching + eyeglasses: 0.109 (0.05 to 0.17) Eyeglasses only: 0.085 (0.02 to 0.15) *Mean (SD) best corrected visual acuity 6 months after trial end* Patching + eyeglasses (n=53): 0.170 (0.13) Eyeglasses only (n=51): 0.197 (0.16) No treatment (n=50): 0.170 (0.15) Mean difference (95% CI) from no treatment: Patching + eyeglasses: 0.0004 (-0.06 to 0.05) Eyeglasses only: 0.03 (-0.09 to 0.03) *Mean (SD) best corrected visual acuity according to baseline severity at end of trial* *Mild acuity loss at baseline* Patching + eyeglasses (n=33): 0.18 (0.11) Eyeglasses only (n=35): 0.16 (0.14) No treatment (n=33): 0.22 (0.17) Mean difference (95% CI) from no treatment: Patching + eyeglasses: 0.045 (-.02 to 0.11) Eyeglasses only: 0.58 (-0.02 to 0.13) *Moderate acuity loss at baseline* Patching + eyeglasses (n=21): 0.22 (0.13) Eyeglasses only (n=20): 0.31 (0.17) No treatment (n=22): 0.42 (0.19) Mean difference (95% CI) from no treatment: Patching + eyeglasses:0.203 (0.10 to 0.30) Eyeglasses only: 0.112 (-0.002 to 0.23)

Appendix E Table 14. Results of Randomized, Controlled Trials That Evaluate Treatment of Amblyopia, Its Risk Factors, and Refractive Error (KQ 4)

Author, Year Study Name	Intervention (N) Comparison (N)	Results
Clarke et al, 2003[115] (cont'd)		*Mean (SD) best corrected visual acuity according to baseline severity at 6 months after trial end* *Mild acuity loss at baseline* Patching + eyeglasses (n=32): 0.16 (0.12) Eyeglasses only (n=31): 0.13 (0.12) No treatment (n=28): 0.13 (9.08) Mean difference (95% CI) from no treatment: Patching + eyeglasses:-0.03 (-0.08 to 0.03) Eyeglasses only: 0.00 (-0.8 to 0.05) *Moderate acuity loss at baseline* Patching + eyeglasses (n=21): 0.19 (0.14) Eyeglasses only (n=20): 0.30 (0.18) No treatment (n=22): 0.22 (0.20) Mean difference (95% CI) from no treatment: Patching + eyeglasses: 0.03 (-.07 to 0.14) Eyeglasses only: -0.08 (-0.19 to 0.04) *Mean change in best corrected visual acuity following 52 weeks of treatment, according to baseline severity* *Mild acuity loss at baseline* Patching + eyeglasses (n=31): 0.23 (0.17) Eyeglasses only (n=31): 0.24 (0.14) No treatment (n=30): 0.19 (0.17) Mean difference (95% CI) from no treatment: Patching + eyeglasses: 0.04 (-0.06 to 0.13) Eyeglasses only: 0.05 (-0.03 to 0.13) *Moderate acuity loss at baseline* Patching + eyeglasses (n=20): 0.52 (0.19) Eyeglasses only (n=18): 0.35 (0.20) No treatment (n=21): 0.25 (0.21) Mean difference (95% CI) from no treatment: Patching + eyeglasses: 0.27 (0.14 to 0.39) Eyeglasses only: 0.11 (-0.03 to 0.24)

Appendix E Table 14. Results of Randomized, Controlled Trials That Evaluate Treatment of Amblyopia, Its Risk Factors, and Refractive Error (KQ 4)

Author, Year Study Name	Intervention (N) Comparison (N)	Results
Wallace et al, 2006[116] PEDIG	2 hours continuous patching/day with ≥1 hour of near activities (n=87) Control (n=93) Continued use of eyeglasses if needed, regardless of randomization group	Overall at end of trial *Mean % change (SD) in lines from baseline* Patching (N=85): 1.1 (1.6) Control (N=88): 0.5 (1.7) *Mean (SD) logMAR acuity* Patching (N=85): 0.44 (0.22) Control (N=88): 0.51 (0.28) Mean difference (95% CI) in logMAR acuity, adjusted for baseline acuity: 0.07 (0.02 to 0.12) Baseline amblyopic eye acuity at end of trial 20/40-20/100 *Mean % change (SD) in lines from baseline* Patching (N=71): 1.1 (1.5) Control (N=71): 0.4 (1.5) *Mean (SD) logMAR acuity* Patching (N=71): 0.38 (0.17) Control (N=71): 0.41 (0.16) Mean difference (95% CI) in logMAR acuity, adjusted for baseline acuity: 0.06 (0.01 to 0.11) 20/125-20/400 *Mean % change (SD) in lines from baseline* Patching (N=14): 1.2 (1.9) Control (N=17): 0.6 (2.1) *Mean (SD) logMAR acuity* Patching (N=14): 0.74 (0.19) Control (N=17): 0.93 (0.26) Mean difference (95% CI) in logMAR acuity, adjusted for baseline acuity: 0.08 (-0.09 to 0.25) Overall during followup *Mean (SD) improvement in lines from baseline to best measured acuity in amblyopic eye* Patching (N=84): 2.2 (1.8) Control (N=87): 1.3 (1.4) Difference (95% CI) in mean best logMAR acuity, adjusted for baseline acuity: 0.10 (0.05 to 0.14) Baseline amblyopic eye acuity during followup 20/40-20/100 *Mean (SD) improvement in lines from baseline to best measured acuity in amblyopic eye* Patching (N=70): 2.1 (1.6) Control (N=72): 1.3 (1.3) Difference (95% CI) in mean best logMAR acuity, adjusted for baseline acuity:0.07 (0.02 to 0.12)

Appendix E Table 14. Results of Randomized, Controlled Trials That Evaluate Treatment of Amblyopia, Its Risk Factors, and Refractive Error (KQ 4)

Author, Year Study Name	Intervention (N) Comparison (N)	Results
Wallace et al, 2006[116] PEDIG (cont'd)		20/125-20/400 *Mean (SD) improvement in lines from baseline to best measured acuity in amblyopic eye* Patching (N=14): 2.7 (1.3) Control (N=15): 1.2 (1.9) Difference (95% CI) in mean best logMAR acuity, adjusted for baseline acuity: 0.02 (0.01 to 0.39) Proportion of patients with ≥2 lines of improvement in visual acuity: patching 38/85 (44.7%) vs. control 18/88 (20.5%)

Abbreviations: CI=confidence interval; hr=hour; KQ=Key Question; N=number; PACT=prism and alternate cover test; p=p-value; PEDIG=Pediatric Eye Disease Investigator Group; SD=standard deviation; SPCT=simultaneous prism and cover test; Tx=treatment; vs.=versus.

Appendix E Table 15. Adverse Events Reported in Randomized, Controlled Trials That Evaluate Treatment of Amblyopia, Its Risk Factors, and Refractive Error (KQ 5)

Author, Year Study Name	Adverse Events
Awan et al, 2005[117]	*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
Clarke et al, 2003[115]; Hrisos et al, 2004[118]	*Proportion of patients with 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%)
Wallace et al, 2006[116] PEDIG	Withdrawals at 5 weeks: patching 2/87 (2.3%) vs. control 5/93 (5.4%) Withdrawals due to adverse events 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.

Abbreviations: hr=hour; p=p-value; PEDIG=Pediatric Eye Disease Investigator Group; vs.=versus.