

Screening for Visual Impairment in Children Younger than Age 5 Years: Update of the Evidence from Randomized Controlled Trials, 1999–2003, for the U.S. Preventive Services Task Force

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Background

In 2001, the U.S. Preventive Services Task Force (USPSTF) developed draft recommendations on screening for visual impairment in children younger than age 5 years, drawing on systematic reviews of the evidence trials and well-conducted observational studies. The evidence pertaining to this topic was originally summarized for the USPSTF in a manuscript covering publications on screening for visual impairment through the end of 1999.³ To help the USPSTF finalize their draft recommendations, the literature review was updated through June 2003, focusing on the randomized controlled trial (RCT) evidence that served as the basis for the draft recommendations.

This update of the evidence, written in 2003, focuses on the question of whether screening for amblyopia and associated conditions in children younger than age 5 years leads to better vision outcomes. This question has been added to the analytic framework from the original Systematic Evidence Review (Figure 1).³ The other key questions in the original evidence review were not systematically reviewed for this update. However,

new RCTs that address treatment effectiveness and performance of screening tests in the context of a screening program are cited here, since there is now more evidence of their effectiveness than was available in 2001. Only RCTs were systematically reviewed for this update of the evidence.

Methods

Search Strategy

References suggested by experts or professional organizations following the review of the 2001 report were reviewed for inclusion. In addition, the research team used the search strategies from the 2001 report, and developed appropriate update search strategies for MEDLINE® (1999–June 2003) and the Cochrane systematic review and RCT registry databases (1999–June 2003) (Appendix).

Inclusion and Exclusion

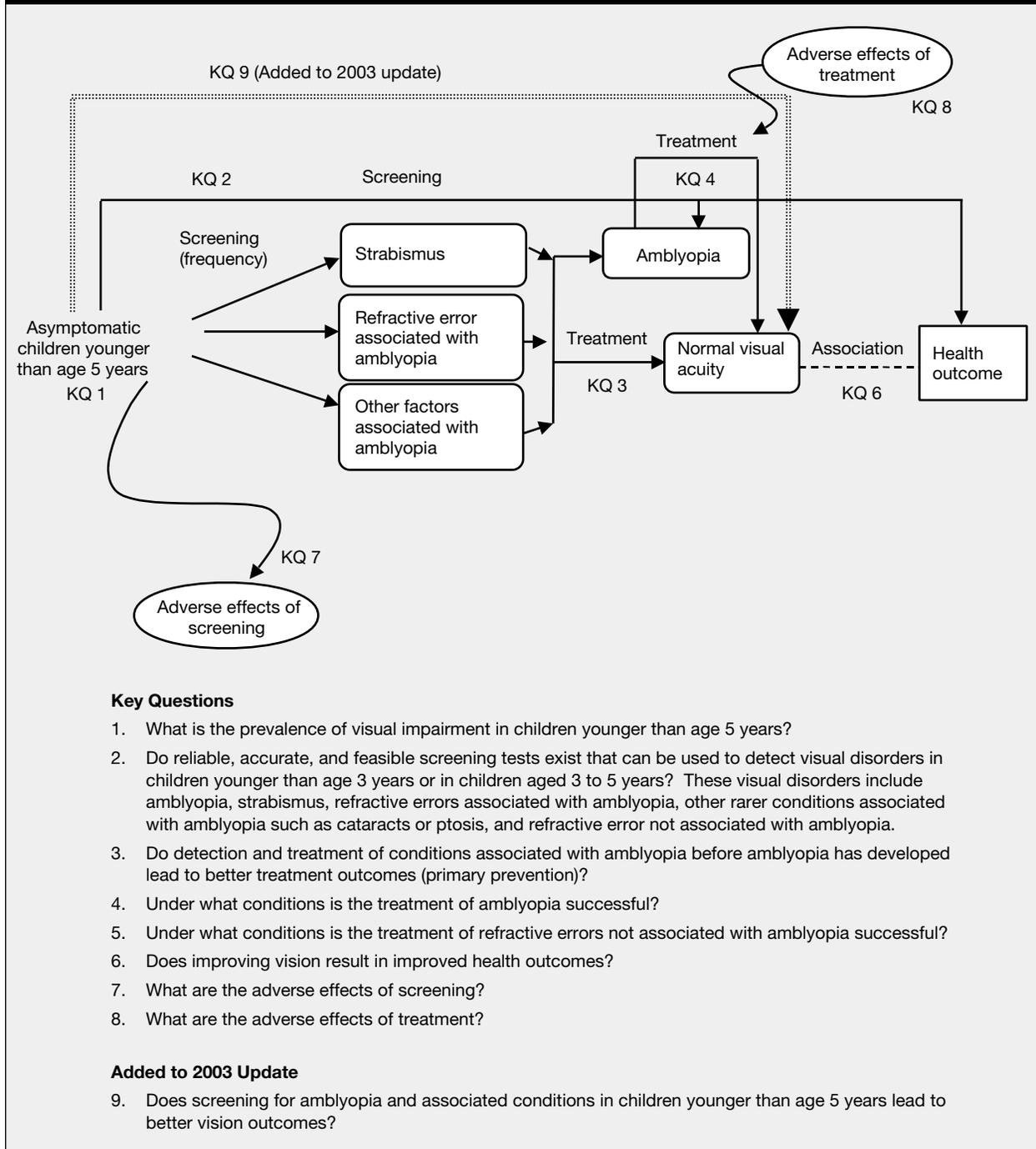
Captured titles and/or abstracts were downloaded and imported into the EndNote® program to create a vision screening update library. Titles and/or

Systematic Evidence Reviews serve as the basis for U.S. Preventive Services Task Force (USPSTF) recommendations on clinical prevention topics. The USPSTF tailors the scope of these reviews to each topic. The USPSTF determined that an update of the evidence was needed to assist in updating its 1996 recommendations on screening for visual impairment.¹

To assist the USPSTF, the Oregon Evidence-based Practice Center, under contract to the Agency for Healthcare Research and Quality (AHRQ), performed a targeted review of the literature published on this topic from 1999 to 2003. This update of the evidence and the updated recommendation statement² are available through the AHRQ Web site (www.preventiveservices.ahrq.gov) and in print through subscription to the *Guide to Clinical Preventive Services, Third Edition: Periodic Updates*. The subscription costs \$60 and can be ordered through the AHRQ Publications Clearinghouse (call 1-800-358-9295, or e-mail ahrqpubs@ahrq.gov). The recommendation is also posted on the Web site of the National Guideline Clearinghouse™ (www.guideline.gov).

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Figure 1. Screening for Amblyopia Analytic Framework and Key Questions (KQ)



abstracts were reviewed using specific inclusion and exclusion criteria (Appendix). Full text papers were retrieved for RCTs of screening for amblyopia that included children aged 5 years and younger, and included a follow-up assessment with appropriate

vision outcomes. Studies were excluded if they were not RCTs, did not include children aged 5 years or younger, or included only high-risk populations (ie, those with low birth weight). Eligibility criteria were reapplied to the full-text articles.

Data Abstraction

Information on the number and characteristics of participants, definition of amblyopia, screening tools and screening intervals, interventions, and results was abstracted from included studies.

Quality Rating

Criteria developed by the USPSTF were used to rate study quality (Appendix). Information on randomization, maintenance of comparable groups, attrition, and analysis was dually reviewed by research team members. Disagreements on quality ratings were discussed until consensus was reached. Studies rated as being of “good” or “fair” quality are mentioned in this update of the evidence.

Results

Two hundred fifty-four abstracts and titles were identified; 42 full-text articles were retrieved for additional review: 10 from suggestions of experts and professional organizations, 28 from the MEDLINE search, and 4 from the Cochrane searches. Of these papers, 2 fair-quality studies (1 trial, 2 publications) met inclusion criteria for screening for amblyopia in preschool children (Table 1). Although not the focus of this review, 6 additional studies assessed the sensitivity and specificity of preschool screening tools, and 3 compared treatment interventions for preschool amblyopia (RCT described in Table 2). Quality ratings for the studies described in this update of the evidence are in Table 3.

Screening

A recently published, nested RCT of screening was rated as being of fair quality by USPSTF criteria. From the Avon Longitudinal Study of Parents and Children (ALSPAC) based in southwest England, 3,490 children born during the last 6 months of the cohort study were randomized into an intensive, visual-screening group or control group.⁴ Children in the intensive group were invited to participate in screenings at a research clinic at 8, 12, 18, 25, 31, and 37 months of age. During the screenings, an orthoptist conducted an examination and a battery of tests appropriate to the age of the

child. Children in the control group were offered similar testing by an orthoptist at age 37 months only. All children received the usual recommended surveillance by their general practitioners and health visitors and were offered screening for reduced visual acuity by a school nurse at school entry (aged 4–5 years). Any child failing an acuity test or cover test was referred to the hospital eye service. All children were invited to a final vision assessment at age 7.5 years. Amblyopia was defined in 2 different ways (Table 1).

Amblyopia at age 7.5 years was less prevalent in the intensive screening group than in the control group (Amblyopia A: 1.45% vs 2.66%, $P = 0.06$; Amblyopia B: 0.63% vs 1.81%, $P = 0.02$). The cumulative incidence of amblyopia in each group was similar. Residual amblyopia was more likely in the control group (despite treatment) than in the intensive group. Mean visual acuities in the worse-seeing eye were better for children in the intensive group who had been treated for amblyopia than for treated children in the control group (0.15 vs 0.26 LogMAR units, $P < 0.001$). A higher proportion of children who were treated for amblyopia had been seen in the eye clinic before the age of 3 years in the intensive group than in the control group (48% vs 13%, $P = 0.0002$).

Earlier data from the ALSPAC study,⁵ rated to be of fair quality, evaluated the number of children from each group confirmed to have strabismus or amblyopia before the age of 37 months. Sensitivities of individual tests within the intervention program were also evaluated. The intensive screening group detected more children with amblyopia than the control group (1.6% vs 0.5%, $P < 0.01$). Screening in the intensive group was more specific than in the control group (4.5% false-positive results vs 7.5%, $P < 0.01$). The cover test and visual acuity test were always more than 99% specific, but had poor sensitivity until age 37 months. Before age 37 months, photorefractive was found to be more sensitive than acuity testing. The cover test, with either photorefractive or acuity testing at 37 months, provided the best sensitivity and specificity (82%–84% sensitivity; 97%–98% specificity; 63%–73% positive predictive value [PPV]; 99% negative predictive value [NPV]).

Table 1. RCTs of Amblyopia Screening in Children Younger than Age 5 Years Published Since 1999

Author, Year	N	Population	Setting	Exclusions	Definitions of Amblyopia
Williams et al, 2002 ⁴	3,490	Newborns and their mothers; nested RCT in ALSPAC; trial included children born during the last 6 mos of the study period	Southwest England	Born during the first 15 mos of cohort study; parents declined, sibling already in study	Amblyopia A: interocular difference in acuity ≥ 0.2 LogMAR; Amblyopia B: visual acuity in amblyopic eye worse than 0.3 LogMAR

ALSPAC, Avon Longitudinal Study of Parents and Children; CI, confidence interval; GP, general practitioner; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value; RCT, randomized controlled trial.

Treatment

The Amblyopia Treatment Study (ATS), rated to be of good quality, is an RCT that evaluated patching versus atropine treatment in 409 children aged 3 to 7 years with moderate amblyopia.⁶ Children were recruited from community- and university-based practices throughout North America. Visual acuity testing was conducted using an ATS protocol administered by a study-certified tester. Seven days later, children were randomly assigned to patching or atropine treatment. Patching treatment included wearing a patch for 6 hours a

day. Atropine treatment used atropine sulfate 1%, 1 drop per day. Adjustments in treatment were made based on patient responses and study criteria. Follow-up visits occurred at 5, 16, and 26 weeks (primary outcome).

In both the patching and the atropine group, visual acuity in the amblyopic eye significantly improved from baseline to 6 months. In the patching group, the mean change in visual acuity was 3.16 lines (95% confidence interval [CI], 2.95–3.37). In the atropine group, the mean change in visual acuity was 2.84 lines (95% CI, 2.61–3.07).

Table 1. RCTs of Amblyopia Screening in Children Younger than Age 5 Years Published Since 1999 (cont)

Intervention	Outcomes	Results	Study Quality
Intensive orthoptic screening in 2,029 (8, 12, 18, 25, 31, 37 mos) vs control screening in 1,490 (usual care and 1 orthopic exam at 37 mos); all screenings: cover test and non-cycloplegic autoretraction; 8, 12 mos: Cardiff Cards; 18, 25, 31 mos: Cardiff Cards and Kays Picture test; 37 mos: Kays Picture (enhanced) and HOTV letters; any child failing acuity or cover tests were referred to hospital eye service; referrals were not made based on autoretraction testing until 37 mos	All children assessed at 7.5 yrs with LogMAR; outcomes include prevalence of amblyopia and visual acuity in worse eye after treatment	<p>Amblyopia at 7.5 yrs was less prevalent in intensive screening group than control group; Amblyopia A: 1.45% intensive vs 2.66% control ($P = 0.06$); Amblyopia B: 0.63% intensive vs 1.81% control ($P = 0.02$)</p> <p>Cumulative incidence of amblyopia in each group was similar; residual amblyopia was more likely despite treatment in control (10/40) than intensive group (3/40); Amblyopia A: OR = 1.56 (95% CI, 0.6–3.92); Amblyopia B: OR = 4.11 (1.04–16.29)</p> <p>Mean visual acuities in the worse seeing-eye were better for children who had been treated for amblyopia in the intensive group than for similar children in the control group (0.15 vs 0.26 LogMAR units; $P < 0.001$)</p> <p>Higher proportion of the children who were treated for amblyopia had been seen in the eye clinic before 3 yrs of age in the intensive group than in the control group (48% vs 13%, $P = 0.0002$)</p>	<p>Fair</p> <p>Almost half did not have the 7.5 yr follow-up examination in both the intensive and usual care groups; completers differed from non-completers; not known if completers in intensive group differed from those in usual care group</p>

continue

The mean treatment group difference in 6-month LogMAR acuity was 0.034 (95% CI, 0.005–0.064). Seventy-nine percent of the patching group and 74% of the atropine group met the criteria for treatment success (95% CI for differences in percentages, –4% to 13%).

At 6 months, visual acuity in the sound eye was decreased from baseline by 1 line in 7% of the patching group and in 15% of the atropine group. Visual acuity was decreased by 2 or more lines in 1% of the patching group and in 9% of the atropine group ($P < 0.001$). Both treatments were

well-tolerated. Atropine had a slightly higher degree of acceptability, as indicated by a parental questionnaire, and better adherence than patching.

Conclusions

Important RCTs have been published about screening for amblyopia in children since the literature review represented in the 2001 summary of evidence considered by the USPSTF. These studies, summarized in Table 4, specifically fill evidence gaps outlined by the USPSTF.

Table 1. RCTs of Amblyopia Screening in Children Younger than Age 5 Years Published Since 1999 (cont)

Author, Year	N	Population	Setting	Exclusions	Definitions of Amblyopia
Williams et al, 2001 ⁵	3,490	Children born in the last 6 mos of the ALSPAC study	Southwest England	Born during the first 15 mos of cohort study; parents declined, sibling already in study	Interocular difference of 0.01 LogMAR units or equivalent using a recognition test with full spectacle correction

References

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(Available on the AHRQ Web site at: www.ahrq.gov/clinic/serfiles.htm.)

Table 1. RCTs of Amblyopia Screening in Children Younger than Age 5 Years Published Since 1999 (cont)

Intervention	Outcomes	Results	Study Quality
<p>Control group (n = 1,461): usual care by GPs or nurses (questions on family history, observation of visual behavior, cover test) at 8 and 18 mos, orthoptic exam at 37 mos</p> <p>Intervention group (n = 2,029): usual care and orthoptic testing at 8, 12, 18, 25, 31, 37 mos; for visual acuity: observing behavior when either eye occluded (all screenings); Cardiff Cards (8,12, 18, 25, 31 mos); Kays Picture test (25, 31 mos); for ocular alignment: cover test (all screenings); for stereopsis: Lang tests 1 & 2 (18, 25, 31 mos); Frisby test: (12, 18, 25, 31 mos); for motor fusion: 20 Dioptre base-out test (all screenings); non-cycloplegic photorefraction: (all screenings); referrals based on testing criteria</p>	<p>Number of children from each group referred to the Eye Hospital and diagnosed with strabismus or amblyopia before 37 mos</p> <p>Sensitivities of program estimated by final orthoptic assessment at 37 mos</p>	<p>Intensive group yielded more children with amblyopia (1.6% vs 0.5%, $P < 0.01$) and was more specific than the control group (4.5% false positives vs 7.5% for controls, $P < 0.01$); cover test with either photorefraction or acuity testing at 37 mos provided the best sensitivity and specificity: 82%–84% sensitivity, 97%–98% specificity, 63%–73% PPV, 99% NPV</p>	<p>Fair</p>

Table 2. RCTs of Amblyopia Treatment in Children Younger than Age 5 Years Published Since 1999

Author, Year	N	Population	Setting	Exclusions	Definitions of Amblyopia
Pediatric Eye Disease Group, 2002 ⁶	409	Children aged 3–7 yrs with moderate amblyopia	47 clinical sites in North America	Ocular cause for visual acuity; prior intraocular surgery; myopia in either eye; Down Syndrome; known skin reaction to patch or bandage adhesive, or allergy to atropine or other cycloplegics; more than 2 mos of amblyopia therapy in the past 2 yrs; aged 7 yrs or older; not able to measure visual acuity with Amblyopia Treatment Study visual acuity testing protocol; refractive error not corrected for at least 4 wks; does not meet study criteria for amblyopia associated with strabismus, refractive error/anisometropia, or both	Amblyopia associated with strabismus, refractive error/anisometropia, or both; visual acuity in the amblyopic eye \leq 20/40 or \geq 20/100; visual acuity in the sound eye \geq 20/40; intereye acuity difference \geq 3 LogMAR lines

CI, confidence interval; RCT, randomized controlled trial.

Table 2. RCTs of Amblyopia Treatment in Children Younger than Age 5 Years Published Since 1999 (cont)

Intervention	Outcomes	Results	Study Quality
<p>Visual acuity testing protocol 7 days prior to randomization to patch for 6 hrs/day or atropine sulfate 1% 1 drop/day; adjustments in treatment based on patient responses and study criteria; follow-up visits at 5, 16, 26 wks (primary outcome) with additional follow-up at 18 mos, with at least 1 visit every 6 mos</p>	<p>Visual acuity score in LogMAR units in the amblyopic and sound eye after 6 mos of treatment; successful treatment defined by amblyopic eye's visual acuity 20/30 or better or improvement of 3 or more lines from baseline; also evaluated effect of treatment on child and parent by questionnaire, adherence to treatment, and adverse reactions</p>	<p>Improved visual acuity in the amblyopic eye in both the patching and atropine groups: patching group mean change in visual acuity was 3.16 lines (95% CI, 2.95–3.37); atropine group mean change in visual acuity was 2.84 lines (95% CI, 2.61–3.07); improvement occurred faster in the patch group; mean treatment group difference in 6 mos LogMAR acuity was 0.034 (95% CI, 0.005–0.064); 79% of patching group and 74% of atropine group met criteria for treatment success (95% CI for differences in percentages, –4% to 13%); at 6 mos, visual acuity in the sound eye was decreased from baseline by 1 line in 14 patients (7%) in patching group; 30 patients (15%) in atropine group; and by 2 or more lines in 3 patients (1%) and 17 patients (9%), respectively ($P < 0.001$); this difference did not persist with further follow-up; both treatments were well tolerated; atropine had a slightly higher degree of acceptability on a parental questionnaire and better adherence than patching</p>	<p>Good</p>

Table 3. Quality Rating Scores

Author, Year	Comparable Groups Assembled (Adequate Randomization, Allocation Concealment, or Distribution of Confounders)?	Maintenance of Comparable Groups (Attrition, Crossovers, Adherence, Contamination)?	Important Loss to Follow-up (Differential, Overall)?
Williams et al, 2002 ⁴	Yes/no; pseudo-random (last digit in day of mother's date of birth) Orthoptists had no knowledge of what group the children were in, rules of allocation, or children's screening history	Not known; completers more likely to have educated mothers, not teenaged mothers, live in owner-occupied residence, breast-fed for at least 3 mos, family history of strabismus or sight problems, weighed > 2,500 grams ($P < 0.001$); not known how comparable between groups	Yes; 1,088/2,029: 54% of intensive screening group completed study, 826/1,490: 55% of control group completed study
Williams et al, 2001 ⁵	Yes/no; pseudo-random (last digit in day of mother's date of birth) Orthoptists had no knowledge of what group the children were in, rules of allocation, or children's screening history	Intensive group slightly less affluent than controls; attendees more affluent than non-attendees in each group	Yes; 54% of intensive group and 64% of control group attended the final assessment at 37 mos; 31% of intensive group and 35% of control group never attended an assessment
Pediatric Eye Disease Group, 2002 ⁶	Yes; permuted-block design	Yes	No; 97% follow-up patch; 98% atropine

Table 3. Quality Rating Scores (cont)

Measures Equal, Reliable, Valid, Including Masking of Outcomes?	Clear Definition of Interventions?	Important Outcomes Considered?	Intention-to-Treat Analysis (or Adjustment for Potential Confounders)?	Quality Rating
Yes	Yes	Yes	Yes	Fair
Yes	Yes	Yes	Yes	Fair
Yes Primary visual acuity outcome measure was masked in 97% of cases	Yes	Yes	Yes	Good

Table 4. Summary Table of Targeted Review of RCTs Addressing Screening and Treatment for Visual Impairment in Children Younger than Age 5 Years

Issue	Previous Assessment	Current Update
Is treatment for amblyopia effective?	Most children in treatment show improvement, although the literature is poor. There have not been RCTs looking at efficacy of different forms of treatment.	The Amblyopia Treatment Study, a good-quality head-to-head comparison RCT, indicated that 79% of children with moderate amblyopia treated with patching and 74% treated with atropine achieved visual improvement meeting criteria for treatment success. Treatment was well-tolerated and acceptable, and adherence was good.
Do formal screening programs identify cases earlier than they would come to clinical diagnosis?	No direct studies on this, but screening programs have substantial yields of previously undiagnosed cases.	A fair-quality nested RCT comparing intensive screening with usual care in the UK indicated higher detection rates and fewer false-positive rates among children aged 0 to 3 years in the intensive screening group.
Does early treatment improve outcomes?	Animal data indicates sensitive period and case series provides conflicting information.	Long-term follow-up of children in the nested RCT, comparing intensive screening with usual care and 1-time orthopic screening at age 37 months, in the UK, indicated improved treatment outcomes for those in the intensive group; this group received treatment at earlier ages.

Appendix

Search Strategy

Database: MEDLINE®

Dates: 1999–April 2003

- 1 exp AMBLYOPIA/ (584)
- 2 limit 1 to (human and English language and yr=1999–2003) (286)
- 3 limit 2 to (all infant <birth to 23 months> or preschool child <2 to 5 years>) (169)
- 4 limit 3 to (clinical trial or meta analysis or practice guideline or randomized controlled trial or review) (34)
- 5 limit 1 to (human and abstracts) (446)
- 6 limit 5 to (all infant <birth to 23 months> or preschool child <2 to 5 years>) (257)
- 7 6 not 3 (118)
- 8 from 3 keep 1–169 (169)
- 1 vision tests/ or vision screening/ or exp Vision Disorders/di (2888)
- 2 limit 1 to (human and English language and (all infant <birth to 23 months> or preschool

- child <2 to 5 years>) and yr=1999–2003) (281)
- 3 limit 2 to (clinical trial or meta analysis or practice guideline or randomized controlled trial or review) (53)
- 4 “Sensitivity and Specificity”/ (70623)
- 5 exp “Outcome Assessment (Health Care)”/ (139719)
- 6 2 and (4 or 5) (51)
- 7 3 or 6 (96)
- 8 from 7 keep 1–96 (96)

Database: Cochrane Library

–Controlled clinical trial registry (CCTR)

–Systematic reviews (CDSR)

Yrs: 1999–2003

Key Words: “Amblyopia” and “Preschool”

Inclusion and Exclusion Criteria for Abstracts About Screening

INCLUDE:

- 1 Amblyopia/Preschool (lazy eye and other terms may apply)

EXCLUSIONS:

- 2 Not an RCT
- 3 Surgery study
- 4 Treatment study

- 5 Not our Scope/Not amblyopia
- 6 Not Ages 0–5
- 7 High risk population
- 8 Screening test other than for amblyopia
- 9 Animal study
- 10 Non-English abstract
- 11 Other

Appendix

Criteria for Grading the Internal Validity of Individual Studies*

Randomized Controlled Trials (RCTs) and Cohort Studies

Criteria:

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

Definition of ratings based on above criteria:

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

considered; and appropriate attention to confounders in analysis. In addition, for RCTs, intention-to-treat analysis is used.

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

Poor: Studies will be graded “poor” if any of the following fatal flaws 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. For RCTs, intention-to-treat analysis is lacking.

In general, a “good” study is one that meets all criteria well. A “fair” study is one that does not meet (or it is not clear that it meets) at least 1 criterion but has no known fatal flaw. “Poor” studies have at least 1 fatal flaw.

*Harris RP, Helfand M, Woolf SH, et al. Current methods of the U.S. Preventive Services Task Force: a review of the process. *Am J Prev Med.* 2001;20:21–35.

Definitions

Amblyopia

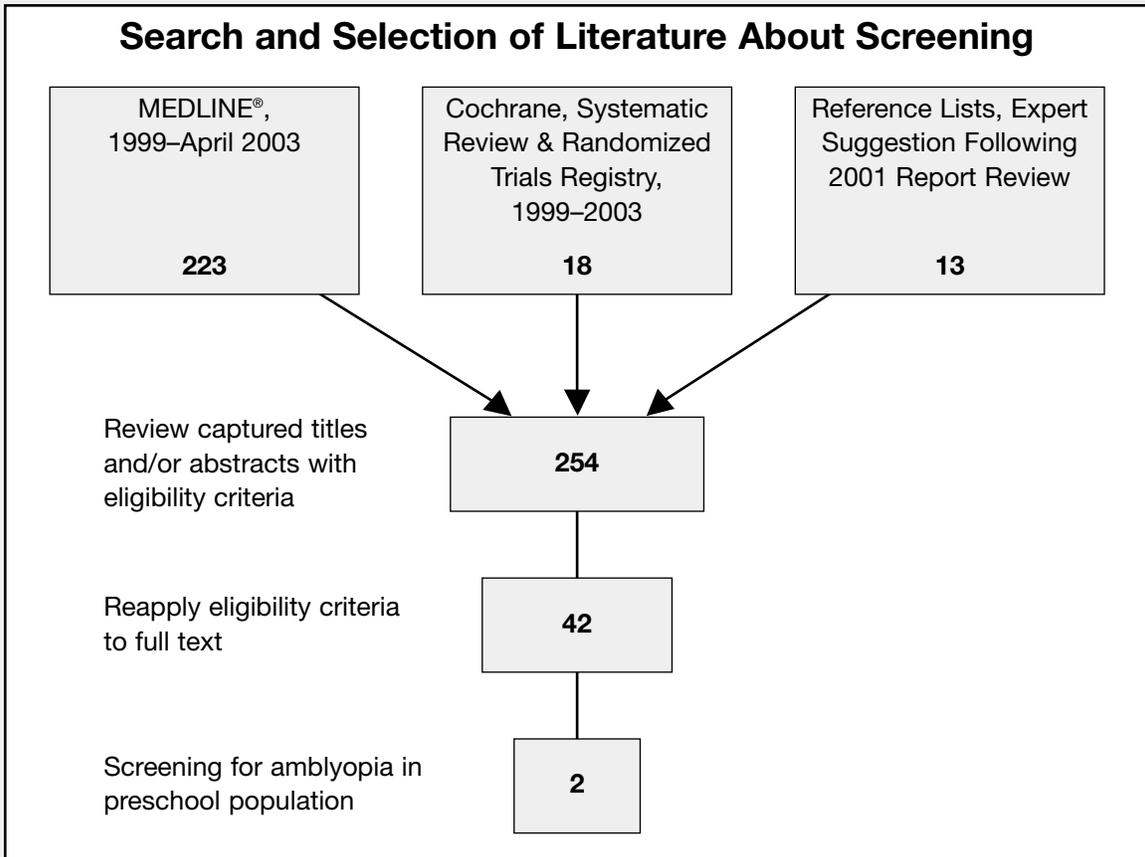
- Functional amblyopia: difference of 2 or more Snellen lines between the 2 eyes.¹
- More than 1 line difference between the 2 eyes.²

- Reduced visual acuity that is not instantly alleviated by wearing spectacles, in an otherwise apparently healthy eye.³
- Amblyopia A: difference in acuity between the 2 eyes is 2 or more lines on the chart (0.2 LogMAR).

Appendix

- Amblyopia B: visual acuity in the amblyopic eye is worse than 0.3 LogMAR.
 - Reduced visual acuity in 1 or both eyes due to abnormal binocular interaction.⁴
 - Impairment of vision without detectable organic lesion of the eye.⁵ Types: alcoholic, arsenic, nutritional deficiency, color, nocturnal, quinine, reflex, strabismic (resulting from suppression of vision in 1 eye to avoid diplopia, tobacco, toxic, traumatic, uremic).
 - A condition of reduced Snellen acuity for which there is no evidence of an organic cause. This clinical definition is restricted to 1 kind of visual loss, which is recognition acuity for high-contrast targets. Psychophysicists suggested a more useful definition of amblyopia as “a developmental anomaly involving primarily those cortical mechanisms involved in form and shape perception.”⁶
 - Reduced acuity in 1 or both eyes without any clear ocular lesion.⁷
 - A form of defective central visual processing, manifested as decreased visual acuity in 1 eye.⁸
- Squint**
- Strabismus.⁵
- Strabismus**
- Deviation of the eye that the patient cannot overcome. The visual axes assume a position relative to each other different than that required by the physiological conditions. The various forms of strabismus are spoken of as tropias, their direction being indicated by the appropriate prefix, as cyclotropia, esotropia (cross-eyed), exotropia, hypertropia, and hypotropia.
 - The most common cause of amblyopia.⁹

Search and Selection of Literature About Screening



Appendix

References

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