

APPENDIX 1. Medline and Embase Search

Index test: (1)

Vision Tests[Mesh:noexp] OR Diagnostic Techniques, Ophthalmological[MAJR:noexp] OR ((Refraction, Ocular[MAJR] OR Visual Acuity[MAJR]) AND (exam*[tw] OR test[tw] OR tests[tw] OR assessment*[tw]))

Index screening: (2)

Vision Screening[Mesh] OR ((screening[tw] OR Mass Screening[Mesh]) AND (eye[tw] OR vision[tw] OR ocular[tw] OR visual[tw] OR ophthalmic[tw]))

Target condition: (3)

Amblyopia[Mesh] OR amblyopia[tw] OR Strabismus[Mesh] OR strabismus[tw] OR Refractive Errors[Mesh] OR refractive-error*[tw] OR refractive-disorder*[tw] OR lazy-eye*[tw] OR squint[tw] OR cross-eye*[tw] OR astigmatism[tw] OR presbyopia[tw] OR myopia[tw] OR hyperopia[tw] OR anisometropia[tw] OR ocular-alignment[tw] OR Vision Disorders/diagnosis[MAJR:noexp] OR Eye Diseases/diagnosis[MAJR:noexp]

Context applicable keywords: (4)

Evidence-Based Practice[Mesh] OR evidence-based[tw] OR Early Diagnosis[Mesh:noexp] OR early-diagnosis[tw] OR early-diagnostic[tw] OR undetected[tw] OR uncorrected[tw] OR visual-impairment[tw] OR “Referral and Consultation”[Mesh] OR Early Medical Intervention[Mesh] OR Risk Factors[Mesh] OR Age of Onset[Mesh] OR Time Factors[Mesh] OR Advisory Committees[Mesh] OR guideline[pt] OR practice-guideline[pt] OR “Consensus Development Conference”[pt] OR guideline*[tw] OR consensus[tw] OR recommendation*[tw] OR Ophthalmology[Mesh:noexp] OR Optometry[Mesh:noexp] OR optometrist*[tw] OR ophthalmologist*[tw] OR pediatrician[tw] OR paediatrician[tw] OR Primary Health Care[Mesh] OR ((comprehensive[tw] OR routine[tw] OR periodic[tw] OR population-based[tw] OR whole-population[tw] OR universal[tw] OR gold-standard[tw] OR Asymptomatic Diseases[Mesh] OR asymptomatic[tw] OR schedule[tw]) AND (eye[tw] OR vision[tw] OR ocular[tw] OR visual[tw] OR ophthalmic[tw]))

Target age group: (5)

Child, Preschool[Mesh] OR Infant[Mesh] OR preschool[tw] OR pre-school[tw] OR kindergarten[tw] OR kindergarden[tw] OR Pediatrics[Mesh] OR pediatric*[tw] OR paediatric*[tw] OR children[tw]

Limits: (6)

(English[lang] OR French[lang]) AND ("1995/01/01"[PDAT] : "3000/12/31"[PDAT])

Final Medline search

(1 OR 2) AND (3 OR 4) AND 5 AND 6

The Embase Search was the same as the Medline search, but without the Mesh terms and excluding Medline records.

APPENDIX 2. Literature search strategy: Inclusion and exclusion criteria

Inclusion criteria: Studies of children with interventions completed from 0 to 5 years of age; well-conducted clinical trials and observational studies; studies of amblyopia, amblyogenic risk factors, and refractive error; research articles published in peer-reviewed journals written in English or French; studies performed in primary care and population-based settings; studies of screening tests typically available in primary care settings (e.g. visual acuity tests, red reflex, and cover test) or examination techniques used by optometrists and ophthalmologists (e.g. retinoscopy, etc.); studies with the following outcomes: improved visual acuity, reduced amblyopia, improved school performance, and quality of life.

Exclusion criteria: Studies in children aged ≥ 6 years ; articles on ocular complications of other diseases (e.g. diabetes); articles on subsets of patients with known ocular diseases (e.g. diabetes, glaucoma, retinopathy of prematurity, age-related macular degeneration); articles not focused on visual outcomes; articles evaluating the utility or cost-effectiveness of a particular screening digital or instrument-based tool (e.g. teleophthalmology, hand-held screening devices, digital screening devices, Retinomax autorefractor); articles evaluating screening programs (e.g. school-based, long-term care institution-based); articles addressing treatment or patient adherence to treatment; articles from countries with a significantly different ethnic composition and/or healthcare system than Canada's; articles describing existing programs; articles describing jurisdictional policies; opinion pieces or editorials; chart reviews; articles in languages other than French or English; articles on vision loss prevention; articles directed toward school nurses or orthoptists; policy papers; articles on healthcare resource or manpower issues; articles on uptake of guideline recommendations; articles on focus group or survey data; and articles considered to be outdated.

APPENDIX 3. Criteria for assigning grade of evidence (based on GRADE guidelines)¹⁷

Types of evidence	<ul style="list-style-type: none"> • Randomized trial = high • Observational study = low • Any other evidence = very low
Decrease* grade if...	<ul style="list-style-type: none"> • Serious or very serious limitation to study quality • Important inconsistency • Some or major uncertainty about directness • Imprecise or sparse data • High probability of reporting bias
Increase grade if...	<ul style="list-style-type: none"> • Strong evidence of association – significant relative risk of >2 (<0.5) based on consistent evidence from two or more observational studies, with no plausible confounders (+1) • Very strong evidence of association – significant relative risk of >5 (<0.2) based on direct evidence with no major threats to validity (+2) • Evidence of a dose response gradient (+1) • All plausible confounders would have reduced the effect (+1)
Range	<ul style="list-style-type: none"> • High-quality evidence • Moderate-quality evidence • Low-quality evidence • Very low-quality evidence

* Each quality criteria can reduce the quality by 1 or, if very serious, by 2 levels.

APPENDIX 4. Grading of recommendations according to the strength of the recommendation (1–2) with implications, and the quality of the evidence (confidence in estimate of effect, A–C); based on GRADE Guidelines^{18,19}

Grade of recommendation (Implication)	Estimate of Effect	Evidence Quality
1A: Strong recommendation, high-quality evidence (Applies to most patients)	Very strong evidence of significant relative risk.	Evidence from >1 well-performed RCT, or overwhelming evidence in some other form. Further research is unlikely to change confidence in the estimates of effect.
1B: Strong recommendation, moderate-quality evidence (Applies to most patients)	Strong evidence of significant relative risk.	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, or imprecision), or very strong evidence of some other research design. Further research (if performed) may change the estimate of effect.
1C: Strong recommendation, low-quality evidence (Applies to most patients)	Benefits appear to outweigh risks and burdens, or vice versa.	Evidence from observational studies, unsystematic clinical experience, or RCTs with serious flaws. Further research is likely to change the estimate of effect.
2A: Weak recommendation, high-quality evidence (Does not apply to all patients)	Benefits closely balanced with risks and burdens.	Evidence from >1 well-performed RCT, or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of effect.
2B: Weak recommendation, moderate-quality evidence (Alternative approaches may be better)	Benefits closely balanced with risk and burdens, with some uncertainty in the estimates of benefits, risk and burdens.	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, or imprecision), or very strong evidence of some other research design. Further research (if performed) may change the estimate of effect.
2C: Weak recommendation, low-quality evidence (Alternative approaches may be better)	Uncertainty in the estimates of benefits, risks and burdens; benefits may be closely balanced with risks and burdens.	Evidence from observational studies, unsystematic clinical experience, or RCTs with serious flaws. Further research is likely to change the estimate of effect.

RCT = randomized controlled trial

APPENDIX 5. Summary of findings: Ages and intervals for ocular assessment and visual outcomes

OUTCOME: PREVALENCE OF AMBLYOPIA						
Reference (Study design)	Number of participants Age at screening	Prevalence (screened)	Prevalence (unscreened or control)	Relative effect	Overall study rating (GRADE)	Comments
De Koning HJ, et al. Effectiveness of screening for amblyopia and other eye disorders in a prospective birth cohort study. <i>J Med Screen</i> 2013;20:66–72. (Prospective cohort)	2964 of the original RAMSES cohort (4624) attended final examination at 7 years. Multiple screenings available from 1–72 months (preverbal and preschool) Final outcome assessed at 7 years	Severe amblyopia (VA >0.3 LogMAR): 0.7 to 1.2% at 7 years	Amblyopia: 2.0 to 3.9% (not measured in study, but reported from non-screened situations)	Not estimable	Moderate	<ul style="list-style-type: none"> No control group Study shows a dose-response effect in that children who attended more screenings had lower rates of amblyopia at 7 years
Groenewoud JH, et al. Rotterdam Amblyopia Screening Effectiveness Study: detection and causes of amblyopia in a large birth cohort. <i>Invest Ophthalmol Vis Sci</i> 2010;51:3476–84. (Same prospective cohort as De Koning et al above)	Same as above In this study, preschool screening from age 3 contributed most to amblyopia detection.	Amblyopia (interocular acuity difference >2 LogMAR): 100/2964 (3.4%) cumulative incidence from birth to 7 years		Not estimable	Low	<ul style="list-style-type: none"> No control group Of 100 amblyopia cases, 83 detected before age 7 56/83 referred due to screening, 26/83 self-referred Refractive error was most common cause of amblyopia
Eibschitz-Tsimhoni M, et al. Early screening for amblyogenic risk factors lowers the	808 in screened cohort and 782 in control cohort (no screening).	Severe amblyopia (BCVA ≤20/60): 0.1%	Severe amblyopia: 1.7 %	Amblyopia was 2.6 times more likely to be present in	Moderate	<ul style="list-style-type: none"> Children who were screened had less amblyopia and the amblyopia that was

prevalence and severity of amblyopia. <i>J AAPOS</i> 2000;4:194–99. (Prospective cohort)	Participants were screened at 1–2.5 years of age. Final outcome assessed for screened and not screened cohorts at 8 years of age.	Amblyopia: 1.0%	Amblyopia: 2.6%	cohort that was not screened		present was much less severe
Sloot F, et al. Effect of omission of population-based eye screening at age 6–9 months in the Netherlands. <i>Acta Ophthalmol</i> 2015;93:318–21. (Prospective cohort)	Screened cohort: 6059 children screened at 1–2 months, 3–4 months, and 6–9 months. Unscreened cohort: 5842 children were examined only if observed eye problem or positive family history.	Amblyopia: 10/6059 (0.17%)	Amblyopia: 6/5482 (0.11%)		Low	<ul style="list-style-type: none"> • The rate of referral to orthoptist or ophthalmologist was similar between the cohorts (58/6059 or 0.96% children screened, 48/5482 or 0.88% children unscreened) • Referrals were mostly due to observed strabismus
Williams C, et al. Amblyopia treatment outcomes after screening before or at age 3 years: follow-up from randomised trial. <i>BMJ</i> 2002;324: 1549. (RCT in nested cohort)	Children estimated to be born from 1991 to 1992 who were residents of Avon, England (ALSPAC). Two groups: Intensive early orthoptic screening (n = 2029) at 8,12,18, 25, 31 and 37 months of age vs. control group (n	Severe amblyopia (VA in amblyopic eye worse than 0.3 LogMAR): 7/1088 (0.63%) Amblyopia (interocular difference in acuity ≥ 0.2 LogMAR): 16/1088* (1.45%)	Severe amblyopia: 15/826 (1.81%) Amblyopia: 22/826 (2.66%)	Amblyopia was 1.8 times more likely to be present in control group	Moderate	<ul style="list-style-type: none"> • *Only 55% of the initial intensive group and 54% of the control group attended the final assessment

	= 1490) screened at 37 months. Prevalence of amblyopia determined at 7.5 years of age.					
Williams C, et al. Amblyopia treatment outcomes after preschool screening v school entry screening: observational data from a prospective cohort study. <i>Br J Ophthalmol</i> 2003;87:988–93. (Prospective cohort)	Part of Avon longitudinal study; ~14,000 children born from 1991 to 1992 were recruited (85% of those eligible). Children were screened at 4-5 years and examined at 7.5 years. Results reported for 6125 children, those not included in the previous study.	Amblyopia (interocular difference in best acuity ≥ 0.2 LogMAR): 11/1019 (1.1%) VA in worse eye >0.3 LogMAR ($<6/12$): 7/1019 (0.7%) VA in worse eye >0.18 LogMAR ($<6/9$): 19/1019 (1.9%) (Data from Table 2 of paper)	Amblyopia: 100/5062 (2.0%) VA in worse eye >0.3 LogMAR ($<6/12$): 65/5062 (1.3%) >0.18 LogMAR ($<6/9$): 171/5062 (3.4%)	Adjusted odds ratio (95% CI) Amblyopia: 0.63 (0.32 to 1.23) VA in worse eye >0.3 LogMAR ($<6/12$): 0.72 (0.22 to 1.60) >0.18 LogMAR ($<6/9$): 0.65 (0.38 to 1.10)	Moderate	<ul style="list-style-type: none"> Well-designed and analyzed cohort study that is of direct relevance to the study question
Zaba JH, et al. Comparing the effectiveness of vision screenings as part of the school entrance physical examination to comprehensive vision examinations in children ages 3 to	Exploratory study in Kentucky: survey-based reports on 1,469 entrance vision examinations performed for school-aged children (3–6 years).	Prevalence of any vision problem: 300/1386 (21.6%) 63 had amblyopia (other visual diagnoses were not identified)			Very low	<ul style="list-style-type: none"> No description of screening program Sent surveys to 466 eye care professionals, but only got responses from 37 (low sample size) Surveys were completed by the doctor, the doctor’s assistant, or the parents. Self-reported

<p>6: An exploratory study. <i>Optometry</i> 2007;78:514–22.⁷⁰</p> <p>(Cross-sectional)</p>						<p>data are susceptible to recall bias</p>
<p>OUTCOME: PREVALENCE OF AMBLYOPIA AND RISK FACTORS</p>						
<p>Atkinson J, et al. Infant hyperopia: detection, distribution, changes and correlates—outcomes from the Cambridge Infant Screening Programs. <i>Optom Vis Sci</i> 2007;84:84–96.</p> <p>(Prospective cohort)</p>	<p>Two population screening programs in England:</p> <p>First program: 3166 infants initially screened at 7–8 months (74% of children born 1981–1983). Follow-up between 1–3 years and VA testing at 4 years of age.</p> <p>Second program: 5142 infants screened at 8 months (76% of children born 1992–1994) and then up to 11 follow-up visits by 7 years of age.</p>	<p>First program (hyperopic infants (without spectacle wear) at 4 years of age: Prevalence of strabismus: 21%</p> <p>Prevalence of amblyopia: 68%</p> <p>Those who wore spectacles had decreased prevalence of strabismus (6.3%) and amblyopia (28.6%)</p> <p>Second program (hyperopic children (without spectacle wear) at 7 years of age:</p>	<p>First program emmetropic control group: Prevalence of strabismus: 1.6%</p> <p>Prevalence of amblyopia: 11.1%</p> <p>Second program emmetropic control group:</p>		<p>Low</p>	<ul style="list-style-type: none"> • Little to no description of the control groups in either screening program • 4 to 5.5% of 6- to 9-month old infants had 3.5D of hyperopia of more in both cohorts • Spectacle correction did not affect emmetropization to 3.5 years

		<p>Prevalence of strabismus: 17%.</p> <p>Prevalence of amblyopia: 68%</p> <p>Those who wore spectacles had decreased prevalence of amblyopia (17.1%), but no change in strabismus.</p>	<p>Prevalence of strabismus: 0.5%</p> <p>Prevalence of amblyopia: 0.5%</p>			
<p>Donahue SP. Relationship between anisometropia, patient age, and the development of amblyopia. <i>J Ophthalmol</i> 2006;142:132–40.</p> <p>(Cross-sectional)</p>	<p>5548 of 119,311 (4.65%) Tennessee children (aged 1-6 years) were referred for full eye examinations after positive result from state-wide preschool photoscreening program (performed by volunteers).</p> <p>4140/5548 (74.7%) were examined by either an optometrist or ophthalmologist.</p>	<p>Anisometropia (refractive error >1.0 diopter): 792/4140 (19.13%) with no co-existing strabismus.</p> <p>Prevalence of amblyopia in those with anisometropia: 454/724 (62.7%)</p> <p>By age 3, nearly 2/3 of children with >1.0 diopter anisometropia had developed amblyopia (at least 2-line decrease in acuity).</p> <p>Prevalence of amblyopia increased with age</p>			Low	<ul style="list-style-type: none"> • Potential selection bias – children who attended screenings were volunteers (no information on % of eligible children were screened) • No comparison group – only children who failed the screening were referred for a full eye examination • Many children had missing data and were excluded from the final report

		among anisometropic children				
Irving EL. Value of routine eye examinations in asymptomatic patients. <i>Optom Vis Sci</i> 2016;93(7):660–66. (Cross-sectional)	Asymptomatic patients (N = 2656) presenting for regular eye examinations at the University of Waterloo Optometry Clinic from 2007–2008. 0.4 to 93.9 years (median 38.5 years).	Spectacle prescription changes: 1078/2656 (41%) Change in ocular status/care: 1535/2656 (58%) Significant change in ocular status/care was associated with increasing age and assessment interval.			Low	<ul style="list-style-type: none"> Clinical population not representative of general population, only of those seeking care
Pai AS, et al. Amblyopia prevalence and risk factors in Australian preschool children. <i>Ophthalmology</i> . 2012;119:138–44. (Cross-sectional)	Based on Sydney Paediatric Eye Disease Study (2007 to 2009), door to door census. 2461 children between 6 and 72 months at time of recruitment. Results reported for 1422 children, 1039 children excluded due to low VA testability.	Prevalence of amblyopia: 27/1422 (1.9%) Mean spherical equivalent for the amblyopic eyes was +3.57 diopters.		Amblyopia was significantly associated with: <ul style="list-style-type: none"> hyperopia (odds ratio [OR], 15.3; 95% CI, 6.5–36.4) astigmatism (OR, 5.7; 95% CI, 2.5–12.7) anisometropia (OR, 27.8; 95% CI, 11.2–69.3), and strabismus (OR, 13.1; 95% CI, 4.3–40.4). 	Very Low	<ul style="list-style-type: none"> Large number of children excluded from this study may lead to underestimation of amblyopia

<p>Huang J, et al; Vision in Preschoolers (VIP) Study Group. Collaborators (143) Risk factors for astigmatism in the Vision in Preschoolers Study. <i>Optom Vis Sci</i> 2014;91:514–21.</p> <p>(Cross-sectional)</p>	<p>Vision In Preschoolers Study (VIP) 2001 to 2004. Multicenter study of children in Head Start, includes children who failed and a random sampling (~20%) of those who did not fail.</p> <p>Children from 36 to 72 months, N=4040.</p>	<p>Prevalence of astigmatism: 687/4040 (17%) (83.8% with-the-rule astigmatism)</p>		<p>There was a trend of an increasing percentage of astigmatism among older children (linear trend $p=0.06$).</p>	<p>Low</p>	<ul style="list-style-type: none"> Head Start is a national program in the United States that serves low-income families
<p>Pascual M, et al; Vision In Preschoolers (VIP) Study Group. Risk factors for amblyopia in the vision in preschoolers study. <i>Ophthalmology</i> 2014;121:622–9.e1</p> <p>(Cross-sectional)</p>	<p>VIP study 2001–2004. Children from 3–5 years (N = 3869).</p>	<p>Prevalence of unilateral amblyopia: 296/3869 (7.7%)</p> <p>Prevalence of bilateral amblyopia: 144/3869 (3.7%)</p>		<p>The following were independently associated with increased risk of unilateral amblyopia:</p> <ul style="list-style-type: none"> Presence of strabismus ($p<0.0001$) Greater magnitude of significant refractive errors (myopia, hyperopia, astigmatism, and anisometropia, each $p<0.00001$) 	<p>Low</p>	<p>The VIP Study was designed to over-represent children with vision disorders so likely overestimates the absolute risk of amblyopia for the general population</p>
<p>VIP Study Group. Does assessing eye alignment along with</p>	<p>Early paper from VIP Study 2001–2003.</p>	<p>Prevalence of amblyopia: 60/4040 (1.5%)</p>			<p>Low</p>	<ul style="list-style-type: none"> Same concerns as previously stated

refractive error or visual acuity increase sensitivity for detection of strabismus in preschool vision screening? <i>Invest Ophthalmol Vis Sci</i> 2007;48:3115–25.	Children aged 3 to <5 years (N = 4040).	Prevalence of strabismus: 157/4040 (3.9%)				
OUTCOME: VISUAL ACUITY						
Kirk VG, et al. Preverbal photoscreening for amblyogenic factors and outcomes in amblyopia treatment. <i>Arch Ophthalmol</i> 2008;126:489–92. (Retrospective cohort)	From February 1996 to February 2006, 21,367 children were photoscreened in Alaska: <ul style="list-style-type: none"> • 6.9% were referred for a complete eye examination (only those who failed) • 10,620 were younger than 48 months when screened • 411 of the children referred before 48 months were older than 6 years at study conclusion • 94 (22.9%) were included in this study 	Children photoscreened before age 2 years (n = 36) had a mean treated visual acuity of 0.17 logMAR, significantly better than that of children screened between ages 25-48 months (n = 58) with a mean 0.26 logMAR		Not estimable	Low	<ul style="list-style-type: none"> • Potential study bias - less than one-quarter of potential participants were included • Despite similar levels of amblyogenic risk factors, the proportion of children failing to reach a visual acuity of 20/40 was significantly less among those screened before age 2 years (5%) than in those screened from ages older than 2.0 years and younger than 4.0 years (17%)

BCVA = best corrected visual acuity

RAMSES = Rotterdam Amblyopia Screening Effectiveness Study
RCT = randomized controlled trial
VA = visual acuity