NIPH
Norwegian Institute of Public Health

2018

REPORT

SYSTEMATIC REVIEW:

Vision screening in children
under the age of 18

NIPH
Norwegian Institute of Public Health

Key messages

The Norwegian Directorate of Health are updating their guideline on vision screening for children under the age of 18, and have therefore commissioned this systematic overview which aim is to summarise, and critically appraise, evidence from studies that compare the effect of screening with no screening (or screening of different intensity). We included five studies (one non-randomised controlled trial with a follow up study, and three cohort studies), including a total of 18,497 children, who were aged 6 months to 8 years at follow up. Screening history, screening tests used, and timing of screening varied across studies. Only single studies contributed data to each comparison. No study evaluated the effects of school-screening.

Main findings:

- It is uncertain whether vision screening of children results in more amblyopia cases being identified, as compared to no screening or fewer screenings (4 studies; very low-certainty evidence).

- Vision screening of preschoolers may possibly result in more visual deficits being identified, as compared to no screening (1 study; low-certainty evidence).

- It is uncertain whether vision screening of children results in improved referral, as compared to no screening or fewer screenings (2 studies; very low-certainty evidence).

- It is also uncertain whether vision screening of children results in improved treatment outcomes, as compared to no screening (one study; very low-certainty evidence).

We cannot, based on the very low to low certainty of evidence from the few studies included in this review, draw any firm conclusions on the effects of vision screening in children, or of different screening intensity. Future studies should use a randomised study design, or if that is not feasible, use consecutive birth cohorts to ensure comparability of groups.

Executive summary

Background

There is a lack of consensus concerning the effects, and cost-effectiveness, of vision screening in children, as well as the optimal age, the frequency and the intervals, at which to carry out screening. In Norway, all children are screened at birth, at 6 weeks of age, at 3 months, and at the age of 4 at the mandatory health checks. In contrast to guidance in the other Scandinavian countries, the Norwegian Guideline for Vision Screening in children recommends fewer pre-school screening events, and does not include any recommendations for screening of schoolchildren. Vision screening of children at different ages fulfil different purposes, e.g. preschool screening to detect amblyopia (lazy eye), and related conditions, and screening of schoolchildren to detect refractive errors (blurred vision), and progressive visual deficits. Younger children are at risk of permanent impaired vision if deficits are not identified in time, while older children do not risk permanent visual impairment if not screened. Un-corrected visual deficits in young children may have a negative impact not only on children's sensorimotor development, but also on their intellectual and social development. This report is a systematic review of the effects of vision screening in children on the detection of disease and treatable deficits, referral to appropriate treatment, and follow up of the children's vision.

Objective

The overall objective of this systematic review was to summarise and critically appraise the existing evidence for the effects of vision screening in children under the age of 18, on the detection of disease and treatable visual deficits, referral to adequate treatment, and follow up of these children.

Method

We conducted a systematic review in accordance with the Cochrane handbook and the handbook of the Division of Health Services at the Norwegian Institute of Public Health. We searched for studies in six electronic databases up to May 2018. Two au-

thors independently screened all titles, and thereafter assessed the full texts of possible eligible studies. One review author extracted data onto a standardised data extraction form, and a second review author checked the accuracy of the data. The same two authors independently assessed the quality of the included studies using the Cochrane EPOC risk of bias tool for non-randomised controlled trials, and ROBINS-1 tool for cohort studies. We assessed the certainty of the included evidence using the GRADE tool (Grading of Recommendations Assessment, Development and Evaluation). Disagreements were solved through discussion between authors.

Results

We included five heterogeneous studies in this systematic review. These studies (one non-randomised controlled trial with a follow up study, and three cohort studies) provided data for five comparisons, i.e. only single studies contributed data for each comparison. All studies evaluated the effect of screening of young children (i.e. before school start), and none evaluated the effects of school-screening. The studies reported three primary outcomes: amblyopia prevalence/visual deficits (5 studies); referrals (2 studies) and treatment outcomes (one study). The certainty of the evidence for all the primary outcomes was overall very low.

Comparison 1: Vision screening at 1-2.5 years of age vs. no screening: outcomes assessed at 8 years of age (one study)

One study reported fewer amblyopia cases among 8-year old children previously screened at 1-2.5 years of age (8/808; 1.0%), as compared to previously unscreened children (20/782; 2.6%; RR (95% CI): 0.39 (0.17 to 0.87); P=0.0098) [1].

The same study also reported lower prevalence of more severe amblyopia in previously screened children (1/808; 0.1%), as compared to in unscreened children (13/78; 21.7%); RR (95% CI): 0.07 (0.01 to 0.57); P=0.01. The authors did not provide any information on the number of children in the unscreened group who had been diagnosed with amblyopia and treated. This study also reported referrals, number of children diagnosed and treated for amblyopia, but only for the screened group.

Comparison 2: Screening at 4-4.5 years of age vs. no screening: effects assessed at 5.5 years of age

One study [2] reported that fewer of the children who had been screened 6-12 months previously had visual deficits (78/763 children; 10%), as compared to unscreened children (112/743; 15%; RR (95% CI): 0.68 (0.52 to 0.89); P=0.005. The authors provided no further information on the type of visual deficits, apart from the severity of deficits.

Comparison 3: Screening 6-9 months vs. omitting screening at 6-9 months: effects assessed at 9 months

One study [3] reported a similar proportion of children that after referral were diagnosed with amblyopia combined with strabismus in the screened group (10/ 6,059; 0.17%) as in the unscreened group (6/5,482 infants; 0.11%); RR (95% CI): 1.51 (0.55 to 4.15), P=0.43.

The same study reported a similar proportion of referrals among infants screened at 6-9 months (58/6,059; 0.96%), as among those with no screening at 6-9 months (48/5,482; 0.88%); RR (95% CI): 1.09 (0.75 to 1.61), P=0.65. However, the confidence interval around the effect estimate, for both amblyopia prevalence and referrals, was wide, with the effect ranging from being in favour of the screening to a non-favourable effect.

Comparison 4: Intensive screening (at 8, 12, 18, 25, and 31 months) vs. no screening (visual surveillance only): effects assessed at 37 months

One study [4] reported that more toddlers with amblyopia were identified in the intensive screening programme (33/2,029; 1.6 %), as compared to in the unscreened group (8/1,461; 0.5%); RR (95% CI): 2.97 (1.38 to 6.41), P<0.006. Note that the results, which refer to an increased number of amblyopia cases identified through intensive screening, as compared to visual surveillance only (by health visitors and GPs), was considered a desired result.

The same study [4] reported in total fewer referrals among children in the intensive screening group (147/2,029; 7.2%), as compared to among control group participants (135/1,461; 9.2%); RR (95% CI):0.77 (0.60 to 0.98), P=0.03.

Comparison 5: Intensive screening (at 8, 12, 18, 25, and 31 months) vs. no screening (visual surveillance only): effects assessed at 7.5 years of age (follow-up study)

Fewer amblyopia cases were reported at follow up [5], among 7.5 year old children in the intensive screening group (22/1088; 2.0%), than in the group of unscreened children (37/826; 4.48%); RR (95% CI): 0.45 (0.27 to 0.76), P=0.003. A problem with this study was large losses to follow up.

The same study [5] also reported that a similar proportion in both groups received patches (intensive screening: 40/1088; 3.7% vs. unscreened: 40/826¸4.8%); RR (95% CI): 0.76 (0.49 to 1.17), P=0.21, and fewer cases with residual amblyopia in the intensive group (3/40), as compared to in the unscreened group (10/40); RR (95% CI): 0.30 (0.09 to 1.01), P=0.05. In addition, the mean visual acuities (in the worse seeing eye) was better for children in the intensive group than for similar children in the control group (mean acuity 0.15 (95% CI; 0.085 to 0.215) vs. 0.26 (0.173 to 0.347) LogMAR units; P < 0.001).

The certainty of evidence from the five included studies and for the primary outcomes (amblyopia prevalence, referrals and treatment outcomes) was very low to low, which means that we have low confidence in the results.

Discussion

We included only five heterogeneous non-randomised studies in this systematic review (one NRCT with a follow up study, and three controlled cohort studies), which all evaluated the effect of vision screening of younger children, and none the effect of school-screening.

The included studies were heterogeneous in terms of populations, timing of the screening, screening history of the children, screening tests used and in the profession of the screeners. This, and the fact that only single studies provided data for each comparison prevented meta-analysis.

The certainty of the included evidence was very low to low, and it is therefore not possible to draw any firm conclusion on the effects of screening as compared to no screening, or to different screening intensity.

Conclusion

The results are based on very low to low-certainty evidence from five heterogeneous non-randomised studies, and we cannot therefore draw any firm conclusions on whether or not vision screening in children lead to improved eye health (i.e. lower prevalence of amblyopia and other vision deficits), as compared to no screening (or fewer screenings). Future studies should use a randomised study design, or if that is not feasible, use consecutive birth cohorts to ensure the comparability of groups.

Hovedfunn (norsk)

Helsedirektoratet oppdaterer sin retningslinje om synsundersøkelse for barn under 18 år, og har derfor bestilt denne systematiske oversikten, som har som mål å oppsummere og kritisk vurdere dokumentasjon fra studier som sammenligner effekten av screening med ingen screening (eller forskjellig screeningsintensitet).

Vi inkluderte fem studier (én ikke-randomisert kontrollert studie med oppfølgingsstudie, og tre kohortstudier). Totalt inkluderte studiene 18,497 barn i alderen 6 måneder til 8 år. Screeninghistorie, screeningtester, og tidspunkt for screening varierte mellom studiene. Hver studie ga data for én enkelt sammenligning. Ingen av studiene evaluerte effekten av screening av skolebarn.

Hovedfunn:

- Det er usikkert om synsscreening fører til at flere barn med amblyopi blir identifisert, sammenlignet med ingen screening eller færre screeninger (4 studier; svært lav tillit til dokumentasjonen).

- Synsscreening av førskolebarn kan føre til at flere barn med synsdefekter (visuelle svekkelser) blir identifisert, sammenlignet med ingen screening (1 studie; lav tillit til dokumentasjonen).

- Det er usikkert om synsscreening av barn fører til forbedret henvisningspraksis, sammenlignet med ingen screening eller færre screeninger (2 studier; svært lav tillit til dokumentasjonen).

- Det er usikkert om synsscreening av barn fører til bedre behandlingsresultater, sammenlignet med ingen screening (1 studie; svært lav tillit til dokumentasjonen).

Vi kan ikke, basert på lav til svært lav tillit til dokumentasjonen fra de få inkluderte studiene, trekke noen sikre konklusjoner om effekten av synsscreening av barn, eller av forskjellig screeningsintensitet. Fremtidige studier bør bruke et randomisert studiedesign, eller hvis det ikke er mulig, bruke konsekutive fødselskohorter for å sikre sammenlignbare grupper.

Sammendrag (norsk)

Synsscreening av barn yngre enn 18 år: en systematisk oversikt

Bakgrunn

Det mangler konsensus om effekten og kostnadseffektiviteten av synsscreening av barn. Det er også uenighet om den optimale alderen for screening, samt hvor ofte og med hvilke tidsintervall det skal utføres screening. I Norge screenes barn for synsdefekter kort tid etter fødselen, og ved 6-ukers, 3-måneders, og 4 års alder som en del av den obligatoriske helsekontrollen. I motsetning til retningslinjene i de andre skandinaviske landene, anbefaler den norske faglige retningslinjen for synsundersøkelse av barn færre screeninger av førskolebarn, og det foreligger ikke anbefalinger om screening av barn i skolealder. Synsscreening av barn i ulike aldre har ulike formål, f.eks. er det primære formålet med screening av 4-åringer å oppdage amblyopi og relaterte tilstander, mens screening av skolebarn primært gjennomføres for å oppdage brytningsfeil. Yngre barn risikerer permanent nedsatt syn hvis synsdefekter ikke fanges opp tidlig, mens eldre barn ikke risikerer permanent synsnedsettelse hvis de ikke screenes. Uidentifiserte synsproblemer kan innvirke negativt på yngre barns sensorimotoriske, intellektuelle og sosiale utvikling. Denne rapporten er en systematisk oversikt over effekter av synsscreening av barn for å identifisere sykdom og synsproblemer som kan behandles, inkludert om dette fører til henvisning, adekvat behandling og oppfølging av barns syn.

Problemstilling

Det overordnede målet med denne systematiske oversikten var å oppsummere og kritisk vurdere den eksisterende dokumentasjonen for effekt av synsscreening hos barn (0 til 18 år) for å identifisere sykdom og synsproblemer som kan behandles, inkludert om dette fører til henvisning, adekvat behandling og oppfølging av disse barnas syn.

Metode

Vi gjennomførte en systematisk oversikt i samsvar med Cochrane-håndboken og håndboken for område for helsetjenester i Folkehelseinstituttet. Vi søkte etter primærstudier i seks elektroniske databaser fram til mai 2018. To forfattere screenet alle titler og abstrakt uavhengig av hverandre, og vurderte deretter de relevante artiklene i fulltekst. En oversiktsforfatter hentet ut data på et standardisert skjema (GMF), og den andre oversiktsforfatteren sjekket riktigheten av uthentingen (KYD). De samme to forfattere vurderte uavhengig av hverandre kvaliteten på de inkluderte studiene ved hjelp av Cochranes risiko for systematiske skjevheter verktøy (ikke-randomiserte kontrollerte studier), og ROBINS-1 verktøyet (kohort studier). Vi vurderte vår tillitt til dokumentasjonen ved hjelp av GRADE-verktøyet (Grading of Recommendations Assessment, Development and Evaluation). Uenigheter ble løst ved diskusjon mellom forfattere.

Resultat

Vi inkluderte fem studier i denne systematiske oversikten. Vår tillitt til dokumentasjonen for alle de primære utfallene (prevalens av amblyopi, henvisninger og behandlingsutfall) var lav til svært lav. Alle studiene evaluerte effekten av screening utført før skolestart, og ingen evaluerte effekten av skole-screening. Studiene rapporterte tre primære utfall: prevalens av amblyopi / synsdefekter (5 studier); henvisninger (2 studier) og behandlingsresultater (én studie).

Synsscreening ved 1-2,5 års alder sammenlignet med ingen screening, utfall vurdert ved 8 års alder

Én studie oppga data for denne sammenligningen, og rapporterte færre tilfeller av amblyopi blant 8 år gamle barn som var screenet ved 1-2,5 års alder (8/808, 1,0%), sammenlignet med barn som ikke tidligere var screenet (20/782; 2,6%): RR (95% CI): 0,39 (0,17 til 0,87), P = 0,0098 [1].

Den samme studien rapporterte også lavere forekomst av mer alvorlig amblyopi hos screenede barn (1/808; 0,1%), sammenlignet med hos ikke screenede barn (13/782; 1,7%); RR (95% CI): 0,07 (0,01 til 0,57), P = 0,01. Av småbarna som ble identifisert til å være i risikogruppen for å utvikle amblyopi når de ble screenet ved 1-2,5 års alder (N = 18), hadde 13 småbarn ikke et amblyogent visuelt tap, mens fem hadde amblyogent synstap ved 8 år. Forfatterne ga ingen informasjon om antall barn i gruppen som ikke hadde blitt screenet, og som hadde blitt diagnostisert med amblyopi og behandlet. Denne studien rapporterte også henvisninger, men bare for den screenede gruppen.

Synsscreening ved 4-4,5 års alder sammenlignet med ingen screening, utfall vurdert ved 5,5 års alder

Én studie [2] rapporterte at færre av barna som hadde blitt screenet 6-12 måneder tidligere hadde synssvekkelser (78 /763 barn, 10%), sammenlignet med barn som ikke ble screenet (112/743, 15%); RR (95% CI): 0,68 (0,52 til 0,89), P = 0,005. Forfatterne oppga kun alvorlighetsgraden av synsproblemene.

Synsscreening ved 1-2, 3-4 og 6-9 måneders alder sammenlignet med utelatelse av screening ved 6-9 måneder, utfall vurdert ved 9 måneders alder

Én studie [3] rapporterte en tilsvarende andel av barn som etter henvisning ble diagnostiserte med amblyopi kombinert med strabisme i den screenede gruppen (10/6.059; 0,17%) som i den ikke screenede gruppen (6/5,482 spedbarn, 0,11%); RR (95% CI): 1,51 (0,55 til 4,15), P = 0,43.

Samme studie rapporterte en tilsvarende andel henvisninger blant tidligere screenede spedbarn (58/6.059; 0.96%), som blant de uten screening ved 6-9 måneder (48/5,482; 0,88%); RR (95%): 1,09 (0,75 til 1,61), P = 0,65. For både prevalens av amblyopi og henvisninger var imidlertid konfidensintervallet rundt effektestimatet bredt, fra en effekt som indikerte en gunstig effekt til en ikke-gunstig effekt.

Intensiv synsscreening (ved 8, 12, 18, 25 og 31 måneder) sammenlignet med ingen screening (kun synsovervåkning), utfall vurdert ved 37 måneders alder

Én studie [4] rapporterte at flere småbarn med amblyopi ble identifisert i det intensive screeningprogrammet (33/2, 029, 1,6%), sammenlignet med i den ikke-screenede gruppen (8/1,461; 0,5%); RR (95% CI): 2,97 (1,38 til 6,41), P <0,006. Merk at resultatene, som refererer til økt antall amblyopi identifisert ved intensiv screening, sammenlignet med kun visuell overvåking (av helsepersonell og lege), regnes som et ønsket resultat.

Den samme studien [4] rapporterte totalt færre henvisninger blant barn i den intensive screeninggruppen (147/2 029, 7,2%), sammenlignet med i kontrollgruppen (135/1 461, 9,2%); RR (95% CI): 0,77 (0,60 til 0,98), P = 0,03.

Intensiv synsscreening (ved 8, 12, 18, 25 og 31 måneder) sammenlignet med ingen screening (kun synsovervåkning), utfall vurdert ved 7,5 års alder (oppfølgingsstudie)

Færre tilfeller av amblyopi ble rapportert ved oppfølging [5], blant 7,5 år gamle barn fra den intensive screeningsgruppen (22/1088, 2,0%), enn hos ikke screenede barn (37/826; 4,48%); RR (95% CI): 0,45 (0,27 til 0,76), P = 0,003.

Den samme studien [5] rapporterte også at en tilsvarende andel i begge gruppene mottok lappebehandling (intensiv synsscreening: 40/1088; 3,7% versus, synsovervåkning: 40/826, 4,8%); RR (95% CI): 0,76 (0,49 til 1,17), P = 0,21 og færre tilfeller med gjenværende amblyopi i intensivgruppen (3/40) sammenlignet med i den ikke-screenede gruppen (10/40); RR (95% CI): 0,30 (0,09 til 1,01), P = 0,05. I tillegg var

de gjennomsnittlige synsskarpheten (i øyet med dårligst syn) bedre for barn i intensivgruppen enn for tilsvarende barn i den ikke screenede gruppen (gjennomsnittlig skarphet 0,15 (95% CI; 0,085 til 0,215) versus 0,26 (95% CI; 0,173 til 0,347) LogMAR-enheter; $P < 0,001$).

Vår tillit til dokumentasjonen for de primære utfallene (prevalens av amblyopi, henvisninger og behandlingsresultater) var lav til svært lav, noe som betyr at vi ikke stoler på resultatene.

Diskusjon

Kun fem ikke-randomiserte studier (en NRCT og fire kontrollerte kohortstudier) møtte inklusjonskriteriene for denne systematiske oversikten. Alle studiene evaluerte effekter av synsscreening av unge barn, og ingen av studiene evaluerte effekter av skolescreening.

De inkluderte studiene var heterogene med hensyn til populasjoner, timing av screening, barnas screeningshistorie, hvilke screeningstester som ble brukt og profesjonen for de som utførte screeningen. Dette, og det faktum at bare enkelte studier oppga data for hver sammenligning forhindret metaanalyse.

Tilliten til den inkluderte dokumentasjonen var lav til svært lav, og det er derfor ikke mulig å trekke noen sikker konklusjon om effekten av screening sammenlignet med ingen screening eller med forskjellig intensitet av screening.

Konklusjon

Den lave til svært lave tilliten til dokumentasjonen fra kun fem ikke-randomiserte studier, gir ikke pålitelig svar på om screening av barn kan resultere i bedre øyehelse (dvs. lavere prevalens av amblyopi og andre synssvekkelser), sammenlignet med ingen screening (eler færre screeninger). Fremtidige studier bør bruke et randomisert studiedesign, eller hvis det ikke er mulig, bruke konsekutive fødselskohorter for å sikre sammenlignbare grupper.

Table of contents

Preface

The Norwegian Directorate of Health commissioned a systematic review of available research on the effects of vision screening for children under the age of 18 from the Division of health services, within the Norwegian Institute of Public Health. This evidence review will make up the background documentation for the updated national guidelines for vision screening in children.

The Division for health services follows a standard approach in dealing with systematic reviews, which is described in the manual "Slik oppsummerer vi forskning." We may use standard formulations when we describe the method, results and discussion of the findings. The Norwegian Directorate for Health, in collaboration with the Division of Health Services, at the Norwegian Institute of Public Health, has a process for faster access to relevant and up-to-date systematic reviews to be used in guideline work. In according to this process we do not write an extensive introductory chapter, discussion chapter or comprehensive list of definitions.

The project group consisted of:
- Project coordinator: Senior researcher, Gerd M Flodgren, Division of Health Services, The Norwegian Institute of Public Health (NIPH)
- Statistician/Researcher, Kristoffer Y Ding, Division of Health Services, NIPH

We would like to acknowledge the following people: research librarian Hilde Strømme for help with developing the search strategy and running the searches, internal peer referees Øyvind Melien and Rigmor Berg, external peer referees Karin Amlie Sandvand, Senior consultant at the Eye section, Vestfold Hospital, and Gro Horgen Vikesdal, Assistant professor at the Department of Optometry, Radiography, and Lighting design, Univerity of South-Eastern Norway for their helpul input on the review.

Declared conflicts of interest:
None of the authors or referees declared any conflicts of interest.

Research director	*Department director*	*Project coordinator*
Kåre Birger Hagen	Kjetil Brurberg	Gerd M Flodgren

Objective

The overall objective of this systematic review was to summarise and critically appraise the existing evidence for the effects of vision screening in children under the age of 18, on the detection of disease and treatable deficits, referrals, and follow up of these children.

Definitions:
'Vision screening' is a short examination that can indicate the presence of a vision deficit or a potential vision problem. It does not provide an exact diagnosis, but can indicate a need of an appointment with an ophthalmologist or optometrist for a comprehensive eye examination.

'Treatable visual deficits' include e.g. amblyopia, strabismus, and refractive errors. Colour vision deficiency, on the other hand, is a condition that cannot be corrected, and screening for this condition is therefore outside the scope of this systematic review.

We have used the Oxford dictionary's definition of a child, which is "a young human being below the age of puberty or below the legal age of majority». In Norway, as in many other countries, this would refer to individuals under the age of 18.

In addition, we have defined *an infant* as a young human being between 1 and 12 months of age, *a toddler* as a young child between 1 and 3 years of age, and a *pre-schooler* a child 3 years old and up to 5 to 7 years of age, depending on when school starts in different countries.

Background

The aim of vision-screening programs for children is early detection of disease and treatable visual deficits, timely referral to adequate treatment and follow up [6]. There is however, a lack of consensus regarding the effects, and cost-effectiveness, of universal screening programs [7, 8]. U*niversal* screening programs, as opposed to targeted screening of high risk populations, include all children of a certain age.

Description of the problem

Visual deficits (in particular amblyopia), can have negative effects on the sensorimotor development of young children, as well as on their intellectual and social development [9-11]. Common visual deficits in pre-school children that can be detected through screening, are amblyopia, strabismus, and refractive errors [9]. Amblyopia (or lazy eye), which is the most common cause of visual impairment in children, is a functional reduction in visual acuity resulting from an abnormal visual development early in life [12]. Treatment of amblyopia is most effective when initiated early [13].

There is a lack of consensus concerning the effects of visual screening in children, as well as the optimal age [14, 15], the frequency, and spacing, at which it is to be carried out. In Norway, all children are screened at 6 weeks, 3 months, and again at age 4 at the mandatory health check [16]. In contrast to the vision screening guidance in Sweden, Denmark, and Finland, the Norwegian Guideline for Vision Screening in children involves comparatively fewer screening events in total, and include no recommendation for screening of school-aged children [17]. In Norway, referral to an eye examination is based on indications of poor vision, expressed by the child, its parents or teachers, or if the child has dyslexia, hearing loss or other disabilities (1).

Vision screening of children at different ages fulfil different purposes; e.g. screening of infants to detect congenital cataract [18], screening of pre-school children to detect amblyopia, and conditions that may lead to amblyopia, while screening of school-children is primarily used to detect refractory errors [19]. It should however be noted that lack of screening have completely different consequences for different age groups. While younger children are at risk of permanent impaired vision (even with ideal glasses), if important visual deficits are not detected and treated in time, children who are older do not run the same risk of permanent visual impairment if

not screened. We have defined a person with impaired vision as "someone with a severe reduction in vision that cannot be corrected with standard glasses or contact lenses and reduces a person's ability to function at certain or all tasks". There is some new evidence from a large longitudinal Indian study, suggesting that schoolchildren's eye-sight is getting increasingly myopic [20]. However, it is unclear whether these findings can be generalised to a Norwegian context, and if universal screening is the best way to solve the problem.

How the intervention might work?

Visual screening programs may improve the eye health of children through early detection of disease and treatable visual deficits, timely referral for adequate treatment, and follow up of relevant children [6].

Most high-income countries have vision-screening programs in place, but these may differ in both content and scope. Worldwide, there is large variation in screening practices, both across and within countries [6, 21]. For example, in both Canada [14], and Australia [6], the screening practices vary widely, which may give rise to inequities in eye health among children from different regions.

According to an inventory of current paediatric vision screening in Europe, a majority of participating countries (35 of 39) have national screening programmes in place, with half of the countries reporting a 95% coverage or more [10, 14]. Vision screening was in the participating countries performed at different points in time (e.g. preschool screening between 3 and 7 years of age), by varying professions (most often ophthalmologists, paediatricians and nurses), and using a number of different (age-relevant) vision acuity tests (e.g. Picture chart, Lea Hyvarinen chart (picture), Landolt C, Tumbling E, Konstantin Moutakis, Sheridan Gardiner and Snellen)[10].

Why is it important to do this review?

The Norwegian Directorate of Health is updating the National Guideline for Vision screening in Children [16], and wishes to gain knowledge about new, and the complete evidence regarding the effects (and cost-effectiveness) of vision screening programs. This systematic review will assist this process by updating the evidence upon which this guidance will be based.

Early detection, and treatment, of visual deficits (especially amblyopia) have the potential to improve vision development, by decreasing both the prevalence and severity of amblyopia [12]. If detection is improved by more screenings, more children will receive treatment and improved vision development. It is therefore important to summarise the existing evidence on the effects of vision screening in children, so as

to ensure that the updated guideline is based on documentation that includes the most recent research evidence.

In a recent Cochrane systematic review, the authors searched for randomised studies evaluating the effects of vision screening versus no screening for school-aged children and adolescents, but found no eligible studies [7]. In another Cochrane review the authors searched for randomised studies evaluating amblyopia prevalence among previously screened and unscreened children at school start, but identified no eligible studies [8]. It is therefore desirable to search for both randomised and non-randomised controlled studies comparing the effect of vision screening with no screening (or different intensity of screening) in children under the age of 18 (i.e. both pre-school and school-age children).

Method

We conducted this systematic review in accordance with the methods described in the Cochrane Handbook for Systematic Reviews of Interventions [22] and in the Division of Health Services' handbook [23] as specified below. The protocol for this systematic review may be found at https://www.fhi.no/prosjekter/synsscreening-av-barn---prosjektbeskrivelse/.

Literature search

Research librarian Hilde Strømme developed the search strategy (which was peer reviewed by research librarian Lien Nguyen), planned and systematically searched for relevant publications in the following databases:
- Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Trials Register)
- MEDLINE (Ovid)
- Embase (Ovid)
- SveMed+
- DARE, EED, and HTA database (via the Cochrane Library)
- Epistemonikos

All databases were searched from their respective inception date and up to May 2018.

Searching other sources

We searched for grey literature in OpenGrey and GreyLit, In addition we searched the reference lists of included studies and of other relevant publications, and tried to contact experts in the field

The complete search strategy is provided in Appendix 1.

Inclusion criteria

Study designs that were considered eligible for inclusion:
- Systematic reviews (SRs)
- Randomised controlled trials (RCT)
- Non-randomised controlled trials (NRCT)
- Controlled before-after studies (CBA)

- Interrupted time series studies (ITS)
- Cohort studies (with a control group)

Population:	Children under the age of 18
Intervention:	Vision screening (conducted in any setting, and by any trained personnel, using any standardised tests).
Comparison:	i) No screening
	ii) Different screening intensity
Outcome:	Detection of disease and treatable visual deficits; referral to appropriate treatment and follow up, vision (treatment) outcomes
Language:	We considered all relevant studies for inclusion regardless of language. (see additional criteria below)

Additional inclusion criteria:
- Only CBAs with at least two intervention sites and two control sites were considered for inclusion.
- Only ITS studies with at least three data points before the intervention and three data points after the intervention were onsidered for inclusion.
- Only studies published in a language mastered by people in our team, colleagues in our unit, or colleagues at the Norwegian Institute of Public Health, were eligible.
- For self-reported (subjective) outcomes, we only included those that had been measured using standardised instruments.

Exclusion criteria

We excluded studies that evaluated the effects of targeted screening: i.e. screening targeted at specific populations of children considered to be at greater risk for developing visual deficits (e.g. premature children, children with low birth weight, or those with a first degree relative with amblyopia). We excluded conference abstracts and other publications without results in full text.

Selection of studies

We downloaded all titles and abstracts retrieved by the electronic searches into the reference management program EndNote and removed duplicates. The review authors (GF and KYD) independently assessed the eligibility of all the remaining titles and abstracts for inclusion using the Rayyan software [24]. We obtained full text copies of potentially relevant studies, and assessed these against the inclusion criteria (see above). We resolved disagreements on the eligibility of studies by discussion among review authors. We documented studies read in full text, and subsequently excluded, in a table along with the reasons for exclusion.

Risk of bias assessment

The review authors (GMF and KYD), independently assessed the risk of bias of each included study in accordance with the guidance in Chapter 8 of the Cochrane Handbook for Systematic Reviews of Interventions [25]. We used the Cochrane Effective Practice and Organisation of Care (EPOC) group's risk of bias tool [26] for assessing the Non-randomised controlled trial (NRCT), and the Robins-1 tool for the cohort studies [27]. We assigned an overall assessment of the risk of bias (high, unclear or low risk of bias) to each of the primary outcomes reported in the included studies using the approach suggested in Chapter 8 of the Cochrane Handbook [25]. We resolved any disagreements through consensus.

Data extraction and analysis

One review author (GMF) extracted data from each included study into a standardised data extraction form (http://epoc.cochrane.org/resources/epoc-resources-review-authors), and a second review author (KYD) controlled the accuracy of the data. We resolved disagreements through consensus.

We extracted the following data from the included primary studies:
- Full reference; study design;
- Characteristics of the population e.g. no of participants, age, gender, ethnicity;
- Type of vision deficits e.g. *amblyopia, myopia*, *strabismus*, *refractive errors*;
- Country, and screening context i.e. healthcare setting or school healthcare;
- Characteristics of the intervention e.g. number and spacing of screening events, vision tests used (including failure thresholds applied for specific tests), and whether or not the tests used were considered age appropriate;
- Profession and qualifications of those performing the screening;
- Type of comparison (no screening, different screening intensity);
- Outcomes (detection of vision deficits, referrals and follow up, vision (treatment) outcomes etc.).

For dichotomous outcomes, we expressed the results as a risk ratio (RR) with 95% confidence interval (CI). No continuous outcomes were included. We evaluated the heterogeneity of the material by looking at population, intervention, comparison and outcomes. Since it was not feasible to pool the data from the heterogeneous studies, we provided a descriptive analysis with presentation of the studies in the text, and in tables with results and quality assessments.

Grading the certainty of evidence

Two review authors (GMF and KYD) independently assessed the certainty of the evidence (i.e. to what degree we can have confidence in that the results estimate the true effect) using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) handbook [28], and tool [29].

Evidence from randomised controlled trials start as high certainty evidence, evidence from observational studies start at low certainty. Both may be downgraded depending on five criteria in GRADE that are used to determine the certainty of the evidence: i) methodological study quality as assessed by review authors, ii) degree of inconsistency, iii) indirectness, iv) imprecision, and v) publication bias. Upgrading of results from observational studies (with no study limitations) is possible according to GRADE if there is a large effect estimate, or a dose-response gradient, or if all possible confounders would only diminish the observed effect and that therefore the actual effect most likely is larger than what the data suggest.

In accordance with the GRADE approach, we graded the certainty of evidence as high, moderate, low, or very low, which is defined in the following way:

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

As the one NRCT, its follow-up study, as well as the three controlled cohort studies provided evidence of very low to low quality, we have reported the results for all studies taken together in the Summary of findings table. This was done in order to be able to give an overall grading of the evidence for the effects of screening as compared to no screening or to fewer screenings.

Results

Search results

The literature searches yielded 2,664 unique citations. Based on titles and abstracts we directly excluded 2,643 irrelevant studies that did not meet our inclusion criteria. We assessed 21 studies in full text, and excluded 16 of the 21 studies after scrutiny. We have reported these studies, along with the reasons for exclusion, in Appendix 2. We identified five studies (reported in seven publications) that were eligible for inclusion in this systematic review. See Fig 1.
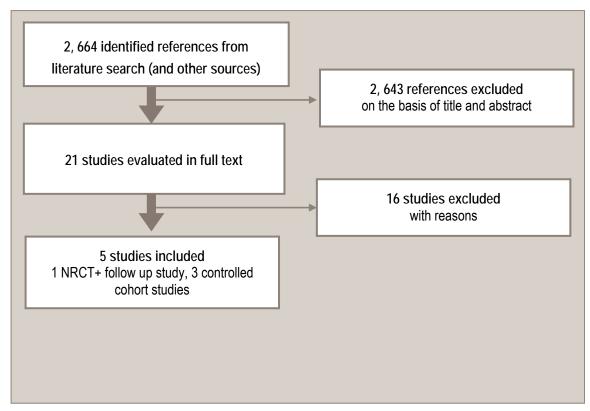

Figure 1. PRISMA study flow diagram describing the study selection process.

Description of included studies

See Table 1 and Table 2 below.

Five studies were included in this systematic review [1-5]. One of the studies [5], was a follow up of a previously published study by the same authors [4]. Four of the included studies were published between 1980 and 2002 [1, 2, 4, 5]. One recent study was published in 2015 [3]. See Appendix 3 for a list of included studies.

We found two additional publications that belonged with two of the included studies [30, 31], which however did not contribute any relevant data to this report.

Study designs and settings

One of the included studies was a non-randomised controlled trial nested within a large cohort study [4], and one was a follow up study of mentioned trial[5]. Three were controlled cohort studies [1-3], and one was a prospective population-based study that included two consecutive birth cohorts [3].

Two studies were conducted in England [4, 5], one in Israel [1], one in Canada [2], and one in the Netherlands [3].

Screening was conducted at child welfare clinics [1], at health centres as part of general infant health screening [3], and at hospital clinics [4, 5]. In one study the setting was not specified [2].

Populations

In total 18,497 children were recruited in the studies included in this review, of which 8,660 were screened and 9,837 were unscreened. One study [3] included infants (age 6 to 9 months), one [4], included toddlers (age 37 months), and a third study [2] included pre-schoolers (age 5.5 years). Two studies included school-children that were 7.5 to 8 years of age [1, 5].

Description of the screening

Timing and intensity of the screening

As mentioned earlier: three of the included studies included infants, toddlers or pre-schoolers [2-4], and two studies school-children [1, 5]. The latter two did not evaluate the effect of school-screening, but followed up on the effect of pre-school screening at 1-2.5 years of age [1], and the effects of an intensive screening programme (5 screenings between 8 and 31 months of age). [4] The study that included pre-schoolers (5-5.5 years of age) evaluated the effects of a previous screening (6-12 months earlier), but it was not clear whether the children had been screened before the age of 4 [2]. One study evaluated the effects of omitting one of three population-based vision screenings (at 6-9 months) from an extensive

screening programme (with two previous screenings at 1-2 months and at 3-4 months) [3]. None of the included studies evaluated the effects of school screening.

Vision screening tests used

A number of different screening tests were used in the included studies, to assess children of different ages (ranging from 6-9 months to 8 years of age). We found little or no information regarding the 'age-appropriateness' of the tests used. For details on the type of tests used see table 1 Characteristics of included studies below.

Criteria for referral/failure thresholds

Three of the included studies reported the failure thresholds/referral criteria applied for the screening tests [2, 4, 5], while two studies did not [1, 3]. For details on the actual referral thresholds see table 1 Characteristics of included studies below.

Sensitivity and specificity of screening tests

One study [1] reported the sensitivity and specificity of the screening test for amblyopia to be 85.7% and 98.6% respectively (positive predictive value: 62.1%, and negative predictive value: 99.6%). One study [4], reported that the intervention programme was more specific than the control programme (95% vs. 92%, p<0.01). Further, the authors reported poor sensitivity of the cover test and the visual acuity test for children younger than 37 months (but 99% specific), and higher sensitivity of the photo-refraction test than that of the visual acuity test for children younger than 37 months, and that the specificity at 31-37 months was high (>95%). Three studies [2] [3, 5] did not report the sensitivity or the specificity of the screening tests used.

Definitions of amblyopia (or visual deficits)

One study [1] defined amblyopia as"corrected visual acuity of ≤5/10 (20/40), or >1 line difference in corrected visual acuity between both eyes".

One study defined amblyopia in two ways: i) 0.2 LogMAR interocular difference in acuity (two lines on the chart) or more; and ii) worse than 0.3 LogMAR visual acuity in the amblyopic eye [5].

Two studies did not provide a definition of amblyopia [3, 4]. One study only reported the proportion of children with mild, moderate to severe 'visual impairment', which were defined as VA 20/40 and VA 20/50+ respectively [2].

Vision screeners

The vision screeners were ophthalmologists or orthoptists (who were also the authors [1]), trained public health nurses [2], public health physicians or public nurses [3], and orthoptists [4, 5].

Comparisons

Most studies compared screening (at different intensity/spacing) with no screening: two studies compared (one) early screening with no screening [1, 2].

One study [1], which aimed to determine the impact of early screening on prevalence of amblyopia in schoolchildren, compared the prevalence of amblyopia in an *8-year-old* population previously screened at 1-2.5 years of age, with an unscreened population of the same age.

One study [2], which aimed to determine whether children (approximately *5.5 years* of age) who had been screened 6 to 12 months earlier, had fewer vision problems compared to an unscreened cohort of the same age.

One study [3], which aimed to determine the effect of *omitting* one of three early population-based eye screenings, compared one birth cohort screened *at 6-9 months* with a birth cohort not screened at 6-9 months (all infants were screened at 1-2 months and 3-4 months).

One study [4], which aimed to determine the effect of intensive screening (5 screening events between 8 and 31 months), compared the effect of an intensive screening programme (children were offered screening at 8, 12, 18, 25 and 31 months), with visual surveillance on amblyopia prevalence and referral rate *at 37 months.* Visual surveillance involved specific examinations of the child at ages 8 and 18 months, asking about family history, observing visual behaviours, using a cover test, and ad hoc referrals if a problem was suspected at any time.

One study [5], which followed-up on the intensive screening programme (described above), compared the amblyopia prevalence among children *7.5 years of age*, who had been part of the intensive screening programme [4], with children of the same age who previously had received visual surveillance only.

Table 1. Screening history of participating children and follow up assessment (N=5)

| | Number and timing of screening events | | | | | | | |
| | Infants | | | Toddlers | | Pre-schoolers | | Preschool-School aged children |
Author Year	1-2 months	3-4 months	6-12 months	14-30 months	31-36 months	37-45 months	4-4.5 years	5.5 -8 years
Eib-schitz-Tsimhoni 2000 [1]				Once (intervention group)				All children examined at 8 years
Feld-mann 1980 [2]							Once (intervention group)	All children examined at 5.5 years)
Sloot 2015 [3]	Once (both groups)	Once (both groups)	Once (intervention group) *					

Williams 2001 [4]			Twice (intervention group)	Twice (intervention group)	Once (intervention group)	All children examined at 37months		
Williams 2002 [5]			Twice (intervention group)	Twice (intervention group)	Twice (intervention group)			All children examined at 7.5 years

* Data extracted from screening registers, as part of a population-based screening program.

Outcomes

Primary

Four of the included studies reported amblyopia prevalence [1, 3-5], and one of these also reported the prevalence of severe amblyopia [1]. One study reported the prevalence of mild, and moderate to severe visual deficits, but did not describe the type of visual deficits further [2]. Three studies reported referrals [1, 3, 4]. One study reported two different treatment outcomes [5].

Secondary outcomes

No study reported effects of screening on quality of life, academic performance, or treatment compliance. Two studies reported screening compliance [3, 4], and one compliance with referral [3].

Table 2. Characteristics of included studies (N=5)

Author Year	Population	Intervention	Comparison	Outcomes
Eibschitz-Tsimhoni 2000 *Country*: Israel *Study design*: controlled cohort study	*Total* N=1,590 *Screened*: N=808 (of whom 99.6%, N=779 did not have amblyopia at the age of 8, while 0.4%, N=3 children had amblyopia) *Unscreened*: N=782 *Age*: 8 year old *Gender*: no information *Ethnicity*: no information	*Screening*: Screening at the age of 8 (children previously screened at 1-2.5 years of age) *Vision tests used*: • Hirschberg corneal reflex test • Monocular fixation-and-following test • Ductions and versions examination • Cover-uncover test • Alternate cover test • Retinoscopy without cycloplegia *Failure/referral thresholds*: no information Profession of screener: an ophthalmologist or an ortoptist trained in retinoscopy *Definition of amblyopia*: as corrected visual acuity of ≤5/10 (20/40), or >1 line difference in corrected visual acuity between both eyes.	No screening	Primary outcomes:' • Amblyopia (all) • More severe amblyopia (with visual acuity of ≤5/15 (20/60)) • Referral and treatment (screened population only) Other outcomes: • Amblyopia not previously identified at infant screening • Screening sensitivity • Screening specificity
Feldmann 1980	*Total N*=1,488 *Screened:* N= 745 children	*Screening*: Two screening events, with 6 to 12 months in between	No screening (scheduled to be	Primary outcomes: • Visual deficits (mild, and moderate to severe)

Country: Canada *Study design:* Controlled cohort study	from the Hamilton area (17 schools); *Mean age:* 66.4 months; *Gender:* Ratio boys/girls; 1.17 *Un-screened:* N= 743 children from the Burlington area (18 schools) *Mean age:* 65.6 months *Gender:* Ratio boys/girls; 1.04 *Ethnicity:* similar race and ethnicity in the two cohorts, and children matched for age, sex and socioeconomic status	*Vision tests used:* • Illiterate Eye Chart Tumbling E *Failure/referral thresholds:* Vision of 20/40 in either or both eyes =mild impairment; and 20/50 or more in either or both eyes=moderate impairment. Profession of screeners: trained nurse-tester/public health nurse Definition of amblyopia: no	screened after the study)	Other outcomes: • Number (%) with glasses
Sloot 2015 *Country:* the Netherlands *Study design:* controlled cohort study	Total N: 11,811 *Screened:* N=6,188; *Unscreened:* N=5,623 *Mean age:* 9 months at last screening Gender, Ethnicity: and Socio-economic status similar Dropout: Screened group: N=129 (2.1%); Unscreened group: N=148 (2.5%)	*Screening:* at 1-2, 3-4 months, and at general health screening at 6-9 months *Vision tests used:* the VOV test which at 1–2 and 3– 4 months comprises: • inspection of the eyes, • pupillary reflexes, • eye motility • red fundus reflex testing and and at 6– 9 months comprises: • inspection of the eyes, • pupillary reflexes, • eye motility, • Hirschberg test, • cover test and • pursuit movements *Failure /referral thresholds:* not reported Profession of screeners: preventive trained child healthcare physicians and nurses Definition of amblyopia: no	Screening at 1-2 months, at 3-4 months (screening at 6-9 months omitted). No screening at 6 to 9 months i.e. different screening intensity: 2 screenings instead of 3 between 1 and 9 months	Primary outcomes: • Referrals • Number of diagnsed Amblyopia (combined with strabismus) cases Other outcomes: • Uncompliant with referral or unknown diagnosis • Ophthalmologic diagnosis • Drop-outs • Children screened in the unscreened group • Children not screened in the screened group
Williams 2001 *Country:* England *Study design:* NRCT	Total No of participants: N=3,490 Intensive screening program: N=2,029; Control:1,461 *Mean age:* up to 37 months *Gender and ethnicity:* no infor-	*Screening:* 5 screening events; at the ages of 8, 12, 18, 25 and 31 months *Vision test used:* • Visual acuity using behaviour when either eye were occluded (all ages), Cardiff Cards (8, 12, 18 25, and 31 months) • Kay pictures (25 and 31 months)	No screening: visual surveillance only (and ad hoc referrals)	Primary outcomes: • No of children with Amblyopia • Referrals

	mation, but randomly selected from a birth cohort	• Ocular alignment with the cover test (all ages) , Stereopsis with Langs test 1 and 2 (18, 25 and 31 month) • the Frisby test (12, 18, 25 and 31 months) • Motor fusion with the 20 Dioptre base-out test (all ages) • Non-cycloplegic photorefraction (using the Topcon PR 2000 paediatric refractometer) Note: The latter three were only collected to allow later analysis of their potential effectiveness as screening tests. Failure /referral thresholds: For suspected strabismus: any manifest deviation, any latent esophoria, a poorly controlled or large (>10 pd),latent exophoria. For reduced visual acuity: 1. Objection to occlusion of one eye more than the other, 2.ar-diff cards result below 0.9 logMAR at 12 months, 0.6 at 18 months, 0.4 at 25 months and 0.3 at 31 months, and 3.Kays picture results below empirically set levels of 6/12 at 25 months and 6/9 at 31 months. Profession of screeners: orthoptists (and health visitors and GPs in the control group)		
Williams 2002 *Country:* England *Study design:* Follow up of NRCT	Total no of participants: 3,490 Intensive screening program: N=2,029; Control (no previous screening):1,461	Follow-up screening at 7.5 years of age (intensive group) *Vision tests used:* Log MAR (log10 minimum angle of resolution, using ETDRS charts) at 4 m was measured, with glasses if worn, both with and without a pinhole *Failure thresholds:* "If the better (smaller Log MAR score) acuity obtained either with or without pinhole for either eye was 0.2 or worse or if there was a difference between the best acuity of the two eyes of 0.2 or more, the child was seen again in a further research clinic where *cyclopaedic retinoscopy and fundoscopy* were carried out. Glasses, referral to the hospital eye service, or both were offered if needed. If the best visual acuity of either eye was better than 0.2 but improved by 0.2 or more with the pinhole, the child's carer	Vision assessed at 7.5 years of age (no previous screening)	Primary outcomes: • Number of children with amblyopia • Vision outcomes (treated/non-treated) • Visual acuity in the worse eye • Previous treatment wth patching • Eye clinic visits

		was advised to see an opti-cian and given a referral note describing the study findings."		

Conflict of interest and study funding

Four of the included studies did not provide any information on possible conflicts of interest, or funding of the study. Only in one study [3] the authors declared no conflicts of interest.

Risk of bias assessment

Cohort studies

All three cohort studies were at low risk of bias [1-3]. See Appendix 4 for details.

Non-randomised controlled trials

The one included NRCT [4] , and its follow up study [5], were both at high risk of bias, mostly due to large losses to follow-up. See Appendix 5 for details.

Ethics

We did not address ethical considerations of vision screening in this systematic review.

Effects of the interventions

Primary outcomes

See Table 3 Results, and Summary of findings Table 4 below.
Five heterogeneous studies provided data for five different comparisons, i.e. only a single study provided data for each comparison (see below). All studies evaluated the effects of screening conducted before school start, and none evaluated the effects of school-screening. The studies reported three primary outcomes: amblyopia prevalence/visual deficits (5 studies); referrals (2 studies) and treatment outcomes (one study).

Comparison 1: Screening at 1-2.5 years of age vs. no screening: effects assessed at 8 years of age (one study)

Prevalence of amblyopia

Eibschitz-Tsimhoni [1] reported that fewer amblyopia cases were identified in 8-year old children previously screened at 1-2.5 years of age (8/808; 1.0%), as compared to previously unscreened children (20/782; 2.6%); RR (95% CI): 0.39 (0.17 to 0.87), P=0.0098.

True and false positive, and false negative

At the previous screening (at 1-2.5 years), 29 toddlers (3.58%) with suspected amblyopia were identified, of which 18 (2.2% of total) after further examination were confirmed to be at risk of amblyopia and thereafter treated (true positive). Eleven of the 29 toddlers were false positives i.e. they did not have any amblyogenic risk factors. Three children (0.4%) were found to have amblyopia when screened again at 8 years of age (false negative). The authors provided no information on the number of true or false positive children from the unscreened group that had been identified and referred during the study period.

Referrals

The number of referrals was only reported for the screened group.

Treatment outcomes

Eibschitz-Tsimhoni [1] also reported lower prevalence of more severe amblyopia in screened children (0.1%; 1/808; 0.1%), as compared to in unscreened children (1.7%; 13/782; 1.7%); RR (95% CI): 0.07 (0.01 to 0.57), P=0.01. Of the toddlers identified, when screened at age 1-2.5 years, as being at risk of amblyopia and treated (N=18), 13 toddlers had no amblyogenic visual loss, while five had amblyogenic visual loss at 8 years of age. The authors did not provide any information on the number of children in the unscreened group who had been diagnosed with amblyopia and treated, without having been screened.

Comparison 2: Screening at 4-4.5 years of age vs. no screening: effects assessed at 5.5 years of age (one study)

Prevalence of visual deficits

Feldman [2] reported that fewer of the children who had been screened 6-12 months previously had visual deficits (78 /763 children; 10%), as compared to unscreened children (112/743; 15%); RR (95% CI): 0.68 (0.52 to 0.89), P=0.005. The prevalence of mild visual deficits (20/40) was similar for screened children (54/763; 7%), and unscreened children (69/743; 9%); while fewer children in the screened group (24; 3%) than in the unscreened group (43; 6%) had moderate to severe vision problems (P<0.01). The authors provided no further information on the type of visual deficits (i.e. the diagnoses).

Referrals

Not reported.

Treatment outcomes

Fifty-eight percent more of the screened children (12; 1.6%) were wearing glasses, as compared to the unscreened children (19; 2.5%), but it was not clear if this was a treatment outcome i.e. it was unclear if they had been given glasses before or after the previous screening.

Comparison 3: Screening at 6-9 months vs. no screening at 6-9 months: effects assessed at 9 months (one study)

Prevalence of amblyopia

Sloot 2015 [3] reported a similar proportion of children who after referral were diagnosed with amblyopia combined with strabismus in the group of infants screened at 6-9 months (10/6,059; 0.17%) as in the group not screened at 6-9 months (6/5,482 infants; 0.11%); RR (95% CI): 1.51 (0.55 to 4.15), P=0.43. All children were, in accordance with the population-based screening programme, screened at 1-2 months, and 3-4 months of age. However, the confidence interval was wide, with the effect ranging from favouring the screening to a non-favourable effect.

One infant in the screened group (0.1%), who had amblyopia, or had been treated for amblyopia, had severe amblyopia, as compared to 13 (1.7%) children in the unscreened group; RR (95 % CI): 0.07 (0.01 to 0.57), P=0.01. Severe amblyopia was defined as visual acuity ≤5/15 (20/60) in the amblyopic eye.

Referrals

Sloot 2015, reported a similar proportion of referrals among the infants who were screened at 6-9 months (5876,059; 0.96%), as among those with no screen at 6-9 months (48/5,482; 0.88%); RR (95%): 1.09 (0.75 to 1.61), P=0.65. However, the confidence interval was wide, with the effect ranging from being in favour of the screening to a non-favourable effect.

Parents to nine infants (15.5%) in the screened group, and to 6 infants (12.5%) in the unscreened group did not comply with referral (or had unknown diagnosis), i.e. they did not bring their infant to the specialist for confirmation of diagnoses and treatment.

Twenty-six (44.8%) infants in the screened group and 26 (54.2%) in the unscreened group received no ophthalmologic diagnosis. Twenty-three (39.7%) screened infants received an ophthalmologic diagnosis, compared to 16 (33.3%) unscreened infants.

Treatment outcomes

Not reported

It should be noted that in this study [3] 524 (8.6%) children in the 'screened group' were not screened, and 434 (7.9%) children in the 'unscreened group' were screened. Also, for 1,596 children (29.1%) in the 'unscreened group' it was unclear whether or not they had been screened. Drop out was 2.1% in the screened group and 2.5% in the unscreened group.

Comparison 4: Intensive screening (at 8, 12, 18, 25, and 31 months) vs. no screening (visual surveillance only): effects assessed at 37 months (one study)

Prevalence of amblyopia

Williams 2001 [4] reported that more toddlers with amblyopia were identified in the intensive screening programme, at age 37 months (33/2,029; 1.6 %) as compared to in the unscreened group (8/1,461; 0.5%) who received visual surveillance only; RR (95% CI): 2.97 (1.38 to 6.41), P<0.006. Note that the results, which refer to an increased number of amblyopia cases identified through intensive screening, as compared to visual surveillance only (by health visitors and GPs), is considered a desired result.

The authors also reported that more children referred from the control group (who received visual surveillance by GPs and health visitors) were found to be false positives (110/1461; 7.5% vs. 92/2029; 4.5%, p<0.01).

Referrals

In Williams 2001 [4] there were in total fewer referrals at follow up among children in the intensive screening group (147/2,029; 7.2%; 117 referrals among intervention group attenders [N=1,408], and 30 referrals from non-attenders [N=621}), as compared to among control group participants (135/ 1,461; 9.2%); RR (95% CI):0.77 (0.60 to 0.98), P=0.03.

Treatment outcomes

Not reported.

Comparison 5: Screening (at 8, 12, 18, 25, 31 months) vs. no screening (visual surveillance only): effects assessed at 7.5 years of age (one follow-up study)

Prevalence of amblyopia

Williams 2002 [5], reported, in a follow up study, fewer amblyopia (all types) cases among 7.5 year old children in the intensive screening group (22/1088; 2.0%), than in the group of unscreened children (37/826; 4.48%); RR (95% CI): 0.45 (0.27 to 0.76), P=0.003.

Referrals

Data not useable.

Treatment outcomes

Williams 2002 [5] reported that patches were given to a similar proportion of children in the intensive screening group (40/1088; 3.7%), as in the unscreened group (40/826¸4.8%); RR (95% CI): 0.76 (0.49 to 1.17), P=0.21. The proportions of untreated amblyopia (no patching) in the intensive (4 children) and control groups (6 children) was also similar (P=0.42).

Williams also reported fewer cases with residual amblyopia in the intensive group (3/40), as compared to in the unscreened group (10/40); RR (95% CI): 0.30 (0.09 to 1.01), P=0.05.

In addition, the mean visual acuities (in the worse seeing eye) was better for children in the intensive group than for similar children in the control group (mean acuity 0.15 [95% CI 0.085 to 0.215] vs. 0.26 [0.173 to 0.347] LogMAR units; P=0.001).

Table 3 Results: prevalence of amblyopia, or other visual deficits, referrals, and treatment outcomes in screened vs. unscreened children at follow up (N=5).

Author Year	No participants	Risk Ratio (RR) (95% CI)		
		No (%) with amblyopia (or visual deficits)	No (%) referred	Treatment outcomes
Eibschitz-Tsumhoni 2000 [1]	Screened: 808; Unscreened: 742	Followed up after 5.5 to 7 years (i.e.at age 8 years): Screened (at 1-2.5 years years): 8 (1.0%); Unscreened: 20 (2.6%); RR (95% CI): 0.39 [0.17 to 0.87], P=0.02 No (%) with severe amblyopia*: Screened: 1 (0.1%)); Unscreened: 13 (1.7%): RR (95 % CI): 0.07 [0.01 to 0.57], P=0.01 *Visual acuity ≤5/15 (20/60)	Only data for the screened group pro-vided.	-
Feldman 1980 [2]	Screened: 763 ; Unscreened: 743	Followed up after 6 to 12 months (i.e. at age 5.5 years) No (%) with visual defi-cits: Screened (at 4-4.5 years): 78 (10%); Un-screened: 112 (15%); RR (95% CI): 0.68 [0.52 to 0.89], P=0.005	-	-
Sloot 2015 [3]	Screened:6,059; Unscreened: 5,482	Followed up after 3 months (at the age of 9 months): Screened (at 1-2, 3-4 and 5-9 months): 10 (0.17%); Unscreened (at 6-9 months, but screened at 1-2, and 3-4 months): 6 (0.11%); RR (95% CI): 1.51 [0.55 to 4.15], P=0.43	Screened: 58 (0.96%); Unscreened (no screen-ing at 6-9 months): 48 (0.88 %); RR (95%): 1.09 (0.75 to 1.61), P=0.65.	-
Williams 2001 [4]	Screened:2,029 ; Unscreened: 1,461	Followed up after 6 months (i.e. at the age of 37 months):	Screened: 147 (7.2%) (117/1408 attenders, and 30/621 non-attend-ers); Unscreened:135 (9.2%); RR (95% CI):	-

		Screened (at 8, 12, 18, 25, and 31 months): 33 ; Unscreened (visual surveillance only): 8; RR (95% CI): 2.97 [1.38 to 6.41], p=0.006	RR (95% CI):0.77 (0.60 to 0.98), P=0.03	
Williams 2002 [5]	Screened:2,029 ; Unscreened: 1,461 Note: Follow up of Williams 2001.	Followed up after approximately 4.5 years (i.e. at age 7.5 years) Screened (as in Williams 2001 above): 22 (2.0 %); Unscreened: 37 (4.5 %); RR (95% CI): 0.45 (0.27 to 0.75), P=0.003	No useable referral data.	**No (%) treated with patching:** Screened: 40 (3.7%): Unscreened: 40 (4.8%):RR (95% CI): 0.76 [0.49 to 1.17], P=0.21 **No (%) with residual amblyopia:** Screened: 3/40 (7.5%); Unscreened: 10/40 (25%); RR (95% CI): 0.30 [0.09 to 1.01], P=0.05.

Secondary outcomes

No secondary outcomes were reported in the included studies (i.e. no studies reported on quality of life, or academic performance).

Drop-out, fidelity, and compliance

Drop-out

In one study a similar proportion of children dropped out from the screened group (129/6,188 children; 2.1%), either due to having moved, no screening record, or non-use of the child healthcare clinic, as from the control group (141/5,623; 2.5%) [3].

In one study the number of children who dropped out were large in both the intensive group (941/2029;46.4%) as well as in the control group (665/1490; 44.6%) [4], and it was unclear how many of these children who took part in the follow up study at age 7.5 years [5].

Two studies [1, 2], provided no information on drop out from the study.

Fidelity

In one study, 69 percent of children (N=2,029) in the intensive screening group attended at least one of five screening opportunities that were offered. Fifty-four percent (N=1,089) of intervention children, and 64 percent (N=939) of control children attended the final assessment. Six-hundred and twenty-one of 2,029 children (30.5%) from the intervention group, and 522 of 1461 children from the control group (35.7%) did not attend any clinic [4].

Compliance to referral

In one study [3] the number of infants (and parents) uncompliant with referral (or unknown diagnosis), were nine (15.5%) in the screened group and six (12.5%) in the unscreened group [3].

Grading of the evidence

All primary outcomes in the cohort-studies were judged to be at low to very low certainty of evidence. The one NRCT also provided very low to low certainty evidence. The reasons for downgrading the already low certainty of evidence were mainly high risk of bias, and imprecision. See Appendix 6 for details.

Table 4. Summary of findings table (N=5)

Effects of vision screening for children vs. no screening (or fewer screening events)			
Population: infants, toddlers, pre-schoolers, and school children **Settings:** England, Canada, the Netherlands, and Israel **Intervention:** screening, different screening intensity/omitting screening **Comparison:** no screening, or lower screening intensity **Outcomes:** amblyopia prevalence, other visual deficits, referrals, treatment outcomes			
Outcomes	Effect	Number of participants (studies)	Certainty of the evidence (GRADE*)
Amblyopia	Un-pooled results from four heterogeneous studies (three cohort studies and one NRCT) suggest that it is uncertain whether vision screening may lead to lower prevalence of amblyopia in children, as compared to no screening.	16,572 (4 studies)	⊕⊖⊖⊖ Very low[1]
Other visual deficits	Results from a single study suggest that screening may possibly lead to lower prevalence of vision deficits, as compared to no screening.	1,506 (1 study)	⊕⊕⊖⊖ Low[2]
Referrals	Un-pooled results from two heterogeneous studies suggest that it is uncertain whether screening improve referrals.	15,301 (2 studies)	⊕⊖⊖⊖ Very low[3]
Treatment outcomes	Results from one study, reporting two different treatment outcomes (residual amblyopia, and patching), suggest that it is uncertain whether screening improves vision treatment outcomes.	3,490 (1 study)	⊕⊖⊖⊖ Very low[4]
* GRADE Working Group grades of evidence			
1 We downgraded the certainty of evidence one step due to high to moderate risk of bias from a majority of studies, and due to imprecision (i.e. from low to very low as observational studies start at low) 2 The certainty of evidence was low due to the observational study design. 3 We downgraded the certainty of evidence one step due to high risk of bias and imprecision. 4 We downgraded the certainty of evidence one step due to high risk of bias.			

Discussion

Summary of main results

We included five heterogeneous non-randomised studies in this systematic review. Meta-analysis was not feasible due to differences in populations, interventions and comparisons. The unpooled results for amblyopia prevalence, referrals and treatment (vision) outcomes constitute very-low to low certainty evidence, and can therefore not provide a reliable indication on whether or not screening may lead to improved eye health.

Overall completeness and applicability of evidence

Study designs, settings, and populations

We could not identify any relevant randomised studies on the topic. Thus, only non-randomised and observational evidence are included in this systematic review, i.e. study designs that provide evidence of lower quality since it is more susceptible to bias.

All included studies were conducted in high income countries, and none in low- or middle income countries (LMICs). This despite the fact that eye disorders and childhood blindness is a much more significant problem in LMICs [32].

In Norway there is no supplementary screening of children between 6 weeks and 4 years of age, while a majority of the included studies evaluated screening of children in that age group. Only one of the included studies [2] evaluated a comparison that may be more relevant for Norwegian conditions (screening at 4-4.5 years versus no screening). The results of this study indicates that screening of children in this age group may possibly lead to fewer vision problems, but the certainty of this evidence is low.

All studies evaluated the effects of early screening or pre-school screening, and no studies evaluated the effects of neonatal screening, or screening of school aged children. One study, which evaluated the effect of omitting one screening event in an otherwise comprehensive screening programme, suffered from contamination (i.e.

some children in the 'unscreened' group were screened, and some children in the 'screened' group were not, and for a non-negligible number of children, the screening status was unclear. In addition, if amblyopia had been detected at 6-9 months, it would have been too early for treatment effects to have been noticeable at the age of 9 months.

Vision screening: screeners, screening tests, screening intensity, sensitivity and specificity of tests

The profession of the screeners differed across studies, and constituted public health nurses, public health physicians, optometrists, and ophthalmologists. Those who were not specialists, all appeared to have received at least some training.

The screening tests used differed widely across the included studies, but since children of different ages were screened, this was maybe to be expected. There are however, according to a recent paper [33], two current best practice vision screening methods for children aged 36 to younger than 72 months: 1) monocular visual acuity testing using single HOTV letters or LEA Symbols, or 2) instrument-based testing using the Retinomax auto refractor or the SureSight Vision Screener with the Vision in Pre-schoolers [33]. LEA symbols, which is one of the most commonly used tests, were not used in any of the included studies, which may be due to the fact that most of the studies are relatively old.

The amblyopia definitions, and the failure thresholds used for referral (when reported) varied across studies.

As mentioned earlier, each included study contributed data to a single comparison. In three of the five included studies the standard screening programme was not described, and the total number of screening events was therefore unclear: e.g. in one study and for children screened at age 4-4.5 and for whom screening was repeated at 5 -5.5 years of age, it was unclear whether or not the 'unscreened children' had been screened as infants or toddlers.

Comparisons

Different follow up (range 3 months to 7 years) and different comparison interventions; no screening, visual surveillance only, or two early screenings vs three screenings, makes comparisons of the effect of interventions difficult.
There is a problem with using cohort studies when comparing vision screening with no screening, as this precludes any baseline measure of outcomes (i.e. amblyopia prevalence at baseline). One cannot therefore be certain that the cohorts were comparable in the first place. In the case of a consecutive controlled birth cohort conducted in the same region (with the same socioeconomic mix), like in the study by Sloot 2015 [3], this is less of a problem.

Outcomes

Amblyopia prevalence (or visual deficits)

The amblyopia prevalence reported in four of the five included studies differed greatly across studies: from 0.17% to 2.0% in screened children, and from 0.11% to 4.5% in unscreened children. One study reported 10% prevalence of visual deficits among children previously screened 6-12 months earlier (and 15% prevalence among unscreened children). These differences may be due to the variety of screening tools used (and thresholds used to define amblyopia), the number of previous screening events (the process of early screening and treatment), the children's age at the time of the screening, the experience and training of screeners, etc.. It may possibly also be due to the fact that some amblyopia cases develop at a later time [34]. The study that reported the lowest amblyopia prevalence (0.11%), was conducted in a country with one of the most extensive vision screening programmes in Europe, and where infants in the screened as well as in the unscreened group had been previously screened at 1-2 months, and again at 3-4 months, why it may not be surprising to find a very low prevalence 3-6 months later. In addition, this was the most recently published study, and therefore most likely to be most up to date in terms of screening guidelines, and methods/tools used etc.

Referrals

Three of the included studies reported on referrals, but one of them only for the screened group. It must be considered very unlikely that none of the unscreened children would have been referred (and treated) for example due to concerns raised by the parents, even if they were not screened. In the two studies that reported referrals for both groups, the proportion of children who were referred to a specialist ranged from 0.96% to 7.2% in the screened group and from 0.88% to 9.2% in the unscreened group. It is of course expected that a study with very low amblyopia prevalence (see above), also would report a very low referral rate.

In one study that compared intensive screening conducted by orthoptists with visual surveillance by GPs and health visitors, the number of false positives referred to specialist was significantly greater in the control group, which possibly may be due to differences in the skill and experience of those conducting the screening, or in the screening methods/tools used. A large number of false positive screens may give rise to unnecessary extra costs for the healthcare system.

Treatment outcomes

Treatment outcomes (patching and residual amblyopia) were reported in only one of the five included studies. A similar number of children in both groups were treated with patching, and a similar number were not. But, since treatment adherence was not reported, it is impossible to say whether the residual amblyopia was due to ineffective treatment, or non-compliance with treatment.

Quality of the evidence

All included studies were non-randomised, and typically therefore provide lower quality evidence as compared to randomised studies. The certainty of the evidence for our primary outcomes (i.e. amblyopia prevalence, referrals and treatment outcomes) was overall very low, mostly due to high risk of bias and imprecision.

Potential biases in the review process

We conducted a comprehensive and systematic search for studies that evaluated the effects of vision screening in children as compared to no screening (or different intensity or spacing of screening). A research librarian developed the search strategy, and conducted the search, which had no language restrictions. We also searched the reference lists of included studies and of other relevant publications, and contacted experts in the field. In addition, two authors independently screened all the references for inclusion, which makes it less likely that we may have missed any relevant studies. To minimise bias we also assessed the risk of bias and graded the certainty of the evidence in duplicate. No studies were excluded due to language.

Agreements and disagreements with other studies or reviews

We found no randomised studies eligible for inclusion, which is consistent with the two Cochrane systematic reviews on the topic, [7, 8]. In our review, we also searched for non-randomised study designs. The very low certainty of evidence from the studies included in our review makes it difficult to draw any firm conclusions about how useful screening is in improving the eye health of children. This, our conclusion is also in agreement with a HTA-report from 2012 on the effects of vision screening in pre-school children that conclude that "rigorous evidence is still lacking to conclusively evaluate the effectiveness of screening" and that "the best practice for conducting screening remains unclear" [35].

Conclusion

The evidence reported in this systematic review are of very low to low certainty, and we can therefore not draw any firm conclusions on whether or not vision screening of children under the age of 18 may lead to improved eye health (i.e. lower prevalence of amblyopia/ other vision deficits). The optimal timing, spacing and frequency of screening, i.e. the most effective screening practice remains unclear.

Identified research gaps

We found no randomised studies that compared screening with no screening. Comparing screening with 'no screening' does not necessarily mean that those that receive 'no screening' are not screened at all, and therefore at greater risk of eye problems, but that the number and spacing of screenings are different.

One example, is the recent publication by Sloot [3], which reported results from a study conducted in the Netherlands, where an extensive screening program is in place. The ethics committee gave green light to omit one screening event from one of the birth cohorts (who already had been screened twice within a relatively short period of time). The parents were free to decline participation in the study and to require that their child received the full screening programme. Also, in case of observed eye problems (by either parent or physician), or a history of vision problems in the family, the child healthcare physicians would perform eye exams also in intervention group children.

Another example, is where there is real uncertainty about the additional effect of screening interventions, like in Norway, where there is only a single screening at 4 years, it would still be ethically correct to randomise some children to one or more additional screenings, while other children are randomised to not receive the additional screening(s) (usual care) for the time period of the trial. Obviously, if results of the trial indicate that one option is better than another, all children would be considered for the one option most effective.

Future studies should use:

- A randomised study design to ensure the comparability of groups, or if a randomised design is not feasible, a consequetive birth cohort study
- Up-to-date and evidence based screening tools
- Skilled, and blinded screeners

Future studies should report:
- Sufficient information on the characteristics of participants (so comparability across groups can be assessed)
- Details of the screening program that is in place i.e. the standard vision screening program (i.e. the full screening history of children)
- The sensitivity and specificity of the screening tools
- The failure thresholds od screening tests that are used for referral
- The number of false positive, true positive and false negative screens (when screening is repeated)
- The numbers referred to specialist for confirmation of diagnosis and treatment (in both groups)
- The number of children compliant with referral
- The number of children treated
- The number of children compliant with treatment
- The treatment (vision) outcome
- Fidelity to repeated screening (in intensive screening programs)
- Drop-out from screening, and reasons for droput if available
- Cost and cost-effectiveness

It is maybe also possible to gain some knowledge on the effect of different screening intensity/school-screening by for example comparing the amblyopia prevalence in Norwegian school children (who have received only one pre-school screening), or Norwegian adolescents (who have received no school-screening), with that of children in other Scandinavian countries with more frequent pre-school screening, and where school screening is in place.

Implications for practice

There are, due to the very low to low certainty of evidence from a limited number of included studies, few implications for practice that can be drawn from the results of this systematic review. However, the results of a single study evaluating screening of 4-4.5 year old children, indicate that the current screening practice in Norway, i.e. screening of 4 year old children at the mandatory health check, may possibly lead to more children with eye problems being identified, which in turn could lead to fewer (and less severe) visual deficits in children.

References

1. Eibschitz-Tsimhoni, M., et al., *Early screening for amblyogenic risk factors lowers the prevalence and severity of amblyopia.* Journal of Aapos: American Association for Pediatric Ophthalmology & Strabismus, 2000. **4**(4): p. 194-9.
2. Feldman, W., et al., *Effects of preschool screening for vision and hearing on prevalence of vision and hearing problems 6-12 months later.* Lancet, 1980. **2**(8202): p. 1014-6.
3. Sloot, F., et al., *Effect of omission of population-based eye screening at age 6-9 months in the Netherlands.* Acta Opthalmologica, 2015. **93**(4): p. 318-21.
4. Williams, C., et al., *Screening for amblyopia in preschool children: Results of a population-based, randomised controlled trial.* Ophthalmic Epidemiology, 2001. **8**(5): p. 279-295.
5. Williams, C., et al., *Amblyopia treatment outcomes after screening before or at age 3 years: follow up from randomised trial.* BMJ, 2002. **324**(7353): p. 1549.
6. Hopkins, S., Sampson , G.P, Hendicott, P, Wood , J.M, *Review of guidelines for children's*

vision screenings. Clin Exp Optom 2013. **96**: p. 443-9.

7. Evans, J., Morjaria, P, Powell, C, *Vision screening for correctable visual acuity deficits in school-age children and adolescents.*
. Cochrane Database of Systematic Reviews 2018(2).

8. Powell, C., Hatt, S.R, *Vision screening for amblyopia in childhood.* Cochrane Database of Systematic Reviews 2009(3).

9. Institute of Health Economics, *The safety and effectiveness of preschool vision screening.* 2012, Institute of Health Economics: Edmonton.

10. Sloot, F., Hoeve, H.L, de Kroon, M. L, Goedegebure, A, Carlton, J, Griffiths, H.J, Simonsz, H.J, *Inventory of current EU paediatric vision and hearing screening programmes.* Journal of Medical Screening, 2015. **22**(2): p. 55-64.

11. White, S.L.J., wood, J.M, Black, A.A, Hopkins, S, *Vision screening outcomes of Grade 3 children in Australia: Differences in academic achievement.* International Journal of Educational Research, 2017. **83**: p. 154-9.

12. Coats, D.K., Paysse, E.A *Amblyopia in children: Classification, screening, and evaluation.* UpToDate 2018 [cited 2018 16.04.18 at https://www.uptodate.com/contents/amblyopia-in-children-classification-screening-and-evaluation].

13. Coats, D., Paysse, EA,, *Amblyopia in children: classification, screening and evaluation*, ed. R. Saunders, Armsby, CA. 2018.

14. Mema, S.C., McIntyre, L, Musto, R, *Childhood Vision Screening in Canada: Public Health Evidence and Practice.* Can J Public Health, 2011. **103**(1): p. 40-5.

15. Nørregaard, J.C., Kruse, M, Olsen, J, *Synscreening af førskolebarn- en kommenteret udenlandsk medicinsk teknologivurdering*, in *Kommenterert Udenlandsk Medicinsk Teknologivurdering*. 2010, Sundhetsstyrelsen, Monitorering & Medicinsk teknologivurdering: København.

16. Sosial- og Helsedirektoratet, *Retningslinjer for undersøkelse av syn, hørsel og språk hos barn*, Helsedirekoratet, Editor. 2005: Oslo.

17. Socialstyrelsen, *Sammanställning av vägledande dokument för barn- och skolhälsovård– Danmark, England, Finland, Norge och Sverige*. 2012, Socialstyrelsen: Sverige.

18. Cagini, C., et al., *Red reflex examination in neonates: evaluation of 3 years of screening.* International Ophthalmology, 2017. **37**(5): p. 1199-1204.

19. Logan, N.S., Gilmartin, B, *School vision screening, ages 5–16 years: the evidence-base for content, provision and efficacy.* Ophthalmic and Physiological Optics, 2004. **24**(6): p. 481-92.

20. Saxena, R., et al., *Incidence and progression of myopia and associated factors in urban school children in Delhi: The North India Myopia Study (NIM Study).* PLoS ONE [Electronic Resource], 2017. **12**(12): p. e0189774.

21. Sharma, A., Congdon, N, Patel, M, Gilbert, C, *School-based approaches to the correction of refractive error in children.* Survey of Ophtalmology, 2012. **57**(3): p. 272-83.

22. Cochrane Collaboration, *Cochrane Handbook for Systematic Reviews of Interventions* J.P.T. Higgins, Green, S Editor. 2011.

23. Kunnskapssenteret, *Slik oppsummerer vi forskning*, in *Håndbok for Nasjonalt kunnskapssenter for helsetjenesten* 2015.

24. Ouzzani, M., Hammady, H, Fedorowicz, Z , Elmagarmid, A *Rayyan — a web and mobile app for systematic reviews.* Systematic reviews, 2016. **5**: p. 210.

25. Cochrane Collaboration, *Chapter 8: Assessing risk of bias in included studies*, in *Cochrane Handbook for Systematic Reviews of Interventions*, J.P.T. Higgins, Green, S Editor. 2011, Cochrane Collaboration.

26. Cochrane Effective Practice and Organisation of Care group (EPOC). *Suggested risk of bias criteria for EPOC reviews. EPOC resources for review authors.* 2017 [cited 2018 Accessed 18 April 2018 at epoc.cochrane.org/epoc-resources-review-authors].

27. Sterne, J., Hernán, MA, Reeves, BC, Savović, J, Berkman, ND, Viswanathan, M, et al *ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions.* British Medical Journal, 2016. **355**: p. i4919.

28. The GRADE Working Group, *GRADE handbook for grading quality of evidence and strength of recommendations*, H.

Schünemann, Brożek, J, Guyatt, G, Oxman, A, Editor. 2013.

29. The GRADE Working Group, *GRADEpro GDT: GRADEpro Guideline Development Tool [Software].* 2015, McMaster University(developed by Evidence Prime, Inc.): Canada.

30. Sloot, F., et al., *The effect of omitting an early population-based vision screen in the Netherlands: A micro-simulation model approach.* Journal of Medical Screening, 2017. **24**(3): p. 120-126.

31. Williams, C., et al., *Amblyopia treatment outcomes after preschool screening v school entry screening: observational data from a prospective cohort study.* British Journal of Ophthalmology, 2003. **87**(8): p. 988-93.

32. World Health Organisation. *Blindness and vision impairment prevention.* 2018 accessed the 17 of August 2018 at http://www.who.int/blindness/causes/priority/en/index3.html].

33. Cotter, S.A., et al., *Vision Screening for Children 36 to <72 Months: Recommended Practices.* Optometry and Vision Science, 2015. **92**(1): p. 6-16.

34. Coats, D., Paysse, EA, . *Amblyopia in children: classification, screening, and evaluation.* 2018 [cited accessed the 21 August 2019 at https://www.uptodate.com/contents/amblyopia-in-children-classification-screening-and-evaluation.

35. *The safety and effectiveness of preschool vision screening* Health Technology Assessment Database, 2012.

36. Abrahamsson, M., et al., *A longitudinal study of a population based sample of astigmatic children. I. Refraction and amblyopia.* Acta Ophthalmologica, 1990. **68**(4): p. 428-34.

37. Allen, S.M., *The effectivity of screening a comparative study of visual screening.* British Orthoptic Journal, 1990(47): p. 57-60.

38. Colak, E. and H. Gursoy, *Truncated logistic regression for matched case-control studies using data from vision screening for school children.* Biomedical Research (India), 2017. **28**(15): p. 6808-6812.

39. Falkenberg, H.K., T. Langaas, and E. Svarverud, *Outcomes of large sample vision screening among school children aged 7-15 years in Norway.* Investigative Ophthalmology and Visual Science, 2014. **55 (13)**: p. 5570.

40. Gjelle, J.V.B., et al., *Prevalence of refractive errors and self-reported near-work, indoor and outdoor activities in Norwegian adolescents.* Investigative Ophthalmology and Visual Science, 2016. **57 (12)**: p. 3985.

41. Glewwe, P.W., KL. Lee, J., *The Impact of Providing Vision Screening and Free Eyeglasses on Academic Outcomes: Evidence from a Randomized Trial in Title I Elementary Schools in Florida.* Journal of Policy Analysis & Management, 2018. **37**(2): p. 265-300.

42. Goodman, L., et al., *Vision screening at two years does not reduce the prevalence of*

reduced vision at four and a half years of age. Clinical & Experimental Optometry, 2017. **28**: p. 28.

43. Huang, C.H., et al., *Economic evaluation on vision screening for preschool children.* Value in Health, 2010. **13 (7)**: p. A563.

44. Kemper, A.R., et al., *Improving the rate of preschool vision screening: an interrupted time-series analysis.* Pediatrics, 2011. **128**(5): p. e1279-84.

45. Kohler, L. and G. Stigmar, *Visual disorders in 7-year-old children with and without previous vision screening.* Acta Paediatrica Scandinavica, 1978. **67**(3): p. 373-7.

46. de Koning, H.J., et al., *Effectiveness of screening for amblyopia and other eye disorders in a prospective birth cohort study.* Journal of Medical Screening, 2013. **20**(2): p. 66-72.

47. Maqsud, M.A. and G.E. Arblaster, *The incidence and visual acuity outcomes of children identified with ametropic amblyopia by vision screening.* Journal of Aapos: American Association for Pediatric Ophthalmology & Strabismus, 2015. **19**(2): p. 104-7.

48. Nishimura, M., D. Maurer, and A.M.F. Wong, *An evaluation of a school-based screening program to detect amblyopia and refractive errors in kindergarten children.* Investigative Ophthalmology and Visual Science. Conference, 2017. **58**(8).

49. Svarverud, E., T. Langaas, and H.K. Falkenberg, *The effectiveness of vision screening for visual problems in school children.* Investigative

Ophthalmology and Visual Science, 2014. **55 (13)**: p. 5569.

50. Telleman, M.A.J., et al., *Visual acuity measurement at 36 months in population-wide eye screening in the Netherlands: 17-22% failure rate.* Investigative Ophthalmology and Visual Science. Conference, 2017. **58**(8).

Appendix

Appendix 1. Search strategy

Search strategies

Embase 1974 to 2018 May 07

Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Date: 8 May 2018

1	(Vision Screening/ or ((Mass Screening/ or Neonatal Screening/ or Population Surveillance/) and exp Vision, Ocular/)) use ppez	2051
2	((screening/ or mass screening/ or newborn screening/) and exp vision/) use oemezd	1671
3	((vision or visual) adj3 screen*).mp.	6954
4	or/1-3	8343
5	(exp Infant/ or exp Child/ or Adolescent/) use ppez	3286807
6	(exp child/ or adolescent/) use oemezd	3270672
7	(child* or adolescen* or preadolescent* or pediatric* or paediatric* or boy? or girl? or kid? or juvenil* or under?age* or infant? or newborn? or neonate* or toddler* or Pre-adolescen* or minor? or prepubescen* or pre-pubescen* or preteen* or pre-teen* or preschool* or pre-school* or pupil? or schoolage* or school-age* or schoolchild* or school-child* or schooler* or teen? or teenager* or teen-ager* or underage* or under-age* or youngster* or youth or young people or young person* or ((primary or secondary or elementary or middle or high) adj school student*)).tw,kw,kf.	5085459
8	or/5-7	8252780
9	4 and 8	4052
10	((animals/ or (rat or rats or mouse or mice).ti.) not (animals/ and humans/)) use ppez	4496532
11	(exp experimental organism/ or animal tissue/ or animal cell/ or exp animal disease/ or exp carnivore disease/ or exp bird/ or exp experimental animal welfare/ or exp animal husbandry/ or animal behavior/ or exp animal cell culture/ or exp mammalian disease/ or exp mammal/ or exp marine species/ or nonhuman/ or animal.hw. or (rat or rats or mouse or mice).ti.) not human/	10282334
12	9 not (10 or 11)	4027

13	remove duplicates from 12	2825

Cochrane Database of Systematic Reveiws

Cochrane Central Register of Controlled Trials

DARE

HTA database

NHS EED

All via The Cochrane Library

Date: 8 May 2018

#1	([mh "Vision Screening"] or (([mh ^"Mass Screening"] or [mh ^"Neo-natal Screening"] or [mh ^"Population Surveillance"]) and [mh "Vision, Ocular"]))	135
#2	((vision or visual) near/3 screen*):ti,ab,kw	369
#3	((vision or visual) near/3 screen*)	421
#4	#1 or #2	369
#5	#1 or #3	421
#6	([mh Infant] or [mh Child] or [mh ^Adolescent])	109869
#7	(child* or adolescen* or preadolescent* or pediatric* or paediatric* or boy or boys or girl or girls or kid or kids or juvenil* or (under next age*) or infant or infants or newborn or newborns or neonate* or toddler* or pre-adolescen* or minor or minors or prepubescen* or pre-pubescen* or preteen* or pre-teen* or preschool* or pre-school* or pupil or pupils or schoolage* or school-age* or school-child* or school-child* or schooler* or teen or teens or teenager* or teen-ager* or underage* or under-age* or youngster* or youth or young people or (young next person*) or ((primary or secondary or elementary or middle or high) next school student*)):ti,ab,kw	234205
#8	(child* or adolescen* or preadolescent* or pediatric* or paediatric* or boy or boys or girl or girls or kid or kids or juvenil* or (under next age*) or infant or infants or newborn or newborns or neonate* or toddler* or pre-adolescen* or minor or minors or prepubescen* or pre-pubescen* or preteen* or pre-teen* or preschool* or pre-school* or pupil or pupils or schoolage* or school-age* or school-child* or school-child* or schooler* or teen or teens or teenager* or teen-ager* or underage* or under-age* or youngster* or youth or young people or (young next person*) or ((primary or secondary or elementary or middle or high) next school student*))	250276
#9	(#1 or #2) and (#7 or #7) in Cochrane Reviews (Reviews and Protocols) and Trials	166
#10	(#1 or #3) and (#6 or #8) in Other Reviews, Technology Assessments and Economic Evaluations	37

Epistemonikos

Date: 8 May 2018

Searched in Title/Abstract:

((vision OR visual) AND screen*) AND (child* or adolescen* or preadolescen* or pediatric* or paediatric* or boy or boys or girl or girls or kid or kids or juvenil* or infant or infants or newborn or newborns or neonate* or toddler* or pre-adolescen* or minor or minors or prepubescen* or pre-pubescen* or preteen* or pre-teen* or preschool* or pre-school* or pupil or pupils or schoolage* or school-age* or schoolchild* or schoolchild* or schooler* or teen or teens or teenager* or teen-ager* or underage* or underage* or youngster* or youth)

Appendix 2. List of excluded studies

Study First author (reference no.)	Cause for exclusion of study
Abrahamsson 1990 [36]	No comparison with no screening or different screening intensity.No control group.
Allen 1990 [37]	Ineligible study design. Survey only.
Colak 2017 [38]	No comparison with no screening or different screening intensity. Comparison of different statistical methods.
Falkenberg 2014[39]	No comparison with no screening or different screening intensity. Looks at prevalence of vision problems in schoolchildren.
Gielle 2016 [40]	No comparison with no screening or different screening intensity. Looks at prevalence of vision problems in schoolchildren and relation to selfreported near work, and in and outdoor activities.
Glewwe 2018 [41]	RCT. Compares the effects of vision screening with that of vision screening accompanied by eye exams and eyeglasses. No data for group with no screening.
Goodman 2017 [42]	Do not evaluate the effects of universal screening, but of targeted screening for a specific condition.
Huang 2010 [43]	Conference abstract only. Economic evaluation of vision screening.
Kemper 2010 [44]	Looks at ways of standardising screening. Evaluates training of screeners. No comparison screening vs. no screening.
Køhler 1978 [45]	No established controlled group at the start of the study.
De Koning [46]	Prospective (controlled) birth cohort. Compares with prevalence rates in the literature (retrospective data).
Maqsud 2015 [47]	Only about amblyopia incidence among screened population and treatment effects (not a comparative study).
Nishimura 2017 [48]	Conference abstract only. Randomised controlled study. Assesses the efficacy of vision screening in children aged 3 to 6 years.
Svarverud 2014 [49]	Conference abstract only. Unclear if cross-sectional or other study design.
Sloot 2017 [30]	Microsimulation based on data from another study by the same author.
Telleman 2017 [50]	Conference abstract only. Controlled cohort study. Probably building on the study by Sloot 2015 (check)

Appendix 3. List of included studies (N=5)

Study First author (reference no.)	Citation
Eibschitz-Tsimhoni et al.2000 [1]	*Early screening for amblyogenic risk factors lowers the prevalence and severity of amblyopia.* Journal of Aapos: American Association for Pediatric Ophthalmology & Strabismus, 2000. 4(4): p. 194-9.
Feldman et al 1980 (24)	*Effects of preschool screening for vision and hearing on prevalence of vision and hearing problems 6-12 months later.* Lancet, 1980. 2(8202): p. 1014-6.
Sloot et al.2015 (25)	*Effect of omission of population-based eye screening at age 6-9 months in the Netherlands.* Acta Opthalmologica, 2015. 93(4): p. 318-21.
Williams et al 2001 (26)	*Screening for amblyopia in preschool children: Results of a population-based, randomised controlled trial.* Ophthalmic Epidemiology, 2001. 8(5): p. 279-295.
Williams et al. 2002 (28)	*Amblyopia treatment outcomes after preschool screening v school entry screening: observational, or another one?*

Appendix 4. Risk of bias - Cohort studies

RoB items- Cohort studies (assessed with ROBINS-1 Tool)				
	Eibschitz-Tsim-honi 1999	**Feldman 1980**	**Sloot 2015**	
Confounding	LOW RISK	LOW RISK	LOW RISK	
Selection of participants into the study	LOW RISK	LOW RISK	LOW RISK	
Classification of intervention	LOW RISK	LOW RISK	LOW RISK	
Deviations from intended intervention	LOW RISK	LOW RISK	LOW RISK	
Missing data	LOW RISK	LOW RISK	LOW RISK	
Measurement of outcomes	MODERATE RISK	LOW RISK	LOW RISK	
Selection of the reported results	LOW RISK	LOW RISK	LOW RISK	
Overall risk of bias	**MODERATE RISK**	**LOW RISK**	**LOW RISK**	

Appendix 5. Table Risk of bias - NRCTs

RoB items- Non-randomised controlled studies (assessed with the Cochrane EPOC Risk of bias tool)				
	Williams 2001	Williams 2002*		
Random sequence generation	HIGH RISK	HIGH RISK		
Allocation concealment	UNCLEAR RISK	UNCLEAR RISK		
Blinding of participants and personnel	N/A	N/A		
Blinding of outcome assessment	LOW RISK	LOW RISK		
Incomplete outcome data	HIGH RISK	HIGH RISK		
Baseline characteristics similar	UNCLEAR RISK	UNCLEAR RISK		
Baseline outcome data similar	N/A (or UNCLEAR as no baseline data)	N/A (or UNCLEAR as no baseline data)		
Selective outcome reporting	LOW RISK	LOW RISK		
Other bias	LOW RISK	LOW RISK		
Overall risk of bias	**HIGH RISK**	**HIGH RISK**		

*Williams 2002 was a follow up study of Williams 2001

Appendix 6. GRADE evidence profiles

Author Year	Risk of bias	Inconsistency	Imprecision	Indirectness	Publication bias	Certainty of evidence
	Amblyopia (and other vision deficits)					
Eibschitz-T 2000	Moderate	No	No	No	No	Low
Feldman 1980	Low	No	No	No	No	Low
Sloot 2015	Moderate	No	Severe	No	No	Very low
Williams 2001 (NRCT)	High	No	Moderate	No	No	Very low
Williams 2002	High	No	Moderate	No	No	Very low
	Referrals					
Eibschitz-T 2000						
Feldman 1980						
Sloot 2015	Moderate	No	Severe	No	No	Very low
Williams 2001- (NRCT)	High	No	No	No	No	Low
Williams 2002	Data not useable.					
	Vision (treatment) outcomes					
Eibschitz-T 2000	Moderate	No	No	No	No	Very low
Feldman 1980						
Sloot 2015						
Williams 2001 (NRCT)						
Williams 2002	High	No	No	No	No	Very low

NIPH