



*UK National
Screening Committee*

Childhood vision screening

External review against programme appraisal criteria for the UK National Screening Committee

Version: 3 – Consultation document

Authors: Ameenat L Solebo, Jugnoo S Rahi

Date: 27th Feb 2019

The UK National Screening Committee secretariat is hosted by Public Health England.

About the UK National Screening Committee (UK NSC)

The UK NSC advises ministers and the NHS in the 4 UK countries about all aspects of [population screening](#) and supports implementation of screening programmes.

Conditions are reviewed against [evidence review criteria](#) according to the UK NSC's [evidence review process](#).

Read a [complete list of UK NSC recommendations](#).

UK NSC, Floor 5, Wellington House, 133-155 Waterloo Road, London, SE1 8UG

www.gov.uk/uknsc

Twitter: [@PHE_Screening](#) Blog: phescreening.blog.gov.uk

For queries relating to this document, please contact: phe.screeninghelpdesk@nhs.net

© Crown copyright 2016

You may re-use this information (excluding logos) free of charge in any format or medium, under the terms of the Open Government Licence v3.0. To view this licence, visit [OGL](#) or email psi@nationalarchives.gsi.gov.uk. Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

Published **February 2019**

Contents

About the UK National Screening Committee (UK NSC)	2
Plain English summary	5
Executive summary	6
Purpose of the review	6
Background	6
Focus of the review	7
Recommendation under review	7
Findings and gaps in the evidence of this review	8
Recommendations on screening	9
Evidence uncertainties	10
Introduction and approach	11
Background	11
Objectives	13
Methods	16
Databases/sources searched	21
Question level synthesis	22
Part One	22
Criterion 13 — harms of childhood vision screening	22
Eligibility for inclusion in the review	22
Description of the evidence	23
Discussion of findings	24
Summary of Findings Relevant to Criterion 13: Criterion not met	26
Part Two	27
Criterion 1 — long-term adverse impact of amblyopia	27
Eligibility for inclusion in the review	28
Description of the evidence	28
Discussion of findings	30
Summary of Findings Relevant to Criterion 1: Criterion not met	37
Criterion 11 — clinical effectiveness of childhood vision screening	39
Eligibility for inclusion in the review	39
Description of the evidence	40
Discussion of findings	41
Summary of Findings Relevant to Criterion 11: Criterion not met	42
Criterion 14 — cost-effectiveness of childhood vision screening	42
Eligibility for inclusion in the review	43
Description of the evidence	43
Summary of Findings Relevant to Criterion 14: not met	44
Review summary	45

Conclusions and implications for policy	45
Limitations	46
Appendix 1 — Search strategy	47
Electronic databases	47
Search Terms	48
Appendix 2 — Included and excluded studies	53
PRISMA flowchart	53
Appendix 3 — Summary and appraisal of individual studies	61
Appraisal for quality and risk of bias	80
Appendix 4 – UK NSC reporting checklist for evidence summaries	104
References	108

Plain English summary

Amblyopia (known as lazy eye) is a childhood condition of reduced vision, usually affecting one eye. This happens because the eye does not develop a strong link with the brain. The most common conditions that cause amblyopia are squint and long/short sightedness. Treatment is with glasses and/or patches to cover the better seeing eye or eye drops to blur it. The patching or eye drops allow the weaker eye to develop stronger links in the brain. The brain is more able to respond in younger children. If amblyopia treatment is delayed, the reduced vision may become permanent. If an amblyopic individual loses vision in the good eye from any other cause later in life, they will be left with poor vision.

Currently, the UK National Screening Committee (NSC) recommends screening of children's eyes when they are 4 to 5 years old. This is to detect reduced vision in one or both eyes. All children who fail the vision test are referred on to a specialist. The main problem found by screening is amblyopia.

The UK NSC last looked at vision screening in 2012. There was little evidence on the:

1. long-term negative impact of amblyopia with or without treatment
2. clinical and cost effectiveness of childhood vision screening
3. the benefits versus the harms of childhood vision screening

The aim of this review was to look at new evidence and decide whether the current recommendation should change.

The review found that there was still little evidence on the harms of childhood vision screening. There may be a high number of children told they have poor vision when they do not. There may also be a high number of children who are not brought for a follow up check.

The review also found that amblyopia can have a negative impact on:

1. eye movements, resulting in slower reading speed (but comprehension is not worse)
2. hand-eye co-ordination activities in experimental settings

There was no evidence of other important negative long-term outcomes of amblyopia.

There was little evidence on the clinical effectiveness of screening. There was also no evidence on the cost-effectiveness of screening.

The evidence found in this review is not enough to change the recommendations.

Executive summary

Purpose of the review

The purpose of this document is to review the evidence on childhood screening for reduced vision.

Part one is a high level triage review of the current vision screening programme. In line with the UK NSC processes for existing programmes, this part of the review scans the literature to identify 'red flags' around the harms of childhood vision screening, which suggest that further exploration of programme cessation may be necessary. These reviews have a surveillance function and are not intended as comprehensive reviews of the programme.

Part two is a more comprehensive review examining the literature on important evidence gaps identified in the previous review.

Background

The UK NSC recommendation is that all children aged 4 to 5 years old should undergo testing to detect reduced vision in one or both eyes so that they can be referred for diagnostic examination and treatment as necessary. The key target disorder for this programme is amblyopia. Individuals with amblyopia have reduced vision due to disturbance of the normal developmental processes in the brain's visual neural pathways during the most vulnerable period of early childhood. In the UK, the majority of children with visual impairment in both eyes are detected in the first year of life, or as part of the diagnosis of another associated disorder, or because the child is noted to have difficulty seeing. However, amblyopia is not detected through these pathways. It is a condition that most commonly affects vision in only one eye. As the brain ignores the information coming in from the amblyopic eye, children do not realise that there is a problem until the vision is tested.

Poor vision in one eye increases the lifelong risk of 'complete' blindness due to later loss of vision in the good eye. Early detection of amblyopia is necessary to avoid permanent visual deficit by allowing treatment to be undertaken within the sensitive period of neuroplasticity (growth and change) in the visual system. The most common conditions predisposing to amblyopia are strabismus (squint) and refractive error (problems focusing due to long or short-sightedness). In rare cases, however, amblyopia can arise from 'form deprivation' caused by structural abnormalities such as congenital cataract. Children with refractive amblyopia undergo correction of the refractive error. Unilateral amblyopia is also treated with penalisation of the better seeing eye (through eye patches or defocusing eye drops). This takes advantage of the physiological 'competitive' relationship between the visual pathways serving the two eyes, and enables the vision in the amblyopic eye to improve. Structural anomalies are treated surgically. In some cases, the

amblyopia is multifactorial, and all necessary modes of intervention will be used, with surgery followed by refractive correction and ending with penalisation.

Focus of the review

The current review update aims to synthesise and appraise the available evidence published since July 2012 (when the previous UK NSC review search was completed). This evidence summary includes studies published up to 14th August 2018. It considers 4 questions. One is a triage review question around the harms of childhood vision screening to assess whether further exploration is needed for programme cessation. The remaining 3 rapid review questions are around the long-term impact of amblyopia, and the clinical and cost effectiveness of screening:

1. What harms do individuals experience after participating in a childhood vision screening programme for vision defects? (criterion 13)
2. What is the long-term adverse impact of amblyopia with and without treatment? (criterion 1)
3. What is the clinical effectiveness of vision screening in children aged 4 to 5 years? (criterion 11)
4. What is the cost-effectiveness of vision screening in children aged 4 to 5 years? (criterion 14)

Recommendation under review

Currently, the UK NSC recommends vision screening for children aged 4 to 5 years in an orthoptic led screening service, with testing using a crowded logMAR acuity chart. This was based on the findings of the 2012 review, which concluded that:

- Amblyopia can increase the risk of vision impairment or blindness due to subsequent loss of vision in individual's non-amblyopic eye.
- Screening at ages under 4 years may increase the proportion of children with normal vision who, because of their developmental status, 'fail' vision screening necessitating further examination to accurately assess their vision and rule out amblyopia, thus increasing opportunity and economic costs. Screening later than the age of 4 to 5 years is likely to result in poorer outcomes in children with moderate and severe amblyopia, and is unlikely to confer benefit in terms of increased reliability of testing.

However, the review also highlighted that there remained limited evidence on the clinical effectiveness of screening at ages 4 to 5 years old or that the overall benefits of childhood vision screening at this age would outweigh any harms. There was also an absence of evidence on the

long-term adverse impact of amblyopia in the absence or presence of childhood treatment and on the cost effectiveness of screening.

Findings and gaps in the evidence of this review

The main conclusions of this review were as follows:

Part One

1. There is currently an absence of specific evidence on the harms of childhood vision screening as practiced within current UK NSC recommendations. The evidence on harms is limited to inconsistent evidence on non-attendance to subsequent diagnostic examination (ranging from 20% to 61%) and false positive numbers following screening (ranging from 15% to 39%). These data came from studies which are not directly applicable to recommended practice in the UK. **Criterion 13: Not met**

Part Two

2. From 18 studies, the review found that amblyopia diagnosed through screening at age 4 to 5 years old can have a negative impact on the type of eye movements which are used to track words across a page when reading, compared with individuals without amblyopia. Amblyopic eyes make larger, less accurate 'fine tuning' movements, 'over-shoot' their intended target, and perform slower at searching tasks. These eye movement difficulties are consistent with reports of slower reading speed in individuals with amblyopia. However, reading comprehension is not affected. There was also evidence that loss of depth perception due to reduced vision in one eye can negatively impact hand-eye co-ordination activities within experimental settings. However, the 'real-life' consequences of this remain unclear. Finally, there was limited evidence suggesting that there was no impact of amblyopia on educational outcomes and self-esteem. This evidence summary did not identify any evidence of the impact of amblyopia on the patient perceived disutility, general health, quality of life, adverse health events, or specific occupational restrictions.

There was also no evidence on any outcomes of untreated amblyopia versus treated amblyopia. Consequently, the impact of amblyopia treatment remains unclear. The papers on outcomes which have highest applicability to the UK setting, and the lowest risk of bias were, conversely, those least able to inform on the impact on treatment, as participants within these studies all received routine management after diagnosis of amblyopia in early childhood. However, it may not be possible to identify new high level evidence on outcomes of amblyopia in treated versus untreated populations, as it would

be unethical to randomise children to no treatment when treatment is clinically recommended. **Criterion 1: Not met**

3. There was an absence of direct evidence on the clinical effectiveness of screening. There is weak but consistent evidence from 2 observational studies which suggests that populations which undergo childhood vision screening have statistically lower prevalence of amblyopia in adulthood than historical controls (difference of 0.45% in 1 study and 1.34% in another). However, causal relationships between the two are not proven. Furthermore, there was no evidence on the effect of screening on quality of life, socioeconomic outcomes, behavioural and functional outcomes, or patient-perceived disutility of amblyopia or of bilaterally poor vision due to loss of vision in the better eye of an amblyopic individual later in life. **Criterion 11: Not met**
4. There was no evidence on the cost effectiveness of vision screening. **Criterion 14: Not met**

Recommendations on screening

This updated analysis of the evidence for vision defects screening in children against the UK NSC criteria did not identify sufficient evidence to support a change in the previous recommendation. The main reasons for this are a failure to identify any harms from childhood vision screening.

Limitations

This review has used a rapid evidence review approach. Such an approach may result in under-ascertainment of available evidence. However, hand searching of the reference sections of identified studies was undertaken, which should have ensured a capture of available evidence. This review excluded those articles not written in English. However, the review should still have captured evidence from populations sufficiently similar to that found within the target population for the screening programme.

Articles were screened by a single reviewer. A second reviewer examined all included articles, 20% of excluded articles and any articles where there was uncertainty about inclusion or exclusion. This provided validation of the evidence selection process, and has ensured that articles where the eligibility was unclear were reviewed twice.

Evidence uncertainties

This review identified the following evidence gaps in the evidence base on the 4 questions assessed:

- The harms of vision screening at age 4 to 5 years
- The real-life educational, socioeconomic, quality of life or other functional consequences of amblyopia
- The clinical effectiveness of vision screening for children aged 4 to 5 years
- The cost effectiveness of vision screening for children aged 4 to 5 years

Introduction and approach

Background

The majority (>97%) of children with significantly reduced vision affecting both eyes are diagnosed early in childhood due to the concerns of carers / care-givers, or in the context of the routine universal Newborn and Infant Physical Examinations.(1) However, children with amblyopia do not experience sight loss, rather they simply grow up without vision developing to its full potential. These children are unlikely to be aware of the poorer vision in their amblyopic eye and unlikely to be picked up.

Amblyopia is a disorder characterised by failure of normal visual development, affecting the vision in one, or less commonly, both eyes.(2) Childhood visual maturation is dependent on presentation of a clear, focused image to the visual system during the sensitive period of the developmental “window” of neuroplasticity. This window ‘opens’ in early infancy, and the system is progressively less sensitive as the child grows. Visual blur from defocus (refractive disorders), and/or a failure to maintain alignment of the eyes (strabismus), and/or structural disorders of the eye, such as cataract (form deprivation) can all obscure the visual signal entering the eyes(s). Should this occur during the sensitive period, the child will develop amblyopia. Failure to correct the amblyogenic insult will result in irreversibly poor vision. However, the long-term adverse impact of amblyopia is unclear, especially the disutility associated with amblyopia.

The majority of the population based studies within industrialised nations report an amblyopia prevalence of 2% to 5%, dependent on amblyopia definition, as well as study methods and study population characteristics (e.g. the existence of a national screening programme).(2) Amblyopia is defined using visual acuity. The internationally accepted ‘unit’ for measuring acuity in children is LogMAR (**L**ogarithm of the **M**inimum **A**ngle of **R**esolution). ‘Normal’ adult vision is 0.0 logMAR, which is equivalent to 6/6 Snellen (Snellen being the older scale for measuring acuity in the UK). This adult level is typically reached by 5 to 6 years of age. ‘Normal’ neonate vision is 1.0 logMAR (10 times worse than adult acuity).(3) There exists no internationally agreed minimum visual acuity threshold for the diagnosis of amblyopia. Within the UK and other high income countries, a threshold of acuity worse than 0.2 logMAR has been used to select a meaningful definition of amblyopia. Health care settings in other countries have used thresholds varying from 0.2 to 0.4 logMAR.(2)

Early detection of amblyopia enables the intervention required to maintain normal visual development trajectories. These interventions comprise glasses, occlusion and penalisation. First, a period of ‘refractive adaptation’ is typically needed whereby glasses are used to correct refractive error to gradually improve the strength of the visual system. Second, children with unilateral

amblyopia who do not have refractive error, or who have not improved following refractive adaptation, are treated with occlusion or penalisation of the better eye. Occlusion is performed with eye-patches in front of the better eye while penalisation is undertaken using defocusing drops (Atropine) in the better eye. It may take several months (or over a year) before the full treatment effect is seen.

Current policy context and previous reviews

As amblyopia requires early treatment, but is typically asymptomatic in affected children, the UK National Screening Committee (UK NSC) recommends screening for vision defects in children. The primary aim of this programme is to detect children at risk of unilaterally impaired vision due to amblyopia. However, the programme also enables detection of any condition causing impaired vision in either or both eyes.

The current UK NSC policy is that children aged 4 to 5 years old undergo vision testing using a crowded logMAR testing chart, and that those with vision worse than 0.2 logMAR in one or both eyes undergo diagnostic examination. Diagnostic examination comprises refraction, examination of eye movements and binocular function and assessment of eye health. The programme is undertaken at 4 to 5 years as treatment undertaken before 4 years of age does not confer significantly better vision while a delay in treatment for children aged 4 to 5 years old with more severe amblyopia may lead to worse outcomes (see below).

Although a childhood vision screening programme has been in place in the UK for decades, there remain uncertainties in the evidence base for this screening programme. In 2008, a systematic review as part of a Health Technology Assessment (HTA) report concluded that there was an absence of good quality research into ‘the associated disability, or the efficacy of available treatments’ for amblyopia and recommended that the UK NSC should consider whether to discontinue existing vision screening programmes.⁽⁴⁾

A subsequent evidence review carried out in 2012,⁽²⁾ concluded that there was insufficient evidence to discontinue the vision screening programme for the following reasons:

1. “in population terms, the major impact of amblyopia lies in its importance as an avoidable risk factor for subsequent visual impairment which can arise through loss of vision in the non-amblyopic eye (the lifetime risk of subsequent visual impairment and blindness is 2 to 3 times higher than for those without amblyopia)”
2. “the focus of amblyopia treatment should remain intervention within the early sensitive period of childhood so as to avoid permanent visual deficit in the amblyopic eye, thus screening for reduced vision at 4 to 5 years enables those with established amblyopia to be detected at a sufficiently early stage so as to allow effective treatment”

3. “superiority of crowded logMAR optotype testing as a screening tool, which is acceptable to the population and for which the distribution of test values in the target population is known”
4. “overall, treatment undertaken before 4 years of age does not confer significantly better vision in either the short or long-term than treatment started between 4 and 6 years, but a delay in treatment for children aged 4 to 5 years old may lead to worse outcomes for children with severe amblyopia. Importantly, it is these children with severe amblyopia who have the greater lifetime risk of disabling bilateral visual impairment should visual loss occur in the better seeing eye”

Following this review, the UK NSC recommended that work should be undertaken to standardise childhood screening. As a result, the UK NSC set up a Vision Screening Advisory Group to produce materials to support the consistent implementation of high quality vision screening services, including screening and diagnosis pathways and quality standards. This included screening conducted in an orthoptic led service and use of the logMAR chart as a screening test, with a threshold of 0.2 logMAR.

However, similar to the 2008 HTA review, the 2012 UK NSC review also highlighted that there remained limited evidence about a number of UK NSC appraisal criteria, specifically:

1. “Balance between the benefit gained by individuals from the screening programme and any harms, for example from over diagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications.”
2. “Long-term adverse impact of amblyopia with and without treatment, with a significant evidence gap on the disutility associated with amblyopia either in childhood or beyond into adult life. It was also difficult to quantify and compare the psychological harm of amblyopia treatment with the negative impact and disutility of amblyopia”
3. “Effectiveness of the screening programme in reducing morbidity.”
4. “Economic balance of the opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) in relation to expenditure on medical care as a whole (i.e. value for money).”

Objectives

Part One

The UK NSC assesses the viability of all national screening programmes every three years. The starting point for these reviews is a triage review, which is a high level review that scans the literature to identify ‘red flags’ suggesting that further exploration of programme cessation may be necessary. Triage reviews have a surveillance function and are not intended as comprehensive

reviews of the programme. Therefore, in line with UK NSC triage review processes for existing programmes, part one of the review will involve 1 question that will search for evidence that indicates that a childhood vision screening programme may cause harm in the screened population (table 1).

Part Two

As the previous review found important evidence gaps for the childhood screening programme, the purpose of the second part of the review is to search for evidence addressing the remaining 3 key gaps for childhood screening for vision defects since the previous UK NSC review (table 1):

1. the long-term outcomes of amblyopia — with and without treatment
2. the clinical effectiveness of childhood vision screening
3. the cost-effectiveness of childhood vision screening

Table 1. Key questions for the evidence summary, and relationship to UK NSC screening criteria

	Criterion	Key questions	Studies Included
THE CONDITION			
1	The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease.	What is the long-term adverse impact of amblyopia with and without treatment?	18
THE SCREENING PROGRAMME			
11	There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity. Where screening is aimed solely at providing information to allow the person being screened to make an “informed choice” (e.g. Down’s syndrome, cystic fibrosis carrier screening), there must be evidence from high quality trials that the test accurately measures risk. The information that is provided about the test and its outcome must be of value and readily understood by the individual being screened.	What is the clinical effectiveness of vision screening in children aged 4 to 5 years?	3
13	The benefit gained by individuals from the screening programme should outweigh any harms for example from over diagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications.	What harms do individuals experience after participating in a childhood vision screening programme?	2
14	The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (i.e. value for money). Assessment against this criterion should have regard to evidence from cost benefit and/or cost effectiveness analyses and have regard to the effective use of available resource.	What is the cost-effectiveness of vision screening in children aged 4 to 5 years?	0

Methods

The current review was conducted by AL Solebo and JS Rahi, in keeping with the UK National Screening Committee evidence review process. Database searches were conducted on 06/09/2018 to identify studies relevant to the questions detailed in

Table 1. Hand searching of the reference sections of eligible studies identified through database searches had successfully identified additional evidence sources for the 2012 review. Hand searching of the reference sections of identified studies was again undertaken for this review.

Eligibility for inclusion in the review

Eligibility criteria for each question are presented in Table 2 below. All eligible studies published in the English language from 27/07/2012 onwards were included.

The following review process was followed:

1. Each abstract was reviewed against the inclusion/exclusion criteria by 1 reviewer (ALS). Where the applicability of the inclusion criteria was unclear, the article was included at this stage in order to ensure that all potentially relevant studies were captured. A second independent reviewer provided input in cases of uncertainty, and validated 20% of the first reviewer's screening decisions. Any disagreements were resolved by discussion until a consensus was met.
2. Full-text articles required for the full-text review stage were acquired.
3. Each full-text article was reviewed against the inclusion/exclusion criteria by 1 reviewer (ALS), who determined whether the article was relevant to 1 or more of the review questions. A second independent reviewer (JSR) provided input in cases of uncertainty, and validated 20% of the first reviewer's screening decisions. Any disagreements were resolved by discussion until a consensus was met.

Table 2. Inclusion and exclusion criteria for the key questions.
For all questions, target condition is Amblyopia

Key question	Inclusion criteria					Exclusion criteria
	Population Target condition	Intervention	Comparator	Outcome	Study type	
1) What harms do individuals experience after participating in a childhood vision screening programme for vision defects?	Individuals who participated in a vision screening programme when they were aged 4 to 5 years.	A universal childhood screening programme for vision defects	None or any	Harms from screening, defined as a clinical risk, a social complication or a reason for disinvestment	Systematic reviews, Randomised controlled trials, or Large prospective cohort studies. Lower quality of evidence only if they report a significant finding and there is no higher quality evidence	Non-human studies, papers not available in the English language, letters, editorials and communications, grey literature and conference abstracts.
2) What is the long-term adverse impact of amblyopia with and without treatment?	Individuals diagnosed with amblyopia when they were aged 4 to 5 years	a) No treatment, or b) Any treatment	None	a) Visual acuity or impairment b) Quality of life c) Socio-economic outcomes (education and employment) d) Behavioural and functional outcomes e) Patient perceived disutility f) General health g) Adverse health events e.g. road traffic accidents and falls	Cohort studies, Cross-sectional studies, Case-control studies, or Systematic reviews of the above	Non-human studies, papers not available in the English language, letters, editorials and communications, grey literature and conference abstracts.

				h) Specific occupational restrictions (versus employment per se)		
3) What is the clinical effectiveness of vision screening in children aged 4 to 5 years?	Asymptomatic participants aged 4 to 5 years	Universal screening by formal visual acuity testing for vision defects.	a) Symptomatic care, or b) Another version of universal childhood screening for vision defects than the one described as the intervention in the study	a) Prevalence of vision defects, visual acuity, or impairments b) Quality of life c) Socio-economic outcomes d) Behavioural and functional outcomes e) Patient-perceived disutility f) General health	In order of preference: Systematic reviews of randomised controlled trials Randomised controlled trials If above not found: Non-randomised intervention studies Cohort studies Systematic reviews of the above	Studies that only include participants with specific diseases (such as dyslexia or deafness) or organic eye defects (such as congenital glaucoma, cataract) Non-human studies, papers not available in the English language, letters, editorials and communications, grey literature and conference abstracts.
4) What is the cost-effectiveness of vision screening in children	General population (any age or gender)	Universal childhood screening for vision defects using formal visual acuity	a) Symptomatic care, or b) Another version of universal childhood screening for	Cost-effectiveness, e.g. incremental cost, incremental effectiveness (measured in quality-adjusted life-years [QALYs]), incremental cost-effectiveness ratios (cost per QALY).	Economic evaluations	Non-human studies, papers not available in the English language, letters,

aged 4 to 5 years?	testing at age 4 to 5 years.	vision defects than the one described as an intervention in the report.	editorials and communications, grey literature and conference abstracts.
--------------------	------------------------------	---	--

Appraisal for quality/risk of bias tool

The following tools were used to assess the quality and risk of bias of each study included in the review

- randomised controlled trials (RCTs): Cochrane Collaboration's "Risk of Bias" Tool
- interventional non-RCTs: Downs and Black checklist
- observational non-interventional studies: Critical Appraisal Skills Programme (CASP) Checklist

Databases/sources searched

Medline, Embase, Cochrane, and PsychInfo were searched for studies published since 27/07/2012. The search strategy is presented in 0.

Question level synthesis

Part One

Criterion 13 — harms of childhood vision screening

The benefit gained by individuals from the screening programme should outweigh any harms, for example from over diagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications

Question 1 – What harms do individuals experience after participating in a childhood vision screening programme?

The aim of this question or part one of the review update is to assess the viability of childhood vision screening programme. To do so, this review will identify 'red flags' reported in the literature suggesting that further exploration of programme cessation may be necessary. In the childhood vision screening programme, 'red flags' would include any harms due to over diagnosis, overtreatment, false positives, false reassurance, uncertain findings, and problems with the programme.

The scope of this question around the harms of undergoing vision screening has been set at screening in children aged 4 to 5 years. The natural history of visual development in children with and without amblyopia is that physiological age-related maturation of vision occurs. A significant number of children aged 3 years will have subnormal levels of vision, but this will improve naturally at a later age.(5, 6) This maturation should not be confused with improvements in acuity due to treatment. Thus, the sensitivity and specificity of vision screening to detect truly reduced vision will vary by age.

The 2012 UK NSC review did not identify any evidence on the potential harms of the vision screening programme, and recommended that population based studies be undertaken in order to examine this issue.

Eligibility for inclusion in the review

Eligible studies were those which looked at universal programmes of vision screening in children 4 to 5 years old, and reported on harms from screening, defined as a clinical risk, a social complication or a reason for disinvestment. Systematic reviews, RCTs, and large prospective cohort studies were included.

Description of the evidence

Database searches yielded 4925 results, of which 35 were judged to be relevant to this question. Of these, 6 abstracts met the criteria for full text review for this question. Following full text review, papers on the harms from treatment alone were excluded as this would not necessarily be reflective of screening. Of the 6 studies selected for full text review, 3 were judged to be eligible for inclusion. These 3 studies, comprising 2 retrospective cohort studies,(7, 8) and 1 prospective observational study,(9) all assessed outcomes for children who had undergone vision screening at age 4 to 5 years and had been referred for diagnostic examination.

0contains a full PRISMA flow diagram (

Figure 1), along with a table of the included publications and details of which questions these publications were identified as being relevant to (

Table 5. Summary of 7).

Methodological quality of included studies

A detailed description of methodological quality as assessed using the Critical Appraisal Skills Programme checklist is presented in Appendix 3, table 10. For all of the 3 included papers, a key area of bias within the study methodology was selective reporting. No study examined outcomes for children who had 'passed' the vision screening test but only reported outcomes for those who had 'failed'. All 3 studies also had in common a high frequency of missing data.

Discussion of findings

A study-level summary of data extracted from each included publication is presented in 'Summary and appraisal of individual studies **Error! Reference source not found.**'. The only harms of screening reported in these eligible observational studies were the number of children who did not attend their diagnostic examination and the number of children who screened 'false positive' (i.e. the number or proportion of children who failed screening but were found not to have any abnormalities in their subsequent diagnostic examination).

The uptake rate for diagnostic examination referrals varied across the 3 studies. In 2 retrospective studies, attendance at subsequent diagnostic ophthalmic examination for those who 'failed' vision screening (i.e. tested positive for reduced vision) was 78%, (556/698, 95% CI 77% to 82%) in a New Zealand setting(8) and 39% (36/93, 95% CI 30% to 49%) in a North American setting.(7) In the prospective study, which was set in the UK, 327/415 (79%, 95% CI 75% to 82%) of children who 'failed' their screening vision tests attended hospital eye services for diagnostic examination. All of the 3726 children in the UK study were aged 4 to 5 years,(9) whilst 70% of the 2933 children in the American study were aged 4 to 5 years.(7) The mean age at screening in the New Zealand study was 52 ±4 months, range 3 years to 6 years.(8) These 3 studies were unable to explore predictors of attendance as they had limited data on those who did not attend. A low uptake rate of diagnostic examination is made more important given the known relationship between vulnerable social position and both poorer utilisation of health care and higher burden of disease.(10) (11) (12)

With respect to false positive results, it was only possible to describe the proportion of children who had failed screening who were then found to be disease free. There was no follow up of those who tested negative so it was not possible to calculate the number of false negative children. It was also not possible to calculate the traditional false positive rate (false positive/(false positive + true negative)). Of those who attended their diagnostic examination, the proportion of false positives found across the studies was 38/260 (15%, 95% CI 11% to 19%) in the UK study,(9) 214/556 (39%, 95% CI 35% to 43%) in the New Zealand study,(8) and 12/36 (33%, 95% CI 20 to 50%) in the North American study.(7)

These variable false positive proportions highlight the key issue of the applicability of these 3 studies. All of the included studies used pass/fail criteria which differed from those currently recommended by the UK NSC for UK childhood vision screening. The study populations described in the UK and New Zealand studies underwent vision testing, examination of eye movement and binocular vision function.(8, 9) Children in these studies therefore underwent diagnostic examination within the 'screening test'. As a result, the reported false-positive numbers may not be directly generalisable to the current UK programme, which uses a screening test of reduced vision. The USA study did involve a screening test for reduced vision without diagnostic examination. However, the investigators used a more restrictive pass threshold (0.3 logMAR) than that in the UK and may, as a result, have a lower false positive number than would be expected for a UK based programme.(7)

This review did not identify any investigations of other harms from childhood vision screening such as over treatment, false reassurance, a social complication or a reason for disinvestment. There were no studies which investigated the balance of the harms and benefits of childhood screening programmes or of the cessation of vision screening programmes.

Summary of Findings Relevant to Criterion 13: Criterion not met*

Similar to the 2012 review, the current review found that there is an absence of specific evidence on the harms of childhood vision screening as practiced within current UK NSC recommendations.

A weak evidence base of only 3 studies was available to assess this criterion. These studies were only able to report on non-attendance and the number of false positives. They found that non-attendance varied between 21% and 61% and the rate of false positives varied between 15% and 39% across the studies. The studies were not only inconsistent, but they also had a moderate risk of bias, due to the high proportion of missing data and the retrospective study design of 2 of the 3 studies. Finally, 2 studies used 'screening tests' which involved diagnostic examination, while the other used the same test as the UK but a different threshold for referral, limiting the applicability of findings on false positive numbers. Therefore, these studies may not be generalisable to the UK childhood vision screening programme.

Overall, there was insufficient evidence to assess the harms of screening. Consequently, this criterion is not met and programme cessation should not currently be explored further.

* Met -for example, this should be applied in circumstances in which there is a sufficient volume of evidence of sufficient quality to judge an outcome or effect which is unlikely to be changed by further research or systematic review.

Not Met - for example, this should be applied in circumstances where there is insufficient evidence to clearly judge an outcome or effect or where there is sufficient evidence of poor performance.

Uncertain -for example, this should be applied in circumstances in which the constraints of an evidence summary prevent a reliable answer to the question. An example of this may be when the need for a systematic review and meta-analysis is identified by the rapid review.

Part Two

Criterion 1 — long-term adverse impact of amblyopia

The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease

Question 2 - What is the long-term adverse impact of amblyopia with and without treatment?

The aim of this question was to explore the long-term impact of amblyopia in order to understand the severity of the condition, and thus its importance. The negative impact of amblyopia was to be assessed when a) untreated, to understand natural history and b) treated, to understand the impact of treatment.

The 2012 UK NSC review reported that beyond the lifetime risk of visual impairment or blindness due to loss of vision in the better-seeing eye,(2) it was unclear how unilateral amblyopia impacts on an individual. Unilaterally poor vision generally results in loss of depth perception (stereopsis).(13) Visual clues such as shadow and perspective parallax may enable other ways of appreciating depth. There have not been reports of ‘real-world’ impact (i.e. beyond experimental settings) of impaired stereopsis in individuals with amblyopia. The review also reported a limited literature which points to a relatively mild disutility associated with amblyopia or with associated stereopsis either in childhood or beyond into adult life. The review concluded that based on the literature at the time, the major impact of amblyopia in population terms lay in its importance as a preventable risk factor for subsequent visual impairment or blindness due to loss of vision in the non-amblyopic eye through injury and disease.

Regarding the impact of treatment on the long-term outcomes of amblyopia, the 2012 UK NSC review reported that amblyopia was not associated with achieved educational level, employment, social mobility, socialisation or behavioural problems. There was limited evidence of relatively mild disutility associated with amblyopia.

As explained above, the previous and current UK NSC update reviews have focused on amblyopia alone as there is little benefit of screening and treatment for other conditions that could affect children aged 4 to 5, for the following reasons.

- Refractive visual defects

There is no evidence of benefit with intervention for refractive errors of mild myopia (short-sightedness) and hypermetropia (long-sightedness) at age 4 to 5 years. These refractive disorders are associated with good distance vision in both eyes,(14) and thus will not be detected through a screening programme for which the test is distance acuity. Moderate childhood hypermetropic refractive errors may be associated with impaired near vision which results in relative depth perception defects,(15) but it is uncertain if these defects persist in these children, as hypermetropia will naturally improve with increasing age as the eyes grow in size.

- Defects in 'secondary' visual functions

Children can have secondary visual function defects such as problems with colour vision. As there are currently no interventions able to restore colour vision, the benefit of screening for the defect is limited.

Although amblyopia is the main target disorder for the screening programme, any other disorder, such as functionally significant refractive error (error which is sufficiently severe to negatively impact visual development) would be detected through the current UK NSC programme which detects all-cause reduced acuity because of the detection of the resultant amblyopia.(2) Many disorders causing significant visual impairment, such as cataract, cerebral visual impairment, and retinopathy of prematurity would be detected before age 4 to 5 years through the Newborn and Infant Physical Examination programme(1) or through surveillance of high risk populations.(16)

Eligibility for inclusion in the review

Eligible studies were those which involved individuals diagnosed with amblyopia when they were aged 4 to 5 years who either did or did not receive treatment. Studies had to be investigating the outcomes of visual acuity or impairment, quality of life, socioeconomic outcomes, behavioural and functional outcomes, patient perceived disutility, general health, adverse health events, and specific occupational restrictions. Included study designs were cohort studies, cross-sectional studies, case-control studies, or systematic reviews of the above study designs.

Description of the evidence

Database searches yielded 25 results eligible for full text review. Eighteen studies were then judged to be eligible for inclusion and data extraction. The review identified 7 studies able to provide evidence on outcomes in children with amblyopia which has undergone treatment following diagnosis at 4 to 5 years of age. There were 11 studies in which reviewers were not able to determine if or when treatment was undertaken. Findings from these articles have been reported

separately. There were no studies that were explicitly on children with untreated amblyopia. The report contains a full PRISMA flow diagram (

Figure 1), along with a table of the included publications and details of which questions these publications were identified as being relevant to (

Table 5. Summary o8).

Reasons for excluding studies after review of full text were failure to report on outcomes for affected children, or descriptions of outcomes limited to those children who had undergone late treatment, or description of outcomes which carried no evidence of impact on function or development (Appendix 2, table 8).

Methodological quality of included studies

A detailed description of methodological quality as assessed using the Critical Appraisal Skills Programme checklist is presented in table 10. The majority of the 7 included papers able to report on outcomes following treatment are at low risk of bias with regards to study objectives, selected methodology, recruitment of cases and measurement of exposures and outcomes. For almost all of these papers, however, there is a high risk of confounding, with limited consideration or adjustment for the factors which could be influencing the outcomes of interest, such as severity of amblyopia, concordance with treatment or form of treatment. There is also considerable uncertainty around the selection and recruitment of controls. For the other 11 studies, the biases are compounded by the limited data on participant treatment history and age at diagnosis. The overall risk of bias is moderate to high for these 11 papers. Despite this, there is some consistency in the findings of the selected studies on the negative impact of amblyopia on selective aspects of vision-related function.

Discussion of findings

A study-level summary of data extracted from each included publication is presented in ‘Summary and appraisal of individual studies **Error! Reference source not found.**’.

Outcomes in treated populations

In 7 of the studies identified, children had been diagnosed with amblyopia at the ages of 4 to 5 years and had then undergone treatment, or were undergoing treatment at the time of the study. This evidence summary did not identify any eligible studies on the impact of treated amblyopia on any dimension of an individual’s quality of life, patient perceived disutility, general health, adverse health events e.g. road traffic accidents and falls, or specific occupational restrictions (versus employment per se). This evidence summary also did not identify any eligible studies on the impact of treated amblyopia on behavioural outcomes such as engagement with health care or self-care behaviours. The evidence review did find eligible studies around visual acuity or impairment, socioeconomic outcomes (education and employment), and functional outcomes. These findings are summarised below. Outcomes were categorised as related to:

- visual functions such as acuity, stereopsis, or eye movement

- other functions such as hand-eye co-ordination
- socioeconomic outcomes such as education or employment

Visual functional outcome

This evidence summary identified no studies reporting on the impact of treated amblyopia on binocular visual acuity (i.e. visual impairment) for children treated for amblyopia which is diagnosed through screening at the age of 4 to 5 years.

Two prospective cross-sectional studies were able to inform on other aspects of visual function, specifically eye movements, uniocular acuity, and stereopsis. Both had a moderate to high risk of bias due to failure to describe participant selection, or to deal appropriately with possible confounders.

One study reported that amblyopia resulted in unstable eye movements.(17) In general, eyes have many different modes of movement. These include locked on gaze (staying fixed on something of interest), involuntary tendency to drift off fixation, microsaccades (involuntary, very small movements they use to correct themselves), saccades (larger, jerky movements to change position quickly, for example, when reading a page of text) and pursuit gaze (move smoothly to track a moving object). The authors found that eye movements were less stable in the bad eyes of 52 amblyopic children versus 40 controls ($F[2,123]=5.4$, $p=0.005$). However, no negative impact was seen when children had both their eyes open. The gaze instability seen in amblyopia may explain findings on reading speed presented later in this review.(17)

The other study reported on the effect of treatment on uniocular acuity and stereopsis. Amongst a cohort of 85 children with amblyopia, refractive adaptation (glasses wear) resulted in a mean of 2 logMAR lines of improvement. Stereoacuity improved in 25 children (38%) who received refractive adaptation, 19 (28%) who received occlusion (patching), and 38 (45%) who underwent refractive adaptation and/or occlusion.(13) These outcomes are consistent with others reported by the 2012 review.

Other functional outcomes

Four prospective cross-sectional studies reported on eye movement related visual tasks.(18-21) One study found a negative impact on hand eye co-ordination in an experimental setting when children attempted to reach for cylindrical items with both eyes open. Amongst 55 amblyopic children, performance was slower when compared to 28 controls.(20) Severity of amblyopia accounted for much of the variance (adjusted $R^2=0.16$, $b=0.43$, $t=2.5$, $p=0.017$). Some of these children were still undergoing treatment. Older (aged 7 to 9 years) patients with “cured” amblyopia

(that is, from children who had successfully completed the course of treatment) and had improved stereoacuties all performed equally as well as their age matched controls.(20)

Two small studies undertaken by the same North American clinical research team reported on reading speed in treated amblyopic children (25 in 1 study(18) and 29 in the other(19)) compared with non-amblyopic children (15 non-amblyopic anisometropic children and 25 normal controls in 1 study(18) and 23 treated strabismus without amblyopia and 21 normal controls in another(19)) aged 8 to 13 years. With both eyes open, amblyopic children read 20% to 25% more slowly than non-amblyopic children. This was true whether the amblyopia was due to refractive causes (anisometropia) or strabismus. Anisometropic amblyopia was 24% slower (mean 149 ± 42 words/min) than non-amblyopic anisometropic children (mean 196 ± 80 words/min, $p=0.024$), and 22% slower than normal control children (mean 191 ± 65 words/min, $p<0.020$). Children with strabismic amblyopia read statistically more slowly (mean 148 ± 52 words/minute) than strabismic children without amblyopia (mean 198 ± 71 words/minute, $p=0.004$), and normal control children (mean 204 ± 62 words/minute, $p=0.002$). 'Normal' (fellow) eye fixation instability was seen in children with amblyopia, and was associated with a slower reading speed. In contrast to the findings on reading speed, comprehension rates did not differ between groups, so the functional impact of amblyopia mediated by reading speed is not clear. The authors also found that there was no association between reading speed and acuity.(18, 19)

In both these studies, reading speed in non-amblyopic and amblyopic children was assessed with the child wearing infrared goggles and silently reading paragraphs of text from a booklet held at 35 to 40cm from the face. Age at onset was not reported, but it can be assumed that they were 4 years old as these geographical areas have had a vision screening programme since 1989 (<https://www.dshs.texas.gov/vhs/vision-require.aspx>). The limitation of these studies is that there was no adjustment for socioeconomic background or IQ. History of amblyopia therapy was not reported for participants, so it was not clear if the 'non-amblyopes' with strabismus and anisometropia were in fact 'successfully treated' amblyopes. Thus, these investigations are unable to directly demonstrate reading speeds in those with 'fully' treated amblyopia versus 'partly' treated amblyopia.

Finally, 1 study investigated the functional outcome of visuo-auditory integration. Speech perception is dependent not only on audio but also on visual input and the successful integration of input from both 'senses'. In the McGurk effect, visuo-auditory integration is demonstrated by an illusory 'blended' perception when different auditory and visual stimuli are presented. In those with normal visual-auditory integration, an audio track playing the sound /pa/ (as in *pat*) presented simultaneously with a separate video track of a person articulating /ka/ (as in *cat*), produces the illusory perception of hearing a fusion sound /ta/ (as in *tap*). This study investigated 33 treated children, and reported that, although older children without amblyopia, and those with late onset amblyopia, perceive the illusion, whereas over half of the children with early onset amblyopia did

not perceive the illusion. The broader impact of failing to perceive the McGurk effect is as yet unclear.(21) but visuo-auditory integration has been described as a marker of good multisensory speech perception, a key element of communication and socialisation (i.e., why some may say "Look at me when I'm talking to you").(21) (22)

Socioeconomic outcomes (education and employment)

There was only 1 identified prospective longitudinal birth cohort study in this review that was able to report findings on the long-term functional and socioeconomic outcomes of individuals with amblyopia (1032 New Zealand participants, of whom 175 had amblyopia). (23) The study investigated the long-term outcomes of motor ability, reading ability, self-esteem, highest educational qualification, and self-reported occupation. Follow ups were done at ages 5, 7, 9, 11, 13, 15, 18, 21, 26 and 32 years when 972 (96%) of the 1015 living study participants were assessed. Amblyopia was determined through parent completed visual health questionnaires undertaken at ages 3 to 15 years old, and visual assessments undertaken at 7, 9, 11 and 15 years. Overall there was little evidence of a negative impact in adulthood. Despite the slower reading speed reported in children with amblyopia,(18) in this cohort study, children with amblyopia were able to recognise as many word as those without amblyopia when tested using the Burt 'reading test' (a word recognition test) as applied at ages 11, 13, 15 and 18 years (adjusted ANOVA using overall outcome $F[3,721]=0.704$, $p=0.550$). Amblyopia was also not associated with measures of adult socioeconomic status based on self-reported occupation ($\chi^2=7.283$, $p=0.61$), or with self-esteem (Rosenberg Self-Esteem Scale, association of poor self-esteem and amblyopia $\chi^2=2.584$, $p=0.460$). Finally, there was no statistically significant association between amblyopia and childhood motor ability score when assessed using a combined score from the individual's Bayley Motor Scale at age 3 years, McCarthy Motor Scale at age 5 years, and Basic Motor Ability Test at ages 7 and 9 years (ANOVA showed no effect of amblyopia grouping on combined childhood motor ability score, $F[3,911]=1.691$, $p=0.16$). However, poor stereoacuity, which was more commonly seen in those with amblyopia, was negatively associated with childhood motor ability ($F[6,894]=3.447$, $p=0.002$). (23)

In this study, as amblyopia was not detected through a whole population screening programme, only diagnosed amblyopia would have been detected. Exact age at diagnosis is not reported. Of the 175 with amblyopia, 31 individuals had 'recovered amblyopia' (amblyopia or patching prior to age 7 years, but no amblyopia measured at ages 9 to 15 years, implying successful treatment), and 108 possible amblyopia (fluctuating visual acuity measures between ages 7 to 15 years). This highlights one of the key limitations of studies on long-term outcome in amblyopia where there is insufficient follow up, as we know that some children with amblyopia can fluctuate, either improving, or experiencing losses in previously gained vision because of failure to maintain amblyopia maintenance therapy.

Another limitation of the study was that a power calculation was not presented. There may have been insufficient statistical power to interrogate these associations for the relatively small number of amblyopic children in the study.(23)

Outcomes in populations in whom the treatment history is unclear

This review identified 11 studies which reported on outcomes for individuals with amblyopia, but lacked sufficient detail to determine age at treatment onset, or age at diagnosis for participants with amblyopia. Although by definition, amblyopia is a disease of early childhood onset, diagnosis may occur too late to enable treatment to be effective. Additionally, these studies were unable to report on or differentiate between outcomes for treated versus untreated individuals. Whilst these studies, are unable to directly inform the question of outcome with treatment and outcome without treatment they do help to deepen our understanding of the broader natural history of amblyopia, and support the findings reported within the other 7 studies. This evidence summary did not identify any eligible studies on the impact of treated amblyopia on patient perceived disutility, quality of life, general health, adverse health events e.g. road traffic accidents and falls, specific occupational restrictions (versus employment per se). The evidence review did find eligible studies around visual functional outcomes. These findings are summarised below.

Visual functional outcomes

The review identified 6 studies around visual functional outcomes. There was 1 retrospective cross-sectional study on stereoacuity outcomes in amblyopic individuals with an unclear treatment history.(24) The study found that, consistent with the findings of Stewart et al,(13) when compared to 72 children with non-amblyopic anisometropia (NA), and 73 normal subjects without anisometropia, 35 children with amblyopic anisometropia (AA), had poorer stereopsis ($641.71 \text{ arc sec} \pm 1443.58$, 76.25 ± 55.78 , and 54.52 ± 20.00 , respectively; AA vs. NA, $p < 0.001$, and AA vs. control, $p < 0.001$, Kruskal–Wallis test). Treatment history was not reported for individuals with anisometropia (that is, the children classified as NA may have had successfully treated amblyopia). Thus, it is unclear whether outcomes reported were for treated amblyopia.(24)

One prospective cross-sectional study reported on the ability of 21 individuals with amblyopia and 10 controls to perform a visual search task. Amblyopic individuals were divided into mild ($n=9$), moderate ($n=8$), and severe ($n=4$). Viewing a scene with the amblyopic eye only was associated with diminished search ability (number of differences identified: controls: 4.73 ± 2.5 ; mild amblyopia: 3.60 ± 2.2 ; moderate: 2.61 ± 2.03 ; severe: 0.77 ± 1.39 , $p < 0.0001$, ANOVA).(25)

Finally, the review identified 4 studies, comprising 3 prospective cross-sectional studies,(26) (27) (28) and 1 retrospective cross-sectional study,(29) which reported fixation instability in amblyopic individuals. All these studies are at moderate risk of bias due to a high risk of confounding, with limited consideration or adjustment for the factors which could be influencing the outcomes of interest, such as severity of amblyopia, treatment history, age at diagnosis, and uncertainty around the selection and recruitment of cases and controls. All studies are small, involving fewer than 30 individuals with amblyopia. All of them report abnormal gaze patterns in amblyopic eyes of affected individuals. One of these studies reported abnormal eye movements in children with unilateral amblyopia when using both eyes at the same time.(28) Shaikh et al. examined 19 children with amblyopia aged 4 to 15 and 9 controls aged 5 to 10, and found that the ‘normal’ fellow eye in children with even mild amblyopia showed unstable ‘scanning’ type movements (i.e. those used in reading). Whilst the correlation was strong, there was no ‘dose-dependent’ relationship between severity of amblyopia and movement stability, that is, there was no strengthening of correlation as severity increased (mild amblyopia: $r=0.82$, $p<0.0001$; moderate amblyopia: $r=0.76$, $p<0.0001$; severe amblyopia: $r=0.69$, $p<0.0001$). (28) These studies support the evidence that amblyopia results in poorer ‘scanning’ eye movements, which may then lead to slower reading speeds. The other studies have not found an association between smooth pursuit type gaze,(26) or errors in targeted gaze and amblyopia.(27)

Other functional outcomes

A series of 4 prospective cross-sectional studies in adults identified that amblyopia was associated with delays in hand-eye co-ordination. When asked to reach for targets on a screen under both monocular and binocular viewing, these studies found that amblyopic participants showed delays in reaching a target and reduced precision.(30-33) The earlier studies reported consistent findings from relatively small study populations (fewer than 30 amblyopic individuals). In the largest and most recent study, involving 55 adults with amblyopia (22 anisometropic, 18 strabismic, 15 mixed mechanism), 14 adults with strabismus without amblyopia, and 22 visually-normal control adults, the lack of precision appeared to be associated with disordered fixation changes.(30) Amblyopia was associated with deficits in reaching for a target presented on a screen when the individual had both eyes open (binocular viewing). Multivariate analysis revealed that the best fitting model that accounted for 35% of total variance in precision had 2 predictors: acuity of the amblyopic eye and eye deviation ($\beta_{\text{Amblyopic eye acuity}}=0.06$, $\beta_{\text{deviation}}=0.001$ on regression analysis, $p<0.0001$). Amblyopic individuals were ‘over-shooting’ when attempting to fixate on targets, and requiring additional corrective saccadic eye movements.(30) This difficulty in re-orienting gaze is again consistent with the lower reading speed reported in children with amblyopia.(18, 19) However, none of these studies articulated or demonstrated the ‘downstream’ real life educational or functional implications.

One study on the visuo-auditory integration was identified, which again reported an association between amblyopia and failure to perceive the McGurk effect. This study recruited 28 'young' children aged 4 to 9 years (mean 6.3 ± 1.3 years), 12 older children (mean 11.5 ± 2 years), and 22 adults (mean 33 ± 10.9 years) and 66 age matched controls (24 young children, 17 older children, 25 adults). Fewer participants with amblyopia (72%, $\pm 3\%$) were able to perceive the McGurk effect when compared to the control group (85%, $\pm 2\%$), which was statistically significant on unadjusted ANOVA ($p < 0.0024$). Increasing age, amongst both amblyopes and visually normal individuals, was associated with greater susceptibility, suggesting a maturing of integration.

Summary of Findings Relevant to Criterion 1: Criterion not met†

At present, the major impact of amblyopia in population terms lies in its importance as an avoidable risk factor for subsequent visual impairment which can arise through loss of vision in the non-amblyopic eye. This review has provided an update of the evidence base on the impact of amblyopia. The review identified 18 papers able to report on long-term outcomes for amblyopia. The studies consistently found a negative impact of amblyopia to fixation stability in the weaker eye (12 studies) and scanning eye movements when individuals have both eyes open (3 studies). Amblyopic eyes make larger, less accurate 'fine tuning' movements, 'over-shoot' their intended target, and perform slower at searching tasks (6 studies). This is, in turn, consistent with the evidence of reduced reading speed in amblyopic individuals (2 studies). There was also high level confirmation of the well recognised loss of stereovision seen in amblyopia (1 study). Amblyopia related loss of stereovision was associated with restriction of hand-eye co-ordination reliant functions within experimental settings (8 studies). However, the 'real-life' consequences of these outcomes are unclear.

However, the review found only 1 paper eligible to report on the broader impact of amblyopia, which found no association between amblyopia and self-esteem, socioeconomic outcomes or other functional outcomes. There was also no evidence on patient perceived disutility, quality of life, general health, visual acuity per se, adverse health events e.g. road traffic accidents and falls or specific occupational restrictions (versus employment per se). Furthermore, none of these papers were explicitly on untreated amblyopia. Seven papers were on screened and treated amblyopia and in 11 studies it was not possible to determine whether the population had undergone treatment. Thus, this evidence summary is unable to comment on the impact of untreated amblyopia or on the impact of amblyopia treatment. The reviewers acknowledge that it may not be possible to identify new, applicable, high level evidence on outcomes of amblyopia in treated versus untreated populations as it would be unethical to randomise children to no treatment when the effectiveness of treatment in improving acuity, and the time sensitive nature of treatment, are now well recognised.

The evidence base was at moderate to high of bias. The 7 papers for which the treatment history of participants is clear were at low to moderate risk of bias while the 11 papers

† **Met** -for example, this should be applied in circumstances in which there is a sufficient volume of evidence of sufficient quality to judge an outcome or effect which is unlikely to be changed by further research or systematic review.

Not Met - for example, this should be applied in circumstances where there is insufficient evidence to clearly judge an outcome or effect or where there is sufficient evidence of poor performance.

Uncertain -for example, this should be applied in circumstances in which the constraints of an evidence summary prevent a reliable answer to the question. An example of this may be when the need for a systematic review and meta-analysis is identified by the rapid review.

where it was unclear to determine treatment have moderate to high risk of bias. The 7 papers for which treatment history of participants is reported have median ages of treatment commencement which are typical of a UK population in which amblyopia is diagnosed through screening. However, the applicability of the remaining 11 studies to a population undergoing screening and resultant diagnosis and treatment at age 4 to 5 years is unclear.

As a result of the risk of bias, applicability concerns and the major gaps in evidence, the complete long-term impact of amblyopia is still unclear. Therefore, this criterion is not met.

Criterion 11 — clinical effectiveness of childhood vision screening

There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity.

Question 3 – What is the clinical effectiveness of vision screening in children aged 4 to 5 years

The aim of this question was to assess the clinical effectiveness of vision screening.

The 2012 UK NSC review did not find any randomised controlled trials of the effectiveness of childhood vision screening at ages 4 to 5 years in reducing morbidity. Morbidity would include reduced vision in both or one eyes and the associated negative consequences such as poor stereoacuity, or visual impairment due to loss of vision in the better eye of those with unilateral amblyopia.

The highest level evidence for any vision screening programme remains the Rotterdam AMblyopia Screening Effectiveness (RAMSES) longitudinal cohort study, which followed 4624 children born in 1996 and 1997 through a (now abandoned) intensive vision screening and surveillance programme in which the eyes and vision are examined at ages 9, 14, 24, 36, 45 to 54 and 60 months. Seventy seven per cent of amblyopic children had improved vision by age 7.(34) This intensive programme is not however an appropriate model for comparison with the current UK screening programme, as it is continued surveillance starting from the age of 9 months, versus targeted whole population screening occurring at age 4 to 5 years in the UK. The surveillance programme would therefore carry substantial differences in effectiveness, as well as different risks of harm and benefit.

Eligibility for inclusion in the review

The reviewers included interventional studies which involved asymptomatic participants aged 4 to 5 years undergoing universal screening by formal visual acuity testing. They included studies that assessed the outcomes of prevalence of vision defects, visual acuity, or impairments, quality of life, socioeconomic outcomes, behavioural and functional outcomes, patient perceived disutility and general health. With respect to study design, they included randomised trials and systematic reviews of these, and if they did not find any of these, they included non-randomised intervention studies and cohort studies as well as systematic reviews of these.

The reviewers excluded studies that only included participants with specific diseases (such as diabetes, dyslexia, deafness or congenital diseases) or organic eye defects (such as congenital glaucoma, cataract and retinoblastoma).

Description of the evidence

Database searches yielded 15 results, of which 4 were judged to be relevant to this question and eligible for full text review. Of these 4, 2 cross-sectional studies were eligible for inclusion on the effect of screening on the prevalence of amblyopia in adulthood.

The search did not identify interventional trials. There were also no studies on the effectiveness of screening on visual acuity or impairments, quality of life, socioeconomic outcomes, behavioural and functional outcomes, patient perceived disutility and general health.

0contains a full PRISMA flow diagram (

Figure 1), along with a table of the included publications and details of which questions these publications were identified as being relevant to this criterion (

Table 5. Summary o9).

Methodological quality of included studies

A detailed description of methodological quality as assessed using the Critical Appraisal Skills Programme checklist is presented in table 10. The 2 included studies are consistent in their findings and their low risk of bias with regards to study methodology and cohort selection. However, for both studies, there is a high risk of bias with regards to potential limitations around confounding and the inference of causal relationships.

Discussion of findings

A study-level summary of data extracted from each included publication is presented in ‘Summary and appraisal of individual studies **Error! Reference source not found.**’.

The review identified 2 observational studies, 1 from Denmark (n=2295 total population sample)(35) and 1 from Israel (n=107896 total population sample).(36) For both studies, investigators compared prevalence of amblyopia amongst population based cohorts for those who reached school age before and after the commencement of a pre-school vision screening.(35, 36) Both groups reported a statistically lower prevalence of amblyopia following the introduction of a vision screening programme. Amongst the 494 Danish participants who would have been systematically screened, prevalence of amblyopia in adulthood was 0.44%. By contrast, 1.78% of 2295 adults who had not undergone screening before age 6 years had amblyopia.(35) In Israel, the prevalence of amblyopia was 1.2% (95% CI 1.07% to 1.23%) amongst adults born between 1971 and 1985 who had not undergone screening, with a decline to 0.8% (95% CI 0.73% to 0.90%, $p<0.001$) in adults born between 1986 and 1994, who had undergone screening.(36)

These studies had a moderate risk of bias, as they may be limited by the use of historical controls. Individual data were not available on participation in a screening programme and this was inferred from the screening programme for the country at the time. Population heterogeneity and confounding bias could exist, therefore, a causal relationship between the introduction of the screening programme and reduction in amblyopia prevalence is not proven. Other confounding factors may be contributing to the findings, particularly other health statuses. Improving general child health statuses may explain the lower prevalence of amblyopia.(2) Additionally 1 study is not directly applicable to the UK NSC’s childhood vision screening programme. The screening population in the Danish article was 3 to 4 years old (potentially resulting in more ‘false positives’), and the vision threshold for screening failure used was vision worse than 0.3 LogMAR (potentially resulting in lower ascertainment of ‘cases’).(35)

Summary of Findings Relevant to Criterion 11: Criterion not met[‡]

This review found a weak evidence base of only 2 cross-sectional studies on the effectiveness of childhood vision screening on the prevalence of amblyopia in adulthood. There were no studies on the effectiveness of screening on visual acuity, impairments, quality of life, socioeconomic outcomes, behavioural and functional outcomes, patient perceived disutility, and general health and no randomised controlled trials.

Both studies consistently found a reduced prevalence of adulthood amblyopia in cohorts who reached school age after the commencement of screening compared with cohorts who reached school age before it. However, this evidence base has a moderate risk of bias, due to the use of historical controls. Improving general population health may have resulted in lower prevalence of amblyopia in those populations who had undergone screening versus older population who were not screened for poor vision. In addition, 1 of the 2 studies used 'screening tests' which involved diagnostic examination, limiting the applicability of findings on the clinical effectiveness of screening.

Due to the scarcity of applicable evidence, the review concludes that there is an absence of evidence on the clinical effectiveness of the vision screening at age 4 to 5 years as recommended by the UK NSC. Thus, this criterion is not met.

Criterion 14 — cost-effectiveness of childhood vision screening

The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole

Question 4 – What is the cost-effectiveness of vision screening in children aged 4 to 5 years?

The aim of this review was to assess the evidence on the costs of vision screening when balanced with the gains.

The 2012 UK NSC review did not identify any applicable robust evidence on the cost-effectiveness of childhood vision screening as recommended by the UK NSC. An analysis undertaken in the UK in 2008 had estimated the cost-effectiveness of screening to be very poor, at a cost per quality-

[‡] **Met** -for example, this should be applied in circumstances in which there is a sufficient volume of evidence of sufficient quality to judge an outcome or effect which is unlikely to be changed by further research or systematic review.

Not Met - for example, this should be applied in circumstances where there is insufficient evidence to clearly judge an outcome or effect or where there is sufficient evidence of poor performance.

Uncertain -for example, this should be applied in circumstances in which the constraints of an evidence summary prevent a reliable answer to the question. An example of this may be when the need for a systematic review and meta-analysis is identified by the rapid review.

adjusted life-year (QALY) of £134,963.(4) This estimate was highly sensitive to both the disutility value of amblyopia and the disutility of visual impairment due to loss of vision in the non-amblyopic eye. A 2% reduction in utility due to amblyopia would result in the estimated QALY cost falling to £17000.(4) The disutility estimate of ‘unscreened’ and thus untreated versus ‘screened’ amblyopia is unknown.

This review update sought to identify any available evidence on the cost-effectiveness of vision screening in children aged 4 to 5 years compared with symptomatic care, or the cost-effectiveness of different vision screening programmes in children aged 4 to 5 years.

Eligibility for inclusion in the review

Eligible studies were those which involved universal childhood screening for vision defects using formal visual acuity testing at age 4 to 5 years, and which reported outcomes on cost-effectiveness, e.g. incremental cost, incremental effectiveness (measured in quality-adjusted life-years [QALYs]), incremental cost-effectiveness ratios (cost per QALY).

Description of the evidence

Database searches yielded 2 results, of which none were judged to be eligible for inclusion for this question. One study was excluded because it examined cost-effectiveness of vision screening for older children, whilst the second examined the cost-effectiveness of follow up care models for children who had failed vision screening tests.

Summary of Findings Relevant to Criterion 14: not met[§]

As no studies were identified, the review concludes that there is an absence of evidence on the cost effectiveness of the vision screening at age 4 to 5 years as recommended by the UK NSC. Thus, this criterion is not met.

[§] Met -for example, this should be applied in circumstances in which there is a sufficient volume of evidence of sufficient quality to judge an outcome or effect which is unlikely to be changed by further research or systematic review.

Not Met - for example, this should be applied in circumstances where there is insufficient evidence to clearly judge an outcome or effect or where there is sufficient evidence of poor performance.

Uncertain -for example, this should be applied in circumstances in which the constraints of an evidence summary prevent a reliable answer to the question. An example of this may be when the need for a systematic review and meta-analysis is identified by the rapid review.

Review summary

Conclusions and implications for policy

This report is an update review on systematic childhood screening for visual defects. Evidence has been reviewed against select UK NSC criteria for appraising the viability, effectiveness and appropriateness of a screening programme. This review assessed key questions to determine if new evidence published since 2012 suggests that reconsideration of the current screening programme for childhood vision screening in the UK is required.

The findings of this review are not sufficient to support any changes to the current UK NSC childhood vision screening programme.

1. There is currently an absence of specific evidence on the harms of childhood vision screening as practiced within current UK NSC recommendations. The evidence on harms is limited to inconsistent evidence on non-attendance to subsequent diagnostic examination (ranging from 20% to 61%) and false positive numbers following screening (ranging from 15% to 39%). These data came from 3 studies, 2 of which were not directly applicable to recommended practice in the UK.
2. This review found that amblyopia diagnosed through screening at age 4 to 5 years old can have a negative impact on the type of eye movements which are used to track words across a page when reading, which are consistent with reports of reduced reading speed in individuals with amblyopia. However, reading comprehension is unchanged. There was also evidence that loss of depth perception due to reduced vision in one eye can negatively impact hand-eye co-ordination activities within experimental settings. The 'real-life' consequences of this remain unclear.
3. There was limited evidence showing no association between amblyopia and long-term socio-economic status, or self-esteem, and no evidence of the impact of amblyopia on the patient's self-perceived disutility, general health, quality of life, adverse health events or specific occupational restrictions. Furthermore, none of these papers explicitly included untreated amblyopia. Therefore, a key element which remains unclear is the impact of amblyopia treatment on outcomes beyond visual acuity in the treated eye. However, it may not be possible to identify new, applicable, high level evidence on outcomes of amblyopia in treated versus untreated populations as trials would be unethical.
4. There remains an absence of evidence on the clinical and cost effectiveness of vision screening at age 4 to 5 years as recommended by the UK NSC. There is weak but consistent evidence which suggests that populations which undergo childhood vision screening have lower prevalence of amblyopia.

5. With regards to cost effectiveness, the key question remains the perceived disutility of amblyopia, or of bilaterally poor vision due to loss of vision in the better eye of an amblyopic individual later in life.

The review has identified key remaining gaps in the evidence. Future research is needed to better understand the implication of vision screening in 4 to 5 years old:

- What are the harms of vision screening at age 4 to 5 years?
- What are the real-life educational, socioeconomic, quality of life or other functional consequences of amblyopia?
- What is the clinical effectiveness of vision screening for children aged 4 to 5 years?
- What is the cost effectiveness of vision screening for children aged 4 to 5 years?

Limitations

For this rapid review, the searching was limited to bibliographic databases and hand searching of the reference sections of eligible studies. Grey literature sources were not searched. Only studies written in English language were included, however, within the 2012 UK NSC review, few studies in other languages were identified, and these studies were inapplicable to a UK setting due to differences in condition definition and screening test.⁽²⁾ This review should have captured evidence from populations sufficiently similar to that found within the target population for the screening programme.

Articles were screened by a single reviewer. A second reviewer examined all included articles, 20% of excluded articles and any articles where there was uncertainty about inclusion or exclusion. This provided validation of the evidence selection process, and has ensured that robust review of articles where the eligibility was unclear.

This rapid review was guided by a protocol developed a priori. The search strategies were peer-reviewed by another senior information specialist using the PRESS form. Standard, systematic approaches for study selection, data extraction, and validity assessment were used.

Appendix 1 — Search strategy

Electronic databases

The search strategy included searches of the databases shown in Table 2. MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print and Embase.

Table 2. Summary of electronic database searches and dates

Database	Platform	Searched on date	Date range of search
MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print	Ovid SP	20/09/2018	27/02/2012 to Present
Embase	Ovid SP	20/09/2018	27/02/2012 to Present
The Cochrane Library, including: - Cochrane Database of Systematic Reviews (CDSR) - Cochrane Central Register of Controlled Trials (CENTRAL) - Database of Abstracts of Reviews of Effects (DARE)	Wiley Online	20/09/2018	CDSR: 2012 to present
PsychInfo	Ovid SP	20/09/2018	27/02/2012 to Present

Search Terms

Search terms included combinations of free text and subject headings

Search terms for MEDLINE, MEDLINE In-Process, MEDLINE Daily, Psychinfo and Embase are shown in Table 3, and search terms for the Cochrane Library databases are shown in

Mapping of search terms to the review questions:

Question 1	What harms do individuals experience after participating in a childhood vision screening programme for vision defects?
Search A: #16, #22 Search B: #11	
Question 2	What is the long-term adverse impact of amblyopia with and without treatment? *Include contextual information on visual defects (in general and specifically amblyopia), what they constitute, their short-term impact and what is known about the long-term impact
Search A: #16, #26 Search B: #6, #7	
Question 3	What is the clinical effectiveness of vision screening in children aged 4 to 5 years?
Search A: #16, #22 Search B: #11	
Question 4	What is the cost-effectiveness* of vision screening in children aged 4 to 5 years? *Dependent on disease frequency
Search A: #24, #28 Search B: #5, #12	

Table 4.

Table 3. Search strategy for MEDLINE, MEDLINE In-Process, MEDLINE Daily, Epub Ahead of Print and Embase

Search terms	Results
1) (randomi?ed or randomi?ed control* trial*).tw	90355
2) Cohort/ or cohort.tw	522271
3) (case-control or longitudinal).tw	541582
4) Randomized Controlled Trials as Topic/	20270
5) 1 or 2 or 3 or 4	1073627
6) child/ or child, preschool/	2068632
7) Amblyopia/ or amblyopia.tw	8669
8) Refractive Errors/	32122
9) exp Strabismus/ or squint.tw	22599
10)Hyperopia/ or hypermetropia.tw	4726
11)Myopia/ or myopia.tw	21235
12)Anisometropia/ or anisometropia.tw	1801
13)Eyeglasses/ or (spectacles or glasses).tw	18446
14)(visual* adj impair*).tw	43503
15)7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	115788
16)5 and 6 and 15	2223
17)(Amblyopia or Refraction or Refractive or Strabismus or Squint or Vision or Blindness).tw	235888
18)Mass Screening/	146016
19)screen*.ti	155460
20)exp Vision Tests/	101868
21)18 or 19 or 20	338641
22)6 and 17 and 21	12642
23)Cost Effectiveness/ or Cost Effective.tw	165817
24)23 and (7 or 22)	141
25)Quality of Life.tw	278911
26)25 and 15	2821
27)(prevalence or surveillance).tw	783434
28)7 and 27	547
29)16 or 22 or 24 or 26 or 28	17046
30)limit 29 to yr="2012 -Current"	4968

Total results: 4968

Mapping of search terms to the review questions:

Question 1	What harms do individuals experience after participating in a childhood vision screening programme for vision defects?
Search A: #16, #22 Search B: #11	
Question 2	What is the long-term adverse impact of amblyopia with and without treatment? *Include contextual information on visual defects (in general and specifically amblyopia), what they constitute, their short-term impact and what is known about the long-term impact
Search A: #16, #26 Search B: #6, #7	
Question 3	What is the clinical effectiveness of vision screening in children aged 4 to 5 years?
Search A: #16, #22 Search B: #11	
Question 4	What is the cost-effectiveness* of vision screening in children aged 4 to 5 years? *Dependent on disease frequency
Search A: #24, #28 Search B: #5, #12	

Table 4. Search strategy for the Cochrane Library Databases (Searched via the Wiley Online platform)

Search terms	Results
1. Amblyopia	590
2. (Prevalence OR surveillance):ti,ab,kw	41848
3. Treatment OR Therapy OR Management	814010
4. Quality of Life	88093
5. #1 AND #2	74
6. #1 AND #3	444
7. #1 AND #4	75
8. Vision screening	1197
9. Child	112302
10. Cost Effectiveness	39696
11. #8 AND #9	351
12. #8 AND #10	387
13. #5 OR #6 OR #7 OR #11 OR #12	827
14. (#13), from 2012 to 2018	542
Total: 542 results	

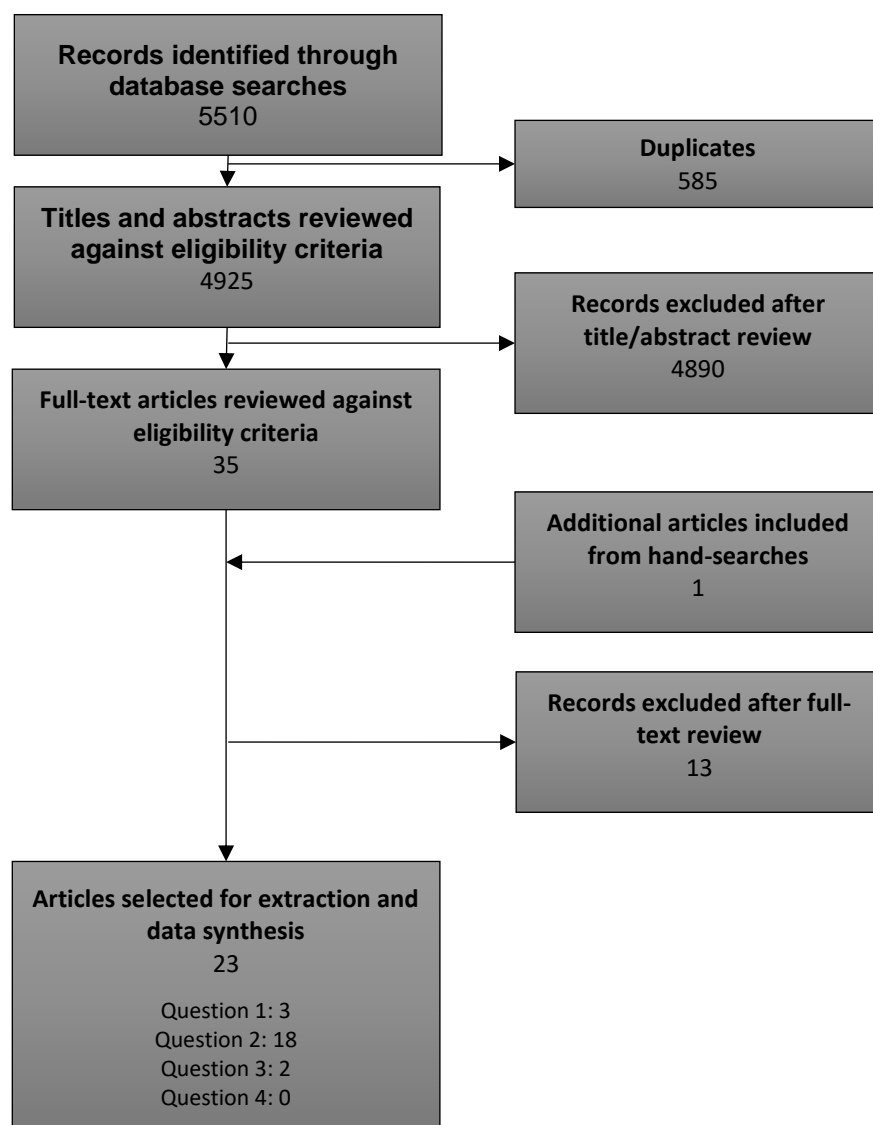
5510 Results were imported into EndNote and de-duplicated. Total 4925 individual titles identified

Appendix 2 — Included and excluded studies

PRISMA flowchart

Figure summarises the volume of publications included and excluded at each stage of the review. Publications that were included or excluded after the review of full-text articles are detailed below.

Figure 1. Summary of publications included and excluded at each stage of the review



Publications included after review of full-text articles

The 23 publications included after review of full-texts are summarised in

Table 5. Summary of below.

Studies were prioritised for extraction and data synthesis. It was planned a priori that the following approach would be taken to prioritise studies for extraction:

1. Systematic reviews and meta-analyses would be considered the highest quality of evidence if any were found. Following this, study designs would be prioritised for each question in the order listed in **Error! Reference source not found.**
2. Studies relating to epidemiology would be prioritised if they considered a UK population, followed by studies from Western populations analogous to the UK.

Publications not selected for extraction and data synthesis are detailed in

Table 5. Summary o6 below.

Table 5. Summary of publications included after review of full-text articles, and the question to which each publication was identified as being relevant

Study	The condition	The test	The intervention	The screening programme	Implementation criteria	Comments
Hered 2013	-	-	-	Q1	-	-
Langeslag-Smith, 2015	-	-	-	Q1	-	-
Touffeeq 2014	-	-	-	Q1	-	-
Kelly 2017	Q2	-	-	-	-	-
Kelly 2015	Q2	-	-	-	-	-
Subramanian 2013	Q2	-	-	-	-	-
Stewart 2013	Q2	-	-	-	-	-
Grant 2014	Q2	-	-	-	-	-
Burgmeier 2015	Q2	-	-	-	-	-
Wilson 2013	Q2	-	-	-	-	-
Gonzalez 2012	Q2	-	-	-	-	-
Narinesingh 2015	Q2	-	-	-	-	-
Chen 2018	Q2	-	-	-	-	-
Jeon 2017	Q2	-	-	-	-	-
Raashid 2016	Q2	-	-	-	-	-
Niechwiej-Szwedo 2012	Q2	-	-	-	-	-
Niechwiej-Szwedo 2014	Q2	-	-	-	-	-
Niechwiej-Szwedo 2014	Q2	-	-	-	-	-
Niechwiej-Szwedo 2017	Q2	-	-	-	-	-

Chung 2015	Q2	-	-	-	-	-
Shaikh 2016	Q2	-	-	-	-	-
Piano 2015	Q2	-	-	-	-	-
Piano 2016	Q2	-	-	-	-	-
Hoeg 2015	-	-	-	Q3	-	-
Shapira 2018	-	-	-	Q3	-	-

Publications excluded after review of full-text articles

Of the 36 publications included after the review of titles and abstracts, 11 were ultimately judged not to be eligible for this review. These publications, along with reasons for exclusion, are listed in Table 6.

Table 6. Publications excluded after review of full-text article

Reference	Reason for exclusion
de Koning, H. J., et al. (2013). "Effectiveness of screening for amblyopia and other eye disorders in a prospective birth cohort study." J Med Screen 20(2): 66-72(34)	Not universal vision screening at age 4-5years: programme of repeated eye / vision examinations from age 1m - 72 months, thus not comparable to NSC recommendations
Chen, Y., et al. (2016). "Longitudinal Impact on Quality of Life for School-aged Children with Amblyopia Treatment: Perspective from Children." Curr Eye Res 41(2): 208-214³(37)	Children diagnosed at age 7 to 12 yrs, undergoing treatment outside the target range for NSC screening programme, with description of impact of treatment and visual level on quality of life. Thus not generalisable to outcomes for children undergoing treatment after diagnosis through screening at age 4 to 5 years. No comparison of quality of life between amblyopic children and age matched norms
Longmuir, S., et al. (2013). "Effect of occlusion amblyopia after prescribed full-time occlusion on long-term visual acuity outcomes." J Pediatr Ophthalmol Strabismus 50(2): 94-101(38)	Harms of one method of intensive treatment reported only. Study population did not undergo screening
van de Graaf, E. S., et al. (2017). "Differences in quality-of-life dimensions of Adult Strabismus Quality of Life and Amblyopia & Strabismus Questionnaires." Graefes Arch Clin Exp Ophthalmol 255(9): 1851-1858.(39)	Report of validation process, rather than results of administration of metric. Thus no report of quality of life outcomes. Also mode of, or age at detection not reported.
Singman, E., et al. (2013). "Association between accommodative amplitudes and amblyopia." Strabismus 21(2): 137-139. (40)	Children aged 3-14 with amblyopia: age at diagnosis, history of treatment, mode of detection not reported. No age matched controls: article described worsening accommodation with worsening acuity in amblyopia rather than association between accommodation and amblyopia per se

Piano, M. E., et al. (2015). "Perceptual Visual Distortions in Adult Amblyopia and Their Relationship to Clinical Features." Invest Ophthalmol Vis Sci 56(9): 5533-5542.(41)	Adults with amblyopia, age at onset, history of treatment, mode of detection not reported. There is no evidence of a functional impact of perceptual visual distortion, beyond its possible use as a marker of poor stereopsis
Piano, M. E., et al. (2016). "Perceived Visual Distortions in Juvenile Amblyopes During/Following Routine Amblyopia Treatment." Invest Ophthalmol Vis Sci 57(10): 4045-4050(42)	Adults with amblyopia, age at onset, history of treatment, mode of detection not reported. No evidence of functional impact of perceptual visual distortion, beyond its possible use as a marker of poor stereopsis
Webber, A. L., et al. (2016). "Fine Motor Skills of Children With Amblyopia Improve Following Binocular Treatment." Invest Ophthalmol Vis Sci 57(11): 4713-4720. (43)	Report on the impact of late treatment, thus not extrapolable to children undergoing treatment following diagnosis through screening at age 4 to 5 yrs Whole population vision screening programme commenced following completion of this Australian study, thus uncertain mode of detection or age at diagnosis for children late treatment
Bogdanici, S. T., et al. (2015). "School integration for children with amblyopia." Rom J Ophthalmol 59(1): 48-51. (44)	Reported on school results for children with amblyopia but no validated metric and no control group or data from general population so unable to reach any conclusions about impact of amblyopia
Bogdanici, S. T., et al. (2015). "Quality of life for amblyopic children and their parents." Rev Med Chir Soc Med Nat Iasi 119(1): 214-220. (45)	Reported on quality of life for children with amblyopia but no validated metric and no control group or data from general population so unable to reach any conclusions about impact of amblyopia
Maqsd, M. A. and G. E. Arblaster (2015). "The incidence and visual acuity outcomes of children identified with ametropic amblyopia by vision screening." J aapos 19(2): 104-107. (46)	Only reported outcomes for subgroup of those who failed screening
Kemper AR, Crews JE, Strickland B, Saaddine JB. Vision screening among children aged 6 years--Medical Expenditure Panel Survey, United States, 2009-2010. MMWR supplements. 2014;63(2):43-6.(47)	Cost-effectiveness of vision screening for older children rather than children aged 4 to 5 yrs
Lowry EA, de Alba Campomanes AG. Cost-effectiveness of School-Based Eye Examinations in Preschoolers Referred for Follow-up From Visual Screening. JAMA ophthalmology. 2016;134(6):658-64.(48)	Cost-effectiveness of follow up care models for children who had failed vision screening tests, rather than cost-effectiveness of screening per se

Appendix 3 — Summary and appraisal of individual studies

Data Extraction

Table 7. Studies relevant to criterion 13, review question 1

Study reference	Study design and country	Screening test	Population characteristics	Proportion of children who (a) failed screening and (b) underwent diagnostic examination	False positive number	Comments
Hered 2013 (7)	Retro-spective cohort study USA	Crowded logMAR chart at age 3-5yrs. Threshold for positive screen: vision worse than 0.3 logMAR	Children aged 3-5yrs receiving well-child examinations within secondary care clinics. n=5896 eligible, of whom 2933 underwent vision screening. 30% aged 3yrs, remaining 70% aged 4-5yrs.	(a) 93 (3.2%) failed screening (b) 36/93 (39%) attended for ophthalmology examination	12/36 had no abnormality.	Different threshold used for pass fail (0.3 versus 0.2 in UK programme)
Langeslag -Smith, 2015(8)	Retro-spective cohort study New Zealand	Crowded logMAR chart plus orthoptic examination. Threshold for positive screen: vision worse than 0.2, or strabismus	Children aged 3-6 yrs attending pre-school well child examinations. n=5572 eligible for children, of whom 4916 received screening. Average age at screening was 52±4 months, range 37-70.	(a) 698 (14%) failed screening, (b) 556/698 (78%) attended for diagnostic examination within Hospital eye services	214/556 had normal vision	Children underwent orthoptic diagnostic examination, thus not directly comparable to practice as currently recommended
Toufeeq 2014(9)	Pros-pective observ-	Crowded logMAR chart at age 4-5yrs plus orthoptic examination. Threshold for positive screen: vision	Children aged 4-5yrs registered with a GP within an NHS Trust.	(a) 415 (11%) failed screening (b) 327/415 (79%) attended for diagnostic	38/260 children had no abnormality.	

	ational study UK	worse than 0.2, strabismus, or absence of binocularity	n=4171 eligible, of whom 3726 underwent screening	examination within Hospital eye services Data available for 260 children who attended		
--	---------------------	--	---	--	--	--

Table 8. Studies relevant to criterion 1, review question 2

Study reference	Study design, Country, setting	Population characteristics	Definition of exposure (Amblyopia)	Details of impact metric	Impact of exposure	Comments
OUTCOMES WITH TREATMENT						
Socio-economic and other functional outcomes						
Wilson 2013(23)	Prospective longitudinal birth cohort, New Zealand, Primary and secondary care	1032 individuals, of whom 97 had classic amblyopia and 175 modern amblyopia (see next column for description). 31 individuals had 'recovered modern amblyopia' (ie successfully responded to treatment, 36 amblyopia, and 108 possible amblyopia (ie fluctuating levels of vision between detection and adulthood).	Amblyopia as detected through visual health questionnaire undertaken at 3 and 5 years, and categorised using vision at 7-9 years. Vision worse than 6/12 (0.3) classic amblyopia, vision worse than 6/9 (0.2) modern amblyopia. Within each definition, four amblyopia groups: 1) no amblyopia; 2) recovered amblyopia – amblyopia or patching prior to age 7 years, but no amblyopia measured at ages 9–15 years,	Motor ability was scored using a combined score from the individual's Bayley Motor Scale at age 3 years, the McCarthy Motor Scale at age 5 years, and the Basic Motor Ability Reading ability as assessed with Burt reading test at ages 11, 13, 15 and 18 years Test at ages 7 and 9 years. Self-Esteem measured with Rosenberg Self-Esteem Scale. Socioeconomic status based on self-reported occupation at 21, 26 and 32 years	SEC and Other health outcomes: There was no statistically significant association between amblyopia and childhood motor ability score. Amblyopia was not associated with reading ability, or with self-esteem as measured at ages 11 and 13 years or with measures of adult socioeconomic status. Poor stereoacuity (<100 arc sec) was seen in 6/15, 40% with amblyopia, 17/63, 27% with possible amblyopia, and	There was no description of history of treatment for those with persistent amblyopia, thus the difference seen between recovered amblyopia and persistent amblyopia groups may not be due to 'exposure' to treatment.

			implying successful treatment; 3) amblyopia – constantly reduced vision; 4) possible amblyopia – fluctuating visual acuity measures between ages 7–15 years.		1/11, 9% with recovered amblyopia, 13/786, 1.7% without amblyopia. Stereoacuity was positively associated with childhood motor ability ($F [6,894] = 3.5, p=0.002$).	
Visual acuity and stereoacuity						
Stewart 2013(13)	Prospective observational longitudinal study, UK, NHS secondary care centres	85 children, mean age at referral 5.1+/- 1.5 years. 33 aged 4-6 years. In 21 children (mean age, 5.6 +/- 1.2 years), amblyopia was associated with anisometropia; in 29 mean age, 4.7+/-1.2 years), with strabismus; and in 35 (mean age, 5.3 +/- 1.5 years), with both anisometropia and strabismus (mixed) Treated population	Children aged 3-7 years with strabismic, anisometropic or mixed amblyopia: visual acuity of 0.1 log units or lower in worst eye and/or interocular difference of at least 0.1 log units, who underwent refractive therapy (spectacles full time for 18 weeks) or occlusion therapy. Within this was a subgroup of	Visual function outcome: acuity and stereoacuity	Refractive adaptation (glasses wear) resulted in a mean of 2 lines improvement (0.22+/-0.18 logMAR). Stereoacuity improved in 45% of treated children: improvement by at least one octave, the amount required to exceed test-retest variability, was achieved by 25 children (38%) who received refractive adaptation, 19 (28%) who	Treated population. No subgroup analysis of results for children aged 4- yrs, but regression analysis showed no statistically significant difference in stereoacuity outcomes across age groups (<48m, 48-72, >72m). Independent of age, poor stereoacuity was associated with poor visual acuity in the amblyopic eye, with a 1 logMAR decrease of visual acuity on average corresponding to a decrease in

			children aged 48-72 months (4-6yrs).		received occlusion, and 38 (45%) who underwent refractive adaptation and/or occlusion	stereoacuity of 0.51 log arcsec. Consistent with findings from previous 2012 review. These findings are however not long term.
Eye position						
Subramanian 2013(17)	Prospective cross sectional study, USA, Secondary care health centre	Children between the ages of 5 and 17 years with strabismus and / or anisometropia, and an age matched control group: 89 children, amblyopia in 7/31 with strabismus, 21/29 with anisometropia, 24/29 with both conditions. 40 control children. Treated population.	Anisometropic, strabismic or mixed amblyopia as diagnosed by ophthalmologist prior to the age of 7yrs, and defined as interocular difference of >0.2 logMAR, vision worse than 0.2.	Visual function outcome: Fixation stability was measured using a retinal camera and mapping of the area of the retina involved in movements during monocular fixation on an object. The smaller the area (bivariate contour ellipse, BCEA), the more stable the fixation.	Mean BCEA for amblyopic children was significantly larger than for normal control and non-amblyopic children ($F[2,123]=5.4$, $p=0.005$). Children had 3 times greater fixation instability during attempted steady gaze with amblyopia eyes than when fixing with their fellow eyes and compared to non-amblyopic controls. Fixation instability was associated with poorer visual acuity in the amblyopic eye. There was no	Treated population. Age at onset not reported: again, this research was undertaken in Texas, all children would have reached the age of 4yrs following introduction of the state vision screening programme. All affected children had been prescribed treatment for their amblyopia. The broader functional impact of monocular fixation instability is unclear.

					evaluation of fixation stability during binocular fixation (i.e. gaze with both eyes open).	
Hand eye co-ordination in experimental setting						
Grant 2014(20)	Prospective cross sectional study, UK, NHS secondary care centre	55 children with anisometropic, strabismic or mixed amblyopia: either undergoing (n=24) or recently completed (n=31) treatment, and 28 were normally sighted controls. Of the 30 amblyopic children aged 5-6yrs, 8 had anisometropia, and 22 strabismus. Of the 25 amblyopic children aged 7-9yrs, 11 had anisometropia, and 14 strabismus. Treated population	Amblyopia as detected prior to 5yrs and confirmed by Hospital Eye Services	Functional outcome: Participants reached for and precision grasped cylindrical household objects of “small” (24 mm) or “large” (48 mm) diameter, but similar (100 mm) height, placed at a “near” and “far” locations.	Movement duration, time to peak velocity, and grip patterns were recorded. Performance with both eyes open were better than with monocular viewing for all but the amblyopes aged 5-7yrs. Binocular performance was slower in amblyopic children, with severity of amblyopia accounting for much of the variance in movement duration (adjusted $R^2=0.16$, $b=0.43$, $t=2.5$, $p=0.017$). 5-6yr old children with amblyopia made significantly more total	Treated population. No definite report of age at diagnosis for children with amblyopia, or mode of detection, but health care environment within which this research was undertaken involves whole population screening of vision at age 4-5yrs

					<p>reaching errors than their age-matched controls particularly when using both eyes. Regression analysis suggested that poor stereovision was the sole factor responsible for the increased total reach errors in these patients (adjusted $R^2=0.16$, $b=0.50$, $t=3.0$, $p=0.007$). Average data obtained from the older (aged 7-9yrs) patients with “cured” stereoacuities (three of whom had residual mild or moderate amblyopia) were all within the upper bound 95% confidence limits of (i.e., indistinguishable from) age-matched controls.</p>	
Reading speed						
Kelly 2017(19)	Prospective cross	Non-amblyopic and amblyopic school-age	Amblyopia as diagnosed by	SEC / Educational outcome: Reading	Amblyopic anisometropic	Treated population. Age at onset not

	sectional study, USA, Secondary care health centre	children treated for anisometropia, and age matched control group: 65 children; 25 amblyopic anisometropic children (mean age, standard deviation [SD], 9.8, 1.4 years), 15 non-amblyopic anisometropic children (10.1, 1.8 years), and 25 normal controls (mean age, 9.7, 1.5 years)	ophthalmologist prior to the age of 7yrs, associated with anisometropia, and defined as interocular difference of >0.2 logMAR, vision worse than 0.2. Unilateral amblyopes only	was assessed with the child wearing infrared goggles and silently reading paragraphs of text from a booklet held at 35-40cm from face, with comprehension later tested by examiners.	children read 24% slower (mean, 149 +/- 42 words/min) than non-amblyopic anisometropic children (mean, 196 +/- 80 words/min; $p=0.024$), and 22% slower than normal control children (mean, 191 +/- 65 words/min; $p<0.020$). 'Normal' (fellow) eye fixation instability was seen in children with amblyopia, as was increased eye movement ('forward saccades'). These factors were associated with a slower reading speed. Comprehension did not differ between groups.	reported, so unclear how many of these children were diagnosed between ages 4-5yrs, and whether they were diagnosed through screening. However, since 1989, the Texas State Vision Screening Program requires that all children enrolled for the first time in any public, private, parochial, or denominational school or in a licensed child care centre or care home must be screened on reaching their 4th birthday (https://www.dshs.texas.gov/vhs/vision-require.aspx). Screening is undertaken using a crowded logMAR chart at distance. Threshold for positive screen: vision worse than 20/30 (0.2). All children in the study would have reached age of 4yrs following
--	--	---	---	--	---	---

						the introduction of the programme. All affected children had been prescribed treatment for their amblyopia
Kelly 2015(18)	Prospective cross sectional study, USA, Secondary care health centre	Non-amblyopic and amblyopic school-age children treated for strabismus, and age matched control group : 73 children: 29 amblyopia (mean age with standard deviation [SD], 9.4 ± 1.2 years, range 8.0–12.4 years), 23 treated strabismus without amblyopia (9.8 ± 1.4 years; 2–12.3 years), and 21 normal controls (10.1 ± 1.4 years, 8.1–12.5 years) Treated population	Amblyopia as diagnosed by ophthalmologist prior to the age of 7yrs, and defined as an interocular difference in visual acuity of ≥ 0.2 LogMAR vision worse than 0.2 logMAR. Unilateral amblyopes only	SEC / Educational outcome: Reading was assessed with the child wearing infrared goggles and silently reading paragraphs of text from a booklet held at 35-40cm from face, with comprehension later tested by examiners.	Reading speed was significantly different between groups ($F_{2,70} = 6.58$, $P = 0.002$). Amblyopic children read significantly more slowly (mean, 148 ± 52 words/minute) than strabismic children without amblyopia (mean, 198 ± 71 words/minute; $P = 0.004$), and normal control children (mean, 204 ± 62 words/minute; $P = 0.002$). Increased eye movements ('forward saccades') were seen in amblyopic children. Comprehension for all children within the study was $\geq 80\%$.	Treated population. All affected children had been prescribed treatment for their amblyopia. Findings are consistent with those reported by same research group.(21)
Other functional outcomes: visuo-auditory integration						

Burgmeier 2015(21)	Retrospective observational longitudinal study, USA, secondary care centres	Children aged over 3 years old with amblyopia. 33 participants with amblyopia mean age 7yrs +/- 1.5yrs, range 3-9. Study population subgroups: children whose onset of amblyopia was prior to 5 years of age (group 1, n=21) and children whose onset of amblyopia was on or after 5 years of age (group 2, n=5). Group 1 was further subdivided into 2 subgroups: those whose amblyopia responded to treatment before 5 years of age (group 1A, n=3) and those whose amblyopia was unresolved at 5 years of age (group 1B, n=19). 9 controls, mean age 8yrs +/- 3.4, range 4-14. Treated population	Amblyopia, recognised through pre-school screening examination, defined as difference in vision of at least 2 Snellen lines, with or without history of treatment	Functional outcome: The McGurk effect, in which visual-auditory integration is demonstrated by an illusory 'blended' perception of different auditory and visual stimuli, was used as an outcome measure. A stimulus presenting an audio track playing the sound /pa/ and a separate video track of a person articulating /ka/, producing the perception of hearing a fusion sound /ta/ in those with normal visual-auditory integration.	All 9 controls perceived the illusion, whilst 11 of the 24 children with amblyopia (46%) perceived it. All of the 5 late onset amblyopia children and all 3 children in whom early onset amblyopia had been treated by age 5yrs could perceive the illusion. There was no association between stereoacuity / vision level in the amblyopic eye and perception of the illusion.	Treated population. Type of pre-school screening (age of participants and tests used) undertaken not described. Although the broader functional consequences of abnormal visuo-auditory integration are unclear, abnormal visuoauditory integration is a marker of abnormal audiovisual perception, particularly in the perception of speech
OUTCOMES WHERE TREATMENT HISTORY IS UNCLEAR						
Visual functional outcome: Stereoacuity						

Jeon 2017(24)	Retrospective cross sectional study, South Korea, secondary care centre.	107 children aged 5-16yrs with anisometropia NA=non-amblyopic anisometropia, n = 72 AA=amblyopic anisometropia, n = 35 And 73 normal subjects without anisometropia	Amblyopia not defined	Stereopsis using Titmus stereotest	The mean stereopsis was significantly worse in the AA group than in the NA and control groups (641.71arc sec \pm 1443.58, 76.25 \pm 55.78, and 54.52 \pm 20.00, respectively; AA vs.NA, P < 0.001, and AA vs. control, P < 0.001, Kruskal–Wallis test).	Treatment history was not reported for individuals with anisometropia (that is, they may have had successfully treated amblyopia.
Visual functional outcome: Visual search tasks						
Chen 2018(25)	Prospective cross sectional study, USA, secondary care centre.	21 individuals with amblyopia and 10 controls. Amblyopic individuals divided into mild (n=9), moderate (n=8), and severe (n =4)	Defined as vision worse than 0.2 logMAR	Visual search tasks: identifying 10 differences between two otherwise identical scenes.	Monocular viewing through amblyopic eyes was associated with diminished ability to identify differences on visual search. Number of differences identified: controls: 4.73 \pm 2.5; mild amblyopia: 3.60 \pm 2.2; moderate: 2.61 \pm 2.03; severe: 0.77 \pm 1.39, P< 0.0001, ANOVA.	Age at presentation and mode of detection not described for amblyopic individuals

Visual functional outcome: Eye position						
Gonzalez 2012(29)	Retrospective cross sectional study, USA, secondary care centre, to investigate in amblyopia	13 adults with amblyopia, and 20 visually normal controls.	Amblyopia based on adult vision worse than 0.2	Eye position stability in binocular gaze measured using eye tracking (size of movement of fixed points at back of the eye) and screen. Measured on an inverse log scale, with number nearer 0 meaning more movement.	Individuals with amblyopia exhibited a significant decrease in fixation stability in the amblyopic eye, and exhibited binocular summation with the fellow but not with the amblyopic eye. ANOVA analysis of variance $F(1.95,23.39) = 26.68$, $P < 0.001$, partial $\eta^2 = 0.69$. The decrease in fixation stability in the amblyopia group was attributed to slow eye drifts.	Broader functional impact is unclear, as the fellow eye fixation stability in amblyopes was similar to controls. Age at presentation and mode of detection not reported
Raashid 2016(26)	Prospective cross sectional study, Canada, secondary care centre	11 adults with anisometropic amblyopia, and 14 visually normal observers	Amblyopia was defined as an interocular visual acuity difference of greater than or equal to 0.18 logMAR.	Tracking of eye following target on screen	Although smooth pursuit gaze was delayed in amblyopic eyes, (206 +/- 20 ms vs 183 +/- 17 ms, $P < 0.002$) Binocular (both eyes open) smooth	Adults with anisometropic amblyopia, no report of age at onset / diagnosis or mode of detection, within region where there is no uniform childhood

					pursuit not significantly different in amblyopic adults.	vision screening (Ontario, Canada)
Chung 2015(27)	Prospective cross sectional study.	16 controls. 14 with anisometropic amblyopia, 14 with strabismic amblyopia	Difference between two eyes (interocular difference) of 0.2 logMAR	Frequency and size of errors of 'landing' on target, amplitude and size of microsaccades (movements to maintain fixation), and amplitude and speed of slow drifts (involuntary movements off target between saccades).	There was no significant difference between the non-amblyopic eyes of amblyopic children and control children.	Individuals with amblyopia, age at diagnosis and mode of detection not reported
Shaikh 2016(28)	Prospective cross sectional study, USA, Secondary care health centre	Children with amblyopia aged 4-15 (n=19), and controls aged 5-10 (n=9)	Visual acuity worse than LogMAR 0.17 in the amblyopic eye, and interocular difference of 2 or more logMAR lines	Eye movement recordings during tracking on a screen	Abnormal fixation movements were seen in children with amblyopia in both the amblyopic and the fellow eye. The subjects with amblyopia had a significant decrease in microsaccade frequency (the physiological movement to maintain fixation). The variance and velocity of ocular 'drifting' (slow involuntary	Children with amblyopia aged 4-15, no evidence of associated screening programme, no report of age at onset / diagnosis, or onset of treatment

					movements between fixation attempts) were increased even when amblyopic participants were using their better seeing eye (mild amblyopia: $r = 0.82$, $p < 0.0001$; mod amblyopia: $r = 0.76$, $p < 0.0001$; severe amblyopia: $r = 0.69$, $p < 0.0001$)	
Visual functional outcome: hand eye co-ordination						
Niechwiej - Szwedo 2012(31)	Prospective cross sectional study, Canada, secondary care health centre	14 with strabismic amblyopia, 13 with strabismus only, and 14 visually normal	Amblyopia was defined as an interocular visual acuity difference of greater than or equal to 0.18 logMAR.	Saccade performance: tracking eye movements on reaching for a target presented on a screen.	Reach precision was significantly worse in patients with severe amblyopia during amblyopic eye viewing. Amblyopic patients without stereopsis needed to initiate secondary ("corrective") saccadic eye movements under binocular viewing conditions more frequently than visually normal participants. These	Adults with anisometropic amblyopia, no report of age at onset / diagnosis or mode of detection, within region where there is no uniform childhood vision screening (Ontario, Canada)

					secondary saccades improved the final precision of saccade gaze.	
Niechwiej-Szwedo 2014(33)	Prospective cross sectional study, Canada, secondary care health centre	16 with strabismic amblyopia, 14 with strabismus only, and 16 visually normal	Amblyopia was defined as an interocular visual acuity difference of greater than or equal to 0.18 logMAR.	Reaching pattern and peak acceleration of hands during visually-guided reaching exercise using tracking screen	Monocular viewing with the amblyopic eye was associated with slower and less precise reaching patterns. Participants with strabismic amblyopia also had reduced peak acceleration when reaching for targets viewed binocularly. This may have been a secondary compensatory mechanism to allow them to attain similar reaching precisions as those seen in non-amblyopes.	Adults with anisometropic amblyopia, no report of age at onset / diagnosis or mode of detection, within region where there is no uniform childhood vision screening (Ontario, Canada)
Niechwiej-Szwedo 2014(32)	Prospective cross sectional study, Canada, secondary	16 with strabismic amblyopia, 14 with strabismus only, and 16 visually normal	Amblyopia was defined as an interocular visual acuity difference of greater than or equal to 0.18 logMAR.	Pattern of temporal eye-hand coordination during reaching exercise using tracking screen	Amplitude and time to peak velocity of reach were higher during amblyopic eye viewing than during other	Adults with anisometropic amblyopia, no report of age at onset / diagnosis or mode of detection, within region where there is

	care health centre				viewing conditions. There were no significant associations between amblyopia and temporal patterns on binocular viewing.	no uniform childhood vision screening (Ontario, Canada)
Niechwiej-Szwedo 2017(30)	Prospective cross sectional study, Canada, secondary care health centre	55 adults with amblyopia (22 anisometropic, 18 strabismic, 15 mixed mechanism), 14 adults with strabismus without amblyopia, and 22 visually-normal control adults	Amblyopia was defined as an interocular visual acuity difference of greater than or equal to 0.18 logMAR.	Deficits on reaching for target on tracking screen	Amblyopia was associated with deficits in reaching for a target presented on a screen when the individual had both eyes open (binocular viewing). Multivariate analysis revealed that the best fitting model that accounted for 35% of total variance in precision had 2 predictors: acuity of amblyopic eye (b amblyopic eye acuity 0.060, $P < 0.0001$), and eye deviation. Amblyopic eye acuity alone accounted for 22% of the variance in	Adults with anisometropic amblyopia, no report of age at onset / diagnosis or mode of detection, within region where there is no uniform childhood vision screening (Ontario, Canada)

					the univariate analysis.	
Other functional outcomes: visuo-auditory integration						
Narinesingh 2015(49)	Retrospective crosssectional study, USA, secondary care centres,	28 'young' children aged 4-9yrs (mean 6.3+/-1.3yrs), 12 older children (mean 11.5+/-2yrs), and 22 adults (mean 33+/-10.9yrs) and 66 age matched controls (24 young children, 17 older children, 25 adults).	Visual acuity of 0.18 logMAR (20/30) or worse in the amblyopic eye, as well as an intraocular difference (IOD) greater than or equal to 0.2 logMAR.	Susceptibility to the McGurk effect, in which visual-auditory integration is demonstrated by an inability to distinguish between incongruent auditory and visual stimuli. A stimulus presenting an audio track playing the sound /pa/ and a separate video track of a person articulating /ka/), producing the perception of hearing a fusion sound /ta/ in those with normal visual-auditory integration.	Fewer participants with amblyopia (72%+/-3%) were able to perceive the McGurk effect when compared to the control group (85%+/-2%). Increasing age, amongst both amblyopes and visually normal individuals, was associated with greater susceptibility to the illusion.	Age at presentation and mode of detection not described for amblyopic individuals

Table 9. Studies relevant to criterion 11.

Study reference	Study design, Country	Population characteristics	Intervention (screening programme)	Comparator	Definition of amblyopia	Study results / outcomes	Comments
Hoeg 2015(35)	Population based cross-sectional study, Denmark	All adults aged 30 years and over in 2010 (n=2295) and a random sample of 25% of adults aged 20–29 from the municipality of Næstved, Denmark (n=3826 who were randomly selected to participate in the Danish Rural Eye Study, DRES).	Systematic screening at age 3-4yrs (as undertaken from 1978 within Denmark)	No systematic screening before age 6yrs	Amblyopia in adulthood confirmed through examination in 2010-2013 and defined as interocular acuity difference of 2-lines, with worse than 0.3 in the worse seeing eye, in addition to one or more of the following factors: strabismus/previous strabismus surgery; anisometropia and/or evidence of past or present visual axis obstruction for >1 week in early childhood.	Amongst the 494 participants who would have been systematically screened, prevalence of amblyopia in adulthood was 0.44%. Amongst the 2295 who had not undergone screening before age 6yrs, 1.78% had amblyopia.	Causal relationship between introduction screening programme and reduction in amblyopia prevalence not proven: improvements in general health may be key contributing factor.
Shapira 2018(36)	Population based cross-sectional study, Israel	Military conscripts aged 16–19yrs, born between 1971 and 1994, who completed the medical profiling process in the years 1988–2012. N=107896 young adults who presented	Compulsory vision screening before age 6yrs (as undertaken in Israel since early 1990s)	No systematic screening before age 6yrs	Unilateral amblyopia was defined as vision worse than 6/9 (0.2 logMAR) in either eye or as an interocular difference of two lines or more. Bilateral amblyopia defined as vision worse than 6/9 in both eyes. Moderate = worse than 6/12 (0.3),	The prevalence of amblyopia was 1.2% (95% CI–1.07% to 1.23%) in the population born between 1971 and 1985, with a decline to 0.8% (95% CI–0.73% to 0.90%, p<0.001) in the population born	

		at the recruitment centre in 1988. Mean age 17+/- 0.6yrs			severe worse than 6/24 (0.5).	between 1986 and 1994. This decline can be attributed to a drop in unilateral amblyopia prevalence from 1% (95% CI– 0.86% to 1.01%) to 0.6% (95% CI– 0.58% to 0.73%, $R^2=0.93$, $p<0.001$), while bilateral amblyopia prevalence remained relatively stable (~0.2%, 95% CI–0.18% to 0.23%, $p=0.12$). Prevalence of severe amblyopia did not change and as ~0.18% (95% CI–0.16% to 0.21%) across years	
--	--	--	--	--	-------------------------------	--	--

Appraisal for quality and risk of bias

Quality assessments of included studies are reported below.

Table 5. Quality assessment of included studies using the Critical Appraisal Skills Programme checklist for observational studies

Hered , R. W. and D. L. Wood (2013). "Preschool vision screening in primary care pediatric practice." Public Health Rep 128(3): 189-197(12)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	To determine the effectiveness of vision screening for pre-school children
Did the authors use an appropriate method to answer their question?	N	High	Retrospective cohort with no follow up of those who test negative on screening
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Children aged 3-5yrs receiving well-child examinations
Were the controls selected in an acceptable way?	n/a		
Was the exposure accurately measured to minimise bias?	Y	Low	Assessment of monocular acuity using crowded LogMAR chart within secondary care clinic
Was the outcome accurately measured to minimise bias?	Y	Low	Threshold for reduced vision: worse than 0.3
Have the authors identified all important confounding factors?	n/a		
Have they taken account of the confounding factors in the design and/or analysis?	n/a		
Was the follow up of subjects complete enough?	N	High	no follow up of those who test negative on screening
Section B: What are the results?			
Are the results precise?	Y	Low	
Do you believe the results?	Y	Low	

Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Y		Crowded logMAR test
Do the results of this study fit with other available evidence?	Unclear		Evidence on false positive rate of childhood vision screening is missing
Langeslag-Smith, M. A., et al. (2015). "Preschool children's vision screening in New Zealand: a retrospective evaluation of referral accuracy." BMJ Open 5(11): e009207(11)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	To assess the accuracy of preschool vision screening in a large, ethnically diverse, urban population of pre-school children
Did the authors use an appropriate method to answer their question?	N	High	Retrospective cohort with no follow up of those who test negative on screening
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Children aged 3-6 yrs attending pre-school well child examinations
Were the controls selected in an acceptable way?	n/a		
Was the exposure accurately measured to minimise bias?	Y	Low	Assessment of monocular acuity using crowded logMAR chart plus orthoptic examination (cover test, binocularity test, stereopsis test).
Was the outcome accurately measured to minimise bias?	Y	Low	Threshold for reduced vision: worse than 0.2 logMAR or failed orthoptic exam
Have the authors identified all important confounding factors?	n/a		
Have they taken account of the confounding factors in the design and/or analysis?	n/a		
Was the follow up of subjects complete enough?	N	High	no follow up of those who test negative on screening
Section B: What are the results?			
Are the results precise?	Y	Low	
Do you believe the results?	Y	Low	
Section C: Will the results help (applicability)?			

Applicable to UK screening test of interest?	N		Children underwent orthoptic diagnostic assessment, thus not directly comparable to practice as currently recommended.
Do the results of this study fit with other available evidence?	Unclear		Existing evidence on false positive rate of childhood vision screening involve heterogeneous 'screening' tests
Touffeeq, A. and A. J. Oram (2014). "School-entry vision screening in the United Kingdom: practical aspects and outcomes." Ophthalmic Epidemiol 21(4): 210-216(10)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	To describe and assess an orthoptist-led vision screening service for reception children and report outcomes
Did the authors use an appropriate method to answer their question?	N	High	Prospective cohort with no follow up of those who test negative on screening
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Children aged 4-5yrs registered with a GP within an NHS Trust
Were the controls selected in an acceptable way?	n/a		
Was the exposure accurately measured to minimise bias?	Y	Low	Assessment of monocular acuity using crowded logMAR chart plus orthoptic examination (cover test).
Was the outcome accurately measured to minimise bias?	Y	Low	Threshold for reduced vision: worse than 0.2 logMAR or failed orthoptic exam
Have the authors identified all important confounding factors?	n/a		
Have they taken account of the confounding factors in the design and/or analysis?	n/a		
Was the follow up of subjects complete enough?	N	High	no follow up of those who test negative on screening
Section B: What are the results?			
Are the results precise?	Y	Low	
Do you believe the results?	Y	Low	
Section C: Will the results help (applicability)?			

Applicable to UK screening test of interest?	N		Although UK based, children underwent diagnostic examination, thus not directly comparable to practice as currently recommended. Time between screening and HES not reported: for some children normal vision may have been due to maturation of visual function rather than a false positive test for reduced vision at screening.
Do the results of this study fit with other available evidence?	Unclear		Existing evidence on false positive rate of childhood vision screening involve heterogeneous 'screening' tests
Kelly, K. R., et al. (2017). "Slow reading in children with anisometropic amblyopia is associated with fixation instability and increased saccades." J aapos 21(6): 447-451.e441.(21)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	To evaluate whether slow reading was associated with ocular motor dysfunction in children with amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Prospective cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Undergoing treatment for anisometropic amblyopia
Were the controls selected in an acceptable way?	Unclear	Unclear	No details on recruitment of controls
Was the exposure accurately measured to minimise bias?	Y	Low	Amblyopia as diagnosed by ophthalmologist prior to the age of 7yrs, associated with anisometropia, and defined as interocular difference of >0.2 logMAR, vision worse than 0.2. Unilateral amblyopes only
Was the outcome accurately measured to minimise bias?	Y	Low	Reading was assessed with the child wearing infrared goggles and silently reading paragraphs of text from a booklet held at 35-40cm from face, with comprehension later tested by examiners.
Have the authors identified all important confounding factors?	N	High	No: eg ethnicity / IQ / socioeconomic status

Have they taken account of the confounding factors in the design and/or analysis?	N	High	See above
Was the follow up of subjects complete enough?	n/a		
Section B: What are the results?			
Are the results precise?	Y		
Do you believe the results?	Y		
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Y		
Do the results of this study fit with other available evidence?	Y		Consistent with other evidence on impact of amblyopia on eye gaze and resultant impact on reading speed. However, wider educational impact is unclear.
Kelly, K. R., et al. (2015). "Amblyopic children read more slowly than controls under natural, binocular reading conditions." J aapos 19(6): 515-520.(22)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	To evaluate whether slow reading was associated with ocular motor dysfunction in children with amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Prospective cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Undergoing treatment for anisometropic amblyopia
Were the controls selected in an acceptable way?	Unclear	Unclear	No details on recruitment of controls
Was the exposure accurately measured to minimise bias?	Y	Low	Amblyopia as diagnosed by ophthalmologist prior to the age of 7yrs, associated with anisometropia, and defined as interocular difference of >0.2 logMAR, vision worse than 0.2. Unilateral amblyopes only
Was the outcome accurately measured to minimise bias?	Y	Low	Reading was assessed with the child wearing infrared goggles and silently reading paragraphs of text from a booklet held at 35-40cm from face, with comprehension later tested by examiners.

Have the authors identified all important confounding factors?	N	High	No: eg ethnicity / IQ / socioeconomic status
Have they taken account of the confounding factors in the design and/or analysis?	N	High	See above
Was the follow up of subjects complete enough?	n/a		
Section B: What are the results?			
Are the results precise?	Y		
Do you believe the results?	Y		
Section C: Will the results help (applicability)?			
Applicable to UK population of interest?	Y		
Do the results of this study fit with other available evidence?	Y		Consistent with other evidence on impact of amblyopia on eye gaze and resultant impact on reading speed. However, wider educational impact is unclear.
Subramanian, V., et al. (2013). "A quantitative study of fixation stability in amblyopia." Invest Ophthalmol Vis Sci 54(3): 1998-2003.(20)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	To evaluate the association between fixation instability and amblyopia in children
Did the authors use an appropriate method to answer their question?	Y	Low	Prospective cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Children undergoing treatment for amblyopia
Were the controls selected in an acceptable way?	Unclear	Unclear	Recruitment method is unclear
Was the exposure accurately measured to minimise bias?	Y	Low	Anisometropic, strabismic or mixed amblyopia as diagnosed by ophthalmologist prior to the age of 7yrs, and defined as interocular difference of >0.2 logMAR, vision worse than 0.2.
Was the outcome accurately measured to minimise bias?	Y	Low	Fixation stability was measured using a retinal camera and mapping of the area of the retina

			involved in movements during monocular fixation on an object.
Have the authors identified all important confounding factors?	N	High	Eg Ethnicity / refractive error / Retinal architecture not captured
Have they taken account of the confounding factors in the design and/or analysis?	N	High	See above
Was the follow up of subjects complete enough?	n/a		
Section B: What are the results?			
Are the results precise?	Y		
Do you believe the results?	Y		
Section C: Will the results help (applicability)?			
Applicable to UK population of interest?	Y		
Do the results of this study fit with other available evidence?	Y		Consistent with other evidence on impact of amblyopia on eye gaze and resultant impact on reading speed. However, wider educational impact is unclear.
Stewart, C. E., et al. (2013). "The effect of amblyopia treatment on stereoacuity." J aapos 17(2): 166-173(16)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	To determine the response to therapy for amblyopia as a function of age and category of amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Prospective observational longitudinal study, UK, NHS secondary care centres
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Children aged 3-7 years with strabismic, anisometropic or mixed amblyopia: visual acuity of 0.1 log units or lower in worst eye and/or interocular difference of at least 0.1 log units. Within this was a subgroup of children aged 48-72 months (4-6yrs).
Were the controls selected in an acceptable way?	n/a		
Was the exposure accurately measured to minimise bias?	Y	Low	Refractive therapy: spectacles full time for 18 weeks. Occlusion therapy: 6 hours occlusion per day.

Was the outcome accurately measured to minimise bias?	Y	Low	Acuity and stereoacuity
Have the authors identified all important confounding factors?	N	Unclear	Excluded those with previous occlusion therapy or coexisting ocular disease, but no capture of socioeconomic status
Have they taken account of the confounding factors in the design and/or analysis?	Y	Low	Excluded those with previous occlusion therapy or coexisting ocular disease, adjusted for age / concordance with treatment
Was the follow up of subjects complete enough?	N	High	Study follow up ends at 18 weeks
Section B: What are the results?			
How precise are the results?	Y		
Do you believe the results?	Y		
Section C: Will the results help (applicability)?			
Applicable to UK population of interest?	Y		UK population within study
Do the results of this study fit with other available evidence?	Y		Consistent with other evidence on negative impact of untreated amblyopia on stereopsis
Grant, S., et al. (2014). "Age- and stereovision-dependent eye-hand coordination deficits in children with amblyopia and abnormal binocularity." Invest Ophthalmol Vis Sci 55(9): 5687-57015.(23)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	N	High	Study objective described as: to examine factors contributing to eye–hand coordination deficits in children with amblyopia and impaired stereovision. However, hand-eye coordination was assessed using experimental settings with no clear description of how this impacted with real life activities
Did the authors use an appropriate method to answer their question?	Y	Low	Prospective cross sectional study with amblyopes and controls.
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Children undergoing treatment
Were the controls selected in an acceptable way?	Unclear	Unclear	

Was the exposure accurately measured to minimise bias?	N	High	Amblyopia not defined in this paper.
Was the outcome accurately measured to minimise bias?	Y	Low	Participants reached for and precision grasped cylindrical household objects of “small” (24 mm) or “large” (48 mm) diameter, but similar (100 mm) height, placed at a “near” and “far” locations. Speed and trajectory captured
Have the authors identified all important confounding factors?	N	High	No formal assessment of global motor skills of cases or controls
Have they taken account of the confounding factors in the design and/or analysis?	N	High	See above
Was the follow up of subjects complete enough?	n/a		
Section B: What are the results?			
Are the results precise?	Y		
Do you believe the results?	Y		
Section C: Will the results help (applicability)?			
Applicable to UK population of interest?	Y		UK population within study
Do the results of this study fit with other available evidence?	Y		Consistent with other evidence on negative impact of amblyopia on reaching exercises within experimental settings
Burgmeier R., et al. (2015). "The effect of amblyopia on visual-auditory speech perception: why mothers may say "Look at me when I'm talking to you". JAMA Ophthalmol 133(1): 11-16.(24)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	To determine whether a history of amblyopia is associated with abnormal visual-auditory speech integration
Did the authors use an appropriate method to answer their question?	N	High	Retrospective study: prospective cross sectional would have been more appropriate
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Children aged over 3 years old with amblyopia, recognised through pre-school screening examination
Were the controls selected in an acceptable way?	Y	Low	Controls were recruited through preschool-screening eye examinations

Was the exposure accurately measured to minimise bias?	Y	Low	Amblyopia (defined as difference in vision of at least 2 Snellen lines) with or without history of treatment
Was the outcome accurately measured to minimise bias?	Y	Low	The McGurk effect, in which visual-auditory integration is demonstrated by an illusory 'blended' perception of different auditory and visual stimuli, was used as an outcome measure
Have the authors identified all important confounding factors?	Y	Low	
Have they taken account of the confounding factors in the design and/or analysis?	Y	Low	Excluded from participating in study
Was the follow up of subjects complete enough?	n/a		
Section B: What are the results?			
Are the results precise?	Y		
Do you believe the results?	Y		
Section C: Will the results help (applicability)?			
Applicable to UK population of interest?	Y		
Do the results of this study fit with other available evidence?	Y		Consistent with emerging evidence on impact of early life abnormal vision on visuo-auditory integration
Shaikh, A. G., et al. (2016). "Abnormal Fixational Eye Movements in Amblyopia." PLoS One 11(3): e0149953.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Fixation behaviour
Did the authors use an appropriate method to answer their question?	Y	Low	Eye movement tracking
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Recruitment in secondary care: can infer that some children had treatment, but age at which treatment given unclear
Were the controls selected in an acceptable way?	Unclear	Unclear	Not described in detail
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment not described

Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective measurement
Have the authors identified all important confounding factors?	N	High	Treatment/ age diagnosis not considered, or severity of vision
Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above
Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			
Are the results precise?	Y	Low	Measurements of different parameters of gaze
Do you believe the results?	Y	Low	Consistent with other evidence on gaze in amblyopia
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Unclear		Age at onset / mode of detection not reported. However, other clinical characteristics (eg general health status of cohort) may be similar as it is set in a higher income country
Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on gaze in amblyopia
Chung, S. T., et al. (2015). "Characteristics of fixational eye movements in amblyopia: Limitations on fixation stability and acuity?" Vision Res 114: 87-99.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Fixation behaviour
Did the authors use an appropriate method to answer their question?	Y	Low	Eye movement tracking errors
Was/were the cohort / cases recruited in an acceptable way?	Unclear	Unclear	Relationship between recruitment / treatment unclear
Were the controls selected in an acceptable way?	Unclear	Unclear	Not described in detail
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment not described
Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective measurement

Have the authors identified all important confounding factors?	N	High	Treatment/ age diagnosis not considered (although vision level has been considered)
Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above
Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			
Are the results precise?	Y	Low	Measurements of errors made in gaze 'landing' on target position.
Do you believe the results?	Y	Low	Consistent with other evidence on gaze in amblyopia
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Unclear		Age at onset / mode of detection not reported. However, other clinical characteristics (eg general health status of cohort) may be similar as it is set in a higher income country
Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on gaze in amblyopia
Niechwiej-Szwedo, E., et al. (2017). "Effects of Reduced Acuity and Stereo Acuity on Saccades and Reaching Movements in Adults With Amblyopia and Strabismus." Invest Ophthalmol Vis Sci 58(2): 914-921.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Eye position and reaching behaviour in adults with amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Target on a screen, cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Unclear	High	Unclear how these adults were identified / approached / recruited: particularly important for disease of childhood onset
Were the controls selected in an acceptable way?	Unclear	High	Selection process not described
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment not described
Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective outcome measure

Have the authors identified all important confounding factors?	N	High	Treatment/ age diagnosis not considered. Presence of depth perception vision has been identified
Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above
Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			
Are the results precise?	Y	Low	Objective measures used
Do you believe the results?	Y	Low	Consistent with other evidence on gaze in amblyopia
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Unclear		Adults with amblyopia, no report of age at onset / diagnosis or mode of detection, within region where there is no uniform childhood vision screening (Ontario, Canada)
Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on eye gaze in amblyopia
Niechwiej-Szwedo, E., et al. (2014). "Effects of strabismic amblyopia and strabismus without amblyopia on visuomotor behavior: III. Temporal eye-hand coordination during reaching." Invest Ophthalmol Vis Sci 55(12): 7831-7838.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Eye position and reaching behaviour in adults with amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Target on a screen, cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Unclear	High	Unclear how these adults were identified / approached / recruited: particularly important for disease of childhood onset
Were the controls selected in an acceptable way?	Unclear	High	Selection process not described
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment not described
Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective outcome measure

Have the authors identified all important confounding factors?	N	High	Treatment/ age diagnosis not considered. Presence of depth perception vision has been identified
Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above
Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			
Are the results precise?	Y	Low	Objective measures used
Do you believe the results?	Y	Low	Consistent with other evidence on gaze in amblyopia
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Unclear		Adults with amblyopia, no report of age at onset / diagnosis or mode of detection, within region where there is no uniform childhood vision screening (Ontario, Canada)
Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on eye gaze in amblyopia
Niechwiej-Szwedo, E., et al. (2014). "Effects of strabismic amblyopia on visuomotor behavior: part II. Visually guided reaching." Invest Ophthalmol Vis Sci 55(6): 3857-3865.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Eye position and reaching behaviour in adults with amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Target on a screen, cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Unclear	High	Unclear how these adults were identified / approached / recruited: particularly important for disease of childhood onset
Were the controls selected in an acceptable way?	Unclear	High	Selection process not described
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment not described
Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective outcome measure

Have the authors identified all important confounding factors?	N	High	Treatment/ age diagnosis not considered. Presence of depth perception vision has been identified
Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above
Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			
Are the results precise?	Y	Low	Objective measures used
Do you believe the results?	Y	Low	Consistent with other evidence on gaze in amblyopia
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Unclear		Adults with amblyopia, no report of age at onset / diagnosis or mode of detection, within region where there is no uniform childhood vision screening (Ontario, Canada)
Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on eye gaze in amblyopia
Niechwiej-Szwedo, E., et al. (2012). "Effects of strabismic amblyopia and strabismus without amblyopia on visuomotor behavior, I: saccadic eye movements." Invest Ophthalmol Vis Sci 53(12): 7458-7468.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Eye position in adults with amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Target on a screen, cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Unclear	High	Unclear how these adults were identified / approached / recruited: particularly important for disease of childhood onset
Were the controls selected in an acceptable way?	Unclear	High	Selection process not described
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment not described
Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective outcome measure
Have the authors identified all important confounding factors?	N	High	Treatment/ age diagnosis not considered. Presence of depth perception vision has been identified

Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above
Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			
Are the results precise?	Y	Low	Objective measures used
Do you believe the results?	Y	Low	Consistent with other evidence on gaze in amblyopia
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Unclear		Adults with amblyopia, no report of age at onset / diagnosis or mode of detection, within region where there is no uniform childhood vision screening (Ontario, Canada)
Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on gaze in amblyopia
Raashid, R. A., et al. (2016). "The Initiation of Smooth Pursuit is Delayed in Anisometropic Amblyopia." Invest Ophthalmol Vis Sci 57(4): 1757-1764.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Eye position and reaching behaviour in adults with amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Target on a screen, cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Unclear	High	Unclear how these adults were identified / approached / recruited: particularly important for disease of childhood onset
Were the controls selected in an acceptable way?	Unclear	High	Selection process not described
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment not described
Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective outcome measure
Have the authors identified all important confounding factors?	N	High	Treatment/ age diagnosis not considered. Presence of depth perception vision has been identified

Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above
Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			
Are the results precise?	Y	Low	Objective measures used
Do you believe the results?	Y	Low	Consistent with other evidence on gaze in amblyopia
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Unclear		Adults with amblyopia, no report of age at onset / diagnosis or mode of detection, within region where there is no uniform childhood vision screening (Ontario, Canada)
Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on gaze in amblyopia
Jeon, H. S. and D. G. Choi (2017). "Stereopsis and fusion in anisometropia according to the presence of amblyopia." Graefes Arch Clin Exp Ophthalmol 255(12): 2487-2492.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Stereopsis in anisometropic children with / without amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Validated tests, cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Unclear	High	Unclear how participants selected
Were the controls selected in an acceptable way?	Unclear	High	Selection process not described
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment not described
Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective outcome measure
Have the authors identified all important confounding factors?	N	High	Treatment/ age diagnosis not considered.
Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above

Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			
Are the results precise?	Y	Low	Objective measures used
Do you believe the results?	Y	Low	Consistent with other evidence on stereopsis in amblyopia
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Unclear		No report of age at onset / diagnosis or mode of detection, within region where there is no uniform childhood vision screening (South Korea)
Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on stereopsis in amblyopia
Chen D, Otero-Millan J, Kumar P, Shaikh AG, Ghasia FF. Visual Search in Amblyopia: Abnormal Fixational Eye Movements and Suboptimal Sampling Strategies. Invest Ophthalmol Vis Sci. 2018 Sep 4;59(11):4506-4517			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Fixation eye movements in individuals with amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Screen based tests, cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Unclear	High	Unclear how participants selected
Were the controls selected in an acceptable way?	Unclear	High	Selection process not described
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment not described
Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective outcome measure
Have the authors identified all important confounding factors?	N	High	Treatment/ age diagnosis not considered.
Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above
Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			

Are the results precise?	Y	Low	Objective measures used
Do you believe the results?	Y	Low	Consistent with other evidence on eye position in amblyopia
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Unclear		No report of age at onset / diagnosis or mode of diagnosis. But similar health setting (USA)
Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on gaze in amblyopia
Narinesingh, C., et al. (2015). "Developmental Trajectory of McGurk Effect Susceptibility in Children and Adults With Amblyopia." Invest Ophthalmol Vis Sci 56(3): 2107-2113.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Visuo-auditory integration in those with amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Validated test, cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Unclear	High	Unclear how participants selected
Were the controls selected in an acceptable way?	Unclear	High	Selection process not described
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment for amblyopia not described, but subgroup analysis by age
Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective outcome measure
Have the authors identified all important confounding factors?	N	High	Age at diagnosis and therefore treatment commencement not considered.
Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above
Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			
Are the results precise?	Y	Low	Objective measures used
Do you believe the results?	Y	Low	Consistent with other evidence on visuoauditory integration
Section C: Will the results help (applicability)?			

Applicable to UK screening test of interest?	Unclear		No report of age at onset / diagnosis or mode of detection. But similar health setting (USA)
Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on visuoauditory integration in amblyopia
Gonzalez, E. G., et al. (2012). "Eye position stability in amblyopia and in normal binocular vision." Invest Ophthalmol Vis Sci 53(9): 5386-5394.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Stability of eye gaze in individuals with amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Screen based tests, cross sectional study
Was/were the cohort / cases recruited in an acceptable way?	Unclear	High	Unclear how participants selected
Were the controls selected in an acceptable way?	Unclear	High	Selection process not described
Was the exposure accurately measured to minimise bias?	N	High	Age at onset / diagnosis / treatment not described – particularly important for adult participants with disorder of early childhood onset
Was the outcome accurately measured to minimise bias?	Y	Low	Outcome defined, objective outcome measure
Have the authors identified all important confounding factors?	N	High	Treatment/ age diagnosis not considered.
Have they taken account of the confounding factors in the design and/or analysis?	N	High	As above
Was the follow up of subjects complete enough?	n/a		Cross sectional study
Section B: What are the results?			
Are the results precise?	Y	Low	Objective measures used
Do you believe the results?	Y	Low	Consistent with other evidence on eye position in amblyopia
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Unclear		No report of age at onset / diagnosis or mode of diagnosis. But similar health setting (USA)

Do the results of this study fit with other available evidence?	Y	Low	Consistent with other studies on gaze in amblyopia
Wilson, G. A. and D. Welch (2013). "Does amblyopia have a functional impact? Findings from the Dunedin Multidisciplinary Health and Development Study." Clin Exp Ophthalmol 41(2): 127-134.			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	Long term outcomes amblyopia
Did the authors use an appropriate method to answer their question?	Y	Low	Longitudinal birth cohort
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Birth cohort
Were the controls selected in an acceptable way?	n/a		Birth cohort study
Was the exposure accurately measured to minimise bias?	N	Moderate	Amblyopia as detected through visual health questionnaire completed by parents / carers and undertaken when child 3 and 5 years old. Possibility of measurement bias
Was the outcome accurately measured to minimise bias?	Y	Low	Validated outcome metric
Have the authors identified all important confounding factors?	Y	Low	Including gender, age, health status
Have they taken account of the confounding factors in the design and/or analysis?	Y	Low	Considered factors in analyses of outcome
Was the follow up of subjects complete enough?	Y	Low	Follow up birth to mid adulthood
Section B: What are the results?			
Are the results precise?	Y	Low	Several outcomes measures, reported findings with point estimates and some assessment of error
Do you believe the results?	Y	Low	No association between amblyopia and motor ability / reading skills (or rather, word recognition) / SEC status, findings all consistent. Also reported poorer stereoacuity in successfully treated amblyopia versus persistent amblyopia.
Section C: Will the results help (applicability)?			

Applicable to UK screening test of interest?	Unclear	Moderate	Yes: However, as population did not undergo screening, uncertain whether treatment started at 4 to 5 years old. Therefore unsure as to whether impact of treatment would be applicable to practice in the UK for those who fail screening and have treatment.
Do the results of this study fit with other available evidence?	Y	Low	Some evidence of better stereoacuity with treated amblyopia.
Hoeg, T. B., et al. (2015). "Danish Rural Eye Study: the association of preschool vision screening with the prevalence of amblyopia." Acta Ophthalmol 93(4): 322-329.(28)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	To determine the prevalence of amblyopia in Denmark before and after the initiation of the Danish national preschool vision screening programme
Did the authors use an appropriate method to answer their question?	Y	Low	Population based cross sectional study (although cohort study would be more robust)
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	All adults aged 30 years and over in 2010 and a random sample of 25% of adults aged 20–29 from the municipality of Næstved, Denmark.
Were the controls selected in an acceptable way?	n/a		
Was the exposure accurately measured to minimise bias?	Y	Low	Systematic screening at age 3-4yrs
Was the outcome accurately measured to minimise bias?	Y	Low	Amblyopia in adulthood confirmed through examination in 2010-2013 and defined as interocular acuity difference of 2-lines, with worse than 0.3 in the worse seeing eye, in addition to one or more of the following factors: strabismus/ previous strabismus surgery; anisometropia of ≥ 1.00 dioptres (D) spherical equivalent (SE); anisohypermetropia, ≥ 3.00 D SE; anisomyopia, or > 1.50 D anisoastigmatism; and/or evidence of past or present visual axis obstruction for > 1 week in early childhood.
Have the authors identified all important confounding factors?	N	High	Other health status

Have they taken account of the confounding factors in the design and/or analysis?	N	High	See above
Was the follow up of subjects complete enough?	Y	Low	Prevalence of amblyopia not expected to change with longer follow up
Section B: What are the results?			
Are the results precise?	Y		
Do you believe the results?	Y		Believe that prevalence is lower, but not in the causal relationship between screening and amblyopia prevalence
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Y		
Do the results of this study fit with other available evidence?	Y		Consistent with Shapira below(29)
Shapira, Y., et al. (2018). "Amblyopia and strabismus: trends in prevalence and risk factors among young adults in Israel." Br J Ophthalmol 102(5): 659-666.(29)			
Question	Assessment (Y, N, unclear)	Risk of Bias (low, high, unclear)	Supporting info
Section A: Are the results of the study valid?			
Did the study address a clearly focused issue?	Y	Low	To estimate the prevalence of amblyopia, strabismus and amblyopia risk factors (ARFs) among young adults in Israel and to analyse trends over time of prevalence rates
Did the authors use an appropriate method to answer their question?	Y	Low	Population based cross sectional study (although cohort study would be more robust)
Was/were the cohort / cases recruited in an acceptable way?	Y	Low	Military conscripts aged 16–19yrs, born between 1971 and 1994
Were the controls selected in an acceptable way?	n/a		
Was the exposure accurately measured to minimise bias?	Y	Low	Compulsory vision screening before age 6yrs (as undertaken in Israel since early 1990s)
Was the outcome accurately measured to minimise bias?	Y	Low	Unilateral amblyopia was defined as vision worse than 6/9 (0.2 logMAR) in either eye or as an interocular difference of two lines or more. Bilateral amblyopia defined as vision worse than 6/9 in both

			eyes. Moderate = worse than 6/12 (0.3), severe worse than 6/24 (0.5).
Have the authors identified all important confounding factors?	N	High	Other health status
Have they taken account of the confounding factors in the design and/or analysis?	N	High	See above
Was the follow up of subjects complete enough?	Y	Low	Prevalence of amblyopia not expected to change with longer follow up
Section B: What are the results?			
Are the results precise?	Y		
Do you believe the results?	Y		Believe that prevalence is lower, but not in the causal relationship between screening and amblyopia prevalence
Section C: Will the results help (applicability)?			
Applicable to UK screening test of interest?	Y		
Do the results of this study fit with other available evidence?	Y		Consistent with Hoeg above(28)

Appendix 4 – UK NSC reporting checklist for evidence summaries

All items on the UK NSC Reporting Checklist for Evidence Summaries have been addressed in this report. A summary of the checklist, along with the page or pages where each item can be found in this report, is presented in Table 6.

Table 6. UK NSC reporting checklist for evidence summaries

	Section	Item	Page no.
1.	TITLE AND SUMMARIES		
1.1	Title sheet	Identify the review as a UK NSC evidence summary.	Title page
1.2	Plain English summary	Plain English description of the executive summary.	5
1.3	Executive summary	Structured overview of the whole report. To include: the purpose/aim of the review; background; previous recommendations; findings and gaps in the evidence; recommendations on the screening that can or cannot be made on the basis of the review.	6
2.	INTRODUCTION AND APPROACH		
2.1	Background and objectives	Background – Current policy context and rationale for the current review – for example, reference to details of previous reviews, basis for current recommendation,	11

		recommendations made, gaps identified, drivers for new reviews	
		Objectives – What are the questions the current evidence summary intends to answer? – statement of the key questions for the current evidence summary, criteria they address, and number of studies included per question, description of the overall results of the literature search.	13
		Method – briefly outline the rapid review methods used.	
2.2	Eligibility for inclusion in the review	State all criteria for inclusion and exclusion of studies to the review clearly (PICO, dates, language, study type, publication type, publication status etc.) To be decided <i>a priori</i> .	16-19
2.3	Appraisal for quality/risk of bias tool	Details of tool/checklist used to assess quality, e.g. QUADAS 2, CASP, SIGN, AMSTAR.	20
3.	SEARCH STRATEGY AND STUDY SELECTION (FOR EACH KEY QUESTION)		
3.1	Databases/sources searched	Give details of all databases searched (including platform/interface and coverage dates) and date of final search.	16 and 20
3.2	Search strategy and results	Present the full search strategy for at least one database (usually a version of Medline), including limits and search filters if used. Provide details of the total number of (results from each database searched), number of duplicates removed, and the final number of unique records to consider for inclusion.	43-46

3.3	Study selection	State the process for selecting studies – inclusion and exclusion criteria, number of studies screened by title/abstract and full text, number of reviewers, any cross checking carried out.	16-19
4.	STUDY LEVEL REPORTING OF RESULTS (FOR EACH KEY QUESTION)		
4.1	Study level reporting, results and risk of bias assessment	For each study, produce a table that includes the full citation and a summary of the data relevant to the question (for example, study size, PICO, follow-up period, outcomes reported, statistical analyses etc.). Provide a simple summary of key measures, effect estimates and confidence intervals for each study where available. For each study, present the results of any assessment of quality/risk of bias.	53-95
5.	QUESTION LEVEL SYNTHESIS		
5.1	Description of the evidence	For each question, give numbers of studies screened, assessed for eligibility, and included in the review, with summary reasons for exclusion.	Q1- 22 Q2 – 26 Q3 – 37 Q4 - 39
5.2	Combining and presenting the findings	Provide a balanced discussion of the body of evidence which avoids over reliance on one study or set of studies. Consideration of 4 components should inform the reviewer's judgement on whether the criterion is 'met', 'not met' or 'uncertain': quantity; quality; applicability and consistency.	Q1- 22 Q2 – 27 Q3 – 37 Q4 - 39
5.3	Summary of findings	Provide a description of the evidence reviewed and included for each question, with reference to their eligibility for inclusion.	Q1 – 24 Q2 – 34 Q3 – 38

		Summarise the main findings including the quality/risk of bias issues for each question. Have the criteria addressed been 'met', 'not met' or 'uncertain'?	Q4 – 40
6.	REVIEW SUMMARY		
6.1	Conclusions and implications for policy	Do findings indicate whether screening should be recommended? Is further work warranted? Are there gaps in the evidence highlighted by the review?	41
6.2	Limitations	Discuss limitations of the available evidence and of the review methodology if relevant.	42

References

1. Rahi JS, Cumberland PM, Peckham CS, Impoving detection of blindness in childhood: the British Childhood Vision Impairment study. *Pediatrics*. 2010;126(4):e895-903.
2. Solebo AL, Cumberland PM, Rahi JS. Whole-population vision screening in children aged 4-5 years to detect amblyopia. *Lancet* (London, England). 2015;385(9984):2308-19.
3. Pan Y, Tarczy-Hornoch K, Cotter SA, Wen G, Borchert MS, Azen SP, et al. Visual acuity norms in pre-school children: the Multi-Ethnic Pediatric Eye Disease Study. *Optometry and vision science : official publication of the American Academy of Optometry*. 2009;86(6):607-12.
4. Carlton J, Karnon J, Czoski-Murray C, Smith KJ, Marr J. The clinical effectiveness and cost-effectiveness of screening programmes for amblyopia and strabismus in children up to the age of 4-5 years: a systematic review and economic evaluation. *Health technology assessment* (Winchester, England). 2008;12(25):iii, xi-194.
5. Awan M, Proudlock FA, Gottlob I. A randomized controlled trial of unilateral strabismic and mixed amblyopia using occlusion dose monitors to record compliance. *Investigative ophthalmology & visual science*. 2005;46(4):1435-9.
6. Clarke MP, Wright CM, Hrisos S, Anderson JD, Henderson J, Richardson SR. Randomised controlled trial of treatment of unilateral visual impairment detected at preschool vision screening. *BMJ* (Clinical research ed). 2003;327(7426):1251.
7. Hered RW, Wood DL. Preschool vision screening in primary care pediatric practice. *Public health reports* (Washington, DC : 1974). 2013;128(3):189-97.
8. Langeslag-Smith MA, Vandal AC, Briane V, Thompson B, Anstice NS. Preschool children's vision screening in New Zealand: a retrospective evaluation of referral accuracy. *BMJ open*. 2015;5(11):e009207.
9. Toufeeq A, Oram AJ. School-entry vision screening in the United Kingdom: practical aspects and outcomes. *Ophthalmic epidemiology*. 2014;21(4):210-6.
10. Ellis DA, McQueenie R, McConnachie A, Wilson P, Williamson AE. Demographic and practice factors predicting repeated non-attendance in primary care: a national retrospective cohort analysis. *The Lancet Public health*. 2017;2(12):e551-e9.
11. O'Colmain U, Low L, Gilmour C, MacEwen CJ. Vision screening in children: a retrospective study of social and demographic factors with regards to visual outcomes. *The British journal of ophthalmology*. 2016;100(8):1109-13.
12. Sharma A, Congdon N, Patel M, Gilbert C. School-based approaches to the correction of refractive error in children. *Survey of ophthalmology*. 2012;57(3):272-83.
13. Stewart CE, Wallace MP, Stephens DA, Fielder AR, Moseley MJ. The effect of amblyopia treatment on stereoacuity. *Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus*. 2013;17(2):166-73.
14. Afsari S, Rose KA, Gole GA, Philip K, Leone JF, French A, et al. Prevalence of anisometropia and its association with refractive error and amblyopia in preschool children. *The British journal of ophthalmology*. 2013;97(9):1095-9.
15. Kulp MT, Ying GS, Huang J, Maguire M, Quinn G, Ciner EB, et al. Associations between hyperopia and other vision and refractive error characteristics. *Optometry and vision science : official publication of the American Academy of Optometry*. 2014;91(4):383-9.
16. Solebo AL, Rahi J. Epidemiology, aetiology and management of visual impairment in children. *Archives of disease in childhood*. 2014;99(4):375-9.
17. Subramanian V, Jost RM, Birch EE. A quantitative study of fixation stability in amblyopia. *Investigative ophthalmology & visual science*. 2013;54(3):1998-2003.
18. Kelly KR, Jost RM, De La Cruz A, Birch EE. Amblyopic children read more slowly than controls under natural, binocular reading conditions. *Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus*. 2015;19(6):515-20.
19. Kelly KR, Jost RM, De La Cruz A, Dao L, Beauchamp CL, Stager D, Jr., et al. Slow reading in children with anisometropic amblyopia is associated with fixation instability and increased saccades. *Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus*. 2017;21(6):447-51.e1.
20. Grant S, Suttle C, Melmoth DR, Conway ML, Sloper JJ. Age- and stereovision-dependent eye-hand coordination deficits in children with amblyopia and abnormal binocularity. *Investigative ophthalmology & visual science*. 2014;55(9):5687-57015.
21. Burgmeier R, Desai RU, Farner KC, Tiano B, Lacey R, Volpe NJ, et al. The effect of amblyopia on visual-auditory speech perception: why mothers may say "Look at me when I'm talking to you". *JAMA ophthalmology*. 2015;133(1):11-6.
22. Marian V, Hayakawa S, Lam TQ, Schroeder SR. Language Experience Changes Audiovisual Perception. *Brain sciences*. 2018;8(5).
23. Wilson GA, Welch D. Does amblyopia have a functional impact? Findings from the

