ClinicalEvidence

Amblyopia

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ABSTRACT

INTRODUCTION: Amblyopia is commonly associated with squint (strabismus) or refractive errors resulting in different visual inputs to each eye during the sensitive period of visual development (<7–8 years of age). The cumulative incidence is estimated at 2% to 4% in children aged up to 15 years. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of interventions to detect amblyopia early? What are the effects of medical treatments for amblyopia? We searched: Medline, Embase, The Cochrane Library, and other important databases up to May 2008 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations, such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 16 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: active vision therapy; glasses alone or with occlusion; penalisation; screening; and targeted vision screening.

QUESTIONS

INTERVENTIONS

Footnote

*Categorisation based on consensus. Limited RCT evidence available.

Key points

- Amblyopia is reduced visual acuity not immediately correctable by glasses, in the absence of ocular pathology.

  It is commonly associated with squint (strabismic amblyopia), refractive errors resulting in different visual inputs to each eye during the sensitive period of visual development (refractive amblyopia), or with cataract or ptosis (stimulus deprivation amblyopia).

  The cumulative incidence is estimated at 2% to 4% in children aged up to 15 years.

- Vision screening before school entry may increase detection rates of amblyopia compared with no screening. However, pre-school screening may not improve treatment outcomes at 7 years compared with school-entry screening.

  We don't know whether children with a higher risk of eye problems should be targeted for vision screening.

- Most evidence is available for children under 7 years of age, in whom wearing glasses for up to 30 weeks can improve amblyopia and may cure it. Children with suspected amblyopia who have clinically important refractive error are prescribed glasses; therefore most data available on other interventions assess their effectiveness in combination with glasses.

- Occlusion (covering the fellow eye using a patch) may be more effective than glasses alone in children up to 13 years of age not fully treated with glasses. Further data assessing occlusion in combination with near-vision tasks such as encouraging the child to do close work while wearing their patch confirm that combined interventions are more effective than glasses alone in younger children.

  Some older children might improve with treatment, although there are few data available to support this.

  Prescribing occlusion for the fellow eye for longer periods every day is no more effective at improving amblyopia than prescribing shorter periods of daily occlusion, but success rates increase in proportion to objectively measured compliance.

Penalisation with atropine may be as effective as occlusion when given in combination with other interventions for improving amblyopia in children aged under 7 years who are not fully treated with glasses.

We don't know whether near-vision tasks are effective alone as adjuvant treatment to glasses for amblyopia. Near-vision tasks may further enhance visual acuity when added to occlusion or penalisation but the contribution of near-vision tasks to the effects of these combination interventions remains unclear.

DEFINITION

Amblyopia is reduced visual acuity not immediately correctable by glasses, in the absence of ocular pathology. [1] It is associated with complete or partial lack of clear visual input to one eye (stimulus deprivation amblyopia or unilateral/anisometropic refractive amblyopia), or, less often, to both eyes (bilateral refractive amblyopia), or to conflicting visual inputs to the two eyes (strabismic amblyopia). The severity of amblyopia is often classified according to the visual acuity in the affected eye, using visual-acuity testing. “Mild” amblyopia is often classified as being visual acuity of 6/9 to 6/12, “moderate” amblyopia as being worse than 6/12 to 6/36, and “severe” amblyopia as being worse than 6/36. Different studies use different definitions of severity, but most assume normal vision (6/6 or better) in the fellow eye. One line of letters or symbols (usually 4 or 5) in a visual-acuity chart constitutes 0.1 LogMAR units. A change in 0.2 LogMAR units is often quoted as being the smallest clinically important change in visual acuity, although some studies use a change of 0.1 LogMAR units or greater, which might be considered clinically marginal. **Diagnosis:** Amblyopia is diagnosed by testing visual acuity in each eye separately, with the person wearing an adequate refractive correction, and after exclusion of ocular pathology. [2] Amblyopia is defined in terms of visual acuity, but other visual functions are affected as well. [3]

INCIDENCE/ PREVALENCE

It is estimated that the cumulative incidence is 2% to 4% in children up to 15 years of age. [4] [5] The population prevalence is affected by whether there have been any interventions to prevent or treat the condition.

AETIOLOGY/ RISK FACTORS

Amblyopia is associated with degraded visual input, either caused by high refractive error (unilateral refractive amblyopia, also known as ametropic amblyopia), by different refractive errors in each eye (anisometropic amblyopia), or by conflicting visual inputs between the eyes because of squint (strabismic amblyopia). [2] Amblyopia can also be associated with an obstruction to the visual axis — for example, by ptosis or cataract (known as stimulus deprivation amblyopia). In a multicentre RCT of 409 children aged 3 to 6 years treated for amblyopia, 38% were strabismic, 37% were anisometropic, and 24% were both strabismic and anisometropic. [6] Whereas strabismus and anisometropia are common causes of amblyopia, less common causes include ptosis, congenital cataract, and corneal injury or dystrophy, accounting for only up to 3% of cases. [7]

PROGNOSIS

Amblyopia is commonly regarded as untreatable after 7 to 8 years of age, although there is some evidence that treatment can be effective in children aged 7 to 12 years. [8] Recovery of normal vision becomes progressively less likely in older children. Successfully treated amblyopia might regress in about a quarter of children. [9] The lifetime risk of blindness because of loss of the better-seeing eye is 1.2% (95% CI 1.1% to 1.4%). [10] If the better-seeing eye is lost, the visual acuity of 10% of amblyopic eyes can improve. [11]

AIMS OF INTERVENTION

To detect amblyopia early; to initiate treatment for amblyopia at a stage when treatment is likely to be effective (ideally between 3 and 5 years of age, and under 7 years of age).

OUTCOMES

Early detection: number of cases of amblyopia detected and treated; **treatment:** visual acuity; interocular acuity difference; binocularity; stereopsis; compliance with treatment; adverse effects of treatment.

METHODS

Clinical Evidence search and appraisal May 2008. The following databases were used to identify studies for this systematic review: Medline 1986 to May 2008, Embase 1986 to May 2008, and The Cochrane Library, Issue 2, 2008. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD), Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment (HTA), and NICE. The contributor also performed a hand search for systematic reviews in The Cochrane Library, Issue 4, 2008. Abstracts of the studies retrieved were assessed independently by an information specialist using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: systematic reviews (including systematic reviews of observational studies), RCTs, and prospective and retrospective cohort studies in any language, containing more than 20 individuals, and with a follow-up of more than 50%. There was no minimum length of follow-up. We included open studies. We searched for studies including children and adults. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We

have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 16).

QUESTION **What are the effects of interventions to detect amblyopia early?**

OPTION **SCREENING VERSUS USUAL CARE**

Prevalence of amblyopia

Screening compared with no screening Screening before 3 years of age may reduce the prevalence of amblyopia by the age of 8 years (low-quality evidence).

Repeated screening compared with usual surveillance Repeated vision screening before 3 years of age increases the detection rates of amblyopia by 3 years of age compared with usual care (high-quality evidence).

Early screening compared with later screening Screening at 3 years of age and at school entry (4–5 years of age) may not reduce the overall prevalence of amblyopia by 7 years of age compared with screening at school entry alone (very-low quality evidence).

Visual acuity

Repeated screening compared with usual care Repeated vision screening before 3 years of age may improve visual acuity at 7 years of age (moderate-quality evidence).

For GRADE evaluation of interventions for amblyopia, see table, p 16 .

Benefits:

Screening versus no screening:
We found no systematic review or RCTs. One comparative, unmatched retrospective cohort study compared a group of 8-year-old children who had visual screening between 12 and 30 months of age with a group of children not offered screening. The prevalence of amblyopia (defined as corrected acuity 6/12 or worse, or >1 line difference in corrected acuity between the eyes) was 5/808 (1%) in children who had been screened in infancy compared with 20/782 (3%) in children with no screening (P = 0.0098). [12]

Pre-school repeated screening versus usual care (surveillance by a health visitor):
We found two systematic reviews. [1] [13] The first systematic review (search date 2005) found no RCTs that matched its inclusion criteria. [1] The second systematic review (updated search date 2003) identified one RCT (3490 children) comparing repeated vision screening before 3 years of age (at 8, 12, 18, 25, and 31 months) versus usual care (surveillance by a health visitor at 8 and 18 months). [13] The RCT found that repeated screening significantly improved the yield of children confirmed to have amblyopia by 3 years of age compared with surveillance (33/2029 [2%] from the repeated screening group *v* 8/1461 [1%] from the surveillance group; P < 0.01). [14] A follow-up study involving 1917/3490 (55%) of participants who returned for repeat assessment at 7.5 years of age found that, after treatment, visual acuity in children from the group offered repeated screening was significantly better than that in children from the group offered surveillance (mean acuity in the treated eye: 0.15 LogMAR units in the screening group *v* 0.26 LogMAR units in the surveillance group; P < 0.001). Significantly fewer children offered repeated screening compared with surveillance were still amblyopic (worse than 6/12) at 7 years (6/1088 [1%] with screening *v* 15/826 [2%] with surveillance; P = 0.02). [15]

Pre-school plus school-entry screening versus school-entry screening alone:
We found no systematic review or RCTs. We found one prospective cohort study conducted parallel to the RCT identified by the systematic review [13] above. It assessed the effects at 7.5 years of vision screening at 3 years and at school entry (4–5 years) versus vision screening at school entry alone. [16] At 7.5 years, 8042 children attended for assessment; 1917 were assessed as part of the RCT (reported above), leaving 6125, 44 of whom were excluded from the analysis because of a known developmental delay, organic eye disease, or developmental syndromes. In the analysis of the remaining 6081 children, 1516/6081 (25%) had been offered orthoptic pre-school screening, 4565/6081 (75%) had not, and only 1019/6081 (17%) offered screening had actually received it. The study found that offering pre-school screening was not effective at population level in reducing the prevalence of amblyopia by 7 years of age. However, the limited power of the study makes the negative finding difficult to interpret. There was no significant difference in rates of amblyopia between children offered pre-school screening and those not offered screening (proportion of children with visual acuity of amblyopic eye worse than 6/12: 1.3% in the group not offered screening *v* 1.2% in the group offered screening; absolute numbers not reported; P = 0.59). [16]

Harms:

Screening versus no screening:
The study gave no information about adverse effects. [12]

Screening versus surveillance:
The RCT identified by the review [13] found significantly fewer false-positive referrals in the repeated screening group by 3 years of age compared with the surveillance group (92/2029 [5%] with screening *v* 110/1461 [8%] with surveillance; P < 0.01). [14]

Early screening versus late screening:
The prospective cohort study gave no information about adverse effects. [16]

Comment: **Clinical guide:**
Although there was a benefit associated with the intensive intervention used in the RCT, [14] such intensive intervention is not practicable in a clinical setting. Further research is needed to determine whether more practicable screening protocols could be cost effective.

Owing to the lack of data, there is currently no clear consensus regarding vision screening, although the review undertaken in the US in 2003 concluded that, on balance, population screening was justified for children aged under 5 years of age and should be offered. [13] In the UK, the 2006 Hall report "Health for All Children" recommends an orthoptic-led vision test for children between ages 4 and 5 years pending further reliable data. [17] Conversely, other systematic reviews have concluded that no recommendations can be made without further evidence. [7] [18] [19]

The uptake of population screening programmes is often poor, [4] [16] and amblyopia has been found to be as prevalent in defaulters as in attenders. [20]

OPTION TARGETED VISION SCREENING VERSUS MASS SCREENING

We found no clinically important results from RCTs or cohort studies about the effects of targeted vision screening compared with mass screening for early detection of amblyopia.

For GRADE evaluation of interventions for amblyopia, **see table, p 16 .**

Benefits: We found no systematic review, RCTs, or cohort studies.

Harms: We found no systematic review, RCTs, or cohort studies.

Comment: **Clinical guide:**
Siblings of children with eye problems have a greater risk of eye problems themselves, [21] [22] and children born prematurely have a greater risk of various eye problems compared with children born at term. [23] It is presently unclear whether these groups should be targeted for vision screening, and local practices vary. However, it is recommended that children with developmental disorders, hearing loss, or other syndromes have multidisciplinary assessments that include testing visual function. [24]

QUESTION What are the effects of medical treatments for amblyopia?

OPTION GLASSES

Visual acuity
Glasses compared with no glasses Wearing glasses may improve the best-corrected visual acuity of the worse-seeing eye compared with no treatment after 1 year (moderate-quality evidence).

Glasses plus occlusion compared with no treatment Glasses plus patching may improve visual acuity after 1 year in children aged 3 to 5 years with unilateral uncorrected visual acuity deficit (moderate-quality evidence).

Glasses alone compared with glasses plus occlusion plus near-vision tasks Glasses alone are less effective at improving visual acuity after 1 year compared with adding patching to glasses plus near-vision tasks, with or without penalisation of the fellow eye, in children aged 3 to 7 years (moderate-quality evidence).

Glasses alone compared with glasses in combination with occlusion plus penalisation plus near-vision tasks Glasses alone are less effective at improving visual acuity compared with patching plus penalisation with atropine plus near-vision tasks after 24 weeks in children aged 7 to 13 years, but are as effective as patching plus penalisation plus near-vision tasks in children aged over 13 years (moderate-quality evidence).

Glasses alone compared with longer or shorter duration of occlusion in children wearing glasses Glasses alone may be as effective at improving visual acuity after 12 weeks as prescribed patching for 6 hours a day plus glasses, or as effective as prescribed patching for 3 hours plus glasses (very low-quality evidence).

Adverse effects

Teasing from school friends is reported for some children.

Note
All children with suspected amblyopia should be offered refractive correction if they have a clinically important refractive error.

For GRADE evaluation of interventions for amblyopia, see table, p 16 .

Benefits:

Glasses versus no treatment:
We found one systematic review (search date 2008), [18] which identified one RCT. [25] We also found three cohort studies. [26] [27] [28]

The RCT (177 children aged 3–5 years with uncorrected visual acuity in the affected eye 6/9–6/36) identified by the review compared glasses alone versus no treatment, and also compared occlusion plus glasses versus no treatment (see option on occlusion, p 6 , for data on this comparison). [25] It found that wearing glasses alone for 1 year resulted in a small but significant improvement in the best-corrected visual acuity of the worse-seeing eye compared with no treatment (mean difference in best-corrected acuity between groups: 0.085 LogMAR units, 95% CI 0.02 LogMAR units to 0.15 LogMAR units; analysis of 164/177 [93%] children; adjusted for analysis of multiple comparisons). [25] Although the treatment effect for all children together was clinically marginal, in a planned subgroup analysis, those with initial uncorrected acuity loss of 6/18 to 6/36 had a clinically meaningful improvement in mean acuity of 0.20 LogMAR units (95% CI 0.1 LogMAR units to 0.3 LogMAR units) with treatment, whereas those with better uncorrected acuity loss at recruitment showed no effect of treatment (mean change in LogMAR units: +0.045, 95% CI –0.02 to +0.11). The RCT found no significant difference in stereoacuity among the groups at 52, 54, or 78 weeks (linear P values for the 3 groups: P = 0.346 at 52 weeks; P = 0.172 at 54 weeks; and P = 0.324 at 78 weeks). [29]

In the first cohort study (94 children aged 3–8 years with anisometropic or strabismic amblyopia; interocular acuity difference of at least 0.1 LogMAR unit), 64 children were prescribed glasses for an 18-week period, with monitoring of visual acuity taking place every 6 weeks. [26] The study found that 14/64 (22%) children developed equal vision in both eyes after wearing glasses alone for 18 weeks. [26]

The second cohort study (84 children aged 3–6 years with anisometropic amblyopia [visual acuity in the amblyopic eye of 6/12–6/75] and no strabismus) found that wearing glasses alone improved the best-corrected visual acuity in the amblyopic eye by two or more lines in 65/84 (77%) children, and reduced the interocular acuity difference by two or more lines in 56/84 (67%) children. [27] The longest duration of improvement before stabilisation of vision was 30 weeks.

The third cohort study (113 children aged 3–9 years with bilateral refractive amblyopia [mean visual acuity 0.50 [20/63]) found that 79/113 (70%) children who wore glasses alone had visual acuity of 20/25 or better at 1 year. [28]

Glasses plus occlusion versus no treatment:
See benefits of occlusion, p 6 .

Glasses alone versus occlusion plus near-vision tasks (plus glasses if needed):
See benefits of occlusion, p 6 .

Glasses alone versus adding occlusion plus penalisation plus near-vision tasks to glasses:
See benefits of occlusion, p 6 .

Harms:

Glasses versus no treatment:
In a separate publication, [30] the authors of the RCT assessed emotional impact in 144/177 (81%) children whose parents completed a questionnaire. Parents reported that equal numbers of 4-year-old children were teased at school in both the no treatment and glasses groups (2/51 [4%] in the no treatment group *v* 2/47 [4%] in the glasses group; P value across the 3 groups = 0.455). There was no significant difference in mean Rutter behaviour scores (used to assess emotional and behavioural difficulties) between the groups (P = 0.458). [30]

None of the cohort studies gave information on adverse effects. [26] [27] [28]

Glasses plus occlusion versus no treatment:
See harms of occlusion, p 6 .

Glasses alone versus occlusion plus near-vision tasks (plus glasses if needed):
See harms of occlusion, p 6 .

Glasses alone versus adding occlusion plus penalisation plus near-vision tasks to glasses:
See harms of occlusion, p 6 .

Comment:

Clinical guide:
The wearing of refractive correction (glasses or contact lenses), if needed, assists in the diagnosis of amblyopia because visual acuity loss associated with amblyopia cannot be immediately corrected by glasses. Observational data support the effectiveness of glasses alone in treating amblyopia by contrasting the gains in acuity obtained after prolonged wearing of glasses with the expected gain caused by increasing age, or after repeated vision testing (learning effect).

OPTION OCCLUSION (PATCHING)

Visual acuity
Occlusion plus glasses compared with no treatment Patching plus glasses may improve visual acuity after 1 year in children aged 3 to 5 years with unilateral uncorrected visual acuity deficit (moderate-quality evidence).

Occlusion compared with penalisation Prescribed occlusion for 6 hours each day and daily penalisation with atropine are equally effective at improving visual acuity after 6 months in children aged 3 to 7 years with amblyopia who also wear glasses (moderate-quality evidence).

Occlusion plus glasses plus near-vision tasks compared with glasses alone Adding patching to glasses plus near-vision tasks with or without penalisation of the fellow eye improves visual acuity after 1 year in children aged 3 to 7 years (moderate-quality evidence).

Occlusion plus penalisation plus near-vision tasks compared with glasses alone Patching plus penalisation with atropine plus near-vision tasks improves visual acuity after 24 weeks in children under 13 years, but is no more effective than glasses alone in children aged 7 to 13 years (moderate-quality evidence).

Longer or shorter duration of prescribed occlusion compared with no occlusion Prescribed patching for 3 or 6 hours a day plus glasses may be no more effective at improving visual acuity after 12 weeks, although we cannot be sure as results may be confounded by compliance (very low-quality evidence).

Longer versus shorter duration of prescribed occlusion Prescribed longer durations of occlusion (6 hours to all day) are no more effective at improving visual acuity compared with prescribed shorter durations of occlusion (2–6 hours) after 3 to 4 months (high-quality evidence).

Note
We found no direct information about whether occlusion is better than no active treatment in children with amblyopia.

Adverse effects
Compliance with patching can be low, and beneficial effects may be seen only in proportion to compliance. Lasting adverse effects of patching (such as reverse amblyopia) are rare, but some children may be teased at school.

For GRADE evaluation of interventions for amblyopia, see table, p 16 .

Benefits:

Occlusion versus no treatment:
We found three systematic reviews of children with either unilateral refractive amblyopia (search date 2008), [18] stimulus deprivation amblyopia (search date 2006), [7] or strabismus amblyopia (search date 2007), [19] which identified no RCTs (see comment below). We found no cohort studies. Occlusion is rarely prescribed alone (see clinical guide below).

Occlusion plus glasses versus no treatment:
We found three systematic reviews of children with either unilateral refractive amblyopia (search date 2008), [18] strabismic amblyopia (search date 2007), [19] or stimulus deprivation amblyopia (search date 2006). [7] Two of the reviews identified no RCTs. [7] [19] We found no cohort studies.

The review of unilateral refractive amblyopia [18] identified one RCT (177 children aged 3–5 years with unilateral uncorrected visual acuity of 6/9–6/36) comparing occlusion plus glasses versus no treatment. [25] The RCT also compared glasses alone versus no treatment (see option on glasses, p 4).

The RCT found that occlusion plus glasses for 1 year resulted in a significant improvement in the visual acuity of the worse-seeing eye compared with no treatment (mean difference in visual acuity between the patching plus glasses and no treatment groups in LogMAR units: 0.11, 95% CI 0.05

to 0.17; P < 0.001; analysis of 164/177 [93%] children; adjusted for analysis of multiple comparisons). [25] Although the treatment effect for all children together was clinically marginal, in a planned subgroup analysis, those with initial acuity loss of 6/18 to 6/36 had a clinically meaningful improvement in mean acuity of 0.20 LogMAR units (95% CI 0.1 LogMAR units to 0.3 LogMAR units) with treatment, whereas those with less severe acuity loss at recruitment showed no effect of treatment (mean change in LogMAR units: +0.045, 95% CI –0.02 to +0.11). The RCT found no significant difference in stereoacuity among the groups at 52, 54, or 78 weeks (linear P values for the 3 groups: P = 0.346 at 52 weeks; P = 0.172 at 54 weeks; and P = 0.324 at 78 weeks). [29] There was also no significant difference in final acuity among the groups 6 months after the end of the trial, after treatment was offered to all children if needed.

Occlusion plus near-vision tasks (plus glasses if needed) versus glasses alone:
We found three systematic reviews of children with either unilateral refractive amblyopia (search date 2008), [18] strabismic amblyopia (search date 2007), [19] or stimulus deprivation amblyopia (search date 2006). [7]

One of the reviews identified no RCTs. [19]

The other reviews [7] [18] identified the same single RCT (180 children aged 3–6 years with amblyopia: best-corrected visual acuity in the amblyopic eye 6/12–6/120; a difference in visual acuity between the eyes of 3 lines or more; and strabismus, anisometropia, or both) comparing occlusion (patching) of the fellow eye for 2 hours a day plus 1 hour of near-vision tasks plus wearing glasses, if needed, versus glasses alone. [31]

The RCT found that patching plus near-vision tasks (with glasses, if needed) significantly improved vision in the amblyopic eye at 5 weeks compared with wearing glasses alone (mean difference in visual acuity between the groups in LogMAR units: 0.07; 95% CI 0.02 to 0.12; P = 0.006). Although this effect is small, the study was not designed to determine the maximum effect of occlusion treatment, but rather to establish whether occlusion was of benefit, while minimising the time that occlusion treatment was withheld from the control group. [31] The RCT included a secondary cohort of 63 children with less severe amblyopia (2-line difference in visual acuity between the eyes). In this cohort, patching plus near-vision tasks significantly increased the proportion of children with reduced (improved) interocular difference of one line or less compared with glasses alone (21/33 [64%] with patching plus near-vision tasks *v* 5/29 [17%] with glasses alone; P < 0.001). [31]

Occlusion plus glasses plus penalisation plus near-vision tasks versus glasses alone:
We found three systematic reviews of children with either unilateral refractive (search date 2008), [18] strabismic amblyopia (search date 2007), [19] or stimulus deprivation amblyopia (search date 2006). [7] Two of the reviews identified no RCTs. [7] [19] We found no cohort studies.

The third review [18] identified one RCT (507 children aged 7–17 years with strabismic, anisometropic, or mixed amblyopia [amblyopic eye visual acuity 6/12–6/120]). [8] It compared glasses plus 24 weeks of occlusion (patching) prescribed for 2 to 6 hours a day plus penalisation with atropine (if under 13 years old) plus 2 to 6 hours of near-vision tasks versus glasses alone.

The RCT found that adding patching plus penalisation plus near-vision tasks to glasses significantly increased the proportion of children with improved amblyopia compared with glasses alone (404 children under 13 years old improved by at least 2 lines: 106/201 [53%] with treatment *v* 50/203 [25%] with glasses alone; adjusted OR 4.19, 95% CI 2.63 to 6.67; P < 0.001). However, in the 13- to 17-year-old age group (who did not receive penalisation), similar proportions of children improved with patching plus glasses compared with glasses alone (103 children, visual acuity improved by at least 2 lines: 14/55 [26%] with patching plus glasses *v* 11/48 [23%] with glasses alone; P = 0.22). [8]

Occlusion versus penalisation in children wearing glasses:
See benefits of penalisation, p 10 .

Longer or shorter periods of prescribed occlusion versus no occlusion in children also wearing glasses and prescribed near-vision tasks:
We found no systematic review but found one RCT. [32] The RCT (60 children aged 2–7 years with strabismic or mixed amblyopia; visual acuity in the amblyopic eye of 6/12–6/48) compared three interventions: patching for 3 hours plus glasses, patching for 6 hours plus glasses, and glasses alone. [32] It found no significant difference in the percentage of change in amblyopia at 12 weeks between patching for 3 hours plus glasses or patching for 6 hours plus glasses and glasses alone (P = 0.43 for 3-hour patching *v* no patching; P = 0.16 for 6-hour patching *v* no patching; absolute numbers not reported). [32] However, objectively measured compliance with patching was low, and

when effective patching hours were considered, visual acuity increased by 8.3% for each hour of effective daily patching over the 12-week period (P < 0.001). [32]

Longer versus shorter prescribed occlusion in children also wearing glasses and prescribed near-vision tasks:
We found two systematic reviews of children with either unilateral refractive (search date 2008) [18] or stimulus deprivation amblyopia (search date 2006). [7] The review of stimulus deprivation amblyopia identified no RCTs. [7] The review of unilateral refractive amblyopia identified three RCTs, [33] [34] [35] and we found one additional RCT [32] comparing different time periods of prescribed occlusion, objectively measured occlusion (patching) of the fellow eye, or both.

In the first two RCTs, [33] [34] conducted by the same group, all children also wore glasses; optimal refractive error correction for at least 1 month prior to enrolment was a requirement for entry into the trials.

The first RCT identified by the review [18] (189 children aged 3–6 years with any type of moderate amblyopia [visual acuity 6/12–6/24]) compared prescribing 2 hours versus 6 hours of daily patching for 4 months. [33] Both groups were also prescribed at least 1 hour a day of near-visual activities. The RCT found no significant difference between prescribing 2- and 6-hour patching in visual acuity outcomes (improvement in visual acuity of the amblyopic eye averaged 2.40 LogMAR lines in both groups; P = 0.98). [33]

The second RCT identified by the review [18] (175 children aged 3–6 years with severe amblyopia of any type [visual acuity 6/30–6/120]) compared prescribing full-time patching (all hours or all but 1 waking hours) versus prescribing 6 hours' patching daily for 4 months. [34] Both groups were prescribed at least 1 hour a day of near-visual activities. The RCT found improvements in visual acuity in children prescribed both full-time and 6-hour patching, with no significant difference between groups (improvement in amblyopic eye visual acuity averaged 4.8 lines in the 6-hour patching group *v* 4.7 lines in the full-time patching group; P = 0.45). [34]

The third RCT identified by the review [18] (80 children aged 3–8 years with unilateral refractive or strabismic amblyopia, or both, and at least 0.1 LogMAR units difference in acuity between each eye) compared maximal (12 hours a day) versus substantial (6 hours a day) occlusion. [35] Prior to randomisation into the trial, all participants wore glasses for 18 weeks; the authors of the trial surmised that this was the time frame during which all measurable improvement to visual acuity in response to glasses alone would have occurred. The RCT found no significant difference in visual acuity at 18 weeks between maximal and substantial occlusion (mean change: 0.24 LogMAR units with 12 hours' occlusion *v* 0.26 LogMAR units with 6 hours' occlusion).

The additional RCT (60 children aged 2–7 years with strabismic or mixed amblyopia; visual acuity in the amblyopic eye of 6/12–6/48) compared three interventions: patching for 3 hours plus glasses, patching for 6 hours plus glasses, and glasses alone. [32] It found no significant difference in the percentage of change in amblyopia at 12 weeks between prescribed patching for 3 hours plus glasses and prescribed patching for 6 hours plus glasses; P = 0.99, absolute numbers not reported). [32] However, objectively measured compliance with patching was low, and when effective patching hours were considered, visual acuity increased by 8.3% for each hour of effective daily patching over the 12-week period (P < 0.001). [32]

Near-vision tasks versus no near-vision tasks in children receiving occlusion:
See benefits of near-vision tasks, p 12 .

Harms:

Occlusion versus no treatment:
We found no RCTs.

Occlusion plus glasses versus no treatment:
The RCT comparing patching plus glasses plus penalisation or glasses alone versus no treatment [25] also assessed the emotional impact of patching plus glasses versus glasses alone in a separate publication. [30] It found that significantly more children were occasionally or more often upset by patching plus glasses compared with glasses alone (85% with patching plus glasses *v* 19% with glasses alone at 4 years of age; P = 0.03; and 62% with patching plus glasses *v* 26% with glasses alone at 5 years of age; P = 0.01). [30] There was no significant difference in mean Rutter behaviour scores (used to assess emotional and behavioural difficulties) between the groups (P = 0.458). [30]

Occlusion plus near-vision tasks (plus glasses if needed) versus glasses alone:
The RCT found no significant difference between patching plus glasses and glasses alone in the proportion of children with reduced visual acuity in the fellow eye at 5 weeks (visual acuity decreased by 2 lines or more: 2/87 [2%] with patching *v* 6/93 [7%] with glasses alone; P = 0.28). [31] In total,

2/87 (2%) children required spectacle-mounted occluders because of skin irritation caused by the patch. [31]

Occlusion plus glasses plus penalisation plus near-vision tasks versus glasses alone:
The RCT reported that 4/201 (2%) children under 13 years (404 children in total; occlusion plus glasses plus penalisation *v* 1/203 [1%] children who received glasses alone) reported intermittent binocular diplopia. All instances had resolved in all but one child by 24 weeks. [8]

Occlusion versus penalisation in children wearing glasses:
See harms of penalisation, p 10 .

Different time periods of prescribed occlusion versus each other in children also wearing glasses and prescribed near-vision tasks:
The first RCT identified by the review also reported no inverse amblyopia. [33] In the second RCT, amblyopia treatment scores for social stigma were worse in the prescribed 6-hour patching group compared with the prescribed 2-hour patching group (P = 0.01), but in the third RCT, scores for social stigma were similar in both groups (P = 0.10). [33] [34]

However, the second RCT reported that prescribed patching time had to be reduced in 6/90 (7%) children for reasons that included possible reverse amblyopia or skin irritation. [33] The RCT found no significant difference between prescribing 2-hour daily patching compared with prescribing 6-hour daily patching in the proportion of children with reduced visual acuity in the fellow eye at 4 months (visual acuity decreased by 2 or more lines: 6/95 [6%] with 2-hour patching *v* 8/94 [9%] with 6-hour patching; P = 0.59). [33]

The third RCT identified by the review reported that “no adverse events occurred” (no further data reported). [35]

The additional RCT comparing prescribed full-time daily patching (all hours, or all but 1 waking hours) versus prescribed 6-hour daily patching also found similar proportions of children with reduced fellow-eye visual acuity at 4 months (visual acuity decreased by 2 or more lines: 3/85 [4%] with 6-hour patching *v* 9/90 [10%] with full-time patching; P = 0.14). With further follow-up, only 1/90 (1%) children treated with full-time occlusion had slightly worse vision in their fellow eye. [34]

The additional RCT reported no inverse amblyopia (reduction in acuity of the fellow eye so that it is worse than the originally amblyopic eye) or patch allergy. [32]

Near-vision tasks versus no near-vision tasks in children carrying out occlusion:
See harms of near-vision tasks, p 12 .

Comment:

Clinical guide:
All children with suspected amblyopia should be offered refractive correction if they have a clinically significant refractive error. [2] [3] Thresholds for giving glasses for smaller refractive errors differ among practitioners, but there is broad agreement that glasses should be prescribed for more substantial refractive errors. We therefore found no studies assessing the effects of occlusion alone for the treatment of amblyopia. In children under 7 years with amblyopia of 6/12 or worse, there is consistent evidence that, in children prescribed glasses, successfully applied occlusion, often in combination with near-vision tasks, achieves better results than wearing glasses alone. However, stereopsis (depth perception) did not improve in the RCTs in which it was included as an outcome. Therefore, the belief that treating amblyopia improves binocularity (the ability to fuse images from the 2 eyes) was not borne out in these studies.

Compliance:
In recent years, evidence has mounted that compliance with patching treatment (which can be objectively monitored with occlusion dose monitors) is crucial for the success of treatment. When interpreting results from studies comparing treatments, it is important to consider whether compliance with occlusion was measured objectively, or estimated from parental reports. In studies measuring occlusion time objectively, the data suggest a dose–response relationship between duration of patching and improvement in acuity, at least within certain limits. Studies with no objective data on compliance report equivalence of prescribed patching regimens, but the results might be confounded by differentially poor compliance. One RCT comparing 12- versus 6-hour occlusion assessed compliance using occlusion dose monitors. [35] It reported that, although analyses comparing prescribed durations of occlusion found no significant difference in outcomes between 12- and 6-hour occlusion, the analysis of actual received occlusion dose found a significantly worse visual outcome in children who received under 3 hours' occlusion a day compared with children who received 3 to 6 hours, or 6 to 12 hours (mean difference in LogMAR units with 3–6 hours *v* <3 hours: 0.07, 95% CI 0.06 to 0.12; P = 0.04; mean difference in LogMAR units with 6–12 hours *v* <3 hours: 0.15, 95%

CI 0.12 to 0.18; P = 0.01). The authors of this RCT suggested that obtaining an initial dose of 3 to 4 hours a day of occlusion (possibly less in children aged <4 years) should be a clinical priority, but that actual doses greater than this may not confer any extra benefit.

Recurrence after successful occlusion:
In a prospective cohort study (69 children aged <8 years with previously successfully treated anisometropic or strabismic amblyopia [improvement in visual acuity 3 or more LogMAR units when treatment stopped]), 25% of children in whom occlusion was successful had a recurrence of their amblyopia within 1 year (absolute numbers not reported). [36] Recurrence was significantly higher in children with better visual acuity at cessation of treatment (RR 0.68 per line of worse visual acuity, 95% CI 0.51 to 0.90), a greater degree of improvement in visual acuity with previous treatment (RR 1.50 per line increase in previous acuity, 95% CI 1.10 to 2.00), and a history of previous recurrence (RR 2.70, 95% CI 1.50 to 4.90; all RRs adjusted for intensity of treatment and length of weaning). Having good stereoacuity or being straight-eyed after treatment did not appear to reduce the risk of recurrence. [36]

OPTION PENALISATION (WITH ATROPINE OR OPTICAL PENALISATION)

Visual acuity
Penalisation using atropine compared with occlusion Daily penalisation using atropine and prescribed occlusion for 6 hours each day are equally effective at improving visual acuity after 6 months in children aged 3 to 7 years with amblyopia who also wear glasses (moderate-quality evidence).

Penalisation using atropine plus occlusion plus near-vision tasks compared with glasses alone Penalisation with atropine plus patching plus near-vision tasks improves visual acuity after 24 weeks in children aged 7 to 13 years, but is no more effective than glasses alone in children aged over 13 years (moderate-quality evidence).

Daily penalisation with atropine compared with less frequent regimen Daily penalisation with atropine is no more effective at improving visual acuity after 4 months than penalisation with atropine at weekends alone in children under 7 years old with amblyopia (moderate-quality evidence).

Penalisation with atropine compared with optical penalisation Atropine is more effective at improving visual acuity at 6 months than optical penalisation (moderate-quality evidence).

Adverse effects
Severe adverse effects of atropine treatment are rare. Parentally reported compliance with treatment is better and negative psychosocial effects are fewer with atropine compared with patching.

Note
We found no clinically important information about the effects of penalisation compared with no treatment, placebo, or glasses.

For GRADE evaluation of interventions for amblyopia, see table, p 16 .

Benefits:

Penalisation with atropine or optical penalisation versus no treatment:
We found two systematic reviews of penalisation in children with either unilateral refractive (search date 2008) [18] or strabismic amblyopia (search date 2006). [19] Neither review identified any RCTs. We found no cohort studies.

Penalisation with atropine versus occlusion (in children wearing glasses):
We found no systematic review. We found one large RCT (419 children aged 3–6 years with strabismic, refractive, or mixed amblyopia; visual acuity in the amblyopic eye: 6/12–6/30) comparing penalisation (using daily atropine) versus occlusion (patching) for 6 hours daily. [37] All participants also wore glasses. The RCT found that visual acuity in the amblyopic eye improved in both groups by approximately three lines after 6 months. It found that penalisation was slightly less effective than patching in increasing mean visual acuity after 6 months, although the difference between groups was of borderline significance and is clinically unimportant (mean difference in mean visual acuity between the patching and atropine groups in LogMAR units: 0.034, 95% CI 0.005 to 0.064; P value not reported). [37] Subgroup analyses reported in a second publication found that treatment was not affected by age, type of amblyopia, initial visual acuity, or eye colour. [38]

The RCT used a quality-of-life questionnaire — the Amblyopia Treatment Index questionnaire — to assess the acceptability of treatment and its impact on the child and family (reported in a third publication). [39] It found that Amblyopia Treatment Index scores were better (lower) in the atropine group compared with those for patching (5-point scale where high = bad: social stigma: mean 1.84 with atropine *v* 3.09 with patching; P < 0.001; difficulty with compliance: mean 1.99 with atropine

v 2.46 with patching; P < 0.001; and adverse effects: mean 2.11 with atropine *v* 2.35 with patching; P = 0.02).

Further weaker support for the equivalence of penalisation and patching is reported from one retrospective cohort study comparing non-matched groups of children under 13 years old who received either penalisation alone, occlusion followed by penalisation, or part-time occlusion (prescription of 2–6 hours of patching daily). In this study, 75 children who had been treated with full-time atropine, intermittent atropine, or optical penalisation were compared with 30 children who had been treated with part-time occlusion. The difference between groups in mean interocular acuity at long-term follow-up (range 0.1–9.2 years) was 0.3 LogMAR lines (reported as not significant; P value not reported). [40]

Adding penalisation with atropine plus occlusion plus near-vision tasks to glasses versus glasses alone:
See benefits of occlusion, p 6 .

Daily penalisation with atropine versus less frequent regimens (in children wearing glasses):
We found no systematic review but found one RCT [41] and one retrospective cohort study. [42]

The RCT (168 children <7 years of age with amblyopia of 6/12–6/24) compared daily atropine versus weekend atropine. [41] It found no significant difference in amblyopic eye visual acuity at 4 months (both groups improved by approximately 2 lines; mean difference in acuity between the groups in LogMAR units: 0, 95% CI –0.04 to +0.04). After 4 months, similar proportions of children in each group had vision in their amblyopic eye that was equal to or better than the fellow eye (39/83 [47%] with daily atropine *v* 45/85 [53%] with weekend atropine; P = 0.54). There was similar depth perception in each group (measured by stereopsis performance tests). [41]

Daily penalisation with atropine versus less frequent regimens or versus optical penalisation (in children wearing glasses):
The retrospective cohort study (163 children with strabismic amblyopia) compared full-time versus intermittent atropine instillation 1 to 3 days a week versus optical penalisation for at least 6 months. Most children also wore glasses. The study found that all three types of penalisation reduced the severity of amblyopia after 6 months (mean improvement in interocular acuity difference: 1.9–2.7 LogMAR units; 3 group P < 0.05), and improvement was similar in all three groups after controlling for age and severity of amblyopia at the initial visit. [42]

Penalisation with atropine versus optical penalisation:
We found one RCT (70 children with strabismic or anisometropic amblyopia; visual acuity in the amblyopic eye at least 20/60) comparing penalisation using atropine twice weekly versus optical penalisation for 6 months. It was unclear whether children receiving penalisation with atropine also wore glasses. Assessment of 63/70 (90%) children who completed the trial found that atropine significantly improved visual acuity at 6 months compared with optical penalisation (mean improvement: 3.4 LogMAR lines with atropine *v* 1.8 LogMAR lines with optical penalisation; P < 0.01). [43]

Harms:

Penalisation with atropine or optical penalisation versus no treatment:
We found no RCTs or cohort studies.

Penalisation with atropine versus occlusion (in children wearing glasses):
The RCT reported that 2/204 (1%) children changed to homatropine from atropine because of adverse effects. [37] It found that 26% of children receiving atropine reported ocular adverse events, including light sensitivity, lid or conjunctival irritation, or, rarely, eye pain. Moderate or severe skin irritation was reported in 6% of children receiving patching.

The RCT also found that atropine significantly increased reduction of the fellow-eye acuity compared with patching at 6 months (fellow-eye acuity reduction by 2 or more lines: 17/194 [9%] children with atropine *v* 3/208 [1%] children with patching; P < 0.01 for reduction in acuity of 1 or more line). [37] Treatment to improve the vision of the fellow eye was given to only one child in the atropine group and, by 6 months, visual acuity in the fellow eye of all children who had received atropine penalisation had returned to within one line of baseline acuity. [37]

The RCT reported that similar proportions of children receiving atropine and patching developed a new strabismus at distance viewing after 6 months of treatment (12/90 [13%] receiving atropine *v* 13/97 [13%] receiving patching). Of these, only one child in each group developed an ocular deviation of greater than 8 dioptres. [37]

The RCT assessed refractive error at 2 years in 282/419 (67%) participants and found no significant difference between penalisation using atropine and occlusion in mean refractive change in the

sound eye (mean change in refractive error from baseline: +0.10 D with atropine *v* +0.08 D with occlusion; mean difference: +0.02 D, 95% CI –0.20 D to +0.17 D). However, these results must be treated with caution as there were no participants with untreated sound eyes for comparison. Treatment (penalisation or occlusion) was at investigator discretion between 6 months and 2 years, so some mixing of interventions may have occurred. [44]

The cohort study gave no information on adverse effects. [40]

Adding penalisation with atropine plus occlusion plus near-vision tasks to glasses versus glasses alone:
See harms of occlusion, p 6 .

Daily penalisation with atropine versus less frequent regimens (in children wearing glasses):
The RCT reported that one child receiving daily atropine changed to homatropine because of facial flushing and fever. [41] Ocular adverse events, most commonly light sensitivity, were reported by 13/83 (16%) children in the daily atropine group compared with 25/85 (29%) children in the weekend atropine group. [41] The RCT found that 4/168 (2%) children had reduced visual acuity in the fellow eye after 4 months, but found no significant difference between daily atropine compared with weekend atropine (P = 0.99). [41] After 5 or 8 months of follow-up, the visual acuity in the fellow eye of 2/168 (1%) children (1 child from each group) remained two lines or more worse than at baseline. [41] New ocular misalignments appeared during treatment in 13/168 (8%) children. [41]

Daily penalisation with atropine versus less frequent regimens or versus optical penalisation (in children wearing glasses):
The retrospective cohort study gave no information on adverse effects. [42]

Penalisation with atropine versus optical penalisation:
The RCT found that 1/31 (3%) children receiving atropine had reverse amblyopia. It found no cases in the children receiving optical penalisation (significance of difference between groups not assessed). [43]

Comment:

Clinical guide:
In general, occlusion treatment (with glasses, if needed) is the mainstay of management for amblyopia. Most practitioners use penalisation with atropine as an option for children who do not comply with patching, if their amblyopia is not severe, rather than as a first-line treatment. The RCTs showing equivalence between occlusion and atropine penalisation may alter practice, so that atropine is more widely used.

OPTION NEAR-VISION TASKS

Visual acuity
Compared with no near-vision tasks We don't know how effective near-vision tasks are as adjuvant treatment for amblyopia compared with no near-vision tasks (moderate-quality evidence).

Near-vision tasks plus occlusion plus glasses compared with glasses alone Adding near-vision tasks plus patching to glasses with or without penalisation of the fellow eye improves visual acuity after 1 year in children aged 3 to 7 years (moderate-quality evidence).

Near-vision tasks plus occlusion plus penalisation compared with glasses alone Near-vision tasks plus patching plus penalisation with atropine improves visual acuity after 24 weeks in children aged under 13 years, but is no more effective than glasses alone in children aged over 13 years (moderate-quality evidence).

For GRADE evaluation of interventions for amblyopia, see table, p 16 .

Benefits:

Near-vision tasks versus no near-vision tasks in children prescribed occlusion or wearing glasses:
We found one systematic review (search date not reported; references cover 1955–2003), which identified no RCTs. [45] We also found one subsequent RCT. [46]

The review identified two case series (219 people; 200 in 1 study, 19 in the other) assessing the effectiveness of near-vision tasks (defined as individualised, non-invasive, therapeutic procedures intended to correct or improve various eye conditions) in combination with occlusion and/or refractive correction. The specific components of near-vision tasks in one case series were: watching motion pictures and stills, tracing, copying pictures and drawings, and threading beads. In the other case series, the tasks included hand–eye co-ordination training and “binocular therapy”, “ocular motility training”, “accommodative therapy”, and “fixation training”. [45] The case series did not account for potential confounders such as baseline differences in visual acuity between groups and compliance.

Follow-up was inadequate. The systematic review found insufficient evidence to assess the efficacy of vision therapy for the treatment of amblyopia.

The subsequent RCT (64 children aged 3–7 years with anisometropic, strabismic, or combined amblyopia) compared near-vision tasks versus no near-vision tasks in children receiving 2-hour daily occlusion (patching). [46] The RCT found no significant difference between groups in visual acuity at 4 weeks, although visual acuity was better in children performing near-vision tasks (mean improvement: 2.6 LogMAR lines with near-vision tasks *v* 1.6 LogMAR lines with no near-vision task; P = 0.07). Visual acuity was a secondary outcome in the RCT and it was therefore underpowered to detect the smallest clinically meaningful difference between groups.

Near-vision tasks plus occlusion with or without glasses versus glasses alone:
See benefits of occlusion, p 6 .

Near-vision tasks plus glasses plus occlusion plus penalisation versus glasses alone:
See benefits of occlusion, p 6 .

Harms:

Near-vision tasks versus no near-vision tasks in children carrying out occlusion or wearing glasses:
The review gave no information on adverse effects of near-vision tasks for the adjuvant treatment of amblyopia. It did, however, warn that although near-vision tasks did not worsen existing eye conditions, children prescribed such tasks might delay seeking medically indicated treatment, or might have unrealistic expectations about the role of the tasks.

Near-vision tasks plus occlusion with or without glasses versus glasses alone:
See harms of occlusion, p 6 .

Near-vision tasks plus glasses plus occlusion plus penalisation versus glasses alone:
See harms of occlusion, p 6 .

Near-vision tasks versus no near-vision tasks in children carrying out occlusion:
The RCT gave no information on adverse effects. [46]

Comment: None.

GLOSSARY

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.
Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Penalisation involves blurring of the fellow eye with a cycloplegic agent (such as atropine) or with a spectacle lens that over or under corrects the true refractive error. Both methods of penalisation prevent the eye having a sharply focussed image, although light is still received as normal.
Very low-quality evidence Any estimate of effect is very uncertain.
Visual acuity testing is carried out with charts using letters or standard pictures or symbols. Modern tests that incorporate crowding and LogMAR (logarithm of the minimum angle of resolution) size scaling are more accurate. One line of letters or symbols (usually 4 or 5) constitutes 0.1 LogMAR units and roughly approximates to one line on a Snellen chart, although this conversion factor is inaccurate and should only be used as a crude guide to interpretation. Given the variability in test performance within individuals, a change in 0.2 LogMAR units is often quoted as being the smallest clinically important change, although some studies use a change of 0.1 LogMAR or greater, which might be considered clinically more marginal. Change of less than 0.1 LogMAR unit is not clinically important and could be accounted for by test–retest variability.

SUBSTANTIVE CHANGES

Glasses One cohort study added found that visual acuity was better at 1 year in over two-thirds of children who wore glasses. [28] Categorisation unchanged (Likely to be beneficial, based on consensus).
Occlusion (patching) Three systematic reviews added [7] [18] [19] identified the same RCTs as previously found by *Clinical Evidence*. One further RCT identified [35] found no significant difference in visual acuity at 18 weeks between 12 and 6 hours' prescribed occlusion, but added to the evidence for a dose response when actual hours of received occlusion can be measured. Categorisation unchanged; occlusion in combination with penalisation and near-vision tasks categorised as Beneficial compared with glasses alone.
Penalisation One RCT added found that penalisation using atropine improved visual acuity at 6 months compared with optical penalisation. [43] Categorisation unchanged (Likely to be beneficial).

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Competing interests: CW is the author of two papers (one RCT and one study) cited in this review.

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TABLE **GRADE evaluation of interventions for amblyopia**

Important outcomes	**Prevalence of amblyopia, visual acuity, and adverse effects**								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consis-tency**	**Direct-ness**	**Effect size**	**GRADE**	**Comment**
What are the effects of interventions to detect amblyopia early?									
1 (1590) [12]	Prevalence of ambly-opia	Screening *v* no screening	2	0	0	0	0	Low	
1 (3490) [14] [15]	Prevalence of ambly-opia	Repeated screening *v* usual care	4	0	0	0	0	High	
1 (6081) [16]	Prevalence of ambly-opia	Pre-school screening *v* school-entry screening	2	–1	0	0	0	Very low	Quality point deducted for very unequal distribution of children in comparison groups (results in 25% offered pre-school screening compared with those in 75% not offered it)
1 (3490) [14] [15]	Visual acuity	Repeated screening *v* usual care	4	–1	0	0	0	Moderate	Quality point deducted for loss to follow-up in assessment of this outcome
What are the effects of medical treatments for amblyopia?									
4 (455) [25] [26] [27] [28]	Visual acuity	Glasses *v* no glasses	4	–1	0	0	0	Moderate	Quality point deducted for inclusion of non-randomised studies
1 (164) [25]	Visual acuity	Glasses plus occlusion *v* no treat-ment	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (180) [31]	Visual acuity	Occlusion plus glasses plus near-vision tasks *v* glasses alone	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (507) [8]	Visual acuity	Occlusion plus penalisation plus near-vision tasks *v* glasses alone	4	0	–1	0	0	Moderate	Consistency point deducted for conflicting results for different age groups
1 (60) [32]	Visual acuity	Longer or shorter periods of pre-scribed occlusion *v* no occlusion	4	–2	–1	0	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Consis-tency point deducted as finding of lack of difference with different duration of treat-ment may have been confounded by com-pliance
4 (524) [32] [33] [34] [35]	Visual acuity	Longer *v* shorter duration of pre-scribed occlusion	4	0	0	0	0	High	
1 (419) [37]	Visual acuity	Penalisation with atropine*v* occlu-sion	4	–1	0	0	0	Moderate	Quality point deducted for incomplete re-porting of results
2 (331) [41]	Visual acuity	Daily penalisation with atropine *v* less frequent regimens	4	–1	0	0	0	Moderate	Quality point deducted for inclusion of non-randomised study
1 (70) [43]	Visual acuity	Penalisation with atropine *v* optical penalisation	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
3 (283) [45] [46]	Visual acuity	Near-vision tasks *v* no no near-vi-sion tasks	4	–1	0	0	0	Moderate	Quality point deducted for inclusion of non-randomised evidence

Important outcomes	Prevalence of amblyopia, visual acuity, and adverse effects								
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consis-tency	Direct-ness	Effect size	GRADE	Comment

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion.
Consistency: similarity of results across studies.
Directness: generalisability of population or outcomes.
Effect size: based on relative risk or odds ratio.