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Topical and oral steroids for otitis media with effusion (OME) in children

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Abstract

Background

Otitis media with effusion (OME) is an accumulation of fluid in the middle ear cavity, common amongst young children. The fluid may cause hearing loss. When persistent, it may lead to behavioural problems and a delay in expressive language skills. Management of OME includes watchful waiting, medical, surgical and other treatments, such as autoinflation. Oral or topical steroids are sometimes used to reduce inflammation in the middle ear.

Objectives

To assess the efficacy (benefits and harms) of topical and oral steroids for the treatment of otitis media with effusion.

Search methods

The Cochrane ENT Information Specialist searched the Cochrane ENT Register; CENTRAL; Ovid MEDLINE; Ovid Embase; Web of Science; ClinicalTrials.gov; ICTRP and additional sources for published and unpublished studies. The date of the search was 20 January 2023.

Selection criteria

We included randomised controlled trials (RCTs) and quasi-randomised trials in children aged 6 months to 12 years with unilateral or bilateral OME. We included studies that compared topical or oral steroids with either placebo or watchful waiting (no treatment).

Data collection and analysis

We used standard Cochrane methods. Our primary outcomes were determined following a multi-stakeholder prioritisation exercise and were: 1) hearing, 2) OME-specific quality of life and 3) systemic corticosteroid side effects. Secondary outcomes were: 1) persistence of OME, 2) other adverse effects (including local nasal side effects), 3) compliance or adherence to treatment, 4) receptive language skills, 5) speech development, 6) cognitive development, 7) psychosocial skills, 8) listening skills, 9) generic health-related quality of life, 10) parental stress, 11) vestibular function and 12) episodes of acute otitis media. We used GRADE to assess the certainty of evidence for each outcome.

Although we included all measures of hearing assessment, the proportion of children who returned to normal hearing was our preferred method to assess hearing, due to challenges in interpreting the results of mean hearing thresholds.

Main results

We included 26 studies in this review (2770 children). Most studies of oral steroids used a course of prednisolone for 7 to 14 days. Studies of nasal steroids used a variety of preparations (beclomethasone, fluticasone and mometasone) for between 2 weeks and 3 months. Here we report our primary outcomes and main secondary outcome, at the longest reported follow-up time.

Oral steroids compared to placebo

Oral steroids probably result in little difference in the proportion of children with normal hearing after 12 months (69.7% of children with steroids, compared to 61.1% of children receiving placebo, risk ratio (RR) 1.14, 95% confidence interval (CI) 0.97 to 1.33; 1 study; 332 participants, moderate-certainty evidence). There is probably little difference in quality of life related to OME (mean difference (MD) in OM8-30 score 0.07, 95% CI -0.2 to 0.34; 1 study; 304 participants; moderate-certainty evidence).

Oral steroids may reduce the number of children with persistent OME at 6 to 12 months of follow-up, but the size of the effect was uncertain (absolute risk reduction ranging from 13.3% to 45%, number needed to treat (NNT) of between 3 and 8; low-certainty evidence). The evidence was very uncertain regarding the risk of systemic corticosteroid side effects and we were unable to conduct any meta-analysis for this outcome.

Oral steroids compared to no treatment

Oral steroids may result in little or no difference in the persistence of OME after three to nine months (74.5% children receiving steroids, compared to 73% of those receiving placebo, RR 1.02, 95% CI 0.89 to 1.17; 2 studies; 258 participants; low-certainty evidence). The evidence on adverse effects was very uncertain. We did not identify any evidence on hearing or disease-related quality of life.

Nasal steroids compared to placebo

We did not identify data on the proportion of children who returned to normal hearing. However, the mean change in hearing threshold after two months was -0.3 dB lower (95% CI -6.05 to 5.45; 1 study; 78 participants; very low-certainty evidence). The evidence suggests that nasal steroids make little difference to disease-specific quality of life after nine months (OM8-30 score, MD 0.05 higher, 95% CI -0.36 to 0.46; 1 study; 82 participants; low-certainty evidence).

The evidence is very uncertain regarding the effect of nasal steroids on persistence of OME at up to one year. Two studies reported this: one showed a potential benefit for nasal steroids, the other showed benefit with placebo (2 studies; 206 participants). The evidence was also very uncertain regarding the risk of corticosteroid-related side effects, as we were unable to provide a pooled effect estimate.

Nasal steroids compared to no treatment

We did not identify data on the proportion of children who returned to normal hearing. However, the mean difference in final hearing threshold after four weeks was 1.95 dB lower (95% CI -3.85 to -0.05; 1 study; 168 participants; low-certainty evidence). Whilst nasal steroids may reduce the persistence of OME after eight weeks of follow-up, the evidence was very uncertain (58.5% of children receiving steroids, compared to 81.3% of children with no treatment, RR 0.72, 95% CI 0.57 to 0.91; 2 studies; 134 participants). We did not identify any evidence on disease-related quality of life or adverse effects.

Authors' conclusions

Overall, oral steroids may have little effect in the treatment of OME, with little improvement in the number of children with normal hearing and no effect on quality of life. There may be a reduction in the proportion of children with persistent disease after 12 months of follow-up. However, this benefit may be small and must be weighed against the potential for adverse effects associated with oral steroid use.

The evidence for nasal steroids was all low- or very low-certainty. It is therefore less clear if nasal steroids have any impact on hearing, quality of life or persistence of OME. Evidence on adverse effects was very limited.

OME is likely to resolve spontaneously for most children. The potential benefit of treatment may therefore be small and should be balanced with the risk of adverse effects. Future studies should aim to determine which children are most likely to benefit from treatment, rather than offering interventions to all children.

Plain language summary

Oral or nasal steroids for glue ear in children

Key messages

Taking steroids in tablet or syrup form (by mouth) may have little impact on hearing and quality of life for children with glue ear. Steroids may reduce the number of children who have glue ear after 6 to 12 months, but we are uncertain how large this reduction might be.

Using a steroid nasal spray may also make little difference to hearing or quality of life, although the evidence is not as robust. It is also unclear whether nasal steroids affect the number of children with glue ear after longer-term follow-up.

Due to a lack of robust evidence, it is difficult to know how many people might suffer from harm from these treatments. However, when steroids are used for other conditions, they are associated with well-recognised side effects. This should be considered when deciding whether or not to use these treatments.

What is OME?

Glue ear (or 'otitis media with effusion', OME) is a common condition affecting young children. Fluid collects in the middle ear, causing hearing impairment. As a result of their poor hearing, children may have behavioural difficulties and delays in their speech development.

How is OME treated?

Most of the time, OME does not need any treatment and the symptoms will get better with time. In children with persistent OME, different treatments have been explored, including medications or surgery.

What did we want to find out?

We wanted to find out whether steroids were better than placebo (sham or dummy treatment) or no treatment for children with OME.

We also wanted to see if there were any unwanted effects associated with taking steroids.

What did we do?

We searched for studies that compared steroids taken as a tablet or nasal spray with placebo or no treatment in children with OME. We compared and summarised the study results, and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We found 26 studies, including 2770 children.

Oral steroids compared to placebo

We found that oral steroids probably make little difference to the number of children who have normal hearing after one year of follow-up. Normal hearing was seen in 69.7% of children who received steroids and 61.1% of children who received placebo. There is also likely to be very little difference between the two groups in quality of life (related to glue ear).

The evidence suggests that oral steroids might reduce the number of children who have glue ear after 6 to 12 months of follow-up, but the results from the studies were very different - so we do not know how big the reduction might be. The evidence on side effects of oral steroids was not robust. From the evidence in this review we were not able to determine what the chance of side effects would be.

Oral steroids compared to no treatment

We found fewer studies here, and there was no information on hearing or quality of life. After up to nine months, there may be little difference in the number of children who still have glue ear (74.5% of children who received steroids, compared to 73% of those who received no treatment). Again, the evidence on side effects was not robust.

Nasal steroids compared to placebo

We are unsure whether nasal steroids have any effect on hearing, as the evidence was not robust. Nasal steroids may make little difference to quality of life after nine months of follow-up. We are uncertain whether nasal steroids affect the number of children with persistent glue ear at up to one year, as the evidence from two studies was conflicting. We are not sure whether there may be a risk of harm with this treatment, as the studies did not clearly report side effects.

Nasal steroids compared to no treatment

We only have information on hearing at up to four weeks of follow-up, which may not be long enough to really assess this treatment. However, at this stage, there might be little difference in hearing between children who receive nasal steroids or no treatment. We are also unsure whether nasal steroids affect the number of children with persistent glue ear after eight weeks. We did not identify any information on quality of life or side effects of treatment from these studies.

What are the limitations of the evidence?

The studies used lots of different types of medication, for different lengths of time. We do not know if some of these may be more effective than others. We do not have good evidence on side effects of these treatments, but they may cause problems for some children.

How up-to-date is this evidence?

The evidence is up-to-date to January 2023.

Summary of findings

Summary of findings 1

Oral steroids compared to placebo for otitis media with effusion (OME) in children

Oral steroids compared to placebo for otitis media with effusion (OME) in children

Patient or population: children with otitis media with effusion (OME)
Setting: outpatient
Intervention: oral steroids
Comparison: placebo

Outcomes	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)			Certainty of the evidence (GRADE)	What happens
		With placebo	With oral steroid	Difference		
Normal hearing Follow-up: 12 months (medium-term) № of participants: 332 (1 RCT)	RR 1.14 (0.97 to 1.33)	61.1%	69.7% (59.3 to 81.3)	8.6% more (1.8 fewer to 20.2 more)	⊕⊕⊕⊖ Moderate[1]	Oral steroids probably result in little or no difference to the return to normal hearing at 12 months, when compared to placebo.
Disease-specific quality of life (total OM8-30, lower score is more favourable)	—	The mean disease-specific quality of life was -0.29	—	MD 0.07 higher (0.2 lower to 0.34 higher)	⊕⊕⊕⊖ Moderate[2]	Oral steroids probably result in little or no difference in disease-specific quality of life at 12 months, when

Follow-up: 12 months (medium-term) № of participants: 304 (1 RCT)						compared to placebo.
Persistence of OME Follow-up: range 6 months to 12 months (medium-term) № of participants: 352 (2 RCTs)	Two studies indicated that persistence of OME may be reduced in those who received steroids, but the size of the effect was very different, ranging from a RR of 0.18 (persistence of OME in placebo group of 67%, compared to 12% of those receiving steroids) to a RR of 0.86 (persistence of OME in placebo group of 93.8% compared to 80.5% of those receiving steroids).				⊕⊕⊖⊖ Low[3]	Oral steroids may reduce the persistence of OME in the medium term, when compared with placebo, but the size of the effect is very uncertain.
Adverse event: systemic corticosteroid side effects Follow-up ranged from 12 days to 12 months № of participants: 264 (3 RCTs)	Without reporting directly on the incidence of systemic corticosteroid side effects, three trials provided information from which it may be reasonable to assume none occurred. One reported an asthma attack as the only serious adverse event, and reported an adjusted OR of 0.59 (95% CI 0.28 to 1.27) for having no adverse effects (adjusted for site and age group at recruitment; data pooled across all follow-up time points of 1, 2, 3, 4 and 5 weeks) (OSTRICH). One trial reported that none of the adverse events were classified as serious (Hemlin 1997), and one further trial reported that no significant adverse effects were seen in any study participant (Niederman 1984). Further information is provided in Table 1.				⊕⊖⊖⊖ Very low[4,5]	The evidence is very uncertain about the risk of systemic corticosteroid side effects with the use of oral steroids.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **OME:** otitis media with effusion; **OR:** odds ratio; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Downgraded one level for imprecision as the optimal information size (OIS) was not reached (< 300 events) and the confidence interval crossed one decision threshold (RR 1.25).

[2]Downgraded one level for imprecision as the OIS was not reached (< 400 participants).

[3]Downgraded two levels for imprecision as the OIS was not reached (< 400 participants) and an estimate of the effect size was not possible, due to a narrative synthesis.

[4]Downgraded by one level for detection bias.

[5]Downgraded by two levels for imprecision as this was a narrative synthesis with zero reported events.

Summary of findings 2

Oral steroids compared to no treatment for otitis media with effusion (OME) in children

Oral steroids compared to no treatment for otitis media with effusion (OME) in children

Patient or population: children with otitis media with effusion (OME)
Setting: outpatient
Intervention: oral steroids
Comparison: no treatment

Outcomes	Relative effect	Anticipated absolute effects* (95% CI)			Certainty of the	What happens

	(95% CI)	Without oral steroids	With oral steroids	Difference	evidence (GRADE)	
Persistence of OME (3 to 9 months - medium-term) № of participants: 258 (2 RCTs)	RR 1.02 (0.89 to 1.17)	73.0%	74.5% (65 to 85.4)	1.5% more (8 fewer to 12.4 more)	⊕⊕⊖⊖ Low[1,2]	The evidence suggests that oral steroids may result in little or no difference in the persistence of OME in the medium term, when compared with no treatment.
Adverse event: systemic corticosteroid side effects Follow-up: 1 month № of participants: 40 (1 RCT)	One trial reported that none of 40 participants given oral prednisolone in a tapering course over two weeks reported adverse effects over one month of follow-up (Acharya 2020). Further information is available in Table 1.				⊕⊖⊖⊖ Very low [3] [4]	The evidence is very uncertain about the effect of a two-week tapering course of prednisolone on the risk of systemic corticosteroid side effects at one month of follow-up.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Downgraded by one level for a risk of performance bias.

[2]Downgraded by one level for imprecision, as the optimal information size (OIS) was not reached (< 300 events).

[3]Downgraded by two levels for a risk of performance and detection bias (arising from lack of blinding and brief follow-up).

[4]Downgraded by two levels for very serious imprecision, due to a narratively reported outcome, with zero reported cases amongst a small sample size.

Summary of findings 3

Nasal steroids compared to placebo for otitis media with effusion (OME) in children

Nasal steroids compared to placebo for otitis media with effusion (OME) in children

Patient or population: children with otitis media with effusion (OME)
Setting: outpatient
Intervention: nasal steroids
Comparison: placebo

Outcomes	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)			Certainty of the evidence (GRADE)	What happens
		Without nasal steroids	With nasal steroids	Difference		
Change in hearing threshold; assumed ICC = 0.5 Follow-up: 2 months (short-term)	—	The mean change in hearing threshold (short-term), ICC = 0.5, without nasal steroid was -7.6 dB	—	MD 0.3 dB lower (6.05 lower to 5.45 higher)	⊕⊖⊖⊖ Very low[1,2]	The evidence is very uncertain about the effect of nasal steroids on change in hearing threshold at 2 months, when compared with placebo.

№ of participants: 78 (1 RCT)						
Disease-specific quality of life (total OM8-30 score, lower score is more favourable) Follow-up: 9 months (medium-term) № of participants: 82 (1 RCT)	—	The mean disease-specific quality of life (medium-term) without nasal steroid was 2.87	—	MD 0.05 higher (0.36 lower to 0.46 higher)	⊕⊕⊖⊖ Low[2,3]	The evidence suggests that nasal steroids result in little to no difference in disease-specific quality of life at 9 months, when compared to placebo.
Persistence of OME Follow-up: up to 1 year (medium-term) № of participants: 206 (2 RCTs)	Two studies reported this outcome, but the results were conflicting. One study showed some benefit to intranasal steroids, whilst the other showed a potential increase in the number of children with persistent OME.				⊕⊖⊖⊖ Very low[4,5]	The evidence is very uncertain about the effect of nasal steroids on persistence of OME at up to 12 months, when compared to placebo.
Adverse event: systemic corticosteroid side effects Follow-up: range 9 months to 2 years № of participants: 157 (2 RCTs)	Without reporting directly on the incidence of systemic corticosteroid side effects, two trials provided information from which it may be reasonable to assume none occurred. One trial reported that there were no serious adverse events and that growth rate was unaffected over two years (Scadding 2014). A second trial reported that there were no serious adverse events, suspected serious adverse reactions or related hospitalisations (Williamson 2009).				⊕⊖⊖⊖ Very low[3,6]	The evidence is very uncertain about the risk of systemic corticosteroid side effects with nasal steroids over two years.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **ICC:** intracluster correlation coefficient; **MD:** mean difference; **RR:** risk ratio;

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Downgraded by two levels for risk of bias, due to the potential for selection bias, detection bias and reporting bias.

[2]Downgraded by one level for imprecision, as the optimal information size (OIS) was not reached (< 400 participants).

[3]Downgraded by one level due to the risk of attrition bias.

[4]Downgraded by one level for risk of bias, due to concerns over reporting bias and attrition bias.

[5]Downgraded by two levels for imprecision, as this was a narrative synthesis (therefore no estimate of effect could be provided) and the OIS was not reached (< 300 events).

[6]Downgraded by two levels for very serious imprecision as this is a narrative synthesis, with zero events in either of two studies.

Summary of findings 4

Nasal steroids compared to no treatment for otitis media with effusion (OME) in children

Nasal steroids compared to no treatment for otitis media with effusion (OME) in children						
Patient or population: children with otitis media with effusion (OME) **Setting:** outpatient **Intervention:** nasal steroids **Comparison:** no treatment						
Outcomes	**Relative effect (95% CI)**	**Anticipated absolute effects* (95% CI)**			**Certainty of the evidence (GRADE)**	**What happens**
		Without nasal steroids	**With nasal steroids**	**Difference**		
Final hearing threshold (air-bone gap, very short-term); assumed ICC = 0.5 Follow-up: 4 weeks № of participants: 168 (1 RCT)	—	The mean air-bone gap without nasal steroid was 9.46	—	MD 1.95 lower (3.85 lower to 0.05 lower)	⊕⊕⊖⊖ Low[1,2]	Nasal steroids may make little or no difference to final hearing threshold at 4 weeks when compared to no treatment.
Persistence of OME (short-term); assumed ICC = 0.5 Follow-up: range 6 weeks to 8 weeks № of participants: 134 (2 RCTs)	RR 0.72 (0.57 to 0.91)	81.3%	58.5% (46.3 to 73.9)	22.8% fewer (34.9 fewer to 7.3 fewer)	⊕⊖⊖⊖ Very low[3,4]	The evidence is very uncertain about the effect of nasal steroids on persistence of OME at 6 to 8 weeks, when compared to no treatment.
***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** confidence interval; **ICC:** intracluster correlation coefficient; **MD:** mean difference; **RR:** risk ratio						
GRADE Working Group grades of evidence **High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect. **Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. **Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.						

[1]Downgraded by one level for risk of bias, due to concerns over performance and detection bias.

[2]Downgraded by one level for imprecision, as the optimal information size (OIS) was not reached (< 400 participants).

[3]Downgraded by two levels for risk of bias, due to concerns over performance, detection and selection bias.

[4]Downgraded by one level for imprecision, as the OIS was not reached (< 300 events) and the confidence interval crosses one decision threshold (0.80).

Background

Description of the condition

Otitis media with effusion (OME) is a common condition in early childhood. The condition, also known as 'glue ear' or serous otitis media, is defined as "the presence of fluid in the middle ear without signs or symptoms of acute infection" (Rosenfeld 2016).

A key clinical feature of OME is hearing loss, due to decreased mobility of the tympanic membrane and consequent loss of sound conduction (Rosenfeld 2016). Other symptoms that may be attributable to OME include balance (vestibular) problems and ear discomfort (Rosenfeld 2016). When symptoms persist, they may lead to poor school performance

and affect a child's daily activities, social interactions and emotions, possibly leading to a poorer quality of life for the child (Rosenfeld 2000).

It is thought that up to 80% of children have had OME by the age of four years, but a decline in its prevalence is observed for children beyond six years of age (Williamson 2011). Most episodes of OME in children resolve spontaneously within three months, however approximately 35% of children will have more than one episode of OME and, furthermore, 5% to 10% of episodes will last for more than a year (Rosenfeld 2016). Children with OME following an episode of untreated acute otitis media (AOM) have a 59% rate of resolution by one month rising to 74% by three months, while children with newly diagnosed OME of unknown duration demonstrate a resolution rate of 28% by three months and up to 42% by six months (Rosenfeld 2003). The condition is more prevalent in children with Down syndrome or cleft palate (Flynn 2009; Maris 2014). Atopy has been considered a potential risk factor for OME in children (Kreiner-Møller 2012; Marseglia 2008; Zernotti 2017).

Diagnosis of OME is typically by clinical examination including (pneumatic) otoscopy and/or tympanometry in primary care. Following diagnosis, there will often be a period of active observation for at least three months. During the observation period the care provider may offer a non-surgical intervention such as hearing aids or autoinflation. The National Institute for Health and Care Excellence (NICE) and the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) do not currently recommend the use of antibiotics, antihistamines, decongestants or corticosteroids for OME as there is insufficient evidence to suggest they are effective treatments (NICE 2008; Rosenfeld 2016). If OME has not resolved within the three-month observation period, the child may be referred for further management/active intervention. This may include hearing aid provision or review by an ENT surgeon for consideration for myringotomy, ventilation tubes insertion and/or adenoidectomy. The choice of active intervention varies considerably. Earlier active intervention may be considered for children at increased risk of developmental difficulties (see Rosenfeld 2016 for a list of 'at-risk' factors).

This Cochrane Review focusses on topical and oral steroids as treatment for OME in children. This review forms part of a suite of five reviews of OME treatment, which will address those interventions identified in a prioritisation exercise as being most important and in need of up-to-date Cochrane Reviews, namely ventilation tubes, adenoidectomy with or without ventilation tubes, autoinflation, antibiotics, and topical and oral steroids (Cochrane ENT 2020).

Description of the intervention

Steroids have been used with the intention of reducing the inflammatory cascade that causes Eustachian tube dysfunction and middle ear effusion (Vanneste 2019). They have been administered systemically as an oral preparation and topically as a nasal spray.

How the intervention might work

Chronic inflammation in the middle ear produces inflammatory mediators, including arachidonic acid metabolites. Steroids may exert a beneficial effect on middle ear effusion by stabilising membrane phospholipid breakdown, thus preventing the formation of arachidonic acid and, in turn, inflammatory mediators (Rosenfeld 1991). In addition, steroids may have an effect on OME by shrinking peritubal lymphoid tissue, promoting secretion of Eustachian tube surfactant, and reducing the viscosity of middle ear fluid (Rosenfeld 1991). Whilst systemic steroids may have a direct effect on the middle ear, intranasal steroids are likely to exert their effect locally through reduction of nasal or adenoid tissue inflammation which may in turn improve Eustachian tube function and promote resolution of OME.

Why it is important to do this review

A Cochrane Review assessing topical and oral steroids for hearing loss associated with OME was published in 2011 (Simpson 2011). This review included 12 studies (nine for

oral steroids and three for topical intranasal steroids), none of which documented hearing loss associated with OME prior to randomisation. The authors concluded that "while oral steroids, especially when used in combination with an oral antibiotic, lead to a quicker resolution of OME in the short term, there is no evidence of a longer-term benefit and no evidence that they relieve symptoms of hearing loss". The authors also found no evidence of short- or long-term benefit from the use of topical intranasal steroids either alone or in combination with an antibiotic.

Since the Cochrane Review was published (Simpson 2011), the findings from a number of randomised controlled trials (RCTs) have been published including those from the OSTRICH study (Francis 2018), a RCT of the effects of a short course of oral steroids for hearing loss in 389 children with persistent OME, and from a second RCT that evaluated the effects of oral and intranasal steroids in 290 children with OME (Hussein 2017).

A prioritisation exercise undertaken in 2020 identified a review of topical and oral steroids as a top priority (Cochrane ENT 2020). It is therefore timely to update the evidence.

Objectives

To assess the effects (benefits and harms) of topical and oral steroids for otitis media with effusion (OME) in children.

Methods

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) and quasi-randomised trials (where trials were designed as RCTs, but the sequence generation for allocation of treatment used methods such as alternative allocation, birth dates and alphabetical order). We included studies that randomised by participant or by cluster. For cross-over studies, we included data from the first phase of the study only (prior to cross-over).

Types of participants

Children aged 6 months to 12 years with unilateral or bilateral OME. If a study included children aged younger than 6 months or older than 12 years, we included the study if the majority of children fit our inclusion criteria or if the trialists presented outcome data by age group. We included all children regardless of any comorbidity such as Down syndrome or cleft palate.

Clinical diagnosis of OME was confirmed by oto(micro)scopy or tympanometry, or both.

Types of interventions

Intervention

Topical (intranasal) and oral steroids.

Comparator

The comparators are placebo or no treatment.

We are interested in the following comparisons:

- oral steroids versus placebo;
- oral steroids versus no oral treatment.
- topical (intranasal) steroids versus placebo;
- topical (intranasal) steroids versus no topical treatment;

If study participants also received other treatments - for example antibiotics, mucolytics or decongestants - we included these studies if both arms received identical treatments.

Types of outcome measures

We analysed the following outcomes in the review, but we did not use them as a basis for including or excluding studies. We assessed all outcomes at very short term (< 6 weeks), short term (≤ 3 months), medium term (> 3 months to ≤ 1 year) and long term (> 1 year).

Primary outcomes

- Hearing, measured as:
    - Proportion of children whose hearing has returned to normal, with normal hearing defined as 20 dB HL or less (assessed using age-appropriate tests).
    - Hearing threshold.

We anticipated that study data for these outcomes may be derived from a variety of assessment methods. To avoid loss of important evidence, we extracted all such data for analysis. However, we gave consideration to the appropriateness of pooling different types of data in meta-analysis. Our selection of primary outcomes was based principally upon clinical importance, but also permits applicability across a variety of age-appropriate assessment methods, and considers the types of outcome data that were most likely to be available. Accordingly, we regarded the proportion of participants whose hearing returned to normal as the most important measure of hearing impact. We considered medium- and long-term outcome data as the most clinically important.

- Disease-specific quality of life measured using a validated instrument, for example:
    - OM8-30 (Haggard 2003);
    - Otitis Media-6 (Rosenfeld 1997).
- Adverse events - systemic corticosteroid side effects.

Secondary outcomes

- Presence/persistence of OME.
- Adverse events - local nasal side effects.
- Receptive language skills, measured using a validated scale, for example:
    - Peabody Picture Vocabulary Test - Revised (Dunn 2007);
    - relevant domains of the Reynell Developmental Language Scales (Reynell 1985);
    - relevant domains of the Preschool Language Scale (PLS) (Zimmerman 1992);
    - relevant domains of the Sequenced Inventory of Communication (SCID) (Hedrick 1984).
- Speech development, or expressive language skills, measured using a validated scale, for example:
    - Schlichting test (Schlichting 2010);
    - Lexi list (Schlichting 2007);
    - relevant domains of the Reynell Developmental Language Scales (Reynell 1985);
    - relevant domains of the PLS (Zimmerman 1992);
    - relevant domains of the SCID (Hedrick 1984).
- Cognitive development, measured using a validated scale, for example:
    - Griffiths Mental Development Scales (Griffiths 1996);
    - McCarthy General Cognitive Index (McCarthy 1972);

    - Bayley Scales of Infant and Toddler Development (Bayley 2006).
- Psychosocial outcomes, measured using a validated scale, for example:
    - the Social Skills Scale of the Social Skills Rating System (Gresham 1990);
    - Child Behaviour Checklist (Achenbach 2011);
    - Strengths and Difficulties Questionnaire (Goodman 1997);
    - Pediatric Symptom Checklist (Jellinek 1988).
- Listening skills, for example listening to stories and instructions effectively. Given that there are few validated scales to assess listening skills in children with OME, we will include any methods used by trialists.
- Generic health-related quality of life assessed using a validated instrument, for example:
    - EQ-5D (Rabin 2001);
    - TNO AZL Children's QoL (TACQOL) (Verrips 1998);
    - TNO AZL Pre-school children QoL (TAPQOL) (Fekkes 2000);
    - TNO AZL Infant Quality of Life (TAIQOL) (TNO 1997);
    - Infant Toddler Quality of Life Questionnaire (ITQOL) (Landgraf 1994);
    - Child Heath Questionnaire (CHQ) (Landgraf 1996).
- Parental stress, measured using a validated scale, for example:
    - Parenting Stress Index (Abidin 1995).
- Vestibular function:
    - balance;
    - co-ordination.
- Number of doctor-diagnosed acute otitis media episodes within a specified time frame.

These outcomes were identified as the most important in two studies that aimed to develop a core outcome set for children with OME (Bruce 2015; Liu 2019). As this review forms part of a suite of reviews of interventions for OME, not all outcomes are relevant for all reviews.

Search methods for identification of studies

The Cochrane ENT Information Specialist conducted systematic searches for randomised controlled trials and controlled clinical trials. There were no language, publication year or publication status restrictions. We contacted original authors for clarification and further data if trial reports were unclear and we arranged translations of papers where necessary. The date of the search was 20 January 2023.

Electronic searches

The Information Specialist searched:

- the Cochrane ENT Register (searched via the Cochrane Register of Studies to 20 January 2023);
- the Cochrane Central Register of Controlled Trials (CENTRAL) (searched via the Cochrane Register of Studies to 20 January 2023);
- Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) (1946 to 20 January 2023);
- Ovid EMBASE (1974 to 23 January 2023);
- Web of Science, Web of Science (1945 to 20 January 2023);

- ClinicalTrials.gov, www.clinicaltrials.gov:
    - searched via the Cochrane Register of Studies to 20 January 2023;
    - searched via www.clinicaltrials.gov to 20 January 2023;
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP), https://apps.who.int/trialsearch/:
    - searched via the Cochrane Register of Studies to 20 January 2023;
    - searched via https://apps.who.int/trialsearch/ to 20 January 2023.

The Information Specialist modelled subject strategies for databases on the search strategy designed for CENTRAL. The search strategies were designed to identify all relevant studies for a suite of reviews on various interventions for otitis media with effusion. Where appropriate, they were combined with subject strategy adaptations of the highly sensitive search strategy designed by Cochrane for identifying randomised controlled trials and controlled clinical trials (as described in the Technical Supplement to Chapter 4 of the *Cochrane Handbook for Systematic Reviews of Interventions* version 6.1) (Lefebvre 2020). Search strategies for major databases including CENTRAL are provided in Appendix 1.

Searching other resources

We scanned the reference lists of identified publications for additional trials and contacted trial authors where necessary. The Information Specialist also ran non-systematic searches of Google Scholar to retrieve grey literature and other sources of potential trials.

We did not perform a separate search for adverse effects. We considered adverse effects described in included studies only.

Data collection and analysis

Selection of studies

The Cochrane ENT Information Specialist used Cochrane's Screen4Me workflow to help assess the search results. Screen4Me comprises three components:

1. Known assessments – a service that matches records in the search results to records that have already been screened in Cochrane Crowd and been labelled as 'a RCT' or as 'not a RCT'.
2. The machine learning classifier (RCT model) (Wallace 2017), available in the Cochrane Register of Studies (CRS-Web), which assigns a probability of being a true RCT (from 0 to 100) to each citation. For citations that are assigned a probability score below the cut-point at a recall of 99% we will assume these to be non-RCTs. For those that score on or above the cut-point we will either manually dual screen these results or send them to Cochrane Crowd for screening.
3. Cochrane Crowd is Cochrane's citizen science platform where the Crowd help to identify and describe health evidence. For more information about Screen4Me and the evaluations that have been done, please go to the Screen4Me website on the Cochrane Information Specialist's portal and see Marshall 2018, McDonald 2017, Noel-Storr 2018 and Thomas 2017.

At least two review authors independently screened titles and abstracts retrieved by the search to identify potentially relevant studies. At least two review authors then independently evaluated the full text of each potentially relevant study to determine whether it met the inclusion/exclusion criteria for this review. Any differences were resolved by discussion and consensus, with the involvement of a third author where necessary.

Screening eligible studies for trustworthiness

Two review authors appraised all studies meeting our inclusion criteria for trustworthiness using a screening tool developed by Cochrane Pregnancy and Childbirth. This tool includes specified criteria to identify studies that are considered sufficiently trustworthy to be included in the review (see Figure 1 and Appendix 2). For any studies that were assessed as being potentially 'high risk', we attempted to contact the study authors to obtain further information or address any concerns. In the protocol for this review, we stated that if we were unable to contact the authors, or there was persisting uncertainty about the study, then it would not be included in the review, and that we would perform a sensitivity analysis to assess the effect on our findings of including/excluding studies.

However, we only identified six studies without any concerns regarding trustworthiness (Berman 1990; Cengel 2006; Macknin 1985; Mandel 2002; OSTRICH; Williamson 2009). We did identify a further five studies where we were unable to fully assess the baseline characteristics of participants (Acharya 2020; Choung 2008; Hemlin 1997; Lambert 1986; Schwartz 1980) or the numbers randomised to each group (Niederman 1984; Podoshin 1990), but otherwise had no concerns over trustworthiness.

The remaining studies all had a least one concern with trustworthiness when using the tool. This included:

- Limited baseline characteristics, so that we were unable to assess the groups for similarity (and an additional concern - see below) (Ahmed 2022; Hussein 2017; Karlidag 2002; Khanam 2022; Puhakka 1985; Saffar 2001).
- Concerns over baseline data (Barati 2011, where there was a numeric difference of two between groups for all characteristics).
- No trial registration, for studies published since 2010 (Ahmed 2022; Barati 2011; Beigh 2013; Bhargava 2014; Hussein 2017; Khanam 2022; Scadding 2014) or retrospective registration (Rahmati 2017).
- Full follow-up, without adequate explanation (Bhargava 2014; Karlidag 2002; Puhakka 1985; Rahmati 2017; Saffar 2001; Stuart 1995).
- Equal numbers allocated to each group without mention of blocked randomisation (Ahmed 2022; Barati 2011; Beigh 2013; Hussein 2017; Khanam 2022; Lildholdt 1982).

We were unsure whether this high level of studies with concerns reflected a genuine problem with the data from these studies, or whether the assessment tool was perhaps too sensitive. We note that this tool, and others used for the same purpose, has not yet been validated.

Consequently we decided to include all of the studies in the main analyses of this review, but we did investigate the effect of excluding studies with concerns over trustworthiness on the overall results (see Sensitivity analysis).

Data extraction and management

Two review authors independently extracted outcome data from each study using a standardised data collection form. Where a study had more than one publication, we retrieved all publications to ensure complete extraction of data. Any discrepancies in the data extracted by the two authors were checked against the original reports, and differences were resolved through discussion and consensus, with recourse to a third author where necessary. If required, we contacted the study authors for clarification. We included key characteristics of the studies, such as the study design, setting, sample size, population and the methods for defining or collecting outcome data in the studies.

We extracted data on study findings according to treatment assignment, irrespective of whether study participants complied with treatment or received the treatment to which they were randomised.

In addition to extracting pre-specified information about study characteristics and aspects of methodology relevant to risk of bias, we extracted the following summary statistics for each trial and outcome:

- For continuous data: the mean values, standard deviation and number of patients for each treatment group at the different time points for outcome measurement. Where endpoint data were not available, we extracted the values for change-from-baseline data instead. If values for the individual treatment groups were not reported, where possible we extracted summary statistics (e.g. mean difference) from the studies.
- For binary data: we extracted information on the number of participants experiencing an event, and the number of participants assessed at that time point. If values for the individual treatment groups were not reported, where possible we extracted summary statistics (e.g. risk ratio) from the studies.
- For ordinal scale data: we did not identify data analysed using ordinal scales for this review.

We pre-specified time points of interest for the outcomes in this review. Where studies reported data at multiple time points, we took the longest available follow-up point within each of the specific time frames.

Assessment of risk of bias in included studies

Two authors undertook assessment of the risk of bias of the included studies independently, with the following taken into consideration, as guided by the *Cochrane Handbook for Systematic Reviews of Interventions* (Handbook 2011):

- sequence generation;
- allocation concealment;
- blinding;
- incomplete outcome data;
- selective outcome reporting; and
- other sources of bias.

We used the Cochrane risk of bias tool in RevMan 5.3 (RevMan 2014), which involves describing each of these domains as reported in the study and then assigning a judgement about the adequacy of each entry: 'low', 'high' or 'unclear' risk of bias.

Measures of treatment effect

We summarised dichotomous data, such as presence of OME, as risk ratios (RR) and 95% confidence intervals (CI) and we continuous data as a mean difference (MD) and 95% CI. For the outcomes presented in the summary of findings tables, we have provided both the relative and absolute measures of effect.

Unit of analysis issues

For this review we anticipated that the unit of analysis would be the child. However, some studies reported findings by ear and therefore we have used both the child and ear as the unit of analysis.

All studies randomised participants to antibiotics or no treatment/placebo at the level of the child, as this is an intervention which affects both ears. Some studies in this review included children with bilateral OME, either exclusively (Ahmed 2022; Bhargava 2014; Hussein 2017; Khanam 2022; OSTRICH), or as a proportion of included participants (Cengel 2006; Choung 2008; Hemlin 1997; Karlidag 2002; Lildholdt 1982; Mandel 2002; Stuart 1995). This gave rise to a number of issues regarding the unit of analysis, as some studies reported outcomes (particularly the persistence of OME) for each ear.

We considered that outcomes for ears within the same individual were likely to be correlated, for example if a child had resolution of OME in one ear they may be more likely to experience resolution in the contralateral ear. There is not complete independence between ears of the same individual. Standard meta-analysis techniques

assume that all data are independent. Therefore inclusion of the raw data (for the number of ears) is likely to overestimate the precision of any effect and result in a excessively narrow confidence interval.

To account for this correlation, we used suggested methods in the *Cochrane Handbook for Systematic Reviews of Interventions* (Handbook 2011), which are more commonly employed in the analysis of cluster-randomised trials. We treated individuals who contributed two ears to the analysis (all of those with bilateral disease) as a 'cluster' of two data points. We then attempted to account for the correlation in these clusters, by assuming a certain correlation between ears of the same individual. We could not identify a figure for this correlation in the published literature, so we used an estimated correlation of 0.50 in the main analysis, but conducted sensitivity analyses using correlations of 0 and 1, to test the limits of this assumption. We then reduced the effective size of the trials by the 'design effect', which accounts for correlation between ears and the average cluster size (which would be 2 for trials where all children had bilateral disease, and less than 2 if trials included a mixture of children with bilateral and unilateral disease).

Dealing with missing data

We attempted to contact study authors by email where data on an outcome of interest to the review were not reported but the methods described in the paper suggest that the outcome was assessed. We did the same if not all data required for meta-analysis were reported.

Assessment of heterogeneity

We assessed clinical heterogeneity by examining the included studies for potential differences in the types of participants recruited, interventions or controls used, and the outcomes measured. We assessed statistical heterogeneity by considering both the I^2 statistic, which calculates the percentage of variability that is due to heterogeneity rather than chance, with values over 50% suggesting substantial heterogeneity, and the P value from the Chi^2 test (Higgins 2021).

Assessment of reporting biases

We assessed reporting bias as within-study outcome reporting bias and between-study publication bias.

Outcome reporting bias (within-study reporting bias)

We assessed within-study reporting bias by comparing the outcomes reported in the published report against the study protocol or trial registry, when this could be obtained. If the protocol or trial registry entry was not available, we compared the outcomes reported to those listed in the methods section of the published report. If results were mentioned but not reported in a way that allowed analysis (e.g. the report only mentions whether the results were statistically significant or not), we sought further information from the study authors. If no further information could be found, we noted this as being a 'high' risk of bias. If there was insufficient information to judge the risk of bias we noted this as an 'unclear' risk of bias (Handbook 2011).

Publication bias (between-study reporting bias)

We planned to produce a funnel plot to explore possible publication biases if we were able to pool 10 or more studies in a single analysis. However, we did not include sufficient studies in any meta-analysis to warrant this.

Data synthesis

Where two or more studies reported the same outcome we performed a meta-analysis using Review Manager 5 (RevMan 2014). We report pooled effect measures for dichotomous outcomes as a risk ratio (RR) using the Mantel-Haenszel methods. For continuous outcomes measured we report a mean difference (MD). We used a random-effects model.

Where it was not possible to pool the findings from studies in a meta-analysis, we present the results of each study and provide a narrative synthesis of findings.

Subgroup analysis and investigation of heterogeneity

We planned the following subgroup analyses if sufficient data were available in trial reports:

- children with mild hearing loss versus moderate or worse;
- children with allergy versus those without (using the trialists own definition);
- children aged up to four years versus children aged four years and over;
- children with previous ventilation tubes versus those without ventilation tubes;
- children with cleft palate versus children without;
- children with Down syndrome versus children without.

However, we did not find any data suitable for conducting most of these subgroup analyses. No studies provided subgroup data for children with different features (for example, for those with mild hearing loss, compared to those with moderate or worse hearing loss). Many of the studies did not provide sufficient background information (for example, on hearing level) for us to conduct subgroup analysis at the level of the individual study. Where data were provided, studies often recruited a mixed population that encompassed all subgroups (for example, most studies recruited children aged 2 to 10 years, not specifically children aged ≤ 6 years or older than 6 years).

Sensitivity analysis

We planned to carry out the following sensitivity analyses to assess whether our findings were robust to decisions made regarding analyses and inclusions of studies:

- impact of model chosen: we compared the results using a random-effects versus a fixed-effect model;
- inclusion of studies at high risk of bias: we planned to compare the results including all studies versus excluding studies at overall high risk of bias, that is four or more of the seven domains of bias are rated as high risk (see Assessment of risk of bias in included studies).
- inclusion of studies considered at high probability of trustworthiness, as assessed by the Trustworthiness Screening Tool (Figure 1).

The results of these analyses are presented in Table 2.

Summary of findings and assessment of the certainty of the evidence

Two independent authors used the GRADE approach to rate the overall certainty of evidence using GRADEpro GDT (https://gradepro.org/). The certainty of evidence reflects the extent to which we are confident that an estimate of effect is correct, and we applied this in the interpretation of results. There are four possible ratings: high, moderate, low and very low. A rating of high certainty of evidence implies that we are confident in our estimate of effect and that further research is very unlikely to change our confidence in the estimate of effect. A rating of very low certainty implies that any estimate of effect obtained is very uncertain.

The GRADE approach rates evidence from RCTs that do not have serious limitations as high certainty. However, several factors can lead to the downgrading of the evidence to moderate, low or very low. The degree of downgrading is determined by the seriousness of these factors:

- study limitations (risk of bias);
- inconsistency;
- indirectness of evidence;

- imprecision; and
- publication bias.

When assessing imprecision, we used a minimally important difference of a risk ratio (or odds ratio) of 0.8 or 1.25 for dichotomous outcomes. For most continuous data we considered a minimally important difference to be half of the standard deviation for the control/comparator group. The exception to this was hearing thresholds, where a difference of 10 dB HL was used as the minimally important difference.

We include summary of findings tables, constructed according to the recommendations described in Chapter 14 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2021), for the following comparisons:

- oral steroids versus placebo;
- oral steroids versus no oral treatment;
- topical (intranasal) steroids versus placebo;
- topical (intranasal) steroids versus no topical treatment.

We included the following four outcomes in the summary of findings tables:

- hearing;
- disease-specific quality of life;
- presence/persistence of OME;
- adverse events - systemic corticosteroid side effects.

Results

Description of studies

Results of the search

The searches (January 2023 and September 2021) retrieved a total of 7441 records. This reduced to 4157 after the removal of duplicates. The Cochrane ENT Information Specialist sent all 4157 records to the Screen4Me workflow. The Screen4Me workflow identified 68 records as having previously been assessed: 50 had been rejected as not RCTs and 34 had been assessed as possible RCTs. The RCT classifier rejected an additional 1514 records as not RCTs (with 99% sensitivity). The Cochrane Crowd assessed the remaining 2443 references, rejecting 1313 as not RCTs and identifying 1130 as possible RCTs. Following this process, the Screen4Me workflow had rejected 2877 records and identified 1280 possible RCTs for title and abstract screening.

	Possible RCTs	Rejected
Known assessments	34	50
RCT classifier	2559	1514
Cochrane Crowd	1130	1313
Total	1280	2877

We identified 76 additional duplicates. We screened the titles and abstracts of the remaining 1204 records. We discarded 886 records and assessed 318 full-text records. We subsequently discarded an additional 236 records and identified an additional five duplicates.

We excluded 34 records (linked to 30 studies) with reasons recorded in the review (see Excluded studies).

We included 26 studies (40 records) where results were available (Acharya 2020; Ahmed 2022; Barati 2011; Beigh 2013; Berman 1990; Bhargava 2014; Cengel 2006; Choung 2008; Hemlin 1997; Hussein 2017; Karlidag 2002; Khanam 2022; Lambert 1986; Lildholdt 1982; Macknin 1985; Mandel 2002; Niederman 1984; OSTRICH; Podoshin

1990; Puhakka 1985; Rahmati 2017; Saffar 2001; Scadding 2014; Schwartz 1980; Stuart 1995; Williamson 2009).

We identified one ongoing study. See Characteristics of Ongoing studies for further details.

We identified two studies that remain in awaiting assessment because we did not have enough information to determine eligibility (Koay 1998; Tawfik 2002).

A flow chart of study retrieval and selection is provided in Figure 2.

Included studies

Details of the studies included in this review are provided in Characteristics of included studies and summarised in Table 3.

Study design

Almost all the studies included in this review were parallel-group RCTs. We identified two cross-over RCTs (Berman 1990; Schwartz 1980), however we only utilised data from the first phase of these studies, prior to cross-over (see Types of studies).

Most studies included two groups of interest (either nasal steroids compared to placebo or no treatment, or oral steroids compared to placebo or no treatment). One study included a comparison of both oral steroid and intranasal steroid with watchful waiting, therefore was included in two comparisons of interest (Acharya 2020). A number of other studies included additional groups that were not applicable to this review, such as antibiotics, montelukast and myringotomy (Hemlin 1997; Hussein 2017; Karlidag 2002; Khanam 2022; Podoshin 1990; Puhakka 1985; Rahmati 2017)

Location

Studies were conducted all across the world. We identified six studies conducted in the USA (Berman 1990; Lambert 1986; Macknin 1985; Mandel 2002; Niederman 1984; Schwartz 1980), and three each from the UK (OSTRICH; Scadding 2014; Williamson 2009) and Iran (Barati 2011; Rahmati 2017; Saffar 2001). Two studies were from India (Beigh 2013; Bhargava 2014), and a further two from Turkey (Cengel 2006; Karlidag 2002). The remaining studies were conducted in Australia (Stuart 1995), Bangladesh (Khanam 2022), Denmark (Lildholdt 1982), Egypt (Ahmed 2022), Finland (Puhakka 1985), Israel (Podoshin 1990), Nepal (Acharya 2020), Saudi Arabia (Hussein 2017), South Korea (Choung 2008) and Sweden (Hemlin 1997).

Number of participants

The number of participants enrolled in each study varied considerably:

- 25 to 50 participants: Khanam 2022; Macknin 1985; Niederman 1984; Saffar 2001; Schwartz 1980 and Stuart 1995.
- 51 to 100 participants: Barati 2011; Beigh 2013; Berman 1990; Bhargava 2014; Cengel 2006; Choung 2008; Lambert 1986; Lildholdt 1982; Puhakka 1985 and Rahmati 2017.
- 101 to 150 participants: Acharya 2020; Hemlin 1997; Mandel 2002; Podoshin 1990.
- 151 to 250 participants: Ahmed 2022; Hussein 2017; Scadding 2014; Williamson 2009.

The largest study was the OSTRICH study, which recruited 380 participants.

Duration of follow-up

Again, the duration of follow-up and timing of outcome assessment was very varied. The shortest studies included between seven days and five weeks of follow-up (Acharya 2020; Ahmed 2022; Barati 2011; Berman 1990; Hemlin 1997; Lambert 1986; Mandel 2002; Niederman 1984; Rahmati 2017; Schwartz 1980). A number of studies conducted follow-up at between six weeks and three months (Beigh 2013; Cengel 2006; Karlidag

2002; Khanam 2022; Lildholdt 1982; Macknin 1985; Podoshin 1990; Puhakka 1985; Stuart 1995).

Only a small number of studies carried out follow-up for longer than three months. This included six-month follow-up for Bhargava 2014, Choung 2008 and Saffar 2001, and nine-month follow-up for Hussein 2017 and Williamson 2009. The OSTRICH study assessed final follow-up at 12 months. One study conducted follow-up at two years, but no outcome data were reported on the outcomes of interest to this review (Scadding 2014).

Participants

All studies included a majority of participants with our target age range of between 6 months and 12 years old. A few studies included some children who were slightly older or younger than our target population:

- Berman 1990 (from 5 months of age to 12 years, mean age around 3 years).
- Cengel 2006 (from 3 to 15 years, mean age of 6 to 7 years).
- Lambert 1986 (from 2 to 15 years, mean 5 to 6 years).
- Lildholdt 1982 (from 4 to 14 years, mean 6.5 years).
- Niederman 1984 (from 2 to 14 years).

The duration of OME was not stated for the majority of studies, although some studies did require a specific duration of symptoms prior to enrolment - predominantly either three months (Ahmed 2022; Bhargava 2014; Cengel 2006; Hemlin 1997; Khanam 2022; OSTRICH; Scadding 2014) or six to eight weeks (Berman 1990; Lambert 1986; Niederman 1984; Podoshin 1990).

Most studies appeared to recruit children with either bilateral or unilateral disease. A few specifically enrolled children with bilateral disease (Ahmed 2022; Bhargava 2014; Hussein 2017; Khanam 2022; OSTRICH; Williamson 2009).

Little information was provided regarding previous treatment, although four studies specifically recruited children who had no response to prior treatment, including at least two courses of antibiotics (Berman 1990; Cengel 2006; Saffar 2001) or other 'medical treatment' (not described further, Bhargava 2014).

Intervention and comparator

Oral steroid versus placebo

Eleven studies assessed this comparison (Berman 1990; Hemlin 1997; Lambert 1986; Macknin 1985; Mandel 2002; Niederman 1984; OSTRICH; Podoshin 1990; Puhakka 1985; Saffar 2001; Schwartz 1980). The majority used treatment with oral prednisolone at a dose of between 0.5 mg/kg and 1.5 mg/kg per day, for between 6 and 14 days (Berman 1990; Lambert 1986; Mandel 2002; OSTRICH; Podoshin 1990; Puhakka 1985; Saffar 2001; Schwartz 1980). Two studies used dexamethasone instead of prednisolone for 13 days of treatment (Macknin 1985; Niederman 1984). Many studies used a regime that included a tapering dose towards the end of the treatment period. One study used a single dose of 6 mg oral betamethasone (Hemlin 1997).

Six studies included background treatment of antibiotics for all participants in the study - those receiving steroids and those receiving placebo (Berman 1990; Hemlin 1997; Mandel 2002; Podoshin 1990; Puhakka 1985; Schwartz 1980). The overall effect estimated in these studies is still relevant for a comparison of steroids versus placebo. However, it should be borne in mind that, if antibiotics were particularly effective at treating OME, any additional effect of steroids may not be easily detected.

Oral steroid versus no treatment

Three studies provided data for this comparison (Acharya 2020; Choung 2008; Hussein 2017). All used treatment with oral prednisolone, for between 7 and 14 days. One study used a tapering dose regime (Acharya 2020).

Again, one study in this comparison also provided all participants with a course of antibiotics, which may modify the effect estimates seen (Choung 2008).

Nasal steroid versus placebo

Six studies assessed this comparison (Bhargava 2014; Khanam 2022; Lildholdt 1982; Scadding 2014; Stuart 1995; Williamson 2009). They used different preparations of intranasal steroids, including beclomethasone (Lildholdt 1982; Stuart 1995), fluticasone (Scadding 2014) and mometasone (Bhargava 2014; Khanam 2022; Williamson 2009). The duration of treatment also varied from a minimum of two weeks (Scadding 2014) up to three months (Williamson 2009). The participants in these studies did not receive additional, concomitant medication as part of the study protocol.

Nasal steroid versus no treatment

Seven studies assessed this comparison, including one three-armed trial, which also provided data for the comparison of oral steroids and no treatment (Acharya 2020). Most studies used mometasone (Acharya 2020; Ahmed 2022; Beigh 2013; Cengel 2006; Rahmati 2017); the remaining two studies assessed beclomethasone (Barati 2011; Karlidag 2002). The duration of treatment was one month for most studies (Acharya 2020; Ahmed 2022; Barati 2011; Rahmati 2017), six weeks for two studies (Beigh 2013; Cengel 2006), and eight weeks for the final study (Karlidag 2002).

Three studies also provided all participants with concomitant treatment of antibiotics for between one and eight weeks (Ahmed 2022; Barati 2011; Karlidag 2002).

Outcomes

Hearing

Hearing was measured rather inconsistently across the studies, which often precluded meta-analysis. Very few studies reported our preferred outcome measure of the proportion of children with a return to normal hearing. This was only described by the OSTRICH study (the number of children with acceptable hearing) and Podoshin 1990, where it was reported as the proportion of children with complete closure of the air-bone gap. A number of studies did report on final hearing thresholds using either pure tone audiometry (Khanam 2022; Lildholdt 1982; Mandel 2002; OSTRICH), or the air-bone gap (Ahmed 2022).

We were unable to include data from several studies, due to insufficient information on the variance of the estimates (Beigh 2013), no description of the number of participants in whom the outcome was measured (Berman 1990) or both (Bhargava 2014). One study only provided a narrative description of the results (Stuart 1995).

Disease-specific health-related quality of life

A single study measured this outcome. The OSTRICH study used the OM8-30 questionnaire to assess quality of life (Timmerman 2008), as it relates to otitis media with effusion. Limited information regarding the scoring of this questionnaire is available. It appears that a type of standardised score is used, but the full range of potential scores and the minimally important difference is unclear. The authors indicate that lower (more negative) scores represent worse quality of life.

Serious adverse events: systemic steroid side effects

Adverse effects were poorly and inconsistently reported across the studies. Many did not report on adverse effects at all, meaning that we were unsure whether these had been assessed but not reported, or whether no adverse effects were identified. Furthermore, the reporting of adverse effects meant that it was difficult to determine whether side effects were considered to be related to steroid use, or not. We therefore took an inclusive approach, and have included all adverse effects reported in the studies. These are presented in Table 1 and Table 4. However, the variety of symptoms reported meant that no meta-analysis was possible for this outcome.

Persistence of OME

Assessment of the persistence of OME also varied across the studies, which may lead to some clinical heterogeneity in the effect sizes seen. We included data according to the authors' definition of 'persistent OME'. However, it should be noted that this was assessed as a type B tympanogram for some studies (including Acharya 2020; Berman 1990; Cengel 2006; Hussein 2017; Saffar 2001), and a "non-type A" (i.e. type B or C) tympanogram for other studies (such as Ahmed 2022; Karlidag 2002; Khanam 2022; OSTRICH). Some studies included only those children with type B or C2 tympanograms as 'persistent OME' (Barati 2011; Williamson 2009).

In addition, there was variation in how persistent OME was assessed for children with bilateral disease: the majority of participants for most studies. Some studies assessed each ear separately (see Unit of analysis issues), whilst others assessed persistence at the level of the child. For children in whom OME resolved in one ear (i.e. the disease changed from bilateral to unilateral), some studies classed these children as having persistent disease (Hussein 2017), and others classed them as having resolved disease (OSTRICH; Williamson 2009). A full description of methods used to classify children with bilateral disease was not available from many studies.

Generic health-related quality of life

Only two studies assessed this outcome. Bhargava 2014 used the Glasgow Children's Benefit Inventory (Kubba 2004). This is a 24-item questionnaire that assesses the change in quality of life following an intervention. Scores range from -100 (maximum harm) to +100 (maximum benefit). The PedsQL™ (https://www.pedsql.org/) was used in the OSTRICH study. Scores for this instrument range from 0 to 100, with higher scores representing better quality of life. The minimally important difference has been proposed to be a change of 4.5 points (Varni 2003). The Health Utilities Index 3 (Feeny 2002; Horsman 2003) was also used in the OSTRICH study. This assesses health on a scale of 0 (dead) to 1 (perfect health). For their analysis, the study authors used a dichotomous scale, comparing the proportion of children with a score of perfect health between the two groups.

Episodes of acute otitis media

Few studies assessed this outcome. Lambert 1986 reported on the proportion of children in whom a specific number of episodes of otitis media was exceeded. Berman 1990, Mandel 2002 and Niederman 1984 considered the proportion of children who had an episode by two to four weeks of follow-up.

Other outcomes

None of the studies included in this review assessed developmental outcomes, including receptive and expressive language skills, cognitive development, psychosocial outcomes or listening skills. In addition, no studies considered parental stress or vestibular function.

Excluded studies

We excluded 30 studies (linked to 34 references) from this review. See Excluded studies for further details. The main reason for exclusion is listed below:

We excluded 13 studies as they were not RCTs (Al-Zaidi 2023; Crawford-Faucher 2010; El-Anwar 2015; Gibson 1996; Iino 1989; Paradise 1997; Parlea 2012; Persico 1978; Salmen 2021; Schwartz 1980a; Shubich 1996; Stenstrom 2005; Zocconi 1994)

Four studies were commentaries and did not report results of a trial (Damoiseaux 2010; Hughes 2019; Isaacs 2018; Mayor 2018).

Six studies included an irrelevant intervention, and did not assess the effect of topical or oral steroids, although some were included in other reviews in this suite (Ardehali 2008; Daly 1991; Endo 1997; Marchisio 1998; Rohail 2006; Velepic 2011).

Six studies enrolled participants who did not fit our inclusion criteria, including:

- children with recurrent acute otitis media (Ferrara 2005; Tracy 1995);
- children with an effusion immediately following an episode of acute otitis media (Giebink 1990);

- studies in which not all participants had a diagnosis of OME (Gluth 2011; Shapiro 1982);
- adult participants (Han 2009).

Finally, we excluded one study for an incorrect comparator, as co-interventions were not identical between the two groups (Yeldandi 2001).

Risk of bias in included studies

All studies had at least some concerns regarding risk of bias. See Figure 3 for a summary of the risk of bias across all included studies, and Figure 4 for detailed assessments for each study.

Allocation

Only five studies provided sufficient description of the randomisation process and methods used to conceal group allocation. We rated these at low risk of selection bias (Macknin 1985; OSTRICH; Scadding 2014; Stuart 1995; Williamson 2009). Whilst a number of other studies appeared to use adequate randomisation methods, there was not a clear description of allocation concealment and we rated this domain at unclear risk of bias (Acharya 2020; Barati 2011; Beigh 2013; Berman 1990; Bhargava 2014; Hussein 2017; Khanam 2022; Niederman 1984). Many studies provided no information regarding the randomisation process, so we rated this domain at unclear risk of bias.

Blinding

Ratings were mixed across the studies. We rated a large number of studies at high risk of performance and detection bias: as a placebo was not used, participants, study personnel and outcome assessors were aware of group allocation (Acharya 2020; Barati 2011; Beigh 2013; Bhargava 2014; Cengel 2006; Choung 2008; Karlidag 2002; Podoshin 1990; Puhakka 1985; Rahmati 2017).

However, some studies did ensure that participants and outcome assessors remained blind to treatment allocation throughout the trial and we rated these at low risk of bias (Lildholdt 1982; OSTRICH; Scadding 2014; Stuart 1995; Williamson 2009).

Incomplete outcome data

We rated this domain at lower risk of bias overall, as we judged 13 studies to have no concerns over attrition bias. However, we noted that attrition was, understandably, more of a problem in the studies with a longer duration of follow-up, including Scadding 2014 and Williamson 2009.

Selective reporting

For most studies, we were unable to identify a published protocol. Therefore, we could not assess whether the authors had adhered to their planned analysis when reporting the results. Consequently, we rated many studies at unclear risk of bias for this domain. Three studies did report according to their pre-specified analysis plan (Acharya 2020; OSTRICH; Williamson 2009). We rated three studies at high risk of bias, due to lack of reporting of pre-specified outcome measures (Rahmati 2017), or unclear and selective reporting of outcome measures, which precluded meta-analysis (Bhargava 2014; Lildholdt 1982).

Other potential sources of bias

We rated many studies at high risk of bias for this domain due to the short follow-up time, which would not allow an appropriate comparison of the two treatment strategies (steroids versus watchful waiting or placebo). We considered that a follow-up time of at least three months was required, in order to give sufficient time for the potential for natural resolution of the disease. However, this duration of follow-up was not completed for most of the studies in this review.

Effects of interventions

Oral steroid versus placebo

Eleven studies assessed this comparison (Berman 1990; Hemlin 1997; Lambert 1986; Macknin 1985; Mandel 2002; Niederman 1984; OSTRICH; Podoshin 1990; Puhakka 1985; Saffar 2001; Schwartz 1980). However, our outcomes of interest were not reported by all studies, therefore very limited meta-analysis was possible.

Hearing

Return to normal hearing

Up to six weeks

One study assessed the proportion of children in whom hearing was 'acceptable' in at least one ear after five weeks of follow-up (OSTRICH). The risk ratio (RR) for a return to normal hearing in those who received oral steroids was 1.22 (95% confidence interval (CI) 0.92 to 1.60; absolute effect 32.8% of participants in the placebo group, compared to 40% in the steroid group; number needed to treat (NNT) 14; 1 study; 363 participants; Analysis 1.1; low-certainty evidence). A similar effect size was seen when adjusting for baseline differences (Analysis 1.2).

One further study reported data at this time point, but we were unable to include the data in a meta-analysis, as the denominator for each group was unclear, and there were discrepancies in the size of the groups reported in the article. Berman 1990 assessed the proportion of children whose hearing returned to normal using speech awareness thresholds or speech reception thresholds. A significant difference was reported for children assessed with speech awareness thresholds (86% of ears with normal hearing amongst those who received steroids, compared to 42% of ears with normal hearing amongst those who received placebo), but not for those children assessed with speech reception thresholds (92% of ears for those who received steroids, compared to 89% of ears for those who received placebo). It should be noted that 33% of ears had normal hearing at baseline, and that all participants in this study also received antibiotics.

The OSTRICH study provided some data suitable for subgroup analysis for this outcome. We assessed whether the use of oral steroids had different effects in children with allergy (atopy), but the effect estimates were similar for both groups (Analysis 1.22).

Up to three months

One study assessed the proportion of children with complete resolution of the air-bone gap after two months of follow-up. The difference between the groups was trivial, although the confidence intervals were wide (RR 0.98, 95% CI 0.61 to 1.58; 1 study; 99 participants; Analysis 1.3; very low-certainty evidence).

Up to one year

Finally, the OSTRICH study also conducted follow-up at 12 months after completion of a seven-day course of steroids. The risk ratio for return to normal hearing in those who had received steroids was 1.14 (95% CI 0.97 to 1.33; 1 study; 332 participants; Analysis 1.4; moderate-certainty evidence). However, it should be noted that the proportion of children in the control group with normal hearing was also high (61.1% of children receiving placebo, compared to 69.4% of children receiving steroids).

Hearing threshold

Up to six weeks

Final hearing threshold was also reported by the OSTRICH study, but the difference between the two groups was trivial after short-term follow-up (mean difference (MD) 0.56 dB HL lower, 95% CI -2.55 to 1.43; 1 study; 364 participants; Analysis 1.5; low-certainty evidence). A similar effect was seen after adjusting for confounders (Analysis 1.6).

Again, the study by Berman 1990 also reported this outcome, but we could not include the data in a meta-analysis. The authors reported a significant difference in speech awareness thresholds at two weeks of follow-up (mean difference -5.8 dB HL better for those receiving steroids), but no significant change in speech reception thresholds (mean difference +1 dB HL worse for those receiving steroids).

OME-specific quality of life

One study assessed OME-specific quality of life, using the OM8-30 questionnaire (OSTRICH). This was completed by parents, on behalf of the child. As described above, limited details on the method for scoring this questionnaire were available and we were unable to identify a minimally important difference. It appears that the scores are reported on a standardised scale, so we have used Cohen's effect sizes to help interpret this measure.

Up to six weeks

After five weeks of follow-up, OM8-30 scores were 0.16 higher (worse) in the oral steroid group (95% CI -0.07 to 0.39; 1 study; 359 participants; Analysis 1.7; low-certainty evidence). It is unclear how clinically significant this difference is, as the authors do not report the full range for this score, nor suggest what difference in score would be regarded as clinically meaningful. If we assume that this is reported on a standardised scale, then an effect size of 0.16 would be considered a trivial difference between the two groups.

Up to one year

The same study assessed disease-specific quality of life at 12 months of follow-up. The mean difference between the groups was 0.07 points higher (worse) for those receiving steroids, but the confidence intervals were wide (-0.20 to 0.34; 1 study; 304 participants; Analysis 1.8; moderate-certainty evidence).

Persistence of OME

Eleven studies reported this outcome, at various follow-up times. However, we noted that different definitions of 'persistent effusion' were used across the studies (see Included studies above).

Up to six weeks

Persistence of OME at up to six weeks may be slightly lower in those who receive steroids. However, the evidence was very uncertain and most children in both groups still had a persistent effusion at this time point (82.3% in the placebo group, compared to 71.8% in the steroid group, RR 0.72, 95% CI 0.51 to 1.02; 7 studies; 786 participants; I^2 = 90%; Analysis 1.9; very low-certainty evidence). As anticipated, there was substantial heterogeneity in this analysis, which resolved slightly when considering the different definitions of 'persistence' used across the studies. Sensitivity analyses to account for different ways of assessing persistence made little different to the overall effect estimates (Analysis 1.10; Analysis 1.11).

The study by Mandel 2002 provided a small amount of information regarding our subgroups of interest for this outcome. We were able to analyse whether the effect size varied for children with allergy (positive skin tests) versus those without, and for children aged < 4 versus those aged ≥ 4 years (Analysis 1.23; Analysis 1.24). However, we did not find evidence for a difference between these subgroups.

Up to three months

Only three studies assessed persistence of OME at this time point. The proportion of children with persistent OME was also slightly lower for those receiving steroids, but the confidence intervals were very wide (proportion with persistent OME 68% versus 55%; RR 0.81, 95% CI 0.50 to 1.30; 3 studies; 211 participants; I^2 = 80%; Analysis 1.12; very low-certainty evidence). Again, sensitivity analyses to account for different correlation in the data between ears of the same individual, or different ways of assessing persistence, made little difference to the overall estimate (Analysis 1.13; Analysis 1.14; Analysis 1.15).

Up to one year

Two studies reported the persistence of OME at up to 12 months. The difference in results from the two studies was considerable and the evidence is therefore very uncertain. Pooling of the data resulted in a very substantial I^2 value, and the confidence intervals for the fixed-effect and random-effects model were very different. We therefore took the decision not to pool these data.

One study showed a modest benefit from oral steroids, but the rate of persistent effusion was still high in both groups at 12 months of follow-up (93.8% in the placebo group, 80.5% in the steroid group, RR 0.86, 95% CI 0.79 to 0.94; 1 study; 263 participants; Analysis 1.16).

The second study showed a very marked benefit from oral steroids, with a RR of 0.18 (95% CI 0.06 to 0.54; absolute effects show persistence in 67% of children receiving placebo, compared to 12% of children receiving steroids; 1 study; 49 participants; Analysis 1.16). Children included in this trial had not responded to two courses of oral antibiotics, therefore may represent a subpopulation of all children with OME. However, it is also unclear how 'persistence' of OME was defined.

Number of doctor-diagnosed episodes of acute otitis media

Up to six weeks

This outcome was only assessed at very short-term follow-up. The pooled result showed little difference in the proportion of children who developed acute otitis media between the two groups, although the confidence interval was very wide and the evidence was very uncertain (absolute effects 5.9% in the placebo group compared to 5.7% in the steroid group; RR 0.97, 95% CI 0.31 to 3.10; 3 studies; 207 participants; I^2 = 54%; Analysis 1.17; very low-certainty evidence).

Generic quality of life

One study used two different questionnaires to assess generic quality of life.

Up to six weeks

The Pediatric Quality of Life Inventory (PedsQL) considers physical functioning, emotional functioning, social functioning and school functioning (https://www.pedsql.org/). The raw scores are transformed to a scale of 1 to 100, with higher scores representing better quality of life. The minimally important difference has been suggested to be a change of 4.5 points. A trivial difference was seen between the groups at this time points (MD -0.9, 95% CI -3.86 to 2.06; 1 study; 358 participants; Analysis 1.18; low-certainty evidence).

The Health Utilities Index 3 (HUI3) was also used (Feeny 2002). This assesses health on a scale of 0 (dead) to 1 (perfect health). For this analysis, the study authors used a dichotomous scale, comparing the proportion of children with a score of perfect health between the two groups. The risk ratio for a perfect score in those receiving steroids compared to placebo was 1.06 (95% CI 0.70 to 1.60; absolute effects 21.3% in the control group, compared to 22.6% in the steroid group; 1 study; 319 participants; Analysis 1.20; very low-certainty evidence).

Up to one year

Results were similar at up to one year follow-up, with both questionnaires indicating a very small or trivial difference between the two groups (PedsQL MD -0.27, 95% CI -2.74 to 3.28; 1 study; 303 participants; Analysis 1.19; moderate-certainty evidence, and HUI3 RR 1.10, 95% CI 0.79 to 1.53; 1 study; 292 participants; Analysis 1.21; moderate-certainty evidence).

Adverse events

Adverse events were reported inconsistently across the studies. Systemic corticosteroid side effects was one of our primary outcomes. However, it was often unclear if reported side effects were considered to be related to corticosteroid use or not. We therefore took

an inclusive approach to adverse event reporting and extracted data on all adverse effects reported by the studies. These are reported in Table 1.

Oral steroid versus no treatment

Three studies provided data for this comparison (Acharya 2020; Choung 2008; Hussein 2017). However, the only outcome assessed was the persistence of OME.

Persistence of OME

Up to six weeks

A single study assessed the persistence of OME after four weeks of treatment. The risk ratio for persistence in those who had received oral steroids was 0.48 (95% CI 0.32 to 0.73; 82.5% of children receiving no treatment, compared to 39.6% of children receiving steroids; 1 study; 80 participants; Analysis 2.1; very low-certainty evidence).

Up to three months

One further study assessed this outcome after three months of follow-up and found a trivial difference between the two groups (persistence in 86% of children receiving no treatment, compared to 85% of those receiving steroids; RR 0.99, 95% CI 0.88 to 1.11; 1 study; 192 participants; Analysis 2.2; low-certainty evidence).

Up to one year

Two studies conducted slightly longer-term follow-up, and assessed this outcome at between three and nine months. Overall the risk ratio for persistence was 1.02 (95% CI 0.89 to 1.17; 73% of children receiving no treatment, compared to 74% of those receiving steroids; 2 studies; 258 participants; Analysis 2.3; low-certainty evidence).

Adverse events

Both Acharya 2020 and Hussein 2017 stated that no adverse effects of oral steroids were reported in study participants. Choung 2008 did not report on adverse events.

Nasal steroids versus placebo

Six studies assessed this comparison (Bhargava 2014; Khanam 2022; Lildholdt 1982; Scadding 2014; Stuart 1995; Williamson 2009). However, not all studies reported on our outcomes of interest.

Hearing

No studies used our preferred primary outcome of proportion of children with normal hearing. The only available data considered mean final hearing threshold.

Hearing threshold

Up to three months

One study reported on the change in hearing threshold after two months follow-up. Very little difference was seen between the two groups, with a mean difference of -0.3 dB HL for those who received steroids, but the evidence was very uncertain (95% CI -6.05 to 5.45; 1 study; 78 participants; Analysis 3.1; very low-certainty evidence). Sensitivity analyses varying the correlation between ears of the same individual made little difference to the estimate (Analysis 3.2; Analysis 3.3).

A second study assessed the final hearing threshold after three months of follow-up and found a benefit to steroids but, again, the evidence was very uncertain (MD -14.95, 95% CI -17.32 to -12.58; 1 study; 40 participants; Analysis 3.4; very low-certainty evidence).

The study Stuart 1995 provided no useable data for meta-analysis. However, the authors stated "there was a greater improvement in hearing levels in the treatment group compared to the controls. This difference was most marked at the end of the study [12 weeks]".

< 12 months

Bhargava 2014 assessed the pure tone average hearing threshold after 24 weeks of follow-up. However, no variance was reported and the number of participants in each group was not stated. The authors' own analysis indicated that there was a significant difference between the two groups, with a mean hearing threshold of 5.2 dB HL in those receiving steroids and 11.6 dB HL for those receiving placebo (1 study; 62 participants; very low-certainty evidence).

Disease-specific health related quality of life

A single study assessed this outcome, using the sum of seven domains from the OM8-30 questionnaire (behaviour, speech and language, school prospects, parental quality of life, global health, respiratory symptoms and ear problems). The full range of scores for this questionnaire was not available, nor was the minimally important difference. Lower scores are stated to represent better quality of life. We assume that results are presented with a form of standardised score and can be interpreted using Cohen's effect sizes.

Up to three months

The mean difference in score was -0.07 (95% CI -0.49 to 0.35; 1 study; 82 participants; low-certainty evidence). We considered that this was likely to represent a trivial difference between the two groups.

Up to 12 months

The mean difference in score was 0.05 (95% CI -0.36 to 0.46; 1 study; 82 participants; low-certainty evidence). Again, this was thought likely to represent a trivial difference between the two groups.

Persistence of OME

Up to six weeks

One study assessed this outcome after one month and found very little difference between the groups (82% children in the no treatment group with persistence, compared to 80% of children in the nasal steroids group; RR 0.98, 95% CI 0.80 to 1.20; 1 study; 89 participants; Analysis 3.7; very low-certainty evidence). Accounting for different levels of correlation between ears of the same individual made little difference to the overall estimates (Analysis 3.8; Analysis 3.9).

Up to three months

Three studies reported at this time point. Overall, nasal steroids may reduce the chance of persistent OME after up to three months of follow-up, but the evidence was very uncertain. Of children receiving placebo, 58% had persistent OME, compared to 46% of those receiving intranasal steroids (RR 0.80, 95% CI 0.51 to 1.26; 3 studies; 286 participants; Analysis 3.10; low-certainty evidence).

Up to one year

Two studies assessed the persistence of OME after longer-term follow-up. However, the results were very different, therefore we took the decision not to pool the data.

- Bhargava 2014 assessed the persistence of OME after six months of follow-up. Persistence was reduced for those who had received nasal mometasone furoate for 24 weeks (50% of those receiving placebo, compared to 7% of those receiving steroids; RR 0.13, 95% CI 0.03 to 0.53; 1 study; 62 participants; Analysis 3.13). All participants in this study had adenoid hypertrophy and had failed to respond to previous treatments, which may account for some clinical heterogeneity between the two studies.
- Williamson 2009 assessed persistence at nine months of follow-up, for children who had received three months of mometasone furoate. Of children in the placebo group, 35% had persistent effusion, compared to 44% of those who received steroids (RR 1.28, 95% CI 0.85 to 1.93; 1 study; 144 participants; Analysis 3.13).

Overall, we considered the evidence for this outcome to be very uncertain, as we were unable to pool the data, and the studies indicated opposing directions of effect.

Adverse effects

As described above, adverse effects were inconsistently reported across the different studies. It was not possible to discern whether authors considered certain reported symptoms to be related to the treatment. Therefore, we took an inclusive approach to data collection for adverse events and show all reported adverse effects in Table 4.

Nasal steroids versus no treatment

Final hearing threshold

Up to six weeks

A single study reported on the final hearing threshold (as assessed with the air-bone gap) after one month of follow-up, and found a mean difference of -1.95 dB HL (95% CI -3.85 to -0.05; 1 study; 168 participants; Analysis 4.1; very low-certainty evidence).

The study Beigh 2013 also provided a description of final hearing threshold, but with no measure of the variance in the two groups. This could not be included in a meta-analysis. Nonetheless, the authors reported a significant difference ($P < 0.05$) between the two groups, with a mean air-bone gap of 8 dB for the group receiving steroids, compared to 20 dB for those receiving no treatment.

Up to three months

Again, Beigh 2013 provided a description of final hearing threshold, but with no measure of the variance in the two groups. After nine weeks of follow-up there was no longer a significant difference between the two groups, with an air-bone gap of 18 dB in those receiving steroids, compared to 24 dB in the no treatment group ($P > 0.05$; 1 study; 92 participants; very low-certainty evidence).

Persistence of OME

Up to six weeks

Overall, nasal steroids may reduce the proportion of children with persistent OME at up to one month of follow-up, but the evidence was very uncertain. The pooled results from five studies showed a risk ratio of 0.62 (95% CI 0.44 to 0.86; 70% of children in the control group, compared to 44% of children in the nasal steroid group; 5 studies; 562 participants; $I^2 = 74\%$; Analysis 4.2; very low-certainty evidence). Sensitivity analyses accounting for different correlation between ears of the same individual showed very similar results (Analysis 4.3; Analysis 4.4).

Up to three months

Two studies looked at the persistence of OME at up to three months and also found a reduction for those who received steroids, but the evidence was very uncertain (RR 0.72, 95% CI 0.57 to 0.91; 81% of children in the control group, compared to 59% of children in the steroid group; 2 studies; 134 participants; $I^2 = 0\%$; Analysis 4.5; very low-certainty evidence). Again, sensitivity analyses accounting for different correlation between ears showed minimal change (Analysis 4.6; Analysis 4.7).

Adverse events

Data pertaining to potential adverse effects of treatment are described in Table 4.

Discussion

Summary of main results

Oral steroid versus placebo

Oral steroids probably make little difference to the proportion of children whose hearing returns to normal after one year of follow-up. A similar effect is seen at earlier time points, although the evidence is less certain. The evidence also shows that there is likely to be little or no difference in disease-specific quality of life and generic quality of life after one year of follow-up. Overall, persistence of OME did appear to be lower in those children who received oral steroids at up to six weeks, up to three months and up to one year of follow-up, but the evidence was less certain. It should also be noted that persistent disease was common in both groups at all follow-up times and the size of any benefit may be small. The evidence regarding episodes of acute otitis media was uncertain, but there may be little difference between those who receive steroids and those who do not. The evidence on adverse effects (including systemic corticosteroid side effects) was very uncertain, but we did not identify major concerns over side effects.

Oral steroid versus no treatment

The evidence for this comparison was all low- or very low-certainty. After six weeks of follow-up, fewer children who received oral steroids had persistent OME, but the difference was trivial after 3 to 12 months of follow-up. Very limited information was available on adverse effects of treatment, so we were unable to draw any conclusions about the risk of side effects. No other outcomes were assessed for this comparison.

Nasal steroid versus placebo

No studies reported on our preferred measure of hearing, the return to normal hearing. The effect of nasal steroids on final hearing threshold was very uncertain. Nasal steroids may have little impact on disease-specific quality of life at up to 12 months of follow-up. The effect on persistence of OME was uncertain, with studies showing no difference at one month of follow-up, some benefit after three months of follow-up and conflicting results at 12 months of follow-up (one study showing benefit, another showing potential harm). As above, the evidence on adverse effects (including systemic corticosteroid side effects and nasal irritation) was very uncertain, but we did not identify major concerns over side effects.

Nasal steroid versus no treatment

Again, we did not identify any data on the return to normal hearing, and the evidence on final hearing threshold was very uncertain. Persistence of OME was lower for those children who received nasal steroids at up to six weeks and up to three months, but the evidence was also very uncertain. Very limited information was available on adverse effects of treatment, so we were unable to draw any conclusions about the risk of side effects. No other outcomes were assessed for this comparison.

Overall completeness and applicability of evidence

It should be noted that the studies included in this review used a variety of different doses, preparations and duration of oral and nasal steroids. We were unable to determine if the efficacy (or harms) of these different regimens varied. However, this may reflect standard clinical practice, where a range of different doses and durations of treatment may be used.

Although we included 26 studies in this review, very limited pooling of data was possible. We did not identify any evidence on developmental outcomes, including language skills, cognition and psychosocial outcomes. However, it is likely that these outcomes are of major importance to children with OME and their parents. The only outcome that was consistently reported by most studies was the presence of OME. However, there were sparse data on patient-reported outcomes, such as quality of life.

Few studies reported on hearing and almost none reported our preferred outcome measure, the number of children who returned to normal hearing. We have concerns that assessment of hearing using the mean difference in final hearing threshold (or mean

change in hearing threshold) may not be the most appropriate way to assess hearing. OME has a high spontaneous resolution rate. Consequently, we would anticipate that the change in hearing threshold for most children will be similar across the groups, as many children will improve with or without treatment. Therefore, even if a subset of children had substantial benefit from the intervention, the overall mean difference between the two groups would appear to be small. When assessed using the mean difference, the marked benefit seen in a subgroup of participants is ‘diluted’ by the children who get better regardless of treatment. Therefore, an apparently small mean difference between the two groups may actually be consistent with a substantial change in the number of children in whom hearing returns to normal.

As discussed below, a number of studies included in this review treated participants in the study with concomitant antibiotics. This may impact on the overall results, if antibiotics were considered to have a strong effect on OME, or if there may be synergistic effects between antibiotics and steroids.

Quality of the evidence

Most of the evidence included in this review was considered low- or very low-certainty. This was predominantly due to the small size of the studies included, which led to wide confidence intervals and imprecision in the overall effect estimates. We also identified a number of concerns over the risk of bias with some of the studies included, which was reflected in the GRADE ratings.

Potential biases in the review process

We are aware that a number of studies included in this review administered a course of antibiotics to all participants in the study. Therefore, the comparisons of interest were (as pre-specified in our review protocol) of steroids versus no treatment or placebo, but with a background treatment of antibiotics. There is the potential, therefore, that this additional treatment may introduce some bias in the effect estimates. Firstly, there is the possibility that the use of antibiotics may mask a potential benefit (or harm) from steroids. If antibiotics had a strong effect on symptoms of OME, then we would expect substantial change in both the intervention and control groups - and any additional benefit (or harm) of steroids may not be seen. The companion review in this suite, which addresses the use of antibiotics for OME, did find some evidence for a reduction in persistence of OME with the use of antibiotics (Mulvaney 2022a). A second possibility is that there may be some synergistic (or antagonistic) effects between the two medications, such that the use of steroids with antibiotics is more (or less) effective than steroids used alone. Therefore, the inclusion of these studies may have an impact on the results of this review, although it was in keeping with our protocol.

Agreements and disagreements with other studies or reviews

The conclusions of the review are similar to those of the previous Cochrane review on this topic, which identified a potential short-term benefit to oral steroids for 'resolution of OME', but no evidence of benefit for hearing or long-term effects (Simpson 2011).

Authors' conclusions

Implications for practice

Although oral steroids may slightly reduce the persistence of otitis media with effusion (OME) in the short term, the evidence suggests that they have little effect on hearing and quality of life. The impact in the longer term is less certain.

The evidence for nasal steroids was also uncertain. However, nasal steroids may have little effect on hearing and disease-related quality of life, and the effect on persistence of OME is

unclear.

The risk of adverse effects with a course of oral or nasal steroids is very uncertain, and is likely to depend on the route of administration and duration of treatment. Although data available in this review were limited, the use of oral steroids (especially prolonged or repeated courses) is recognised to cause potential harm, such as osteoporosis or growth retardation. The potential for harm should always be considered when deciding on a treatment strategy.

Implications for research

This review forms part of a suite of five reviews which consider interventions for OME (Galbraith 2022; MacKeith 2022a; MacKeith 2022b; Mulvaney 2022a; Mulvaney 2022b). Here we present implications for research in this field which are shared across the suite of reviews:

1. 1. As OME is a fluctuating condition with high rates of resolution and recurrence, and a highly variable impact on children, clinical trials (and, in particular, randomised controlled trials) may not be the research design of choice. Instead, evidence may be better obtained from surgical or clinical registries (for example, see Schmalbach 2021) or prospective cohort studies, with the use of 'big data'. These data sets may also be used to help identify subgroups of children who are at greater risk of persistent disease or long-term consequences of OME. A clearer understanding of possible subgroups of children is needed to better target interventions to those who need them most, whilst avoiding over-treatment for those in whom spontaneous resolution is anticipated.
2. 2. Adverse effects of interventions are important, and should always be assessed. However, randomised controlled trials are also not the best method to consider these - especially when events are rare. Observational studies with longer follow-up and larger numbers of participants are needed to provide more robust evidence on the frequency of side effects.
3. It is encouraging that a core outcome set has been developed in this field (Bruce 2015; Liu 2019). Guidance on *how* to measure the different outcomes would also be helpful for future research.
4. Comparison of mean hearing thresholds is widely used in research to assess the impact of different interventions on hearing. However, this outcome measure risks underestimating the potential impact of interventions on hearing. Small changes in mean hearing thresholds may be consistent with a substantial improvement in the number of children whose hearing returns to normal - particularly in a condition with a high spontaneous resolution rate. We would encourage researchers to assess hearing with the proportion of children in whom hearing returns to normal, in preference to mean hearing thresholds.

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Editorial and peer reviewer contributions

[To be completed after peer review/sign-off] Cochrane ENT supported the authors in the development of this review.

The following people conducted the editorial process for this article:

- Sign-off Editor (final editorial decision): [NAME, AFFILIATION];
- Managing Editor (selected peer reviewers, collated peer reviewer comments, provided editorial guidance to authors, edited the article): [NAME, AFFILIATION];
- Copy Editor (copy editing and production): [NAME, AFFILIATION];
- Peer reviewers (provided comments and recommended an editorial decision): [NAME, AFFILIATION] (clinical/content review)*, [NAME, AFFILIATION] (consumer review), [NAME, AFFILIATION] (methods review), [NAME, AFFILIATION] (search review). [NUMBER] of additional peer reviewers provided [CLINICAL/CONTENT/CONSUMER/METHODS/SEARCH] peer review, but chose not to be publicly acknowledged.

Data and analyses

Comparison 1

Oral steroid versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Normal hearing (very short-term)	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.2 Normal hearing (very short-term, adjusted OR)	1		Odds Ratio (IV, Random, 95% CI)	Subtotals only
1.3 Normal hearing defined as complete improvement in air-bone gap (short-term)	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.4 Normal hearing (medium-term)	1	332	Risk Ratio (M-H, Random, 95% CI)	1.14 [0.97, 1.33]
1.5 Hearing threshold (very short-term)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.6 Hearing threshold (difference in adjusted	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
mean, very short-term)				
1.7 Disease-specific quality of life (very short-term)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.8 Disease-specific quality of life (medium-term)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.9 Persistence of OME (very short-term)	7	786	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.51, 1.02]
1.9.1 Persistence undefined	1	41	Risk Ratio (M-H, Random, 95% CI)	0.40 [0.23, 0.68]
1.9.2 Persistence in one or both *affected* ears	2	113	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.24, 2.00]
1.9.3 Persistence defined as effusion in *all affected* ears	2	480	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.52, 1.43]
1.9.4 Persistence defined as effusion in *either or both* ears	2	152	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.63, 0.97]
1.10 Sensitivity analysis: Persistence of OME (very short-term); persistence in all affected ears (Berman 1990)	7	786	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.50, 1.02]
1.10.1 Persistence undefined	1	41	Risk Ratio (M-H, Random, 95% CI)	0.40 [0.23, 0.68]
1.10.2 Persistence in one or both *affected* ears	1	60	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.70, 1.82]
1.10.3 Persistence defined as	3	533	Risk Ratio (M-H,	0.68 [0.36, 1.29]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
effusion in *all affected* ears			Random, 95% CI)	
1.10.4 Persistence defined as effusion in *either or both* ears	2	152	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.63, 0.97]
1.11 Sensitivity analysis: Persistence of OME (very short-term); effusion in both ears (Niederman 1984)	7	786	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.51, 1.02]
1.11.1 Persistence undefined	1	41	Risk Ratio (M-H, Random, 95% CI)	0.40 [0.23, 0.68]
1.11.2 Persistence in one or both *affected* ears	2	113	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.24, 2.00]
1.11.3 Persistence defined as effusion in *all affected* ears	2	480	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.52, 1.43]
1.11.4 Persistence defined as effusion in *either or both* ears	1	132	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.62, 1.01]
1.11.5 Persistence defined as effusion in *both ears (whether affected at baseline or not)*	1	20	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.37, 1.33]
1.12 Persistence of OME (short-term); ICC = 0.5	3	211	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.50, 1.30]
1.12.1 Persistence in any ear	2	112	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.20, 2.43]
1.12.2 Persistence defined as effusion in the worst ear	1	99	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.65, 1.16]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.13 Sensitivity analysis: Persistence of OME (short-term); ICC = 1.0	3	199	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.52, 1.30]
1.13.1 Persistence in any ear	2	100	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.19, 2.54]
1.13.2 Persistence defined as effusion in the worst ear	1	99	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.65, 1.16]
1.14 Sensitivity analysis: Persistence of OME (short-term); ICC = zero	3	230	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.47, 1.30]
1.14.1 Persistence in any ear	2	131	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.19, 2.49]
1.14.2 Persistence defined as effusion in the worst ear	1	99	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.65, 1.16]
1.15 Sensitivity analysis: Persistence of OME (short-term); persistence in all affected ears (Macknin 1985)	3	211	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.47, 1.30]
1.15.1 Persistence defined as effusion *in any ear*	1	63	Risk Ratio (M-H, Random, 95% CI)	0.40 [0.20, 0.80]
1.15.2 Persistence defined as effusion *in the worst ear*	1	99	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.65, 1.16]
1.15.3 Persistence defined as effusion in *all affected ears*	1	49	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.91, 1.22]
1.16 Persistence of OME (medium-term)	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.16.1 Persistence defined as effusion in both affected ears	1	303	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.79, 0.94]
1.16.2 Persistence undefined	1	49	Risk Ratio (M-H, Random, 95% CI)	0.18 [0.06, 0.54]
1.17 Acute otitis media (very short-term)	3	207	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.97 [0.31, 3.10]
1.18 Generic health-related quality of life (PedsQL, very short-term)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.19 Generic health-related quality of life (PedsQL, medium-term)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.20 Generic health-related quality of life (HU13, very short-term)	1	319	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.70, 1.60]
1.21 Generic health-related quality of life (HU13, medium-term)	1	292	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.79, 1.53]
1.22 Subgroup analysis: Normal hearing: allergy versus none (very short-term)	1	363	Risk Ratio (M-H, Random, 95% CI)	1.22 [0.92, 1.61]
1.22.1 Allergy	1	120	Risk Ratio (M-H, Random, 95% CI)	1.33 [0.81, 2.21]
1.22.2 No allergy	1	243	Risk Ratio (M-H, Random, 95% CI)	1.17 [0.84, 1.63]
1.23 Subgroup analysis: Persistence	1	120	Risk Ratio (M-H,	0.82 [0.59, 1.14]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
of OME: allergy versus none (very short-term)			Random, 95% CI)	
1.23.1 Allergy	1	51	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.70, 1.33]
1.23.2 No allergy	1	69	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.50, 0.96]
1.24 Subgroup analysis: Persistence of OME: age < 4 versus ≥ 4 (very short-term)	1	64	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.64, 1.06]
1.24.1 Age <4	1	21	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.44, 1.54]
1.24.2 Age ≥4	1	43	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.62, 1.09]

Comparison 2

Oral steroid versus no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Persistence of OME (very short-term)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.1.1 Persistence undefined	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.2 Persistence of OME (short-term)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.2.1 Persistence in one or both ears	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2.3 Persistence of OME (medium-term)	2	258	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.89, 1.17]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
2.3.1 Persistence undefined	1	66	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.76, 1.72]	
2.3.2 Persistence in one or both ears	1	192	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.87, 1.16]	

Comparison 3

Nasal steroid versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
3.1 Change in hearing threshold (short-term); ICC = 0.5	1	78	Mean Difference (IV, Random, 95% CI)	-0.30 [-6.05, 5.45]	
3.2 Sensitivity analysis: Change in hearing threshold (short-term); ICC=1.0	1	61	Mean Difference (IV, Random, 95% CI)	-0.30 [-6.80, 6.20]	
3.3 Sensitivity analysis: Change in hearing threshold (short-term); ICC=zero	1	107	Mean Difference (IV, Random, 95% CI)	-0.30 [-5.21, 4.61]	
3.4 Final hearing threshold (short term)	1	40	Mean Difference (IV, Random, 95% CI)	-14.95 [-17.32, -12.58]	
3.5 Disease-specific quality of life (short-term)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected	
3.6 Disease-specific quality of life (medium-term)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected	
3.7 Persistence of OME (very short-term); ICC=0.5	1	89	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.80, 1.20]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.8 Sensitivity analysis: Persistence of OME (very short-term); ICC=1.0	1	70	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.79, 1.26]
3.9 Sensitivity analysis: Persistence of OME (very short-term); ICC=zero	1	123	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.83, 1.17]
3.10 Persistence of OME (short-term)	3	286	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.51, 1.26]
3.10.1 Analysis per child	2	212	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.33, 1.26]
3.10.2 Analysis per ear	1	74	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.83, 1.53]
3.11 Sensitivity analysis: Persistence of OME (short-term); ICC=1.0	3	270	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.50, 1.29]
3.11.1 Analysis per child	2	212	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.33, 1.26]
3.11.2 Analysis per ear	1	58	Risk Ratio (M-H, Random, 95% CI)	1.16 [0.83, 1.62]
3.12 Sensitivity analysis: Persistence of OME (short-term); ICC=zero	3	314	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.51, 1.29]
3.12.1 Analysis per child	2	212	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.33, 1.26]
3.12.2 Analysis per ear	1	102	Risk Ratio (M-H,	1.15 [0.89, 1.49]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
			Random, 95% CI)		
3.13 Persistence of OME (medium-term)	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected	
3.13.1 Persistence undefined	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected	
3.13.2 Persistence in both ears	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected	
3.14 Adverse event: nasal bleeding (medium-term)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected	
3.15 Generic health-related quality of life (medium-term)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected	

Comparison 4

Nasal steroid versus no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
4.1 Final hearing threshold (up to 6 weeks)	1	168	Mean Difference (IV, Random, 95% CI)	-1.95 [-3.85, -0.05]	
4.2 Persistence of OME (very short term); ICC=0.5	5	562	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.44, 0.86]	
4.2.1 Persistence in any or both ears	1	122	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.61, 1.26]	
4.2.2 Persistence undefined	2	164	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.29, 0.65]	
4.2.3 Persistence in any *affected* ear	2	276	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.37, 1.12]	

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.3 Sensitivity analysis: Persistence of OME (very short term); ICC=1.0	5	465	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.44, 0.86]
4.3.1 Persistence in any or both ears	1	92	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.58, 1.33]
4.3.2 Persistence undefined	2	164	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.29, 0.65]
4.3.3 Persistence in any *affected* ear	2	209	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.37, 1.13]
4.4 Sensitivity analysis: Persistence of OME (very short term); ICC=zero	5	757	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.45, 0.87]
4.4.1 Persistence in any or both ears	1	184	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.65, 1.18]
4.4.2 Persistence undefined	2	164	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.29, 0.65]
4.4.3 Persistence in any *affected* ear	2	409	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.37, 1.12]
4.5 Persistence of OME (short-term); ICC=0.5	2	134	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.57, 0.91]
4.5.1 Persistence in *affected* ears	2	134	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.57, 0.91]
4.6 Sensitivity analysis: Persistence of OME (short-term); ICC=1.0	2	104	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.54, 0.91]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size	
4.6.1 Persistence in *affected* ears. ICC 1.0	2	104	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.54, 0.91]	
4.7 Sensitivity analysis: Persistence of OME (short-term); ICC=zero	2	192	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.60, 0.87]	
4.7.1 Persistence in *affected* ears. ICC zero	2	192	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.60, 0.87]	

History

Protocol first published: Issue 4, 2022

Contributions of authors

Caroline A Mulvaney: drafted the protocol. Screened the search results and selected studies, conducted data extraction, carried out statistical analyses and GRADE assessment. Drafted the text of the review.

Kevin Galbraith: drafted the protocol. Screened the search results and selected studies, conducted data extraction, carried out statistical analyses and GRADE assessment. Drafted the text of the review.

Katie Webster: screened the search results and selected studies. Drafted the text of the review.

Mridul Rana: conducted data extraction. Reviewed and edited the text of the review.

Rachel Connolly: conducted data extraction. Reviewed and edited the text of the review.

Ben Tudor Green: conducted data extraction. Reviewed and edited the text of the review.

Tal Marom: reviewed the protocol. Reviewed the analyses and reviewed and edited the text of the review.

Mat Daniel: reviewed the protocol. Reviewed the analyses and reviewed and edited the text of the review.

Roderick P Venekamp: co-wrote and edited the protocol. Reviewed the analyses and reviewed and edited the text of the review.

Anne GM Schilder: co-wrote and edited the protocol. Reviewed the analyses and reviewed and edited the text of the review.

Samuel MacKeith: drafted the protocol. Screened the search results and selected studies. Reviewed the analyses and reviewed and edited the text of the review.

Declarations of interest

Caroline A Mulvaney: none known.

Kevin Galbraith: none known.

Katie Webster: none known.

Mridul Rana:

Rachel Connolly:

Ben Tudor-Green:

Tal Marom: none known.

Mat Daniel: has a financial interest in Aventamed, a company that produces a ventilation tube insertion device.

Roderick P Venekamp: is an Editor for Cochrane Acute Respiratory Infections and Cochrane ENT, but had no role in the editorial process for this review.

Anne GM Schilder: Professor Anne Schilder was joint Co-ordinating Editor of Cochrane ENT until April 2020, but had no role in the editorial process for this review. Her evidENT team at the UCL Ear Institute is supported by the National Institute of Health Research (NIHR) University College London Hospitals (UCLH) Biomedical Research Centre (BRC), with research projects being supported by the NIHR, Wellcome Trust, RNiD, ENT UK and industry. She is the National Specialty Lead for the NIHR Clinical Research Network ENT and Surgical Specialty Lead for ENT for the Royal College of Surgeons of England's Clinical Research Initiative. In her role as director of the NIHR UCLH BRC Deafness and Hearing Problems Theme, she advises CRO, biotech and pharma companies in the hearing field on clinical trial design and delivery.

Samuel MacKeith: treats patients with OME in his NHS and private practice and is Assistant Co-ordinating Editor of Cochrane ENT but has not been involved in the editorial process for this review.

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Internal sources

- No sources of support provided

External sources

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Differences between protocol and review

In our protocol we planned to use the Trustworthiness Tool developed by Cochrane Pregnancy and Childbirth to determine which studies would be included in the main analyses (Mulvaney 2022b). As described in the text, we used this tool to assess the studies, but did not use it to determine whether a study should be included in the main analysis.

Characteristics of studies

Characteristics of included studies [ordered by study ID]

Acharya 2020

Study characteristics	
Methods	Four-arm, parallel-group, randomised controlled trial

	One arm of this trial considered a separate intervention (antibiotics, antihistamines and decongestants) - data pertaining to this arm have not been extracted for the purposes of this review

Participants	**Setting:**
	Single-centre, conducted in an ENT department at a university hospital in Nepal between September 2018 and February 2020
	Sample size:
	• **Number randomised:**
	  ◦ 160 participants total
	  ◦ 120 participants relevant to this review
	• **Number completed:**
	  ◦ 160 participants total
	  ◦ 120 participants relevant to this review
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Intranasal steroids group: mean 6 years
	  ◦ Oral steroids group: mean 7.3 years
	  ◦ Watchful waiting group: mean 7.1 years
	  ◦ Overall: 6.84 years (SD 2.97)
	• **Gender:**
	  ◦ Intranasal steroids group:
	  ▪ 14 males (35%)
	  ▪ 26 females (65%)
	  ◦ Oral steroids group:
	  ▪ 15 males (37.5%)
	  ▪ 25 females (62.5%)
	  ◦ Watchful waiting group:
	  ▪ 24 males (60%)
	  ▪ 16 females (40%)
	Inclusion criteria:
	Aged 1 to 12 years diagnosed with otitis media with effusion. OME was diagnosed by consultant otolaryngologist based on history, clinical examination and tympanometry. Diagnosis of OME was made when tympanometry showed B type curve in children suspected to have OME from history (hearing loss, occasional mild earache or deteriorating school performance over last few months) and clinical examination (dull, lusterless, mild retracted tympanic membrane with visible blood vessels in pars tensa adjacent to annulus and absent mobility).
	Exclusion criteria:
	• Lack of consent
	• Cleft palate
	• Down syndrome or any cranio-facial developmental disorder
	• History of ear surgery
	• Systemic disorders like diabetes
	• Treatment with steroids in the last 6 weeks

Interventions	**Intranasal steroids group (n = 40 randomised, n = 40 completed)** Mometasone furoate 50 µg/puff for a month. They were instructed to use one puff (50 µg mometasone) per nostril per day Parents/guardians and the children were taught on how to use the spray **Oral steroids group (n = 40 randomised, n = 40 completed)** Oral prednisolone at the rate of 1 mg per kg per day in 2 divided doses for a week followed by 0.5 mg per day for next 1 week **Watchful waiting group (n = 40 randomised, n = 40 randomised)**

	Parent/guardian and participants of group D were counselled about the condition and its management options and were advised for observation for a month without active treatment

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Not reported
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of children with persistence of OME**
	  ◦ Tympanometry at 1 month (children with A, As or C curve were labelled as improved whereas those with B curve were considered to have persistent OME)
	Other outcomes reported in the study:
	• Antibiotic-antihistamine nasal decongestant combination as a treatment option
	• Cost-effectiveness of treatment options

Funding sources	Not reported
Declarations of interest	None reported
Notes	**Research integrity checklist** • No retractions or expressions of concern were identified • This trial was prospectively registered (NCT03590912) • Limited baseline characteristics are described, but we do not have concerns over excessive similarity between the groups • The authors state that "telephone calls were made in between to reduce loss to follow up", which may account for full follow-up • No implausible results were noted • Block randomisation was used to allocate equal numbers to each group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The children who fulfilled the selection criteria were randomly divided into four parallel groups by block randomization, with blocks of four by a resident not involved in the study. The blocks were generated randomly by an author, who was not directly involved in treatment of patient, according to computer generated random numbers" Comment: computer-generated random numbers.
Allocation concealment (selection bias)	High risk	Comment: small block size (blocks of 4, therefore 1:1 ratio for allocation) and an unblinded trial, therefore recruitment to different groups would have been predictable.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no placebo was used. Participants and study personnel would have been aware of treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: open-label trial with no placebo. No description of blinding of outcome assessors, therefore we assume that outcome assessors were unblinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: full follow-up is reported.

Selective reporting (reporting bias)	Low risk	Comment: results are reported in accordance with the trial registration.
Other bias	High risk	Comment: follow-up is inadequate to allow appropriate comparison of steroids and no intervention. Outcomes reported at this stage may be more likely to favour the active intervention, as insufficient time has elapsed to allow for spontaneous resolution.

Ahmed 2022

Study characteristics	
Methods	Two-arm, parallel-group, randomised controlled trial with 4 weeks duration of treatment and follow-up

Participants	**Setting:**
	Single-centre, conducted in an ENT department at a university hospital in Egypt between October 2018 and September 2021
	Sample size:
	• **Number randomised:**
	  ◦ 168 participants
	• **Number completed:**
	  ◦ 168 participants
	Participant (baseline) characteristics:
	• **Age**
	  ◦ Intranasal steroids group: 4.28 years (SD 1.74)
	  ◦ Control group: 5.91 years (SD 1.62)
	• **Hearing threshold at baseline (air-bone gap)**
	  ◦ Intranasal steroids group:
	  ▪ Right ear: 15.1 dB (SD 7.2)
	  ▪ Left ear: 18.4 dB (SD 6.9)
	  ◦ Control group:
	  ▪ Right ear: 13.9 dB (SD 7.1)
	  ▪ Left ear: 14.1 dB (SD 7.1)
	Inclusion criteria:
	Aged 4 to 12 years old with bilateral OME (including children with type B or type C curves on tympanogram) for at least 3 months
	Exclusion criteria:
	• Children with grade 2/3 adenoid hypertrophy
	• Children with craniofacial abnormalities (e.g. choanal atresia, cleft palate)
	• Children with hypersensitivity to mometasone furoate or amoxicillin-clavulanic acid

Interventions	**Intranasal steroid group (n = 84 randomised, n = 84 completed)** Mometasone furoate aqueous nasal spray, 50 µg/puff, 2 puffs per nostril once daily for 1 month **Control (n = 84 randomised, n = 84 completed)** No intervention **Background interventions provided to both groups:** Participants in both groups also received amoxicillin and clavulanic acid (90 mg/kg/day) for 4 weeks

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Air-bone gap for each ear after 4 weeks follow-up
	• **Disease-specific quality of life**
	  ◦ Not reported

	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of children with persistence of OME**
	  ◦ Tympanometry at 1 month (children with B or C curve were considered to have persistent OME)

Funding sources	No funding was declared
Declarations of interest	The authors have no conflicts to declare
Notes	**Research integrity checklist:** • No retractions or expressions of concern were identified • No prospective trial registration was available • Limited baseline information was reported, but no concerns over excessive similarity between the groups with the data available • No loss to follow-up was reported • No implausible results were identified • Equal numbers of participants were randomised to each group, without any description of blocked randomisation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The subjects were randomly divided into two equal groups. A computer-generated table of random numbers was used for group assignment; if the last digit of the random number was from 0 to 4, assignment was to the 1st group (study group), and if the last digit was from 5 to 9, assignment was to the 2nd group (control group)." Comment: random number table should be an adequate method to randomise.
Allocation concealment (selection bias)	Unclear risk	See quote above. If the random number table was open and accessible, then treatment allocation would have been easily accessible. However, it is not clear if this was the case.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding was used in this study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	There is no statement to indicate that outcome assessors were blinded. As study participants were not blinded to treatment allocation, we assume this was also the case for outcome assessors.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Full follow-up was reported.
Selective reporting (reporting bias)	Unclear risk	No protocol was available to assess for the potential of selective reporting bias.
Other bias	High risk	Follow-up was insufficient to allow for natural resolution in the control group, therefore results may be biased towards the intervention.

Barati 2011

Study characteristics	
Methods	Two-arm, parallel-group, randomised controlled trial with 4 weeks of follow-up
Participants	**Setting:** Single-centre, conducted in a university ENT Department in Iran between March 2004 and March 2005 **Sample size:** • **Number randomised:** 92 participants (N = 106 included before exclusion criteria applied, including exclusion due to loss to follow-up)

	• **Number completed:** 92 participants (14 children absent at follow-up appointment were excluded from study. Unclear from the 14 excluded children how many were lost to follow-up or which group they were in). **Participant (baseline) characteristics:** • **Age:** ◦ Antibiotics, decongestants and intranasal steroids group: mean 5.6 years (SD 1.9) ◦ Antibiotics and decongestants only group: mean 4.5 years (SD 2.1) • **Other measure of hearing status: children with a history of altered response to sounds or hearing loss (reported by parents)** ◦ Antibiotics, decongestants and intranasal steroids group: 26/46 (57%) ◦ Antibiotics and decongestants only group: 18/46 (39%) **Inclusion criteria:** Aged 1 to 10 years with unilateral or bilateral otitis media with effusion assessed using tympanometry and otoscopy. Otologic examinations included the presence of TM retraction and the degree from 0 to 3 for each ear; tympanometry was performed using an impedance audiometer AT235 device, and ears assessed as type A, B, C1 or C2. Children with type A tympanograms for the suspiciously involved ear at initial assessment were excluded from the study. **Exclusion criteria:** • Age < 1 year or > 10 years* • Chronic otitis media in the involved ear • Previous operative surgery on the involved ear • A history of previous adenoidectomy or AOM or a period of taking antibiotics in the last 4 weeks • Type A tympanometry at first for the suspiciously involved ear • Adverse or allergic reactions to amoxicillin • Concomitant use of inhalant corticosteroid sprays (for reducing of the adverse effects of higher dosing levels) • Absence in the follow-up dates *Authors report that “age more than 1 year or less than 10 years” (p511) was part of the exclusion criteria, but this is presumably an error as all participants are between the ages of 1 to 10 years
Interventions	**Antibiotics, decongestants and intranasal steroids group (n = 46 randomised, n = 46 completed)** Amoxicillin suspension or capsule for 10 days: 50 mg/kg per day divided in 3 doses Decongestant for 4 weeks: normal saline drop, 0.25 cc (4 to 5 drops) per nostril twice a day in children 1 to 2 years old; pseudoephedrine syrup, 3 mg/kg per day divided in 3 to 4 doses (lower than standard recommended dosage) for other ages Nasal beclomethasone spray for 4 weeks: 1 puff per nostril twice a day for children 1 to 5 years old; 1 puff per nostril 3 times a day for children 6 to 10 years old **Antibiotics and decongestants only group: (n = 46 randomised, n = 46 completed)** Amoxicillin suspension or capsule for 10 days: 50 mg/kg per day divided in 3 doses Decongestant for 4 weeks: normal saline drop, 0.25 cc (4 to 5 drops) per nostril twice a day in children 1 to 2 years old; pseudoephedrine syrup, 3 mg/kg per day divided in 3 to 4 doses (lower than standard recommended dosage) for other ages
Outcomes	**Primary outcomes relevant to this review:** • **Hearing** ◦ Data not useable. Authors only report "proportion of children with improved symptoms or hearing quality of life" at 4 weeks. • **Disease-specific quality of life** ◦ Not reported • **Adverse event** ◦ Not reported **Secondary outcomes relevant to this review:**

	• **Presence/persistence of OME: proportion of children/ears with persistence of OME**
	  ◦ Otoscopy and tympanometry – assessed according to tympanic retraction and tympanogram type by child at 4 weeks
	  ◦ Tympanometry: type C2 or B tympanogram by ear at 4 weeks
	Other outcomes reported in the study:
	Number of participants who had an improvement in their hearing, according to the parents
	Most common tympanometry result after treatment in each ear

Funding sources	Not reported
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were noted • Prospective trial registration was not identified • Limited baseline characteristics are presented, but no concerns with the available data • Full follow-up was reported as this was a per protocol analysis, and only those participants who completed follow-up were included • No implausible results were noted • Identical numbers of participants were included in each group, even after the exclusion criteria were applied (excluding participants who did not return for follow-up)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The arrangement of cases in the case or control group was performed using random number table." Comment: an appropriate method was used for randomisation.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was reported regarding whether allocation was adequately concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: this was an unblinded study and participants ware aware of their allocated treatment.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: no information provided on blinding of outcome assessors. Lack of blinding of participants is likely to influence primary outcome 'proportion of children with improved symptoms or hearing quality' as this outcome was assessed based on parent- and child-reported improvement. Authors note that the research team filled all questionnaires at each appointment and controlled all otoscopies in the process, and information on blinding of personnel not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no missing outcome data, though this is due to exclusion of children from the study if they did not attend their follow-up appointment. The authors do not report the number of children who were excluded for this reason, and it is not possible to discount the potential that missing outcome data for these participants may be related to their true outcome (although number of participants included in final analyses are the same in each group).
Selective reporting (reporting bias)	Unclear risk	Comment: no trial registration or protocol was identified, therefore unable to assess.
Other bias	High risk	Comment: very limited details on study design and conduct are available. Duration of follow-up is likely to be insufficient to allow time for spontaneous resolution of OME.

Beigh 2013

Study characteristics

Methods	Two-arm, parallel-group, randomised controlled trial with follow-up at 3, 6 and 9 weeks
Participants	**Setting:** Single-centre, conducted in a university hospital ENT Department in India between September 2011 and November 2012 **Sample size:** • **Number randomised:** 92 participants (N = 106 included before exclusion due to loss to follow-up) • **Number completed:** 92 participants (14 children lost to follow-up were excluded from study. Unclear which group/s they were in). **Participant (baseline) characteristics:** • **Age (number in each age category):** ◦ Intranasal steroids group: ▪ 2 to 4 years: 24 ▪ 4 to 6 years: 14 ▪ 6 to 8 years: 8 ◦ No treatment group: ▪ 2 to 4 years: 26 ▪ 4 to 6 years: 14 ▪ 6 to 8 years: 6 • **Gender:** ◦ Intranasal steroids group: ▪ 26 males ▪ 20 females ◦ No treatment group: ▪ 24 males ▪ 22 females • **Other measure of hearing status: mean air-bone gap assessed by pure tone audiometry** ◦ Intranasal steroids group: 20 dB ◦ No treatment group: 22 dB **Inclusion criteria:** Aged 2 to 8 years. Otitis media with effusion diagnosed by otoscopy and tympanometry. **Exclusion criteria:** • Children with congenital syndromes • Children with cleft palate • Children lost to follow-up
Interventions	**Intranasal steroids group (n = 46 randomised, n = 46 completed)** • Intranasal steroids (mometasone nasal spray is stated in the abstract, but dose and frequency not stated) given as treatment for period of 3 weeks • After 3 weeks of treatment, dose of steroids gradually tapered over further 3 weeks • Steroids were stopped after 3 weeks of tapering **Comparator: no treatment (n = 46 randomised, n = 46 randomised)** Children in this group were observed without treatment
Outcomes	**Primary outcomes relevant to this review:** • **Hearing** ◦ Mean (SD) final hearing threshold (dB) (air-bone gap) measure by audiometry at 3 weeks and 9 weeks. No measure of variance was reported, therefore not included in meta-analysis. • **Disease-specific quality of life**

	◦ Not reported • **Adverse event** ◦ Not reported **Secondary outcomes relevant to this review:** • **Presence/persistence of OME: proportion of children/ears with persistence of OME** ◦ Not reported **Other outcomes reported in the study:** Audiometry results were also reported at week 6
Funding sources	Not reported
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions/expressions of concern were noted • No prospective trial registration was identified • Some concerns over baseline data (a difference of 2 is seen between the groups for every baseline characteristic) • The authors excluded participants who were lost to follow-up • Identical numbers of participants were in each group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomization was allocated by random number table, use by the even and odd numbers in equal proportions. The even numbers in random number table represented the control group while the odd numbers represented the study group." Comment: an adequate method was used.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was provided on any methods used to conceal allocation.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: this was an open study and participants were aware of their treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: this was an open study. There is no report that outcome assessors were blinded, therefore we assume that they were aware of the treatment allocation for individual participants.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no missing outcome data, although this is due to exclusion of children from the study if they were lost to follow-up. It is not possible to discount the potential that missing outcome data for these participants may be related to true outcome (though the number of participants included in final analyses are the same in each group).
Selective reporting (reporting bias)	Unclear risk	Comment: no protocol or trial registration was identified.
Other bias	High risk	Comment: the short duration of follow-up may be insufficient to detect a difference between the groups. In addition, there is very little information reported in the article - insufficient information to assess whether an important additional risk of bias exists.

Berman 1990

Study characteristics	
Methods	Two-arm, parallel-group, randomised controlled trial (cross-over at 2 weeks in the event of treatment failure), with follow-up at 2 and 4 weeks Data were only used before any cross-over to the alternate group
Participants	**Setting:**

	Single-centre, conducted in a university hospital ENT Department in the USA between February 1988 and January 1990
	Sample size:
	• **Number randomised:** 68 participants
	• **Number completed:** 53 participants
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Antibiotics and oral steroids group: mean 36 months (SD 29)
	  ◦ Antibiotics group: mean 29 months (SD 23)
	• **Gender:**
	  ◦ Antibiotics and oral steroids group:
	  ▪ 14 males
	  ▪ 12 females
	  ◦ Antibiotics group:
	  ▪ 18 males
	  ▪ 12 females
	• **Bilateral disease**
	  ◦ Antibiotics and oral steroids group:
	  ▪ 18 bilateral
	  ▪ 8 unilateral
	  ◦ Antibiotics group:
	  ▪ 23 bilateral
	  ▪ 4 unilateral
	• **Hearing thresholds: mean speech awareness thresholds (SAT)**
	  ◦ Antibiotics and oral steroids group: mean 25 dB (SD 9.43)
	  ◦ Antibiotics group: mean 28.1 dB (SD 13.65)
	• **Hearing thresholds: mean speech reception thresholds (SRT)**
	  ◦ Antibiotics and oral steroids group: mean 20.5 dB (SD 5.97)
	  ◦ Antibiotics group: mean 20 dB (SD 5.77)
	Inclusion criteria:
	• Children with middle ear effusion for 6 weeks or longer despite multiple courses of antibiotics
	• Received at least 2 courses of antibiotics, one of which was effective against beta-lactamase-producing organisms
	Diagnosis of MEE required at least 2 of the following findings:
	• Absent or diminished tympanic membrane mobility on pneumatic otoscopy, assessed using a hand-held pneumatic otoscope or an otologic operating microscope
	• Type B tympanogram assessed by tympanometry using an impedance audiometer
	• Speech threshold >15 dB HL assessed by audiometry using an age-appropriate audiologic evaluation to document speech awareness thresholds (SAT) or speech reception thresholds (SRT)
	Authors also note that MEE was confirmed using tympanocentesis
	Exclusion criteria:
	Not reported

Interventions	**Antibiotics and oral steroids group (n = 35 randomised, n = 26 completed)** • Trimethoprim-sulfamethoxazole (TMP/SMZ) 5 mg/kg/dose of trimethoprim twice a day for 30 days • Prednisone 0.5 to 1.0 mg/kg/dose twice a day for 7 days • Pills were crushed and given to participants with jelly or fruit

	• Participants with unresolved MEE by follow-up were crossed over to the alternative regimen • Participants with complete resolution were placed on continuous or intermittent (with upper respiratory infection symptoms) amoxicillin prophylaxis (10 mg/kg/dose twice a day) for 3 months **Antibiotics group (n = 33 randomised, n = 27 completed)** • TMP/SMZ 5 mg/kg/dose of trimethoprim twice a day for 30 days • Prednisone placebo (in the form of a similar white pill) for 7 days • Pills were crushed and given to participants with jelly or fruit • Participants with unresolved MEE by 2 week follow-up were crossed over to the alternative regimen **Treatment used before entry into the trial** All participants had received at least 2 courses of antibiotics prior to entry into the study, one of which was effective against beta-lactamase-producing organisms **Background interventions administered to all participants** • All participants received TMP/SMZ 5 mg/kg/dose of trimethoprim twice a day for 30 days • Participants with unresolved MEE by 2 week follow-up were crossed over to the alternative regimen, and therefore some participants received both interventions • Participants with complete resolution were placed on continuous or intermittent (with upper respiratory infection symptoms) amoxicillin prophylaxis (10 mg/kg/dose twice a day) for 3 months. It is unclear whether this was done at 2 weeks or 4 weeks follow-up, or on an individual patient basis whenever MEE resolved
Outcomes	**Primary outcomes relevant to this review:** • **Hearing** ◦ A number of outcomes were assessed, but we could not include them in a meta-analysis, as data on the denominator for each group were not clearly reported ◦ Proportion of ears with hearing returned to normal: speech awareness thresholds (SAT) < 15 dB/ ear at 2 weeks measured by audiometry ◦ Proportion of ears with hearing returned to normal: speech reception thresholds (SRT) < 15 dB/ ear at 2 weeks measured by audiometry ◦ Mean (SD) final hearing thresholds (dB) per ear: SAT (affected ear) at 2 weeks measured by audiometry ◦ Mean (SD) final hearing thresholds (dB) per ear: SRT (affected ear) at 2 weeks measured by audiometry • **Disease-specific quality of life** ◦ Not reported • **Adverse event** ◦ Not reported **Secondary outcomes relevant to this review:** • **Presence/persistence of OME: proportion of children with persistence of OME** ◦ No resolution of middle ear effusion at 2 weeks in both ears (or in one ear when only one was involved) (type B tympanogram) • **Episodes of acute otitis media: mean (SD) number of episodes** ◦ Number with acute otitis media at 2 weeks • **Other adverse effects** ◦ Vomiting: narrative summary reported **Other outcomes reported in the study:** • Number of children with type A, B and C tympanograms at one week follow-up

	• Duration of subsequent follow-up in participants with complete resolution of MEE at 4-week follow-up • Number of children receiving tympanostomy tubes during subsequent follow-up period
Funding sources	This study was supported by Grant RR-69 from the General Clinical Research Center Program of the Division of Research, National Institutes of Health, Bethesda, MD
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concerns were noted • This trial was conducted before 2010, therefore prospective registration was not required • Baseline characteristics of the 2 groups were not excessively similar • Plausible loss to follow-up was reported • No implausible results were identified • The number randomised to each group was not identical

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “The 53 patients were randomly assigned from a random number table provided by a statistician.” Comment: adequate method. Participants were randomised using a random number table.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was provided regarding any methods used to conceal allocation.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “The investigator treating the patient was blinded to the randomisation scheme” Comment: study was double-blind, with participants in the group not receiving prednisone given a similar-looking placebo pill. Participants and study personnel were therefore blinded to allocation.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "All follow-up otoscopic examinations were done by Dr. Nerman". Comment: it is not reported whether the lead author was blind to the treatments received. Additionally, no information is given regarding who performed tympanometry or audiometry, or on the blinding of these assessors. It is unclear how adverse events data were collected.
Incomplete outcome data (attrition bias) All outcomes	High risk	28% of participants were lost to follow-up.
Selective reporting (reporting bias)	Unclear risk	No protocol or trial registration was found.
Other bias	High risk	Comment: The short duration of follow-up may be insufficient to detect a difference between the groups.

Bhargava 2014

Study characteristics	
Methods	Two-arm, parallel-group, randomised controlled trial with 24 weeks follow-up
Participants	**Setting:** Single-centre, conducted in a university hospital ENT Department in India between October 2011 and March 2013 **Sample size:** • **Number randomised:** 62 participants • **Number completed:** 62 participants **Participant (baseline) characteristics:** • **Age:**

	◦ Intranasal steroids: mean 7.28 years (SD 3.17) ◦ Intranasal saline: mean 7.61 years (SD 2.48) • **Gender:** ◦ Intranasal steroids: ▪ 18 (60%) males ▪ 12 (40%) females ◦ Intranasal saline: ▪ 20 (63%) males ▪ 12 (38%) females • **Hearing thresholds: pure tone average** ◦ Intranasal steroids group: mean 20.5 dB ◦ Intranasal saline group: mean 20.4 dB **Inclusion criteria:** Aged 2 to 12 years, with: • Grade 3 and 4 adenoidal hypertrophy according to the Cassano classification • Duration of symptoms for at least 3 months and not responsive to previous medical treatment • Diagnosed with bilateral OME on otoscopy & tympanometry ENT examination including pneumatic otoscopy and tympanometry (modified Jerger's type B or C2). Participants also underwent pure tone audiometry wherever possible and nasopharyngoscopy under local anaesthetic spray (lignocaine spray 15%)/ sedation with midazolam if required using rigid 2.7 mm/4 mm diameter nasal telescope. **Exclusion criteria:** • Previous adenoidectomy • Use of intranasal topical or systemic steroid in the last year • Associated marked tonsillar hypertrophy • Anatomic deformity of the nose or sinonasal disease such as nasal polyposis or inferior turbinate hypertrophy • Craniofacial abnormalities such as cleft lip/cleft palate • Genetic diseases such as Down Syndrome • Acute upper respiratory infection within 2 weeks of enrolling in the study • Patients with any clinically significant metabolic cardiovascular, neurologic, haematologic, gastrointestinal, cerebrovascular or respiratory disease
Interventions	**Intranasal steroids group (n = 30 randomised, n = 30 completed)** • Initial treatment of 2 puffs of mometasone furoate nasal spray (50 µg/puff) in each nostril once a day (a total of 200 µg/day) for first 8 weeks • Followed by a maintenance dose of 2 puffs of mometasone furoate nasal spray in each nostril on alternate days for 16 weeks **Intranasal saline group (n = 32 randomised, n = 32 completed)** • Two puffs of saline nasal spray in each nostril once a day for 8 weeks • Followed by 2 puffs of saline nasal spray on alternate days for 16 weeks
Outcomes	**Primary outcomes relevant to this review:** • **Hearing** ◦ Mean final hearing threshold: pure tone average was assessed using pure tone audiometry at 24 weeks. However, data could not be used as the number in each group and standard deviation were not reported. • **Disease-specific quality of life** ◦ Not reported • **Adverse event** ◦ Not reported **Secondary outcomes relevant to this review:**

	• **Presence/persistence of OME: proportion of children with persistence of OME**
	  ◦ ENT examination including pneumatic otoscopy and tympanometry at 24 weeks
	• **Generic health-related quality of life: mean (SD) change from baseline**
	  ◦ Glasgow Children's Benefit Inventory at 24 weeks
	• **Other adverse effects**
	  ◦ Minor nasal bleeding
	Other outcomes reported in the study:
	• Mean symptom score and change in symptom score (including nasal obstruction score, snoring score, rhinorrhoea score, cough score, OSA score, and total score)
	• Adenoid size
	• Change in OME (not further defined)

Funding sources	Not reported
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were noted • No prospective trial registration was identified • Baseline characteristics were not excessively similar between the 2 groups • No explanation is given for full follow-up • No implausible results were noted • Different numbers of participants were allocated to each group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “The children included in this study were divided into 2 groups randomly by chit selection into group A (study) and the group B (control).”
Allocation concealment (selection bias)	Unclear risk	No information provided on method of concealment to allow an assessment of risk of bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	It appears that participants may have been blinded, through the use of saline spray in the control group. However, no information is given regarding how blinding was maintained, for example, whether identical packaging was used for the intervention and comparator. No information is provided regarding blinding of study personnel, and this is an RCT with only 2 authors, therefore it is reasonably likely that the study personnel were also involved in allocating participants to treatment.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information is provided on whether outcome assessors were blind to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	High risk	Data are missing for hearing outcomes, specifically no SDs are reported and P values are missing from the main text. Only 48 participants underwent PTA testing, and it is unclear to which groups they were allocated.
Selective reporting (reporting bias)	High risk	No protocol or trial registration was found, however results are reported incompletely: Table 1 is referred to for information on the outcome ‘change in quality of life’ but data are not provided. Instead, these results are provided in the main text and in a more difficult to read/ interpret bar graph (figure 4, p 769). There are asterisks in table 1 which presumably refer to further information, but none is provided as there are no footnotes. Authors report data were collected at follow-up every 2 weeks for the first 8 weeks and then monthly for the next 16 weeks, but only data ‘post therapy’ are reported for the outcomes ‘mean hearing loss’ and ‘presence/

		persistence of OME' (p 768). The data collection time-points are not reported for the rest of the outcomes extracted here. Authors report 'Change in OME' in table 1 as an additional outcome but do not explain what this outcome is, how it was assessed, or discuss these results in the text Authors note "The observations were described in terms of mean, median, standard deviation, and 95% confidence interval for continuous data", but only the former is reported in the results (p 768)
Other bias	Low risk	No concerns.

Cengel 2006

Study characteristics	
Methods	Two-arm, parallel-group, quasi-randomised controlled trial with 6 weeks of follow-up

Participants	**Setting:**
	Single-centre, conducted in a University hospital in Turkey between October 2002 and June 2003
	Sample size:
	• **Number randomised:** 122 participants
	  ◦ 63 participants (relevant to this review)
	  ◦ 59 participants (with adenoid hypertrophy, not OME - not assessed in this review)
	• **Number completed:** 122 participants
	  ◦ 63 participants (relevant to this review)
	  ◦ 59 participants (with adenoid hypertrophy, not OME - not assessed in this review)
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Intranasal steroids group:
	  ▪ mean 6.9 years
	  ▪ range 3-15 years
	  ◦ No treatment group:
	  ▪ mean 6
	  ▪ range 3-13 years
	• **Gender:**
	  ◦ Intranasal steroids group:
	  ▪ males: 27/67 (45%)
	  ▪ females: 40/67 (55%)
	  ◦ No treatment group:
	  ▪ males: 25/55 (45%)
	  ▪ females: 30/55 (55%)
	NB. Baseline characteristics for age and gender are for the full cohort, those with adenoid hypertrophy as well as those with OME
	• **Number with bilateral disease**
	  ◦ Antibiotics group: 30/34 (88%)
	  ◦ No treatment group: 26/29 (90%)
	Inclusion criteria:
	Aged 3–15 years on the waiting list for adenoidectomy and/or ventilation tube placement. With documented persistent middle ear effusion by otoscopic examination for a minimum of 3 months at the time of entry in to the study; middle ear pressure less than -150mm H_2O and conductive hearing loss in audiometry supporting the diagnosis of OME; and, treatment with appropriate antibiotics at least twice before.
	Diagnosis:The ears were examined separately by otoscopy for tympanic membrane appearance and mobility was assessed by pneumatic otoscopy. A middle ear pressure

	less than -150mm H_2O and Jerger type B flat tympanogram were considered to support the diagnosis of OME. Conductive-type hearing loss was also thought to indicate the presence of effusion. **Exclusion criteria:** • Previous use of systemic or intranasal steroids • Surgery for these illnesses • Active upper airway infections in the previous 2 weeks • History of immune deficiency, hypersensitivity to mometasone furoate, or any systemic or local contraindication against corticosteroids • A craniofacial anomaly
Interventions	**Intranasal steroids (n = 34 randomised, n = 34 completed)** Intranasal mometasone furoate 100µg/day, one spray in each nostril once a day for 6 weeks **Comparator (n = 29 randomised, n = 29 completed)** No treatment.

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Not reported
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of ears with persistence of OME**
	  ◦ Tympanometry at 6 weeks
	Other outcomes reported in the study:
	• Adenoid/choana ration (A/C)
	• A symptom questionnaire consisted of a parental assessment of the patient's ear pain, ear popping, hearing loss, nasal obstruction, nasal discharge, snoring, mouth breathing and apnoea
	• Other outcomes were assessed for the entire group, including patients with adenoid hypertrophy, therefore are not of relevance to this review

Funding sources	Not reported
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were identified • This trial was published before 2010, so prospective registration was not required • Baseline characteristics of the 2 groups were not excessively similar • Full follow-up was reported, but this may be plausible for such a short duration of follow-up • No implausible results are noted • Different numbers of participants were recruited to each group, but quasi-randomisation was used

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The randomization process involved enrolling every second patient in the waiting list into the treatment and control groups consecutively. However, this method sometimes failed as some of the families did not want their children to be in the groups that they had been placed in and the patients were therefore included in the other group. However, the bias that occurred due to this occasional failure of the

		randomization process was not thought to influence the validity of the study." Comment: non-random allocation.
Allocation concealment (selection bias)	High risk	Quote: "The randomization process involved enrolling every second patient in the waiting list into the treatment and control groups consecutively. However, this method sometimes failed as some of the families did not want their children to be in the groups that they had been placed in and the patients were therefore included in the other group" Comment: allocation was not concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "As the study was designed to have no connection with any of the manufacturers of the drugs or the pharmaceutical industry at all, it was not possible to obtain a placebo, and therefore the study could not be double blinded." Comment: no blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "All the examinations of the patients were carried out by the authors of the paper, therefore the examiners were not blinded." Comment: no blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: There do not appear to be any missing outcome data.
Selective reporting (reporting bias)	Unclear risk	Comment: No protocol or trial registration was found.
Other bias	High risk	Comment: The short duration of follow-up may be insufficient to detect a difference between the groups.

Choung 2008

Study characteristics	
Methods	Five arm, parallel-group, randomised controlled trial with follow-up every 2 weeks for 3 months (for bilateral OME) or 6 months (for unilateral OME)

Participants	**Setting:**
	Single-centre, conducted in a University hospital in South Korea between June 2003 and March 2005
	Sample size:
	• **Number randomised:** 84 participants (100 children were initially included, but the 16 children lost to follow-up were excluded from the study)
	• **Number completed:** 84 participants
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Mean 69.0 months
	  ◦ Range 5 months to 12 years
	• **Gender:**
	  ◦ 57 (68%) males
	  ◦ 27 (32%) females
	• **Number with bilateral disease**
	  ◦ 68 (81%) bilateral
	  ◦ 16 (19%) unilateral
	• **Duration of disease: duration of recent OME**
	  ◦ mean 10.5 weeks (SD 14.8)
	• **Hearing thresholds: pure tone average (air conduction threshold)**
	  ◦ Right ears: mean 26.1 (SD 11.3) dB
	  ◦ Left ears: mean 26.4 (SD 11.0) dB
	• **Hearing thresholds: pure tone average (air-bone gap)**

	◦ Right ears: mean 22.1 (SD 13.6) dB ◦ Left ears: mean 23.8 (SD 12.1) dB **Inclusion criteria:** Children with OME as diagnosed by pneumatic otoscopy, tympanometry and pure tone audiography: • B or C tympanograms • Hearing loss >25dB on pure tone audiometry **Exclusion criteria:** • Children with AOM and fever or otalgia • Children with cleft palate • Children with developmental difficulties • Children with contraindications to medications • Participants lost to follow-up
Interventions	**Antibiotics group (n = 16 completed)** • Amoxicillin-clavulanate syrup (1 cc/kg, Augmex Duo syrup) for 2 weeks **Antibiotics and oral steroids group (n=18 completed)** • Amoxicillin-clavulanate syrup (1 cc/kg, Augmex Duo syrup) for 2 weeks • Prednisolone (1 mg/kg, Solondo) **Antibiotics and antihistamine group (n=15 completed)** • Amoxicillin-clavulanate syrup (1 cc/kg, Augmex Duo syrup) for 2 weeks • Ebastine (0.2 cc/kg, Ebastel) **Antibiotic, steroid and antihistamine group (n=17 completed)** • Amoxicillin-clavulanate syrup (1 cc/kg, Augmex Duo syrup) for 2 weeks • Prednisolone (1 mg/kg, Solondo) • Ebastine (0.2 cc/kg, Ebastel) One additional study arm received mucolytics, but data have not been extracted as not relevant for this review.
Outcomes	**Primary outcomes relevant to this review:** • **Hearing** ◦ Not reported • **Disease-specific quality of life** ◦ Not reported • **Adverse event** ◦ Not reported **Secondary outcomes relevant to this review:** • **Presence/persistence of OME: Proportion of children with persistence of OME** ◦ No resolution of OME when observed over 6 months, using pneumatic otoscopy, tympanography and pure tone audiograph **Other outcomes reported in the study:** Number of children receiving VT insertion Overall resolution according to laterality of disease
Funding sources	Not reported
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were noted • The trial was published before 2010 therefore prospective registration was not required • Baseline characteristics for each group are not reported separately, therefore we are unable to assess similarities between the groups

	• Plausible loss-to-follow-up was reported • No implausible results were noted • Different numbers of participants were randomised to each group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: “After obtaining consent from parents or guardians, we consecutively and randomly prescribed...” Comment: no information reported on sequence generation.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No description of blinding and therefore participants were likely to be aware of their group allocation.
Blinding of outcome assessment (detection bias) All outcomes	High risk	The authors provide no description of blinding of outcome assessment, and therefore it is likely they were unblinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The 16 participants lost to follow-up were excluded from the study, and the reasons for their loss to follow-up not reported. It is therefore unclear whether the reason for the missing outcome data is likely to be related to true outcome.
Selective reporting (reporting bias)	Unclear risk	No protocol or trial registration was found.
Other bias	High risk	It is unclear whether follow-up was consistent for all participants in the trial. Outcome data for different participants may have been collected at different times, therefore this may not be an accurate portrayal of efficacy at 3 months.

Hemlin 1997

Study characteristics

Methods	Three-arm, parallel-group, randomised controlled trial with 10 days of treatment and 12 to 21 days follow-up

Participants	**Setting:**
	Single-centre, conducted in a hospital ENT department in Sweden. No study dates reported.
	Sample size:
	• **Number randomised:** 142 participants
	• **Number completed:** 140 participants
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Antibiotics and oral steroids group: mean 67 months
	  ◦ Antibiotics and placebo group: mean 63 months
	  ◦ Placebo group: mean 63 months
	• **Gender:**
	  ◦ Antibiotics and oral steroids group:
	  ▪ 36 males
	  ▪ 23 females
	  ◦ Antibiotics and placebo group:
	  ▪ 37 males
	  ▪ 24 females
	  ◦ Placebo group:
	  ▪ 14 males
	  ▪ 6 females
	Inclusion criteria:

	Aged 2 to 12 years. Unilateral or bilateral secretory otitis media of at least 3 months duration, confirmed by otomicroscopy and tympanometry. Immobile and pale eardrum on otomicroscopy and a type B tympanogram in at least one of the ears **Exclusion criteria:** • Severe underlying disease • Immunologic deficiency • Cleft palate • Known or suspected allergy to penicillin or cephalosporins • Antibiotic treatment within the preceding 4 weeks • Previous inclusion in the study
Interventions	**Antibiotics and oral steroids group (n = 59 completed)** • Liquid suspension of cefixime (20 mg/mL) administered in a dosage of 8 mg/kg body weight in 2 doses (morning and evening) per day, for 10 consecutive days • Single dose of a betamethasone tablet (6 mg) on the morning of day 10 **Antibiotics and placebo group (n = 61 completed)** • Liquid suspension of cefixime (20 mg/mL) administered in a dosage of 8 mg/kg body weight in 2 doses (morning and evening) per day, for 10 consecutive days • Placebo tablet with a similar appearance to the betamethasone tablet administered on day 10 • Antimicrobial agents other than the study drugs were not allowed during the study period **Placebo group (n = 20 completed)** • Placebo suspension administered in same method to cefixime in other groups • Placebo tablet with a similar appearance to the betamethasone tablet administered on day 10

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Not reported
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Anaphylaxis (presumed to be assessed but not to have occurred)
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of children with persistence of OME**
	  ◦ Not cured of middle ear effusion at 2 weeks, measured using otomicroscopy and tympanometry. Defined as any child who did not have a normal middle ear status – pale eardrum with normal mobility and type A tympanogram or type C with a peak of more than -300 decapascals
	• **Other adverse effects**
	  ◦ Proportion of children with vomiting
	  ◦ Proportion of children with diarrhoea
	  ◦ Proportion of children with dermatitis
	  ◦ Proportion of children with loose stools
	  ◦ Proportion of children with stomach pain
	  ◦ Proportion of children with gastroenteritis
	Other outcomes reported in the study:
	Some longer term outcomes reported, but only for those who were healed at early follow-up

Funding sources	It is noted that ASTRA AB supplied the drugs and patient registration forms, and assisted in the data analysis

Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were noted • This trial was published prior to 2010, therefore prospective registration was not required • Limited baseline characteristics are reported, but no concerns with the available data • Plausible loss to follow-up was reported • No implausible results were identified • Randomisation was stated to be 3:3:1, and numbers are plausible

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Treatment with cefixime or cefixime plus betamethasone or placebo was allocated at random with a ratio of 3:3:1". Comment: No information on generation of random sequence.
Allocation concealment (selection bias)	Unclear risk	No information on how group allocation was concealed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The drugs were dispensed double-blind by a double-dummy technique". Comment: This quote suggests trial personnel dispensing the treatments were blinded. As the study is placebo controlled it also suggests that participants were blinded to allocation.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details regarding whether the outcome assessors were blinded to treatment allocation. Outcomes were not objectively measured.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Reasons for loss to follow-up at 6 weeks and 6 months are not reported, and there is a slight imbalance in the numbers of participants lost to follow-up at each of these time points: 3/ 26 (12%) lost in the cefixime plus betamethasone group versus 1/ 12 (8%) in the cefixime plus placebo group at 6 weeks; 1/ 7 (14%) lost in the cefixime plus betamethasone group versus 0/ 8 (0%) in the cefixime plus placebo group at 6 months. There is potential that the reason for the missing outcome data is related to true outcome for presence/ persistence of OME.
Selective reporting (reporting bias)	Unclear risk	No protocol was available.
Other bias	High risk	High risk of bias for short term follow-up as there is insufficient time to detect a difference between the groups.

Hussein 2017

Study characteristics

Methods	Three-arm, parallel-group randomised controlled trial with one week, and 3 and 9 month follow-up
Participants	**Setting:** Single-centre, Saudi Airlines Medical Centre, Saudi Arabia between June 2013 and November 2016 **Setting:** Single-centre, conducted in a University ENT Department in China between June 2009 and March 2011 **Sample size:** • **Number randomised:** 303 participants total (202 relevant for this review) • **Number completed:** 290 participants **Participant (baseline) characteristics:**

	• **Age:**
	  ◦ Mean 5.7 years
	  ◦ Range 2-11 years
	• **Gender:**
	  ◦ Male to female ratio 1:1.19
	• **Duration of disease**
	  ◦ Antibiotics group: 10.2 days (6.58 SD)
	  ◦ No treatment group: 11.1 days (6.45 SD)
	• **Hearing thresholds**
	  ◦ Antibiotics group: mean 10.2 dB (SD 6.83)
	  ◦ No treatment group: mean 30.6 dB (SD 7.82)
	Inclusion criteria:
	Aged 2 to 11 years. Clinical evidence of bilateral middle-ear effusion, bilateral type B tympanogram and hearing loss of more than 20dB HL.
	Exclusion criteria:
	Down's syndrome, cilial abnormalities such as Kartagener's syndrome, cleft palate, growth retardation, immunodeficiency states, genetic causes of conductive hearing loss, diabetes mellitus, renal failure, hypertension or congestive heart failure, and nasal tumours or frequent epistaxis.
	Children in need of steroids for other medical diseases such as uncontrolled asthma, children who had received a live vaccine in the preceding 4 weeks, children already with ventilation tubes or scheduled or willing to have ventilation tubes in the next 6 months, and children with a history of acute otitis media in the 3 months prior to enrolment in the study.

Interventions	**Oral steroids group (n=101 randomised)** Seven days of oral soluble prednisolone, single daily doses of 1 mg/kg (not exceeding 20 mg for children aged 2–5 years or 30 mg for those aged 6–11 years) **Watchful waiting group (n=101 randomised)** No intervention One further arm received a combination of oral and nasal steroids, but this was not a comparison of interest for this review, therefore data have not been extracted

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Not reported
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of children persistence of OME**
	  ◦ Persistent OME: type B tympanogram plus hearing loss >20dB at 3 and 9 months
	  ◦ Incomplete resolution: type C1 or C2 with or without hearing loss of more than 20dB at 3 and 9 months
	Other outcomes reported in the study:
	Outcome data at 6 weeks and 6 months

Funding sources	Not reported
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were noted • No prospective trial registration was identified • No information is presented on baseline characteristics

	• Plausible loss to follow-up is reported • No implausible results were noted • Identical numbers were randomised to each group, with no report of blocked randomisation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Patients were randomly assigned, using random numbers…” Comment: Adequate method.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were aware of treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: “The audiology evaluation was carried out by the last author, who was blinded regarding the group allocation and treatment of patients”. Comment: the quote suggests that all outcomes were assessed blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Relatively few dropouts, insufficient numbers to substantially alter conclusions.
Selective reporting (reporting bias)	Unclear risk	No protocol available to compare.
Other bias	Low risk	No concerns.

Karlidag 2002

Study characteristics	
Methods	Three-arm, unblinded, parallel group randomised controlled trial with 8 weeks of treatment and follow-up

Participants	**Setting:**
	Single-centre, conducted in Turkey between January to December 2001
	Sample size:
	• **Number randomised:** 42 participants
	• **Number completed:** 42 participants
	An additional 20 patients were randomised to antibiotics alone. These were not included in this review.
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Intranasal steroids and antibiotics group: mean 6.57 years (SD 3.17)
	  ◦ Watchful waiting group: mean 4.58 years (SD 2.30)
	• **Gender:**
	  ◦ Intranasal steroids and antibiotics group:
	  ▪ 14 males
	  ▪ 6 females
	  ◦ Watchful waiting group:
	  ▪ 11 males
	  ▪ 11 females
	Inclusion criteria:
	Aged 2 to 12 years. Diagnosed with otitis media with effusion based on:

	• History: hearing loss, feeling of fullness in the ear, watching TV with a loud volume, apathy, comprehension and speech impairment • Otoscopy: grey, dull or light pink eardrum with thickening, retraction or increased vascularity • Rinne negativity on tuning fork test • Conductive hearing loss • Type B or C tympanogram **Exclusion criteria:** • Previous insertion of VT • Allergy to ampicillin/sulbactam • Antibiotic or nasal spray use in the past 2 weeks • Immune disorders or systemic illnesses
Interventions	**Steroids and antibiotics group (n = 20 randomised, n = 20 completed)** Ampicillin/sulbactam 25 mg/kg/day, administered in 2 divided doses, orally for 8 weeks. Plus budesonide intranasal spray, 200µg/day administered in 2 divided doses for 8 weeks **Antibiotic group (n = 20 randomised, n = 20 completed)** Ampicillin/sulbactam 25 mg/kg/day, administered in 2 divided doses, orally for 8 weeks **Watchful waiting group (n = 22 randomised, n = 22 completed)** Active monitoring

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Not reported
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of ears with persistence of OME**
	  ◦ At 8 weeks

Funding sources	None reported
Declarations of interest	Not reported
Notes	**Research integrity checklist:** • No retractions of expressions of concern • This study was published prior to 2010, therefore prospective registration was not required • Limited baseline characteristics were reported, but we do not have concerns with the available data • Full follow-up was reported, with no reason given • No implausible results were identified • Different numbers of participants were allocated to the groups

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants were "randomly allocated" into 3 groups. No information on sequence generation.
Allocation concealment (selection bias)	Unclear risk	No details on concealment of allocation.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were aware of treatment allocation.

Blinding of outcome assessment (detection bias) All outcomes	High risk	Unblinded trial.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Full follow-up is reported.
Selective reporting (reporting bias)	Unclear risk	No protocol available to compare.
Other bias	High risk	High risk of bias for short term follow-up as there is insufficient time to detect a difference between the groups.

Khanam 2022

Study characteristics	
Methods	Three-arm, parallel-group randomised controlled study with 12 weeks duration of treatment and follow-up. For the purposes of this review only 2 arms are of relevance. The remaining group received a combination of nasal steroid and oral montelukast.
Participants	**Setting:** Single-centre, conducted in the ENT and paediatric department of a tertiary hospital in Bangladesh **Sample size:** • **Number randomised:** 40 participants • **Number completed:** 40 participants **Participant (baseline) characteristics:** • **Age** ◦ Only reported for the whole cohort ◦ Aged 2-3 years: 12 participants ◦ Aged 4-5 years: 22 participants ◦ Aged 5-6 years: 20 participants ◦ Aged 7-8 years: 4 participants ◦ Aged 9-10 years: 1 participant ◦ Aged 11-12 years: 1 participant • **Gender** ◦ 38 males: 22 females • **Hearing threshold** ◦ Nasal steroid group: 33.65 ± 8.12 dB ◦ Control group: 33.3 ± 6.78 dB **Inclusion criteria:** Children aged 2-12 years old diagnosed with bilateral OME for at least 3 months **Exclusion criteria:** Previous intranasal or systemic steroid use Previous surgery for these illnesses Sensorineural hearing loss Nasal polyp, sinusitis, or active upper respiratory tract infection in the preceding 2 weeks History of immunodeficiency Hypersensitivity to mometasone furoate or other steroid Down syndrome or cranio-facial abnormality
Interventions	**Steroid group:** Randomised N=20. Completed N=20. 1 spray mometasone furoate (100 µg/day) into each nostril once daily for 12 weeks **Control group:**

	Randomised N=20. Completed N=20. Nosomist spray (normal saline) used as above
Outcomes	Hearing threshold Persistence of OME
Funding sources	None reported
Declarations of interest	The authors declared no conflicts of interest
Notes	**Research integrity checklist:** • No retractions or expressions of concern were identified • No prospective trial registration was available • Limited baseline information was reported, but no concerns over excessive similarity between the groups with the data available • Plausible loss to follow-up was reported • It appears that equal numbers of participants were randomised to each group, without any description of blocked randomisation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Total 60 children who participated in this study were randomly divided into 3 equal groups by a random number table."
Allocation concealment (selection bias)	Unclear risk	No information is provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Study participants were apparently blinded to intervention. However, there is no information to describe whether study personnel were also blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information is provided to indicate whether outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	6 participants were excluded from the analysis, however, it is unlikely that this would be sufficient to introduce bias to the results.
Selective reporting (reporting bias)	Unclear risk	No protocol was available for comparison.
Other bias	Low risk	No other issues were identified.

Lambert 1986

Study characteristics

Methods	Two-arm, double blind, parallel-group, randomised controlled trial, with follow-up at 7-10 days following treatment completion then at 1 and 3 months for children whose effusion cleared at follow-up

Participants	**Setting:**
	Single-centre, conducted in an otolaryngology clinic in the USA between December 1982 and February 1985
	Sample size:
	• **Number randomised:** 60 participants
	• **Number completed:** 60 participants (at initial follow-up after completion of first treatment regimen
	  ◦ 32 of 32 participants at follow-up after second treatment regimen (of those who experienced treatment failure after the first treatment regimen)
	  ◦ 29 of 36 at longer term follow-up (of those who experienced OME clearance after the first or second treatment regimen)
	Participant (baseline) characteristics:
	Baseline characteristics data are not reported either per treatment group or overall; they are reported according to whether the participants are in the 'prednisone-cleared' (n=18: n=14 participants initially allocated to prednisone, n=4 participants initially allocated to placebo then crossed over to prednisone), 'placebo-cleared' (n=18: n=14 participants initially allocated to placebo, n=4 participants initially allocated to prednisone then crossed over to placebo) or 'failed' (n=24: n=10 initially allocated to placebo then

crossed over to prednisone, n=14 initially allocated to prednisone then crossed over to placebo) groups

- **Age:**
  - Prednisone cleared (n=18):
    - mean 6.7 years
    - range 2-15 years
  - Placebo cleared (n=18):
    - mean 4.9 years
    - range 2-11 years
  - Failed (n=24):
    - mean 6.4 years
    - range 2-14 years
- **Gender:**
  - Prednisone cleared (n=18):
    - 11 (61%) males
    - 7 (39%) females
  - Placebo cleared (n=18):
    - 11 (61%) males
    - 7 (39%) females
  - Failed (n=24):
    - 15 (63%) males
    - 9 (38%) females
- **Duration of disease: middle ear effusion**
  - Prednisone cleared (n=18):
    - mean 2.7 months
    - range 2-6 months
  - Placebo cleared (n=18):
    - mean 2.7 months
    - range 2-4 months
  - Failed (n=24):
    - mean 2.7 months
    - range 2-6 months
- **Hearing thresholds:**
  - Prednisone cleared (calculated from 31/34 ears):
    - mean 28 dB
    - range 13-40 dB
  - Placebo cleared (calculated from 31/34 ears):
    - mean 26 dB
    - range 12-42 dB
  - Failed (calculated from 35/41 ears):
    - mean 37 dB
    - range 10-47 dB
- **Other measure of hearing status: speech reception thresholds**
  - Prednisone cleared:
    - mean 30 dB
    - range 10-45 dB
  - Placebo cleared:
    - mean 25 dB
    - range 10-40 dB
  - Failed:
    - mean 30 dB

	▪ range 10-50 dB **Inclusion criteria:** Aged 2 years or older with suspected middle ear effusion confirmed by physical examination and a flat tympanogram (or by physical examination and >10dB conductive hearing loss), who had effusion for 2 months Otitis media with effusion was confirmed using the following criteria: • Physical examination using pneumatic otoscopy (middle ear effusion was suspected if the tympanic membrane was opaque and did not move in response to the insufflation of air into a sealed external auditory canal) and a flat tympanogram without a peak, OR • Physical examination using pneumatic otoscopy (as above) and >10dB conductive hearing loss, assessed using pure-tone and speech audiometry* Tympanometry was done using a Teledyne Avionics TA-2C electro-acoustic impedance meter, and tympanograms assessed using Jerger or Pittsburgh classification (type B or types 12, 13 or 14, respectively, were assessed as OME) **Exclusion criteria:** • Air-fluid level or air bubbles in the middle ear • Inflammation of the tympanic membrane or otalgia • Atelectasis of the tympanic membrane (adhesive otitis media) • Prior middle ear or mastoid surgery (with the exception of myringotomy, with or without VTs)
Interventions	**Prednisone (oral steroid) group (n = 32 randomised)** • Prednisone elixir (1 mg/cc) for 14 days, administered once daily according to the following schedule: 1.5 mg/kg/day for 4 days; 0.75 mg/kg/day for 4 days; 5 mg or 10 mg (depending on the child's weight) every other day for 6 days • Amoxicillin, either 125 mg or 250 mg, 3 times daily • Participants who had no substantial changes (on examination or audiometrically) at follow-up 7-10 days after completion of initial treatment were crossed over to the alternate regimen for 14 days and received follow-up 7-10 days after treatment completion • Participants who had improved audiometrically but still had otoscopic evidence of MEE after initial or alternate treatment regimen were given a 7-day course of the same medication (steroid dose: 0.75 mg/kg/day for 3 days, then 5 mg or 10 mg (depending on the child's weight) every other day for 4 days) and followed up 7-10 days later • Participants who still had effusions at follow-up after alternate treatment regimen were advised to undergo VT insertion **Placebo group (n = 28 randomised)** • Placebo (cherry flavoured lactose syrup) administered in the same manner as prednisone • Amoxicillin, either 125 mg or 250 mg, 3 times daily • Participants who had no substantial changes (on examination or audiometrically) at follow-up 7-10 days after completion of initial treatment were crossed over to the alternate regimen for 14 days and received follow-up 7-10 days after treatment completion • Participants who had improved audiometrically but still had otoscopic evidence of MEE after initial or alternate treatment regimen were given a 7-day course of the same medication and followed up 7-10 days later • Participants who still had effusions at follow-up after alternate treatment regimen were advised to undergo VT insertion **Treatment used before entry into the trial** • 26/60 children included had histories of VTs (7/ 18 participants in the 'prednisone-cleared group'; 6/ 18 in the 'placebo-cleared group'; 13/ 24 in the treatment failure group) • 47/ 60 children had received antibiotics for their effusion during the 5 weeks preceding entry into the study (14/ 18 participants in the 'prednisone-cleared group'; 14/ 18 in the 'placebo-cleared group'; 19/ 24 in the treatment failure group)

	Background interventions administered to all participants • All participants received either 125 mg or 250 mg amoxicillin 3 times daily as part of their treatment regimen • Participants with unresolved effusion by follow-up were crossed over to the alternative regimen, and therefore some participants received both interventions

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing: mean (range) change in hearing thresholds (dB) from baseline**
	  ◦ Only reported at the end of full follow-up (after cross over) - unable to use these data
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of children with persistence of OME**
	  ◦ Tympanometry, otoscopy and audiometry - 7-10 days after completion of initial treatment regimen or 7-10 days after repetition of initial treatment regime (only for participants who had improved audiometrically after first round of treatment but still had evidence of effusion)
	• **Episodes of acute otitis media: proportion exceeding a specified cut-off value of episodes of AOM**

Funding sources	Not reported
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retraction notices or expressions of concern were identified • Prospective registration was not required (trial published prior to 2010) • Baseline characteristics cannot be compared for the 2 randomised groups, therefore we cannot assess for similarity • Full follow-up is reported, but this may be plausible for short follow-up • No implausible results were identified • Different numbers were randomised to each group

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: “Patients meeting the aforementioned criteria randomly received, in a double-blind fashion, prednisone or placebo for 14 days as the initial treatment”. Comment: no information on random sequence generation
Allocation concealment (selection bias)	Unclear risk	No information on how allocation was concealed.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The author describes this as a double blind trial. A placebo was used, but no information is provided on whether taste/appearance differed between the interventions. This is a single-author RCT, and no information is provided on how results of randomisation were concealed from this author.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information is provided on how blinding was maintained when this was a single-author RCT.
Incomplete outcome data	Low risk	No missing outcome data.

(attrition bias) All outcomes		
Selective reporting (reporting bias)	Unclear risk	No protocol is available.
Other bias	High risk	High risk of bias for short term follow-up as there is insufficient time to detect a difference between the groups.

Lildholdt 1982

Study characteristics	
Methods	Two-arm, double-blind, parallel-group, randomised controlled trial, with follow-up at one and 2 months
Participants	**Setting:** Single-centre, conducted in a private ENT clinic in Denmark during the autumn, winter and spring of 1980 and 1981 **Sample size:** • **Number randomised:** 70 participants • **Number completed:** unclear **Participant (baseline) characteristics:** • **Age:** ◦ Intranasal steroids group: ▪ 4-5 years: 14 ▪ 6-7 years: 11 ▪ ≥8: 10 ◦ Placebo group: ▪ 4-5 years: 12 ▪ 6-7 years: 14 ▪ ≥8: 9 ◦ Overall: ▪ mean 6.5 years ▪ range 4-14 years • **Gender:** ◦ Intranasal steroids group: ▪ 18 (51%) males ▪ 17 (49%) females ◦ Placebo group: ▪ 20 (57%) males ▪ 15 (43%) females • **Hearing thresholds per ear: assessed using pure tone audiometry** ◦ Intranasal steroids group: (n=56 ears) mean 22.5 (SD 9.5) dB ◦ Placebo group: (n=51 ears) mean 26.0 (SD 15.2) **Inclusion criteria:** Aged 4 or more years. Primary cases of unilateral or bilateral middle ear effusion, or a new bout of unilateral or bilateral middle ear effusion in a child with previous disease. No sign of acute infection in the upper airway or the middle ear. Plus all of the following 3 criteria. • Flat tympanogram • Hearing loss at audiometry • Otomicroscopic signs of an effusion **Exclusion criteria:** Not reported
Interventions	**Intranasal steroids group (n = 35 randomised)**

	Beclomethasone dipropionate nasal spray administered twice in each nostril (100µg per nostril) twice a day, for a total of 400µg daily, for one month. The dosage corresponded to that recommended for perennial and seasonal hay fever. **Placebo group (n = 35 randomised)** Placebo nasal spray; it is unclear if participants in this group were instructed to administer this in the same way to the active drug group. **Background interventions administered to all participants** Antibiotics were prescribed to children if a fever was present, but otherwise no other treatment was given

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Mean (SD) change in hearing thresholds (dB): hearing gain per ear at 2 months, measured by pure tone audiometry
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of ears with persistence of OME**
	  ◦ Middle ear condition unchanged (B-B) per ear at one month and 2 months, assessed by tympanometry and otoscopy
	• **Other adverse effects**
	  ◦ Narrative summary reported

Funding sources	It is noted that the medications were provided through Essex Pharma, Denmark, a division of the Schering-Plough Corporation, Kenilworth, NY, USA
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were identified • This trial was published before 2010, so prospective registration was not required • Baseline characteristics of the 2 groups are not excessively similar • Plausible loss to follow-up was reported • No implausible results were identified • Equal numbers of participants were allocated to each group, without the use of blocked randomisation

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: “The commercially available nasal spray was handed over from a large quantity that was consecutively numbered to contain at random either the active drug (A) or the vehicle = placebo (P)”. Comment: it is unclear whether the participants were given alternating sprays in a particular order, or generally how the allocation sequence was generated.
Allocation concealment (selection bias)	High risk	Quote: “The commercially available nasal spray was handed over from a large quantity that was consecutively numbered to contain at random either the active drug (A) or the vehicle = placebo (P). The code for the numbering was not broken until the study had been finished." Comment: adequate allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “The commercially available nasal spray was handed over from a large quantity that was consecutively numbered to contain at random either the active drug (A) or the vehicle = placebo (P). The code for the numbering was not broken until the study had been finished." Comment: adequate blinding of participants and personnel.
Blinding of outcome assessment	Low risk	This is a double-blind trial where participants were exclusively assessed by the trial authors, who did not break the numbering code until after the study was finished.

(detection bias) All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The authors note that 8 participants did not return for the final follow-up at 2 months and that “in a few cases” treatment was discontinued due to the child’s fear of the power of the nasal spray, however they do not report which groups these children were part of (Lildholdt 1982, Table II, p 134). It is therefore also unclear how many children were lost to follow-up. Using the results for the outcome ‘presence/ persistence of OME’, it can be deduced that there are data for 21 fewer ears at 2 months follow-up compared to 1 month follow-up, at least for tympanometry data (10 fewer ears in active treatment group, 11 fewer in placebo group), but it is unclear how many children this equates to, or how this affects the other outcomes. It seems as though missing outcome data are balanced in numbers across intervention groups, but this is not certain and the reasons for missing data across groups are unclear
Selective reporting (reporting bias)	High risk	For the outcome ‘hearing’, parents’ opinions of any changes in the hearing ability of their child were evaluated and authors note there was “no difference between the two groups of treatment” in terms of parental estimate, however these results are not reported quantitatively. Otomicroscopy results are only partly reported narratively, with no quantitative data reported and no indication whether this contributed to interpretation of results. Adverse events data are only reported narratively, with no quantitative data reported. Audiometric results are only reported as an average of results at 1 and 2 months follow-up, not separately for both time points. It is not reported which participants discontinued treatment due to their child’s response to the power of the nasal spray, which may have effected adverse events data.
Other bias	High risk	High risk of bias for short term follow-up as there is insufficient time to detect a difference between the groups. The diagnostic criteria for MEE appears to be different at follow-up to the criteria outlined at baseline. It appears that assessments at follow-up were based solely on tympanometry at follow-up, whereas otomicroscopy and audiometry were also used to define MEE at baseline.

Macknin 1985

Study characteristics	
Methods	Two-arm, double-blind, parallel-group, randomised controlled trial with 6 weeks of follow-up

Participants	**Setting:**
	Single-centre, conducted in a paediatric department of a hospital in the USA between January 1981 and January 1982
	Sample size:
	• **Number randomised:** 49 participants
	• **Number completed:** 49 participants
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Oral steroids group:
	  ▪ mean 42 months
	  ▪ median 34 months
	  ◦ Placebo group:
	  ▪ mean 46 months
	  ▪ median 40 months
	• **Gender:**
	  ◦ Oral steroids group:
	  ▪ 20 males (70%)
	  ▪ 6 females (23%

	◦ Placebo group: ▪ 11 males (48%) ▪ 12 females (52%) • **Number with bilateral disease** ◦ Oral steroids group ▪ bilateral 15 (58%) ▪ unilateral 11 (42%) ◦ Placebo group ▪ bilateral 18 (78%) ▪ unilateral 5 (22%) **Inclusion criteria:** Middle ear effusions had persisted 3 weeks after the diagnosis of nonsuppurative otitis media or 6 weeks after the diagnosis of acute otitis media. Middle ear effusion was defined by Bluestone and Cantekin's algorithm combining pneumatic otoscopy and tympanometry. **Exclusion criteria:** • Patients with tympanostomy tubes in place • Patients having illnesses requiring antimicrobial treatment different from the study regimen, immune deficiencies, current steroid treatment • Temperature greater than 37.7^{o} C (100^{o}F) • Those without a telephone for daily follow-up calls
Interventions	**Oral steroids group (n = 26 randomised, n = 26 completed)** Oral dexamethasone, tapering dose for 13 days. The dosing schedule was 0.15 mg/kg to a maximum of 6 mg once a day for 2 days; 0.075 mg/kg to a maximum of 3 mg once a day for 2 days; 0.0375 mg/kg to a maximum of 1.5 mg once a day for 3 days; and 1.5 mg every other day for 3 doses for patients weighing more than 40kg and 0.0375 mg/ kg to a maximum of 0.75 mg for 3 doses for patients weighing less than 40kg. **Comparator (n = 23, n = 23 completed)** Placebo **Treatment used before entry into the trial** If initially diagnosed with AOM, children were given amoxicillin 50 mg/kg/d divided 3 times a day to a maximum of 250 mg 3 times a day for a total of 10 days
Outcomes	**Primary outcomes relevant to this review:** • **Hearing** ◦ Authors report the proportion of children with improvement of hearing by 10 dB or more at 6 weeks. However, no data on the return to normal hearing or mean hearing threshold were reported • **Disease-specific quality of life** ◦ Not reported • **Adverse event** ◦ Not reported **Secondary outcomes relevant to this review:** • **Presence/persistence of OME: proportion of children with persistence of OME** ◦ Persistence of OME in one or both ears at 6 weeks
Funding sources	Not reported
Declarations of interest	None reported
Notes	Trial terminated after 49 patients as only 6% cure rate in steroid group **Research integrity checklist** • No retractions or expressions of concern were identified • Trial was published before 2010, therefore prospective registration was not required

	• Baseline characteristics of the groups are not excessively similar • Plausible loss to follow-up was reported • No implausible results were identified • Numbers allocated to each group are different

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: ""Randomization was performed by the pharmacist with a table of random numbers designed to balance each stratified characteristic after every four subjects." Comment: a table of random numbers was used to generate the sequence.
Allocation concealment (selection bias)	Low risk	Quote: ""Randomization was performed by the pharmacist with a table of random numbers designed to balance each stratified characteristic after every four subjects." Comment: third party allocation.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The study is described as "double-blind" but it is not clear who is blinded. It is unclear what form the placebo took so it is not possible to determine whether participants and personnel could identify their group allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Tympanometry was performed and interpreted by a "blinded" pediatric audiologist on a calibrated Madsen Z073 impedance bridge." Comment: The study is also described as "double-blind".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is unclear how many children were recruited to the study, data is reported on 49 participants. A further 12 children, approximately, did not complete the study as planned.
Selective reporting (reporting bias)	Unclear risk	No protocol was found.
Other bias	High risk	High risk of bias for short term follow-up as there is insufficient time to detect a difference between the groups. Study was terminated early due to very low cure rate in the first 49 recruited patients. A sample size calculation found that 81 children were needed per group (total of 162).

Mandel 2002

Study characteristics	
Methods	Four arm, parallel-group, randomised controlled trial with 28 days of treatment and follow-up

Participants	**Setting:**
	Single-centre, conducted in a children's hospital in the USA between August 1994 and June 1999
	Sample size:
	• **Number randomised:** 144 participants
	• **Number completed:** 132 participants
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Oral steroids group
	  ▪ 12-23 months: 15 (30.5%)
	  ▪ 2-5 years: 33 (45.2%)
	  ▪ 6-9 years: 25 (34.2%)
	  ◦ Placebo group
	  ▪ 12-23 months: 14 (19.7%)
	  ▪ 2-5 years: 31 (43.7%)
	  ▪ 6-9 years: 26 (36.6%)

	• **Gender:**
	  ◦ Oral steroids group: 41 males (56.2%)
	  ◦ Placebo group: 44 males (62%)
	• **Number with bilateral disease**
	  ◦ Oral steroids group: n=51 (69.9%)
	  ◦ Placebo group: n=50 (70.4%)
	• **Hearing thresholds: Pure Tone Audiometry**
	  ◦ Oral steroids group: n=53
	  ▪ Right: mean 20.31 dB
	  ▪ Left: mean 26.51 dB
	  ◦ Placebo group: n=52
	  ▪ Right: 23.46 dB
	  ▪ Left: 24.84 dB
	• **Other measure of hearing status: Speech Awareness Thresholds**
	  ◦ Oral steroids Group: mean 22.06 (n=17)
	  ◦ Placebo group: mean 20.33 (n=15)
	• **Number of doctor-diagnosed AOM episodes in previous 12 months:**
	  ◦ Oral steroids group: n=59 (80.8%)
	  ◦ Placebo group: n=57 (80.3%)
	Inclusion criteria:
	Aged 1 to 9 years with unilateral or bilateral middle ear effusion
	The determination of the presence or absence of effusion was based on a decision tree algorithm that combined admittance testing and pneumatic otoscopy by a validated otoscopist
	The following set of criteria using tympanometric width (TW) to categorise middle ear status was used: TW ≤150 no OME; TW ≥ 350 =OME; TW between 150 and 350 = diagnose by otoscopy. The finding of fluid levels or bubbles on otoscopic examination superseded the above rules and automatically led to the diagnosis of OME.
	Exclusion criteria:
	• Hypersensitivity or significant adverse reactions to penicillins
	• Previous tonsillectomy and/or adenoidectomy
	• Previous ear surgery other than tympanocentesis or myringotomy with or without tube insertion
	• History of seizure disorder, diabetes mellitus, asthma requiring daily medication, or any health condition that could make entry potentially dangerous
	• Medical conditions with a predisposition for MEE, such as cleft palate, Down syndrome, congenital malformations of the ear, cholesteatoma, or chronic mastoiditis; severe retraction pockets; acute or chronic diffuse external otitis
	• Perforation of the tympanic membrane
	• Intracranial or intratemporal complications of MEE
	• Upper respiratory obstruction attributable to tonsil or adenoid enlargement or both with cor pulmonale, sleep apnoea, or severe dysphagia
	• Conductive hearing loss attributable to destructive changes in the middle ear
	• Sensorineural hearing loss
	• Distance from CHP that would make follow-up difficult
	• History of varicella exposure within the previous 30 days (if never had clinical varicella or varicella vaccine) or clinical varicella in the previous 3 weeks
	• History of measles exposure in the previous 30 days
	• Immunisation in the previous 30 days

Interventions	**Oral steroids plus antibiotics group (n=73 randomised)** Prednisone syrup 0.5 mg/kg given twice a day on days one through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then given once a day on days 11 through 14 (total daily dose 0.5 mg/kg, maximum 15 mg/d) Amoxicillin 40 mg/kg/day in 3 divided doses for 14 days

	Placebo plus antibiotics group (n=71 randomised) Placebo and amoxicillin as above

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing:** mean (SD) final hearing threshold (dB)
	  ◦ Air conduction Pure Tone Audiometry or play audiometry at 4 weeks
	  ◦ Visual reinforcement audiometry at 4 weeks
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of children with persistence of OME**
	  ◦ Presence or absence of effusion based on decision tree algorithm at 4 weeks
	• **Episodes of acute otitis media: Mean number of episodes**
	  ◦ Between 2 and 4 weeks
	• **Other adverse effects**
	  ◦ Hyperactivity
	  ◦ Increased appetite at 2 and 4 weeks
	  ◦ Vomiting at 2 and 4 weeks
	  ◦ Diarrhoea at 2 and 4 weeks
	  ◦ Irritability at 2 and 4 weeks
	  ◦ Abdominal discomfort at 2 and 4 weeks
	  ◦ Hives at 2 and 4 weeks
	  ◦ Other rash at 2 and 4 weeks
	Other outcomes reported in the study:
	Detection of bacterial biofilm in the middle ear

Funding sources	This study was supported by grant DC01693 from the National Institute on Deafness and Other Communication Disorders, National Institutes of Health. Muro Pharmaceutical, Inc (Tewksbury, MA) provided the prednisolone and its placebo for this study. SmithKline Beecham Pharmaceuticals (Collegeville, PA) provided amoxicillin and its placebo for this trial as well as amoxicillin-clavulanate for intercurrent infections.
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were identified • This trial was performed before 2010, therefore prospective registration was not required • Baseline characteristics are not excessively similar between the groups • Plausible loss-to-follow-up was reported • No implausible results were identified • Different numbers were randomised to each group

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: “The children were stratified for age (12–23 months, 2–5 years, 6–9 years), laterality of effusion (unilateral or bilateral), and duration of effusion (2–3 months, ≥4 months, unknown). The stratification scheme resulted in 18 subgroups. Within each subgroup, children were randomly assigned in a double-blind manner, in blocks of 4, to 1 of 4 treatment arms” Comment: No information regarding generation of the random sequence.

Allocation concealment (selection bias)	Unclear risk	No information regarding concealment of allocation. The use of non-permuted blocks of 4, at a group allocation ratio of 1:1:1:1 could be predictable.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants are stated to be blinded to intervention, and placebo is used. No information on blinding of study personnel, but lack of blinding of personnel is unlikely to have affected care.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information is provided regarding when treatment assignment was revealed, and whether outcome assessors were blinded to intervention.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Limited dropout, insufficient to cause bias in the results.
Selective reporting (reporting bias)	Unclear risk	No protocol available to compare.
Other bias	High risk	Short follow-up may give insufficient time for effusion to resolve, therefore bias towards intervention.

Niederman 1984

Study characteristics	
Methods	Two-arm, parallel-group, randomised controlled trial with 13 days of treatment and total follow-up of 5 weeks

Participants	**Setting:**
	Single-centre, conducted in a hospital in the USA between December 1980 and May 1982.
	Sample size:
	• **Number randomised:** 26 participants
	• **Number completed:**
	  ◦ 22 participants at 2 weeks
	  ◦ 20 participants at 5 weeks
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Oral steroids group
	  ▪ mean 46 months
	  ▪ range 26-84 months
	  ◦ Placebo group
	  ▪ mean 75 months
	  ▪ range 29-171 months
	• **Gender:**
	  ◦ Oral steroids group
	  ▪ 9 males
	  ▪ 3 females
	  ◦ Placebo group
	  ▪ 7 males
	  ▪ 3 females
	• **Duration of disease**
	  ◦ Oral steroids group
	  ▪ mean 66 months
	  ▪ range 55-83 months
	  ◦ Placebo group
	  ▪ mean 78 months

	▪ range 64-99 months • **Other measure of hearing status: number with normal hearing (only tested for a subgroup of participants)** ◦ Oral steroids group: 6/6 ◦ Placebo group: 5/6 **Inclusion criteria:** Aged 2 years or older. Initially referred with acute otitis media or nonsuppurative (serous) otitis media. Tympanometric evidence of unilateral effusion persisting in the same ear for 8 weeks, or bilateral effusion persisting for 8 weeks during pre-trial observation period. Diagnosis of middle ear effusion was based on the tympanogram using a “peak” or “no peak” classification. **Exclusion criteria:** • Other medical problems • Craniofacial abnormalities (e.g. cleft palate) • Systemic conditions predisposing to middle ear disease (e.g. immunodeficiency, Down’s syndrome) • Previous otologic surgery
Interventions	**Oral steroids group (n=12 completed at 2 weeks; n=11 at completed 4 weeks)** Tapering dose of oral dexamethasone for 13 days, starting at a max dose of 6 mg: • 0.15 mg/kg per day up to a maximum of 6 mg on days 1 and 2 • 0.075 mg/kg per day (to a max of 3 mg/day) on days 3 and 4 • 0.0375 mg/kg/day (to a max of 1.5 mg per day) on days 5, 6 and 7 • 0.0375 mg/kg/day (to a max of 1.5 mg per day in children over 40kg and 0.75 mg per day in children less than 40kg) on days 9, 11 and 13 **Placebo group (n=10 completed at 2 weeks; n=9 completed at 4 weeks)** Identical in appearance and tastes, and containing the same inactive ingredients. No further information.
Outcomes	**Primary outcomes relevant to this review:** • **Hearing** ◦ Not reported • **Disease-specific quality of life** ◦ Not reported • **Adverse event** ◦ Not reported **Secondary outcomes relevant to this review:** • **Presence/persistence of OME: proportion of children with persistence of OME** ◦ In any ear at 5 weeks • **Episodes of acute otitis media: proportion** ◦ At 2 weeks • **Other adverse effects** ◦ Narrative summary only **Other outcomes reported in the study:** • Adherence to medication • Some data at 2 weeks, but I have extracted the longest data available for our follow-up times • Change in effusion status from 2 to 5 weeks
Funding sources	Biomedical Research Support Grant from NIH Medication and placebo were both provided by the manufacturer, Merck Sharp and Dohme

Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were identified • This trial was published prior to 2010 to prospective trial registration was not required • Baseline characteristics of the groups are not excessively similar • Plausible loss-to-follow-up was reported • No implausible results were identified • The numbers randomised to each group were not explicit, so unclear if they were the same in each group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Children meeting these criteria were randomized (using a list of preselected random numbers) to receive either dexamethasone or placebo” Comment: Random number table was used for randomisation.
Allocation concealment (selection bias)	Unclear risk	No information regarding allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: “All medications were dispensed by a hospital pharmacist in a double-blind design”. Comment: The Participants were apparently blinded to the intervention but there are no specific details regarding whether study personnel were also blinded, therefore rated as unclear. There is a potential for study personnel to interact with participants at 2 weeks follow-up.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	There is no information regarding whether outcome assessors were blinded to the intervention.
Incomplete outcome data (attrition bias) All outcomes	High risk	Although loss to follow-up was relatively low, the missing data do have the potential to make significant differences to the reported result in such a small study.
Selective reporting (reporting bias)	Unclear risk	No protocol was found so it is not possible to assess selective reporting.
Other bias	High risk	Short follow-up may give insufficient time for effusion to resolve, therefore bias towards intervention. Participants with bilateral disease are included, but results are not specified for both ears of individual participants. It is not possible to assess whether there may be some effect on a single ear (which would be beneficial). There were more children with bilateral OME at baseline in the placebo group, which also had a higher rate of bilateral persistence, so there is a risk of detection bias arising because ‘caseness’ was poorly defined.

OSTRICH

Study characteristics	
Methods	Two-arm, double-blind, parallel-group, randomised controlled trial with one week of treatment and follow-up at 5 weeks, and 6-12 months
Participants	**Setting:** Multi-centre study, conducted in ENT or paediatric audiology and audiovestibular medicine clinics, outpatient in the UK between March 2014 and April 2016 **Sample size:** • **Number randomised:** 380 participants (389 children initially randomised, 6 of which were afterwards found to be ineligible due to insufficient hearing loss and 3 of which withdrew and declined the use of their data) • **Number completed:**

- 368 participants by 5 weeks follow-up
- 332 participants by final follow-up at 12 months

Participant (baseline) characteristics:

- **Age:**
  - Oral steroids group: mean 5.30 years (SD 1.60)
    - 2-5 years: 131/193 (68%)
    - 6-8 years: 62/193 (32%)
  - Placebo group: mean 5.08 (SD 1.60)
    - 2-5 years: 133/187 (71%)
    - 6-8 years: 54/187 (29%)
- **Gender:**
  - Oral steroids group:
    - 109 (57%) females
    - 84 (43%) males
  - Placebo group:
    - 102 (55%) females
    - 85 (46%) males
- Bilateral disease:
  - All participants had bilateral disease
- **Duration of disease**
  - Oral steroids group:
    - <6 months: 19 (10%)
    - 6 to <9 months: 22 (12%)
    - 9 to <12 months: 20 (10%)
    - ≥12 months: 131 (68%)
    - missing data: 1 (1%)
  - Placebo group
    - <6 months: 26 (14%)
    - 6 to <9 months: 28 (15%)
    - 9 to <12 months: 18 (10%)
    - ≥12 months: 115 (62%)
    - missing data: 1 (1%)
- **Hearing thresholds: average over 2 ears**
  - Oral steroids group (n=193): mean 36.25 (SD 7.74) dB HL
  - Placebo group (n=187): mean 37.83 (SD 6.93) dB HL
- **Disease-specific quality of life score: OM8-30**
  - Oral steroids group (n=190/193)
    - Total summary score: mean 0.60 (SD 1.03)
  - Placebo group (n=187/187)
    - Total summary score: mean 0.47 (SD 1.04)
- **Generic health-related quality of life: HU13 (8 attributes)**
  - Oral steroids group (n=164/193)
    - Media score: 0.79 (25-75th centiles: 0.66-0.92; Range min-max: 0.10 to 1.00)
  - Placebo group (n=159/187)
    - Median score 0.80 (25-75th centiles: 0.63-0.93; Range min-max: 0.16 to 1.00)
- **Generic health-related quality of life: PedsQL**
  - Oral steroids group (n=189/193)
    - Physical functioning: median 90.6 (25th-75th centiles: 79.7-98.4)
    - Emotional functioning: median 75.0 (25th-75th centiles: 55.0-85.0)

	▪ Social functioning: median 90.0 (25th-75th centiles: 72.5-100.0) ▪ Psychosocial health summary: median 78.3 (25th-75th centiles: 63.4-87.1) ▪ Total summary: median 82.6 (25th-75th centiles: 68.0-90.7) ▪ Missing: 4 ▪ School Functioning: median 70.0 (25th-75th centiles: 58.3-85.0) ▪ Missing: 10 ◦ Placebo group (n=187/187) ▪ Physical functioning: median 90.6 (25th-75th centiles: 78.1-100.0) ▪ Emotional functioning: median 70.0 (25th-75th centiles: 60.0-85.0) ▪ Social functioning: median 90.0 (25th-75th centiles: 75.0-100.0) ▪ Psychosocial health summary: median 78.8 (25th-75th centiles: 63.54-87.5) ▪ Total summary: median 82.1 (25th-75th centiles: 69.0-90.5) ▪ Missing: 0 ▪ School Functioning: median 75.0 (25th-75th centiles: 58.3-90.0) ▪ Missing: 8 **Inclusion criteria:** Aged 2 to 8 years with the following: • symptoms of hearing loss attributable to otitis media with effusion for at least 3 months (or with audiometry-proven hearing loss for at least 3 months) • bilateral otitis media with effusion diagnosed in an ENT or paediatric audiology and AVM clinic on the day of recruitment or during the preceding week • audiometry confirming hearing loss of >20 dB HL (averaged within the frequencies of 0.5, 1, 2, and 4 KHz in both ears) by pure tone audiometry ear-specific insert, visual reinforcement audiometry (VRA), or ear-specific play audiometry; or hearing loss of >25 dB HL (averaged within the frequencies of 0.5, 1, 2, and 4 KHz) by soundfield VRA or soundfield performance/play audiometry in the better-hearing ear, on the day of recruitment or within the preceding 14 days • first time in the OSTRICH trial • parent or carer able to understand and give full informed consent **Exclusion criteria:** • Currently involved in another clinical trial of an investigational medicinal product (CTIMP) or participated in a CTIMP during the last 4 months • Current systemic infection or ear infection • Cleft palate, Down syndrome, diabetes mellitus, Kartagener syndrome or primary ciliary dyskinesia, renal failure, hypertension or congestive heart failure • Confirmed, major developmental difficulties (e.g. tube fed, chromosomal abnormalities) • Existing known sensory hearing loss • Taken oral steroids in the preceding 4 weeks • Had a live vaccine in the preceding 4 weeks if aged <3 years • Condition that increases the risk of adverse effects from oral steroids (i.e. on treatment likely to modify the immune system or be immunocompromised, for example undergoing cancer treatment) • Been in close contact with someone known or suspected to have chickenpox or active shingles during the 3 weeks prior to recruitment and had no prior history of varicella infection or immunisation • Had ventilation tubes • On a waiting list for VT insertion, anticipated having surgery within 5 weeks, and unwilling to delay it
Interventions	**Oral steroids group: (n=193 randomised)** • 7-day course of oral soluble prednisolone (5 mg tablets, manufactured by Waymade PLC trading)

	◦ For children aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days ◦ For children aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days • The daily dose stated was the most commonly used dose in previous studies of OME, and is similar to the standard dose for the treatment of other conditions with inflammatory components (such as asthma) **Placebo group (n=187 randomised)** • 7-day course of placebo matched to prednisolone for consistency, colour, and solubility, as well as visually and in its packaging (manufactured, packaged and supplied by Piramal Healthcare UK Limited) ◦ For children aged 2–5 years: a single daily dose of 4 tablets for 7 days ◦ For children aged >5 years: a single daily dose of 6 tablets for 7 days
Outcomes	**Primary outcomes relevant to this review:** • **Hearing: proportion of children with hearing returned** ◦ Acceptable hearing assessed using audiometry at 5 weeks, 12 months. Acceptable hearing defined as ≤20 dB HL averaged within 4 frequencies in at least 1 ear when assessed by PTA, ear-specific insert VRA, or ear-specific play audiometry, and ≤25 dB HL averaged within the frequencies when assessed by soundfield VRA or soundfield performance/ play audiometry. ◦ Mean (SD) final hearing thresholds (dB) ◦ Mean (SD) change in hearing thresholds from baseline (dB) • **Disease-specific quality of life: OM8-30** ◦ Mean (SD) at endpoint at 5 weeks and 12 months • **Adverse event** ◦ Not reported **Secondary outcomes relevant to this review:** • **Presence/persistence of OME: proportion of children with** ◦ No resolution of OME (persistence of type B or C in both ears) measured by tympanometry at 5 weeks and 12 months • **Generic health-related quality of life:** ◦ Mean (SD) at endpoint: PedsQL at 5 weeks and 12 months ◦ Proportion exceeding a specified cut-off value: HUI3, perfect health at 5 weeks and 12 months • **Other adverse effects: proportion of children with** ◦ Digestion symptoms (Increased appetite, Low appetite, Diarrhoea, Constipation, Nausea) at one week: ◦ Behavioural symptoms (Hyperactive, Tired, Frustration, Change in behaviour, Sleep walking) at one week **Other outcomes reported in the study:** All of the study's outcomes were also reported at 6 months follow-up. The following outcomes were additionally reported (at all time points unless otherwise stated): • Otoscopic outcomes: perforation present in at least one ear; bubbles present behind the ear drum in at least one ear • Insertion of VTs • Health-care consultations related to OME and other resource use • Cronbach's alpha overall symptom score for 8 symptoms (hearing, ear pain, speech, energy levels, sleep, attention span, balance, and being generally unwell). These symptom scores were not all reported separately of one another and therefore relevant outcomes could not be extracted (e.g. balance scores for the outcome vestibular function) • Serious adverse events (1 asthma attack – no between treatment group comparison was made) • Symptom outcomes at 1 week: Respiratory tract infection symptoms (phlegmy cough, cold, sneezing, temperature, nosebleed, conjunctivitis, itchy eyes, or

	generally unwell; headache; parotitis; ear pain on touch or earache; rash, pox, or scarlet fever; flushed cheeks); other symptoms (finger infection; knee pain)
Funding sources	Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research. Authors note the funder had no role in study design, data collection, data analysis, data interpretation, writing of the manuscript, or the decision to submit the manuscript for publication.
Declarations of interest	Christopher C Butler is a National Institute for Health Research (NIHR) senior investigator. Kerenza Hood and Amanda Roberts are members of the NIHR Health Technology Assessment General Board. Kerenza Hood is a member of the NIHR Clinical Trials Unit Standing Committee
Notes	**Research integrity checklist:** • No retractions or expressions of concern were identified • This trial was prospectively registered • Baseline characteristics between the groups were not excessively similar • Plausible loss-to-follow-up was reported • No implausible results were noted • Different numbers of participants were allocated to each group, and randomisation was stratified by site and age of child

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Randomisation was co-ordinated centrally by the South East Wales Trials Unit, Centre for Trials Research. The randomisation schedule was prepared by the trial statistician (TS) and comprised random permuted blocks that were stratified by site and child’s age. The investigational medicinal product (IMP) manufacturer (Piramal Healthcare UK Limited, Grangemouth, UK) was provided with a list of random allocation numbers linking to either the oral steroid or the placebo.” “Randomisation was remote and online” "Sequential pack numbers were randomly assigned (1:1) to the oral steroid or placebo groups by use of computer-generated random permuted block sizes stratified by site and child’s age group (2–5 years vs 6–8 years)".
Allocation concealment (selection bias)	Low risk	Participants received the next sequentially numbered trial pack (which were all in identical packaging) allocated to the participant by the site pharmacy, and a designated member of the OSTRICH trial site team (when possible), or the participant’s parent, collected the pack from the pharmacy on behalf of the participant. Authors note there was no indication of breaches in allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “The placebo was matched for consistency, colour and solubility, as well as visually, in identical packaging to the active treatment. Participants, parents, all clinic staff and members of the OSTRICH trial team remained blinded to treatment allocation.”
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Participants, parents, all clinic staff and members of the OSTRICH trial team remained blinded to treatment allocation". Adverse events outcomes and quality of life outcomes were reported/ assessed by parents, who were blinded to intervention by use of placebo
Incomplete outcome data (attrition bias) All outcomes	Low risk	3% of participants were lost to follow-up at 5 months, 13% were lost to follow-up at 12 months, and 19% did not attend all 3 follow-up appointments. The missing outcome data tended to be balanced between groups except for slight differential loss to follow-up for the 5-week clinic appointment (n=9 in oral steroid group; n=3 in placebo group).
Selective reporting (reporting bias)	Low risk	The study protocol is available and all of the study’s pre-specified (primary and secondary) outcomes that are of interest in the review have been reported. Authors are transparent about where their methods differed from those specified in the protocol and why these changes were made.
Other bias	High risk	High risk of bias for short term follow-up as there is insufficient time to detect a difference between the groups. Low risk of bias for longer term follow-up.

Podoshin 1990

Study characteristics	
Methods	Three-arm, double-blind, parallel-group, randomised controlled trial with 2 weeks of treatment and 2 months follow-up
Participants	**Setting:** Single-centre, conducted in an ENT department in Israel between September 1987 and December 1988 **Sample size:** • **Number randomised:** 150 participants • **Number completed:** 136 participants **Participant (baseline) characteristics:** • **Age:** ◦ Antibiotics plus placebo group: ▪ Mean 7.3 years ▪ Range 4-8 years ◦ Antibiotics plus oral steroids group ▪ Mean 6.5 years ▪ Range 3-7 years ◦ Placebo group: ▪ mean 6.7 ▪ Range 3-7 years • **Gender:** ◦ Antibiotics group: ▪ 27 males ▪ 22 females ◦ Antibiotics plus oral steroids group: ▪ 25 males ▪ 25 females ◦ Placebo group: ▪ 20 males ▪ 17 females **Inclusion criteria:** Aged greater than 4 years. OME of at least 2 months duration, who had received no previous treatment for OME. Diagnosis made by pneumo-otoscopy using a Welch Allyn halogen illuminated otoscope plus presence of a flat tympanogram (type B) **Exclusion criteria:** • Recurrent acute otitis media • Cleft palate • Hypertrophic adenoids (adenoidal nasopharyngeal ratio of greater than 0.73) • Aged less plus than 4 years • Children with signs of fluid lines, air bubbles or yellow fluid, indication an already resolving effusion
Interventions	**Antibiotic plus placebo group (n = 49 completed)** Amoxicillin 50 mg/kg/day plus placebo **Antibiotics plus oral steroids group (n = 50 completed)** As above plus 1 mg/kg prednisolone, reduced by 5 mg every 2 days, therefore tapering course for a total of 14 days. Tablets of prednisolone were pulverised and placed in unmarked gelatin capsules **Placebo group (n = 37 completed)** Two placebos of lactose powder placed in capsules that were identical to those containing the pulverised prednisolone
Outcomes	**Primary outcomes relevant to this review:**

	• **Hearing: proportion of children with hearing returned to normal**
	  ◦ Closure of air-bone gap in worst affected ear at 2 months
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of children with persistence of OME**
	  ◦ Tympanometry: anything other than type A at 2 months (performed only on the ear with the worst air-bone gap)

Funding sources	Not reported
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were identified • The trial was published before 2010, therefore prospective registration was not required • Limited information was available on baseline characteristics • Plausible loss to follow-up was reported • No implausible results were identified • The number randomised to each group was not clear, but may be identical

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "They were treated randomly by our directions". Comment: No further information about generation of a random sequence.
Allocation concealment (selection bias)	Unclear risk	No information on allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Although 2 active medications were used, it appears that only one type of placebo may have been used: "[In the group receiving only placebo…] The placebo consisted of lactose powder placed in capsules that were identical to those containing the pulverized prednisone." It is probable that 'double-blind' referred to blinding of participants and trial personnel administering the treatments, though this was not confirmed. The attrition rate was much higher (13%) in the placebo-only group compared with either the antibiotic and placebo group (2%) or the prednisolone and placebo group (0%). This raises the possibility that participants may have been aware that they were not taking any active treatment.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on blinding of outcome assessors.
Incomplete outcome data (attrition bias) All outcomes	High risk	Substantial dropout in the placebo group, which may be sufficient to introduce bias in the results.
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	High risk	Inadequate duration of follow-up.

Puhakka 1985

Study characteristics

Methods	

	Three-arm, double-blind, parallel-group randomised controlled trial with 2 months follow-up

Participants	**Setting:**
	Single-centre, conducted in a hospital in Finland. Study dates not reported
	Sample size:
	• **Number randomised:** 75 participants (122 ears)
	• **Number completed:** 75 participants (122 ears)
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ mean 4 years and 10 months
	  ◦ range 7 months to 11 years
	• **Gender:**
	  ◦ 49 males (65%)
	  ◦ 26 females (35%)
	• **Number with bilateral disease**
	  ◦ 45 (60%)
	Inclusion criteria:
	Children with secretory middle-ear effusion
	Exclusion criteria:
	Children with an AOM episode during the preceding 3 months

Interventions	**Prednisone and sulfatrimethoprim group (n = 29 (47 ears) randomised, n = 29 (47 ears) completed)** Oral prednisolone: 1 mg/kg body weight/day divided into 3 doses and given as decreasing dose for 6 days. Oral sulfatrimethoprim: 6 mg of trimethoprim and 18.5 mg of sulfadiazine/kg/day divided into 2 doses for 10 days **Sulfatrimethoprim and placebo group (n=22 (35 ears) randomised, n=22 (35 ears) completed)** As above plus placebo **Placebo group (n = 24 (40 ears) randomised, n = 24 (40 ears) completed)** Two placebos, no further details **Treatment used before entry to the trial** Myringotomy on all affected ears at first visit **Background interventions administered to all participants** At the follow-up visits 2, 4 and 8 weeks after starting therapy, myringotomy was performed in all ears in which middle ear fluid detected. Follow-up exams by ENT specialist who performed initial exam

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Not reported
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of ears with persistence of OME**
	  ◦ Cured after 2 weeks, defined as appearance and mobility of tympanic membrane had become normal or if effusion was no longer present at myringotomy
	  ◦ Cured after 8 weeks, defined as appearance and mobility of tympanic membrane had become normal or if effusion was no longer present at myringotomy

	Other outcomes reported in the study: Bacterial cultures of middle ear fluid
Funding sources	Not reported
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retraction notices or expressions of concern were identified • This trial was published prior to 2010, therefore prospective registration was not required • Limited baseline data were available to assess for similarities • Full follow-up was reported • No implausible results were noted • Different numbers were allocated to each group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Children were randomly allocate *(sic)* to three therapy groups" Comment: No information about the sequence generation process to permit judgement.
Allocation concealment (selection bias)	Unclear risk	No information about allocation concealment to permit judgement.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The trial is described as a double-blind study, however it is not clear who is blind. It is possible to blind participants but may not be possible to blind those administering the therapy.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: “Follow-up examinations were always carried out by the ENT specialist who had examined the child initially”. Comment: no description of outcome assessors being blinded to group allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Does not appear to be any data missing.
Selective reporting (reporting bias)	Unclear risk	No protocol is available.
Other bias	High risk	Randomisation occurred at the level of the child, but results are reported at the level of the individual ear. There is no description of correlation between ears, and it is not possible to determine whether an individual child had cure in both ears or only one ear.

Rahmati 2017

Study characteristics	
Methods	Three-arm, parallel-group, randomised controlled trial with one month follow-up The third arm considered combination treatment with montelukast and mometasone, therefore was not relevant for this review

Participants	**Setting:**
	Single-centre, conducted in a University hospital in Iran in 2014
	Sample size:
	• **Number randomised:**
	  ◦ Total 143 participants
	  ◦ 84 participants of interest to this review
	• **Number completed:**
	  ◦ Total 143 participants
	  ◦ 84 participants of interest to this review
	Participant (baseline) characteristics:
	• **Age:**

	◦ Intranasal steroids group: mean 50.7 months (SD 17.58) ◦ No treatment group: mean 41.27 months (SD 15.9) • **Gender:** ◦ Intranasal steroids group: ▪ 24 males (60%) ▪ 16 females (40%) ◦ No treatment group: ▪ 31 males (70.5%) ▪ 13 females (29.5) • **Number with bilateral disease** ◦ Intranasal steroids group ▪ 17 bilateral (42.5%) ▪ 23 unilateral (57.5%) ◦ No treatment group ▪ 17 bilateral (38.6%) ▪ 27 unilateral (61.4%) **Inclusion criteria:** Aged 2 to 6 years with a definite diagnosis of otitis media with effusion with symptoms and examination, including tympanometry **Exclusion criteria:** • Currently using corticosteroids or prophylactic montelukast • Chronic pulmonary or cardiac disease or immune deficiency • Allergic rhinitis • Hypersensitivity to montelukast or corticosteroids • Lack of written informed consent
Interventions	**Intranasal steroids group (n = 40 randomised, n = 40 completed)** Mometasone inhaled, one puff in each side of nose for one month **No treatment group (n = 44 randomised, n = 44 completed)** (Additional third arm received mometasone and montelukast, 59 participants) **Treatment used before entry to the trial** If initially diagnosed with AOM, children were given amoxicillin 50 mg/kg/d divided 3 times a day to a maximum of 250 mg 3 times a day for a total of 10 days
Outcomes	**Primary outcomes relevant to this review:** • **Hearing** ◦ Not reported • **Disease-specific quality of life** ◦ Not reported • **Adverse event** ◦ Not reported **Secondary outcomes relevant to this review:** • **Presence/persistence of OME: proportion of children with persistence of OME** ◦ Improvement based on tympanometry at one month
Funding sources	Hormozgan University of Medical Sciences, Bandar Abbas, Iran
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were noted • Study was registered retrospectively • Baseline characteristics were not excessively similar between the groups.

	• Full follow-up was reported, but follow-up was short • No implausible results were noted • Different numbers were randomised to each group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: ""Participants were randomly assigned into three groups." Comment: insufficient information about the sequence generation process to permit judgement.
Allocation concealment (selection bias)	Unclear risk	Insufficient information about the sequence generation process to permit judgement.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Trial registration states "Masking: Double (Investigator, Outcomes Assessor)". No placebo was used.
Blinding of outcome assessment (detection bias) All outcomes	High risk	There is no mention of blinding in the paper so unlikely that assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There does not appear to be any missing outcome data.
Selective reporting (reporting bias)	High risk	Trial registration states that a secondary outcome is "Frequency of Drug side effects as reported by the children or their parents" but no data is reported. Trial registration was retrospective.
Other bias	High risk	There is a lack of information on methods used to assess (only) outcome, of resolution/persistence of OME. Unclear if this was based on tympanometry, otoscopy or other measures, and how children with different outcomes in each ear were categorised (e.g. one ear resolved, one ear persistent).

Saffar 2001

Study characteristics	
Methods	Two-arm parallel, Single-centre, randomised, placebo-controlled, double-blind trial from Iran
Participants	**Setting**: not reported **Sample size**: • Total number randomised: 49 • Total number who completed trial: 49 **Participants (baseline) characteristics**: • Age range: 2 to 10 years • Male: 23 • Female: 26 • Duration of disease: at least 2 months • Laterality of OME at baseline: not reported **Inclusion criteria**: children 2-10 years old with clinical diagnosis of otitis media with effusion (OME) with or without recent history of acute otitis media (AOM) or antibiotic use. No improvement after 2 pre-trial courses of antibiotic administered by trialists. **Exclusion criteria**: Previous history of chronic cardiopulmonary, immunosuppressive diseases and head and face anatomical defects. Improvement after either one or 2 courses of antibiotic administered before the trial by the trialists. **Diagnostic criteria for OME**: Type B tympanogram and auditory test (>20 dB HL) **Treatment prior to randomisation**: Amoxicillin (80-90 mg/kg/day) for 2 weeks (those who have recently used amoxicillin, prescribed with co-amoxiclav instead, with same dosage and duration). Those who have not shown improvement were re-treated with co-amoxiclav (in patients who were given amoxicillin before) or cotrimoxazole + erythromycin (in patients who were given co-amoxiclav before) for 2 weeks.

Interventions	**Oral steroid**: **(n = 25 randomised, n = 25 completed)** Prednisolone (1 mg/kg), twice a day, for 7 days and tapered within 5 days (12 days in total) **Placebo**: **(n = 24 randomised, n = 24 completed)** Placebo (produced at Sari school of pharmacy) with same dosage and duration of intervention group **Treatment prior to randomisation**: Amoxicillin (80-90 mg/kg/day) for 2 weeks (those who have recently used amoxicillin, prescribed with co-amoxiclav instead, with same dosage and duration). Those who have not shown improvement were re-treated with co-amoxiclav (in patients who were given amoxicillin before) or cotrimoxazole + erythromycin (in patients who were given co-amoxiclav before) for 2 weeks.

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Not reported
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• Persistence of OME at 6 months (type B tympanogram and hearing >20dB HL)

Funding sources	Not reported in translation
Declarations of interest	Not reported in translation
Notes	Data extraction based on translation **Research integrity checklist:** • No retractions or expressions of concern were identified • The trial was published before 2010, therefore prospective registration was not required • Baseline characteristics of the groups are not excessively similar, although few characteristics are reported • Complete follow-up was reported • No implausible results were reported • Different numbers of children were allocated to each group

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported in translation
Allocation concealment (selection bias)	Unclear risk	Not reported in translation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Described as ‘double-blind’. A placebo was used and it is therefore unlikely that participants were aware of treatment allocation. However, it is unclear whether trial personnel were also unaware of treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Described as ‘double-blind’ without further information.
Incomplete outcome data (attrition bias) All outcomes	Low risk	It appears there were no losses to follow-up.
Selective reporting (reporting bias)	Unclear risk	No protocol available
Other bias	Low risk	

		High risk of detection bias as follow-up was too short to judge the extent of natural resolution in the placebo group.

Scadding 2014

Study characteristics	
Methods	Four arm, double blind, parallel-group, randomised controlled trial with up to 2 years of treatment and follow-up

Participants	**Setting:**
	Single-centre, conducted in a specialist glue ear clinic in a hospital in the UK between 1994 and 2003
	Sample size:
	• **Number randomised:** 200 participants
	• **Number completed:** 123 participants
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Nasal steroids group: mean 5.4 years (SD 1.2)
	  ◦ Autoinflation group: mean 5.7 (SD 1.3)
	  ◦ Autoinflation and nasal steroids group: mean 5.9 (SD 1.1)
	  ◦ Placebo group: mean 5.7 (SD 1.3)
	• **Gender:**
	  ◦ Nasal steroids group:
	  ▪ 31 males (60%)
	  ▪ 21 females (40%)
	  ◦ Autoinflation group:
	  ▪ 25 males (48%)
	  ▪ 27 females (52%)
	  ◦ Autoinflation and nasal steroids group:
	  ▪ 29 males (60%)
	  ▪ 19 females (40%)
	  ◦ Placebo group:
	  ▪ 32 males (67%)
	  ▪ 16 females (33%)
	• **Hearing thresholds**
	  ◦ Nasal steroids group:
	  ▪ Right: mean 23.3 (SD 8.5)
	  ▪ Left: mean 24.1 (SD 9.7)
	  ◦ Autoinflation group:
	  ▪ Right: mean 25.9 (SD 10.4)
	  ▪ Left: mean 24.3 (SD 10.1)
	  ◦ Autoinflation and nasal steroids group:
	  ▪ Right: mean 25.2 (12.3)
	  ▪ Left: mean 22.8 (SD 9.9)
	  ◦ Placebo group:
	  ▪ Right: mean 24.8 (SD 12.5)
	  ▪ Left: mean 25.8 (SD 11.8)
	Inclusion criteria:
	Aged 4 to 8 years with at least 3 months of glue ear or more than 2 episodes in the past 6 months; and a type B or C tympanogram
	Exclusion criteria:
	• Cleft palate

	• Down's syndrome • Cystic fibrosis
Interventions	**Nasal steroids group (n=52 randomised; n= 32 completed)** Fluticasone propionate aqueous nasal spray 50µg per spray, one puff per nostril twice daily for 2 weeks (2 puffs per nostril twice daily for children over 35kg), i.e. total daily dose 200µg (or 400µg) initially Then reduced to one puff per nostril (100µg) once daily. "The children were asked to use this on a regular basis". "Those who reported spray use on at least 3 days a week remained in the study" **Autoinflation group (n=52 randomised; n=30 completed**) Otovent auto-inflation device. Used 3 times-daily for the first box of balloons (i.e. 4 to 5 weeks) then stop if hearing not troublesome. Re-establish use if glue ear re-presented, esp after a cold. **Autoinflation and nasal steroids group (n=48 randomised; n=31 completed)** Otovent as above and nasal steroids as above **Placebo group (n=48 randomised; n=30 completed)** Matching placebo

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Not reported
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME**
	  ◦ Persistent hearing loss of greater than 30 dB or grommet insertion at 2 years (data not relevant for this review)
	• **Other adverse effects**
	  ◦ Narrative summary only
	Other outcomes reported in the study:
	• Kaplan Meier plots of survival time without grommets or hearing loss >30dB HL
	• Change in specific symptoms over time
	• Number with recurrent URTIs

Funding sources	Glaxo Smith Kline, Inphormed and Merck
Declarations of interest	This study was conceived by Glenis Scadding and funded by Glaxo Smith Kline (including the salary of Abhijeet Parikh as a PhD student) together with Inphormed who provided Otovent devices free of charge. Merck Sharp and Dohme provided funding for further independent statistical analysis since this was advised by a referee when the paper was originally submitted. Glenis Scadding has received funding from GSK and MSD for other trials, serves on an advisory panel and has lectured for them at meetings. Helen Tate has worked as an independent statistical consultant for Merck, Sharp and Dohme. At the time of the study, DR was a full-time employee of GlaxoSmithKline R&D. None of the other authors has any interests to declare.
Notes	**Research Integrity Checklist** • No retraction notices or expressions of concern were identified • No prospective trial registration was identified. However, although the trial was published after 2010, we note that it was conducted from 1993 to 2003. • Baseline characteristics of the groups were not excessively similar • Some loss to follow-up was reported • No implausible results were reported • Block randomisation was used to allocate participants to the groups, but the numbers are not identical
Risk of bias	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Subjects were randomised to receive FP or matching placebo in a 1:1 ratio according to a computer-generated randomisation schedule using a block size of 8.” “In addition those children entering the trial with an odd number were also given the Otovent device; this part of the study was open.” Comment: adequate method for both.
Allocation concealment (selection bias)	Low risk	Quote: “…computer-generated randomisation schedule using a block size of 8. This was held in the pharmacy, and both subjects and observers were blind as to the nature of this treatment.” Comment: Third party conducted randomisation and allocation. Even though personnel would know that an odd number is allocation to Otovent, it is unlikely that allocation can be interfered with.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “both subjects and observers were blind as to the nature of this treatment. In addition those children entering the trial with an odd number were also given the Otovent device; this part of the study was open. “ Comment: low risk for steroids.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "both subjects and observers were blind as to the nature of this treatment.” Comment: the above statement most likely refers to the steroid intervention.
Incomplete outcome data (attrition bias) All outcomes	High risk	38% loss to follow-up, this may substantially impact results.
Selective reporting (reporting bias)	Unclear risk	No protocol found, so it was not possible to assess selective reporting bias.
Other bias	Low risk	No other concerns.

Schwartz 1980

Study characteristics	
Methods	Two-arm, double-blind, parallel-group, randomised controlled trial with 1-2 weeks treatment and follow-up. Cross-over trial, but only data from the first phase were used.

Participants	**Setting:**
	Multicentre centre, conducted in 2 private practices in the USA between September 1977 and January 1979
	Sample size:
	• **Number randomised:** 41 participants
	• **Number completed:** 40 participants
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ mean 4 years and 9 months
	  ◦ range 14 months to 10 years
	• **Gender:**
	  ◦ 26 males
	  ◦ 14 females
	• **Number with bilateral disease**
	  ◦ 19/40
	Inclusion criteria:
	Children with persistent otitis media with effusion for 3 weeks or more despite use of antimicrobial and/or decongestant therapy. Biphasic pneumo-otoscopy was performed at each visit using a factory modified 3.5 v Welch-Allyn halogen-illuminated otoscope.

	In addition, tympanometric pattern and crossed acoustic reflex thresholds were obtained using a Teledyne acoustic impedance monitor. **Exclusion criteria:** Objective signs of fluid lines, menisci, air bubbles or yellow fluid thus avoiding inclusion of any child with an already resolving effusion
Interventions	**Oral steroids group (n = 24 randomised)** Prednisone 1 mg/kg/day for the first 2 days in a divided dose, 0.75 mg/kg/day for the next 2 days and 5 to 10 mg/day as a single morning dose for the remaining 3 days. If partial clearing another week of prednisone 5 to 10 mg in a single morning dose on alternate days. **Placebo group (n = 17 randomised)** Lactose powder **Treatment used before entry to the trial** All subjects had previously been treated with antimicrobial and/or decongestant therapy **Background interventions administered to all participants** All were treated with sulfisoxazole suspension of 50 mg/kg/day in a twice daily dosage schedule

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Not reported
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of children with persistence of OME**
	  ◦ Assessed at one to 2 weeks
	• **Other adverse effects**
	  ◦ No data, a narrative summary of adverse effects is reported
	Other outcomes reported in the study:
	Some data on correlation of outcome with other variables, but only reported for full follow-up data (not first phase only), therefore does not compare the 2 randomised groups

Funding sources	Upjohn Company, Kalamazoo, Michigan provided Deltasone used in this investigation
Declarations of interest	None reported
Notes	**Research integrity checklist** • No retraction notices or expressions of concern were identified • This study was published prior to 2010, therefore prospective trial registration is not applicable • Baseline characteristics were not reported for each group, therefore we cannot assess for similarities • No loss to follow-up was reported (although follow-up was only 1-2 weeks) • No implausible results were identified • Different numbers were allocated to each group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "…the experimental design was that of a double-blind crossover paradigm in which children were assigned randomly to receive wither prednisone or lactose placebo". Comment: insufficient information provided.
Allocation concealment	Unclear risk	Quote: "Prednisone and lactose placed in unmarked gelatin capsules and placed in identically coded vials by a registered pharmacist".

(selection bias)		Comment: it is unclear if the unmarked capsules and identical vials means that allocation was definitely concealed.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: “Pulverized prednisone tablets (5mg) or lactose powder were packed in unmarked gelatin capsules and place in identically coded vials by a registered pharmacist” Comment: participants are likely to have been blinded. It is unclear who administered the study drug to participants, and whether they were also blinded. Follow-up was short, but management at 1-week follow-up was determined by the observing physician, therefore this could have been altered if the treatment allocation was known. Insufficient information to make a judgement.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome data reported for all children.
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	High risk	Short duration of follow-up, therefore there is a risk of detection bias in favour of resolution for active treatment.

Stuart 1995

Study characteristics	
Methods	Note that 2 studies are described in the same article Both were single-centre, parallel-group RCTs with follow-up of 9-12 weeks

Participants	**Setting:**
	Single-centre, recruitment from preschool and kindergarten class in Australia
	Sample size:
	• **Number randomised:**
	  ◦ study 1989: 26
	  ◦ study 1990: 24
	• **Number completed:**
	  ◦ study 1989: 26
	  ◦ study 1990: 24
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ study 1989:
	  ▪ beclomethasone group: mean 4.8 years, SD 1.2
	  ▪ placebo group: mean 4.5 years, SD 1.0
	  ◦ study 1990:
	  ▪ beclomethasone group: mean 4.89 years, SD 1.43
	  ▪ placebo group: mean 4.65 years, SD 1.08
	• **Gender:**
	  ◦ study 1989:
	  ▪ beclomethasone group: 10 male: 4 female
	  ▪ placebo group: 3 male: 9 female
	  ◦ study 1990:
	  ▪ beclomethasone group: 4 male: 8 female
	  ▪ placebo group: 7 male: 5 female
	• **Hearing thresholds**
	  ◦ Not reported
	Inclusion criteria:

	Abnormal tympanometry (type B or C) in one or both ears **Exclusion criteria:** Not reported
Interventions	**Intervention:** Beclomethasone spray twice daily for 5 weeks (1989 study) or 8 weeks (1990 study) **Comparator:** Compared to placebo spray for the same duration

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Narrative report only
	• **Disease-specific quality of life**
	  ◦ Not reported
	• **Adverse event**
	  ◦ Not reported
	Secondary outcomes relevant to this review:
	None
	Other outcomes reported in the study:
	n/a

Funding sources	No details are given. Medication was provided by Glaxo.
Declarations of interest	No information provided
Notes	**Research integrity checklist:** • No retractions or expressions of concern were identified • This trial was published before 2010 therefore prospective registration was not required • Baseline characteristics of the 2 groups are not excessively similar • There does not appear to be any loss-to-follow-up, and no reason is given for this • No implausible results were identified • Different numbers of participants were allocated to each group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The consenting children were randomised into two groups using a block randomisation with four in each block". "The randomisation code was determined by Glaxo Laboratories, who supplied the beclomethasone and placebo metered dose nasal aerosols in identical packaging, identified only by the numbers 1 to 30. The code was held by Glaxo until the end of the study, neither researchers nor subjects being aware of the aerosols' contents."
Allocation concealment (selection bias)	Low risk	Quote: "The consenting children were randomised into two groups using a block randomisation with four in each block". "The randomisation code was determined by Glaxo Laboratories, who supplied the beclomethasone and placebo metered dose nasal aerosols in identical packaging, identified only by the numbers 1 to 30. The code was held by Glaxo until the end of the study, neither researchers nor subjects being aware of the aerosols' contents."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The randomisation code was determined by Glaxo Laboratories, who supplied the beclomethasone and placebo metered dose nasal aerosols in identical packaging, identified only by the numbers 1 to 30. The code was held by Glaxo until the end of the study, neither researchers nor subjects being aware of the aerosols' contents."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The randomisation code was determined by Glaxo Laboratories, who supplied the beclomethasone and placebo metered dose nasal aerosols in identical packaging, identified only by the numbers 1 to 30. The code was held by Glaxo until the end of the study, neither researchers nor subjects being aware of the aerosols' contents."

Incomplete outcome data (attrition bias) All outcomes	Low risk	There does not appear to be any missing outcome data.
Selective reporting (reporting bias)	Unclear risk	No protocol was found. No trial registration.
Other bias	Unclear risk	Insufficient information. The author was contacted and forwarded some study details to the review authors.

Williamson 2009

Study characteristics	
Methods	Two-arm, double blind, parallel-group, randomised controlled trial

Participants	**Setting:**
	Multi-centre trial, conducted in 99 general practices in the UK between January 2004 and April 2007
	Sample size:
	• **Number randomised:** 217 participants
	• **Number completed:** 144 participants
	Participant (baseline) characteristics:
	• **Age:**
	  ◦ Nasal steroids group: mean 73.3 months (SD 20.2)
	  ◦ Placebo group: mean 72.1 months (SD 18.6)
	• **Gender:**
	  ◦ Nasal steroids group:
	  ▪ 52 males (50%)
	  ▪ 53 females (50%)
	  ◦ Placebo group:
	  ▪ 63 males (56%)
	  ▪ 49 females (44%)
	• **Number with bilateral disease**
	  ◦ All had bilateral disease
	• **Hearing thresholds**
	  ◦ Nasal steroids group (n=84):
	  ▪ Median 30.97
	  ▪ IQR 23.8 to 32.65
	  ◦ Placebo group
	  ▪ Median 30.94
	  ▪ IQR 24.03 to 2.21
	Inclusion criteria:
	Aged 4 to 11 years. Attendance at the GP surgery with at least one prior episode of an ear-related problem including
	• Previous OME
	• Previous AOM
	• Concerns over hearing or speech
	and failed tympanometric screening in both ears
	• Tympanogram B/B or B/C2
	• Initially there was a requirement for failing tympanometry on 2 occasions, 3 months apart (72 children). This was relaxed to encourage recruitment to the study, so later recruits had a single abnormal tympanogram (145). See page 32 of the pdf, or page 18 main text
	Exclusion criteria:

	• Children at high risk of recurrent disease for whom early referral is indicated • Children with cleft palate, Down syndrome, primary ciliary dyskinesia, Kartagener's syndrome and immunodeficiency states • Children with grommets already in place, or referred or listed for grommets • Children who have taken systemic steroids in the previous 3 months or have poorly controlled asthma • Where there are developmental concerns about the child's growth, frequent or recent heavy epistaxis or known hypersensitivity to mometasone
Interventions	**Nasal steroids group (n=105 randomised, n=72 completed)** Topical intranasal mometasone furoate 50µg in each nostril (total daily dose 100µg) once daily for 3 months **Placebo nasal spray group (n=112 randomised, n=72 completed)** Used as above

Outcomes	**Primary outcomes relevant to this review:**
	• **Hearing**
	  ◦ Proportion of children with hearing returned to normal (sweep handheld audiometer) at 3 and 9 months
	  ◦ Mean (SD) final hearing thresholds. Air conduction estimated from tympanometry at 3 and 9 months
	• **Disease-specific quality of life**
	  ◦ OM8-30 total endpoint scores at 3 and 9 months
	• **Adverse event**
	  ◦ No data. Narrative summary available.
	Secondary outcomes relevant to this review:
	• **Presence/persistence of OME: proportion of children with persistence of OME (in both ears)**
	  ◦ Tympanograms B/B or B/C2 or C2/C2 at 3 and 9 months
	• **Receptive language skills:** Not reported
	• **Speech development, or expressive language skills:** Not reported
	• **Cognitive development:** Not reported
	• **Psychological outcomes:** Not reported
	• **Listening skills:** Not reported
	• **Generic health-related quality of life:** Not reported
	• **Parental stress:** Not reported
	• **Vestibular function:** Not reported
	• **Episodes of acute otitis media:** Not reported
	• **Other adverse effects**
	  ◦ Stinging in the nose at one and 3 months
	  ◦ Nosebleed at one and 3 months
	  ◦ Dry throat at one and 3 months
	  ◦ Cough at one and 3 months
	  ◦ Any adverse effect at one and 3 months
	Other outcomes reported in the study:
	• Proportion of participants with resolution of OME at 1, 3 and 9 months
	• Separate scores for subscales of the OM8-30 (including developmental scores and reported hearing difficulty) – not extracted as not considered validated measures of speech/language etc. as only a subset of a QOL scale.
	• Days with Reported hearing loss by parents in diary
	• Reported hearing loss on the OM8-30 scale
	• Days with otalgia
	• Adherence to medication

Funding sources	Health Technology Assessment NIHR HTA programme
Declarations of interest	None reported
Notes	**Research integrity checklist:** • No retractions or expressions of concern were noted • This trial was published prior to 2009 therefore prospective registration was not required • No concerns over similarity of baseline characteristics in the groups • Plausible loss to follow-up was reported • No implausible results were identified • Different numbers of participants were randomised to each group

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quote: “The supplier, Schering-Plough, used a computer generated random number sequence to randomise the intervention and placebo into blocks of four. Each block of four contained two active and two placebo codes in random sequence.” Comment: computer generated random sequence
Allocation concealment (selection bias)	Low risk	Quote: "To ensure blinding was total and complete the study separated all executors from the generator”. “Labelling and use of identical appearance containers, instructions and nasal sprays (also identical smell/taste) were all provided by Schering-Plough according to these codes and were in numbered auditable sequence.” "RNs assigned children in blinded numbered sequence” Comment: sequential numbered codes were used, with identical appearing interventions.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “To ensure blinding was total and complete the study separated all executors from the generator”. “...children were similarly unaware of assignment.” “The randomisation code was not broken at any point (the integrity of the returned code break envelopes from practices was found satisfactory). The study remained completely blinded until the analysis phase.” Comment: participants and study personnel unaware of group assignment
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: “To ensure blinding was total and complete the study separated all executors from the generator”. “The randomisation code was not broken at any point (the integrity of the returned code break envelopes from practices was found satisfactory). The study remained completely blinded until the analysis phase.” Comment: outcome assessors were blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	There is a high rate of attrition (31% and 36% in the steroid and placebo groups respectively over 9 months) in relation to the effect sizes reported. The reasons for losses to follow-up were reported, and these could be related to the outcomes.
Selective reporting (reporting bias)	Low risk	A protocol is available (https://www.journalslibrary.nihr.ac.uk/hta/hta13370/#/app11.) Trial record does state retrospectively registered. However, it is clear that a detailed trial plan occurred for the funder, and differences from this plan are documented in the report, e.g. changes to the protocol.
Other bias	Low risk	No concerns.

AOM: acute otitis media; ENT: ear, nose and throat; MEE: middle ear effusion; SD: standard deviation; TM: tympanic membrane

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Al-Zaidi 2023	ALLOCATION: not an RCT
Ardehali 2008	INTERVENTION: treatment with antibiotics and is relevant for another review in this suite (Mulvaney 2022a)
Crawford-Faucher 2010	ALLOCATION: not randomised
Daly 1991	INTERVENTION: participants received dual therapy with antibiotics and steroids, without an appropriate comparator.
Damoiseaux 2010	STUDY DESIGN: commentary article, not an RCT
El-Anwar 2015	ALLOCATION: not randomised
Endo 1997	INTERVENTION: treatment with antibiotics, and is relevant for another review in this suite (Mulvaney 2022a)
Ferrara 2005	PARTICIPANTS: had recurrent acute otitis media, not OME.
Gibson 1996	ALLOCATION: not randomised
Giebink 1990	PARTICIPANTS: children with effusion after an episode of acute otitis media, not OME.
Gluth 2011	PARTICIPANTS: wrong patient population, does not specifically include children with OME.
Han 2009	PARTICIPANTS: includes adult patients
Hughes 2019	STUDY DESIGN: commentary article, not an RCT
Iino 1989	ALLOCATION: not randomised
Isaacs 2018	STUDY DESIGN: commentary article, not an RCT
Marchisio 1998	INTERVENTION: treatment with antibiotics and is relevant for another review in this suite (Mulvaney 2022a)
Mayor 2018	STUDY DESIGN: commentary article, not an RCT
Paradise 1997	ALLOCATION: not randomised
Parlea 2012	ALLOCATION: not randomised
Persico 1978	ALLOCATION: not randomised
Rohail 2006	INTERVENTION: combination of medical interventions, including steroids, antibiotics, decongestants and antihistamines.
Salmen 2021	ALLOCATION: not an RCT
Schwartz 1980a	ALLOCATION: not randomised
Shapiro 1982	PARTICIPANTS: wrong patient population - not all participants had OME.
Shubich 1996	ALLOCATION: not randomised
Stenstrom 2005	ALLOCATION: not randomised
Tracy 1995	PARTICIPANTS: had recurrent acute otitis media.
Velepic 2011	INTERVENTION: treatment with ventilation tubes and is relevant for another review in this suite (MacKeith 2022b)
Yeldandi 2001	COMPARISON: co-interventions were not identical across the 2 study arms
Zocconi 1994	ALLOCATION: not randomised

Characteristics of studies awaiting classification [ordered by study ID]

Koay 1998

Methods	—
Participants	—
Interventions	—
Outcomes	—
Notes	Unable to obtain full text

Tawfik 2002

Methods	—
Participants	—
Interventions	—
Outcomes	—

Notes	Unable to obtain full text

Characteristics of ongoing studies [ordered by study ID]

NCT03491098

Study name	The Efficacy of Nasal Steroids in Treatment of Otitis Media With Effusion: A Comparative Study (Efficacy)
Methods	Parallel-group, randomised controlled trial from Egypt.
Participants	Estimated enrolment 60 participants. Children aged 4-12 years with OME (type B tympanogram and conductive hearing loss) for at least 2 months. Children with previous ventilation tubes or those with cleft palate will be excluded.
Interventions	**Nasal steroid:** Mometasone furoate spray, one puff in each nostril per day for 8 weeks. **Oral steroid:** Prednisolone 15 mg 3 times daily for 1 week, then tapered dose over a further 2 weeks. **Comparator:** Hypertonic seawater solution spray, one puff in each nostril daily for 8 weeks.
Outcomes	• Hearing loss (measured on an ordinal scale of 0 = no symptoms to 4 = always present) • Nasal obstruction (measured on an ordinal scale of 0 = no symptoms to 4 = always present) • Full ENT history, including snoring, sleep apnoea, difficult suckling in infants, anterior nasal discharge and conductive hearing loss.
Starting date	May 2018. Estimated study completion date was March 2020.
Contact information	Muteea M Bakuwairi bakuwairi2017@gmail.com
Notes	—

Appendices

Appendix 1. Draft search strategies

The search strategies were designed to identify all relevant studies for a suite of reviews on various interventions for Otitis Media with Effusion.

CENTRAL (CRS)	Cochrane ENT Register (CRS)	Medline (Ovid)
1 MESH DESCRIPTOR Otitis Media with Effusion EXPLODE ALL AND CENTRAL:TARGET 2 ("otitis media" adj6 effusion):AB,EH,KW,KY,MC,MH,TI,TO AND CENTRAL:TARGET 3 (OME):TI,TO AND CENTRAL:TARGET 4 (Secretory otitis media):AB,EH,KW,KY,MC,MH,TI,TO AND CENTRAL:TARGET 5 (Serous otitis media):AB,EH,KW,KY,MC,MH,TI,TO AND CENTRAL:TARGET	1 MESH DESCRIPTOR Otitis Media EXPLODE ALL AND INREGISTER 2 ("otitis media" OR OME OR "glue ear" OR middle-ear effusion OR middle-ear perfusion):AB,EH,KW,KY,MC,MH,TI,TO AND INREGISTER 3 #1 OR #2 4 (effusion or Recurrent or persistent or serous or secretory or perfusion):AB,EH,KW,KY,MC,MH,TI,TO AND INREGISTER 5 #3 AND #4	1 exp Otitis Media with Effus 2 ("otitis media" adj6 effusion 3 OME.ti. 4 Secretory otitis media.ab,ti 5 Serous otitis media.ab,ti. 6 Middle-ear effusion.ab,ti. 7 Glue ear.ab,ti. 8 middle-ear perfusion.ab,ti. 9 Otitis Media/ 10 otitis media.ti. 11 9 or 10

6 (Middle-ear effusion):AB,EH,KW,KY,MC,MH,TI,TO AND CENTRAL:TARGET 7 (glue ear):AB,EH,KW,KY,MC,MH,TI,TO AND CENTRAL:TARGET 8 (middle-ear perfusion):AB,EH,KW,KY,MC,MH,TI,TO AND CENTRAL:TARGET 9 MESH DESCRIPTOR Otitis Media AND CENTRAL:TARGET 10 (otitis media):TI,TO AND CENTRAL:TARGET 11 #9 OR #10 AND CENTRAL:TARGET 12 (((effusion or Recurrent or persistent or serous or secretory or perfusion) adj3 otitis)):AB,EH,KW,KY,MC,MH,TI,TO AND CENTRAL:TARGET 13 #11 AND #12 AND CENTRAL:TARGET 14 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #13 AND CENTRAL:TARGET		12 ((effusion or Recurrent or or serous or secretory or per adj3 otitis).ab,ti. 13 11 and 12 14 1 or 2 or 3 or 4 or 5 or 6 o 13 15 randomized controlled tria 16 controlled clinical trial.pt. 17 randomized.ab. 18 placebo.ab. 19 drug therapy.fs. 20 randomly.ab. 21 trial.ab. 22 groups.ab. 23 15 or 16 or 17 or 18 or 19 21 or 22 24 exp animals/ not humans 25 23 not 24 26 14 and 25
Embase (Ovid)	**Web of Science (Web of knowledge)**	**Trial registries (CR**
1 exp secretory otitis media/ 2 ("otitis media" adj6 effusion).ab,ti. 3 OME.ti. 4 Secretory otitis media.ab,ti. 5 Serous otitis media.ab,ti. 6 Middle-ear effusion.ab,ti. 7 glue ear.ab,ti. 8 middle-ear perfusion.ab,ti. 9 otitis media/ 10 otitis media.ti. 11 9 or 10 12 ((effusion or Recurrent or persistent or serous or secretory or perfusion) adj3 otitis).ab,ti. 13 11 and 12 14 1 or 2 or 4 or 5 or 6 or 7 or 8 or 13 15 (random* or factorial* or placebo* or assign* or allocat* or crossover*).tw. 16 (control* adj group*).tw. 17 (trial* and (control* or comparative)).tw. 18 ((blind* or mask*) and (single or double or triple or treble)).tw. 19 (treatment adj arm*).tw. 20 (control* adj group*).tw. 21 (phase adj (III or three)).tw. 22 (versus or vs).tw. 23 rct.tw. 24 crossover procedure/ 25 double blind procedure/ 26 single blind procedure/	11 #10 AND #9 Indexes=SCI-EXPANDED, CPCI-S Timespan=All years 10 #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1 Indexes=SCI-EXPANDED, CPCI-S Timespan=All years 9 TS=(randomised OR randomized OR randomisation OR randomisation OR placebo* OR (random* AND (allocat* OR assign*)) OR (blind* AND (single OR double OR treble OR triple))) Indexes=SCI-EXPANDED, CPCI-S Timespan=All years 8 (TI=(otitis media)) AND TS= ((effusion or Recurrent or persistent or serous or secretory or perfusion) NEAR/3 otitis) Indexes=SCI-EXPANDED, CPCI-S Timespan=All years 7 TOPIC: ((middle-ear perfusion)) Indexes=SCI-EXPANDED, CPCI-S Timespan=All years 6 TOPIC: ((glue ear)) Indexes=SCI-EXPANDED, CPCI-S Timespan=All years 5 TOPIC: ((Middle-ear effusion)) Indexes=SCI-EXPANDED, CPCI-S Timespan=All years 4 TOPIC: ((Serous otitis media)) Indexes=SCI-EXPANDED, CPCI-S Timespan=All years 3 TOPIC: ((Secretory otitis media)) Indexes=SCI-EXPANDED, CPCI-S Timespan=All years	1 ("otitis media" OR OME OR ear" OR middle-ear effusion middle-ear perfusion):AB,EH,KW,KY,MC AND CENTRAL:TARGET 2 (effusion or Recurrent or p serous or secretory or perfusion):AB,EH,KW,KY,MC AND CENTRAL:TARGET 3 #1 AND #2 4 http*:SO AND CENTRAL:T 5 (NCT0* or ACTRN* or ChiC DRKS* or EUCTR* or eudra IRCT* or ISRCTN* or JapicC JPRN* or NTR0* or NTR1* o NTR3* or NTR4* or NTR5* o NTR7* or NTR8* or NTR9* o or UMIN0*):AU AND CENTRAL:TARGET 6 #4 OR #5 7 #3 AND #6

27 randomization/ 28 placebo/ 29 exp clinical trial/ 30 parallel design/ 31 Latin square design/ 32 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 33 exp ANIMAL/ or exp NONHUMAN/ or exp ANIMAL EXPERIMENT/ or exp ANIMAL MODEL/ 34 exp human/ 35 33 not 34 36 32 not 35 37 14 and 36	2 TITLE: (OME) Indexes=SCI-EXPANDED, CPCI-S Timespan=All years 1 TOPIC: ("otitis media" NEAR/6 effusion) Indexes=SCI-EXPANDED, CPCI-S Timespan=All years	
ClinicalTrials.gov	**ICTRP**	
(EXPAND[Concept] "otitis media" OR EXPAND[Concept] "glue ear" OR middle-ear) AND (effusion OR Recurrent OR persistent OR serous OR secretory OR perfusion) | Interventional Studies	(otitis media AND effusion) OR glue ear OR middle-ear effusion OR middle-ear perfusion	

Appendix 2. Tool for screening eligible studies for scientific integrity/trustworthiness

This screening tool has been developed by Cochrane Pregnancy and Childbirth. It includes a set of predefined criteria to select studies that, based on available information, are deemed to be sufficiently trustworthy to be included in the analysis.

Criteria questions	**Assessment**		**Comments and concerns**
	High risk	**Low risk**	
Research governance			
Are there any retraction notices or expressions of concern listed on the Retraction Watch Database relating to this study?	Yes	No	
Was the study prospectively registered (for those studies published after 2010) If not, was there a plausible reason?	No	Yes	
When requested, did the trial authors provide/share the protocol and/or ethics approval letter?	No	Yes	
Did the trial authors engage in communication with the Cochrane Review authors within the agreed timelines?	No	Yes	
Did the trial authors provide IPD data upon request? If not, was there a plausible reason?	No	Yes	
Baseline characteristics			
Is the study free from characteristics of the study participants that appear too similar? (e.g. distribution of the mean (SD) excessively narrow or excessively wide, as noted by Carlisle 2017)	No	Yes	
Feasibility			
Is the study free from characteristics that could be implausible? (e.g. large numbers of women with a rare condition (such as severe cholestasis in pregnancy) recruited within 12 months)	No	Yes	
In cases with (close to) zero losses to follow-up, is there a plausible explanation?	No	Yes	
Results			
Is the study free from results that could be implausible? (e.g. massive risk reduction for main outcomes with small sample size)?	No	Yes	
	No	Yes	

Do the numbers randomised to each group suggest that adequate randomisation methods were used (e.g. is the study free from issues such as unexpectedly even numbers of women 'randomised' including a mismatch between the numbers and the methods, if the authors say 'no blocking was used' but still end up with equal numbers, or if the authors say they used 'blocks of 4' but the final numbers differ by 6)?			
For abstracts only:			
Have the study authors confirmed in writing that the data to be included in the review have come from the final analysis and will not change?	No	Yes	

References

References to studies included in this review

Acharya 2020 {published data only}

[CTG: NCT03590912]

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NCT03590912. Efficacy and cost analysis of steroid spray in treatment of otitis media with effusion [Efficacy and cost analysis of steroid spray in treatment of otitis media with effusion (OME) compared to that of antibiotic, antihistaminic, and nasal decongestant]. Https://clinicaltrials.gov/show/nct03590912 (first received 2018 Jul 18). [CENTRAL: CN-01625711] 9157677

Ahmed 2022 {published data only}

Ahmed MR, Eldeeb WE. Effectiveness of mometasone furoate nasal spray on tympanometric results and hearing loss in children with otitis media with effusion. Egyptian Journal of Otolaryngology 2022;38(1):32. [CENTRAL: CN-02518321] 22461865

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Barati B, Omrani MR, Okhovat AR, Kelishadi R, Hashemi M, Hassanzadeh A, et al. Effect of nasal beclomethasone spray in the treatment of otitis media with effusion. Journal of Research in Medical Sciences 2011;16(4):509-15. [CENTRAL: CN-01777185] 10395489 [EMBASE: 361828890] [PMID: 22091267]

Beigh 2013 {published data only}

Beigh Z, Lattoo M, Yousuf A, Pampori R. Topical nasal steroids for hearing loss associated with otitis media with effusion in children. Indian Journal of Otology 2013;19(3):132-5. [CENTRAL: CN-00873772] 1647615 [EMBASE: 2013602416]

Berman 1990 {published data only}

Berman S, Grose K, Nuss R, Huber-Navin C, Roark R, Gabbard SA, et al. Management of chronic middle ear effusion with prednisone combined with trimethoprim-sulfamethoxazole. Pediatric Infectious Disease Journal 1990 Aug;9(8):533-8. [CENTRAL: CN-00071176] 1006118 [PMID: 2235167]

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2014 Nov-Dec;35(6):766-70. [CENTRAL: CN-01036886] 1767490 [EMBASE: 2014790206] [PMID: 25151658]

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Akyol MU, Cengel S. The role of topical nasal steroid aerosol treatment in children with otitis media with effusion and/or adenoid hypertrophy. 12 months follow-up. In: Proceedings of the 9th International Conference on Pediatric Otorhinolaryngology (ESPO); 2006 Jun 18-21; Paris, France. 2006. [ABSTRACT NUMBER: 329] [CENTRAL: CN-00597474] 1422030

Cengel S, Akyol MU. The role of topical nasal steroids in the treatment of children with otitis media with effusion and/or adenoid hypertrophy. International Journal of Pediatric Otorhinolaryngology 2006 Apr;70(4):639-45. [CENTRAL: CN-00561141] 1390496 [EMBASE: 2006094358] [PMID: 16169093]

Choung 2008 {published data only}

Choung YH, Shin YR, Choi SJ, Park K, et al, et al. Management for the children with otitis media with effusion in the tertiary hospital. Clinical and Experimental Otorhinolaryngology 2008;1(4):201-5. [CENTRAL: CN-00671567] 1478067

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Hemlin C, Carenfelt C, Papatziamos G. Single dose of betamethasone in combined medical treatment of secretory otitis media. Annals of Otology, Rhinology, and Laryngology 1997 May;106(5):359-63. [CENTRAL: CN-00139646] 1074207 [PMID: 9153098]

Papatziamos G, Hemlin C, Carenfelt C. A placebo-controlled study of cetixime and the combination of cefixime and Betamethasone in children with secretory otitis media. In: Recent advances in otitis media. Proceedings of the second extraordinary international symposium on recent advances in otitis media, Japan, Mar 31-Apr 3, 1993. 1994.

Hussein 2017 {published data only}

Hussein A, Fathy H, Amin SM, Elsisy N. Oral steroids alone or followed by intranasal steroids versus watchful waiting in the management of otitis media with effusion. Journal of Laryngology and Otology 2017 Oct;131(10):907-13. [CENTRAL: CN-01412927] 6666616 [EMBASE: 618740433] [PMID: 28807086]

Karlidag 2002 {published data only}

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Figures and tables

Additional tables

Table 1

Adverse event reporting: oral steroid

Adverse event report	Trial	Steroid type, dosage and duration	Comparator	Effect
"Serious" or "severe" adverse event	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	"Only one serious adverse event was reported during the trial: one child in the placebo group had an asthma attack."
	Hemlin 1997	Single dose of a betamethasone tablet (6 mg) on the morning of day 10 (plus antibiotic for 10 days)	Antibiotic and placebo	"One child reported fever and sore throat that was classified as a severe adverse event, but considered to have an unlikely association with treatment given. None of the adverse events were classified as serious."
"Possible side-effects"	Mandel 2002	Prednisone syrup 0.5 mg/kg given twice a day on days one through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then given once a day on days 11 through 14 (total daily dose 0.5 mg/kg, maximum 15 mg/d) plus antibiotic.	Antibiotic and placebo	During weeks 1 and 2: oral steroid+antibiotic: 22/69; antibiotic+placebo: 17/66. RR 1.24 (95% CI 0.72 to 2.11)
"No significant adverse effects"	Niederman 1984	Tapering dose of oral dexamethasone for 13 days, starting at a max dose of 6 mg: 0.15 mg/kg per day up to a maximum of 6 mg on days 1 and 2; 0.075 mg/kg per day (to a max of 3 mg/day) on days 3 and 4; 0.0375 mg/kg/day (to a max of 1.5 mg per day) on days 5, 6 and 7; 0.0375 mg/kg/day (to a max of 1.5 mg per day in children over 40kg and 0.75 mg per day in children less than 40kg) on days 9, 11 and 13.	Placebo	"No significant adverse effects were seen in any study participant."
"No adverse effects"	Acharya 2020	Oral prednisolone 1 mg per kg per day in two divided doses for a week followed by 0.5 mg per day for one week.	No treatment	"No adverse effect was reported from group C (oral steroid)."
	Hemlin 1997	Single dose of 6 mg betamethasone.	No treatment	"No side effects of oral or intranasal steroids were reported in our patients"
	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Adjusted OR[1] 0.59 (95% CI 0.28 to 1.27)
Hyperactive	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Oral steroid: 3/179; placebo: 1/170. RR 2.85 (95% CI 0.30 to 27.12)
	Mandel 2002	Prednisone syrup 0.5 mg/kg given twice a day on days one through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then given once a day on days 11 through 14 (total daily dose 0.5 mg/kg, maximum 15 mg/d) plus antibiotic.	Antibiotic and placebo	During weeks 1 and 2: oral steroid+antibiotic: 10/69; antibiotic+placebo: 6/66. RR 1.59 (95% CI 0.61 to 4.14)
Change in behaviour	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20mg of prednisolone) for 7 days. Aged	Placebo	Oral steroid: 2/179; placebo: 0/170. Peto OR 7.07 (95% CI 0.44 to 113.53)

		>5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days		
Tired	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Oral steroid: 1/179; placebo: 1/170. RR 0.95 (95% CI 0.06 to 15.06)
Frustration	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Oral steroid: 0/179; placebo: 1/170. Peto OR 0.13 (95% CI 0.00 to 6.48)
Irritability	Mandel 2002	Prednisone syrup 0.5 mg/kg given twice a day on days one through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then given once a day on days 11 through 14 (total daily dose 0.5 mg/kg, maximum 15 mg/d) plus antibiotic.	Antibiotic and placebo	During weeks 1 and 2: oral steroid+antibiotic: 1/69; antibiotic+placebo: 2/66. RR 0.48 (95% CI 0.04 to 5.15)
Irritability and polyphagia	Schwartz 1980	Prednisone 1 mg/kg/day for the first two days in a divided dose, 0.75 mg/kg/day for the next two days and 5 to 10 mg/day as a single morning dose for the remaining three days. If partial clearing another week of prednisone 5 to 10 mg in a single morning dose on alternate days.	Placebo	"Only one child treated with the prednisone/sulfa manifested symptoms of irritability and polyphagia; this was the only complication of therapy in the 40 children treated with corticosteroids."
Sleep walking	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Oral steroid: 1/179; placebo: 0/170. Peto OR 7.03 (95% CI 0.14 to 354.59)
No symptoms of changes in behaviour and mood	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Adjusted OR[1] 0.76 (95% CI 0.49 to 1.19)
Increased appetite	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	RR 0.71 (95% CI 0.16 to 3.14)
	Mandel 2002	Prednisone syrup 0.5 mg/kg given twice a day on days one through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then given once a day on days 11 through 14 (total daily dose 0.5 mg/kg, maximum 15 mg/d) plus antibiotic.	Antibiotic and placebo	During weeks 1 and 2: oral steroid+antibiotic: 8/69; antibiotic+placebo: 4/66. RR 1.91 (95% CI 0.60 to 6.05)
Low appetite	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Peto OR 0.13 (95% CI 0.01 to 2.05)
Headache	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of	Placebo	RR 1.27 (95% CI 0.29 to 5.57)

		6 tablets (30 mg of prednisolone) for 7 days		
Vomiting	Berman 1990	Prednisone 0.5-1.0 mg/kg/dose twice a day for 7 days (plus antibiotic)	Antibiotic	"No side effects were noted in patients treated with prednisone and/or TMP/SMZ (antibiotic) other than one patient with a self limited episode of vomiting. The relationship of the vomiting to the TMP/SMZ and prednisone was unclear."
	Hemlin 1997	Single dose of a betamethasone tablet (6 mg) on the morning of day 10 (plus antibiotic for 10 days)	Antibiotic and placebo	Oral steroid+antibiotic: 1/59; antibiotic+placebo: 3/61 RR 0.34 (95% CI 0.04 to 3.22)
	Mandel 2002	Prednisone syrup 0.5 mg/kg given twice a day on days one through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then given once a day on days 11 through 14 (total daily dose 0.5 mg/kg, maximum 15 mg/d) plus antibiotic.	Antibiotic and placebo	During weeks 1 and 2: oral steroid+antibiotic: 3/69; antibiotic+placebo: 2/66. RR 1.43 (95% CI 0.25 to 8.32)
Nausea	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Oral steroid: 1/179; placebo: 0/170. Peto OR 7.03 (95% CI 0.14 to 354.59)
Stomach pain	Hemlin 1997	Single dose of a betamethasone tablet (6 mg) on the morning of day 10 (plus antibiotic for 10 days)	Antibiotic and placebo	Oral steroid+antibiotic: 2/59; antibiotic+placebo: 2/61 RR 1.03 (95% CI 0.15 to 7.10)
Abdominal discomfort	Mandel 2002	Prednisone syrup 0.5 mg/kg given twice a day on days one through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then given once a day on days 11 through 14 (total daily dose 0.5 mg/kg, maximum 15 mg/d) plus antibiotic.	Antibiotic and placebo	During weeks 1 and 2: oral steroid+antibiotic: 1/69; antibiotic+placebo: 2/66. RR 0.48 (95% CI 0.04 to 5.15)
Diarrhoea	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Oral steroid: 2/179; placebo: 2/170. RR 0.95 (95% CI 0.14 to 6.67)
	Hemlin 1997	Single dose of a betamethasone tablet (6 mg) on the morning of day 10 (plus antibiotic for 10 days)	Antibiotic and placebo	Oral steroid+antibiotic: 4/59; antibiotic+placebo: 2/61. RR 2.07 (95% CI 0.39 to 10.87)
Loose stools	Hemlin 1997	Single dose of a betamethasone tablet (6 mg) on the morning of day 10 (plus antibiotic for 10 days)	Antibiotic and placebo	Oral steroid+antibiotic: 2/59; antibiotic+placebo: 2/61. RR 1.03 (95% CI 0.15 to 7.10)
	Mandel 2002	Prednisone syrup 0.5 mg/kg given twice a day on days one through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then given once a day on days 11 through 14 (total daily dose 0.5 mg/kg, maximum 15 mg/d) plus antibiotic.	Antibiotic and placebo	During weeks 1 and 2: oral steroid+antibiotic: 4/69; antibiotic+placebo: 1/66. RR 3.83 (95% CI 0.44 to 33.35)
Gastroenteritis	Hemlin 1997	Single dose of a betamethasone tablet (6 mg) on the morning of day 10 (plus antibiotic for 10 days)	Antibiotic and placebo	Oral steroid+antibiotic: 0/59; antibiotic+placebo: 1/161. Peto OR 0.14 (95% CI 0.00 to 7.05)
Constipation	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of	Placebo	Oral steroid: 1/179; placebo: 1/170. RR 0.95 (95% CI 0.06

		prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days		to 15.06)
No symptoms of nausea, vomiting or indigestion	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Adjusted OR[1] 0.67 (95% CI 0.4 to 1.11)
Dermatitis	Hemlin 1997	Single dose of a betamethasone tablet (6 mg) on the morning of day 10 (plus antibiotic for 10 days)	Antibiotic and placebo	Oral steroid+antibiotic: 1/59; antibiotic+placebo: 0/61. Peto OR 7.64 (95% CI 0.15 to 385.43)
Hives	Mandel 2002	Prednisone syrup 0.5 mg/kg given twice a day on days one through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then given once a day on days 11 through 14 (total daily dose 0.5 mg/kg, maximum 15 mg/d) plus antibiotic.	Antibiotic and placebo	During weeks 1 and 2: oral steroid+antibiotic: 0/69; antibiotic+placebo: 1/66. Peto OR 0.13 (95% CI 0.00 to 6.52)
Rash, pox, or scarlet fever	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Peto OR 0.13 (95% CI 0.01 to 2.05)
Flushed cheeks	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Peto OR 7.03 (95% CI 0.14 to 354.59)
Other rash	Mandel 2002	Prednisone syrup 0.5 mg/kg given twice a day on days one through 10 (total daily dose 1 mg/kg, maximum 30 mg/d), then given once a day on days 11 through 14 (total daily dose 0.5 mg/kg, maximum 15 mg/d) plus antibiotic.	Antibiotic and placebo	During weeks 1 and 2: oral steroid+antibiotic: 4/69; antibiotic+placebo: 2/66. RR 1.91 (95% CI 0.36 to 10.10)
Phlegmy cough, cold, sneezing, temperature, nosebleed, conjunctivitis, itchy eyes, or generally unwell	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	RR 3.32 (95% CI 0.70 to 15.78)
Parotitis	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Peto OR 0.13 (95% CI 0.00 to 6.48)
Ear pain on touch or earache	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	RR 0.95 (95% CI 0.06 to 15.06)
Parent states child not hearing	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Oral steroid: 0/179; placebo: 1/170. Peto OR 0.13 (95% CI 0.00 to 6.48)
Finger infection	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged	Placebo	Oral steroid: 0/179; placebo: 1/170. Peto OR 0.13 (95% CI 0.00 to 6.48)

		>5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days		
Knee pain	OSTRICH	Aged 2–5 years: a single daily dose of 4 tablets (20 mg of prednisolone) for 7 days. Aged >5 years: a single daily dose of 6 tablets (30 mg of prednisolone) for 7 days	Placebo	Oral steroid: 0/179; placebo: 1/170. Peto OR 0.13 (95% CI 0.00 to 6.48)

[1] Adjusted for site and child's age group at recruitment (2–5 years and 6–8 years), data pooled across all follow-up time points (1, 2, 3, 4, and 5 weeks).

Table 2

Sensitivity analyses

Outcome	Main analysis result	Sensitivity analysis	Sensitivity analysis result
Oral steroid versus placebo			
1.9 Persistence of OME (very short-term)	0.72 (0.51 to 1.02)	Fixed-effect model	0.88 (0.82 to 0.94)
1.9 Persistence of OME (very short-term)	0.72 (0.51 to 1.02)	Excluding studies with any concern over trustworthiness	0.77 (0.48 to 1.24)
1.12 Persistence of OME (short-term)	0.81 (0.50 to 1.30)	Fixed-effect model	0.82 (0.67 to 1.01)
Oral steroid versus no treatment			
2.3 Persistence of OME (medium-term)	1.02 (0.89 to 1.17)	Fixed-effect model	1.03 (0.90 to 1.19)
Nasal steroid versus placebo			
3.10 Persistence of OME (short-term)	0.80 (0.51 to 1.26)	Fixed-effect model	0.86 (0.69 to 1.06)
3.10 Persistence of OME (short-term)	0.80 (0.51 to 1.26)	Excluding studies with any concern over trustworthiness	0.88 (0.63 to 1.23)
Nasal steroid versus no treatment			
4.2 Persistence of OME (very short term)	0.62 (0.44 to 0.86)	Fixed-effect model	0.58 (0.50 to 0.68)
4.2 Persistence of OME (very short term)	0.62 (0.44 to 0.86)	Excluding studies at high risk of bias	0.70 (0.46 to 1.07)
4.5 Persistence of OME (short-term)	0.72 (0.57 to 0.91)	Fixed effect model	0.72 (0.57 to 0.91)
4.5 Persistence of OME (short-term)	0.72 (0.57 to 0.91)	Excluding studies with any concern over trustworthiness	0.67 (0.50 to 0.90)
4.5 Persistence of OME (short-term)	0.72 (0.57 to 0.91)	Excluding studies at high risk of bias	0.80 [0.55 to 1.16)

Table 3

Study features

Study	Population	Setting	Intervention	Comparator	Concomitant treatment	Follow-up	Notes
Acharya 2020	Children aged 1-12 years with OME (n = 120)	Single-centre University hospital in Nepal	Intranasal mometasone furoate 50 µg per nostril per day for one month. or Oral prednisone (1 mg/kg/day) for one week, then 0.5 mg/kg/day	No treatment	None reported	One month	One further study arm assessed antibiotics a antihistamir nasal decongesta (not relevar for this revi

			for a further week				
Ahmed 2022	Children aged 4-12 years with bilateral OME (n = 168)	Single-centre University hospital in Egypt	Intranasal mometasone furoate spray, 50 µg/puff, 2 puffs per nostril once daily for one month.	No treatment	Participants in both groups also received amoxicillin and clavulanic acid (90g/kg/day) for 4 weeks.	One month	
Barati 2011	Children aged 1-10 years with OME (n = 92)	Single-centre University hospital in Iran	Intranasal beclomethasone, one puff per nostril (dose not given) for 4 weeks. Twice daily for children aged 1-5 years, three times daily for children aged 6-10 years.	No treatment	All participants also received amoxicillin 50 mg/kg/day for one week and decongestant (nasal saline spray and pseudoephedrine syrup)	Four weeks	
Beigh 2013	Children aged 2-8 years with OME (n = 92)	Single-centre University hospital in India	Intranasal mometasone (dose and frequency not stated) for 3 weeks, then a tapering dose for a further 3 weeks.	No treatment	None reported	9 weeks	
Berman 1990	Children with middle ear effusion for ≥6 weeks despite at least 2 courses of antibiotics (n = 68). Mean age 2.5 to 3 years (range 5 months to 12 years).	Single-centre University hospital in USA	Oral prednisone 0.5-1.0 mg/kg/dose twice daily for 7 days.	Placebo.	Trimethoprim-sulfamethoxazole 5 mg/kg/dose twice daily for 30 days	2 weeks	Participants with unresolved OME by tw week follow up crossed over to the alternative regimen, ar therefore some participants received bo intervention These data were not included in review.
Bhargava 2014	Children aged 2-12 years with at least 3 months of bilateral OME (n = 62).	Single-centre University hospital in India	Intranasal mometasone furoate 50 µg/nostril twice daily for 8 weeks, then reduced to alternate day dosing for a further 16 weeks.	Placebo (nasal saline spray), administered with the same frequency.	None reported	24 weeks	All participa had adenoi hypertrophy and had fai to respond "previous medical therapy".
Cengel 2006	Children aged 3-15 years with at least 3 months of bilateral or unilateral OME (n = 63).	Single-centre University hospital in Turkey	Intranasal mometasone furoate 100 µg daily, one spray in each nostril once a day for 6 weeks.	No treatment	None reported	6 weeks	
Choung 2008	Children aged 5 months to	Single-centre University	Oral prednisolone 1	No treatment	All participants received 2 weeks of amoxicillin-	6 months	Data from t relevant arr have been

	12 years with unilateral or bilateral OME (n = 84).	hospital in South Korea	mg/kg/day for 2 weeks.		clavulanic acid (2 groups also received antihistamine for 2 weeks).		pooled for analysis, to allow a comparisor those who received steroids to those who not.
Hemlin 1997	Children aged 2 to 12 years. Unilateral or bilateral OME of at least 3 months duration (n = 142).	Single-centre hospital in Sweden	Single dose of 6 mg betamethasone.	No treatment	All participants received cefixime 8 mg/kg/day for ten days	2 weeks	Longer follo up was reported, b only for a subset of participants
Hussein 2017	Children aged 2-11 years with bilateral OME (n = 202).	Single-centre hospital in Saudi Arabia	Seven days of oral prednisolone, 1 mg/kg/day.	No treatment	None reported.	9 months	
Karlidag 2002	Children aged 2-12 years with unilateral or bilateral OME (n = 42).	Single-centre hospital in Turkey	Budesonide intranasal spray, 200 µg/day for 8 weeks.	No treatment	All participants received ampicillin/sulbactam 25 mg/kg/day for 8 weeks.	8 weeks	
Khanam 2022	Children aged 2-12 years with bilateral OME for at least 3 months (n = 40).	Single-centre tertiary hospital in Bangladesh	Mometasone furoate 100 µg per nostril per day for 12 weeks.	Saline spray, used with the same frequency	None reported.	12 weeks	One further study arm assessed montelukas (not relevar for this revi
Lambert 1986	Children aged 2-15 years with OME (n = 60	Single-centre study from an ENT clinic in the USA.	Prednisolone once daily for 14 days according to the following schedule: 1.5 mg/kg/day for 4 days; 0.75 mg/kg/day for 4 days; 5 mg or 10 mg (depending on the child's weight) every other day for 6 days	Placebo syrup, administered in the same way.	All participants received either 125 mg or 250 mg amoxicillin 3 times daily for 14 days.	3-6 weeks	Some participants received a second cou of steroids resolution h started but was not complete b 10 days.
Lildholdt 1982	Children aged 4-14 years with uni- or bilateral OME (n = 70).	Single-centre trial from private ENT clinic in Denmark.	Beclomethasone 100 µg per nostril twice daily for one month.	Placebo spray.	None reported.	2 months.	
Macknin 1985	Children (mean age 3 to 4 years) with OME for at least 3 weeks (n = 49)	Single-centre trial from paediatric department of a hospital in the USA.	Oral dexamethasone, tapering dose for 13 days (starting dose 0.15 mg/kg).	Placebo.	None reported.	6 weeks.	Some child in this trial h a middle ea effusion persisting after an episode of AOM.
				Placebo.		4 weeks	

Mandel 2002	Children aged 1-9 years with uni- or bilateral middle ear effusion (n = 144)	Single-centre trial from a children's hospital in the USA.	Prednisone syrup 0.5 mg/kg twice daily for 10 days, then once daily for a further 4 days.		Amoxicillin 40 mg/kg/day in three divided doses for 14 days.		
Niederman 1984	Children aged ≤2 years with OME for at least 8 weeks (n = 26)	Single-centre trial from a hospital in the USA.	Tapering dose of oral dexamethasone for 13 days, starting at a dose of 0.15 mg/kg.	Placebo.	None reported.	5 weeks.	
OSTRICH	Children aged 2-8 years with bilateral OME for at least 3 months (n = 380)	Multi-centre trial conducted at 20 sites across the UK.	7-day course of oral soluble prednisolone (20 mg per day for children aged 2-5, 30 mg per day for those aged >5 years)	Placebo.	None reported.	12 months.	
Podoshin 1990	Children aged 3-8 years with OME for at least 2 months (n = 150)	Single-centre trial conducted in Israel.	14 day tapering dose of oral prednisolone, with initial dose of 1 mg/kg/day.	Placebo.	Amoxicillin 50 mg/kg/day	2 months.	
Puhakka 1985	Children aged 7 months to 11 years with OME (n = 75)	Single-centre trial conducted in Finland.	Oral prednisolone 1 mg/kg/day, given as a tapering dose over 6 days.	Placebo.	Sulfadiazine (18.5 mg/kg/day) and trimethoprim (6 mg/kg/day) for ten days	8 weeks.	Note that a participants received myringotom at the start the trial and any follow-u visit where effusion wa detected.
Rahmati 2017	Children aged 2-6 years with OME (n = 84)	Single-centre trial conducted in Iran.	Nasal mometasone, one puff per nostril daily for one month (dose not stated).	No treatment.	None reported.	1 month.	
Saffar 2001	Children aged 2-10 with OME (n = 49)	Single-centre trial conducted in Iran.	Oral prednisolone 1 mg/kg/day for 7 days, then tapered over next 5 days.	Placebo.	None reported.	6 months.	
Scadding 2014	Children aged 4-8 years with OME for at least 3 months (n = 200)	Single-centre trial conducted from a specialist OME clinic in the UK.	Fluticasone propionate nasal spray 50 µg per nostril twice daily for 2 weeks.	Placebo.	Some children in the trial also received autoinflation as an additional, background treatment.	2 years.	No efficacy data were useable fro this study.
Schwartz 1980	Children aged 1 to 10 years with OME for at least 3 weeks (n = 41)	Two-centre trial from private practices in the USA.	Oral prednisolone, 1 mg/kg/day to start, with a tapering does over 1 week.	Placebo.	Sulfisoxazole 50 mg/kg/day for 1 week.	1-2 weeks.	Some participants received additional prednisolon (5-10 mg o alternate da for 1 week) Unclear ho many participants

							this applies to.
Stuart 1995	Children (mean 4.5 years) with uni- or bilateral OME (n=50)	Single-centre study from Australia.	Nasal beclomethasone twice daily for 5 to 8 weeks (dose not given).	Placebo	None reported.	9-12 weeks.	Note that tv studies are reported in same publication.
Williamson 2009	Children aged 4-11 years with bilateral OME (n = 217)	Multi-centre trial from the UK.	Nasal mometasone furoate 50 µg per nostril once daily for three months.	Placebo.	None reported.	9 months.	

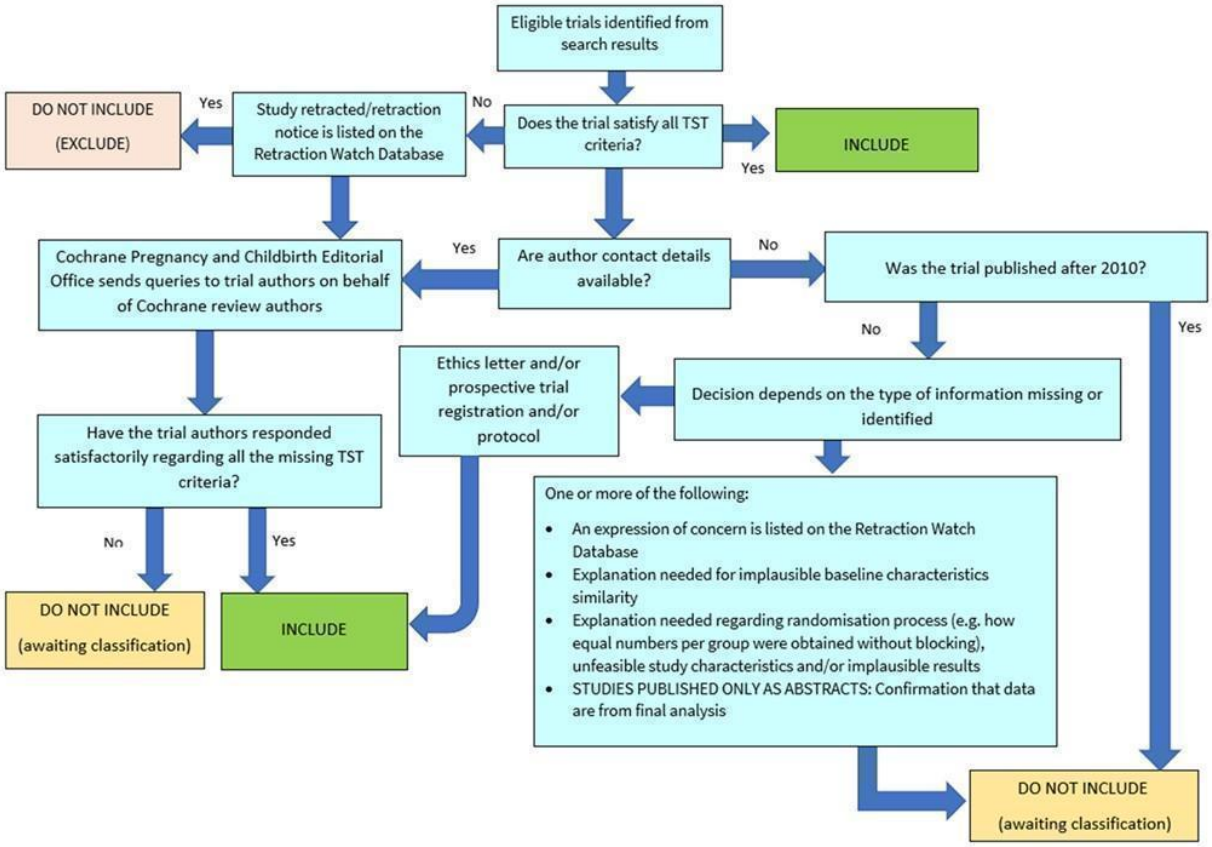
Table 4

Adverse event reporting: intranasal steroid

Adverse event report	Trial	Steroid type, dosage and duration	Comparator	Effect
"No serious adverse events"	Scadding 2014	Fluticasone propionate aqueous nasal spray 50 µg per spray, one puff per nostril twice daily for 2 weeks (2 puffs per nostril twice daily for children over 35kg), i.e. total daily dose 200 µg (or 400 µg) initially; then reduced to one puff per nostril (100 µg) once daily. “The children were asked to use this on a regular basis”. “Those who reported spray use on at least 3 days a week remained in the study”	Placebo	Over 2 years: "There were no serious adverse events in this study."
"No significant adverse effects"	Williamson 2009	Mometasone furoate 50 µg in each nostril (total daily dose 100 µg) once daily for three months.	Placebo	"No serious adverse events, suspected serious adverse reactions or related hospitalisations occurred during the study."
"Reported side-effects"	Williamson 2009	Mometasone furoate 50 µg in each nostril (total daily dose 100 µg) once daily for three months.	Placebo	At 1 month: Nasal steroid: 45/96; placebo: 35/98. RR 1.31 (95% CI 0.93 to 1.84). At 3 months: nasal steroid: 29/86; placebo: 23/86. RR 1.26 (95% CI 0.80 to 1.99)
"No adverse effects"	Lildholdt 1982	Beclomethasone dipropionate nasal spray administered twice in each nostril (100µg per nostril) twice a day, for a total of 400µg daily, for one month.	Placebo	"Apart from that (the child’s response to the power of the nasal spray) complications in the use of the spray were not noticed, especially no signs of mycosis or atrophy of the nasal mucosa occurred."
"No effect on growth"	Scadding 2014	Fluticasone propionate (FP) aqueous nasal spray 50 µg per spray, one puff per nostril twice daily for 2 weeks (2 puffs per nostril twice daily for children over 35kg), i.e. total daily dose 200 µg (or 400 µg) initially; then reduced to one puff per nostril (100 µg) once daily. “The children were asked to use this on a regular basis”. “Those who reported spray use on at least 3 days a week remained in the study”	Placebo	Over 2 years: "The plots of growth rate (not presented) indicated a uniform increase in height over the time period, independent of treatment. The mixed model fitted indicated no significant difference in growth rates between those children receiving FP and those given placebo on either method of analysis."
Nose bleed	Acharya 2020	Mometasone furoate 50 microgram in each nostril once a day for one month.	No treatment	“One case (2.5%) from group B (nasal spray) reported blood tinged nasal discharge which was managed with

				nasal ointment and counselling regarding proper way of using nasal spray.
	Bhargava 2014	Initial treatment of 2 puffs of mometasone furoate nasal spray (50 µg/puff) in each nostril once a day (a total of 200 µg/day) for first 8 weeks, followed by two puffs in each nostril on alternate days for 16 weeks.	Nasal saline	Nasal steroid: 2/30; nasal saline: 3/32. RR 0.71 (95% CI 0.13 to 3.97; Analysis 3.14)
	Scadding 2014	Fluticasone propionate aqueous nasal spray 50 µg per spray, one puff per nostril twice daily for 2 weeks (2 puffs per nostril twice daily for children over 35kg), i.e. total daily dose 200 µg (or 400 µg) initially; then reduced to one puff per nostril (100 µg) once daily. “The children were asked to use this on a regular basis”. “Those who reported spray use on at least 3 days a week remained in the study”	Placebo	"Minor adverse events were recorded, but none was of sufficient severity to cause cessation of the treatment or withdrawal from the trial. The commonest was minor epistaxis which occurred in fewer than 10% of subjects."
	Williamson 2009	Mometasone furoate 50 µg in each nostril (total daily dose 100 µg) once daily for three months.	Placebo	At 1 month: nasal steroid: 8/96; placebo: 7/98. RR 1.17 (95% CI 0.44 to 3.09) At 3 months: nasal steroid: 10/86; placebo: 6/86. RR 1.67 (95% CI 0.63 to 4.38)
Stinging in the nose	Williamson 2009	Mometasone furoate 50 µg in each nostril (total daily dose 100 µg) once daily for three months.	Placebo	At 1 month: nasal steroid: 9/96; placebo: 10/98. RR 0.92 (95% CI 0.39 to 2.16) At 3 months: nasal steroid: 9/86; placebo: 9/86. RR 1.00 (95% CI 0.42 to 2.40)
Dry throat	Williamson 2009	Mometasone furoate 50 µg in each nostril (total daily dose 100 µg) once daily for three months.	Placebo	At 1 month: nasal steroid: 13/96; placebo: 14/98. RR 0.95 (95% CI 0.47 to 1.91) At 3 months: nasal steroid: 10/86; placebo: 7/86. RR 1.43 (95% CI 0.57 to 3.58)
Cough	Williamson 2009	Mometasone furoate 50 µg in each nostril (total daily dose 100 µg) once daily for three months.	Placebo	At 1 month: nasal steroid: 23/96; placebo: 19/98. RR 1.24 (95% CI 0.72 to 2.12) At 3 months: nasal steroid: 19/86; placebo: 11/86. RR 1.73 (95% CI 0.88 to 3.41)
Intolerance of administration	Lildholdt 1982	Beclomethasone dipropionate nasal spray administered twice in each nostril (100µg per nostril) twice a day, for a total of 400µg daily, for one month.	Placebo	"This produced a rather powerful spray, and often a mist would appear through the open mouth; thus the spray reached the rhinopharynx, but many children were scared initially and did not enter the study. In a few cases the treatment was discontinued for that reason."

Figure 1



The Cochrane Pregnancy and Childbirth Trustworthiness Screening Tool

Figure 2

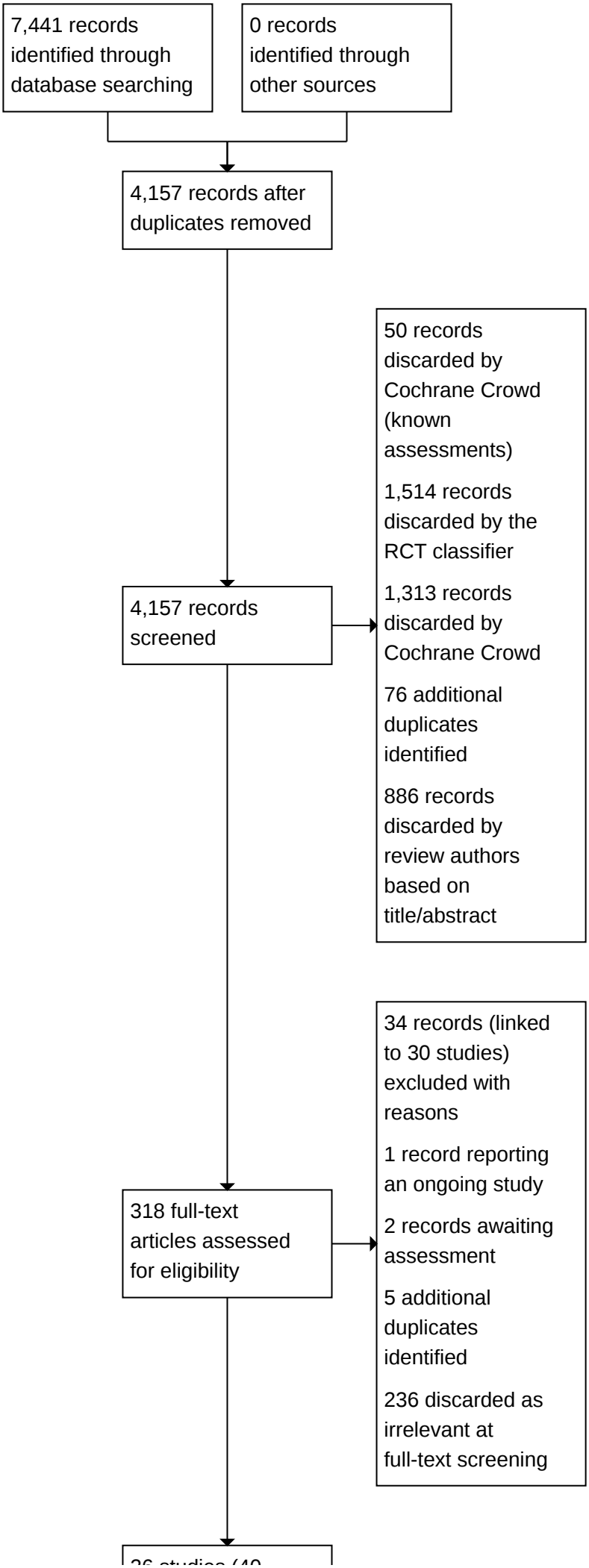
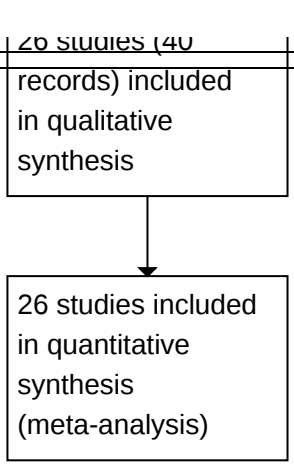
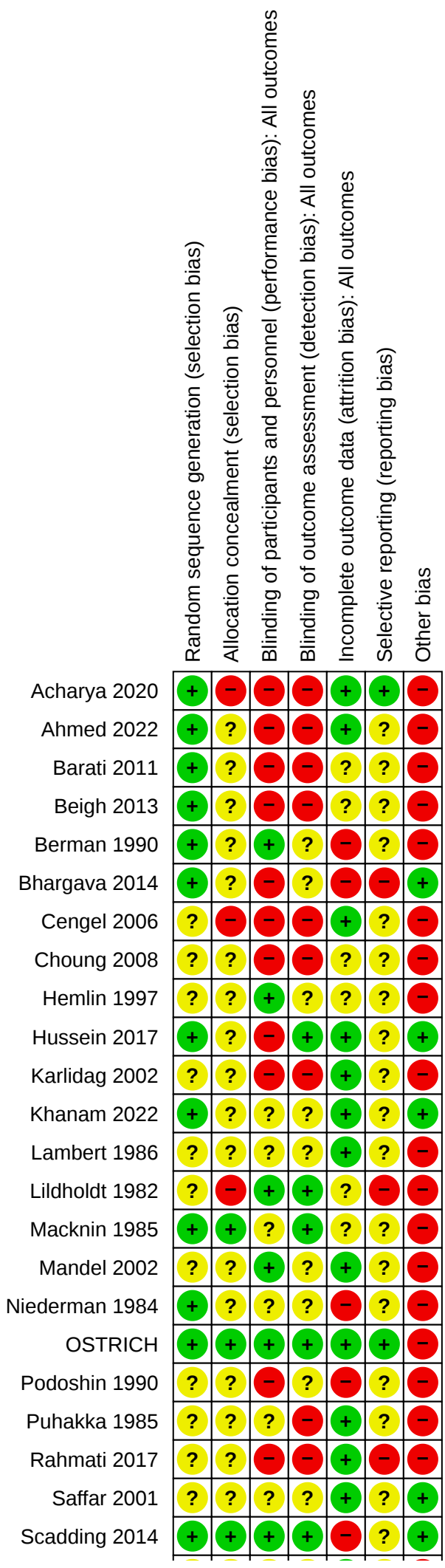

7,441 records identified through database searching
0 records identified through other sources
4,157 records after duplicates removed
4,157 records screened
50 records discarded by Cochrane Crowd (known assessments)
1,514 records discarded by the RCT classifier
1,313 records discarded by Cochrane Crowd
76 additional duplicates identified
886 records discarded by review authors based on title/abstract
318 full-text articles assessed for eligibility
34 records (linked to 30 studies) excluded with reasons
1 record reporting an ongoing study
2 records awaiting assessment
5 additional duplicates identified
236 discarded as irrelevant at full-text screening

Figure 3


26 studies (40 records) included in qualitative synthesis
26 studies included in quantitative synthesis (meta-analysis)


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias): All outcomes
Blinding of outcome assessment (detection bias): All outcomes
Incomplete outcome data (attrition bias): All outcomes
Selective reporting (reporting bias)
Other bias
Acharya 2020
Ahmed 2022
Barati 2011
Beigh 2013
Berman 1990
Bhargava 2014
Cengel 2006
Choung 2008
Hemlin 1997
Hussein 2017
Karlidag 2002
Khanam 2022
Lambert 1986
Lildholdt 1982
Macknin 1985
Mandel 2002
Niederman 1984
OSTRICH
Podoshin 1990
Puhakka 1985
Rahmati 2017
Saffar 2001
Scadding 2014

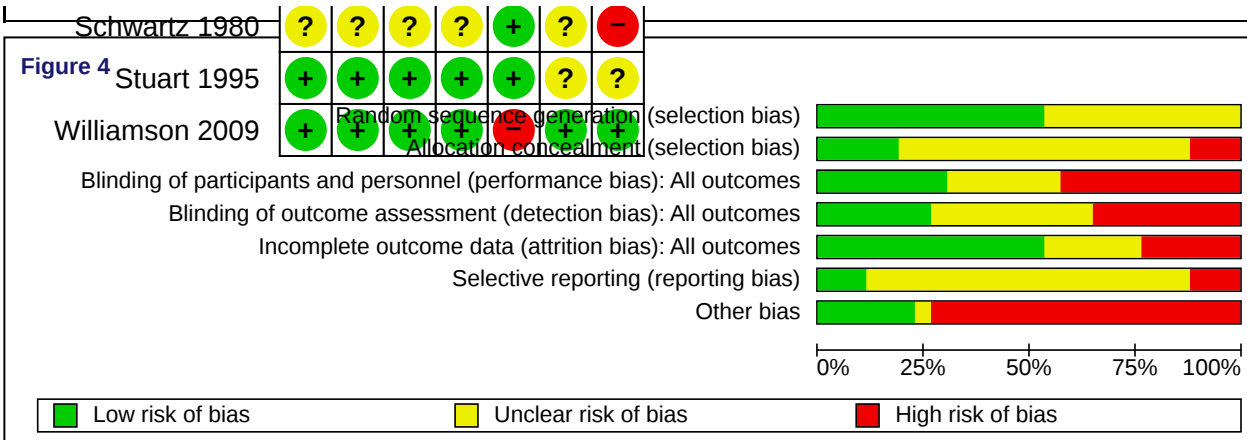
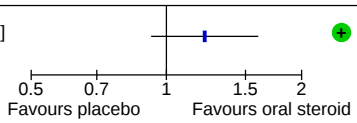


Figure 4

Analysis 1.1

Study or Subgroup	Oral steroid Events	Oral steroid Total	Placebo Events	Placebo Total	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
OSTRICH (1)	73	183	59	180	1.22 [0.92 , 1.60]		+ + + + + + −



Test for subgroup differences: Not applicable

Footnotes

(1) 5 weeks. Bilateral at baseline. Analysis by child. Normal defined as 'acceptable' in one ear.

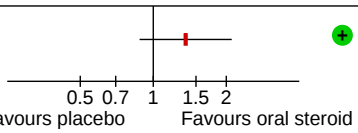
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 1: Normal hearing (very short-term)

Analysis 1.2

Study or Subgroup	log[Odds Ratio]	SE	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A B C D E F G
OSTRICH (1)	0.307485	0.223096	1.36 [0.88 , 2.11]		+ + + + + + −



Test for subgroup differences: Not applicable

Footnotes

(1) 5 weeks. Bilateral at baseline. Reported by child. Adj for site, age group and time since recruitment.

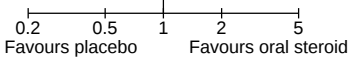
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 2: Normal hearing (very short-term, adjusted OR)

Analysis 1.3

Study or Subgroup	Oral steroid Events	Total	Placebo Events	Total	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
Podoshin 1990 (1)	20	50	20	49	0.98 [0.61 , 1.58]		? ? − ? − ? −



Test for subgroup differences: Not applicable

Footnotes

(1) 2 months. Analysis by child. Normal=complete improvement in air-bone gap in worst ear.

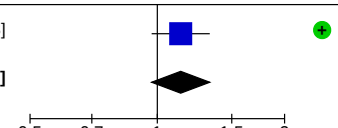
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 3: Normal hearing defined as complete improvement in air-bone gap (short-term)

Analysis 1.4

Study or Subgroup	Oral steroids Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
OSTRICH (1)	118	170	99	162	100.0%	1.14 [0.97 , 1.33]		+ + + + + + −
Total (95% CI)		**170**		**162**	**100.0%**	**1.14 [0.97 , 1.33]**		
Total events:	118		99					



Heterogeneity: Not applicable
Test for overall effect: Z = 1.58 (P = 0.11)
Test for subgroup differences: Not applicable

Footnotes

(1) 12 months. Bilateral at baseline. Analysis by child.

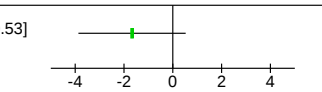
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 4: Normal hearing (medium-term)

Analysis 1.5

Study or Subgroup	Oral steroid Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
OSTRICH (1)	29.32	10.38	183	30.99	11	181	-1.67 [-3.87 , 0.53]		+ + + + + + −



Footnotes

(1) 5 weeks. Bilateral at baseline. Analysis by child. PTA.

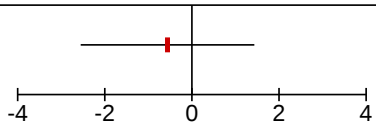
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 5: Hearing threshold (very short-term)

Analysis 1.6

Study or Subgroup	Mean Difference	SE	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
OSTRICH (1)	-0.56	1.017015	-0.56 [-2.55 , 1.43]	



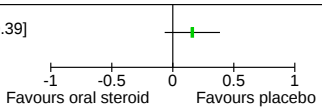
Footnotes

(1) 5 weeks. Analysis by child. Adj for baseline hearing, site, age and time since recruitment.

Comparison 1: Oral steroid versus placebo, Outcome 6: Hearing threshold (difference in adjusted mean, very short-term)

Analysis 1.7

Study or Subgroup	Oral steroid Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
OSTRICH (1)	0.49	1.11	182	0.33	1.08	177	0.16 [-0.07 , 0.39]		+ + + + + + −



Footnotes

(1) 5 weeks. Total OM8-30. Lower score better.

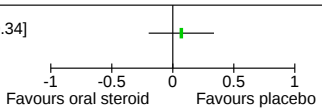
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 7: Disease-specific quality of life (very short-term)

Analysis 1.8

Study or Subgroup	Oral steroid Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
OSTRICH (1)	-0.22	1.18	154	-0.29	1.2	150	0.07 [-0.20 , 0.34]		+ + + + + + −



Footnotes

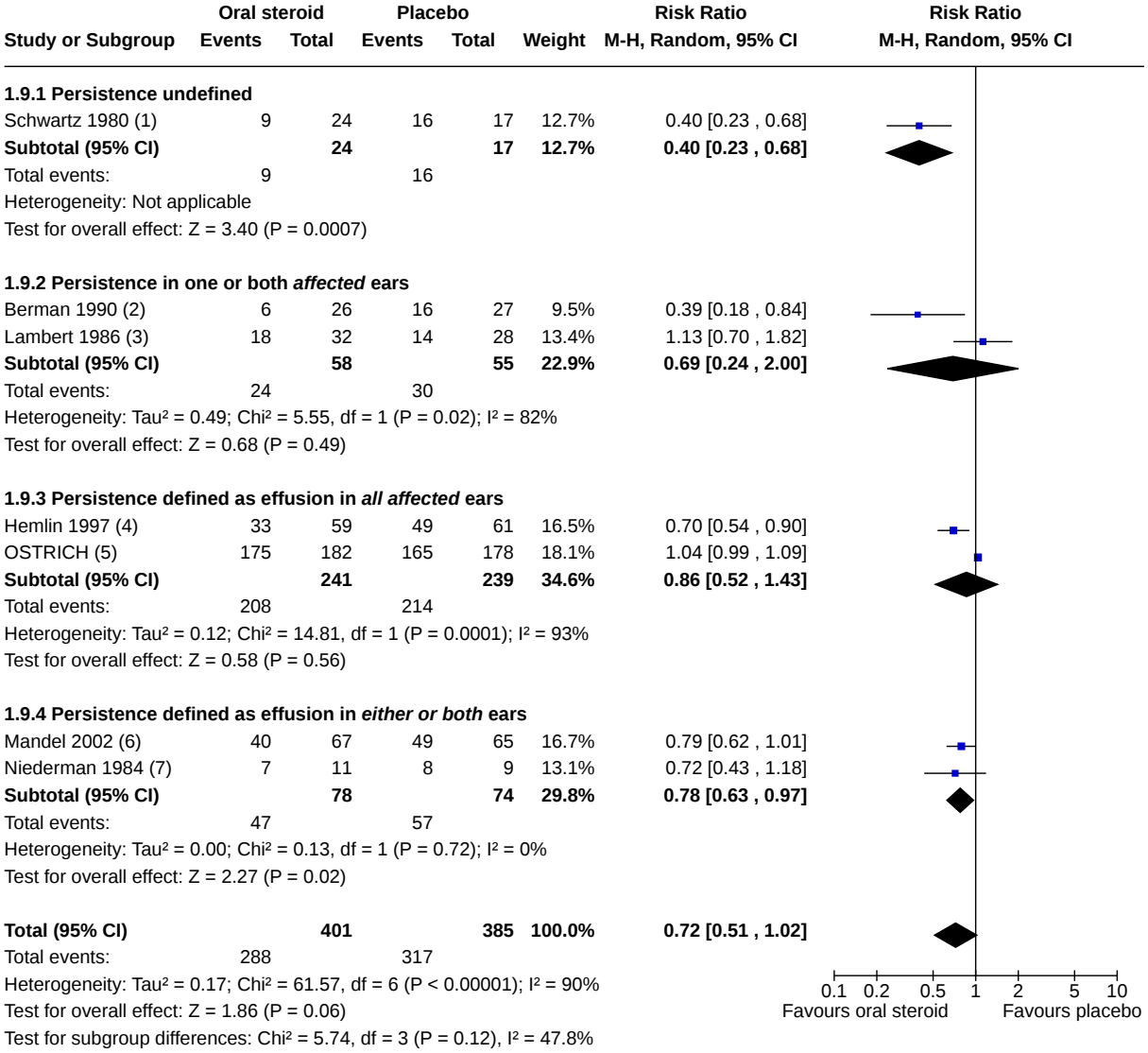
(1) 12 months. Total OM8-30. Lower score is better.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 8: Disease-specific quality of life (medium-term)

Analysis 1.9

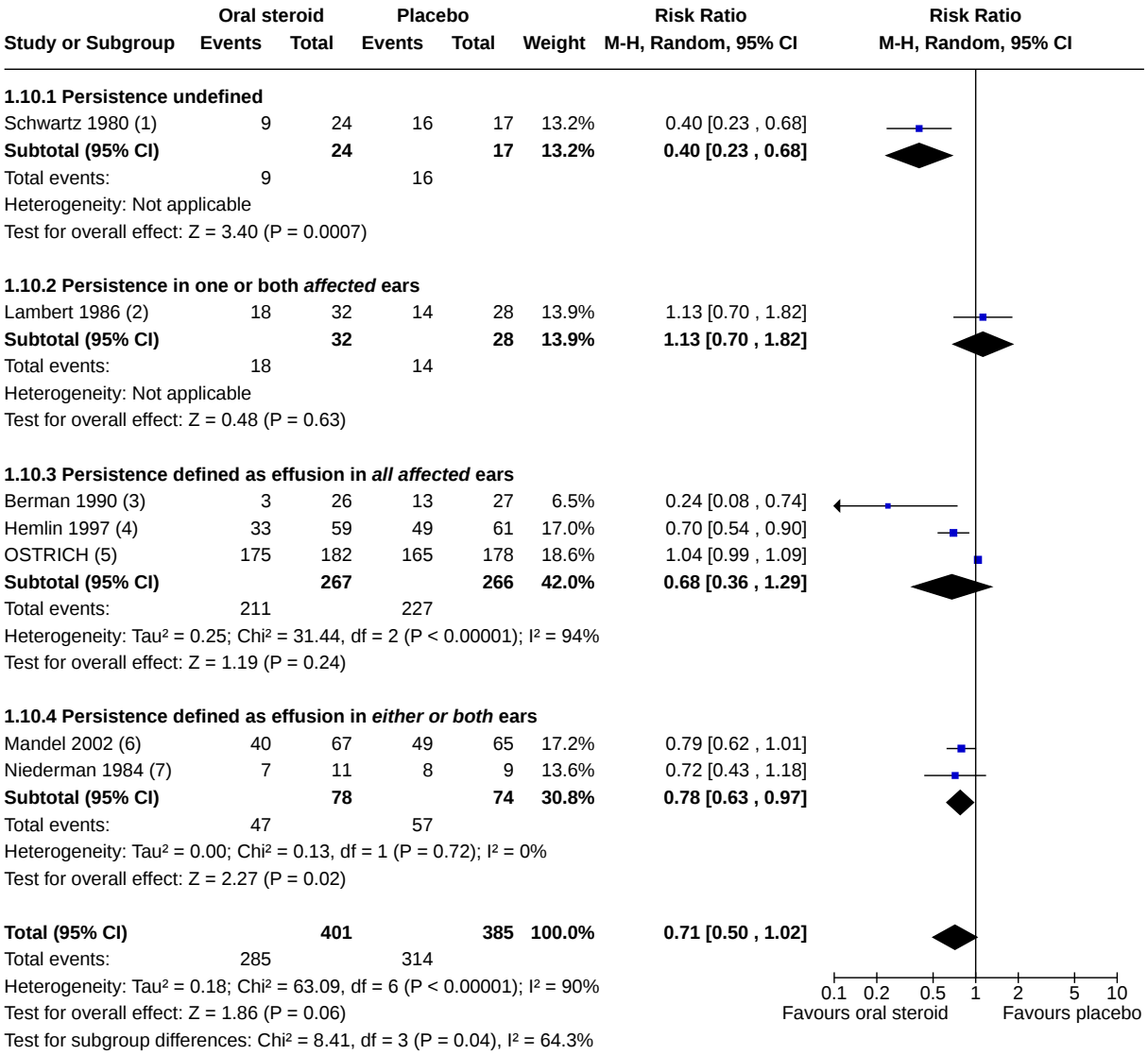


Footnotes

(1) 1 week. Uni- and bilateral at baseline. Reported by child.
(2) 2 weeks. Uni- or bilateral at baseline. Reported by child.
(3) 2 to 3 weeks. Uni- or bilateral at baseline. Analysis by child. Phase 1 only.
(4) 12 to 23 days. Uni-or bilateral at baseline. Analysis by child. Otomicroscopy and tympanometry.
(5) 5 weeks. Bilateral at baseline. Analysis by child. Tympanometry
(6) 4 weeks. Uni- or bilateral at baseline. Analysis by child. Does not include 8 cases of AOM.
(7) 5 weeks. Uni- or bilateral at baseline. Analysis by child.

Comparison 1: Oral steroid versus placebo, Outcome 9: Persistence of OME (very short-term)

Analysis 1.10

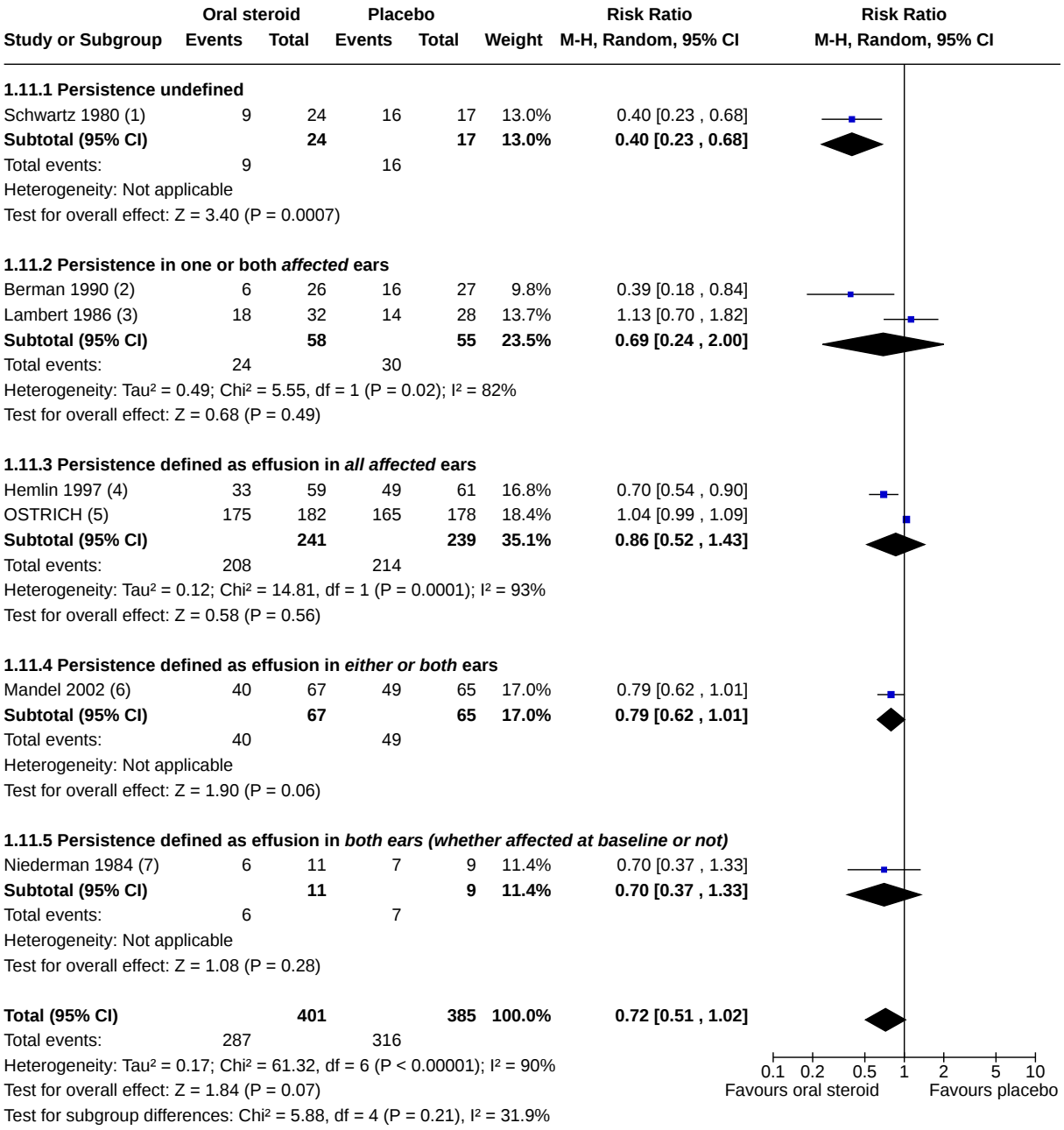


Footnotes

(1) 1 week. Uni- and bilateral at baseline. Reported by child.
(2) 2 to 3 weeks. Uni- or bilateral at baseline. Analysis by child. Phase 1 only.
(3) 2 weeks. Uni- or bilateral at baseline. Analysis by child.
(4) 12 to 23 days. Uni-or bilateral at baseline. Analysis by child. Otomicroscopy and tympanometry.
(5) 5 weeks. Bilateral at baseline. Analysis by child. Tympanometry
(6) 4 weeks. Uni- or bilateral at baseline. Analysis by child. Does not include 8 cases of AOM.
(7) 5 weeks. Uni- or bilateral at baseline. Analysis by child.

Comparison 1: Oral steroid versus placebo, Outcome 10: Sensitivity analysis: Persistence of OME (very short-term); persistence in all affected ears (Berman 1990)

Analysis 1.11

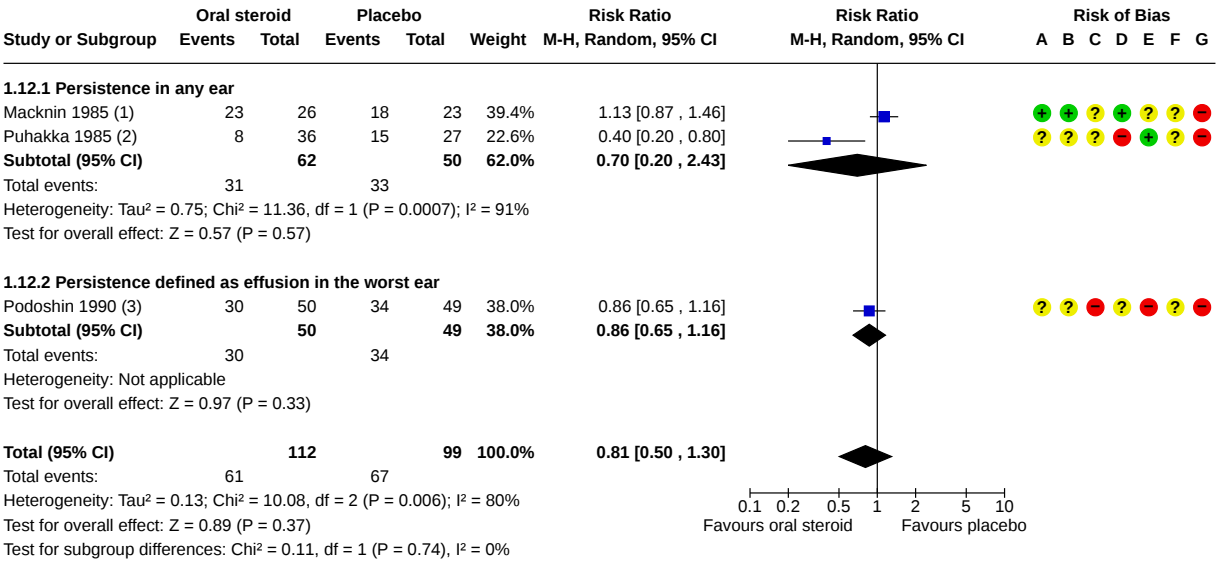


Footnotes

(1) 1 week. Uni- and bilateral at baseline. Reported by child.
(2) 2 weeks. Uni- or bilateral at baseline. Analysis by child.
(3) 2 to 3 weeks. Uni- or bilateral at baseline. Analysis by child. Phase 1 only.
(4) 12 to 23 days. Uni-or bilateral at baseline. Analysis by child. Otomicroscopy and tympanometry.
(5) 5 weeks. Bilateral at baseline. Analysis by child. Tympanometry
(6) 4 weeks. Uni- or bilateral at baseline. Analysis by child. Does not include 8 cases of AOM.
(7) 5 weeks. Uni- or bilateral at baseline. Analysis by child.

Comparison 1: Oral steroid versus placebo, Outcome 11: Sensitivity analysis: Persistence of OME (very short-term); effusion in both ears (Niederman 1984)

Analysis 1.12



Footnotes

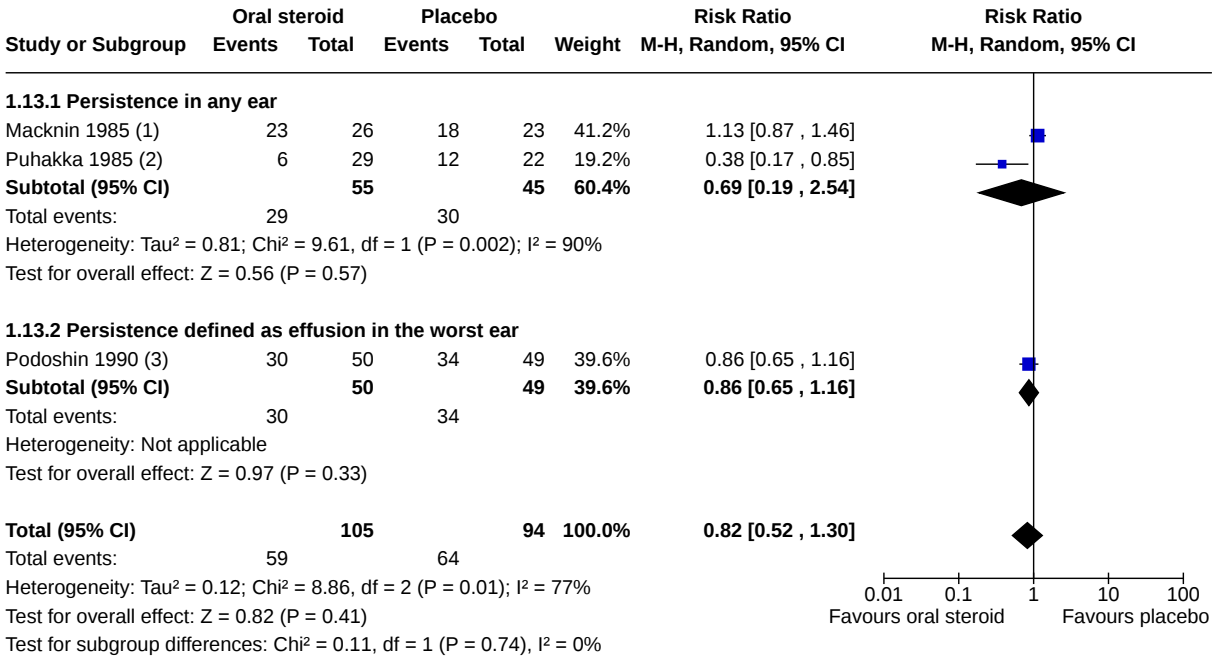
(1) 6 weeks. Uni- or bilateral at baseline. Analysis by child, in any ear.
(2) 8 weeks. Mixed uni- and bilateral. Analysis by ear (assumed ICC of 0.5, DE 1.3), in any ear.
(3) 2 months. Laterality of effusion at baseline not reported. Analysis by child. Tympanometry.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 12: Persistence of OME (short-term); ICC = 0.5

Analysis 1.13



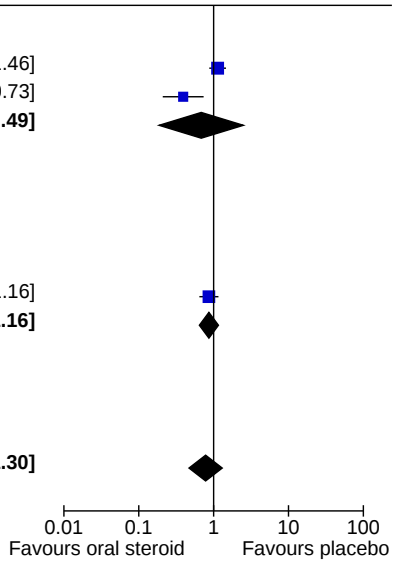
Footnotes

(1) 6 weeks. Uni- or bilateral at baseline. Analysis by child, in any ear.
(2) 8 weeks. Mixed uni- and bilateral. Analysis by ear. Average cluster size=1.6; ICC=1.0; DE=1.6.
(3) 2 months. Laterality of effusion at baseline not reported. Analysis by child. Tympanometry.

Comparison 1: Oral steroid versus placebo, Outcome 13: Sensitivity analysis: Persistence of OME (short-term); ICC = 1.0

Analysis 1.14

Study or Subgroup	Oral steroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.14.1 Persistence in any ear						
Macknin 1985 (1)	23	26	18	23	37.8%	1.13 [0.87 , 1.46]
Puhakka 1985 (2)	10	47	19	35	25.6%	0.39 [0.21 , 0.73]
Subtotal (95% CI)		**73**		**58**	**63.3%**	**0.68 [0.19 , 2.49]**
Total events:	33		37			
Heterogeneity: Tau² = 0.81; Chi² = 14.58, df = 1 (P = 0.0001); I² = 93%						
Test for overall effect: Z = 0.58 (P = 0.56)						
1.14.2 Persistence defined as effusion in the worst ear						
Podoshin 1990 (3)	30	50	34	49	36.7%	0.86 [0.65 , 1.16]
Subtotal (95% CI)		**50**		**49**	**36.7%**	**0.86 [0.65 , 1.16]**
Total events:	30		34			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						
Total (95% CI)		**123**		**107**	**100.0%**	**0.78 [0.47 , 1.30]**
Total events:	63		71			
Heterogeneity: Tau² = 0.16; Chi² = 12.42, df = 2 (P = 0.002); I² = 84%						
Test for overall effect: Z = 0.95 (P = 0.34)						
Test for subgroup differences: Chi² = 0.12, df = 1 (P = 0.73), I² = 0%						



Footnotes

(1) 6 weeks. Uni- or bilateral at baseline. Analysis by child, in any ear.

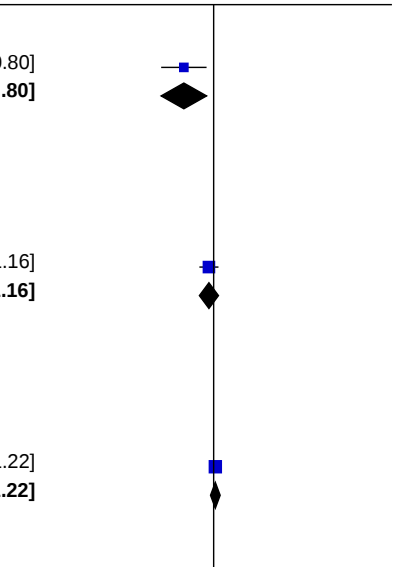
(2) 8 weeks. Mixed uni- and bilateral. Analysis by ear. Average cluster size=1.6; ICC=zero; DE=1.0.

(3) 2 months. Laterality of effusion at baseline not reported. Analysis by child. Tympanometry.

Comparison 1: Oral steroid versus placebo, Outcome 14: Sensitivity analysis: Persistence of OME (short-term); ICC = zero

Analysis 1.15

Study or Subgroup	Oral steroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.15.1 Persistence defined as effusion *in any ear*						
Puhakka 1985 (1)	8	36	15	27	23.4%	0.40 [0.20 , 0.80]
Subtotal (95% CI)		**36**		**27**	**23.4%**	**0.40 [0.20 , 0.80]**
Total events:	8		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.57 (P = 0.01)						
1.15.2 Persistence defined as effusion *in the worst ear*						
Podoshin 1990 (2)	30	50	34	49	36.5%	0.86 [0.65 , 1.16]
Subtotal (95% CI)		**50**		**49**	**36.5%**	**0.86 [0.65 , 1.16]**
Total events:	30		34			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.97 (P = 0.33)						
1.15.3 Persistence defined as effusion in *all affected ears*						
Macknin 1985 (3)	25	26	21	23	40.1%	1.05 [0.91 , 1.22]
Subtotal (95% CI)		**26**		**23**	**40.1%**	**1.05 [0.91 , 1.22]**
Total events:	25		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.69 (P = 0.49)						
Total (95% CI)		**112**		**99**	**100.0%**	**0.78 [0.47 , 1.30]**
Total events:	63		70			
Heterogeneity: Tau² = 0.16; Chi² = 15.86, df = 2 (P = 0.0004); I² = 87%						
Test for overall effect: Z = 0.94 (P = 0.34)						
Test for subgroup differences: Chi² = 7.94, df = 2 (P = 0.02), I² = 74.8%						



Footnotes

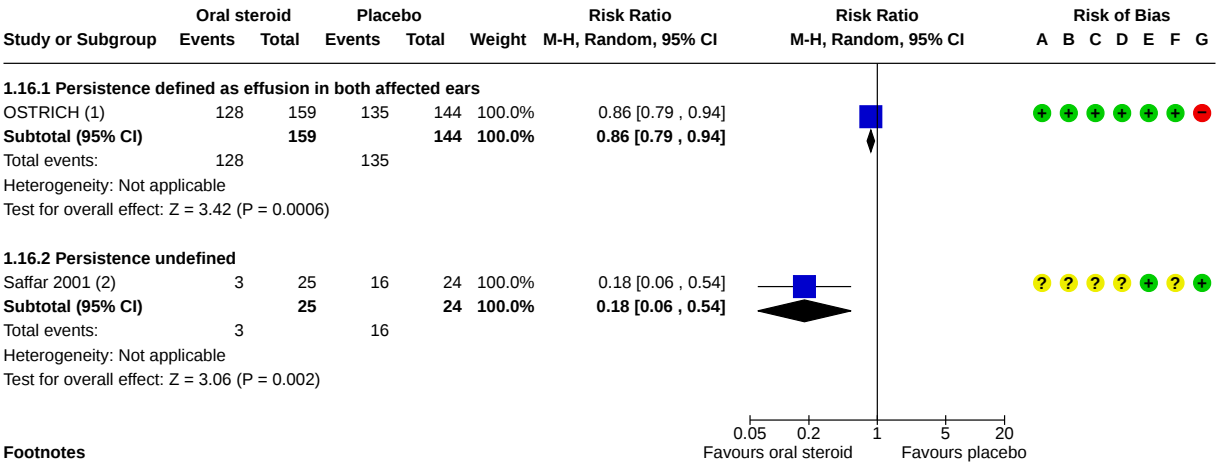
(1) 8 weeks. Mixed uni- and bilateral. Analysis by ear (assumed ICC of 0.5, DE 1.3), in any ear.

(2) 2 months. Laterality of effusion at baseline not reported. Analysis by child. Tympanometry.

(3) 6 weeks. Uni- or bilateral at baseline. Analysis by child.

Comparison 1: Oral steroid versus placebo, Outcome 15: Sensitivity analysis: Persistence of OME (short-term); persistence in all affected ears (Macknin 1985)

Analysis 1.16



Footnotes

(1) 12 months. Bilateral at baseline. Analysis by child. Tympanometry.

(2) 6 months. Laterality of effusion at baseline not reported. Analysis by child. Tympanometry and audiology.

Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

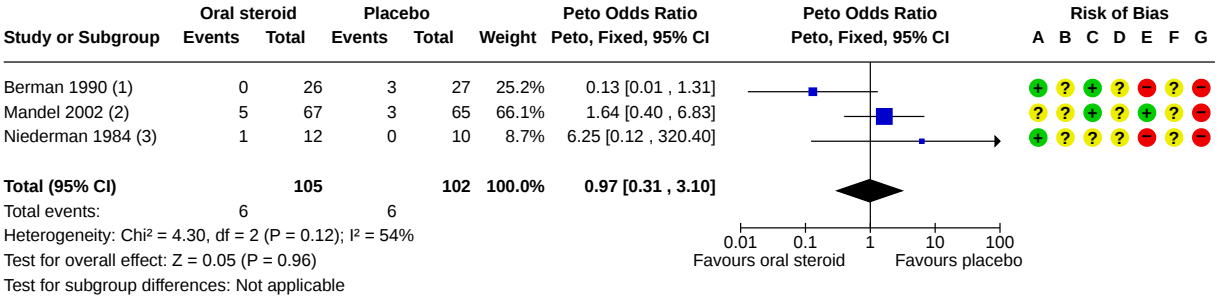
(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 16: Persistence of OME (medium-term)

Analysis 1.17



Footnotes

(1) Uni- or bilateral at baseline. Analysis by child. Proportion who had AOM by 2 weeks.

(2) Uni- or bilateral at baseline. Analysis by child. Proportion who had AOM between 2 and 4 weeks.

(3) Uni- or bilateral at baseline. Analysis by child. Proportion who had AOM by 2 weeks.

Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

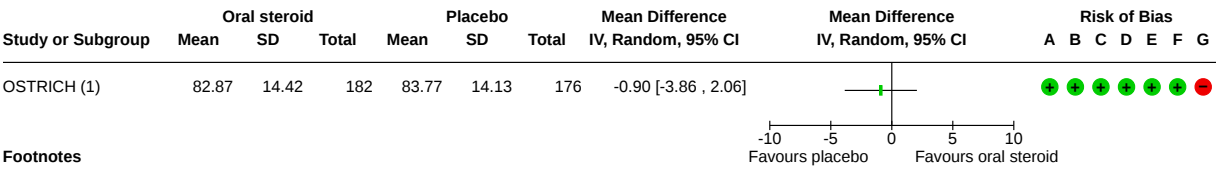
(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 17: Acute otitis media (very short-term)

Analysis 1.18



Footnotes

(1) 5 weeks. Total PedsQL. Higher score is better.

Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

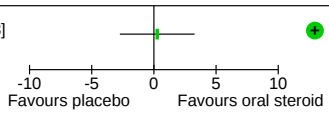
(F) Selective reporting (reporting bias)

(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 18: Generic health-related quality of life (PedsQL, very short-term)

Analysis 1.19

Study or Subgroup	Oral steroid Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F G
OSTRICH (1)	85.7	15.12	154	85.43	11.38	149	0.27 [-2.74 , 3.28]		+ + + + + + −



Footnotes
(1) 12 months. Total PedsQL. Higher score is better.

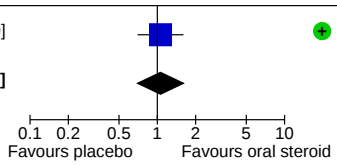
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 19: Generic health-related quality of life (PedsQL, medium-term)

Analysis 1.20

Study or Subgroup	Oral steroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
OSTRICH (1)	37	164	33	155	100.0%	1.06 [0.70 , 1.60]		+ + + + + + −
Total (95% CI)		**164**		**155**	**100.0%**	**1.06 [0.70 , 1.60]**		
Total events:	37		33					

Heterogeneity: Not applicable
Test for overall effect: Z = 0.27 (P = 0.78)
Test for subgroup differences: Not applicable



Footnotes
(1) 5 weeks. Dichotomised (perfect score yes/no).

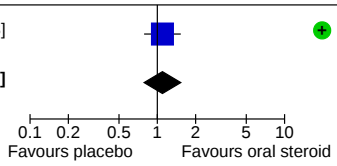
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 20: Generic health-related quality of life (HU13, very short-term)

Analysis 1.21

Study or Subgroup	Oral steroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
OSTRICH (1)	51	150	44	142	100.0%	1.10 [0.79 , 1.53]		+ + + + + + −
Total (95% CI)		**150**		**142**	**100.0%**	**1.10 [0.79 , 1.53]**		
Total events:	51		44					

Heterogeneity: Not applicable
Test for overall effect: Z = 0.55 (P = 0.58)
Test for subgroup differences: Not applicable



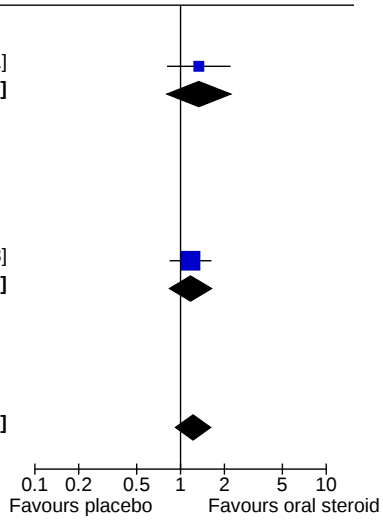
Footnotes
(1) 12 months. Dichotomised (perfect score yes/no).

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 1: Oral steroid versus placebo, Outcome 21: Generic health-related quality of life (HU13, medium-term)

Analysis 1.22

Study or Subgroup	Oral steroid Events	Oral steroid Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.22.1 Allergy						
OSTRICH (1)	27	67	16	53	30.2%	1.33 [0.81 , 2.21]
Subtotal (95% CI)		**67**		**53**	**30.2%**	**1.33 [0.81 , 2.21]**
Total events:	27		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.13 (P = 0.26)						
1.22.2 No allergy						
OSTRICH	46	116	43	127	69.8%	1.17 [0.84 , 1.63]
Subtotal (95% CI)		**116**		**127**	**69.8%**	**1.17 [0.84 , 1.63]**
Total events:	46		43			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.94 (P = 0.35)						
Total (95% CI)		**183**		**180**	**100.0%**	**1.22 [0.92 , 1.61]**
Total events:	73		59			
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 1 (P = 0.67); I² = 0%						
Test for overall effect: Z = 1.40 (P = 0.16)						
Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.67), I² = 0%						



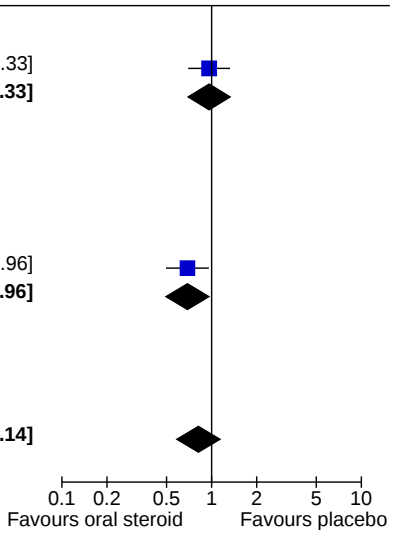
Footnotes

(1) 5 weeks. Atopy versus no atopy.

Comparison 1: Oral steroid versus placebo, Outcome 22: Subgroup analysis: Normal hearing: allergy versus none (very short-term)

Analysis 1.23

Study or Subgroup	Oral steroid Events	Oral steroid Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.23.1 Allergy						
Mandel 2002 (1)	22	30	16	21	50.5%	0.96 [0.70 , 1.33]
Subtotal (95% CI)		**30**		**21**	**50.5%**	**0.96 [0.70 , 1.33]**
Total events:	22		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.23 (P = 0.82)						
1.23.2 No allergy						
Mandel 2002 (2)	18	31	32	38	49.5%	0.69 [0.50 , 0.96]
Subtotal (95% CI)		**31**		**38**	**49.5%**	**0.69 [0.50 , 0.96]**
Total events:	18		32			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.21 (P = 0.03)						
Total (95% CI)		**61**		**59**	**100.0%**	**0.82 [0.59 , 1.14]**
Total events:	40		48			
Heterogeneity: Tau² = 0.03; Chi² = 2.06, df = 1 (P = 0.15); I² = 51%						
Test for overall effect: Z = 1.21 (P = 0.23)						
Test for subgroup differences: Chi² = 2.01, df = 1 (P = 0.16), I² = 50.4%						



Footnotes

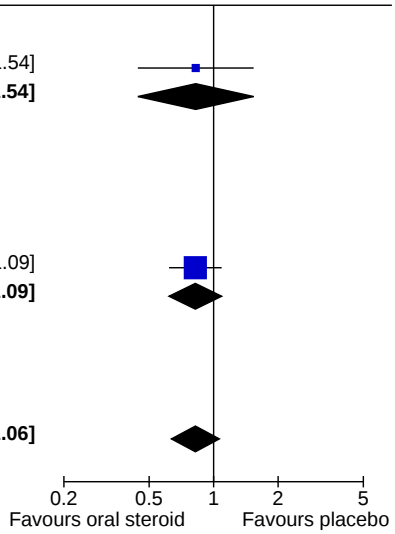
(1) 2 weeks. Positive skin tests.

(2) 2 weeks. Negative skin tests.

Comparison 1: Oral steroid versus placebo, Outcome 23: Subgroup analysis: Persistence of OME: allergy versus none (very short-term)

Analysis 1.24

Study or Subgroup	Oral steroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.24.1 Age <4						
Mandel 2002 (1)	6	10	8	11	17.1%	0.82 [0.44 , 1.54]
Subtotal (95% CI)		**10**		**11**	**17.1%**	**0.82 [0.44 , 1.54]**
Total events:	6		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.61 (P = 0.54)						
1.24.2 Age ≥4						
Mandel 2002 (2)	15	20	21	23	82.9%	0.82 [0.62 , 1.09]
Subtotal (95% CI)		**20**		**23**	**82.9%**	**0.82 [0.62 , 1.09]**
Total events:	15		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.36 (P = 0.17)						
Total (95% CI)		**30**		**34**	**100.0%**	**0.82 [0.64 , 1.06]**
Total events:	21		29			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.99); I² = 0%						
Test for overall effect: Z = 1.49 (P = 0.14)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.99), I² = 0%						



Footnotes

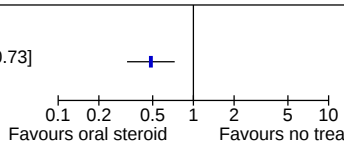
(1) 2 weeks. Age 12 to 23 months.

(2) 2 weeks. Age 6 to 9 years.

Comparison 1: Oral steroid versus placebo, Outcome 24: Subgroup analysis: Persistence of OME: age < 4 versus ≥ 4 (very short-term)

Analysis 2.1

Study or Subgroup	Oral steroid Events	Total	No treatment Events	Total	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
2.1.1 Persistence undefined						
Acharya 2020 (1)	16	40	33	40	0.48 [0.32 , 0.73]	+ − − − + + −



Footnotes

(1) 4 weeks. Laterality at baseline NR. Analysis by child.

Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

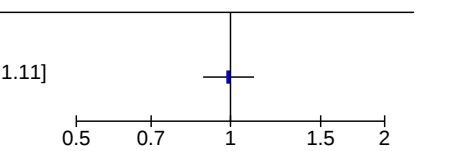
(F) Selective reporting (reporting bias)

(G) Other bias

Comparison 2: Oral steroid versus no treatment, Outcome 1: Persistence of OME (very short-term)

Analysis 2.2

Study or Subgroup	Oral steroid Events	Total	No treatment Events	Total	Risk Ratio M-H, Random, 95% CI
2.2.1 Persistence in one or both ears					
Hussein 2017 (1)	83	97	82	95	0.99 [0.88 , 1.11]



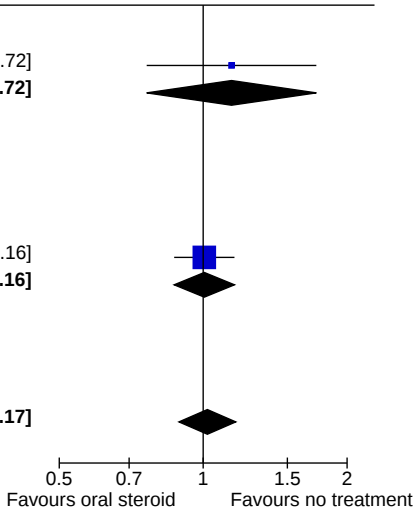
Footnotes

(1) 3 months. Bilateral at baseline. Analysis by child.

Comparison 2: Oral steroid versus no treatment, Outcome 2: Persistence of OME (short-term)

Analysis 2.3

Study or Subgroup	Oral steroid Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
2.3.1 Persistence undefined						
Choung 2008 (1)	22	35	17	31	11.2%	1.15 [0.76 , 1.72]
Subtotal (95% CI)		**35**		**31**	**11.2%**	**1.15 [0.76 , 1.72]**
Total events:	22		17			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.65 (P = 0.51)						
2.3.2 Persistence in one or both ears						
Hussein 2017 (2)	77	97	75	95	88.8%	1.01 [0.87 , 1.16]
Subtotal (95% CI)		**97**		**95**	**88.8%**	**1.01 [0.87 , 1.16]**
Total events:	77		75			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.07 (P = 0.94)						
Total (95% CI)		**132**		**126**	**100.0%**	**1.02 [0.89 , 1.17]**
Total events:	99		92			
Heterogeneity: Tau² = 0.00; Chi² = 0.38, df = 1 (P = 0.54); I² = 0%						
Test for overall effect: Z = 0.29 (P = 0.77)						
Test for subgroup differences: Chi² = 0.35, df = 1 (P = 0.55), I² = 0%						



Footnotes

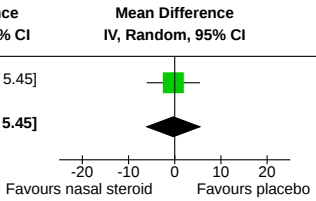
(1) At 3 to 6 months. Uni- or bilateral at baseline. Analysis by child. Two groups combined for each arm.

(2) 9 months. Bilateral at baseline. Analysis by child.

Comparison 2: Oral steroid versus no treatment, Outcome 3: Persistence of OME (medium-term)

Analysis 3.1

Study or Subgroup	Nasal steroid Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Lildholdt 1982 (1)	-7.9	15.4	41	-7.6	10.2	37	100.0%	-0.30 [-6.05 , 5.45]	? - + + ? - -
Total (95% CI)			**41**			**37**	**100.0%**	**-0.30 [-6.05 , 5.45]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.10 (P = 0.92)									
Test for subgroup differences: Not applicable									



Footnotes

(1) 2 mo. Uni- or bilateral at BL. Analysis by ear. Ave cluster size at BL (123 ears)=1.76 (assumed to apply to 107 ears at 2 months). ICC=0.5; DE=1.38.

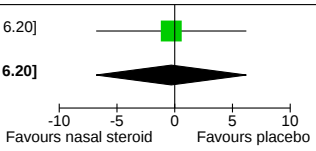
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 1: Change in hearing threshold (short-term); ICC = 0.5

Analysis 3.2

Study or Subgroup	Nasal steroid Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Lildholdt 1982 (1)	-7.9	15.4	32	-7.6	10.2	29	100.0%	-0.30 [-6.80 , 6.20]	? - + + ? - -
Total (95% CI)			**32**			**29**	**100.0%**	**-0.30 [-6.80 , 6.20]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.09 (P = 0.93)									
Test for subgroup differences: Not applicable									



Footnotes

(1) 2 mo. Uni- or bilateral at BL. Analysis by ear. Ave cluster size at BL (123 ears)=1.76 (assumed to apply to 107 ears at 2 months). ICC=1.0; DE=1.76.

Risk of bias legend

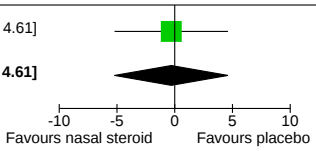
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 2: Sensitivity analysis: Change in hearing threshold (short-term); ICC=1.0

Analysis 3.3

Study or Subgroup	Nasal steroid Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Lildholdt 1982 (1)	-7.9	15.4	56	-7.6	10.2	51	100.0%	-0.30 [-5.21 , 4.61]		? − + + ? − −
Total (95% CI)			**56**			**51**	**100.0%**	**-0.30 [-5.21 , 4.61]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.90)
Test for subgroup differences: Not applicable



Footnotes
(1) 2 mo. Uni- or bilateral at BL. Analysis by ear. Ave cluster size at BL (123 ears)=1.76 (assumed to apply to 107 ears at 2 months). ICC=zero; DE=1.0

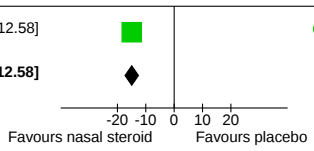
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 3: Sensitivity analysis: Change in hearing threshold (short-term); ICC=zero

Analysis 3.4

Study or Subgroup	Nasal steroid Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Khanam 2022 (1)	14.95	3.35	20	29.9	4.24	20	100.0%	-14.95 [-17.32 , -12.58]		+ ? ? ? + ? +
Total (95% CI)			**20**			**20**	**100.0%**	**-14.95 [-17.32 , -12.58]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 12.37 (P < 0.00001)
Test for subgroup differences: Not applicable



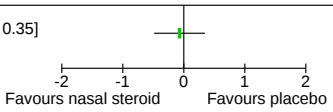
Footnotes
(1) 12 weeks. Pure tone audiometry.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 4: Final hearing threshold (short term)

Analysis 3.5

Study or Subgroup	Nasal steroid Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Williamson 2009 (1)	2.92	0.95	39	2.99	0.97	43	-0.07 [-0.49 , 0.35]		+ + + + − + +



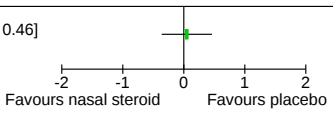
Footnotes
(1) 3 months. Total OM8-30 score. Lower score=better.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 5: Disease-specific quality of life (short-term)

Analysis 3.6

Study or Subgroup	Nasal steroid Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Williamson 2009 (1)	2.92	0.94	39	2.87	0.96	43	0.05 [-0.36 , 0.46]		



Footnotes

(1) 9 months. Total OM8-30 score. Lower score=better.

Risk of bias legend

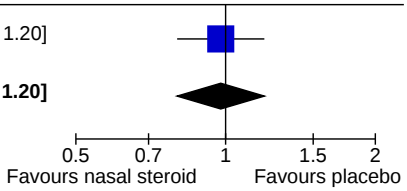
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 6: Disease-specific quality of life (medium-term)

Analysis 3.7

Study or Subgroup	Nasal steroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Lildholdt 1982 (1)	36	45	36	44	100.0%	0.98 [0.80 , 1.20]	
Total (95% CI)		**45**		**44**	**100.0%**	**0.98 [0.80 , 1.20]**	
Total events:	36		36				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.22 (P = 0.83)
Test for subgroup differences: Not applicable



Footnotes

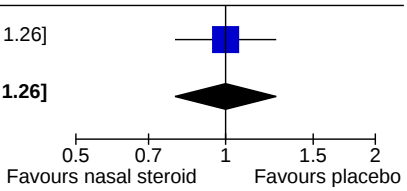
(1) 1 month. Uni- or bilateral at BL. Analysis by ear. Ave cluster size=1.76; ICC=0.5; DE=1.38.

Comparison 3: Nasal steroid versus placebo, Outcome 7: Persistence of OME (very short-term); ICC=0.5

Analysis 3.8

Study or Subgroup	Nasal steroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Lildholdt 1982 (1)	28	35	28	35	100.0%	1.00 [0.79 , 1.26]	
Total (95% CI)		**35**		**35**	**100.0%**	**1.00 [0.79 , 1.26]**	
Total events:	28		28				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)
Test for subgroup differences: Not applicable



Footnotes

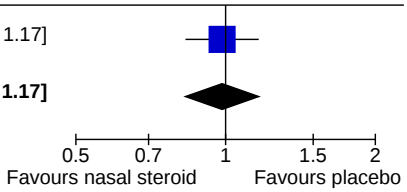
(1) 1 month. Uni- or bilateral at BL. Analysis by ear. Ave cluster size=1.76; ICC=1.0; DE=1.76.

Comparison 3: Nasal steroid versus placebo, Outcome 8: Sensitivity analysis: Persistence of OME (very short-term); ICC=1.0

Analysis 3.9

Study or Subgroup	Nasal steroid Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Lildholdt 1982 (1)	50	62	50	61	100.0%	0.98 [0.83 , 1.17]	
Total (95% CI)		**62**		**61**	**100.0%**	**0.98 [0.83 , 1.17]**	
Total events:	50		50				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.19 (P = 0.85)
Test for subgroup differences: Not applicable

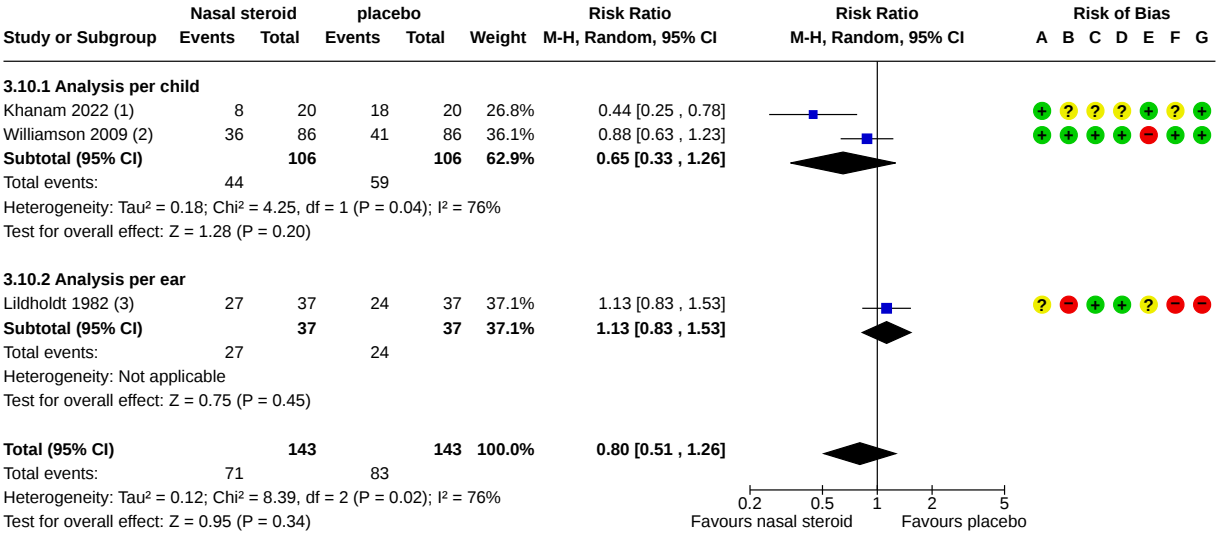


Footnotes

(1) 1 month. Uni- or bilateral at BL. Analysis by ear. Ave cluster size=1.76; ICC=zero; DE=1.0

Comparison 3: Nasal steroid versus placebo, Outcome 9: Sensitivity analysis: Persistence of OME (very short-term); ICC=zero

Analysis 3.10



Footnotes

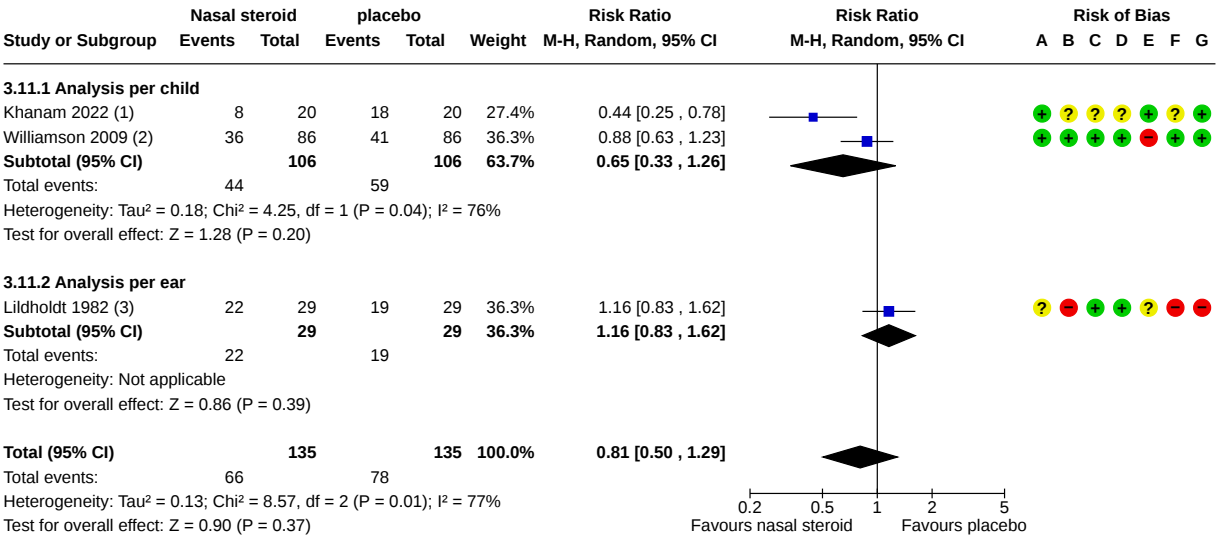
(1) 3 months. All bilateral at baseline. Unclear how persistence was defined.
(2) 3 months. All bilateral at baseline. Persistence in both ears.
(3) 2 mo. Uni/bilateral at BL. Analysis by ear. Ave cluster size at BL (123 ears)=1.76 (assumed applies to 102 ears at 2 months). ICC=0.5; DE=1.38.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 10: Persistence of OME (short-term)

Analysis 3.11



Footnotes

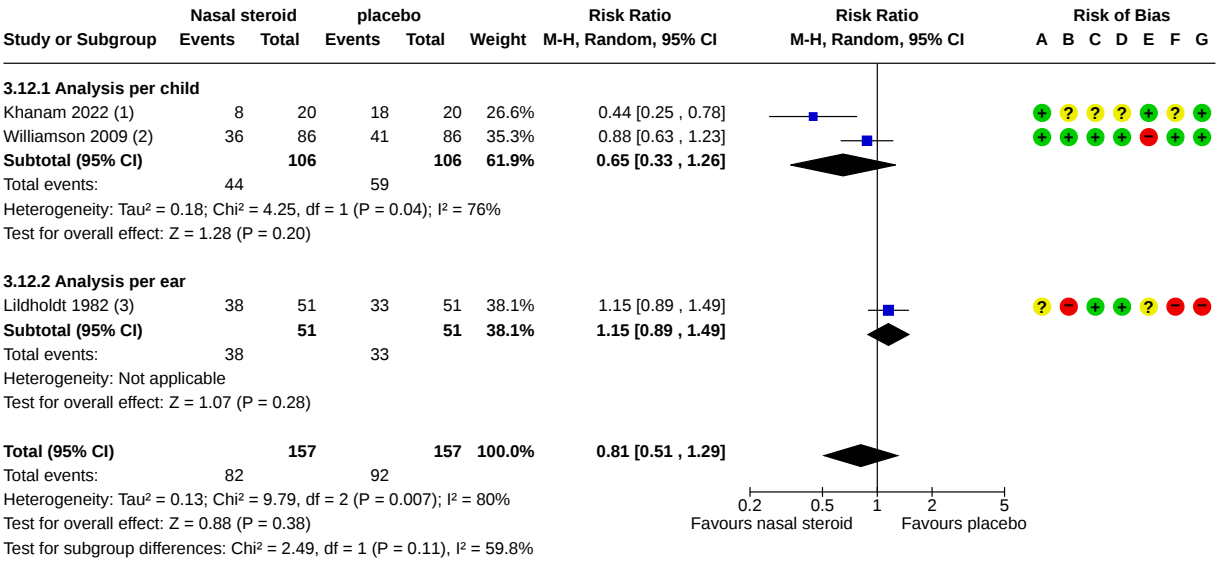
(1) 3 months. All bilateral at baseline. Unclear how persistence was defined.
(2) 3 months. All bilateral at baseline. Persistence in both ears.
(3) 2 mo. Uni/bilateral at BL. Analysis by ear. Ave cluster size at BL (123 ears)=1.76 (assumed applies to 102 ears at 2 months). ICC=1.0; DE=1.76.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 11: Sensitivity analysis: Persistence of OME (short-term); ICC=1.0

Analysis 3.12



Footnotes

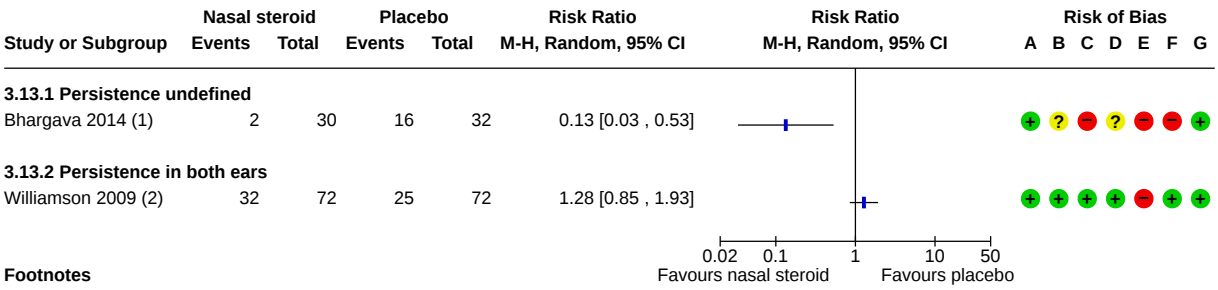
(1) 3 months. All bilateral at baseline. Unclear how persistence was defined.
(2) 3 months. All bilateral at baseline. Persistence in both ears.
(3) 2 mo. Uni/bilateral at BL. Analysis by ear. Ave cluster size at BL (123 ears)=1.76 (assumed applies to 102 ears at 2 months). ICC=zero; DE=1.0.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 12: Sensitivity analysis: Persistence of OME (short-term); ICC=zero

Analysis 3.13



Footnotes

(1) 6 months. Bilateral at baseline. Analysis by child.
(2) 9 months. Analysis by child.

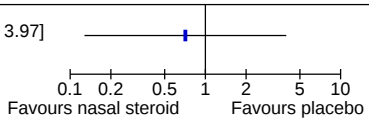
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 13: Persistence of OME (medium-term)

Analysis 3.14

Study or Subgroup	Nasal steroid Events	Total	Placebo Events	Total	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
Bhargava 2014 (1)	2	30	3	32	0.71 [0.13 , 3.97]		



Footnotes

(1) 6 months. Bilateral at baseline. Analysis by child.

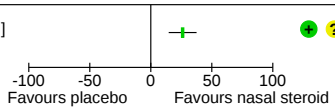
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 14: Adverse event: nasal bleeding (medium-term)

Analysis 3.15

Study or Subgroup	Nasal steroid Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Bhargava 2014 (1)	37.11	25.5	30	11.02	19.8	32	26.09 [14.67 , 37.51]		



Footnotes

(1) 6 months. Glasgow Children's Benefit Inventory. Possible range -100 to +100 (higher=better).

Risk of bias legend

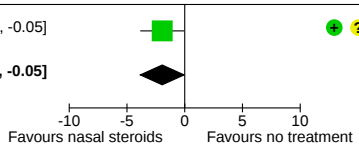
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 3: Nasal steroid versus placebo, Outcome 15: Generic health-related quality of life (medium-term)

Analysis 4.1

Study or Subgroup	Nasal steroids Mean	SD	Total	No treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
Ahmed 2022 (1)	7.51	6.39	84	9.46	6.17	84	100.0%	-1.95 [-3.85 , -0.05]		
Total (95% CI)			**84**			**84**	**100.0%**	**-1.95 [-3.85 , -0.05]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.01 (P = 0.04)
Test for subgroup differences: Not applicable



Footnotes

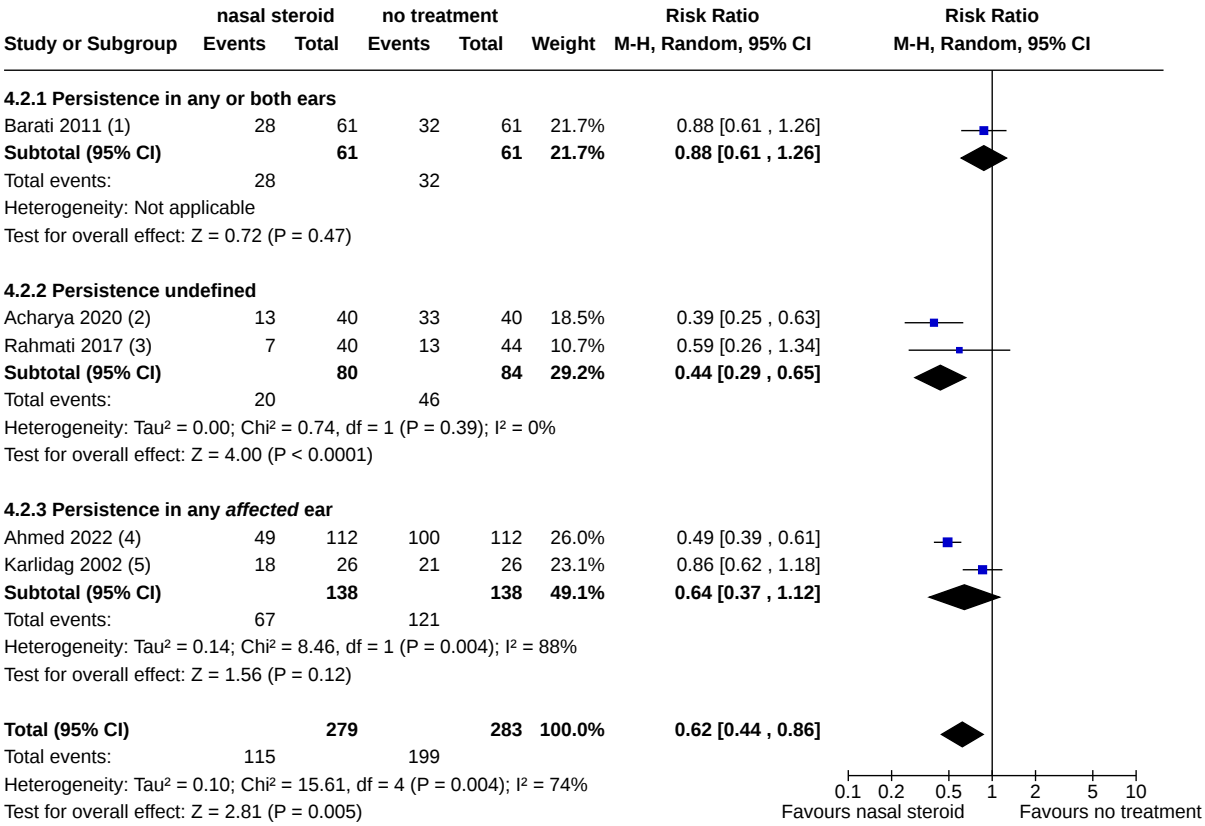
(1) 1 month. Air bone gap. Data pooled from right and left ears, assuming correlation of 0.5 between ears.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Comparison 4: Nasal steroid versus no treatment, Outcome 1: Final hearing threshold (up to 6 weeks)

Analysis 4.2

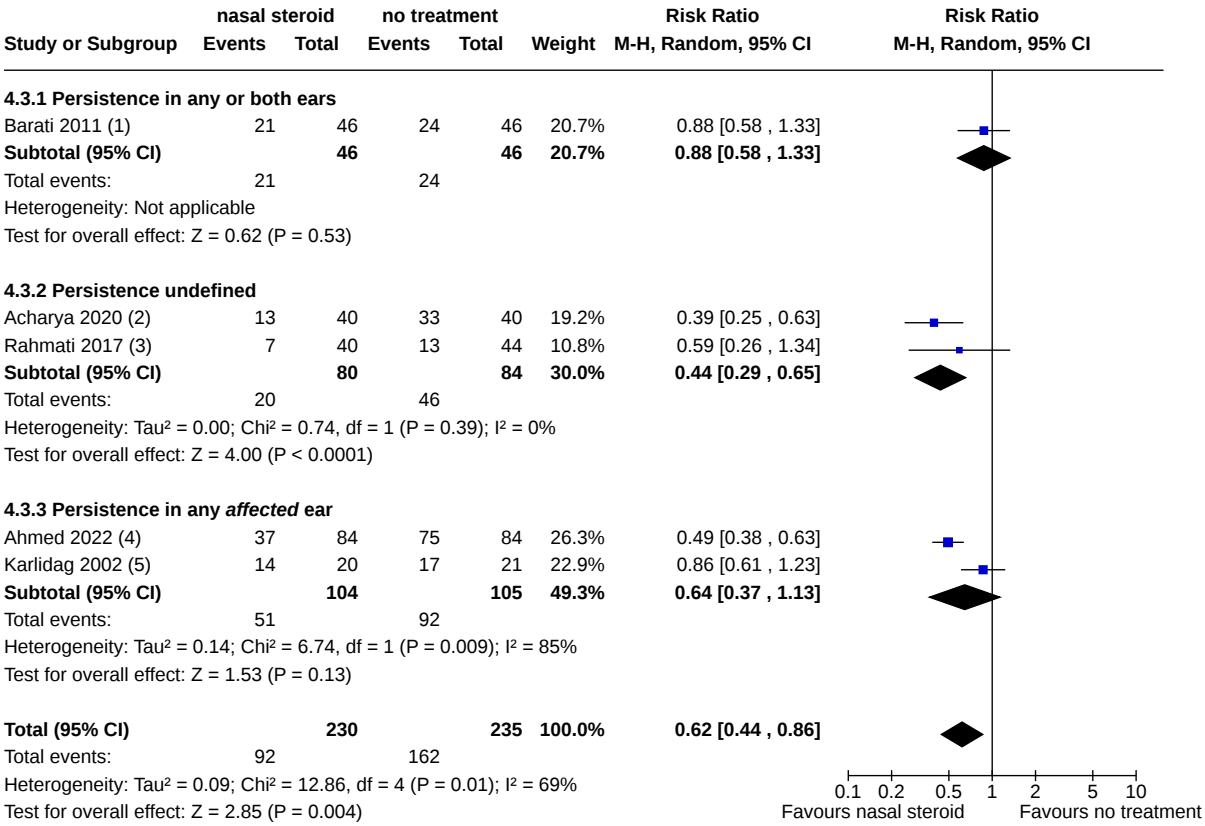


Footnotes

(1) 4 weeks. Uni- or bilateral at baseline. Analysis by ear. Persistence = B or C2 regardless of initial status. ICC 0.5 (DE 1.5)
(2) 4 weeks. Laterality at baseline NR. Analysis by child
(3) 4 weeks. Uni- or bilateral at baseline. Analysis by child.
(4) 1 month. Bilateral at baseline. Analysis by ears. Ave cluster size=2; ICC=0.5; DE=1.5.
(5) 4 weeks. Uni- or bilateral at baseline. Analysis by ears. Ave cluster size=1.8; ICC=0.5; DE=1.4.

Comparison 4: Nasal steroid versus no treatment, Outcome 2: Persistence of OME (very short term); ICC=0.5

Analysis 4.3

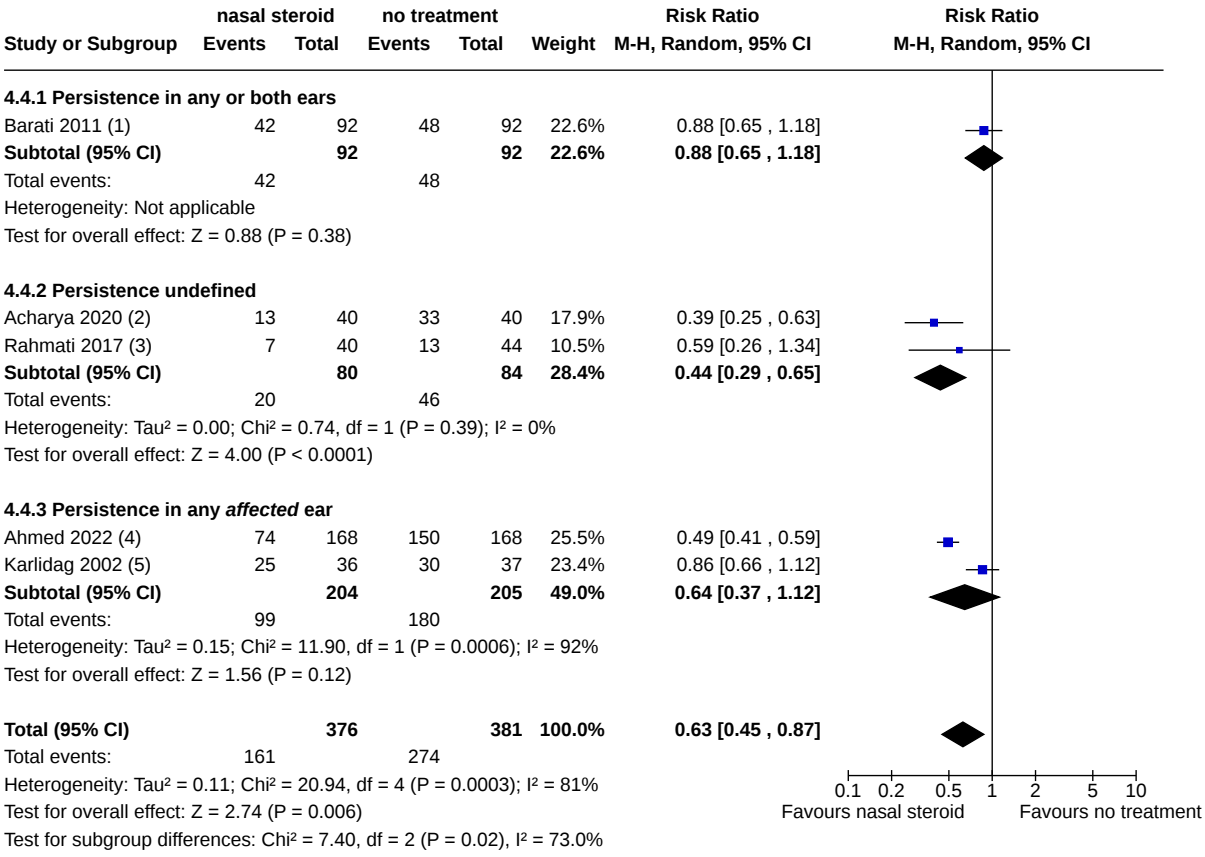


Footnotes

(1) 4 weeks. Uni- or bilateral at baseline. Analysis by ear. Persistence = B or C2 regardless of initial status. ICC 1.0 (DE 2.0)
(2) 4 weeks. Laterality at baseline NR. Analysis by child
(3) 4 weeks. Uni- or bilateral at baseline. Analysis by child.
(4) 4 weeks. Bilateral at baseline. Analysis by ears. Ave cluster size=2; ICC=1.0; DE=2.
(5) 4 weeks. Uni- or bilateral at baseline. Analysis by ears. Ave cluster size=1.8; ICC=1.0; DE=1.8.

Comparison 4: Nasal steroid versus no treatment, Outcome 3: Sensitivity analysis: Persistence of OME (very short term); ICC=1.0

Analysis 4.4

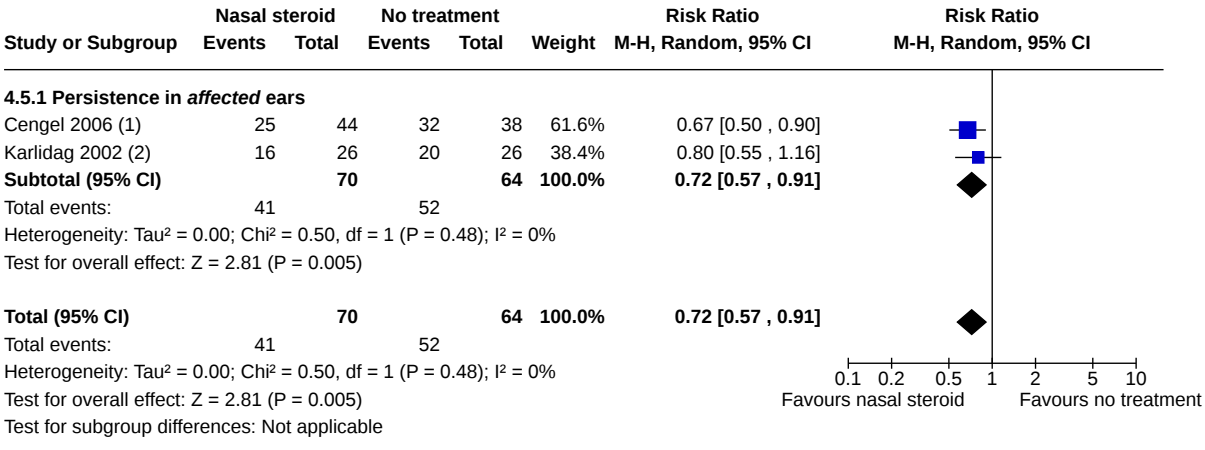


Footnotes

(1) 4 weeks. Uni- or bilateral at baseline. Analysis by ear. Persistence = B or C2 regardless of initial status. ICC 0.0 (DE 1.0)
(2) 4 weeks. Laterality at baseline NR. Analysis by child
(3) 4 weeks. Uni- or bilateral at baseline. Analysis by child.
(4) 4 weeks. Bilateral at baseline. Analysis by ears. Ave cluster size=2; ICC=0; DE=1.
(5) 4 weeks. Uni- or bilateral at baseline. Analysis by ears. Ave cluster size=1.8; ICC=0.0; DE=1.0.

Comparison 4: Nasal steroid versus no treatment, Outcome 4: Sensitivity analysis: Persistence of OME (very short term); ICC=zero

Analysis 4.5



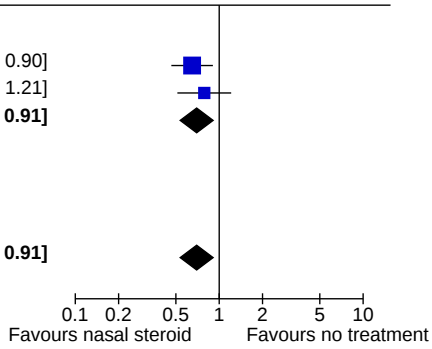
Footnotes

(1) 6 weeks. Uni- or bilateral at baseline. Analysis by ear. Average cluster size=1.9. Assumed ICC=0.5; DE=1.45
(2) 8 weeks. Uni- or bilateral at baseline. Analysis by ear. Average cluster size=1.8; ICC=0.5; DE=1.4

Comparison 4: Nasal steroid versus no treatment, Outcome 5: Persistence of OME (short-term); ICC=0.5

Analysis 4.6

Study or Subgroup	Nasal steroid Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
4.6.1 Persistence in *affected* ears. ICC 1.0						
Cengel 2006 (1)	19	34	25	29	62.7%	0.65 [0.46 , 0.90]
Karlidag 2002 (2)	12	20	16	21	37.3%	0.79 [0.51 , 1.21]
Subtotal (95% CI)		**54**		**50**	**100.0%**	**0.70 [0.54 , 0.91]**
Total events:	31		41			
Heterogeneity: Tau² = 0.00; Chi² = 0.49, df = 1 (P = 0.48); I² = 0%						
Test for overall effect: Z = 2.69 (P = 0.007)						
Total (95% CI)		**54**		**50**	**100.0%**	**0.70 [0.54 , 0.91]**
Total events:	31		41			
Heterogeneity: Tau² = 0.00; Chi² = 0.49, df = 1 (P = 0.48); I² = 0%						
Test for overall effect: Z = 2.69 (P = 0.007)						
Test for subgroup differences: Not applicable						



Footnotes

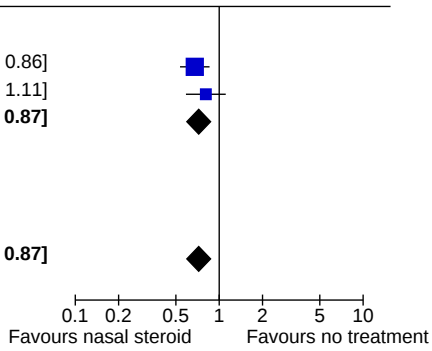
(1) 6 weeks. Uni- or bilateral at baseline. Analysis by ears. Average cluster size=1.9; ICC 1.0 (DE 1.9)

(2) 8 weeks. Uni- or bilateral at baseline. Analysis by ear. Average cluster size=1.8; ICC=1.0; DE=1.8.

Comparison 4: Nasal steroid versus no treatment, Outcome 6: Sensitivity analysis: Persistence of OME (short-term); ICC=1.0

Analysis 4.7

Study or Subgroup	Nasal steroid Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
4.7.1 Persistence in *affected* ears. ICC zero						
Cengel 2006 (1)	37	64	47	55	64.5%	0.68 [0.53 , 0.86]
Karlidag 2002 (2)	22	36	28	37	35.5%	0.81 [0.59 , 1.11]
Subtotal (95% CI)		**100**		**92**	**100.0%**	**0.72 [0.60 , 0.87]**
Total events:	59		75			
Heterogeneity: Tau² = 0.00; Chi² = 0.77, df = 1 (P = 0.38); I² = 0%						
Test for overall effect: Z = 3.39 (P = 0.0007)						
Total (95% CI)		**100**		**92**	**100.0%**	**0.72 [0.60 , 0.87]**
Total events:	59		75			
Heterogeneity: Tau² = 0.00; Chi² = 0.77, df = 1 (P = 0.38); I² = 0%						
Test for overall effect: Z = 3.39 (P = 0.0007)						
Test for subgroup differences: Not applicable						



Footnotes

(1) 6 weeks. Uni- or bilateral at baseline. Analysis by ears. Average cluster size=1.9; ICC 0.0 (DE 1.0)

(2) 8 weeks. Uni- or bilateral at baseline. Analysis by ear. Average cluster size=1.8; ICC=0.0; DE=1.0.

Comparison 4: Nasal steroid versus no treatment, Outcome 7: Sensitivity analysis: Persistence of OME (short-term); ICC=zero