National Institute for Health and Care Excellence

Draft for consultation

Otitis media with effusion in under 12s

[L] Evidence reviews for treating otorrhoea after surgery for hearing loss associated with OME in children

NICE guideline number tbc

Evidence reviews underpinning recommendations 1.6.7 to 1.6.10 in the NICE guideline

March 2023

Draft for consultation

This evidence review was developed by NICE

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ISBN:

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Treating otorrhoea after surgery for hearing loss associated with OME in children

Review question

What interventions are effective for treating otorrhoea (ear discharge) after surgery for otitis media with effusion (OME)-related hearing loss in children under 12 years?

Introduction

The aim of this review is to assess what interventions are effective for treating otorrhoea (ear discharge) after surgery for otitis media with effusion (OME)-related hearing loss in children under 12 years

At the time of development, the term ventilation tube (VT) was used to refer to tubes inserted during surgery for OME. However, the committee agreed that the term grommet should be used as this is likely to be the term that is more familiar to readers of the guideline and would avoid confusion with tubes used to assist with breathing. Therefore, both terms appear in this evidence review.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	All children under 12 years who have otorrhoea after ventilation tube (VT) surgery for OME-related hearing loss.
Intervention	Interventions of interest (alone or in combination): • Antibiotic ear drops with or without corticosteroid • Oral antibiotics • Water precautions (actions to ensure ears are kept dry, for example, wearing ear plugs, swimming cap and headband and avoidance of swimming)
Comparison	• Head-to-head comparisons between the above intervention categories* (alone or in combination) • The above interventions (alone or in combination) versus placebo • The above interventions (alone or in combination) versus no intervention for otorrhoea *Please note, head-to-head comparisons between different interventions within each category (e.g., comparisons between different types of oral antibiotics) were not included, only head-to-head comparisons of interventions from different categories (e.g., an oral antibiotic versus a water precaution intervention)
Outcome	**Critical** • Otorrhoea (ear discharge) resolves • Adverse effects of intervention (including antimicrobial resistance) • Surgical intervention to remove VTs **Important** • Tube blockage • Tube extrusion • Hearing • Quality of life (measured by OM8-30 questionnaire, Health Utilities Index Mark 3 (HUI3) questionnaire, Otitis Media-6 (OM-6) questionnaire, Quality of Life in Children's Ear Problems (OMQ-14) questionnaire, Evaluation of Children's Listening and Processing Skills (ECLiPS) questionnaire, Auditory Behaviour in Everyday Life (ABEL) questionnaire, Early Listening Function (ELF) questionnaire, Parents' Evaluation of Aural/Oral Performance of Children (PEACH) questionnaire, EuroQol 5 Dimensions (EQ-5D) questionnaire, Infant Toddler Quality of Life Questionnaire, or Child Heath Questionnaire)

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1).

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Effectiveness evidence

Included studies

One randomised controlled trial (RCT) was included for this review (van Dongen 2014).

The included study is summarised in Table 2.

The included study compared hydrocortisone-bacitracin-colistin ear drops to oral amoxicillin-clavulanate suspension and initial observation (van Dongen 2014). The study also compared oral amoxicillin-clavulanate suspension to initial observation.

The average age in years of participants in the included study was 4.6.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix J.

Summary of included studies

Summary of the study that was included in this review is presented in Table 2.

Table 2: Summary of included studies.

Study	Population	Intervention	Comparison	Outcomes	Comments
van Dongen 2014 RCT Netherlands	N=230 Children aged 1 to 10 years with tympanostomy tube otorrhoea for up to 7 days Age in years, mean (SD): Hydrocortisone-bacitracin-colistin drops: 4.6 (2.1) Oral amoxicillin-clavulanate suspension: 4.4 (2.0) Initial observation: 4.4 (2.0) Sex (male/female): Hydrocortisone-bacitracin-colistin drops: 50/26 Oral amoxicillin-clavulanate suspension: 40/37 Initial observation: 43/34	<u>Hydrocortisone-bacitracin-colistin drops:</u> 5 drops, 3 times a day, in the discharging ear/ears for 7 days <u>Oral amoxicillin-clavulanate suspension:</u> 30 mg of amoxicillin and 7.5 mg of clavulanate per kg per day in three divided doses for 7 days	<u>Initial observation:</u> Observation for 2 weeks	• Otorrhoea (ear discharge) resolves • Adverse effects of intervention • Quality of life	Population is indirect due to 43% of population with recurrent acute otitis media. Study was conducted from 2009 to 2012.

RCT: randomised controlled trial; SD: standard deviation

See the full evidence tables in appendix D and the forest plots in appendix E.

Summary of the evidence

The evidence was very low quality due to bias arising from measurement of the outcome and deviations from the intended interventions, seriously imprecise findings, and the inclusion of an indirect population. In addition, parts of the study were conducted before 2010.

Hydrocortisone-bacitracin-colistin ear drops compared with oral amoxicillin-clavulanate suspension

Hydrocortisone-bacitracin-colistin ear drops had an important benefit in terms of reducing otorrhoea (the presence of otorrhoea at 2 weeks) and gastrointestinal discomfort (adverse effect of intervention) compared with oral amoxicillin-clavulanate suspension, but it had an important harm in terms of local discomfort or pain during administration (adverse effect of intervention). There was no important difference for other adverse effects of intervention (rash, oral candidiasis and serious adverse events), otorrhoea (recurrent episodes of otorrhoea at 6 months), and quality of life.

Hydrocortisone-bacitracin-colistin ear drops compared with initial observation

Compared with initial observation, hydrocortisone-bacitracin-colistin ear drops had an important benefit in terms of reducing otorrhoea (the presence of otorrhoea at 2 weeks) although there was no important difference in number of recurrent episodes of otorrhoea at 6 months. There was also no important difference for adverse effects of the intervention (serious adverse events) and quality of life.

Oral amoxicillin-clavulanate suspension compared with initial observation

A comparison between oral amoxicillin-clavulanate suspension and initial observation showed no important difference for otorrhoea (at 2 weeks or 6 months), adverse effects of the intervention and quality of life. The outcomes of tube blockage, tube extrusion, hearing and 'surgical intervention to remove ventilation tubes' were not reported by the included study.

See appendix F for full GRADE tables.

Economic evidence

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation given the low cost of the interventions under consideration in this review.

Unit costs

Resource	Unit costs	Source
Ciprofloxacin (as Ciprofloxacin hydrochloride) 2 mg per 1 ml	£6.01	NHS Drugs Tariff March 2023

The committee's discussion and interpretation of the evidence

The outcomes that matter most

Otorrhoea is a common complication after grommet surgery, which may both recur and lead to poor quality of life in children with otitis media with effusion. Therefore, otorrhoea was prioritised as a critical outcome. To treat otorrhoea following grommet surgery, different types of interventions (for example, antibiotic ear drops with or without corticosteroid, oral antibiotics, and water precautions) can be used. However, these interventions may have adverse effects in children (for example, local discomfort, rash, headache, gastrointestinal discomfort, antimicrobial resistance and so on). Therefore, adverse effects of interventions were prioritised as critical outcomes. Requirement of surgical intervention to remove grommet was also prioritised as a critical outcome as it is common in children who undergo grommet placement surgery and may generally have psychological, emotional, and behavioural impacts.

Tube blockage and tube extrusion were selected as important outcomes as they are also common in children who undergo grommet placement surgery and may be related to recurrence of otitis media with effusion. Hearing loss or hearing difficulty is often associated with otitis media with effusion, and this could impact on the child's language and behavioural development. Therefore, hearing was selected as an important outcome. In addition, quality of life was selected as an important outcome as this is a global measure that takes into accounts both beneficial and adverse effects of the interventions.

The quality of the evidence

The quality of the evidence was assessed using GRADE methodology. The evidence for all outcomes identified in this review was very low quality due to bias arising from measurement of the outcome and deviations from the intended interventions, seriously imprecise findings, and the inclusion of indirect populations. In addition, parts of the included study were conducted before 2010.

No evidence was found that reported on the outcomes of tube blockage, tube extrusion, hearing or surgical intervention to remove grommets.

Benefits and harms

There was no evidence available on the effectiveness of water precautions, however the committee agreed it was sensible to keep the ear dry in the event of postoperative otorrhoea after grommet insertion. Despite the lack of evidence, the committee agreed to make a strong recommendation because it is common routine practice to avoid getting wounds and infections wet. The committee agreed that taking care when bathing and washing hair was usually advised (such as directing the shower head away from their head or ears), alongside the use of ear plugs or headbands if in contact in water. The committee agreed that avoiding swimming would also be sensible for the duration that otorrhoea is present, but for children who have otorrhoea repeatedly or for long periods of time, it would be more practical to use ear plugs or head bands to enable the child to learn to swim, as the committee acknowledged the risks associated with children being unable to swim, and to ensure quality of life for children and their families. The committee also noted that normally headbands would be advised over the use of ear plugs, however there was no evidence to support this.

There was very low quality evidence which showed that hydrocortisone-bacitracin-colistin drops had an important benefit in terms of presence of otorrhoea at 2 weeks follow-up compared to an oral amoxicillin clavulanate suspension or to initial observation. The committee discussed the indirectness of the population in van Dongen 2014 and agreed the fact that 43% of the population had acute otitis media (AOM) and not OME was of serious concern. Although the presence of otorrhoea might indicate that an infection is present, the

effectiveness of antibiotics might differ for AOM compared with OME because the site of the infection differs: AOM represents an infection of the middle ear, which might also present with systemic features, but otorrhoea following grommet insertion for OME might represent an infection of the foreign body (i.e., the grommet), rather than the middle ear. The committee also discussed whether otorrhoea was a significant issue for people with OME, and whether the resolution of otorrhoea justified the potential for increasing antibiotic resistance, especially considering the lack of robust evidence of effectiveness of any intervention. Lay members of the committee noted that otorrhoea was very painful for the patient and could cause difficulties for families, and therefore attempts to treat otorrhoea should be made rather than leaving it to clear up by itself. The type of antibiotic and corticosteroid drop used in van Dongen 2014 was not recognised by the committee as being used in standard practice; instead, the committee agreed non-ototoxic antibiotics such as ciprofloxacin were normally prescribed for otorrhoea. They discussed the available evidence regarding adverse effects, which showed that hydrocortisone-bacitracin-colistin drops caused local discomfort or pain during administration in over 20% of all participants who received the intervention, which, in their experience, does not usually occur when applying ciprofloxacin drops. The committee also agreed that noncompliance with treatment was likely to be a risk if administration of the drops was painful. Additionally, the availability of hydrocortisone-bacitracin-colistin ear drops could not be confirmed in the UK, and any topical ear drops containing colistin could not be located on the British National Formulary for Children (BNFC). The committee therefore agreed that non-ototoxic drops such as ciprofloxacin should be considered based on the evidence of effectiveness of topical antibiotics in treating otorrhoea, as well as their knowledge that non-ototoxic antibiotics would have a lower risk of damaging the ear, potentially resulting in hearing loss, tinnitus, or balance disorders. However, the committee agreed it was important to acknowledge that there is no safety data on the use of topical antibiotics when there is damage to the tympanic membrane. The committee also discussed dosage of non-ototoxic topical antibiotic ear drops such as ciprofloxacin, but they felt that they could not add details on dosage to the recommendation as there was variation in practice. However, the committee acknowledged that it was important to include details on how long topical antibiotic ear drops should be used because it is fundamental for antimicrobial stewardship and patient safety. Based on the committee's experience, topical antibiotic ear drops tend to be given for 5 to 7 days in practice. Therefore, the committee recommended 5 to 7 days of non-ototoxic topical antibiotic ear drops in line with current practice.

There was very low quality evidence which showed that oral amoxicillin-clavulanate suspension had no important difference in terms of presence of otorrhoea at 2 weeks follow-up when compared to initial observation. The committee agreed it was not standard practice to prescribe oral antibiotics for otorrhoea because they are usually used to treat an underlying infection, whereas topical treatment should be sufficient to treat otorrhoea after grommet surgery due to the site of the infection, as discussed above. The committee also discussed the available evidence regarding adverse effects, which showed that oral amoxicillin-clavulanate suspension caused gastrointestinal discomfort in nearly a quarter of all participants who received the intervention. The committee agreed that topical ear drops should be preferred over oral antibiotics for people with otorrhoea after grommet surgery, on the basis of the evidence supplemented with their own knowledge and experience that systemic antibiotics are associated with more side effects than topical antibiotics. However, the evidence was not of sufficient quality to recommend that oral antibiotics are not used.

The committee agreed that recurrent otorrhoea was of high concern because repeat infections have an ototoxic effect and the potential to damage the eardrum. The committee therefore discussed whether grommets should be removed when children have recurrent otorrhoea and agreed it would depend on several factors, including the patient's discomfort, the frequency of and time between episodes, family concern, and the weighing of risk of conducting surgery on the child dependant on their age and any comorbidities, versus the potential risks of repeat ear infections. There was a lack of evidence regarding how many recurrent episodes of otorrhoea would indicate the need for removal of grommets, and

therefore, based on their knowledge of current practice, the committee recommended removal when otorrhoea was persistent (recurring) and not responsive to topical antibiotics.

The committee discussed what should happen if children have symptoms additional to otorrhoea such as high temperature, lethargy, complete loss of hearing, dizziness, or other respiratory symptoms. They agreed that these were symptoms of systemic infection and not complications related to grommet surgery. Therefore, the committee agreed it was important to emphasise the fact that the recommendations made apply to otorrhoea in isolation in order to avoid any confusion that could result in failure to treat a more serious infection. The management of systemic infections is outside the scope of this guideline. However, the committee were aware of a number of other NICE guidelines, such as Fever in under 5s and the Sepsis guidelines, that include recommendations relevant to symptoms such as those mentioned here.

Cost effectiveness and resource use

This review question was not prioritised for economic analysis and therefore the committee made a qualitative assessment of the likely cost-effectiveness of their recommendations. Whilst the committee noted that there was no evidence on the effectiveness of water precautions, they recognised that it is common routine practice to advise patients not to get wounds and infections wet. Therefore, given the very low cost of giving this advice alongside other routine patient information, the committee concluded that recommending water precautions for isolated postoperative otorrhoea (ear discharge) after grommet insertion, would be cost-effective for the NHS. However, for children with recurrent otorrhoea the committee reasoned that it would be more practical to recommend the use of headbands or earplugs for when the child was in contact with the water although these would not be provided by the NHS.

The committee reflected that otorrhoea was very painful and could therefore have an important impact on health-related quality of life. They reasoned therefore that an effective low-cost intervention would be likely to represent a cost-effective use of NHS resources and therefore, reflecting the strength of the evidence, they recommended that a non-ototoxic topical antibiotic-containing ear drop treatment could be considered for postoperative otorrhoea after grommet insertion.

The committee were concerned about the ototoxic impact of repeat infections and possible damage to the hearing drum where antibiotics had not worked. Therefore, where this was an issue, they recommended that removal of grommets could be considered. Although, that would involve a surgical procedure they believed the recommendation was likely to be cost-effective because of the potential long-term impact on health-related quality of life from infection that does not respond to antibiotics.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.6.7 to 1.6.10.

References – included studies

Effectiveness

van Dongen 2014

van Dongen, T. M. A., van der Heijden, G. J. M. G., Venekamp, R. P. et al. (2014). A trial of treatment for acute otorrhea in children with tympanostomy tubes, The New England Journal of Medicine 370(8), 723-33

Other

British National Formulary for Children (BNFC)

Paediatric Formulary Committee. BNF for Children (online) London: BMJ Group, Pharmaceutical Press, and RCPCH Publications <http://www.medicinescomplete.com> [Accessed on 31-05-2022]

NICE guideline [NG51]

National Institute for Health and Care Excellence. (2017). Sepsis: recognition, diagnosis and early management [NICE Guideline No. 51]. <https://www.nice.org.uk/guidance/ng51> [Accessed on 31-05-2022]

NICE guideline [NG143]

National Institute for Health and Care Excellence. (2021). Fever in under 5s: assessment and initial management [NICE Guideline No. 143]. <https://www.nice.org.uk/guidance/ng143> [Accessed on 31-05-2022]

Appendices

Appendix A Review protocols

Review protocol for review question: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

Table 3: Review protocol

Field	Content
PROSPERO registration number	CRD42022333940
Review title	The effectiveness of interventions for treating otorrhoea after surgery for hearing loss associated with otitis media with effusion in children
Review question	What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?
Objective	To determine the effectiveness of intraoperative or postoperative interventions at preventing otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years
Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • Epistemonikos • International Health Technology Assessment (INAHTA) database • MEDLINE & MEDLINE In-Process Searches will be restricted by: • OECD geographic study filter • Date limitations: 2010 onwards (see rationale under “Other exclusion criteria”)

Field	Content
	• English language studies • Human studies Other searches: • Inclusion lists of systematic reviews • Citation searches of included studies With the agreement of the guideline committee the searches will be re-run between 6-8 weeks before final submission of the review and further studies retrieved for inclusion. The full search strategies for MEDLINE database will be published in the final review.
Condition or domain being studied	Hearing loss associated with otitis media with effusion
Population	All children under 12 years who have otorrhoea after ventilation tube surgery for OME-related hearing loss.
Intervention	Interventions of interest (alone or in combination): • Antibiotic ear drops with or without corticosteroid • Oral antibiotics • Water precautions (actions to ensure ears are kept dry, for example, wearing ear plugs, swimming cap and headband and avoidance of swimming)
Comparator	• Head-to-head comparisons between the above intervention categories** (alone or in combination) • The above interventions (alone or in combination) versus placebo • The above interventions (alone or in combination) versus no intervention for otorrhoea **Please note, we will not include head-to-head comparisons between different interventions within each category (e.g., comparisons between different types of oral antibiotics), only head-to-head comparisons of interventions from different categories (e.g., an oral antibiotic versus a water precaution intervention)

Field	Content
Types of study to be included	Include published full-text papers: • Systematic reviews of RCTs • RCTs • If insufficient RCTs*: comparative prospective cohort studies with at least 40 participants per arm • If insufficient comparative prospective cohort studies: comparative retrospective cohort studies with at least 40 participants per arm *Non-randomised studies will be considered for inclusion if insufficient RCT evidence is available for guideline decision making. Sufficiency will be judged taking into account factors including number/quality/sample size of RCTs, outcomes reported and availability of data from subgroups of interest. Non-randomised studies will be downgraded for risk of bias if they do not adequately adjust for the following covariates, but will not be excluded for this reason: Age
Other exclusion criteria	• Country limitations: limit studies to OECD high-income countries • Date limitations: 2010 as safety of antibiotics was improved from 2015 (e.g., non-ototoxic antibiotics) and the committee wanted to capture studies leading up to that change. • Language limitations: studies published not in English-language • Conference abstracts will not be considered.
Context	This guidance will fully update the following NICE guideline: Otitis media with effusion in under 12s: surgery (2008; CG60)
Primary outcomes (critical outcomes)	• Otorrhoea (ear discharge) resolves • Adverse effects of intervention (including antimicrobial resistance) • Surgical intervention to remove VTs
Secondary outcomes (important outcomes)	• Tube blockage • Tube extrusion • Hearing

Field	Content
	• Quality of life (measured by OM8-30 questionnaire, Health Utilities Index Mark 3 (HUI3) questionnaire, Otitis Media-6 (OM-6) questionnaire, Quality of Life in Children's Ear Problems (OMQ-14) questionnaire, Evaluation of Children's Listening and Processing Skills (ECLiPS) questionnaire, Auditory Behaviour in Everyday Life (ABEL) questionnaire, Early Listening Function (ELF) questionnaire, Parents' Evaluation of Aural/Oral Performance of Children (PEACH) questionnaire, EuroQol 5 Dimensions (EQ-5D) questionnaire, Infant Toddler Quality of Life Questionnaire, or Child Heath Questionnaire)
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Dual sifting will be performed on at least 10% of records; 90% agreement is required, if capacity allows it. Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs and quasi-RCTs • Cochrane ROBINS-I tool for non-randomised (clinical) controlled trials and cohort studies The quality assessment will be performed by one reviewer, and this will be quality assessed by a senior reviewer.

Field	Content
Strategy for data synthesis	Quantitative findings will be formally summarised in the review. Where possible, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios or odds ratios for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed using the I2 statistic. Alongside visual inspection of the point estimates and confidence intervals, I2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled if the random effects model does not adequately address heterogeneity. The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/ **Minimally important differences (MIDs):** • Validated scales: Published MIDs where available; if not GRADE default MIDs • All other outcomes: GRADE default MIDs

Analysis of sub-groups	Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes:
	• Age
	  ○ Children <2 years vs ≥2 years
	  ○ Children <4 years vs ≥4 years
	  ○ Children <6 years vs ≥6 years
	
	Where evidence is subgrouped the committee will consider on a case by case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee

Field	Content			
	will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.			
Type and method of review	☒	Intervention		
	☐	Diagnostic		
	☐	Prognostic		
	☐	Qualitative		
	☐	Epidemiologic		
	☐	Service Delivery		
	☐	Other (please specify)		
Language	English			
Country	England			
Anticipated or actual start date	31/03/2022			
Anticipated completion date	23/12/2022			
Stage of review at time of this submission	Review stage		Started	Completed
	Preliminary searches		☑	☑
	Piloting of the study selection process		☑	☑
	Formal screening of search results against eligibility criteria		☑	☑
	Data extraction		☑	☑
	Risk of bias (quality) assessment		☑	☑
	Data analysis		☑	☑
Named contact	Named contact: National Guideline Alliance Named contact e-mail: otitis@nice.org.uk			

Field	Content
	Organisational affiliation of the review: National Institute for Health and Care Excellence (NICE) and National Guideline Alliance
Review team members	National Guideline Alliance
Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance which receives funding from NICE.
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10193
Other registration details	None
Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022333940
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
Keywords	Otitis media with effusion, otorrhoea, hearing, quality of life

Field	Content	
Details of existing review of same topic by same authors	None	
Current review status	☐	Ongoing
	☒	Completed but not published
	☐	Completed and published
	☐	Completed, published and being updated
	☐	Discontinued
Additional information	None	
Details of final publication	www.nice.org.uk	

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; GRADE: Grading of Recommendations Assessment, Development and Evaluation; INAHTA: International Health Technology Assessment database; MEDLINE: Medical Literature Analysis and Retrieval System Online; MID: minimally important difference; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; ROBINS-I: risk of bias in non-randomised studies – of interventions; ROBIS: risk of bias in systematic reviews; SD: standard deviation; VT: ventilation tube

Appendix B Literature search strategies

Literature search strategies for review question: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

Clinical search

This was a combined search to cover both this review and the evidence review on the effectiveness of intraoperative and postoperative interventions at preventing otorrhoea after surgery for OME-related hearing loss in children under 12 years.

Database: MEDLINE – OVID interface

Date last searched: 09/11/2022

#	Searches
1	otitis media with effusion/
2	(glue ear or ((middle ear or otitis media) adj2 effusion*) or ome or ((secretory or serous) adj2 otitis media)).ti,ab.
3	1 or 2
4	Cerebrospinal Fluid Otorrhea/ or Mucus/ or Otitis Media, Suppurative/ or Suppuration/
5	(otor* or discharg* or fluid* or leak* or liquor* or moist* or mucoid* or mucopurulen* or mucus* or otoliquor* or purulen* or pus or secret* or suppurat* or weep* or wet*).ti,ab.
6	4 or 5
7	3 and 6
8	Intraoperative Care/ or exp Intraoperative Period/ or exp Monitoring, Intraoperative/ or Perioperative Care/ or Perioperative Period/ or Postoperative Care/ or exp Postoperative Period/ or Secondary Prevention/ or Adenoidectomy/ or exp Otologic Surgical Procedures/
9	(implant* or intraoperat* or intrasurg* or operat* or otosurg* or perioperat* or postoperat* or postsurg* or surg* or prophyl* or postadenoidectom* or postadenotonsillectom* or postmyringoplast* or postmyringostom* or postmyringotom* or posttubulat* or posttympanoplast or posttympanostom* or adenoidectom* or adenotonsillectom* or grommet* or tube* or tubulat* or tympanoplast* or tympanostom* or tonsillectom* or ventilat*).ti,ab.
10	8 or 9
11	7 and 10
12	exp anti-infective agents/ or Bacterial Infections/ or exp beta-Lactams/ or exp Macrolides/ or exp Trimethoprim/
13	(antibacteri* or anti bacteri* or antibiotic* or anti biotic* or antiinfect* or anti infect* or antimicrob* or anti microb* or antimyobacteri* or anti myobacteri or bacteriocid*).ti,ab.
14	(penicillin* or aminoglycoside* or amoxicillin* or amix or amoram or amoxident or galenamox or rimoxallin or amoxil or ampicillin* or clavulan* or coamoxiclav or amoxiclav or augmentin or ticarcillin or timentin or flucloxacillin or fluampicil or magnapen or piperacillin or tazocin or cephalosporin* or cefaclor or distaclor or cefadroxil or baxan or cefalexin or ceporex or keflex or cefamandole or kefadol or cefazolin or kefzol or cefixime or suprax or cefotaxime or claforan or cefoxitin or mefoxin or cefpirome or cefrom or cefpodoxime or orelox or cefprozil or cefzil or cefradine or velosel or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or cefuroxime* or zinacef or zinnat or cefonicid or aztreonam or azactam or imipenem or cilastatin or primaxin or meropenem or meronem or tetracycline* or deteclo or demecleocyclin or ledermycin or doxycycline or vibramycin or minocycline or minocine or oxytetracycline or terramycin or macrolide* or erythromycin* or erymax or erythrocin or erythroped or azithromycin* or zithromax or zedbac or clarithromycin or klaricid or mycifor or telithromycin or sulfisoxazole or ketek or trimoxazole or moxifloxacin or avelox or trimethoprim or cotrimoxazole or monotrim or septrin or trimopan or metronidazole or flagyl or metrolyl or quinolone* or ciprofloxacin or ciproxin or phenoxymethylpenicillin or sulfamethoxazole or oxacillin or cephalothin or sulbactam or ofloxacin or clindamycin or gentamycin or vancomycin or sulfisoxazole).ti,ab.
15	Steroids/ or exp Adrenal Cortex Hormones/ or exp Mineralocorticoids/ or exp Prednisolone/ or exp Pregnenediones/
16	(steroid* or adrenal cortex hormone* or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or aldosterone or aristocort or baycadron or becloforte or beclomet?a?one or aerobec or asmabec or beclazone or becodisks or becotide or clenil modulite or qvar or betamethasone or budelin or bude?onide or calcort or clobetasol or corlan or cortef or cortisol or cortisone or corticosterone or cortodoxone or cortone acetate or cotolone or decadron or deflazacort or delta?one or desonide or dexametha?one or dexsol or efcortesol or entocort or florinef acetate or flumetha?one or flunisolide or flutica?one or fludrocorti?one or hydrocorti?one or hydrocortone or hydroxycorticosteroid* or hydroxypregnenolone or kenalog or medrone or medrol or solu?medrone or depo?medrone or methylpred or methylpredni?olone or mineralcorticoid*or mometa?one or parametha?one or pediapred or prednicot or predni?olone or predni?one or pregnenedione* or pregnenolone* or prelone or pulmicort or solucortef or symbicort or tetrahydrocortisol or triamcinolone).ti,ab.
17	Saline Solution/ or Saline Solution, Hypertonic/ or Sodium Chloride/ or Therapeutic Irrigation/
18	(antiseptic* or anti septic* or clean* or drop* or eardrop* or hypersaline or hypertonic* or hyper tonic* or irrigat* or lavag* or rins* or saline or salt* or seawater or sodium chloride or solution* or toilet* or wash* or water*).ti,ab.
19	Baths/ or Fresh Water/ or Immersion/ or "Oceans and Seas"/ or Seawater/ or Swimming Pools/ or Swimming/ or Water/
20	(swim* or shower* or bath* or dry or dive or diving or nonswim* or immers* or submers* or submerg* or lake* or pond* or creek* or pool* or river* or freshwater* or sea* or ocean* or ingress*).ti,ab.
21	Ear Protective Devices/

#	Searches
22	(protect* or prevent* or precaution* or barrier* or ear mould* or ear mold* or ear plug* or earplug* or earmold* or earmould* or headband* or head band*).ti,ab.
23	or/12-22
24	11 and 23
25	limit 24 to english language
26	(animals/ not humans/) or exp animals, laboratory/ or exp animal experimentation/ or exp models, animal/ or exp rodentia/ or (rat or rats or mouse or mice).ti.
27	25 not 26
28	limit 27 to yr="2010 -Current"

1 **Database: Embase – OVID interface**

2 Date last searched: 09/11/2022

#	Searches
1	exp secretory otitis media/
2	(glue ear or ((middle ear or otitis media) adj2 effusion*) or ome or ((secretory or serous) adj2 otitis media)).ti,ab.
3	1 or 2
4	exp otorrhea/ or mucus/ or suppuration/ or exp suppurative otitis media/
5	(otor* or discharg* or fluid* or leak* or liquor* or moist* or mucoid* or mucopurulen* or mucus* or otoliquor* or purulen* or pus or secret* or suppurat* or weep* or wet*).ti,ab.
6	4 or 5
7	3 and 6
8	exp intraoperative monitoring/ or exp intraoperative period/ or exp perioperative monitoring/ or exp perioperative period/ or exp postoperative period/ or prophylaxis/ or prevention/ or adenoidectomy/ or exp ear surgery/
9	(implant* or intraoperat* or intrasurg* or operat* or otosurg* or perioperat* or postoperat* or postsurg* or surg* or prophyl* or postadenoidectom* or postadenotonsillectom* or postmyringoplast* or postmyringostom* or postmyringotom* or posttubulat* or posttympanoplast or posttympanostom* or adenoidectom* or adenotonsillectom* or grommet* or tube* or tubulat* or tympanoplast* or tympanostom* or tonsillectom* or ventilat*).ti,ab.
10	8 or 9
11	7 and 10
12	exp antiinfective agent/ or bacterial Infection/dt, pc
13	(antibacteri* or anti bacteri* or antibiotic* or anti biotic* or antiinfect* or anti infect* or antimicrob* or anti microb* or antimyobacteri* or anti myobacteri or bacteriocid*).ti,ab.
14	(penicillin* or aminoglycoside* or amoxicillin* or amix or amoram or amoxident or galenamox or rimoxallin or amoxil or ampicillin* or clavulan* or coamoxiclav or amoxiclav or augmentin or ticarcillin or timentin or flucloxacillin or fluampicil or magnapen or piperacillin or tazocin or cephalosporin* or cefaclor or distaclor or cefadroxil or baxan or cefalexin or ceporex or keflex or cefamandole or kefadol or cefazolin or kefzol or cefixime or suprax or cefotaxime or claforan or cefoxitin or mefoxin or cefpirome or cefrom or cefpodoxime or orelox or cefprozil or cefzil or cefradine or velosel or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or cefuroxime* or zinacef or zinnat or cefonicid or aztreonam or azactam or imipenem or cilastatin or primaxin or meropenem or meronem or tetracycline* or deteclo or demecleocyclin or ledermycin or doxycycline or vibramycin or minocycline or minocine or oxytetracycline or terramycin or macrolide* or erythromycin* or erymax or erythrocin or erythroped or azithromycin* or zithromax or zedbac or clarithromycin or klaricid or mycifor or telithromycin or sulfisoxazole or ketek or trimoxazole or moxifloxacin or avelox or trimethoprim or cotrimoxazole or monotrim or septrin or trimopan or metronidazole or flagyl or metrolyl or quinolone* or ciprofloxacin or ciproxin or phenoxymethylpenicillin or sulfamethoxazole or oxacillin or cephalothin or sulbactam or ofloxacin or clindamycin or gentamycin or vancomycin or sulfisoxazole).ti,ab.
15	steroid/ or exp corticosteroid/ or exp prednisolone/ or pregnane derivative/
16	(steroid* or adrenal cortex hormone* or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or aldosterone or aristocort or baycadron or becloforte or beclomet?a?one or aerobec or asmabec or beclazone or becodisks or becotide or clenil modulite or qvar or betamethasone or budelin or bude?onide or calcort or clobetasol or corlan or cortef or cortisol or cortisone or corticosterone or cortodoxone or cortone acetate or cotolone or decadron or deflazacort or delta?one or desonide or dexametha?one or dexsol or efcortesol or entocort or florinef acetate or flumetha?one or flunisolide or flutica?one or fludrocorti?one or hydrocorti?one or hydrocortone or hydroxycorticosteroid* or hydroxypregnenolone or kenalog or medrone or medrol or solu?medrone or depo?medrone or methylpred or methylpredni?olone or mineralcorticoid*or mometa?one or parametha?one or pediapred or prednicot or predni?olone or predni?one or pregnenedione* or pregnenolone* or prelone or pulmicort or solucortef or symbicort or tetrahydrocortisol or triamcinolone).ti,ab.
17	ear drops/ or sodium chloride/ or lavage/
18	(antiseptic* or anti septic* clean* or drop* or eardrop* or hypersaline or hypertonic* or hyper tonic* or irrigat* or lavag* or rins* or saline or salt* or seawater or sodium chloride or solution* or toilet* or wash* or water*).ti,ab.
19	bath/ or fresh water/ or immersion/ or sea water/ or swimming pools/ or swimming/ or water/ or water immersion/
20	(swim* or shower* or bath* or dry or dive or diving or nonswim* or immers* or submers* or submerg* or lake* or pond* or creek* or pool* or river* or freshwater* or sea* or ocean* or ingress*).ti,ab.
21	exp ear protective device/
22	(protect* or prevent* or precaution* or barrier* or ear mould* or ear mold* or ear plug* or earplug* or earmold* or earmould* or headband* or head band*).ti,ab.
23	or/12-22
24	11 and 23
25	limit 24 to english language
26	(animal/ not human/) or nonhuman/ or exp animal experiment/ or exp experimental animal/ or animal model/ or exp rodent/ or (rat or rats or mouse or mice).ti.

#	Searches
27	25 not 26
28	limit 27 to (conference abstract or conference paper or conference review or conference proceeding)
29	27 not 28
30	limit 29 to yr="2010 -Current"

1 **Database: Cochrane Database of Systematic Reviews (CDSR); Cochrane Central**
2 **Register of Controlled Trials (CENTRAL) – Wiley interface**

3 Date last searched: 09/11/2022

ID	Search
#1	MeSH descriptor: [Otitis Media with Effusion] this term only
#2	(("glue ear" or (("middle ear" or "otitis media") near/2 effusion*) or ome or ((secretory or serous) near/2 "otitis media"))):ti,ab,kw
#3	#1 or #2
#4	MeSH descriptor: [Cerebrospinal Fluid Otorrhea] this term only
#5	MeSH descriptor: [Mucus] this term only
#6	MeSH descriptor: [Otitis Media, Suppurative] this term only
#7	MeSH descriptor: [Suppuration] this term only
#8	(otor* or discharg* or fluid* or leak* or liquor* or moist* or mucoid* or mucopurulen* or mucus* or otoliquor* or purulen* or pus or secret* or suppurat* or weep* or wet*):ti,ab
#9	{or #4-#8}
#10	#3 and #9
#11	MeSH descriptor: [Intraoperative Care] this term only
#12	MeSH descriptor: [Intraoperative Period] this term only
#13	MeSH descriptor: [Monitoring, Intraoperative] this term only
#14	MeSH descriptor: [Perioperative Care] this term only
#15	MeSH descriptor: [Perioperative Period] this term only
#16	MeSH descriptor: [Postoperative Care] this term only
#17	MeSH descriptor: [Postoperative Period] this term only
#18	MeSH descriptor: [Secondary Prevention] this term only
#19	MeSH descriptor: [Adenoidectomy] this term only
#20	MeSH descriptor: [Otologic Surgical Procedures] explode all trees
#21	(implant* or intraoperat* or intrasurg* or operat* or otosurg* or perioperat* or postoperat* or postsurg* or surg* or prophyl* or postadenoidectom* or postadenotonsillectom* or postmyringoplast* or postmyringostom* or postmyringotom* or posttubulat* or posttympanoplast or posttympanostom* or adenoidectom* or adenotonsillectom* or grommet* or tube* or tubulat* or tympanoplast* or tympanostom* or tonsillectom* or ventilat*):ti,ab
#22	{or #11-#21}
#23	#10 and #22
#24	MeSH descriptor: [Anti-Infective Agents] this term only
#25	MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#26	MeSH descriptor: [Anti-Infective Agents, Local] explode all trees
#27	MeSH descriptor: [Bacterial Infections] this term only
#28	MeSH descriptor: [beta-Lactams] explode all trees
#29	MeSH descriptor: [Macrolides] explode all trees
#30	MeSH descriptor: [Trimethoprim] explode all trees
#31	(antibacteri* or "anti bacteri*" or antibiotic* or "anti biotic*" or antiinfect* or "anti infect*" or antimicrob* or "anti microb*" or antimyobacteri* or "anti myobacteri*" or bacteriocid*):ti,ab
#32	(penicillin* or aminoglycoside* or amoxicillin* or amix or amoram or amoxident or galenamox or rimoxallin or amoxil or ampicillin* or clavulan* or coamoxiclav or amoxiclav or augmentin or ticarcillin or timentin or flucloxacillin or fluampicil or magnapen or piperacillin or tazocin or cephalosporin* or cefaclor or distaclor or cefadroxil or baxan or cefalexin or ceporex or keflex or cefamandole or kefadol or cefazolin or kefzol or cefixime or suprax or cefotaxime or claforan or cefoxitin or mefoxin or cefpirome or cefrom or cefpodoxime or orelox or cefprozil or cefzil or cefradine or velosel or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or cefuroxime* or zinacef or zinnat or cefonicid or aztreonam or azactam or imipenem or cilastatin or primaxin or meropenem or meronem or tetracycline* or deteclo or demecleocyclin or ledermycin or doxycycline or vibramycin or minocycline or minocine or oxytetracycline or terramycin or macrolide* or erythromycin* or erymax or erythrocin or erythroped or azithromycin* or zithromax or zedbac or clarithromycin or klaricid or mycifor or telithromycin or sulfisoxazole or ketek or trimoxazole or moxifloxacin or avelox or trimethoprim or cotrimoxazole or monotrim or septrin or trimopan or metronidazole or flagyl or metrolyl or quinolone* or ciprofloxacin or ciproxin or phenoxymethylpenicillin or sulfamethoxazole or oxacillin or cephalothin or sulbactam or ofloxacin or clindamycin or gentamycin or vancomycin or sulfisoxazole):ti,ab
#33	MeSH descriptor: [Steroids] this term only
#34	MeSH descriptor: [Adrenal Cortex Hormones] explode all trees
#35	MeSH descriptor: [Mineralocorticoids] explode all trees
#36	MeSH descriptor: [Prednisolone] explode all trees
#37	(steroid* or "adrenal cortex hormone*" or corticosteroid* or corticoid* or glucocorticoid* or glucocorticosteroid* or aldosterone or aristocort or baycadron or becloforte or "beclomet?a?one" or aerobec or asmabec or beclazone or becodisks or becotide or "clenil modulite" or qvar or betamethasone or budelin or bude?onide or calcort or clobetasol or corlan or cortef or cortisol or cortisone or corticosterone or cortodoxone or "cortone acetate" or cotolone or decadron or deflazacort or delta?one or desonide or dexametha?one or dexsol or efcortesol or entocort or "florinef acetate" or flumetha?one or flunisolide or flutica?one or fludrocorti?one or hydrocorti?one or hydrocortone or

ID	Search
	hydroxycorticosteroid* or hydroxypregnenolone or kenalog or medrone or medrol or solu?medrone or depo?medrone or methylpred or methylpredni?olone or mineralcorticoid*or mometa?one or parametha?one or pediapred or prednicot or predni?olone or predni?one or pregnenedione* or pregnenolone* or prelone or pulmicort or solucortef or symbicort or tetrahydrocortisol or triamcinolone):ti,ab
#38	MeSH descriptor: [Saline Solution] this term only
#39	MeSH descriptor: [Saline Solution, Hypertonic] this term only
#40	MeSH descriptor: [Sodium Chloride] this term only
#41	MeSH descriptor: [Therapeutic Irrigation] this term only
#42	(antiseptic* or "anti septic*" or clean* or drop* or eardrop* or hypersaline or hypertonic* or "hyper tonic*" or irrigat* or lavag* or rins* or saline or salt* or seawater or "sodium chloride" or solution* or toilet* or wash* or water*):ti,ab
#43	MeSH descriptor: [Baths] this term only
#44	MeSH descriptor: [Fresh Water] this term only
#45	MeSH descriptor: [Immersion] this term only
#46	MeSH descriptor: [Oceans and Seas] this term only
#47	MeSH descriptor: [Seawater] this term only
#48	MeSH descriptor: [Swimming Pools] this term only
#49	MeSH descriptor: [Swimming] this term only
#50	MeSH descriptor: [Water] this term only
#51	(swim* or shower* or bath* or dry or dive or diving or nonswim* or immers* or submers* or submerg* or lake* or pond* or creek* or pool* or river* or freshwater* or sea* or ocean* or ingress*):ti,ab
#52	MeSH descriptor: [Ear Protective Devices] this term only
#53	(protect* or prevent* or precaution* or barrier* or "ear mould*" or "ear mold*" or "ear plug*" or earplug* or earmold* or earmould* or headband* or "head band*"):ti,ab
#54	{or #24-#53}
#55	#23 and #54
#56	"conference":pt or (clinicaltrials or trialsearch):so
#57	#55 not #56 with Cochrane Library publication date Between Jan 2010 and Nov 2022

Database: Epistemonikos

Date last searched: 09/11/2022

#	Searches
1	(title:(("glue ear" OR (("middle ear" OR "otitis media") AND effusion*) OR ome OR ((secretory OR serous) AND "otitis media"))) OR abstract:(("glue ear" OR (("middle ear" OR "otitis media") AND effusion*) OR ome OR ((secretory OR serous) AND "otitis media")))
2	(title:((otor* OR discharg* OR fluid* OR leak* OR liquor* OR moist* OR mucoid* OR mucopurulen* OR mucus* OR otoliquor* OR purulen* OR pus OR suppurat* OR weep* OR wet*)) OR abstract:((otor* OR discharg* OR fluid* OR leak* OR liquor* OR moist* OR mucoid* OR mucopurulen* OR mucus* OR otoliquor* OR purulen* OR pus OR suppurat* OR weep* OR wet*))
3	1 AND 2
4	date limit: 2010-

Database: International Network of Agencies for Health Technology Assessment (INAHTA)

Date last searched: 09/11/2022

#	Searches
1	"Otitis Media with Effusion"[mhe]
2	((“glue ear” or ((“middle ear” or “otitis media”) and effusion*) or ome or ((secretory or serous) and “otitis media”))
3	1 OR 2
4	(otor* or discharg* or fluid* or leak* or liquor* or moist* or mucoid* or mucopurulen* or mucus* or otoliquor* or purulen* or pus or suppurat* or weep* or wet*)
5	3 AND 4 FROM 2010 TO 2022 AND (English)[Language]

Economic literature search strategy

A global, population-based search was undertaken to find economic evidence covering all parts of the guideline.

Database: MEDLINE – OVID interface

Date last searched: 09/11/2022

#	Searches
1	otitis media with effusion/
2	(glue ear or ((middle ear or otitis media) adj2 effusion*) or ome or ((secretory or serous) adj2 otitis media)).ti,ab.

#	Searches
3	1 or 2
4	Economics/
5	Value of life/
6	exp "Costs and Cost Analysis"/
7	exp Economics, Hospital/
8	exp Economics, Medical/
9	Economics, Nursing/
10	Economics, Pharmaceutical/
11	exp "Fees and Charges"/
12	exp Budgets/
13	budget*.ti,ab.
14	cost*.ti.
15	(economic* or pharmaco?economic*).ti.
16	(price* or pricing*).ti,ab.
17	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
18	(financ* or fee or fees).ti,ab.
19	(value adj2 (money or monetary)).ti,ab.
20	or/4-19
21	exp models, economic/
22	*Models, Theoretical/
23	*Models, Organizational/
24	markov chains/
25	monte carlo method/
26	exp Decision Theory/
27	(markov* or monte carlo).ti,ab.
28	econom* model*.ti,ab.
29	(decision* adj2 (tree* or analy* or model*)).ti,ab.
30	or/21-29
31	20 or 30
32	3 and 31
33	(animals/ not humans/) or exp animals, laboratory/ or exp animal experimentation/ or exp models, animal/ or exp rodentia/ or (rat or rats or mouse or mice).ti.
34	32 not 33
35	limit 34 to english language
36	limit 35 to yr="2000 -Current"

1 **Database: Embase – OVID interface**

2 Date last searched: 09/11/2022

#	Searches
1	exp secretory otitis media/
2	(glue ear or ((middle ear or otitis media) adj2 effusion*) or ome or ((secretory or serous) adj2 otitis media)).ti,ab.
3	1 or 2
4	health economics/
5	exp economic evaluation/
6	exp health care cost/
7	exp fee/
8	budget/
9	funding/
10	budget*.ti,ab.
11	cost*.ti.
12	(economic* or pharmaco?economic*).ti.
13	(price* or pricing*).ti,ab.
14	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
15	(financ* or fee or fees).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	or/4-16
18	statistical model/
19	exp economic aspect/
20	18 and 19
21	*theoretical model/
22	*nonbiological model/
23	stochastic model/
24	decision theory/
25	decision tree/
26	monte carlo method/
27	(markov* or monte carlo).ti,ab.
28	econom* model*.ti,ab.

#	Searches
29	(decision* adj2 (tree* or analy* or model*)).ti,ab.
30	or/20-29
31	17 or 30
32	3 and 31
33	(animal/ not human/) or nonhuman/ or exp animal experiment/ or exp experimental animal/ or animal model/ or exp rodent/ or (rat or rats or mouse or mice).ti.
34	32 not 33
35	limit 34 to english language
36	limit 35 to yr="2000 -Current"

Database: Cochrane Central Register of Controlled Trials (CENTRAL) – Wiley interface

Date last searched: 09/11/2022

ID	Search
#1	MeSH descriptor: [Otitis Media with Effusion] this term only
#2	(("glue ear" or (("middle ear" or "otitis media") near/2 effusion*) or ome or ((secretory or serious) near/2 "otitis media"))):ti,ab,kw
#3	#1 or #2
#4	MeSH descriptor: [Economics] this term only
#5	MeSH descriptor: [Value of Life] this term only
#6	MeSH descriptor: [Costs and Cost Analysis] explode all trees
#7	MeSH descriptor: [Economics, Hospital] explode all trees
#8	MeSH descriptor: [Economics, Medical] explode all trees
#9	MeSH descriptor: [Economics, Nursing] this term only
#10	MeSH descriptor: [Economics, Pharmaceutical] this term only
#11	MeSH descriptor: [Fees and Charges] explode all trees
#12	MeSH descriptor: [Budgets] explode all trees
#13	budget*:ti,ab
#14	cost*:ti
#15	(economic* or pharmaco?economic*):ti
#16	(price* or pricing*):ti,ab
#17	(cost* near/2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)):ab
#18	(financ* or fee or fees):ti,ab
#19	(value near/2 (money or monetary)):ti,ab
#20	{or #4-#19}
#21	MeSH descriptor: [Models, Economic] explode all trees
#22	MeSH descriptor: [Models, Theoretical] this term only
#23	MeSH descriptor: [Models, Organizational] this term only
#24	MeSH descriptor: [Markov Chains] this term only
#25	MeSH descriptor: [Monte Carlo Method] this term only
#26	MeSH descriptor: [Decision Theory] explode all trees
#27	(markov* or "monte carlo"):ti,ab
#28	(econom* next model*):ti,ab
#29	(decision* near/2 (tree* or analy* or model*)):ti,ab
#30	{or #21-#29}
#31	#20 or #30
#32	#3 and #31 with Cochrane Library publication date Between Jan 2000 and Apr 2022

Database: International Network of Agencies for Health Technology Assessment (INAHTA)

Date last searched: 09/11/2022

#	Searches
1	((("Otitis Media with Effusion"[mhe]) OR ((("glue ear" or (("middle ear" or "otitis media") and effusion*) or ome or ((secretory or serous) and "otitis media")))
2	1 and FROM 2000 TO 2022 AND (English)[Language]

Database: NHS Economic Evaluation Database (NHS EED) – CRD interface

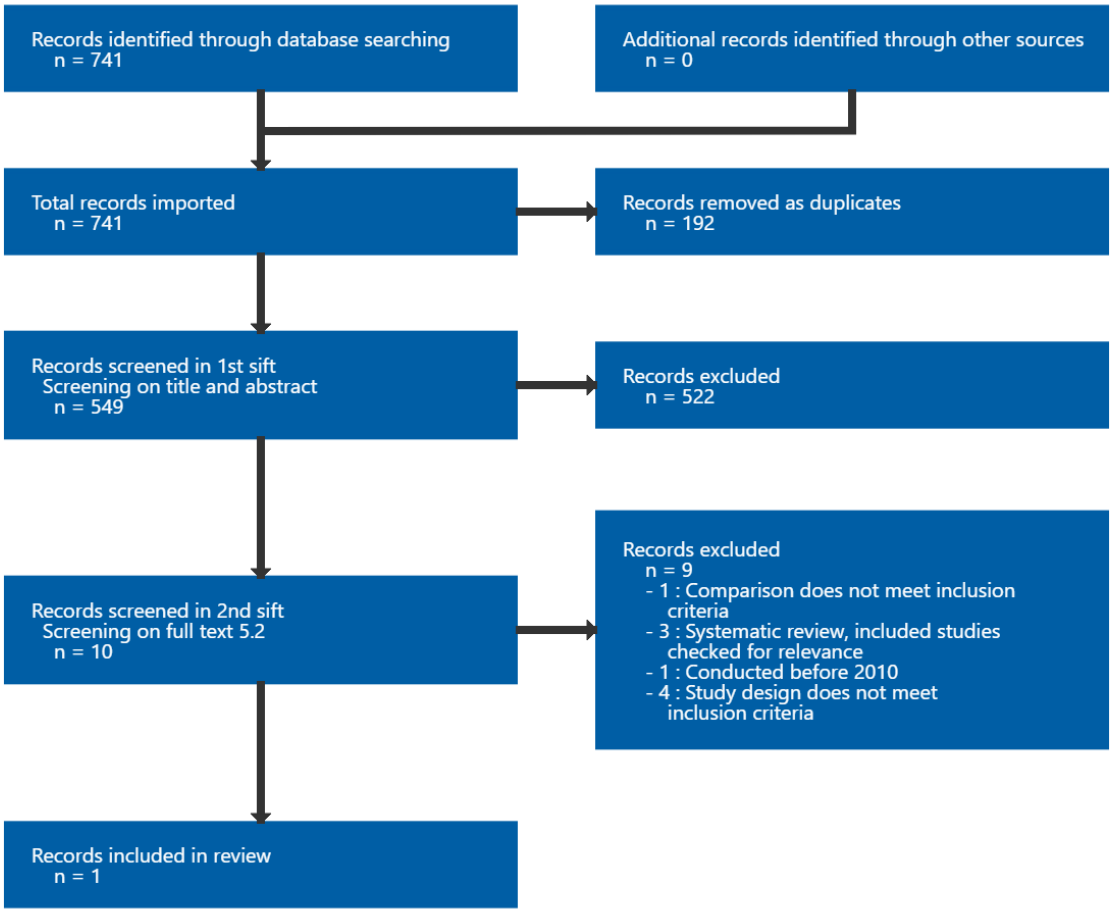
Date last searched: 09/11/2022

Line	Search for
1	MeSH DESCRIPTOR Otitis Media with Effusion EXPLODE ALL TREES
2	((glue ear or ((middle ear or otitis media) and effusion*) or ome or ((secretory or serous) and otitis media))) IN NHS EED
3	#1 OR #2

Appendix C Effectiveness evidence study selection

Study selection for: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

Table 4: Evidence tables

van Dongen, 2014

Bibliographic Reference	van Dongen, Thijs M A; van der Heijden, Geert J M G; Venekamp, Roderick P; Rovers, Maroeska M; Schilder, Anne G M; A trial of treatment for acute otorrhea in children with tympanostomy tubes.; The New England journal of medicine; 2014; vol. 370 (no. 8); 723-33

Study details

Country/ies where study was carried out	Netherlands
Study type	Randomised controlled trial (RCT)
Study dates	June 2009 - May 2012
Inclusion criteria	Children aged 1 to 10 years with tympanostomy tube otorrhoea for up to 7 days
Exclusion criteria	Body temperature >38.5°C, use of antibiotics during previous two weeks, history of tympanostomy tube placement within the previous two weeks, an episode of otorrhoea in the previous four weeks, three or more episodes of otorrhoea in the previous six months, four or more episodes of otorrhoea in the previous year, Down's syndrome, craniofacial anomaly, known immunodeficiency, and history of allergic reaction to study medications
Patient characteristics	N=230 (Hydrocortisone-bacitracin-colistin drops: N=76; Oral amoxicillin-clavulanate suspension: N=77; Initial observation: N=77) Mean age in years (SD):

	Hydrocortisone-bacitracin-colistin drops: 4.6 (2.1) Oral amoxicillin-clavulanate suspension: 4.4 (2.0) Initial observation: 4.4 (2.0) Sex (male/female): Hydrocortisone-bacitracin-colistin drops: 50/26 Oral amoxicillin-clavulanate suspension: 40/37 Initial observation: 43/34 Persistent otitis media with effusion: Hydrocortisone-bacitracin-colistin drops: N=40 Oral amoxicillin-clavulanate suspension: N=50 Initial observation: N=41 Recurrent acute otitis media: Hydrocortisone-bacitracin-colistin drops: N=36 Oral amoxicillin-clavulanate suspension: N=27 Initial observation: N=36
Intervention(s)/control	Hydrocortisone-bacitracin-colistin drops: administered as 5 drops, 3 times a day, in the discharging ear/ears for 7 days Oral amoxicillin-clavulanate suspension: 30 mg of amoxicillin and 7.5 mg of clavulanate per kg per day in three divided doses for 7 days Initial observation: observation for 2 weeks (no assigned medication prescription to fill)
Duration of follow-up	Children were assessed at 2 weeks and 6 months.
Sources of funding	Not industry funded
Sample size	N=230
Other information	Otorrhoea was assessed by otoscopy. The disease-specific health-related quality of life was assessed with the Otitis Media-6 (OM-6) questionnaire, and lower scores indicate better quality of life.

1 *RCT: randomised controlled trial; SD: standard deviation*

Outcomes

Hydrocortisone-bacitracin-colistin drops versus oral amoxicillin-clavulanate suspension versus initial observation: Otorrhoea, adverse effects of intervention and quality of life

Outcome	Hydrocortisone-bacitracin-colistin drops, N = 76	Oral amoxicillin-clavulanate suspension, N = 77	Initial observation, N = 77
Otorrhoea (the presence of otorrhoea; at 2 weeks) Custom value	4/76	34/77	41/75
Otorrhoea (recurrent episodes of otorrhoea; up to 6 months) Custom value	0/76	1/77	1/75
Adverse effects of intervention (local discomfort or pain during administration; up to 2 weeks) Custom value	16/75	0/77	-
Adverse effects of intervention (gastrointestinal discomfort; up to 2 weeks) Custom value	0/75	18/77	-
Adverse effects of intervention (rash; up to 2 weeks) Custom value	2/75	3/77	-
Adverse effects of intervention (oral candidiasis; up to 2 weeks) Custom value	0/75	0/77	-

Outcome	Hydrocortisone-bacitracin-colistin drops, N = 76	Oral amoxicillin-clavulanate suspension, N = 77	Initial observation, N = 77
Adverse effects of intervention (serious adverse events such as local cellulitis, perichondritis, mastoiditis, and intracranial complication; up to 2 weeks) Custom value	0/75	0/77	0/75
Quality of life (changes in the disease-specific health-related quality-of-life scores assessed with the OM-6 questionnaire; at 2 weeks) Median (IQR)	-1 (-14 to 11)	1 (-11 to 18)	0.5 (-15 to 26)

Critical appraisal - Cochrane RoB2

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Randomisation sequence generated by an independent data manager, and the allocation sequence was concealed. No significant differences between groups at baseline.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	High *(Participants and personnel were aware of intervention, and there were changes from assigned intervention: 2/76 in ear drops group, 6/77 in oral suspension group, and 15/77 in initial observation group. Appropriate analysis was used.)*

Section	Question	Answer
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(The data were available for 99% of participants for all outcomes.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low/High *(Methods of measuring the outcomes were appropriate, and no difference in measurement of the outcomes between intervention groups. Outcome assessors were aware of intervention status. Low risk for the presence of otorrhoea at 2 weeks as outcome measurement by otoscopy may not be influenced by knowledge of assigned intervention, and high risk for outcomes reported by parents, such as recurrent otorrhoea, adverse effects, and quality of life, as they may be somewhat subjective and may be influenced by knowledge of assigned intervention.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(There is clear evidence that all eligible reported results for the outcome correspond to all intended outcome measurements and analyses.)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias in at least one domain.)*
Overall bias and Directness	Overall Directness	Indirectly applicable *(Population is indirect due to 43% of recurrent acute otitis media. Study was conducted from 2009 to 2012.)*
Overall bias and Directness	Risk of bias variation across outcomes	None

RoB: risk of bias

Appendix E Forest plots

Forest plots for review question: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

No meta-analysis was conducted for this review question and so there are no forest plots.

Appendix F GRADE tables

GRADE tables for review question: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

Table 5: Evidence profile for comparison: hydrocortisone-bacitracin-colistin drops versus oral amoxicillin-clavulanate suspension

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hydrocortisone-bacitracin-colistin drops	Oral amoxicillin-clavulanate suspension	Relative (95% CI)	Absolute		
Otorrhoea (the presence of otorrhoea) (follow-up 2 weeks)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	no serious imprecision	none	4/76 (5.3%)	34/77 (44.2%)	RR 0.12 (0.04 to 0.32)	389 fewer per 1000 (from 300 fewer to 424 fewer)	VERY LOW	CRITICAL
Otorrhoea (recurrent episodes of otorrhoea) (follow-up 6 months)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	very serious[3]	none	0/76 (0%)	1/77 (1.3%)	POR 0.14 (0 to 6.91)	11 fewer per 1000 (from 13 fewer to 70 more)	VERY LOW	CRITICAL
Adverse effects of intervention (local discomfort or pain during administration) (follow-up 2 weeks)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	no serious imprecision	none	16/75 (21.3%)	0/77 (0%)	POR 9.49 (3.38 to 26.65)	9490 more per 1000 (from 3380 more to 26650 more)[4]	VERY LOW	CRITICAL
Adverse effects of intervention (gastrointestinal discomfort) (follow-up 2 weeks)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	no serious imprecision	none	0/75 (0%)	18/77 (23.4%)	POR 0.11 (0.04 to 0.29)	201 fewer per 1000 (from 152 fewer to 222 fewer)	VERY LOW	CRITICAL
Adverse effects of intervention (rash) (follow-up 2 weeks)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	very serious[3]	none	2/75 (2.7%)	3/77 (3.9%)	RR 0.68 (0.12 to 3.98)	12 fewer per 1000 (from 34 fewer to 116 more)	VERY LOW	CRITICAL
Adverse effects of intervention (oral candidiasis) (follow-up 2 weeks)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	very serious[5]	none	0/75 (0%)	0/77 (0%)	RD 0 (-0.03 to 0.03)	0 fewer per 1000 (from 30 fewer to 30 more)[4]	VERY LOW	CRITICAL
Adverse effects of intervention (serious adverse events such as local cellulitis, perichondritis, mastoiditis, and intracranial complication) (follow-up 2 weeks)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	serious[5]	none	0/75 (0%)	0/77 (0%)	RD 0 (-0.03 to 0.03)	0 fewer per 1000 (from 30 fewer to 30 more)[4]	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hydrocortisone-bacitracin-colistin drops	Oral amoxicillin-clavulanate suspension	Relative (95% CI)	Absolute		
Quality of life (changes in the disease-specific health-related quality-of-life scores assessed with the OM-6 questionnaire) (follow-up 2 weeks; Better indicated by lower values)[7]												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	serious[6]	none	76	77	-	-	VERY LOW	IMPORTANT

CI: confidence interval; IQR: interquartile range; MD: mean difference; POR: Peto odds ratio; RD: risk difference; RR: risk ratio

[1] Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2

[2] Population is indirect due to 43% of population with recurrent acute otitis media, and study was conducted from 2009 to 2012.

[3] 95% CI crosses 2 MIDs

[4] Absolute effect calculated based on risk difference

[5] Sample size <400

[6] Imprecision of the effect estimate based on MIDs not calculable as only median and IQR reported by study. Sample size <400

[7] Relative and absolute effects not calculable as only median and IQR reported by study: hydrocortisone-bacitracin-colistin drops: -1 (-14 to 11); oral amoxicillin-clavulanate suspension: 1 (-11 to 18)

Table 6: Evidence profile for comparison: hydrocortisone-bacitracin-colistin drops versus initial observation

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hydrocortisone-bacitracin-colistin drops	Initial observation	Relative (95% CI)	Absolute		
Otorrhoea (the presence of otorrhoea) (follow-up 2 weeks)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	no serious imprecision	none	4/76 (5.3%)	41/75 (54.7%)	RR 0.1 (0.04 to 0.26)	492 fewer per 1000 (from 405 fewer to 525 fewer)	VERY LOW	CRITICAL
Otorrhoea (recurrent episodes of otorrhoea) (follow-up 6 months)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	very serious[3]	none	0/76 (0%)	1/75 (1.3%)	POR 0.13 (0 to 6.73)	12 fewer per 1000 (from 13 fewer to 70 more)	VERY LOW	CRITICAL
Adverse effects of intervention (serious adverse events such as local cellulitis, perichondritis, mastoiditis, and intracranial complication) (follow-up 2 weeks)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	serious[4]	none	0/75 (0%)	0/75 (0%)	RD 0 (-0.03 to 0.03)	0 fewer per 1000 (from 30 fewer to 30 more)[5]	VERY LOW	CRITICAL
Quality of life (changes in the disease-specific health-related quality-of-life scores assessed with OM-6 questionnaire) (follow-up 2 weeks; Better indicated by lower values)[7]												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	serious[6]	none	76	77	-	-	VERY LOW	IMPORTANT

CI: confidence interval; IQR: interquartile range; MD: mean difference; POR: Peto odds ratio; RD: risk difference; RR: risk ratio

[1] Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2

[2] Population is indirect due to 43% of population with recurrent acute otitis media, and study was conducted from 2009 to 2012.

[3] 95% CI crosses 2 MIDs

[4] Sample size <400

[5] Absolute effect calculated based on risk difference

[6] Imprecision of the effect estimate based on MIDs not calculable as only median and IQR reported by study. Sample size <400

[7] Relative and absolute effects not calculable as only median and IQR reported by study: hydrocortisone-bacitracin-colistin drops: -1 (-14 to 11); initial observation: 0.5 (-15 to 26)

Table 7: Evidence profile for comparison: oral amoxicillin-clavulanate suspension versus initial observation

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral amoxicillin-clavulanate suspension	Initial observation	Relative (95% CI)	Absolute		
Otorrhoea (the presence of otorrhoea) (follow-up 2 weeks)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	serious[3]	none	34/77 (44.2%)	41/75 (54.7%)	RR 0.81 (0.58 to 1.12)	104 fewer per 1000 (from 230 fewer to 66 more)	VERY LOW	CRITICAL
Otorrhoea (recurrent episodes of otorrhoea) (follow-up 6 months)												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	very serious[4]	none	1/77 (1.3%)	1/75 (1.3%)	RR 0.97 (0.06 to 15.29)	0 fewer per 1000 (from 13 fewer to 191 more)	VERY LOW	CRITICAL
Adverse effects of intervention (serious adverse events such as local cellulitis, perichondritis, mastoiditis, and intracranial complication) (follow-up 2 weeks)												
1 (van Dongen 2014)	observational studies	very serious[1]	no serious inconsistency	very serious[2]	serious[5]	none	0/77 (0%)	0/75 (0%)	RD 0 (-0.03 to 0.03)	0 fewer per 1000 (from 30 fewer to 30 more)[6]	VERY LOW	CRITICAL
Quality of life (changes in the disease-specific health-related quality-of-life scores assessed with the OM-6 questionnaire) (follow-up 2 weeks; Better indicated by lower values)[8]												
1 (van Dongen 2014)	randomised trials	very serious[1]	no serious inconsistency	very serious[2]	serious[7]	none	77	77	-	-	VERY LOW	IMPORTANT

CI: confidence interval; IQR: interquartile range; MD: mean difference; POR: Peto odds ratio; RD: risk difference; RR: risk ratio

[1] Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2

[2] Population is indirect due to 43% of population with recurrent acute otitis media, and study was conducted from 2009 to 2012.

[3] 95% CI crosses 1 MID

[4] 95% CI crosses 2 MIDs

[5] Sample size <400

[6] Absolute effect calculated based on risk difference

[7] Imprecision of the effect estimate based on MIDs not calculable as only median and IQR reported by study. Sample size <400

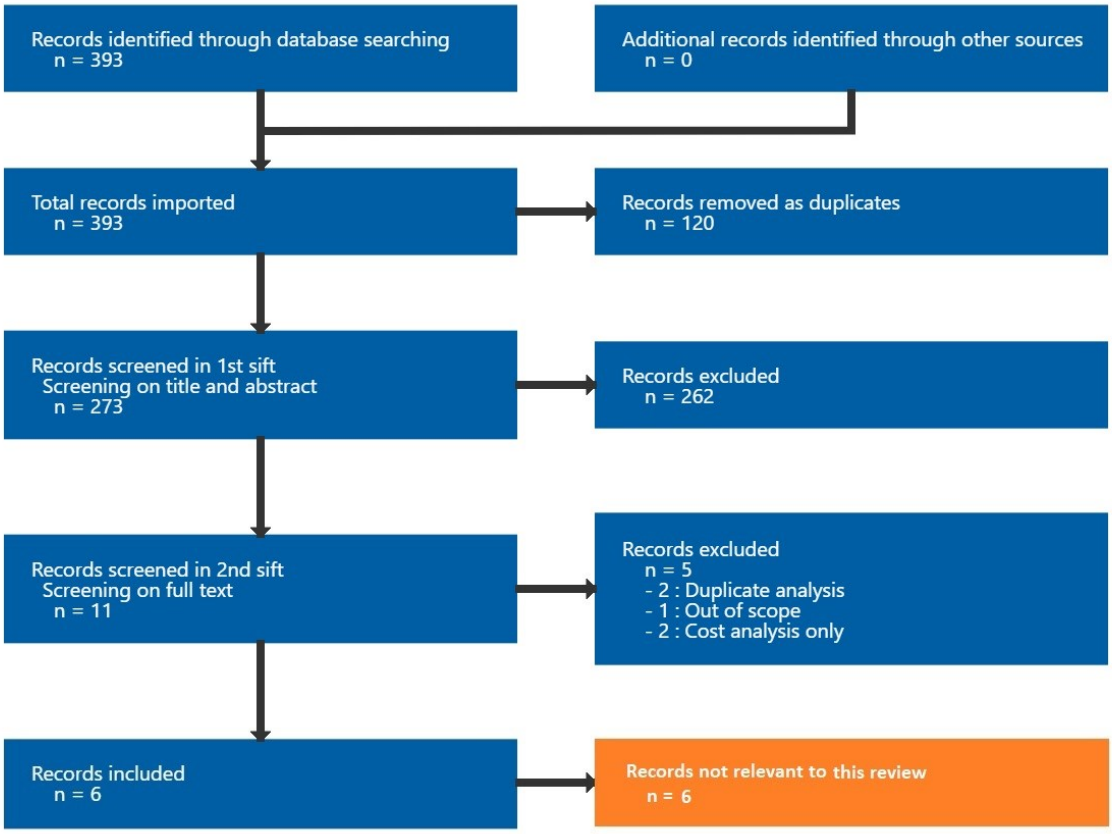
[8] Relative and absolute effects not calculable as only median and IQR reported by study: oral amoxicillin-clavulanate suspension: 1 (-11 to 18); initial observation: 0.5 (-15 to 26)

Appendix G Economic evidence study selection

Study selection for: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

A global search was undertaken to cover all the review questions considered in this guideline, but no economic evidence was identified which was applicable to this review question (see Figure 2).

Figure 2: Study selection flowchart



Appendix H Economic evidence tables

Economic evidence tables for review question: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

No evidence was identified which was applicable to this review question.

Appendix I Economic model

Economic model for review question: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

Excluded effectiveness studies

The excluded studies table only lists the studies that were considered and then excluded at the full-text stage for this review (N=9) and not studies (N=16) that were considered and then excluded from the search at the full-text stage as per the PRISMA diagram in Appendix C for the other review question in the same search.

Table 8: Excluded studies and reasons for their exclusion

Study	Code [Reason]
Alexander, Nathan S, Kulbersh, Brian D, Heath, C Hope et al. (2011) MRSA and non-MRSA otorrhea in children: a comparative study of clinical course. Archives of otolaryngology--head & neck surgery 137(12): 1223-7	- Conducted before 2010 *Study conducted between January 2003 and December 2008*
Chee, Jeremy, Pang, Khang Wen, Yong, Jui May et al. (2016) Topical versus oral antibiotics, with or without corticosteroids, in the treatment of tympanostomy tube otorrhea. International journal of pediatric otorhinolaryngology 86: 183-8	- Systematic review, included studies checked for relevance
Cheng, Jeffrey and Javia, Luv (2012) Methicillin-resistant Staphylococcus aureus (MRSA) pediatric tympanostomy tube otorrhea. International journal of pediatric otorhinolaryngology 76(12): 1795-8	- Study design does not meet inclusion criteria *Non-comparative study*
Dohar, Joseph E and Lu, Chung H (2018) Tube patency: Is there a difference following otic drop administration?. American journal of otolaryngology 39(4): 392-395	- Comparison does not meet inclusion criteria *Tympanostomy tube with/without intraoperative local antibiotic injection plus postoperative otic drops (if post-tube otorrhea observed) vs. tympanostomy tube with/without intraoperative local antibiotic injection; tube patency is only outcome reported and only as ranges; analyses not in PICO*
Rosenfeld, Richard M (2014) Topical antibiotics are superior to oral antibiotics in children with acute tympanostomy tube otorrhea. The Journal of pediatrics 165(1): 208	- Study design does not meet inclusion criteria *Commentary*
Rosenfeld, Richard M (2014) Topical antibiotic therapy is superior to systemic antibiotics for acute tympanostomy tube otorrhoea, but may not be necessary for all children. Evidence-based medicine 19(4): 132	- Study design does not meet inclusion criteria *Commentary*
Steele, Dale W, Adam, Gaelen P, Di, Mengyang et al. (2017) Prevention and Treatment of	- Systematic review, included studies checked for relevance

Study	Code [Reason]
Tympanostomy Tube Otorrhea: A Meta-analysis. Pediatrics 139(6)	
van Dongen, Thijs M A (2017) Topical antibiotic-glucocorticoid is superior to oral antibiotics in tympanostomy-tube otorrhea. The Journal of pediatrics 190: 287-290	- Study design does not meet inclusion criteria *Commentary*
Venekamp, RP, Javed, F, van Dongen, TMA et al. (2016) Interventions for children with ear discharge occurring at least two weeks following grommet (ventilation tube) insertion. Cochrane Database of Systematic Reviews	- Systematic review, included studies checked for relevance

Excluded economic studies

No economic evidence was identified for this review.

Appendix K Research recommendations – full details

Research recommendations for review question: What interventions are effective for treating otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

No research recommendations were made for this review question.