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

Table 3: Review protocol

Field	Content
PROSPERO registration number	CRD42022334005
Review title	The effectiveness of intraoperative or postoperative interventions at preventing otorrhoea after surgery for hearing loss associated with otitis media with effusion in children
Review question	What intraoperative or postoperative interventions are effective at preventing 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

Field	Content
	• Date limitations: 2010 onwards (see rationale under “Other exclusion criteria”) • 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 with confirmed otitis media with effusion (OME) who are undergoing ventilation tube surgery for OME-related hearing loss.
Intervention	Intraoperative interventions*: • Antiseptic and/or saline washouts • Antibiotic ear drops with or without corticosteroid • Systemic antibiotics • Systemic corticosteroids Postoperative interventions*: • Antibiotic ear drops with or without corticosteroid • Oral antibiotics (either immediately after operation or within 6 months) • Water precautions (actions to ensure ears are kept dry, for example, wearing ear plugs, swimming cap and headband and avoidance of swimming) *Interventions alone or in combination

Field	Content
Comparator	• Head-to-head comparisons between the above intraoperative intervention categories** (alone or in combination) • Head-to-head comparisons between the above postoperative intervention categories** (alone or in combination) • The above intraoperative interventions (alone or in combination) versus placebo • The above postoperative interventions (alone or in combination) versus placebo • The above intraoperative interventions (alone or in combination) versus no intervention for preventing otorrhoea • The above postoperative interventions (alone or in combination) versus no intervention for preventing otorrhoea **Please note, we will not include head-to-head comparisons between different interventions within each category (e.g., comparisons between different types of systemic antibiotics), only head-to-head comparisons of interventions from different categories (e.g., a systemic antibiotic versus a systemic corticosteroid)
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:

Field	Content
	• Age • Craniofacial anomalies • Socioeconomic status • Additional sensory or learning needs
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) – frequency (either clinically confirmed or parent-reported) • Adverse effects of intervention (including antimicrobial resistance) • Acceptability
Secondary outcomes (important outcomes)	• Tube blockage • Tube extrusion • Surgical intervention to remove VTs • 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.

Field	Content
	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.
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

Field	Content
	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 0.8 and 1.25 for dichotomous outcomes and 0.5 SD of the control group at baseline for continuous outcomes • All other outcomes: 0.8 and 1.25 for dichotomous outcomes and 0.5 SD of the control group at baseline for continuous outcomes

Analysis of sub-groups	Evidence will be stratified by:
	• Craniofacial anomalies
	• Mucociliary condition such as cystic fibrosis
	
	Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes:
	• Previous episode of otorrhoea
	• Previous episode of acute otitis media
	• Age
	  ○ Children <2 years vs ≥2 years
	  ○ Children <4 years vs ≥4 years
	  ○ Children <6 years vs ≥6 years
	
	Where evidence is stratified or 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=CRD42022334005
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, hearing aids, hearing devices, 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