National Institute for Health and Care Excellence

Draft for consultation

Otitis media with effusion in under 12s

[D] Evidence reviews for natural history of OME-related hearing loss

NICE guideline number tbc

Evidence reviews underpinning recommendations 1.3.1 to 1.3.3 and research recommendation 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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Natural history of OME-related hearing loss

Review question

What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years?

Introduction

The aim of this review is to investigate the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years.

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 present with otitis media with effusion (OME) confirmed by tympanometry, with associated hearing loss.
Intervention	N/A: No intervention (Natural history)
Comparison	N/A
Outcome	**Critical** • Progression of OME-related hearing loss* (e.g., worsening of hearing loss) • Time to progression of OME-related hearing loss* **Important** • Resolution of OME-related hearing loss* • Time to resolution of OME-related hearing loss* • Recurrence of OME-related hearing loss* (following spontaneous resolution of OME-related hearing loss) • Resolution of OME** causing hearing loss* • Time to resolution of OME** causing hearing loss* *OME-related hearing loss to be measured using appropriate developmental hearing assessments **Resolution/recurrence of OME to be confirmed by tympanometry

N/A: not applicable; OME: otitis media with effusion

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).

For time-to-event data, the intention was to pool such data and present the results as summary survival curves, as specified in the review protocol. However, only one included study presented time-to-event data so a summary survival curve could not be generated.

Therefore, this data was converted to proportion data to allow for direct comparison, and where applicable, pooling, with the data from the remaining studies.

Due to the absence of minimally important differences for this review, which are not appropriate for non-comparative data, imprecision was judged based on optimal information size criteria. Evidence was considered seriously imprecise if there were less than 300 events, based on the rule-of-thumb specified in version 3.2 of the GRADE handbook (Schünemann 2009), and very seriously imprecise if there were less than 150 events. The threshold for very serious imprecision was a pragmatic decision, in the absence of a rule-of-thumb being available, based on the fact that this is half the number required for serious imprecision, which would be consistent with approach suggested for continuous outcomes.

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

Epidemiological evidence

Included studies

13 studies were included for this review, 3 observational single group (non-comparative) studies (Alde 2021; Renvall 1982; van Balen 2000), 2 untreated control arms from comparative observational studies (Cooper 2022; Ghedia 2018), and 8 untreated control arms from comparative experimental studies (Dempster 1993; Francis 2018; La Mantia 2018; Maw 1993; Maw 1999; MRC Multi-centre Otitis Media Study Group 2001; O'Shea 1980; O'Shea 1982).

The included studies are summarised in Table 2.

Five studies reported resolution of OME-related hearing loss (Dempster 1993; Francis 2018; La Mantia 2018; O'Shea 1980; O'Shea 1982), 11 studies reported resolution of OME causing hearing loss (Alde 2021; Cooper 2022; Dempster 1993; Francis 2018; Ghedia 2018; La Mantia 2018; Maw 1999; MRC Multi-centre Otitis Media Study Group 2001; O'Shea 1982; Renvall 1982; van Balen 2000), and 1 study reported time to resolution of OME causing hearing loss (Maw 1993). No studies reported recurrence of OME-related hearing loss (following spontaneous resolution of OME-related hearing loss), time to progression of OME-related hearing loss, and time to resolution of OME-related hearing loss.

One study excluded children with cleft palate (Dempster 1993), 1 study excluded children with craniofacial anomalies or cleft palate (Alde 2021), 1 study excluded children with Down's syndrome or craniofacial anomalies (van Balen 2000); 2 studies excluded children with Down's syndrome or cleft palate (Francis 2018; Maw 1999), and 8 studies did not report data on whether participants had Down's syndrome, cleft palate or craniofacial anomalies (Cooper 2022; Ghedia 2018; La Mantia 2018; Maw 1993; MRC Multi-centre Otitis Media Study Group 2001; O'Shea 1980; O'Shea 1982; Renvall 1982).

Two studies included children with first episode of OME within one month before the study (O'Shea 1980; O'Shea 1982), 5 studies included children with persistent OME (at least 3 months) (Alde 2021; Dempster 1993; Francis 2018; La Mantia 2018; Maw 1993), and 6 studies did not report data on type of OME (fluctuating OME or persistent OME) and episode of OME (first episode or recurrent episode) (Cooper 2022; Ghedia 2018; Maw 1999; MRC Multi-centre Otitis Media Study Group 2001; Renvall 1982; van Balen 2000).

About 10% of children had previous grommet insertion in 1 study (Francis 2018), and 1 study included children without grommet (watchful waiting group) (Ghedia 2018). Eleven studies did not report data on whether participants had previous grommet insertion (Alde 2021; Cooper 2022; Dempster 1993; La Mantia 2018; Maw 1993; Maw 1999; MRC Multi-centre Otitis Media Study Group 2001; O'Shea 1980; O'Shea 1982; Renvall 1982; van Balen 2000)

One study included children aged 2 years and over (Maw 1999), 1 study included children aged 6 months to 6 years (van Balen 2000); 1 study included children aged 2 to 9 years (Maw 1993), 1 study included children aged 3 to 9 years (O'Shea 1982), 1 study included children aged 3.3 to 6.8 years (MRC Multi-centre Otitis Media Study Group 2001), 6 studies included children aged 4 years and over (Alde 2021; Cooper 2022; Dempster 1993; Francis 2018; Ghedia 2018; Renvall 1982), and 2 studies included children aged 6 years and over (La Mantia 2018; O'Shea 1980)

Seven studies were from the UK (Cooper 2022; Dempster 1993; Francis 2018; Ghedia 2018; Maw 1993; Maw 1999; MRC Multi-centre Otitis Media Study Group 2001), 2 studies were from Italy (Alde 2021; La Mantia 2018), 2 studies were from USA (O'Shea 1980; O'Shea 1982), 1 study was from Sweden (Renvall 1982), and 1 study was from Netherlands (van Balen 2000).

Resolution of OME-related hearing loss was defined as change in hearing threshold from above to below 20 dB in 2 studies (O'Shea 1980; O'Shea 1982), change in hearing threshold from above to below 20 to 25 dB in 1 study (Francis 2018), and change in hearing threshold from above to below 25 dB in 2 studies (La Mantia 2018; Dempster 1993).

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

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies.

Study	Population	Outcomes	Comments
Alde 2021 Observational single group (non-comparative) study Italy	N=932 (n=59 children with chronic OME: Subgroup A: n=30; Subgroup B: n=29) Children aged 6 months to 12 years who attended paediatric outpatient audiology clinic Age in years, mean (SD): Subgroup A: 4.7 (NR) Subgroup B: 5 (NR) Sex (male/female):	• Resolution of OME causing hearing loss	Follow-up: 9-12 months Duration of OME before the study was more than 6 months. The diagnosis of OME (type B tympanogram) confirmed by tympanometry, otoscopy, and the presence of mild to moderate conductive hearing loss (Subgroup A and B). Resolution of OME was defined as change from type B to type A tympanogram (Subgroup A and B).

Study	Population	Outcomes	Comments
	Subgroup A: 23/7 Subgroup B: 18/11		
Cooper 2022 Untreated control arm from comparative observational study UK	N=513* Children aged 3-11 years seen in the RBFT children's hearing assessment clinic between 23 February 2017 and 22 February 2018 with type B tympanogram and normal ear canal volume in at least one ear Age in years, mean (SD)*: 5.3 (1.5) Sex (male/female)*: 279/234 *Data from untreated control arm	• Resolution of OME causing hearing loss	Follow-up: 3-6 months (mean 5.4 months) Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Resolution of OME was defined as change from type B to non-B tympanogram.
Dempster 1993 Untreated control arm from comparative experimental study UK	N=72 (n=35 from untreated control arm)* Children with average pure tone air conduction thresholds across different frequencies of ≥25 dB HL, an average air-bone gap of ≥15 dB, and type B tympanogram Age in years, mean (SD)*: 5.8 (1.3) Sex (male/female)*: 40/32	• Resolution of OME-related hearing loss • Resolution of OME causing hearing loss	Follow-up: 12 months Participants had persistent bilateral OME for at least 3 months before the study. The diagnosis of OME was confirmed by otoscopy and tympanometry (type B tympanogram). Resolution of OME-related hearing loss was defined as change in hearing threshold from above to below 25 dB. Resolution of OME was defined as change from type B to non-B tympanogram.

Study	Population	Outcomes	Comments
	*Data from whole sample as data from untreated control arm was not reported separately		
Francis 2018 Untreated control arm from comparative experimental study UK	N=187* Children aged 2-8 years with bilateral OME and hearing loss (defined as >20 or >25 dB HL, dependent on methods used) with symptoms of hearing loss for at least 3 months Age in years, mean (SD)*: 5.1 (1.6) Sex (male/female)*: 102/85 *Data from untreated control arm	• Resolution of OME-related hearing loss • Resolution of OME causing hearing loss	Follow-up: 12 months Participants had persistent bilateral OME for at least 6 months before the study. The diagnosis of OME (type B or C tympanogram) was confirmed by tympanometry. Resolution of OME-related hearing loss was defined as change in hearing threshold from above to below 20-25 dB (depending on methods used). Resolution of OME was defined as change from type B or C to type A tympanogram.
Ghedia 2018 Untreated control arm from comparative observational study UK	N=53 (n=106 ears with OME)* Children with diagnosis of PCD and OME in January 2016 Age in years and months, mean (SD)*: 5 years and 6 months (NR) Sex (male/female)**: 50/51 *Data from untreated control arm	• Resolution of OME causing hearing loss	Follow-up (mean): 57 months Duration of OME before the study is unknown. The diagnosis of OME was confirmed by otoscopy (dull tympanic membrane) and tympanometry (type B tympanogram). Resolution of OME was defined as change from type B to non-B tympanogram.

Study	Population	Outcomes	Comments
	**Data from whole sample as data from untreated control arm was not reported separately		
La Mantia 2018 Untreated control arm from comparative experimental study Italy	N=40* Children aged 4-12 years with unilateral or bilateral OME documented for at least 3 months Age in years, mean (SD)*: 7.6 (2.0) Sex (male/female)*: 22/18 *Data from untreated control arm	• Resolution of OME-related hearing loss • Resolution of OME causing hearing loss	Follow-up: 3 months Duration of OME before the study was at least 3 months. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Resolution of OME-related hearing loss was defined as change in hearing threshold from above to below 25 dB. Resolution of OME was defined as change from type B to type A tympanogram.
Maw 1993 Untreated control arm from comparative experimental study UK	N=77* Children aged 2-11 years with pronounced subjective hearing loss, bilateral MEE, and >25 dB pure audiometric or free field hearing loss in each ear at one or more frequencies Age in years, mean (SD): NR, but range**: 2-9 *Data from untreated control arm **Data from whole sample as data from untreated control arm was	• Resolution of OME causing hearing loss	Follow-up: 10 years and 1 month Duration of OME before the study was more than 3 months. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Resolution of OME was defined as change from type B to non-B tympanogram that persisted for 12 months.

Study	Population	Outcomes	Comments
	not reported separately		
Maw 1999 Untreated control arm from comparative experimental study UK	N=90* Children who were born between 1st April 1991 and 31st December 1992 and had bilateral OME, hearing loss, and speech, language, learning or behaviour problems Age in years, mean (SD)*: 2.9 (0.9) Sex (male/female)*: 35/72 *Data from untreated control arm	• Resolution of OME causing hearing loss	Follow-up: 18 months Duration of OME before the study is unknown. The diagnosis of OME (type B or C2 tympanogram) was confirmed by tympanometry. The definition of resolution of OME was defined as change from type B or C2 to type A or C1 tympanogram.
MRC Multi-centre Otitis Media Study Group 2001 Untreated control arm from comparative experimental study UK	N=639* Children with bilateral OME, bilateral hearing loss (pure-tone threshold of 20 dB HL or worse and air-bone gap >10 dB at 1 kHz), and no previous ear or adenoid surgery Age in years, mean (SD): NR, but range*: 3.3-6.8 Sex (male/female)*: 318/321 *Data from whole sample that were followed up over 12-week	• Resolution of OME causing hearing loss (defined as ≥15 dB, ≥20 dB and ≥25 dB in better ear)	Follow-up: 12 weeks Duration of OME before the study is unknown. The diagnosis of OME (bilateral type B or B and C2 tympanogram) was confirmed by tympanometry. Resolution of OME was defined as change from B/B or B/C2 tympanogram and >10 dB air-bone gap at 1 kHz to not meeting these criteria.

Study	Population	Outcomes	Comments
	watchful waiting period (before randomisation)		
O'Shea 1980 Untreated control arm from comparative experimental study USA	N=28* Children with first episode of OME, rectal temperature <38.4 C or oral temperature <37.8 C, no obvious nose or ear deformities, air conduction hearing loss of ≥15 dB but no bone conduction hearing loss of >10 dB Age in years, mean (SD)*: 6 (NR) Sex (male/female)**: 33/22 *Data from untreated control arm **Data from whole sample as data was not reported separately for untreated control arm	• Resolution of OME-related hearing loss	Follow-up: 3 months Duration of OME before the study was less than 1 month. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Resolution of OME-related hearing loss was defined as change in hearing threshold from above to below 20 dB.
O'Shea 1982 Untreated control arm from comparative experimental study USA	N=24* Children with first episode of OME, rectal temperature <38.4 C or oral temperature <37.8 C, no obvious nose or ear deformities, air conduction hearing loss of ≥15 dB but no bone conduction hearing loss of >10 dB	• Resolution of OME-related hearing loss • Resolution of OME causing hearing loss	Follow-up: 1 year Duration of OME before the study was less than 1 month. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Resolution of OME-related hearing loss was defined as change in hearing threshold from above to below 20 dB. Resolution of OME was defined as change from type B to A tympanogram, or from type B to A or C tympanogram.

Study	Population	Outcomes	Comments
	Age in years, mean (SD): NR, but range**: 3-9 Sex (male/female): NR *Data from untreated control arm **Data from whole sample as data was not reported separately for untreated control arm		
Renvall 1982 Observational single group (non-comparative) study Sweden	N=248 (n=223 ears) Children aged 4 years with hearing loss >20 dB HL on pure-tone audiometry and middle ear pressure ≤-150mm H2O on tympanometry/ otomicroscopy Age in years, mean (SD): NR, but study included children aged 4 years Sex (male/female): NR	• Resolution of OME causing hearing loss	Follow-up: 12 weeks Duration of OME before the study is unknown. The diagnosis of OME was confirmed by tympanometry, but authors did not report criteria used. The definition of resolution of OME was not reported.
van Balen 2000 Observational single group (non-comparative) study Netherlands	N=433 Children with bilateral OME and presenting complaints that are frequently associated with OME Age in months and years,	• Resolution of OME causing hearing loss	Follow-up: 3 months Duration of OME before the study is unknown. The diagnosis of OME (B or C2 tympanogram) was confirmed by tympanometry. Resolution of OME was defined as change from type B or C2 to A or C1 tympanogram.

Study	Population	Outcomes	Comments
	mean (SD): NR, but range: 6 months - 6 years Sex (male/female): 230/203		

dB HL: decibel hearing level; MEE: middle ear effusion; NR: not reported; OME: otitis media with effusion; PCD: primary ciliary dyskinesia; RBFT: The Royal Berkshire Hospital NHS Foundation Trust; SD: standard deviation; VT: ventilation tube

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 for all outcomes, except for resolution of OME of unknown duration at 6 months, due to risk of bias in some of the domains of the Joanna Briggs Institute Checklist (JBI) checklist and imprecision due to small number of events. The quality of evidence for resolution of OME of unknown duration at 6 months was low due to risk of bias in some of the domains of the JBI checklist. The evidence was stratified by duration of OME before the study or follow-up, duration of follow-up, definition of resolution used, and unit of analysis (ear or child). None of the studies included children with craniofacial anomalies.

Resolution of OME-related hearing loss

Resolution of OME-related hearing loss in children with OME of <1 month duration before follow-up

Resolution of OME-related hearing loss, defined as change in hearing threshold from above to below 20 dB, was 50% (confidence interval 32% to 68%) by 3 months and 75% (confidence interval 54% to 88%) by 12 months in children with OME of <1 month duration before follow-up.

Resolution of OME-related hearing loss in children with OME of >3 months duration before follow-up

In children with OME of >3 months duration before follow-up, resolution of OME-related hearing loss, defined as change in hearing threshold from above to below 25 dB, was 50% (confidence interval 32% to 68%) by 3 months, 60% (confidence interval 43% to 75%) by 6 months, and 77% (confidence interval 61% to 88%) by 12 months.

Resolution of OME-related hearing loss in children with OME of >12 months duration before follow-up

Resolution of OME-related hearing loss, defined as change in hearing threshold from above to below 20-25 dB (depending on methods used), in children with OME of >12 months duration before follow-up was 33% (confidence interval 26% to 40%) by 1 month, 52% (confidence interval 44% to 59%) by 6 months, and 61% (confidence interval 53% to 68%) by 12 months.

Resolution of OME causing hearing loss

Resolution of OME of <1 month duration before follow-up

At 12 months follow-up, resolution of OME of <1 month duration before follow-up was 29% (confidence interval 18% to 43%) when it was defined as change from type B to type A tympanogram and 77% (confidence interval 63% to 87%) when it was defined as change from type B to type A or C tympanogram.

Resolution of OME of >3 months duration before follow-up

At 3 months follow-up, resolution of OME of >3 months duration before follow-up was 25% (confidence interval 14% to 41%) when defined as change from type B to type A tympanogram. Resolution of OME, defined as change from type B to non-B tympanogram, was 20% (confidence interval 10% to 36%) by 6 months and 31% (confidence interval 18% to 48%) by 12 months. Resolution of OME of >3 months duration before follow-up, defined as change from type B to non-B tympanogram that persisted for 12 months, was as follows:

- 3% (confidence interval 1% to 10%) at 18 months,
- 5% (confidence interval 2% to 13%) at 19 months,
- 6% (confidence interval 3% to 15%) at 23 months,
- 8% (confidence interval 4% to 16%) at 27 months,
- 9% (confidence interval 4% to 18%) at 30 months,
- 10% (confidence interval 5% to 19%) at 31 months,
- 12% (confidence interval 6% to 21%) at 37 months,
- 13% (confidence interval 7% to 22%) at 39 months,
- 14% (confidence interval 8% to 24%) at 42 months,
- 19% (confidence interval 12% to 30%) at 45 months,
- 21% (confidence interval 13% to 31%) at 47 months,
- 22% (confidence interval 14% to 33%) at 48 months,
- 23% (confidence interval 15% to 34%) at 54 months,
- 25% (confidence interval 16% to 35%) at 60 months,
- 27% (confidence interval 19% to 38%) at 61 months,
- 30% (confidence interval 21% to 41%) at 67 months,
- 36% (confidence interval 26% to 48%) at 69 months,
- 39% (confidence interval 29% to 50%) at 73 months,
- 40% (confidence interval 30% to 52%) at 75 months,
- 43% (confidence interval 32% to 54%) at 78 months,
- 45% (confidence interval 35% to 57%) at 81 months,
- 51% (confidence interval 40% to 62%) at 93 months,
- 55% (confidence interval 43% to 65%) at 101 months, and
- 58% (confidence interval 47% to 69%) at 105 months.

Resolution of OME of >6 months duration before follow-up

Resolution of OME of >6 months duration before follow-up, defined as change from type B to type A tympanogram, was 21% to 93% (reasons for heterogeneity unclear) by 12 months.

Resolution of OME of >12 months duration before follow-up

Resolution of OME of >12 months duration before follow-up, defined as change from type B or C to type A tympanogram, was 7% (confidence interval 4% to 12%), 12% (confidence interval 7% to 18%) and 6% (confidence interval 3% to 12%) by 1 month, 6 months and 12 months, respectively.

Resolution of OME of unknown duration before follow-up

Resolution (undefined) of OME of unknown duration before follow-up was 39% (confidence interval 31% to 47%) by 1.5 months. Resolution of OME was 23% (confidence interval 20% to 28%), when defined as change from type B or C2 to type A or C1 tympanogram, and 52% (confidence interval 39% to 64%), when undefined, by 3 months. At 3 months follow-up, resolution of OME causing hearing loss ≥15 dB, ≥20 dB and ≥25 dB in better ear was 33% (confidence interval 30% to 37%), 43% (confidence interval 39% to 47%) and 55% (confidence interval 50% to 60%), respectively, when defined as change from type B/B or B/C2 tympanogram and >10 dB air-bone gap at 1 kHz to not meeting these criteria. Resolution of OME was 50% (confidence interval 46% to 53%) by 6 months when defined as change from type B to non-B tympanogram and 31% (confidence interval 21% to 42%) by 9 months when defined as change from type B or C2 to type A or C1 tympanogram. At 57 months follow-up, resolution of OME, defined as change from type B to non-B tympanogram, was 42% (confidence interval 33% to 51%).

There were a number of outcomes in the protocol that were not reported on by any studies, including progression of OME-related hearing loss (e.g., worsening of hearing loss), time to progression of OME-related hearing loss, time to resolution of OME-related hearing loss, and recurrence of OME-related hearing loss (following spontaneous resolution of OME-related hearing loss).

See appendix F for full GRADE tables.

Economic evidence

Included studies

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 as this review question did not explicitly address a decision between competing alternatives.

The committee's discussion and interpretation of the evidence

The outcomes that matter most

This review aimed to identify natural history (progression, resolution and recurrence) of OME with hearing loss. The committee were aware that hearing loss or hearing difficulty could impact on the child's development and quality of life. Therefore, progression of OME-related hearing loss and time to progression of OME-related hearing loss were prioritised as critical outcomes. Resolution of OME-related hearing loss, time to resolution of OME-related hearing loss, recurrence of OME-related hearing loss (following spontaneous resolution of OME-related hearing loss), resolution of OME causing hearing loss, and time to resolution of OME causing hearing loss were chosen as important outcomes as they are useful indicators of natural history of OME with hearing loss.

The quality of the evidence

The quality of evidence was assessed using GRADE methodology. The evidence was low to very low quality due to risk of bias (e.g., arising from issues with sample frame, participant sampling, reporting of characteristics and setting, and measurement of condition) and imprecision due to small number of events.

No evidence was found for the following outcomes: progression of OME-related hearing loss (e.g., worsening of hearing loss), time to progression of OME-related hearing loss, time to resolution of OME-related hearing loss, or recurrence of OME-related hearing loss (following spontaneous resolution of OME-related hearing loss).

Benefits and harms

The available data on resolution of OME-related hearing loss showed a trend towards greater resolution over longer follow-up periods, and it seemed to follow the linear pattern expected by the committee, based on their experience, independent of unit of analysis (ear and child) and how resolution of OME-related hearing loss was defined. However, the evidence showed wide variation in the rates of resolution of OME causing hearing loss reported across papers. There was a trend towards greater resolution of OME causing hearing loss over longer follow-up periods, but this did not follow the linear pattern that the committee expected. The committee agreed that this may be due to differences in populations across studies and in how resolution was defined, as there was a tendency for resolution rates to be higher in children with OME of less than 1 month duration before follow-up compared with children with persistent OME (>12 months duration before follow-up), and in studies that used less strict definition of resolution (for example, change from type B to non-B tympanogram compared with change from type B to non-B tympanogram that persisted for 12 months). However, the committee were not confident in the available evidence due to the low quality of the evidence, and they made recommendations based on their expert knowledge and experience.

The committee felt that the available evidence was not strong enough to make a change to the currently recommended monitoring and support period (watchful waiting period), which is 3 months, due to the variation across studies and the low quality of the evidence. However, the committee were concerned about the negative impacts of OME-related hearing loss on the child's development and discussed that strategies, such as modifying the environment and listening strategies (see recommendations on information and advice and evidence review N for more details about the strategies), may reduce its impacts during monitoring and support period. The committee discussed that such strategies should be used in both home and educational settings to reduce the impact of hearing loss in all settings and best support the child's development and wellbeing. The committee discussed what action should be taken after the monitoring and support period and felt that this would depend on whether the OME is bilateral or unilateral. In their experience, it is standard practice to reassess hearing loss after 3 months where the OME is bilateral, but they were aware that children with unilateral OME may not need reassessment after 3 months. This is because children with unilateral hearing loss tend to hear well in a normal listening environment without excessive background noise, and there may not be a significant impact on the child's communication and development. In the committee's experience, strategies to minimise the impact of hearing loss may be sufficient in children with unilateral hearing loss. However, the committee acknowledged that OME is a fluctuating condition, and some children may fluctuate between unilateral and bilateral OME. Therefore, the committee made a change to current recommendation, and they agreed that after 3 months of monitoring and support period, during which the strategies mentioned above should be advised, hearing should be reassessed as standard in children with bilateral OME and should also be considered for those with unilateral OME.

The committee were aware that hearing loss may significantly affect day-to-day living for some children. The committee agreed that in these cases, the hearing loss should be addressed as soon as possible to avoid negatively impacting children's development and wellbeing; therefore, they recommended that earlier intervention should be considered for these children, as opposed to waiting 3 months for further assessment of hearing (see the recommendations on management of hearing loss, non-surgical management of OME and surgical management of OME, and evidence reviews E-J for more details about interventions).

In the committee's experience, children with OME do not need further assessment or interventions if there is no hearing loss. Therefore, the committee agreed that at 3 months audiology assessment children with OME and normal hearing should be discharged. However, the committee acknowledged that, as OME is often a fluctuating condition, further hearing assessment may be needed if concerns about hearing occur in the future. The committee discussed that parents should have the opportunity to contact audiology services to discuss the need for further hearing assessment for their child when they are concerned about recurrence of hearing loss. The committee felt that it may reduce delays in identifying recurrent hearing loss and therefore, appropriate interventions to address this and avoid adverse effects on the child's development and wellbeing as people will not have to go through GP referral. However, the committee were aware that there is variation in practice, and audiology services may or may not accept direct referrals depending on when reassessment is needed. They discussed that it is fairly common in practice that audiology services may only accept direct referrals for reassessment within one year after discharge, but reassessment may be carried out by GP if it is after one year. The committee agreed that the recommendation will give the flexibility for audiology services to accept direct referrals or to refer the child back to the GP if this is necessary.

If hearing loss is unilateral at the follow-up assessment, the committee recommended that people continue with the strategies to minimise the impact of hearing loss discussed above and consider another hearing assessment after a further 3 months or follow the recommendations on interventions (see the recommendations on management of hearing loss, non-surgical management of OME and surgical management of OME, and evidence reviews E-J) if there is concern about the impact of hearing loss on day-to-day living and communication. The committee acknowledged that this would give flexibility in providing appropriate care for children with unilateral hearing loss as necessary. However, the committee were aware that some children with unilateral hearing loss that has minimal or no impact on day-to-day living may be discharged at this point, rather than requiring further follow-up, although the committee agreed that they would still advise that strategies to minimise the impact of hearing loss are continued. As children with bilateral hearing loss are at the greatest risk of negative effects on their development and quality of life, the committee recommended following the recommendations on interventions referenced above if hearing loss is bilateral at the 3 months assessment.

The committee acknowledged that heterogeneity would be expected with this type of evidence as any differences in the populations included may affect the natural history. One approach suggested for systematic reviews of observational epidemiological studies is to prioritise studies that are most similar to the population of interest (depending on the purpose of the review) rather than attempting to provide a pooled estimate that may obscure differences between populations and be of minimal use (Munn 2015). Over 50% of the studies included in this review were conducted in the UK (Cooper 2022; Dempster 1993; Francis 2018; Ghedia 2018; Maw 1993; Maw 1999; MRC Multi-centre Otitis Media Study Group 2001); however, the data from these studies were not pooled due to the stratifications based on duration of OME before the study or follow-up, duration of follow-up, definition of resolution used, and unit of analysis (ear or child). Therefore, consideration of the evidence from the UK specifically also did not provide robust evidence, and the committee agreed that further research on the natural history of OME with hearing loss was needed. They discussed that clear understanding of the natural history of OME informed by robust evidence will contribute to optimal management. Therefore, the committee made a research recommendation for progression, resolution, and recurrence of OME with hearing loss (see Appendix K).

Cost effectiveness and resource use

The committee did not consider there was sufficient evidence to determine the optimal watchful waiting period prior to intervention and therefore the current recommendation of 3

months of watchful waiting was maintained. As the recommendations do not alter current practice there will not be a resource impact to the NHS.

The committee considered that earlier intervention than the 3-month reassessment could be cost-effective for children who are experiencing hearing difficulties leading to an adverse impact on health-related quality of life (HRQoL) and day-to-day living. Therefore, they recommended that this could be considered for these children as gains in HRQoL would likely be realised and most additional costs would only be incurred in the event of spontaneous resolution of OME associated hearing loss occurring in such children within the 3-month watchful waiting period, as otherwise intervention would be simply delayed.

The committee also made recommendations on giving advice to minimise the impact of hearing loss in home and educational settings, but the committee reasoned that as this would be provided as part of routine communication with parents that this would not have any resource impact to the NHS.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.3.1, 1.3.2, and 1.3.3 and the research recommendation on progression, resolution and recurrence of OME with and without hearing loss. Other evidence supporting this research recommendation can be found in the evidence review on natural history of OME without hearing loss (see evidence reviews C).

References – included studies

Epidemiological

Alde 2021

Alde, M., Di Berardino, F., Marchisio, P. et al. (2021). Effects of COVID-19 lockdown on otitis media with effusion in children: future therapeutic implications, Otolaryngology - Head and Neck Surgery 165(5), 710-715

Cooper 2022

Cooper, H. E., Grifa, I., Bryant, C. (2022). Use of an autoinflation device does not lead to a clinically meaningful change in hearing thresholds in children with otitis media with effusion, Clinical otolaryngology 47(1), 160-166

Dempster 1993

Dempster, J. H., Browning, G. G., Gatehouse, S. G. (1993). A randomized study of the surgical management of children with persistent otitis media with effusion associated with a hearing impairment, The Journal of Laryngology & Otology 107(4), 284-289

Francis 2018

Francis, N. A., Waldron, C-A., Cannings-John, R. et al. (2018). Oral steroids for hearing loss associated with otitis media with effusion in children aged 2-8 years: the OSTRICH RCT, Health Technology Assessment 22(61), 1-114

Ghedia 2018

Ghedia, R., Ahmed, J., Navaratnam, A. et al. (2018). No evidence of cholesteatoma in untreated otitis media with effusion in children with primary ciliary dyskinesia, International Journal of Pediatric Otorhinolaryngology 105, 176-180

La Mantia 2018

La Mantia, I. and Andaloro, C. (2018). Effects of salso-bromo-iodine thermal water in children suffering from otitis media with effusion: a randomized controlled pilot study, La Clinica Terapeutica 169(1), e10-e13

Maw 1993

Maw, R. and Bawden, R. (1993). Spontaneous resolution of severe chronic glue ear in children and the effect of adenoidectomy, tonsillectomy, and insertion of ventilation tubes (grommets), BMJ 306(6880), 756-760

Maw 1999

Maw, R., Wilks, J., Harvey, I. et al. (1999). Early surgery compared with watchful waiting for glue ear and effect on language development in preschool children: a randomised trial, Lancet 353(9157), 960-963

MRC Multi-centre Otitis Media Study Group 2001

MRC Multi-centre Otitis Media Study Group (2001). Risk factors for persistence of bilateral otitis media with effusion, Clinical Otolaryngology and Allied Sciences 26(2), 147-156

O'Shea 1982

O'Shea, J. S., Langenbrunner, D. J., McCloskey, D. E. et al. (1982). Childhood serous otitis media: fifteen months' observations of children untreated compared with those receiving an antihistamine-adrenergic combination, Clinical Pediatrics 21(3), 150-153

O'Shea 1980

O'Shea, J. S., Langenbrunner, D. J., McCloskey, D. E. et al. (1980). Diagnostic and therapeutic studies in childhood serous otitis media. results of treatment with an antihistamine-adrenergic combination, The Annals of Otology, Rhinology & Laryngology. Supplement 89(3pt2), 285-289

Renvall 1982

Renvall, U., Aniansson, G., Lidén, G. (1982), Spontaneous improvement in ears with middle ear disease, International Journal of Pediatric Otorhinolaryngology 4(3), 245-250

van Balen 2000

van Balen, F. A. and de Melker, R. A. (2000). Persistent otitis media with effusion: can it be predicted? a family practice follow-up study in children aged 6 months to 6 years, The Journal of family Practice 49(7), 605-611

Other

Munn 2015

Munn, Z., Moola, S., Lisay, K. et al. (2015). Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data, International Journal of Evidence-Based Healthcare 13(3), 147-153

Schünemann 2009

Schünemann H., Brożek J., Oxman A., editors. (2009). GRADE handbook for grading quality of evidence and strength of recommendation. Version 3.2 [updated March 2009]

Appendices

Appendix A Review protocols

Review protocol for review question: What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years?

Table 3: Review protocol

Field	Content
PROSPERO registration number	CRD42022341020
Review title	Natural history of OME-related hearing loss
Review question	What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years?
Objective	To determine the natural history of OME-related hearing loss at presentation 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 • MEDLINE • CINAHL • Epistemonikos • International Health Technology Assessment (INAHTA) database • PsycINFO Searches will be restricted by: • OECD geographic study filter • English language

Field	Content
	• Human studies The full search strategies for MEDLINE database will be published in the final review. For each search, the principal database search strategy is quality assured by a second information scientist using an adaptation of the PRESS 2015 Guideline Evidence-Based Checklist.
Condition or domain being studied	Otitis media with effusion in children under 12 years
Population	Inclusion: All children under 12 years who present with otitis media with effusion (OME) confirmed by tympanometry, with associated hearing loss.
Intervention/Exposure/Test	N/A
Comparator/Reference standard/Confounding factors	N/A
Types of study to be included	Include published full-texts: • Systematic reviews of observational single group (non-comparative) studies • Observational single group (non-comparative) studies or untreated control arms from comparative observational studies • If insufficient observational studies*: Systematic reviews or primary studies of untreated control arms from comparative experimental studies • If insufficient observational studies and comparative experimental studies*: Case series Minimum follow-up time of at least 3 months. Outcomes will be extracted for all follow-up points, including those earlier than 3 months. *Sufficiency will be judged based on number of studies reporting different outcomes and data from subgroups of interest
Other exclusion criteria	• Country limitations: limit studies to OECD high- and middle-income countries • Language limitations: limit studies to those published in English-language • Individual case studies will not be considered. • Conference abstracts will not be considered.

Field	Content
Context	This guidance will fully update the following NICE guideline: Otitis media with effusion in under 12s: surgery (2008; CG60)
Primary outcomes (critical outcomes)	• Progression of OME-related hearing loss* (e.g., worsening of hearing loss) • Time to progression of OME-related hearing loss* *OME-related hearing loss to be measured using appropriate developmental hearing assessments
Secondary outcomes (important outcomes)	• Resolution of OME-related hearing loss* • Time to resolution of OME-related hearing loss* • Recurrence of OME-related hearing loss* (following spontaneous resolution of OME-related hearing loss) • Resolution of OME** causing hearing loss* • Time to resolution of OME** causing hearing loss* *OME-related hearing loss to be measured using appropriate developmental hearing assessments **Resolution/recurrence of OME to be confirmed by tympanometry
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. 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

Field	Content
	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 • JBI checklist for prevalence studies for observational single group (non-comparative) 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 of proportion data will be conducted using the metafor package in R (Viechtbauer 2010), which will allow for meta-analysing of data from single group studies. A fixed effects model will be used, and data will be presented as a pooled rate. Heterogeneity in the effect estimates of the individual studies will be assessed using the I^2 statistic (calculated from Cochran's Q). Alongside visual inspection of the point estimates and confidence intervals, I^2 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. Where possible, time-to-event data will be pooled using the metaSurvival package in R (Pandey 2020) and presented as a summary survival curve. 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/ Due to the absence of minimally important differences for this review, imprecision will be judged based on optimal information size (number of events) and importance of outcomes will be assessed qualitatively during committee discussions and documented in the committee's discussion and interpretation of the evidence.

Field	Content

Analysis of sub-groups	Evidence will be stratified by:
	• Craniofacial anomalies
	  ○ Children with Down's syndrome
	  ○ Children with cleft palate
	  ○ Children with other craniofacial anomalies (including achondroplasia)
	  ○ Children without craniofacial anomalies
	Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes:
	• Type of OME
	  ○ Fluctuating OME
	  ○ Persistent OME
	• Episode of OME
	  ○ First episode
	  ○ Recurrent episode
	• Previous intervention
	  ○ Previous grommet insertion
	  ○ No previous grommet insertion
	• Age
	  ○ Children <2 years vs ≥2 years
	  ○ Children <4 years vs ≥4 years
	  ○ Children <6 years vs ≥6 years
	• Country
	• Ethnicity
	• Measurement of hearing (critical outcomes only)

Field	Content			
	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 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	24/05/2022			
Anticipated completion date	28/09/2023			
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		☐	☑

Field	Content
Named contact	Named contact: National Guideline Alliance Named contact e-mail: otitis@nice.org.uk 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=CRD42022341020
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

Field	Content	
	• 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, natural history, progression, resolution, recurrence, hearing loss	
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; CINAHL: Cumulative Index to Nursing and Allied Health Literature; GRADE: Grading of Recommendations Assessment, Development and Evaluation; INAHTA: International Health Technology Assessment database; JBI: The Joanna Briggs Institute Checklist; MEDLINE: Medical Literature Analysis and Retrieval System Online; N/A: not applicable; NICE: National Institute for Health and Care Excellence; OME: otitis media with effusion; PsycINFO: Psychological Information Database; ROBIS: risk of bias in systematic reviews

Appendix B Literature search strategies

Literature search strategies for review question: What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years?

Clinical search

This was a combined search to cover both this review and the evidence review on natural history of OME-related hearing loss in children under 12 years.

Database: MEDLINE – OVID interface

Date last searched: 28/06/2022

#	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	Acoustic Impedance Tests/
5	(tympanomet* or tympanogra* or reflectomet*).ti,ab,kf.
6	(((acoustic or admittance or audio or eardrum* or ear drum* or electroacoustic or frequenc* or impedance or middle ear or otoacoustic or tympanic) adj3 (evaluat* or measur* or method* or screen* or test*)) or DPOAE? or TEOAE?).ti,ab.
7	((acoustic or audio or eardrum* or ear drum* or electroacoustic or frequenc* or middle ear or otoacoustic or sound?) and (admittance or audiomet* or compliance or conductance or emission or immittance or impedance or intermittence or reactance or reflex or resistance or susceptance)).ti,ab.
8	or/4-7
9	3 and 8
10	Incidence/ or exp Disease Progression/ or exp Periodicity/ or Prevalence/ or "Recovery of Function"/ or exp Recurrence/ or Time/ or Time Factors/ or Monitoring, Physiologic/ or Watchful Waiting/
11	(((natural* or spontaneous* or disease* or effusion* or past or period* or persist* or season* or time*) adj5 (histor* or course* or duration* or factor*)) or inciden* or prevalen*).ti,ab.
12	(monitor* or observ* or surveillance or (watch* adj2 (wait* or see)) or (wait adj2 see)).ti,ab.
13	(clinical course or untreated or "not treated" or no intervention* or without intervention* or no treatment* or without treatment* or no therap* or without therap*).ti,ab.
14	(clear* or deteriorat* or develop* or disappear* or evolv* or exacerbat* or fluctuat* or frequen* or infect* or improv* or occur* or progress* or recover* or recur* or reinfect* or relaps* or remission or reoccur* or resolution or resolv* or restor*).ti,ab.
15	or/10-14
16	9 and 15
17	(animals not humans).sh. or exp animals, laboratory/ or exp animal experimentation/ or exp models, animal/ or exp rodentia/ or (rat or rats or mouse or mice).ti.
18	16 not 17
19	limit 18 to english language

Database: Embase – OVID interface

Date last searched: 28/06/2022

#	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	acoustic impedance/ or tympanometry/
5	(tympanomet* or tympanogra* or reflectomet*).ti,ab,kf.
6	(((acoustic or admittance or audio or eardrum* or ear drum* or electroacoustic or frequenc* or impedance or middle ear or otoacoustic or tympanic) adj3 (evaluat* or measur* or method* or screen* or test*)) or DPOAE? or TEOAE?).ti,ab.
7	((acoustic or audio or eardrum* or ear drum* or electroacoustic or frequenc* or middle ear or otoacoustic or sound?) and (admittance or audiomet* or compliance or conductance or emission or immittance or impedance or intermittence or reactance or reflex or resistance or susceptance)).ti,ab.
8	or/4-7
9	3 and 8
10	incidence/ or disease course/ or disease clearance/ or disease duration/ or convalescence/ or recurrent disease/ or recurrent infection/ or remission/ or time/ or time factor/ or patient monitoring/ or watchful waiting/

#	Searches
11	(((natural* or spontaneous* or disease* or effusion* or past or period* or persist* or season* or time*) adj5 (histor* or course* or duration* or factor*)) or inciden* or prevalen*).ti,ab.
12	(monitor* or observ* or surveillance or (watch* adj2 (wait* or see)) or (wait adj2 see)).ti,ab.
13	(clinical course or untreated or "not treated" or no intervention* or without intervention* or no treatment* or without treatment* or no therap* or without therap*).ti,ab.
14	(clear* or deteriorat* or develop* or disappear* or evolv* or exacerbat* or fluctuat* or frequen* or infect* or improv* or occur* or progress* or recover* or recur* or reinfect* or relaps* or remission or reoccur* or resolution or resolv* or restor*).ti,ab.
15	or/10-14
16	9 and 15
17	(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.
18	16 not 17
19	limit 18 to english language
20	limit 19 to (conference abstract or conference paper or conference review or conference proceeding)
21	19 not 20

1 **Database: CINAHL – Ebsco interface**

2 Date last searched: 28/06/2022

#	Query	Limiters/Expanders
S23	S9 AND S22	Limiters - English Language; Exclude MEDLINE records Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S22	S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S21	TX (clear* or deteriorat* or develop* or disappear* or evolv* or exacerbat* or fluctuat* or frequen* or infect* or improv* or occur* or progress* or recover* or recur* or reinfect* or relaps* or remission or reoccur* or resolution or resolv* or restor*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S20	TX ("clinical course" or untreated or "not treated" or "no intervention*" or "without intervention*" or "no treatment*" or "without treatment*" or "no therap*" or "without therap*")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S19	TX (monitor* or observ* or surveillance or (watch* N2 (wait* or see)) or (wait N2 see))	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S18	TX (((natural* or spontaneous* or disease* or effusion* or past or period* or persist* or season* or time*) N5 (histor* or course* or duration* or factor*)) or inciden* or prevalen*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S17	(MH "Monitoring, Physiologic")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S16	(MH "Time") OR (MH "Time Factors")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S15	(MH "Recurrence+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S14	(MH "Recovery+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S13	(MH "Prevalence")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S12	(MH "Periodicity+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S11	(MH "Disease Progression+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S10	(MH "Incidence")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S9	S3 AND S8	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase

#	Query	Limiters/Expanders
S8	S4 OR S5 OR S6 OR S7	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S7	TX ((acoustic or audio or eardrum* or "ear drum*" or electroacoustic or frequenc* or "middle ear" or otoacoustic or sound?) and (admittance or audiomet* or compliance or conductance or emission or immittance or impedance or intermittence or reactance or reflex or resistance or susceptance))	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S6	TX (((acoustic or admittance or audio or eardrum* or "ear drum*" or electroacoustic or frequenc* or impedance or "middle ear" or otoacoustic or tympanic) N3 (evaluat* or measur* or method* or screen* or test*)) or DPOAE? or TEOAE?)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S5	TX (tympanomet* or tympanogra* or reflectomet*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S4	(MH "Acoustic Impedance Tests")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S3	S1 OR S2	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S2	TI ("glue ear " or (("middle ear " or "otitis media ") N2 effusion*) or ome or ((secretory or serous) N2 "otitis media ")) OR AB ("glue ear " or (("middle ear " or "otitis media ") N2 effusion*) or ome or ((secretory or serous) N2 "otitis media "))	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S1	(MH "Otitis Media with Effusion")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase

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

3 Date last searched: 28/06/2022

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
#3	#1 or #2
#4	MeSH descriptor: [Acoustic Impedance Tests] this term only
#5	(tympanomet* or tympanogra* or reflectomet*):ti,ab,kw
#6	(((acoustic or admittance or audio or eardrum* or "ear drum*" or electroacoustic or frequenc* or impedance or "middle ear" or otoacoustic or tympanic) near/3 (evaluat* or measur* or method* or screen* or test*)) or DPOAE? or TEOAE?):ti,ab
#7	((acoustic or audio or eardrum* or "ear drum*" or electroacoustic or frequenc* or "middle ear" or otoacoustic or sound?) and (admittance or audiomet* or compliance or conductance or emission or immittance or impedance or intermittence or reactance or reflex or resistance or susceptance)):ti,ab
#8	{or #4-#7}
#9	#3 and #8
#10	MeSH descriptor: [Incidence] this term only
#11	MeSH descriptor: [Disease Progression] explode all trees
#12	MeSH descriptor: [Periodicity] explode all trees
#13	MeSH descriptor: [Prevalence] this term only
#14	MeSH descriptor: [Recovery of Function] this term only
#15	MeSH descriptor: [Recurrence] explode all trees
#16	MeSH descriptor: [Time] this term only
#17	MeSH descriptor: [Time Factors] this term only
#18	MeSH descriptor: [Monitoring, Physiologic] this term only
#19	MeSH descriptor: [Watchful Waiting] this term only
#20	(((natural* or spontaneous* or disease* or effusion* or past or period* or persist* or season* or time*) near/5 (histor* or course* or duration* or factor*)) or inciden* or prevalen*):ti,ab
#21	(monitor* or observ* or surveillance or (watch* near/2 (wait* or see)) or (wait near/2 see)):ti,ab
#22	("clinical course" or untreated or "not treated" or "no intervention*" or "without intervention*" or "no treatment*" or "without treatment*" or "no therap*" or "without therap*"):ti,ab
#23	(clear* or deteriorat* or develop* or disappear* or evolv* or exacerbat* or fluctuat* or frequen* or infect* or improv* or occur* or progress* or recover* or recur* or reinfect* or relaps* or remission or reoccur* or resolution or resolv* or restor*):ti,ab
#24	{or #10-#23}
#25	#9 and #24
#26	"conference":pt or (clinicaltrials or trialsearch):so
#27	#25 not #26

Database: Epistemonikos

Date last searched: 28/06/2022

#	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:((tympanomet* OR tympanogra* OR reflectomet* OR DPOAE* OR TEOAE* OR acoustic OR admittance OR audio OR audiomet* OR conductance OR eardrum* OR "ear drum*" OR electroacoustic OR emission OR frequenc* OR immittance OR impedance OR intermittence OR "middle ear" OR otoacoustic OR sound* OR reactance OR reflex OR resistance OR susceptance OR tympanic)) OR abstract:((tympanomet* OR tympanogra* OR reflectomet* OR DPOAE* OR TEOAE* OR acoustic OR admittance OR audio OR audiomet* OR conductance OR eardrum* OR "ear drum*" OR electroacoustic OR emission OR frequenc* OR immittance OR impedance OR intermittence OR "middle ear" OR otoacoustic OR sound* OR reactance OR reflex OR resistance OR susceptance OR tympanic)
3	(title:((((natural* OR spontaneous* OR disease* OR effusion* OR past OR period* OR persist* OR season* OR time*) AND (histor* OR course* OR duration* OR factor*)) OR inciden* OR prevalen OR monitor* OR observ* OR surveillance OR (watch* AND (wait* OR see)) OR (wait AND see) OR "clinical course" OR untreated OR "not treated" OR "no intervention" OR "without intervention" OR "no treatment" OR "without treatment" OR "no therapy" OR "without therapy" OR clear* OR deteriorat* OR develop* OR disappear* OR evolv* OR exacerbat* OR fluctuat* OR frequen* OR infect* OR improv* OR occur* OR progress* OR recover* OR recur* OR reinfect* OR relaps* OR remission OR reoccur* OR resolution OR resolv* OR restor*)) OR abstract:((((natural* OR spontaneous* OR disease* OR effusion* OR past OR period* OR persist* OR season* OR time*) AND (histor* OR course* OR duration* OR factor*)) OR inciden* OR prevalen OR monitor* OR observ* OR surveillance OR (watch* AND (wait* OR see)) OR (wait AND see) OR "clinical course" OR untreated OR "not treated" OR "no intervention" OR "without intervention" OR "no treatment" OR "without treatment" OR "no therapy" OR "without therapy" OR clear* OR deteriorat* OR develop* OR disappear* OR evolv* OR exacerbat* OR fluctuat* OR frequen* OR infect* OR improv* OR occur* OR progress* OR recover* OR recur* OR reinfect* OR relaps* OR remission OR reoccur* OR resolution OR resolv* OR restor*)
4	1 AND 2 AND 3

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

Date last searched: 28/06/2022

#	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	(((natural* or spontaneous* or disease* or effusion* or past or period* or persist* or season* or time*) and (histor* or course* or duration* or factor*)) or inciden* or prevalen or monitor* or observ* or surveillance or (watch* and (wait* or see)) or (wait and see) or “clinical course” or untreated or "not treated" or “no intervention” or “no interventions” “without intervention” or “no treatment” or “no treatments” or “without treatment” or “no therapy” or “no therapies” or “without therapy” or “without therapies” or clear* or deteriorat* or develop* or disappear* or evolv* or exacerbat* or fluctuat* or frequen* or infect* or improv* or occur* or progress* or recover* or recur* or reinfect* or relaps* or remission or reoccur* or resolution or resolv* or restor*)
5	3 AND 4 AND (English)[Language]

Database: APA PsycInfo – OVID interface

Date last searched: 28/06/2022

#	Searches
1	middle ear/
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	disease course/ or disease progression/ or exp epidemiology/ or "recovery (disorders)"/ or "relapse (disorders)"/ or exp "remission (disorders)"/ or seasonal variations/ or time/ or monitoring/ or exp treatment effectiveness evaluation/
5	(((natural* or spontaneous* or disease* or effusion* or past or period* or persist* or season* or time*) adj5 (histor* or course* or duration* or factor*)) or inciden* or prevalen*).ti,ab.
6	(monitor* or observ* or surveillance or (watch* adj2 (wait* or see)) or (wait adj2 see)).ti,ab.
7	(clinical course or untreated or "not treated" or no intervention* or without intervention* or no treatment* or without treatment* or no therap* or without therap*).ti,ab.
8	(clear* or deteriorat* or develop* or disappear* or evolv* or exacerbat* or fluctuat* or frequen* or infect* or improv* or occur* or progress* or recover* or recur* or reinfect* or re infect* or relaps* or remission or reoccur* or resolution or resolv* or restor*).ti,ab.
9	or/4-8
10	3 and 9
11	animal.po.
12	(rat or rats or mouse or mice).ti.
13	11 or 12
14	10 not 13

#	Searches
15	limit 14 to english language

1

2 **Economic literature search strategy:**

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

5 **Database: MEDLINE – OVID interface**

6 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	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"

7 **Database: Embase – OVID interface**

8 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.

#	Searches
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.
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

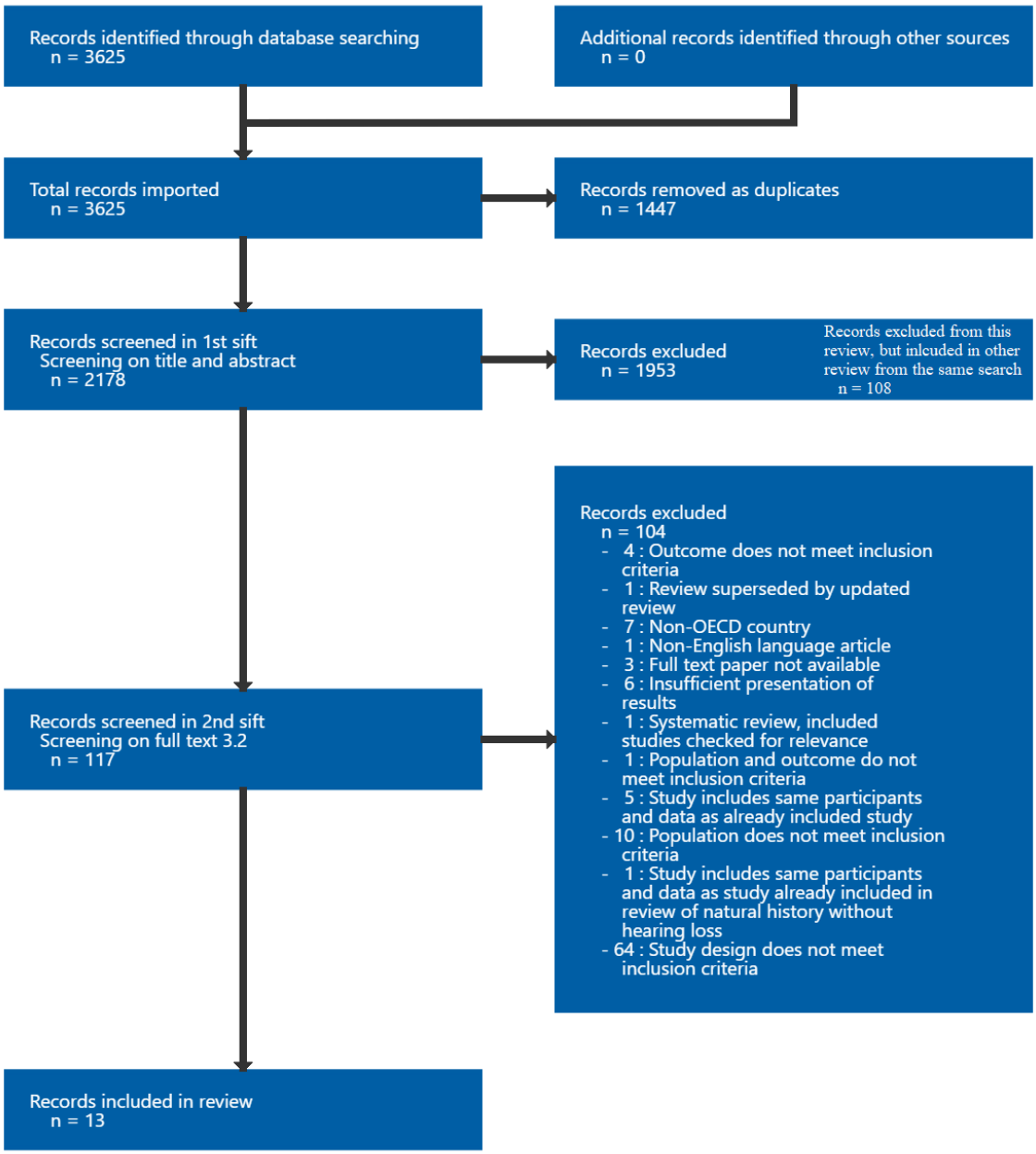
Appendix C Epidemiological evidence study selection

Study selection for: What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years?

Clinical search

This was a combined search to cover both this review and the evidence review on natural history of OME without hearing loss in children under 12 years.

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years?

Table 4: Evidence tables

Alde, 2021

Bibliographic Reference	Alde, M.; Di Berardino, F.; Marchisio, P.; Cantarella, G.; Ambrosetti, U.; Consonni, D.; Zanetti, D.; Effects of COVID-19 Lockdown on Otitis Media With Effusion in Children: Future Therapeutic Implications; Otolaryngology - Head and Neck Surgery (United States); 2021; vol. 165 (no. 5); 710-715

Study details

Country/ies where study was carried out	Italy
Study type	Observational single group (non-comparative) study
Study dates	Retrospective study including the following time periods: June-August 2018, December 2018-February 2019, May-June 2019, June-August 2019, December 2019-February 2020, May-June 2020
Inclusion criteria	Children aged 6 months to 12 years who attended the participating paediatric outpatient audiology clinic (in Milan, Italy) as a first or follow-up visit for hearing, speech, language, or vestibular disorders
Exclusion criteria	Children were excluded if: there was otomicroscopic evidence of tympanosclerosis, cholesteatoma, eardrum perforation, or complete stenosis or atresia of the external auditory canal; there were craniofacial anomalies, cleft palate, or syndromes characterized by anatomic and functional impairment of the eustachian tube; they had received medical treatment or interventions (e.g. antibiotics, steroids, or other medications or interventions) that could have transiently cleared the OME within 2 months before the visit; they showed contraindications to tympanometry, including otitis externa, acute otitis media, otorrhea, recent ear surgery (e.g. myringoplasty, tympanoplasty, and stapedectomy), presence of tympanostomy tubes, and foreign body in the external auditory canal

Patient characteristics	Subgroup A: Children with chronic OME, diagnosed during June–August 2019, reexamined at the clinic during December 2019-February 2020 when OME had not resolved, reevaluated at the clinic May-June 2020. N=30, 23 male and 7 female, mean age 4.7 years. Subgroup B: Children with chronic OME, diagnosed during June-August 2018, reexamined at the clinic during December 2018-February 2019 when OME had not resolved, reevaluated at the clinic May-June 2019. N=29, 18 male and 11 female, mean age 5.0 years. Hearing levels: Not reported
Duration of follow-up	9 to 12 months
Sources of funding	None
Sample size	N=932 (n=59 children with chronic OME: Subgroup A: n=30; Subgroup B: n=29) Subgroup A: N=30 children Subgroup B: N=29 children
Other information	Duration of OME before the study was more than 6 months. The diagnosis of OME (type B tympanogram) confirmed by tympanometry, otoscopy, and the presence of mild to moderate conductive hearing loss. Resolution of OME was defined as change from type B to type A tympanogram.
Outcomes	Resolution of OME causing hearing loss (defined as number of children presenting with a changed tympanogram from type B to type A): 9-12 month follow-up Subgroup A: 28/30 (93.3%) of children showed resolution of OME

	Subgroup B: 6/29 (20.7%) of children showed resolution of OME

1 *OME: otitis media with effusion*

2 **Critical appraisal - Critical appraisal - JBI checklist for prevalence studies**

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	No *(Sample taken from a single tertiary level referral audiologic centre, and characteristics of the population not adequately described)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly)*
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers (particularly for subgroup analyses of interest, i.e., those with OME) were small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Unclear *(Gender and age reported for relevant subgroup (i.e., those with OME). However, further detail not reported, for example, on ethnicity or socioeconomic status)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Diagnoses of OME were based on the presence of all of the following: type B tympanogram (flat); otomicroscopic evidence of middle ear effusion, defined by a yellowish retracted tympanic membrane and by air-fluid level or bubbles in the middle ear; and mild to moderate conductive hearing loss.)*

Section	Question	Answer
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Unclear *(No details reported on those collecting data, e.g., sufficient training)*
Statistical analysis	Was there appropriate statistical analysis?	Yes *(Statistical analysis used was adequate for the design of the study)*
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Unclear *(Initial response rate (for participating in the study) is not reported (retrospective study so no drop-out as such). No reasons for not participating provided, and no comparison of responders versus non-responders)*

1 *JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion*

2 **Cooper, 2022**

Bibliographic Reference	Cooper, Hannah E; Grifa, Ilaria; Bryant, Catriona; Use of an autoinflation device does not lead to a clinically meaningful change in hearing thresholds in children with otitis media with effusion.; Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery; 2022; vol. 47 (no. 1); 160-166

3 **Study details**

Country/ies where study was carried out	UK
Study type	Untreated control arm from comparative observational study "Pragmatic retrospective study with historical controls"
Study dates	Retrospective study including the time period February 2017-February 2019 (control arm (cohort A) identified between February 2017-February 2018 only)

Inclusion criteria	Inclusion criteria for control arm (cohort A): Children seen in the Royal Berkshire Hospital NHS Foundation Trust (RBFT) children's hearing assessment clinic between 23 February 2017 and 22 February 2018 who were aged between 3 and 11 years and had a type B tympanogram with normal ear canal volume in at least one ear
Exclusion criteria	• Patients who did not have follow-up recorded • Patients with no hearing threshold results at first or second appointment • Patients with soundfield results only at first or second appointment • Perforation, occluding wax, ear infection, or grommets at second appointment
Patient characteristics	Cohort A (n=513): Children with a type B tympanogram with normal ear canal volume in at least one ear, who did not receive autoinflation devices: • Sex (male:female): 279:234 • Mean age (SD) at appointment 1 (baseline): 5.3 (1.5) years • Time with OME before inclusion into study: not reported • Number of children with right tympanometry type B: 399/513 (78%) • Number of children with left tympanometry type B: 397/513 (77%) • Right ear hearing thresholds (dB HL; mean (SD)): at 500 Hz: 27.39 (10.26); at 1000 Hz: 25.27 (11.02); at 2000 Hz: 17.09 (11.28); at 4000 Hz: 23.51 (13.44) • Left ear hearing thresholds (dB HL; mean (SD)): at 500 Hz: 26.37 (10.85); at 1000 Hz: 25.17 (11.90); at 2000 Hz: 17.77 (11.86); at 4000 Hz: 24.41 (13.32) Participant characteristics for cohort B (n = 463) were not extracted as these children were in the intervention arm and received autoinflation devices
Duration of follow-up	Between 3 and 6 months. Mean (SD) interval between appointments 1 and 2 for cohort A: 4.54 (1.95) months
Sources of funding	Industry funded
Sample size	N=513 children in cohort A*

	*Data from untreated control arm
Other information	Duration of OME before the study is unknown. All included children received history taking, otoscopy, tympanometry, and pure tone or play audiometry at each appointment. The diagnostic criteria for OME are not explicitly reported, but criteria for inclusion into the study include type B tympanogram, and tympanometric resolution is defined as changing from a type B to type A or C.
Outcomes	Resolution of OME causing hearing loss (3-6 months; number of children)*: Right tympanic resolution: 203/399 (51%) Left tympanic resolution: 194/397 (49%) *Resolution defined as a change from type B tympanogram to a type A or C. Denominators are number of children with type B tympanograms on the relevant side at baseline Reduction in right and left ear hearing thresholds over time (pure-tone average) also available but not extracted as not reported as number with resolution of OME-related hearing loss Data for right and left tympanic resolution was combined in the analysis to provide a single outcome with ears as the unit of analysis.

dB HL: decibel hearing level; OME: otitis media with effusion; RBFT: The Royal Berkshire Hospital NHS Foundation Trust; SD: standard deviation

Critical appraisal - Critical appraisal - JBI checklist for prevalence studies

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	No *(Sample taken from one NHS Foundation Trust, meaning participants would all likely have similar sociodemographic characteristics)*
Participant sampling	Were study participants sampled in an appropriate way?	Not applicable *(All children seen in the RBFT children's hearing assessment clinic between 23 February 2017 and 22 February 2019 were included in cohort A)*

Section	Question	Answer
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers (particularly for subgroup analyses of interest, i.e., those not receiving treatment) were relatively small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Characteristics of the study subjects, including age, gender, hearing loss, and tympanometry type, and setting were described in detail)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Tympanometry used)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Unclear *(No details reported on those collecting data, e.g., sufficient training)*
Statistical analysis	Was there appropriate statistical analysis?	No *(Important information not reported, so that data can only be extracted for number of ears and not for number of children)*
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Unclear *(Number of children lost to follow-up (response rate) not reported and not possible to ascertain from results. Authors only note "There were significantly more missing values for Cohort B at 0.5 and 2 kHz PTA at the second appointment than for Cohort A")*

1 *JBI: The Joanna Briggs Institute Checklist; NHS: National Health Service; PTA: pure tone audiometry; RBFT: The Royal Berkshire Hospital NHS Foundation Trust*
2

1 **Dempster, 1993**

Bibliographic Reference	Dempster, J. H.; Browning, G. G.; Gatehouse, S. G.; A randomized study of the surgical management of children with persistent otitis media with effusion associated with a hearing impairment; The Journal of Laryngology & Otology; 1993; vol. 107 (no. 4); 284-289

2 **Study details**

Country/ies where study was carried out	UK
Study type	Untreated control arm from comparative experimental study
Study dates	August 1986 - February 1989
Inclusion criteria	Children with pure tone air conduction thresholds average over 0.5, 1 and 2 kHz of ≥25 dB HL; an air-bone gap over 0.5, 1 and 2 kHz of ≥15 dB; and type B tympanogram
Exclusion criteria	Children with previous aural surgery or adenoidectomy, symptoms that require surgical intervention (for example, recurrent sore throat), and cleft palate
Patient characteristics	Mean age in years (SD)*: 5.8 (1.3) Sex (male/female)*: 40/32 Degree of hearing loss (mean; SD)**: Air conduction dB HL: 32.4 (7.1); Air bone gap dB: 32.2 (7.0) *Data from whole sample as data from untreated control arm was not reported separately **Data from untreated control arm
Duration of follow-up	12 months

Sources of funding	Not reported
Sample size	Total sample size*: 72 (n=35 from untreated control arm) *Data from whole sample as data from untreated control arm was not reported separately
Other information	Participants had persistent bilateral OME for at least three months before the study. The diagnosis of OME was confirmed by otoscopy and tympanometry (type B tympanogram). Resolution of OME-related hearing loss was defined as pure tone air conduction thresholds average over 0.5, 1 and 2 kHz of <25 dB HL.
Outcomes	Resolution of OME-related hearing loss (number of ears)*: 6 months: 21/35 12 months: 27/35 Resolution of OME causing hearing loss (number of ears)*: 6 months: 7/35 12 months: 11/35 *Data from untreated control arm

1 *dB HL: decibel hearing level; OME: otitis media with effusion; SD: standard deviation*

2 **Critical appraisal - Critical appraisal - JBI checklist for prevalence studies**

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	Unclear *(Unclear that sample frame includes complete registry data)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly (children between the ages of three and a half and 12 were recruited))*

Section	Question	Answer
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers were small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	No *(Age and gender was reported for the whole sample, but not for those with OME from untreated control arm. No further details reported)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Otoscopy and tympanometry used)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Unclear *(No details reported on those collecting data, e.g., sufficient training)*
Statistical analysis	Was there appropriate statistical analysis?	No *(Important information not reported, so that data can only be extracted for number of ears and not for number of children)*
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Unclear *(Initial response rate (for participating in the study) is 98%. 8% (of total study sample) were lost to follow-up or defaulted, and characteristics of those defaulted not reported)*

JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion

Francis, 2018

Bibliographic Reference	Francis, Nick A; Waldron, Cherry-Ann; Cannings-John, Rebecca; Thomas-Jones, Emma; Winfield, Thomas; Shepherd, Victoria; Harris, Debbie; Hood, Kerenza; Fitzsimmons, Deborah; Roberts, Amanda; Powell, Colin Ve; Gal, Micaela; Jones, Sarah; Butler, Christopher C; Oral steroids for hearing loss associated with otitis media with effusion in children aged 2-8 years: the OSTRICH RCT.; Health technology assessment (Winchester, England); 2018; vol. 22 (no. 61); 1-114

1 **Study details**

Country/ies where study was carried out	UK
Study type	Untreated control arm from comparative experimental study
Study dates	March 2014 - April 2016
Inclusion criteria	• Children aged 2-8 years • Symptoms of hearing loss associated with OME for at least 3 months • Diagnosis of bilateral OME confirmed in an ENT or paediatric audiology and AVM clinic on the data of recruitment or during the preceding week • Bilateral hearing loss of >20 dB HL averaged within the frequencies of 0.5, 1, 2 and 4 kHz confirmed by pure-tone audiometry ear-specific insert, visual reinforcement audiometry (VRA) or ear-specific play audiometry, or hearing loss of >25 dB HL averaged within the frequencies of 0.5, 1, 2 and 4 kHz confirmed by soundfield VRA or soundfield performance (or play) audiometry in the better-hearing ear, within the preceding 14 days or on the day of recruitment • First-time participant in the OSTRICH trial • Parent or legal guardian who can understand and provide full informed consent
Exclusion criteria	• Children who participated in another clinical trial of an investigational medicinal product currently or during the last 4 months • Current systemic or ear infection • Cleft palate, Down syndrome, diabetes mellitus, Kartagener syndrome or primary ciliary dyskinesia, renal failure, hypertension or congestive heart failure • Major developmental difficulties (for example, children who were tube fed or had chromosomal abnormalities) • Known existing sensory hearing loss

	• History of oral steroid use in the preceding 4 weeks • History of a live vaccine in the preceding 4 weeks in children aged <3 years, • Condition that increases the risk of adverse events from oral steroids • History of close contact with someone with suspected or known varicella (chickenpox) or active herpes zoster (shingles) during 3 weeks before recruitment in children who had no prior history of varicella infection or immunisation • Already had grommets • Children who were on waiting list for grommet surgery and planning to have it within 5 weeks, and were unwilling to delay it
Patient characteristics	Mean age in years (SD)*: 5.1 (1.6) Sex (male/female)*: 102/85 Previous ventilation tubes surgery*: 19/187 Previous tonsillectomy*: 8/187 Previous adenoidectomy*: 8/187 Antibiotics for an ear infection during the last month*: 13/187 Family history of OME*: 147/187 Atopy*: 56/187 Mean dB HL (SD), from pure tone audiometry in both ears and soundfield average*: 37.83 (6.93) Degree of hearing loss*: Slight (16-25 dB HL): n=8 (4.3%); mild (26-40 dB HL): n=116 (62.0%); moderate (41-55 dB HL): n=63 (33.6%) *Data from untreated control arm
Duration of follow-up	12 months
Sources of funding	Not industry funded

Sample size	Total sample size*: 187 *Data from untreated control arm
Other information	Participants had persistent bilateral OME for <6 months in n=26, 6-<9 months in n=28, 9-<12 months in n=18, and ≥12 months in n=115 children. The diagnosis of OME (type B or C tympanogram) was confirmed by tympanometry. Resolution of OME-related hearing loss (acceptable hearing) was defined as ≤20 dB HL averaged within the frequencies of 0.5, 1, 2 and 4 kHz in at least one ear assessed by pure tone audiometry, ear-specific insert VRA or ear-specific play audiometry, and ≤25 dB HL averaged within the frequencies of 0.5, 1, 2 and 4 kHz assessed by soundfield VRA or soundfield performance/play audiometry.
Outcomes	Resolution of OME-related hearing loss (number of children)*: 5 weeks: 59/180 6 months: 86/166 12 months: 99/162 Resolution of OME causing hearing loss (B or C to A tympanogram in at least one ear) (number of children)*: 5 weeks: 13/178 6 months: 17/147 12 months: 9/144 *Data from untreated control arm

AVM: audiovestibular medicine; dB HL: decibel hearing level; ENT: ear, nose and throat; OME: otitis media with effusion; SD: standard deviation; VRA: visual reinforcement audiometry

Critical appraisal - Critical appraisal - JBI checklist for prevalence studies

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	Yes *(Sample taken from 20 secondary care sites from Wales and England)*

Section	Question	Answer
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly)*
Sample size	Was the sample size adequate?	Yes *(Sample size calculation was reported to determine an adequate sample size)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Characteristics of the study subjects, including age and gender, were reported)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Tympanometry used)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Unclear *(No details reported on those collecting data, e.g., sufficient training)*
Statistical analysis	Was there appropriate statistical analysis?	Yes *(Statistical analysis used was adequate for the design of the study)*
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	No *(12% of participants who were assessed for eligibility declined to participate. 15% (of participants from untreated control arm) were lost to follow-up and non-compliance and had missing outcome data, and their characteristics not reported)*

1 *JBI: The Joanna Briggs Institute Checklist*
2

1 **Ghedia, 2018**

Bibliographic Reference	Ghedia, Reshma; Ahmed, Jahangir; Navaratnam, Annakan; Harcourt, Jonny; No evidence of cholesteatoma in untreated otitis media with effusion in children with primary ciliary dyskinesia.; International journal of pediatric otorhinolaryngology; 2018; vol. 105; 176-180

2 **Study details**

Country/ies where study was carried out	UK
Study type	Untreated control arm from comparative observational study
Study dates	January 2016
Inclusion criteria	Children with a confirmed diagnosis via electron microscopy or genetic analysis of Primary Ciliary Dyskinesia (PCD) and a diagnosis of OME in January 2016
Exclusion criteria	Children with an unconfirmed or presumed PCD diagnosis
Patient characteristics	N=101 children with PCD and OME, n=53 children in group a (watchful waiting): • Sex (male:female): 50:51* • Mean age (SD) at OME diagnosis: 5 years and 6 months • Time with OME before inclusion into study: not reported. Authors note OME diagnosis predated the first PCD clinic in those who had had VTs inserted but no information provided on children in group a • Mean hearing level (dB HL): 25.5 (SD not reported) *Characteristics from whole sample as data was not reported separately for group a
Duration of follow-up	Mean duration of follow up in clinic for group a: 57 months
Sources of funding	Not reported

Sample size	N=53 children (106 ears)* *Data from untreated control arm
Other information	Duration of OME before the study is unknown. OME was diagnosed clinically via otoscopy (dull tympanic membrane) and confirmed with tympanometry (type B curve).
Outcomes	Resolution of OME causing hearing loss (~57 months; number of ears)*: 44/106 *Reported as normal or wax tympanic membrane (i.e., not reported as dull, CSOM or retracted) Reduction in hearing thresholds over time (pure-tone average) also available but not extracted as not reported as number with resolution of OME-related hearing loss

CSOM: chronic suppurative otitis media; dB HL: decibel hearing level; OME: otitis media with effusion; PCD: Primary Ciliary Dyskinesia; SD: standard deviation

Critical appraisal - Critical appraisal - JBI checklist for prevalence studies

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	No *(All children included in study had Primary Ciliary Dyskinesia (PCD) as well as OME)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly)*
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers (particularly for subgroup analyses of interest, i.e., those not receiving treatment) were very small)*

Section	Question	Answer
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	No *(Only age and gender reported (age only reported for whole sample and not those receiving no treatment), though setting described in detail)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Unclear *(Tympanometry used at baseline, unclear if tympanometry was also used to confirm OME at follow-up (results reported according to otoscopy findings))*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Unclear *(All children were reviewed by the senior author of the paper, or the audio-vestibular consultant, but no details reported on training or validity checks)*
Statistical analysis	Was there appropriate statistical analysis?	No *(Important information not reported, so that data can only be extracted for number of ears and not for number of children)*
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Unclear *(Charts for 20/144 (14% of total study sample) could not be found and these children were not included in the study, although data are available for all participants.)*

JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion; PCD: Primary Ciliary Dyskinesia

La Mantia, 2018

Bibliographic Reference	La Mantia, I; Andaloro, C; Effects of salso-bromo-iodine thermal water in children suffering from otitis media with effusion: a randomized controlled pilot study.; La Clinica terapeutica; 2018; vol. 169 (no. 1); e10-e13

1 **Study details**

Country/ies where study was carried out	Italy
Study type	Untreated control arm from comparative experimental study
Study dates	October 2016 – April 2017
Inclusion criteria	• Age 4-12 years • Documented diagnosis of OME (mono- or bilateral), based on clinical history and presence of type B tympanogram, since at least 3 months • Signing by both parents of an informed consent on the aim of the study and its procedure
Exclusion criteria	• Presence of syndromic diseases • Previous adeno-tonsillectomy • Presence of perceptive or mixed hypoacusia • Interfering medications

Patient characteristics	Control group receiving normal 0.9% sodium chloride saline solution (n=40)*:
	• Sex (male:female): 22:18
	• Mean age (SD): 7.6 (2.0) years
	• Time with OME before inclusion into study:
	  ○ ≥3 months: 40/40 (100%)
	• Hearing loss at baseline:
	  ○ Normal hearing (perception of tones up to 25 dB): 9/40 (23%)
	  ○ Mild hypoacusis (hearing loss between 25 and 39 dB): 9/40 (23%)
	  ○ Moderate hypoacusis (hearing loss between 40 and 69 dB): 16/40 (40%)

	○ Severe hypoacusis (hearing loss between 70 and 89 dB): 6/40 (15%) *Data from untreated control arm Patient characteristics for study group (n = 40) were not extracted as these children were in the intervention arm and received treatment
Duration of follow-up	3 months
Sources of funding	None
Sample size	N=40 children (number of ears with OME not reported)* *Data from untreated control arm
Other information	At least 3 months' OME was required for entry into the study. OME was diagnosed based on clinical history and presence of type B tympanogram. Resolution of OME was defined as change from type B to type A tympanogram; improvement was defined as change from type B to type C tympanogram
Outcomes	Resolution of OME-related hearing loss* (3 months; number of children)**: 14/28 (35%) Resolution of OME causing hearing loss*** (3 months; number of children)**: 10/40 (25%) *Measured using tonal audiometry for frequencies ranging between 0.25 and 4 kHz. Resolution defined as perception of tones up to 25 dB **Data from untreated control arm ***Resolution defined as change from type B to type A tympanogram. Disease improvement (change from type B to type C tympanogram) was also reported but not extracted here

1 *OME: otitis media with effusion; SD: standard deviation*

2 **Critical appraisal - Critical appraisal - JBI checklist for prevalence studies**

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	No *(Sample taken from a single ENT Unit, and characteristics of the population not adequately described)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly)*
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers (particularly for subgroup analyses of interest, i.e., those not receiving treatment) were very small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Age and gender of the control group, and the setting were reported in detail)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Tympanometry used)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Unclear *(No details reported on those collecting data, e.g. sufficient training)*
Statistical analysis	Was there appropriate statistical analysis?	Yes *(Statistical analysis used was adequate for the design of the study)*

Section	Question	Answer
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Unclear *(Initial response rate (for participating in the study) is not reported, although data are available for all participants)*

ENT: ear, nose, and throat; JBI: The Joanna Briggs Institute Checklist

Maw, 1993

Bibliographic Reference	Maw, R; Bawden, R; Spontaneous resolution of severe chronic glue ear in children and the effect of adenoidectomy, tonsillectomy, and insertion of ventilation tubes (grommets).; BMJ (Clinical research ed.); 1993; vol. 306 (no. 6880); 756-60

Study details

Country/ies where study was carried out	UK
Study type	Untreated control arm from comparative experimental study
Study dates	April 1983* *They study stated that the first assessment was in April 1983.
Inclusion criteria	Children aged 2-11 years with pronounced subjective hearing loss, bilateral middle ear effusion confirmed by pneumatic otoscopy, non-type A tympanometry, and >25 dB pure audiometric or free field hearing loss in each ear at one or more frequencies
Exclusion criteria	Children who moved out of the area, children with middle ear fluid at the final or last assessment before they were lost to follow up, and children with poor attendance, unreliable/missing preoperative audiometric data, severe obstructive symptoms due to enlarged adenoids or tonsils, and severe problems in the operated ear

Patient characteristics	Age range in years*: 2-9 Mean (SD) hearing threshold at baseline**: 31.86 (8.89) *Data from whole sample as data from untreated control arm was not reported separately **Data from untreated control arm
Duration of follow-up	10 years and 1 month
Sources of funding	Not reported
Sample size	Total sample size*: 77 *Data from untreated control arm
Other information	Participants had persistent bilateral OME confirmed on three preoperative assessments over three months before the study. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry.
Outcomes	Time to resolution of OME causing hearing loss (B to A, C1, or C2 tympanogram that persisted for 12 months; number of children)*: 0 months: Effective number of children at risk: 77; Resolution probability: 0% 18 months: Effective number of children at risk: 75; Resolution probability: 2.7% 19 months: Effective number of children at risk: 73; Resolution probability: 4.9% 23 months: Effective number of children at risk: 72; Resolution probability: 6.3% 27 months: Effective number of children at risk: 71: Resolution probability: 7.7% 30 months: Effective number of children at risk: 70; Resolution probability: 8.6%

	31 months: Effective number of children at risk: 69; Resolution probability: 10.4%
	37 months: Effective number of children at risk: 68; Resolution probability: 11.6%
	39 months: Effective number of children at risk: 67; Resolution probability: 13.2%
	42 months: Effective number of children at risk: 66; Resolution probability: 14.6%
	45 months: Effective number of children at risk: 62; Resolution probability: 19.3%
	47 months: Effective number of children at risk: 61; Resolution probability: 20.3%
	48 months: Effective number of children at risk: 60; Resolution probability: 22.0%
	54 months: Effective number of children at risk: 59; Resolution probability: 23.9%
	60 months: Effective number of children at risk: 57; Resolution probability: 25.3%
	61 months: Effective number of children at risk: 56; Resolution probability: 27.2%
	67 months: Effective number of children at risk: 54; Resolution probability: 29.2%
	69 months: Effective number of children at risk: 48; Resolution probability: 36.8%
	73 months: Effective number of children at risk: 47; Resolution probability: 39.0%
	75 months: Effective number of children at risk: 45; Resolution probability: 40.7%
	78 months: Effective number of children at risk: 44; Resolution probability: 42.6%
	81 months: Effective number of children at risk: 42; Resolution probability: 45.0%
	93 months: Effective number of children at risk: 38; Resolution probability: 50.7%
	101 months: Effective number of children at risk: 35; Resolution probability: 54.4%
	105 months: Effective number of children at risk: 33; Resolution probability: 58.2%

	*Data from untreated control arm. Data extracted from figure; to calculate effective number at risk, constant censoring between the minimum and maximum follow-up points has been assumed due to lack of information about censored events. The data was converted to binary outcome data to allow pooling with other studies as there was not any other time-to-event data included in this review; converted to months for consistency with other studies.

1 *OME: otitis media with effusion*

2 **Critical appraisal - Critical appraisal - JBI checklist for prevalence studies**

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	Unclear *(Unclear that sample frame includes complete registry data)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly)*
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers were small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Age for those with OME was reported)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Tympanometry used)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Unclear *(No details reported on those collecting data, e.g., sufficient training)*

Section	Question	Answer
Statistical analysis	Was there appropriate statistical analysis?	No *(Important information not reported, so that data can only be extracted for number of ears and not for number of children)*
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Unclear *(Initial response rate (for participating in the study) and dropout rate not reported. The Kaplan-Meier survival analysis included ears with incomplete follow-up; however, insufficient information was reported about length of follow-up and censoring.)*

JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion

Maw, 1999

Bibliographic Reference	Maw, R; Wilks, J; Harvey, I; Peters, T J; Golding, J; Early surgery compared with watchful waiting for glue ear and effect on language development in preschool children: a randomised trial.; Lancet (London, England); 1999; vol. 353 (no. 9157); 960-3

Study details

Country/ies where study was carried out	UK
Study type	Untreated control arm from comparative experimental study
Study dates	November 1993 - January 1996
Inclusion criteria	Children who were born between April 1, 1991 and December 31, 1992 and had bilateral OME confirmed by otoscopy and tympanometry, hearing loss, and speech, language, learning or behaviour problems
Exclusion criteria	Children with cleft palate and syndromes (for example, Down's Syndrome, Hunter's, or Hurler's)

Patient characteristics	Mean age in years*: 2.9 (0.9) Sex (male/female)*: 33/45 Current smokers in household*: 35/72 Childhood allergies*: 6/72 Recurrent tonsillitis or sore throat*: 31/72 Mean hearing loss (dB) at 4000 Hz*: Best ear: 34.9; Worst ear: 42.8 *Data from untreated control arm
Duration of follow-up	18 months
Sources of funding	Not industry funded
Sample size	Total sample size*: 90 *Data from untreated control arm
Other information	Duration of OME before the study is unknown. The diagnosis of OME (bilateral type B or C2 tympanograms) was confirmed by tympanometry. 18% of participants from untreated control arm underwent surgery before 9-months assessment, and unclear if they were excluded from final analysis
Outcomes	Resolution of OME causing hearing loss (number of children)*: 9 months: 22/72 *Data from untreated control arm

OME: otitis media with effusion

1 **Critical appraisal - Critical appraisal - JBI checklist for prevalence studies**

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	Unclear *(Unclear that sample frame includes complete registry data)*
Participant sampling	Were study participants sampled in an appropriate way?	Yes *(Complete cohort sampled (children born between April 1, 1991 and December 31, 1992))*
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers were small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Characteristics of the study subjects, including age, and characteristics at birth, were described)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Tympanometry used)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Yes *(Those involved in collecting data were trained in the use of the instruments)*
Statistical analysis	Was there appropriate statistical analysis?	Yes *(Statistical analysis used was adequate for the design of the study)*
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	No *(Initial response rate (for participating in the study) is not reported. 19% (of*

Section	Question	Answer
		participants from untreated control arm) were lost to follow-up, and characteristics of those lost to follow-up not reported)

JBI: The Joanna Briggs Institute Checklist

MRC Multi-centre Otitis Media Study Group 2001

Bibliographic Reference	MRC Multi-centre Otitis Media Study Group; Risk factors for persistence of bilateral otitis media with effusion.; Clinical otolaryngology and allied sciences; 2001; vol. 26 (no. 2); 147-56

Study details

Country/ies where study was carried out	UK
Study type	Untreated control arm from comparative experimental study
Study dates	Not reported
Inclusion criteria	Children with bilateral OME (B or B+C2 tympanogram), bilateral pure-tone threshold of 20 dB HL or poorer associated with an air-bone gap of >10 dB at 1kHz, and no previous ear or adenoid surgery
Exclusion criteria	Not reported
Patient characteristics	Age range in years*: 3.3-6.8 Sex (male/female)*: 318/321 Hearing in the better ear <15 dB HL (ears)*: 12 Hearing in the better ear ≥15 dB HL (ears)*: 629 Hearing in the better ear ≥20 dB HL (ears)*: 597

	Hearing in the better ear ≥25 dB HL (ears)*: 415 *Data from whole sample that were followed up over 12-week watchful waiting period (before randomisation)
Duration of follow-up	12 weeks
Sources of funding	Not reported
Sample size	Total sample size*: 639 *Data from whole sample that were followed up over 12-week watchful waiting period (before randomisation)
Other information	Duration of OME before the study is unknown. The diagnosis of OME (bilateral type B or B and C2 tympanogram) was confirmed by tympanometry. Persistent OME was defined as the presence of bilateral type B or B and C2 tympanograms with >10 dB air-bone gap at 1 kHz, on two separate occasions, 12 weeks apart. To define hearing loss, three cut-offs (≥15 dB, ≥20 dB, and ≥25 dB HL) in air-conduction thresholds in the better ear were used.
Outcomes	Resolution of OME causing hearing loss (hearing loss ≥15 dB HL in the better ear; number of children)*: 12 weeks: 205/617 Resolution of OME causing hearing loss (hearing loss ≥20 dB HL in the better ear; number of children)*: 12 weeks: 255/589 Resolution of OME causing hearing loss (hearing loss ≥25 dB HL in the better ear; number of children)*: 12 weeks: 226/412 *Data from whole sample that were followed up over 12-week watchful waiting period (before randomisation)

1 *OME: otitis media with effusion*

2 **Critical appraisal - Critical appraisal - JBI checklist for prevalence studies**

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	Yes *(Sample taken from 11 otorhinolaryngological trial centres.)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly)*
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers were small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Characteristics of the study participants, including age, gender, and hearing level, were reported)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Tympanometry, audiometry and otoscopy used)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Yes *(Those involved in collecting data were trained in the use of the instruments or they were well-experienced (for example, trained audiology technicians and consultant otolaryngologist))*
Statistical analysis	Was there appropriate statistical analysis?	Yes *(Statistical analysis used was adequate for the design of the study)*

Section	Question	Answer
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Unclear *(Initial response rate (for participating in the study) and dropouts rate not reported.)*

JBI: The Joanna Briggs Institute Checklist

O'Shea, 1980

Bibliographic Reference	O'Shea, J S; Langenbrunner, D J; McCloskey, D E; Pezzullo, J C; Regan, J B; Diagnostic and therapeutic studies in childhood serous otitis media. Results of treatment with an antihistamine-adrenergic combination.; The Annals of otology, rhinology & laryngology. Supplement; 1980; vol. 89 (no. 3pt2); 285-9

Study details

Country/ies where study was carried out	USA
Study type	Untreated control arm from comparative experimental study
Study dates	March 1977 - December 1977
Inclusion criteria	Children diagnosed with the first episode of OME within one month prior to study entry (type B tympanogram), rectal temperature less than 38.4 C or oral temperature less than 37.8 C, no obvious nose or ear deformities, fluid in at least one ear but no bulging tympanic membrane, and air conduction hearing loss of 15 or more decibels but no bone conduction hearing loss of more than 10 dB in at least one ear
Exclusion criteria	Children with type A and type C tympanograms
Patient characteristics	Mean age in years*: 6 Sex (male/female)*: 33/22

	Median decibel loss at low frequencies (not defined)*: 30 *Data from whole sample as data was not reported separately for untreated control arm
Duration of follow-up	3 months
Sources of funding	Not industry funded
Sample size	Total sample size*: 28 *Data from untreated control arm
Other information	Participants were diagnosed with first episode of OME within one month before the study. The diagnosis of OME was confirmed by tympanometry (type B tympanogram), and pneumatic otoscopy.
Outcomes	Resolution of OME-related hearing loss* (number of children)**: 3 months: 14/28 *Resolution was defined as hearing loss less than 20 dB in at least one ear **Data from untreated control arm

1 *OME: otitis media with effusion*

2 **Critical appraisal - Critical appraisal - JBI checklist for prevalence studies**

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	Unclear *(Sample taken from a hospital in a small geographical area)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly)*

Section	Question	Answer
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers were small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Age, and gender for those with OME and the setting were reported in detail)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Tympanometry used)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Unclear *(No details reported on those collecting data, e.g., sufficient training)*
Statistical analysis	Was there appropriate statistical analysis?	Yes *(Statistical analysis used was adequate for the design of the study)*
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Unclear *(Initial response rate (for participating in the study) is not reported. 10% (of total study sample) were lost to follow-up, and characteristics of those lost to follow-up not reported)*

JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion

O'Shea, 1982

Bibliographic Reference	O'Shea, J S; Langenbrunner, D J; McCloskey, D E; Pezzullo, J C; Regan, J B; Childhood serous otitis media: fifteen months' observations of children untreated compared with those receiving an antihistamine-adrenergic combination.; Clinical pediatrics; 1982; vol. 21 (no. 3); 150-3

1 **Study details**

Country/ies where study was carried out	USA
Study type	Untreated control arm from comparative experimental study
Study dates	March 1977 - December 1977
Inclusion criteria	Children diagnosed with the first episode of OME within one month prior to study entry (type B tympanogram), rectal temperature less than 38.4 C or oral temperature less than 37.8 C, no obvious nose or ear deformities, fluid in at least one ear but no bulging tympanic membrane, and air conduction hearing loss of 15 or more decibels but no bone conduction hearing loss of more than 10 dB in at least one ear
Exclusion criteria	Not reported
Patient characteristics	Age range in years*: 3-9 Hearing levels: Not reported *Data from whole sample as data was not reported separately for untreated control arm
Duration of follow-up	1 year
Sources of funding	Not industry funded
Sample size	Total sample size*: 24

	*Data from untreated control arm
Other information	Participants were diagnosed with first episode of OME within one month before the study. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry.
Outcomes	Resolution of OME-related hearing loss* (number of children)**: 1 year: 18/24 Resolution of OME causing hearing loss (B to A tympanogram; number of ears)**: 1 year: 14/48 Resolution of OME causing hearing loss (B to A or C tympanograms; number of ears)**: 1 year: 37/48 *Resolution was defined as hearing loss less than 20 dB in at least one ear **Data from untreated control arm

1 *OME: otitis media with effusion*

2 **Critical appraisal – Critical appraisal – JBI checklist for prevalence studies**

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	Unclear *(Sample taken from a hospital in a small geographical area)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly)*
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers were small)*

Section	Question	Answer
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Characteristics of the study subjects, including age and duration of OME before the study, and the setting were reported in detail)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Tympanometry used)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Unclear *(No details reported on those collecting data, e.g., sufficient training)*
Statistical analysis	Was there appropriate statistical analysis?	Yes *(Statistical analysis used was adequate for the design of the study)*
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Unclear *(Initial response rate (for participating in the study) is not reported. 13% (of total study sample) were lost to follow-up, and characteristics of those lost to follow-up not reported)*

JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion

Renvall, 1982

Bibliographic Reference	Renvall, Ulf; Aniansson, Gunnar; Lidén, Gunnar; Spontaneous improvement in ears with middle ear disease; International Journal of Pediatric Otorhinolaryngology; 1982; vol. 4 (no. 3); 245-250

Study details

Country/ies where study was carried out	Sweden
Study type	Observational single group (non-comparative) study
Study dates	1980
Inclusion criteria	4-year-olds screened at 'healthy-baby-clinics' during 1980, who failed screening (hearing loss >20dBHL on pure-tone audiometry). Ears which were found to have middle ear pressure ≤-150mm H2O on tympanometry/ otomicroscopy were included
Exclusion criteria	Exclusion criteria for children not reported. Ears with middle ear pressures >-150mm H2O, no tympanic membrane retraction and hearing ≤20 dBHL were excluded. Ears with significant bilateral hearing loss which received immediate treatment were excluded from analyses

Patient characteristics	N=248 children with hearing loss:
	• Sex (male:female): not reported
	• Age in years: all participants were 4 years old
	• Time with OME before inclusion into study: not reported
	• Middle ear pressure (tympanogram type) at baseline (number of ears):
	  ○ Normal (>-150mm H2O): 273/496 ears (55%; these ears were excluded)
	  ○ -150 to -400mm H2O: 165/496 ears (33%)*
	  ○ Flat (<-400mm H2O): 58/496 ears (12%)**
	• Hearing levels: Not reported
	
	*61/165 ears were later excluded due to loss to follow-up or having received treatment
	
	**18/58 ears were later excluded due to loss to follow-up or having received treatment
	
	Please note authors do not state the number of children excluded due to loss to follow-up, receiving treatment, or both ears having normal middle ear pressure. Only number of ears excluded is reported

Duration of follow-up	6 and 12 weeks
Sources of funding	Not reported
Sample size	N=248 children (496 ears) with hearing loss. After ear exclusions for otomicroscopically normal tympanic membranes and normal pure tone audiometry, 223 ears were included. The number of children after these exclusions is not reported
Other information	Authors note that children who exhibited a unilateral hearing loss of ≥20 dBHL and/or a retraction pocket and/or middle ear pressure <-150mm H2O did not get any treatment for the duration of the study, however some ears with significant bilateral hearing loss did receive immediate treatment. These ears were excluded from analyses Duration of OME prior to entry into the study not reported. Children failed hearing screening and were then tested using otomicroscopy, tympanogram, and pure-tone audiometry for entry into the study 3-8 weeks later, but it is unclear if participants had OME for those 3-8 weeks Criteria for OME diagnosis not explicitly reported, but all included children were assessed with otomicroscopy, tympanogram, and pure-tone audiometry at baseline, and ears with middle ear pressure ≤-150mm H2O on tympanometry/ otomicroscopy were included in the study. Tympanometry was not used at 6 week follow-up
Outcomes	Resolution of OME causing hearing loss* (number of ears): 6 weeks: 56/144 (10/40 (25%) ears with flat tympanograms at baseline) 12 weeks: 30/58 (6/30 (20%) ears with flat tympanograms at baseline)** *Resolution not explicitly defined by authors, but reported here as change from flat tympanogram (middle ear pressure <-400mm H2O) or middle ear pressure -150 to -400mm H2O, to normal middle ear pressure (>-150m H2O); assessed using otomicroscopy at 6 weeks, and otomicroscopy and tympanometry at 12 weeks. Improvement in middle ear pressure (defined as any positive change to middle ear pressure but did not reach normal middle ear pressure) also reported but not extracted **Results at 12 weeks only presented in study for those ears which did not have normal middle ear pressure at 6 weeks. It is unclear if the ears with normal middle ear pressure at 6 weeks were followed up at 12 weeks

dB HL: decibel hearing level; OME: otitis media with effusion; SD: standard deviation

Critical appraisal - Critical appraisal - JBI checklist for prevalence studies

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	Unclear *(Sample taken from a small geographical area (Goteborg))*
Participant sampling	Were study participants sampled in an appropriate way?	Not applicable *(All children who failed pure-tone screening were initially included in the study)*
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers were small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	No *(Setting described, however for patient characteristics: all participants were 4 years old, but no further details reported)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Tympanometry and otomicroscopy used at baseline and 12-week follow-up, otomicroscopy used at 6 week follow-up)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	No *(Tympanometry only used at baseline and 12-week follow-up, not at 6-week follow-up. Reasoning for this not given. No details reported on those collecting data, e.g., sufficient training)*
Statistical analysis	Was there appropriate statistical analysis?	No *(Important information not reported, so that data can only be extracted for number of ears and not for number of children. Children with normal middle ear pressure at 6 weeks not followed up at 12 weeks)*

Section	Question	Answer
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	No *(Initial response rate (for participating in the study) is not reported. 79/223 ears (35% of total study sample after exclusions for normal middle ear pressure at baseline) were lost to follow-up or received treatment and were therefore excluded)*

JBI: The Joanna Briggs Institute Checklist

van Balen, 2000

Bibliographic Reference	van Balen, F A; de Melker, R A; Persistent otitis media with effusion: can it be predicted? A family practice follow-up study in children aged 6 months to 6 years.; The Journal of family practice; 2000; vol. 49 (no. 7); 605-11

Study details

Country/ies where study was carried out	Netherlands
Study type	Observational single group (non-comparative) study
Study dates	December 1992 - August 1993
Inclusion criteria	Children with bilateral OME confirmed by tympanometry and presenting complaints that are frequently related to OME, including subjective or objective hearing loss, speech and language problems, snoring and mouth breathing, history of recurrent upper respiratory tract infection, history of acute otitis media in the preceding 6 weeks, and family history of otitis media
Exclusion criteria	Children with history of antimicrobial therapy in the preceding 6 weeks, immunodeficiency, craniofacial anomalies, Down's Syndrome, or cystic fibrosis
Patient characteristics	Age range: 6 months - 6 years

	Sex (male/female): 230/203 Hearing loss: 316/433 Upper respiratory tract infection at initial visit: 196/433 Snoring/mouth breathing: 96/433 Acute otitis media in the preceding 6 weeks: 45/433 Family history of OME: 57/433
Duration of follow-up	3 months
Sources of funding	Not reported
Sample size	Total sample size: 433
Other information	Duration of OME before the study is unknown. The diagnosis of OME (B or C2 types) was confirmed by tympanometry.
Outcomes	Resolution of OME causing hearing loss (B or C2 to A or C1 tympanogram; number of children): 3 months: 93/397

1 *OME: otitis media with effusion*

2 **Critical appraisal - Critical appraisal - JBI checklist for prevalence studies**

Section	Question	Answer
Sample frame	Was the sample frame appropriate to address the target population?	Unclear *(Sample was selected by 57 family physicians, no further information (for example, geographical area) provided)*

Section	Question	Answer
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly)*
Sample size	Was the sample size adequate?	No *(No sample size calculation reported, and numbers were relatively small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Characteristics of the study subjects, including age, gender, hearing loss, and history of respiratory tract infection, and setting were described in detail)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	Unclear *(Details not reported for responders versus non-responders so unclear if there was sufficient coverage of the identified sample)*
Identification of condition	Were valid methods used for the identification of the condition?	Yes *(Tympanometry used)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Unclear *(No details reported on those collecting data, e.g., sufficient training)*
Statistical analysis	Was there appropriate statistical analysis?	Yes *(Statistical analysis used was adequate for the design of the study)*
Response rate	Was the response rate adequate, and if not, was the low response rate managed appropriately?	Unclear *(Initial response rate (for participating in the study) is not reported. 3% (of total study sample) were lost to follow-up, and characteristics of those lost to follow-up did not differ significantly from the remaining participants)*

1 *JBI: The Joanna Briggs Institute Checklist*

2

Appendix E Forest plots

Forest plots for review question: What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation 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 is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years?

Table 5: Evidence profile for resolution of OME-related hearing loss in children with OME of <1 month duration before follow-up

Quality assessment							No of patients	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
Resolution of OME-related hearing loss (defined as change in hearing threshold from above to below 20dB) at 3 months; unit of analysis=child											
1 (O'Shea 1980)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	14/28 (50.0%)	0.50 (0.32 to 0.68)	500 per 1000 (from 320 per 1000 to 680 per 1000)	VERY LOW	IMPORTANT
Resolution of OME-related hearing loss (defined as change in hearing threshold from above to below 20dB) at 12 months; unit of analysis=child											
1 (O'Shea 1982)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18/24 (75.0%)	0.75 (0.54 to 0.88)	750 per 1000 (from 540 per 1000 to 880 per 1000)	VERY LOW	IMPORTANT

CI: confidence interval; JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion
[1]Very serious risk of bias in the evidence contributing to the outcomes as per JBI
[2]<150 events

Table 6: Evidence profile for resolution of OME-related hearing loss in children with OME of >3 months duration before follow-up

Quality assessment							No of patients	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
Resolution of OME-related hearing loss (defined as change in hearing threshold from above to below 25dB) at 3 months; unit of analysis=child											

1 (La Mantia 2018)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	14/28 (50.0%)	0.50 (0.32 to 0.68)	500 per 1000 (from 320 per 1000 to 680 per 1000)	VERY LOW	IMPORTANT
Resolution of OME-related hearing loss (defined as change in hearing threshold from above to below 25dB) at 6 months; unit of analysis=ear											
1 (Dempster 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	21/35 (60.0%)	0.60 (0.43 to 0.75)	600 per 1000 (from 430 per 1000 to 750 per 1000)	VERY LOW	IMPORTANT
Resolution of OME-related hearing loss (defined as change in hearing threshold from above to below 25dB) at 12 months; unit of analysis=ear											
1 (Dempster 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	27/35 (77.1%)	0.77 (0.61 to 0.88)	770 per 1000 (from 610 per 1000 to 880 per 1000)	VERY LOW	IMPORTANT

CI: confidence interval; JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion
[1]Very serious risk of bias in the evidence contributing to the outcomes as per JBI
[2]<150 events

Table 7: Evidence profile for resolution of OME-related hearing loss in children with OME of >12 months duration before follow-up

Quality assessment							No of patients	Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**		**Relative (95% CI)**	**Absolute**		
Resolution of OME-related hearing loss (defined as change in hearing threshold from above to below 20-25dB) at 1 month; unit of analysis=child											
1 (Francis 2018)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	59/180 (32.8%)	0.33 (0.26 to 0.40)	330 per 1000 (from 260 per 1000 to 400 per 1000)	VERY LOW	IMPORTANT
Resolution of OME-related hearing loss (defined as change in hearing threshold from above to below 20-25dB) at 6 months; unit of analysis=child											

1 (Francis 2018)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	86/166 (51.8%)	0.52 (0.44 to 0.59)	520 per 1000 (from 440 per 1000 to 590 per 1000)	VERY LOW	IMPORTANT
Resolution of OME-related hearing loss (defined as change in hearing threshold from above to below 20-25dB) at 12 months; unit of analysis=child											
1 (Francis 2018)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	99/162 (61.1%)	0.61 (0.53 to 0.68)	610 per 1000 (from 530 per 1000 to 680 per 1000)	VERY LOW	IMPORTANT

CI: confidence interval; JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion
[1]Very serious risk of bias in the evidence contributing to the outcomes as per JBI
[2]<150 events

Table 8: Evidence profile for resolution of OME of <1 month duration before follow-up

Quality assessment							No of patients	Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**		**Relative (95% CI)**	**Absolute**		
Resolution of OME (defined as change from type B tympanogram to type A tympanogram) at 12 months; unit of analysis=ear											
1 (O'Shea 1982)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	14/48 (29.2%)	0.29 (0.18 to 0.43)	290 per 1000 (from 180 per 1000 to 430 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A or C tympanogram) at 12 months; unit of analysis=ear											
1 (O'Shea 1982)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	37/48 (77.1%)	0.77 (0.63 to 0.87)	770 per 1000 (from 630 per 1000 to 870 per 1000)	VERY LOW	IMPORTANT

CI: confidence interval; JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion
[1]Very serious risk of bias in the evidence contributing to the outcomes as per JBI
[2]<150 events

1 **Table 9: Evidence profile for resolution of OME of >3 months duration before follow-up**

Quality assessment							No of patients	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
Resolution of OME (defined as change from type B tympanogram to A tympanogram) at 3 months; unit of analysis=child											
1 (La Mantia 2018)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/40 (25.0%)	0.25 (0.14 to 0.41)	250 per 1000 (from 140 per 1000 to 410 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 6 months; unit of analysis=ear											
1 (Dempster 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/35 (20.0%)	0.20 (0.10 to 0.36)	200 per 1000 (from 100 per 1000 to 360 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 12 months; unit of analysis=ear											
1 (Dempster 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	11/35 (31.4%)	0.31 (0.18 to 0.48)	310 per 1000 (from 180 per 1000 to 480 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 18 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/77 (2.6%)	0.03 (0.01 to 0.10)	30 per 1000 (from 10 per 1000 to 100 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 19 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/77 (5.2%)	0.05 (0.02 to 0.13)	50 per 1000 (from 20 per 1000 to 130 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 23 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/77 (6.5%)	0.06 (0.03 to 0.15)	60 per 1000 (from 30 per 1000 to 150 per 1000)	VERY LOW	IMPORTANT

Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 27 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/77 (7.8%)	0.08 (0.04 to 0.16)	80 per 1000 (from 40 per 1000 to 160 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 30 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/77 (9.1%)	0.09 (0.04 to 0.18)	90 per 1000 (from 40 per 1000 to 180 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 31 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/77 (10.4%)	0.10 (0.05 to 0.19)	100 per 1000 (from 50 per 1000 to 190 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 37 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/77 (11.7%)	0.12 (0.06 to 0.21)	120 per 1000 (from 60 per 1000 to 210 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 39 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	10/77 (13.0%)	0.13 (0.07 to 0.22)	130 per 1000 (from 70 per 1000 to 220 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 42 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	11/77 (14.3%)	0.14 (0.08 to 0.24)	140 per 1000 (from 80 per 1000 to 240 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 45 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	15/77 (19.5%)	0.19 (0.12 to 0.30)	190 per 1000 (from 120 per 1000 to 300 per 1000)	VERY LOW	IMPORTANT

Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 47 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	16/77 (20.8%)	0.21 (0.13 to 0.31)	210 per 1000 (from 130 per 1000 to 310 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 48 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	17/77 (22.1%)	0.22 (0.14 to 0.33)	220 per 1000 (from 140 per 1000 to 330 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 54 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18/77 (23.4%)	0.23 (0.15 to 0.34)	230 per 1000 (from 150 per 1000 to 340 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 60 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19/77 (24.5%)	0.25 (0.16 to 0.35)	250 per 1000 (from 160 per 1000 to 350 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 61 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	21/77 (27.3%)	0.27 (0.19 to 0.38)	270 per 1000 (from 190 per 1000 to 380 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 67 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	23/77 (29.9%)	0.30 (0.21 to 0.41)	300 per 1000 (from 210 per 1000 to 410 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 69 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	28/77 (36.4%)	0.36 (0.26 to 0.48)	360 per 1000 (from 260 per 1000 to 480 per 1000)	VERY LOW	IMPORTANT

Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 73 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	30/77 (39.0%)	0.39 (0.29 to 0.50)	390 per 1000 (from 290 per 1000 to 500 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 75 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	31/77 (40.3%)	0.40 (0.30 to 0.52)	400 per 1000 (from 300 per 1000 to 520 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 78 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	33/77 (42.9%)	0.43 (0.32 to 0.54)	430 per 1000 (from 320 per 1000 to 540 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 81 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	35/77 (45.5%)	0.45 (0.35 to 0.57)	450 per 1000 (from 350 per 1000 to 570 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 93 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	39/77 (50.6%)	0.51 (0.40 to 0.62)	510 per 1000 (from 400 per 1000 to 620 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 101 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	42/77 (54.5%)	0.55 (0.43 to 0.65)	550 per 1000 (from 430 per 1000 to 650 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram that persisted for 12 months) at 105 months; unit of analysis=child											
1 (Maw 1993)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	45/77 (58.4%)	0.58 (0.47 to 0.69)	580 per 1000 (from 470 per 1000 to 690 per 1000)	VERY LOW	IMPORTANT

1 *CI: confidence interval; JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion*

[1]*Very serious risk of bias in the evidence contributing to the outcomes as per JBI*
[2]*<150 events*

Table 10: Evidence profile for resolution of OME of >6 months duration before follow-up

Quality assessment							No of patients	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
Resolution of OME (defined as change from type B tympanogram to type A tympanogram) at 12 months; unit of analysis=child											
2 (Alde 2021a; Alde 2021b)*	observational	very serious[1]	very serious inconsistency[2]	no serious indirectness	very serious[3]	none	34/59 (57.6%)	Alde 2021a: 0.93 (0.77 to 0.98) Alde 2021b: 0.21 (0.10 to 0.39)	210 to 930 per 1000 (from 100 per 1000 to 980 per 1000)	VERY LOW	IMPORTANT

CI: confidence interval; JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion
**Data reported in one paper, but two separate cohorts included*
[1]*Very serious risk of bias in the evidence contributing to the outcomes as per JBI*
[2]*Very serious heterogeneity unexplained by subgroup analysis*
[3]*<150 events*

Table 11: Evidence profile for resolution of OME of >12 months duration before follow-up

Quality assessment							No of patients	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		Relative (95% CI)	Absolute		
Resolution of OME (defined as change from type B or C tympanogram to type A tympanogram) at 1 month; unit of analysis=child											
1 (Francis 2018)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	13/178 (7.3%)	0.07 (0.04 to 0.12)	70 per 1000 (from 40 per 1000 to 120 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B or C tympanogram to type A tympanogram) at 6 months; unit of analysis=child											
1 (Francis 2018)	untreated control arm from	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	17/147 (11.6%)	0.12 (0.07 to 0.18)	120 per 1000 (from 70 per 1000 to 180 per 1000)	VERY LOW	IMPORTANT

	comparative experimental study										
Resolution of OME (defined as change from type B or C tympanogram to type A tympanogram) at 12 months; unit of analysis=child											
1 (Francis 2018)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/144 (6.3%)	0.06 (0.03 to 0.12)	60 per 1000 (from 30 per 1000 to 120 per 1000)	VERY LOW	IMPORTANT

CI: confidence interval; JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion
[1]Very serious risk of bias in the evidence contributing to the outcomes as per JBI
[2]<150 events

Table 12: Evidence profile for resolution of OME of unknown duration before follow-up

Quality assessment							**No of patients**	**Effect**		**Quality**	**Importance**
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**		**Relative (95% CI)**	**Absolute**		
Resolution of OME (undefined) at 1.5 months; unit of analysis=ear											
1 (Renvall 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	56/144 (38.9%)	0.39 (0.31 to 0.47)	390 per 1000 (from 310 per 1000 to 470 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B or C2 tympanogram to type A or C1 tympanogram) at 3 months; unit of analysis=children											
1 (Van Balen 2000)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	93/397 (23.4%)	0.23 (0.20 to 0.28)	230 per 1000 (from 200 per 1000 to 280 per 1000)	VERY LOW	IMPORTANT
Resolution of OME in children with hearing loss ≥15 dB in better ear (defined as change from B/B or B/C2 tympanogram and >10dB air-bone gap at 1kHz to not meeting this criteria) at 3 months; unit of analysis=child											
1 (MRC Multi-centre Otitis Media Study Group 2001)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	205/617 (33.2%)	0.33 (0.30 to 0.37)	330 per 1000 (from 300 per 1000 to 370 per 1000)	VERY LOW	IMPORTANT
Resolution of OME in children with hearing loss ≥20 dB in better ear (defined as change from B/B or B/C2 tympanogram and >10dB air-bone gap at 1kHz to not meeting this criteria) at 3 months; unit of analysis=child											

1 (MRC Multi-centre Otitis Media Study Group 2001)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	255/589 (43.3%)	0.43 (0.39 to 0.47)	430 per 1000 (from 390 per 1000 to 470 per 1000)	VERY LOW	IMPORTANT
Resolution of OME in children with hearing loss ≥25 dB in better ear (defined as change from B/B or B/C2 tympanogram and >10dB air-bone gap at 1kHz to not meeting this criteria) at 3 months; unit of analysis=child											
1 (MRC Multi-centre Otitis Media Study Group 2001)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	226/412 (54.9%)	0.55 (0.50 to 0.60)	550 per 1000 (from 500 per 1000 to 600 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 3 months; unit of analysis=ear											
1 (Renvall 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	30/58 (51.7%)	0.52 (0.39 to 0.64)	520 per 1000 (from 390 per 1000 to 640 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 6 months; unit of analysis=ear											
1 (Cooper 2022)	observational	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	397/796 (49.9%)	0.50 (0.46 to 0.53)	500 per 1000 (from 460 per 1000 to 530 per 1000)	LOW	IMPORTANT
Resolution of OME (defined as change from type B or C2 tympanogram to type A or C1 tympanogram) at 9 months; unit of analysis=child											
1 (Maw 1999)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	22/72 (30.6%)	0.31 (0.21 to 0.42)	310 per 1000 (from 210 per 1000 to 420 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 57 months; unit of analysis=ear											
1 (Ghedia 2018)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	44/106 (41.5%)	0.42 (0.33 to 0.51)	420 per 1000 (from 330 per 1000 to 510 per 1000)	VERY LOW	IMPORTANT

CI: confidence interval; JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion

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

[2]<150 events

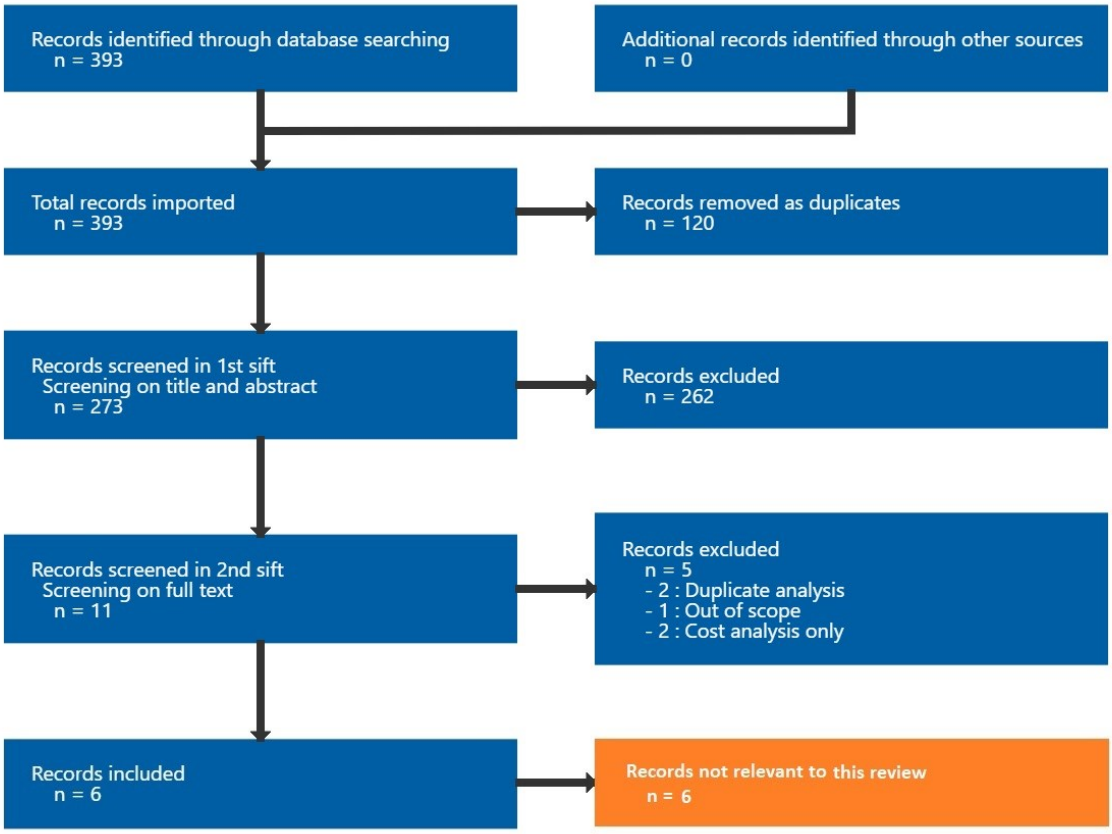
[2]<300-≥150 events

Appendix G Economic evidence study selection

Study selection for: What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation 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 flow chart



Appendix H Economic evidence tables

Economic evidence tables for review question: What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation 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 is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years?

Excluded epidemiological studies

The excluded studies table only lists the studies that were considered and then excluded at the full-text stage for this review (N=104) and not studies (N=108) 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 13: Excluded studies and reasons for their exclusion

Study	Code [Reason]
Aboueisha, Mohamed A, Attia, Abdallah S, McCoul, Edward D et al. (2022) Efficacy and safety of balloon dilation of eustachian tube in children: Systematic review and meta-analysis. International journal of pediatric otorhinolaryngology 154: 111048	- Study design does not meet inclusion criteria *The study investigates the efficacy and safety of balloon dilation of eustachian tube*
Akdogan, Ozgur and Ozkan, Soner (2006) Otoacoustic emissions in children with otitis media with effusion. International journal of pediatric otorhinolaryngology 70(11): 1941-4	- Study design does not meet inclusion criteria *Participants received treatments for OM, so it is not reporting on natural history*
Alper, Cuneyt M, Losee, Joseph E, Seroky, James T et al. (2016) Resolution of Otitis Media With Effusion in Children With Cleft Palate Followed Through Five Years of Age. The Cleft palate-craniofacial journal : official publication of the American Cleft Palate-Craniofacial Association 53(5): 607-13	- Study design does not meet inclusion criteria *All participants had ventilation tubes inserted at the same time as cleft lip or palate repair, so is not reporting on natural history*
Andreasson, L, Bylander, A, Ivarsson, A et al. (1983) Treatment with sulfur hexafluoride in children with serous otitis media. An alternative to tubulation. Archives of otolaryngology (Chicago, Ill. : 1960) 109(6): 358-9	- Study design does not meet inclusion criteria *The study investigates the effectiveness of sulfur hexafluoride during myringotomy*
Anonymous (2001) Pars tensa and pars flaccida retractions in persistent otitis media with effusion. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 22(3): 291-8	- Outcome does not meet inclusion criteria *Reports on the natural history of pars tensa and pars flaccida retractions, rather than OME itself*
Arick, D S and Silman, S (2000) Treatment of otitis media with effusion based on politzerization with an automated device. Ear, nose, & throat journal 79(4): 290-passim	- Study design does not meet inclusion criteria *Follow-up <3 months*
Arick, Daniel S and Silman, Shlomo (2005) Nonsurgical home treatment of middle ear	- Study design does not meet inclusion criteria *Follow-up <3 months*

Study	Code [Reason]
effusion and associated hearing loss in children. Part I: clinical trial. Ear, nose, & throat journal 84(9): 567-passim	
Aslanyan, A.R., Harutunyan, A.G., Shukuryan, A.K. et al. (2018) Correlation of hearing and vestibular disorders in patients with chronic secretory otitis media. New Armenian Medical Journal 12(4): 53-57	- Non-OECD country *Armenia*
Augustsson, I; Nilson, C; Engstrand, I (1990) The preventive value of audiometric screening of preschool and young school-children. International journal of pediatric otorhinolaryngology 20(1): 51-62	- Study design does not meet inclusion criteria *Duration of follow-up <3 months*
Aziz Ashoor, A. and Fuer, F. (2013) Management of otitis media with effusion. Bahrain Medical Bulletin 35(3)	- Non-OECD country *Saudi Arabia*
Bandyopadhyay, T and Raman, E V (2018) Otitis Media with Effusion (OME) in Urban Pediatric Population in a Tertiary Care Centre: A Clinical Study. Indian journal of otolaryngology and head and neck surgery : official publication of the Association of Otolaryngologists of India 70(2): 267-272	- Study design does not meet inclusion criteria *Children were either managed surgically, medically or watchful waiting, but results combined for medical intervention and watchful waiting groups, so cannot extract any data for natural history*
Banigo, A, Hunt, A, Rourke, T et al. (2016) Does the EarPopper(R) device improve hearing outcomes in children with persistent otitis media with effusion? A randomised single-blinded controlled trial. Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery 41(1): 59-65	- Insufficient presentation of results *No usable data on outcomes of interest*
Beigh, Z., Lattoo, M., Yousuf, A. et al. (2013) Topical nasal steroids for hearing loss associated with otitis media with effusion in children. Indian Journal of Otology 19(3): 132-135	- Non-OECD country *India*
Berkman, ND, Wallace, IF, Steiner, MJ et al. (2013) Otitis media with effusion: comparative effectiveness of treatments.	- Study design does not meet inclusion criteria *Includes studies with treated control groups. Included studies checked for relevance.*
Berman, S; Grose, K; Zerbe, G O (1987) Medical management of chronic middle-ear effusion. Results of a clinical trial of prednisone combined with sulfamethoxazole and trimethoprim. American journal of diseases of children (1960) 141(6): 690-4	- Study design does not meet inclusion criteria *Children received medical treatments for OME, so does not report natural history*
Bhargava, Rahul and Chakravarti, Arunabha (2014) A double-blind randomized placebo-controlled trial of topical intranasal mometasone furoate nasal spray in children of adenoidal	- Non-OECD country *India*

Study	Code [Reason]
hypertrophy with otitis media with effusion. American journal of otolaryngology 35(6): 766-70	
Bidarian-Moniri, Armin; Ramos, Maria-Joao; Ejnell, Hasse (2014) Autoinflation for treatment of persistent otitis media with effusion in children: a cross-over study with a 12-month follow-up. International journal of pediatric otorhinolaryngology 78(8): 1298-305	- Study design does not meet inclusion criteria *Follow-up <3 months*
Bidarian-Moniri, Armin, Ramos, Maria-Joao, Goncalves, Ilidio et al. (2013) A new device for treatment of persistent otitis media with effusion. International journal of pediatric otorhinolaryngology 77(12): 2063-70	- Study design does not meet inclusion criteria *Follow-up <3 months.*
Bonci, M and Bozzi, A (1994) Mucoregulatory therapy in secreting disease of the middle ear. Minerva medica 85(3): 83-87	- Full text paper not available
Brooks, D N (1980) Possible long-term consequences of middle ear effusion. The Annals of otology, rhinology & laryngology. Supplement 89(3pt2): 246-8	- Study design does not meet inclusion criteria *The study investigates long-term consequences of middle ear effusion*
Browning, George G, Rovers, Maroeska M, Williamson, Ian et al. (2010) Grommets (ventilation tubes) for hearing loss associated with otitis media with effusion in children. The Cochrane database of systematic reviews: cd001801	- Study design does not meet inclusion criteria *Includes studies with treated control groups. Included studies not checked for relevance as this review has been superseded by ongoing update (which has been checked)*
Cantekin, E I; McGuire, T W; Griffith, T L (1991) Antimicrobial therapy for otitis media with effusion ('secretory' otitis media). JAMA 266(23): 3309-17	- Study design does not meet inclusion criteria *Follow-up period <3 months*
Casselbrant, M L, Brostoff, L M, Cantekin, E I et al. (1985) Otitis media with effusion in preschool children. The Laryngoscope 95(4): 428-36	- Population does not meet inclusion criteria *No hearing loss reported. Included in the review of natural history of OME without hearing loss*
Commins, D.J., Koay, B.C., Bates, G.J. et al. (2000) The role of Mucodyne in reducing the need for surgery in patients with persistent otitis media with effusion. Clinical Otolaryngology and Allied Sciences 25(4): 274-279	- Study design does not meet inclusion criteria *30% and 12% of participants had previous grommet insertion and adenoidectomy, respectively, so does not report on natural history*
Dewan, Karuna and Lieu, Judith (2018) A Clinical Trial of Proton Pump Inhibitors to Treat Children with Chronic Otitis Media with Effusion. The journal of international advanced otology 14(2): 245-249	- Outcome does not meet inclusion criteria *Reports hearing thresholds and requirement for tympanostomy tubes only.*
Edwards, Lowri, Cannings-John, Rebecca, Butler, Christopher et al. (2021) Identifying factors associated with spontaneous restoration of hearing in children with otitis media with	- Study design does not meet inclusion criteria *Participants in control group and intervention group (steroid therapy) were analysed together*

Study	Code [Reason]
effusion. Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery 46(1): 243-248	*and data not presented separately for control group, so does not report natural history*
Fiellau-Nikolajsen, M (1980) Tympanometry in three-year-old children. Prevalence and spontaneous course of MEE. The Annals of otology, rhinology & laryngology. Supplement 89(3pt2): 223-7	- Population does not meet inclusion criteria *Participants without OME-related hearing loss*
Fiellau-Nikolajsen, M (1981) Tympanometry in three-year-old children. The 3-year follow-up of a cohort study. ORL; journal for oto-rhino-laryngology and its related specialties 43(2): 89-103	- Population does not meet inclusion criteria *Participants without OME-related hearing loss*
Francis, NA, Cannings-John, R, Waldron, CA et al. (2018) Oral steroids for resolution of otitis media with effusion in children (OSTRICH): a double-blinded, placebo-controlled randomised trial. Lancet (London, England) 392(10147): 557-568	- Study includes same participants and data as already included study *Francis 2018*
Giebink, GS, Batalden, PB, Le, CT et al. (1990) A controlled trial comparing three treatments for chronic otitis media with effusion. The Pediatric infectious disease journal 9(1): 33-40	- Study design does not meet inclusion criteria *18% of participants had tympanometry tubes, and data not presented separately for those without tympanostomy tubes, so does not report natural history*
Goodey, R.J. and Bowers, M. (1975) Antibiotic treatment of secretory otitis media assessed by impedence audiometry. New Zealand Medical Journal 82(548): 187-188	- Study design does not meet inclusion criteria *The study investigates the effects of antibiotic treatment on average change in pressure after one week*
Gravel, J S and Wallace, I F (2000) Effects of otitis media with effusion on hearing in the first 3 years of life. Journal of speech, language, and hearing research : JSLHR 43(3): 631-44	- Study design does not meet inclusion criteria *Participants had myringotomy, so does not report on natural history*
Hall, A J; Maw, A R; Steer, C D (2009) Developmental outcomes in early compared with delayed surgery for glue ear up to age 7 years: a randomised controlled trial. Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery 34(1): 12-20	- Study design does not meet inclusion criteria *The study investigates the effects of early and delayed surgery on developmental outcomes in children with OME*
Handzic, Jadranka, Radic, Bozo, Bagatin, Tomica et al. (2012) Hearing in children with otitis media with effusion--clinical retrospective study. Collegium antropologicum 36(4): 1273-7	- Study design does not meet inclusion criteria *All children with OME received ventilation tubes and adenoidectomy, so does not report on natural history*
Harrison, H; Fixsen, A; Vickers, A (1999) A randomized comparison of homoeopathic and standard care for the treatment of glue ear in	- Study design does not meet inclusion criteria *Standard care arm received autoinflation and in some cases antibiotics, so does not report on natural history*

Study	Code [Reason]
children. Complementary therapies in medicine 7(3): 132-5	
Hassmann, Elbieta, Skotnicka, Boena, Baczek, Maria et al. (2004) Laser myringotomy in otitis media with effusion: long-term follow-up. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery 261(6): 316-20	- Study design does not meet inclusion criteria *Unclear if diagnosis of OME was confirmed by tympanometry*
Heaf, M; Hutchings, S; Bunch, K (1991) Does nose blowing improve hearing in serous otitis? A community study. The British journal of general practice : the journal of the Royal College of General Practitioners 41(350): 377-9	- Study design does not meet inclusion criteria *OME was not confirmed by tympanometry*
Hsu, G S; Levine, S C; Giebink, G S (1998) Management of otitis media using Agency for Health Care Policy and Research guidelines. The Agency for Health Care Policy and Research. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 118(4): 437-43	- Study design does not meet inclusion criteria *The study investigates adherence to Agency for Health Care Policy and Research guidelines*
Hussein, A, Fathy, H, Amin, S M et al. (2017) Oral steroids alone or followed by intranasal steroids versus watchful waiting in the management of otitis media with effusion. The Journal of laryngology and otology 131(10): 907-913	- Non-OECD country *Saudi Arabia*
Jorissen, M; De Boeck, K; Feenstra, L (1998) Middle ear disease in cystic fibrosis. International journal of pediatric otorhinolaryngology 43(2): 123-8	- Population and outcome do not meet inclusion criteria *38% of participants were aged >12 years, and outcomes of interest not reported*
Kilic, Nihat, Yoruk, Ozgur, Kilic, Songul Comert et al. (2016) Rapid maxillary expansion versus middle ear tube placement: Comparison of hearing improvements in children with resistance otitis media with effusion. The Angle orthodontist 86(5): 761-7	- Outcome does not meet inclusion criteria *Reports hearing thresholds only.*
Kuo, CL, Tsao, YH, Cheng, HM et al. (2014) Grommets for otitis media with effusion in children with cleft palate: a systematic review. Pediatrics 134(5): 983-94	- Non-OECD country *Systematic review included studies from non-OECD countries (China, Hong Kong)*
Lamothe, A, Boudreault, V, Blanchette, M et al. (1981) Serous otitis media: a six week prospective study. The Journal of otolaryngology 10(5): 371-9	- Study design does not meet inclusion criteria *Follow-up period is less than 3 months*

Study	Code [Reason]
Langan, LA, Sockalingam, R, Caissie, R et al. (2007) Occurrence of otitis media and hearing loss among First Nations elementary school children. Canadian Journal of Speech-Language Pathology & Audiology 31(4): 178-185	- Outcome does not meet inclusion criteria *Outcomes of interest not reported*
Le, C T; Freeman, D W; Fireman, B H (1991) Evaluation of ventilating tubes and myringotomy in the treatment of recurrent or persistent otitis media. The Pediatric infectious disease journal 10(1): 2-11	- Insufficient presentation of results *No usable data on outcomes of interest*
Leiberman, A. and Bartal, N. (1986) Untreated persistent middle ear effusion. The Journal of Laryngology & Otology 100(8): 875-878	- Study design does not meet inclusion criteria *Unclear how OME was defined. There is no mention of tympanometry/tympanograms*
Lildholdt, T (1983) Ventilation tubes in secretory otitis media. A randomized, controlled study of the course, the complications, and the sequelae of ventilation tubes. Acta oto-laryngologica. Supplementum 398: 1-28	- Study design does not meet inclusion criteria *Participants received treatments for OME, including medications, adenoidectomy and myringotomy (proportion not reported), so does not report natural history*
Lildholdt, T (1979) Unilateral grommet insertion and adenoidectomy in bilateral secretory otitis media: preliminary report of the results in 91 children. Clinical otolaryngology and allied sciences 4(2): 87-93	- Study design does not meet inclusion criteria *All participants had adenoidectomy, and 7% of control ears had ventilation tubes, so does not report natural history*
Liu, L, Sun, YG, Ma, L et al. (2004) Effect of ventilation tube insertion on otitis media with effusion in cleft palate children. Zhonghua er bi yan hou ke za zhi 39(4): 216-218	- Full text paper not available
Macknin, M L and Jones, P K (1985) Oral dexamethasone for treatment of persistent middle ear effusion. Pediatrics 75(2): 329-35	- Study design does not meet inclusion criteria *Follow-up <3 months*
Mair, Eric A, Moss, Jonathan R, Dohar, Joseph E et al. (2016) Randomized Clinical Trial of a Sustained-Exposure Ciprofloxacin for Intratympanic Injection During Tympanostomy Tube Surgery. The Annals of otology, rhinology, and laryngology 125(2): 105-14	- Study design does not meet inclusion criteria *All children had ventilation tubes inserted, so does not report on natural history.*
Majithia, A, Fong, J, Hariri, M et al. (2005) Hearing outcomes in children with primary ciliary dyskinesia--a longitudinal study. International journal of pediatric otorhinolaryngology 69(8): 1061-4	- Insufficient presentation of results *No usable data on outcomes of interest*
Maw, A R and Bawden, R (1994) Factors affecting resolution of otitis media with effusion in children. Clinical otolaryngology and allied sciences 19(2): 125-30	- Study includes same participants and data as already included study *Maw 1993*
Maw, A R and Bawden, R (1994) The long term outcome of secretory otitis media in children and the effects of surgical treatment: a ten year	- Study includes same participants and data as already included study *Maw 1993*

Study	Code [Reason]
study. Acta oto-rhino-laryngologica Belgica 48(4): 317-24	
Maw, A R and Herod, F (1986) Otoscopic, impedance, and audiometric findings in glue ear treated by adenoidectomy and tonsillectomy. A prospective randomised study. Lancet (London, England) 1(8495): 1399-402	- Study includes same participants and data as already included study *Maw 1993*
Maw, A R and Parker, A (1988) Surgery of the tonsils and adenoids in relation to secretory otitis media in children. Acta oto-laryngologica. Supplementum 454: 202-7	- Study includes same participants and data as already included study *Maw 1993*
McKenna Benoit, Margo, Orlando, Mark, Henry, Kenneth et al. (2019) Amplitude Modulation Detection in Children with a History of Temporary Conductive Hearing Loss Remains Impaired for Years After Restoration of Normal Hearing. Journal of the Association for Research in Otolaryngology : JARO 20(1): 89-98	- Study design does not meet inclusion criteria *All children with OME had VTs, so does not report on natural history. Also, no relevant outcomes reported.*
Mirandola, Prisco, Gobbi, Giuliana, Malinverno, Chiara et al. (2013) Impact of sulphurous water politzer inhalation on audiometric parameters in children with otitis media with effusion. Clinical and experimental otorhinolaryngology 6(1): 7-11	- Population does not meet inclusion criteria *Included children with hearing impairment due to chronic upper airway inflammatory status; results not presented separately for those with OME*
Moller, P (1980) Negative middle ear pressure and hearing thresholds in secretory otitis media. A double-blind crossover study with Lunerin. Scandinavian audiology 9(3): 171-6	- Study design does not meet inclusion criteria *All participants had myringotomy, so does not report natural history*
Møller, P and Dingsør, G (1990) Otitis media with effusion: can erythromycin reduce the need for ventilating tubes?. The Journal of laryngology and otology 104(3): 200-2	- Study design does not meet inclusion criteria *Follow-up <3 months*
NHS Centre for Reviews and, Dissemination (1992) The treatment of persistent glue ear in children.	- Study design does not meet inclusion criteria *Narrative review*
O'Shea, J S, Regan, J B, Langenbrunner, D J et al. (1986) Childhood otitis media with effusion: six-year follow-up. The Journal of otolaryngology 15(5): 303-5	- Study design does not meet inclusion criteria *Participants in control group and intervention group (antihistamine/decongestant) were analysed together and data not presented separately for control group, so does not report natural history*
Paradise, Jack L, Feldman, Heidi M, Campbell, Thomas F et al. (2007) Tympanostomy tubes and developmental outcomes at 9 to 11 years of age. The New England Journal of Medicine 356(3): 248-261	- Study design does not meet inclusion criteria *Unclear how OME was defined. There is no mention of tympanometry/tympanograms*
Parikh, A., Alles, R., Hawk, L. et al. (2000) Treatment of allergic rhinitis and its impact in	- Study design does not meet inclusion criteria

Study	Code [Reason]
children with chronic otitis media with effusion. Journal of Audiological Medicine 9(2): 104-117	*Participants received grommets, intra-nasal steroids or decongestants, so does not report natural history*
Passali, D and Zavattini, G (1987) Multicenter study on the treatment of secretory otitis media with ambroxol. Importance of a surface-tension-lowering substance. Respiration; international review of thoracic diseases 51suppl1: 52-9	- Population does not meet inclusion criteria *Children and adults included, and data not presented separately for children*
Pereira, NM, Maresh, AM, Modi, VK et al. (2022) Tympanostomy tubes in the age of quarantine. International journal of pediatric otorhinolaryngology 154: 111047	- Study design does not meet inclusion criteria *Unclear if diagnosis of OME was confirmed by tympanometry*
Perera, Rafael, Glasziou, Paul P, Heneghan, Carl J et al. (2013) Autoinflation for hearing loss associated with otitis media with effusion. The Cochrane database of systematic reviews: cd006285	- Study design does not meet inclusion criteria *Includes studies with treated control groups. Included studies not checked for relevance as this review has been superseded by ongoing update (which has been checked)*
Rach, G H, Zielhuis, G A, van Baarle, P W et al. (1991) The effect of treatment with ventilating tubes on language development in preschool children with otitis media with effusion. Clinical otolaryngology and allied sciences 16(2): 128-32	- Population does not meet inclusion criteria *The study was conducted in children with OME without hearing loss, so it is included in the review question on natural history of OME without associated hearing loss*
Reading, Richard (2011) Grommets (ventilation tubes) for hearing loss associated with otitis media with effusion in children. Child: Care, Health & Development 37(1): 150-151	- Study design does not meet inclusion criteria *Commentary*
Renou, G, Ketari, M, Toutée, JP et al. (1989) Medical treatment of seromucous otitis. Revue de laryngologie - otologie - rhinologie 110(3): 327-328	- Non-English language article
Renvall, U., Liden, G., Jungert, S. et al. (1975) Impedance audiometry in the detection of secretory otitis media. Scandinavian Audiology 4(2): 119-124	- Study design does not meet inclusion criteria *The study investigates the usefulness of impedance audiometry*
Renvall, U and Holmquist, J (1976) Tympanometry revealing middle ear pathology. The Annals of otology, rhinology, and laryngology 85(2suppl25pt2): 209-15	- Study design does not meet inclusion criteria *The study investigates the usefulness of impedance audiometry*
Renvall, U, Liden, G, Jungert, S et al. (1978) Long-term observation of ears with reduced middle ear pressure. Acta oto-laryngologica 86(12): 104-9	- Study design does not meet inclusion criteria *Long-term observation of ears with reduced middle ear pressure. No outcomes of interested reported*
Robert, J E, Burchinal, M R, Medley, L P et al. (1995) Otitis media, hearing sensitivity, and maternal responsiveness in relation to language during infancy. The Journal of pediatrics 126(3): 481-9	- Study design does not meet inclusion criteria *The study investigates the associations of OME-related hearing loss with language and cognitive impairment*

Study	Code [Reason]
Rosso, Cecilia, Colletti, Liliana, Foltran, Martina et al. (2021) Effects of rapid maxillary expansion on hearing loss and otitis media in cleft palate children. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery	- Study design does not meet inclusion criteria *Participants were prescribed treatments, so does not report on natural history*
Rovers, M M, Straatman, H, Ingels, K et al. (2000) The effect of ventilation tubes on language development in infants with otitis media with effusion: A randomized trial. Pediatrics 106(3): e42	- Study design does not meet inclusion criteria *Control received treatments including, adenoidectomy, antibiotics and nose drops (proportions not reported), so does not report natural history*
Rovers, M M, Straatman, H, Ingels, K et al. (2001) Generalizability of trial results based on randomized versus nonrandomized allocation of OME infants to ventilation tubes or watchful waiting. Journal of clinical epidemiology 54(8): 789-94	- Study design does not meet inclusion criteria *Control received treatments, including adenoidectomy, antibiotics and nose drops (proportions not reported), so does not report natural history*
Rovers, M.M., Straatman, H., Ingels, K. et al. (2001) The effect of short-term ventilation tubes versus watchful waiting on hearing in young children with persistent otitis media with effusion: A randomized trial. Ear and Hearing 22(3): 191-199	- Study design does not meet inclusion criteria *Control received treatments including, adenoidectomy, antibiotics and nose drops (proportions not reported), so does not report natural history*
Sancaktar, O.; Oz, A.A.; Sancaktar, M.E. (2021) Does maxillary expansion improve hearing loss due to otitis media with effusion?. Journal of Experimental and Clinical Medicine (Turkey) 38(2): 159-166	- Population does not meet inclusion criteria *Children aged 10-15 years old; mean age >12 years*
Sanyaolu, LN, Cannings-John, R, Butler, CC et al. (2020) The effect of ventilation tube insertion on quality of life in children with persistent otitis media with effusion. Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery 45(2): 239-247	- Insufficient presentation of results *Data not reported separately for untreated children.*
Saunte, C (1978) Clinical trial with Lunerin mixture and Lunerin mite in children with secretory otitis media. The Journal of international medical research 6(1): 50-5	- Study design does not meet inclusion criteria *OME was not confirmed using tympanometry*
Shekelle, P, Takata, G, Chan L, S et al. (2003) Diagnosis, natural history, and late effects of otitis media with effusion.	- Systematic review, included studies checked for relevance *Diagnostic test accuracy studies included*
Shriberg, Lawrence D, Friel-Patti, Sandy, Flipsen, Peter Jr. et al. (2000) Otitis media, fluctuant hearing loss, and speech-language outcomes: A preliminary structural equation	- Study design does not meet inclusion criteria *The study investigates the effect of early recurrent OME with or without hearing loss on speech and language.*

Study	Code [Reason]
model. Journal of Speech, Language, and Hearing Research 43(1): 100-120	
Silverman, C A and Silman, S (1995) Acoustic-immittance characteristics of children with middle-ear effusion: longitudinal investigation. Journal of the American Academy of Audiology 6(4): 339-45	- Study design does not meet inclusion criteria *The study investigates sensitivity and specificity of the acoustic-immittance measures*
Skinner, D W; Lesser, T H; Richards, S H (1988) A 15 year follow-up of a controlled trial of the use of grommets in glue ear. Clinical otolaryngology and allied sciences 13(5): 341-6	- Study design does not meet inclusion criteria *All participants had adenoidectomy, and if indicated tonsillectomy and/or maxillary antral lavage, so does not report natural history*
Son, Mi Ju, Choi, Songie, Kim, Young-Eun et al. (2016) Herbal medicines for the treatment of otitis media with effusion: a systematic review of randomised controlled trials. BMJ open 6(11): e011250	- Study design does not meet inclusion criteria *None of the included studies included an untreated control arm.*
Steele, D, Adam, GP, Di, M et al. (2017) Tympanostomy Tubes in Children With Otitis Media. AHRQ Comparative Effectiveness Reviews	- Study design does not meet inclusion criteria *Includes studies with treated control arms. Included studies checked for relevance.*
Stephenson, H, Haggard, M, Zielhuis, G et al. (1993) Prevalence of tympanogram asymmetries and fluctuations in otitis media with effusion: implications for binaural hearing. Audiology : official organ of the International Society of Audiology 32(3): 164-74	- Insufficient presentation of results *No usable data on outcomes of interest*
Swedish Council on Health Technology, Assessment (2008) Tympanostomy Tube Insertion for Otitis Media in Children: A Systematic Review. SBU Systematic Review Summaries	- Population does not meet inclusion criteria *Systematic review includes studies of acute otitis media*
Szoke, Henrik, Marodi, Marta, Sallay, Zsuzsa et al. (2016) Integrative versus Conventional Therapy of Chronic Otitis Media with Effusion and Adenoid Hypertrophy in Children: A Prospective Observational Study. Forschende Komplementarmedizin (2006) 23(4): 231-9	- Study design does not meet inclusion criteria *Observational study comparing between two different interventions; no untreated arm (so no data on natural history)*
Szoke, Henrik, Marodi, Marta, Vagedes, Jan et al. (2021) The P.E.A.N.U.T. Method: Update on an Integrative System Approach for the Treatment of Chronic Otitis Media with Effusion and Adenoid Hypertrophy in Children. Antibiotics (Basel, Switzerland) 10(2)	- Study design does not meet inclusion criteria *Comparison with data from a previous study using the same intervention; no untreated arm (so no data on natural history)*
Testa, B., Testa, D., Mesolella, M. et al. (2001) Management of chronic otitis media with effusion: The role of glutathione. Laryngoscope 111(8): 1486-1489	- Study design does not meet inclusion criteria *Participants received treatments for OME, including antibiotics, steroids, and saline-medicated nasal aerosol, so does not report natural history*

Study	Code [Reason]
Tian, X, Liu, Y, Wang, M et al. (2014) [A systematic review of adenoidectomy in the treatment of otitis media with effusion in children]. Lin chuang er bi yan hou tou jing wai ke za zhi = Journal of clinical otorhinolaryngology, head, and neck surgery 29(8): 723-5	- Full text paper not available
Topazio, D., Passali, F., Cama, A. et al. (2019) Intranasal hyaluronic acid improves the audiological outcomes of children with otitis media with effusion. Indian Journal of Otology 25(3): 155-161	- Insufficient presentation of results *Data not reported separately for ears with type B tympanograms.*
Torretta, S., Marchisio, P., Rinaldi, V. et al. (2016) Topical administration of hyaluronic acid in children with recurrent or chronic middle ear inflammations. International Journal of Immunopathology and Pharmacology 29(3): 438-442	- Population does not meet inclusion criteria *Includes children with OME or a history of recurrent AOM. Proportion of those with OME not reported.*
Tos, M (1984) Epidemiology and natural history of secretory otitis. The American journal of otology 5(6): 459-62	- Study includes same participants and data as study already included in review of natural history without hearing loss *Tos 1980; Tos 1982*
van Balen, F A; de Melker, R A; Touw-Otten, F W (1996) Double-blind randomised trial of co-amoxiclav versus placebo for persistent otitis media with effusion in general practice. Lancet (London, England) 348(9029): 713-6	- Study design does not meet inclusion criteria *All children received decongestants, so does not report on natural history*
van den Aardweg, MT, Schilder, AG, Herkert, E et al. (2010) Adenoidectomy for otitis media in children. Cochrane database of systematic reviews (Online): cd007810	- Study design does not meet inclusion criteria *None of the included studies included an untreated control group.*
van Zon, A., van der Heijden, G.J., van Dongen, T.M. et al. (2012) Antibiotics for otitis media with effusion in children. Cochrane database of systematic reviews (Online) 9: cd009163	- Review superseded by updated review
Venekamp, Roderick P, Burton, Martin J, van Dongen, Thijs M A et al. (2016) Antibiotics for otitis media with effusion in children. The Cochrane database of systematic reviews: cd009163	- Study design does not meet inclusion criteria *Includes studies with treated control groups. Included studies not checked for relevance as this review has been superseded by ongoing update (which has been checked)*
Williams, R L, Chalmers, T C, Stange, K C et al. (1993) Use of antibiotics in preventing recurrent acute otitis media and in treating otitis media with effusion. A meta-analytic attempt to resolve the brouhaha. JAMA 270(11): 1344-51	- Population does not meet inclusion criteria *Includes studies on recurrent acute otitis media. Included studies checked for relevance*
Williamson, I (2007) Otitis media with effusion in children. BMJ clinical evidence 2007(nopagination)	- Study design does not meet inclusion criteria *Includes studies with untreated control groups (included studies checked for relevance)*

Study	Code [Reason]
Zheng, Z., Li, Q., Chen, S. et al. (2018) Transformation of audiological characteristics of neonatal otitis media with effusion in 7-month-olds. International Journal of Clinical and Experimental Medicine 11(2): 946-951	- Non-OECD country *China*
Zhou, X, Jin, X, Yang, L et al. (2022) Efficacy and safety of ambroxol hydrochloride in the treatment of secretory otitis media: a systematic review and meta-analysis. Annals of translational medicine 10(3): 142	- Study design does not meet inclusion criteria *None of the included studies included an untreated control arm (all had steroids), so does not report on natural history.*

OME: otitis media with effusion

Excluded economic studies

No economic evidence was identified for this review.

Appendix K Research recommendations – full details

Research recommendations for review question: What is the progression, resolution and recurrence (natural history) of OME-related hearing loss at presentation in children under 12 years?

K.1.1 Research recommendation

What is the progression, resolution and recurrence of OME with and without hearing loss?

K.1.2 Why this is important

See Appendix K of evidence review C.

K.1.3 Rationale for research recommendation

See Appendix K of evidence review C.

K.1.4 Modified PICO table

See Appendix K of evidence review C.