National Institute for Health and Care Excellence

Draft for consultation

Otitis media with effusion in under 12s

[C] Evidence reviews for natural history of OME without hearing loss

NICE guideline number tbc

Evidence reviews underpinning research recommendation in the NICE guideline

March 2023

Draft for consultation

This evidence review was developed by NICE

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Natural history of OME without hearing loss

Review question

What is the progression, resolution and recurrence (natural history) of OME without 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 without 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, without associated hearing loss.
Intervention	N/A: No intervention (Natural history)
Comparison	N/A
Outcome	**Critical** • Progression to OME with associated hearing loss • Time to progression to OME with associated hearing loss **Important** • Resolution of current episode of OME* • Time to resolution of current episode of OME* • Total resolution (no further recurrences) of OME* • Time to total resolution of OME* • Recurrence of OME* (following spontaneous resolution) *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 the approach suggested for continuous outcomes.

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

Epidemiological evidence

Included studies

19 studies were included for this review, 14 observational single group (non-comparative) studies (Birch 1984; Birch 1986; Casselbrant 1985; Fiellau-Nikolajsen 1979; Fiellau-Nikolajsen 1983; Holm-Jensen 1981; Lous 1981; Reves 1985; Thomsen 1981; Tos 1980; Tos 1982; Williamson 1994; Zeisel 1995; Zielhuis 1990), 1 untreated control arm from comparative observational study (Wynings 2022), and 4 untreated control arms from comparative experimental study (Hughes 1984; Leach 2008; Rach 1991; Williamson 2009).

The included studies are summarised in Table 2.

Eighteen studies reported resolution of current episode of OME (Birch 1984; Birch 1986; Casselbrant 1985; Fiellau-Nikolajsen 1979; Fiellau-Nikolajsen 1983; Holm-Jensen 1981; Hughes 1984; Leach 2008; Lous 1981; Rach 1991; Reves 1985; Thomsen 1981; Tos 1980; Tos 1982; Williamson 1994; Williamson 2009; Wynings 2022; Zeisel 1995), 1 study reported time to resolution of current episode of OME (Zielhuis 1990), and 8 studies reported recurrence of OME (following spontaneous resolution) (Casselbrant 1985; Fiellau-Nikolajsen 1979; Fiellau-Nikolajsen 1983; Hughes 1984; Lous 1981; Tos 1980; Tos 1982; Williamson 1994). No studies reported progression to OME with associated hearing loss, time to total resolution of OME or time to these outcomes occurring.

One study included children with normal palatal function (Hughes 1984), 1 study excluded children with craniofacial anomalies (Leach 2008), 1 study excluded children with cleft palate or Down's syndrome (Williamson 2009), and 16 studies did not report data on whether any participants had Down's syndrome, cleft palate or craniofacial anomalies (Birch 1984; Birch 1986; Casselbrant 1985; Fiellau-Nikolajsen 1979; Fiellau-Nikolajsen 1983; Holm-Jensen 1981; Lous 1981; Rach 1991; Reves 1985; Thomsen 1981; Tos 1980; Tos 1982; Williamson 1994; Wynings 2022; Zeisel 1995; Zielhuis 1990).

Two studies included children with persistent OME (Rach 1991; Zeisel 1995), and 17 studies did not report data on type of OME (fluctuating OME or persistent OME) and episode of OME (first episode or recurrent episode) (Birch 1984; Birch 1986; Casselbrant 1985; Fiellau-Nikolajsen 1979; Fiellau-Nikolajsen 1983; Holm-Jensen 1981; Hughes 1984; Leach 2008; Lous 1981; Reves 1985; Thomsen 1981; Tos 1980; Tos 1982; Williamson 1994; Williamson 2009; Wynings 2022; Zielhuis 1990).

About 2% to 12% of children had grommets in 3 studies (Tos 1982; Williamson 1994; Williamson 2009). Four studies excluded children with grommets or who were going to have grommet surgery (Fiellau-Nikolajsen 1983; Rach 1991; Wynings 2022; Zeisel 1995), and 12 studies did not report data on whether participants had previous grommet insertion (Birch 1984; Birch 1986; Casselbrant 1985; Fiellau-Nikolajsen 1979; Holm-Jensen 1981; Hughes 1984; Leach 2008; Lous 1981; Reves 1985; Thomsen 1981; Tos 1980; Zielhuis 1990).

Three studies included children aged less than 2 years (Leach 2008; Wynings 2022; Zeisel 1995), 7 studies included children aged 2 years and over (Casselbrant 1985; Fiellau-Nikolajsen 1979; Fiellau-Nikolajsen 1983; Rach 1991; Thomsen 1981; Tos 1980; Zielhuis 1990), 3 studies included children aged 4 years and over (Birch 1984; Holm-Jensen 1981; Tos 1982), 1 study included children aged 1 to 5 years (Birch 1986), 1 study included children aged 3 months to 6 years (Reves 1985), 2 studies included children aged 6 years and over (Lous 1981; Williamson 2009), 1 study included children aged 5 to 8 years (Williamson 1994), and 1 study did not report ages of participants (Hughes 1984).

Three studies were from the UK (Reves 1985; Williamson 1994; Williamson 2009), 9 studies were from Denmark (Birch 1984; Birch 1986; Fiellau-Nikolajsen 1979; Fiellau-Nikolajsen 1983; Holm-Jensen 1981; Lous 1981; Thomsen 1981; Tos 1980; Tos 1982), 3 studies were from USA (Casselbrant 1985; Wynings 2022; Zeisel 1995), 1 study was from Germany (the British Army of the Rhine) (Hughes 1984), 1 study was from Australia (Leach 2008), and 2 studies were from Netherlands (Rach 1991; Zielhuis 1990).

One study included Aboriginal infants (Leach 2008), and 1 study included black infants (Zeisel 1995). 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
Birch 1984 Observational single group (non-comparative) study Denmark	N=373 (n=116 ears with OME) Children attending day-care centres Age in years, mean (SD)*: 4.3 (NR) Sex (male/female): NR *Reported for total study sample only	• Resolution of current episode of OME	Follow-up: 3 months Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Resolution of OME defined as change from type B to non-B tympanogram.
Birch 1986 Observational single group (non-comparative) study	N=210 (n=40 ears with OME) Children aged 1-7 years who were exclusively minded at home	• Resolution of current episode of OME	Follow-up: 12 weeks Duration of OME before the study is unknown.

Study	Population	Outcomes	Comments
Denmark	or in private day-care or attending preschool class or school Age in years, mean (SD): NR, but range: 1-5 Sex (male/female): NR		The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Resolution of OME defined as change from type B to non-B tympanogram.
Casselbrant 1985 Observational single group (non-comparative) study USA	N=140 (n=134 ears with OME) Preschool children aged 2-6 years Age in years, mean (SD): NR, but range*: 2-6 Sex (male/female)*: 81/59 *Reported for total study sample only	• Resolution of current episode of OME • Recurrence of OME (following spontaneous resolution)	Follow-up: 2 years 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 or recurrence of OME was not reported.
Fiellau-Nikolajsen 1983 Observational single group (non-comparative) study Denmark	N=404 (n=78 children with OME at first examination, and n=166 children with at least one episode of OME during 6-months study period) Only inclusion criterion was reported that children were aged 3 years old. Age in years, mean (SD): NR, but study included children aged 3 years	• Resolution of current episode of OME • Recurrence of OME (following spontaneous resolution)	Follow-up: 6 months Duration of OME before the study is unknown. However, some data was reported for children who had developed OME since previous screening assessments; therefore, it was possible to include duration of OME for this data. The diagnosis of OME was confirmed by impedance audiometry (tympanometry) and pneumatic otoscopy, but authors did not report criteria used. The definition of resolution or recurrence of OME was not reported.

Study	Population	Outcomes	Comments
	Sex (male/female): NR		
Fiellau-Nikolajsen 1979 Observational single group (non-comparative) study Denmark	N=504 (n=91 ears with OME) Only inclusion criterion was reported that children were aged 3 years old. Age in years, mean (SD): NR, but study included children aged 3 years Sex (male/female): NR	• Resolution of current episode of OME	Follow-up: 6 months Duration of OME before the study is unknown The diagnosis of OME (type B tympanogram) confirmed by tympanometry. Resolution of OME defined as change from type B to A tympanogram, or from type B to A or C1 tympanogram.
Holm-Jensen 1981 Observational single group (non-comparative) study Denmark	N=373 (n=93 ears with OME) Children aged 4 years born on the 1st to the 10th of every month in 1975 who were living in 1 of 2 Copenhagen counties Age in years, mean (SD): 4 (NR) Sex (male/female): NR	• Resolution of current episode of OME	Follow-up: 6 months Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) confirmed by tympanometry. Resolution of OME defined as change from type B to A, C1 or C2 tympanogram.
Hughes 1984 Untreated control arm from comparative experimental study Germany (the British Army of the Rhine)	N=16* Children with OME, normal palatal function and no history of ENT surgery Age in years, mean (SD): NR	• Resolution of current episode of OME • Recurrence of OME (following spontaneous resolution)	Follow-up: up to 6 months 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 or recurrence of OME was not reported.

Study	Population	Outcomes	Comments
	Sex (male/female): NR *Data from untreated control arm		
Leach 2008 Untreated control arm from comparative experimental study Australia	N=51* Aboriginal infants aged less than 12 months with unilateral or bilateral OME from three Aboriginal communities Age in months, mean (SD)*: 3.2 (NR) Sex (male/female)*: 30/21 *Data from untreated control arm	• Resolution of current episode of OME	Follow-up: 24 weeks Duration of OME before study was less than 2 weeks. The diagnosis of OME (type B tympanogram) confirmed by tympanometry and otoscopy. Resolution of OME defined as change from type B to non-B tympanogram.
Lous 1981 Observational single group (non-comparative) study Denmark	N=387 (n=100 children with OME) Children who started school (1st grade) in August 1987 in two rural municipalities Age in years, mean (SD): NR, but range*: 6.5-7.5 Sex (male/female)*: 190/197 *Reported for total study sample only	• Resolution of current episode of OME • Recurrence of OME (following spontaneous resolution)	Follow-up: 12 months Onset of OME was known for 117 of 139 episodes, but the duration of OME where this was known was not reported. The diagnosis of OME (type B tympanogram) confirmed by tympanometry. Resolution and recurrence of OME defined as change from type B to non-B tympanogram and change from non-B to type B tympanogram, respectively.
Rach 1991	N=21*	• Resolution of current	Follow-up: 6 months

Study	Population	Outcomes	Comments
Untreated control arm from comparative experimental study Netherlands	Children with bilateral OME Age in years, mean (SD): NR, but study included children aged 2 years Sex (male/female): NR *Data from untreated control arm	episode of OME	Duration of OME before the study: 3-6 months in n=7 children and at least 6 months in n=14 children. The diagnosis of OME (type B tympanogram) confirmed by tympanometry and impedance measurements. Resolution of OME defined as change from type B to non-B tympanogram.
Reves 1985 Observational single group (non-comparative) study UK	N=264 (n=64 children with OME) Children aged 3-6 years who were registered at a GP practice in North-West London Age in years, mean (SD): NR, but range: 3-6 Sex (male/female): NR	• Resolution of current episode of OME	Follow-up: at least 3 months Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) confirmed by tympanometry. Resolution of OME defined as change from type B to A or C tympanogram.
Thomsen 1981 Observational single group (non-comparative) study Denmark	N=184 (n=48 ears with OME) Children aged 2 years born on the 1st to the 10th of every month in 1976 who were living in 1 of 2 Copenhagen municipalities Age in years, mean (SD): NR, but study included children aged 2 years	• Resolution of current episode of OME	Follow-up: 27 months Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) confirmed by tympanometry. Resolution of OME defined as change from type B to A, C1 or C2 tympanogram.

Study	Population	Outcomes	Comments
	Sex (male/female)*: 92/92 *Reported for total study sample only		
Tos 1980 Observational single group (non-comparative) study Denmark	N=372 (n=51 ears with OME*) Infants (2-4 days old) and 2-year-old children Age in years, mean (SD): NR, but study included children aged 2 years Sex (male/female): NR *The study included infant group and children group, but data on outcomes of interest was only reported for the children group.	• Resolution of current episode of OME • Recurrence of OME (following spontaneous resolution)	Follow-up: 9 months in children group Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) confirmed by tympanometry. Resolution of OME defined as change from type B to A tympanogram, from type B to A or C1 tympanogram, and from type B to non-B tympanogram. Recurrence of OME defined as change from non-B to type B tympanogram.
Tos 1982 Observational single group (non-comparative) study Denmark	N=373 (n=87 ears with OME) Children aged 4 years who were born during the first ten days of every month in 1976 Age in years, mean (SD): NR, but study included children aged 4 years Sex (male/female): NR	• Resolution of current episode of OME • Recurrence of OME (following spontaneous resolution)	Follow-up: 12 months Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) confirmed by tympanometry. Resolution of OME defined as change from type B to A tympanogram, from type B to A or C1 tympanogram, and from type B to non-B tympanogram. Recurrence of OME defined as change from non-B to type B tympanogram.

Study	Population	Outcomes	Comments
Williamson 1994 Observational single group (non-comparative) study UK	N=856 (n=50 children or n=67 ears with OME*) Children aged 5-8 years from 1 of 4 schools in southwest Hampshire Age in years, mean (SD): NR, but range: 5-8 Sex (male/female): NR *Data extracted for children with type B tympanogram at screening in Spring 1990 only as this was the only usable data on outcomes of interest	• Resolution of current episode of OME • Recurrence of OME (following spontaneous resolution)	Follow-up: 12 months Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) confirmed by tympanometry. Resolution and recurrence of OME defined as change from type B to non-B tympanogram and change from non-B to type B tympanogram, respectively.
Williamson 2009 Untreated control arm from comparative experimental study UK	N=112* Children aged 4-11 years with a history of OM and OME confirmed by tympanometry Age in months, mean (SD)*: 72.1 (18.6) Sex (male/female)*: 63/49 *Data from untreated control arm	• Resolution of current episode of OME	Follow-up: 9 months Duration of OME before the study is unknown. The diagnosis of OME (B/B or B/C2 types) confirmed by tympanometry. Resolution of OME defined as change from type B or C2 to A or C1 tympanogram.
Wynings 2022 Untreated control arm from comparative observational study	N=94 (n=60 children who developed OME*) Children aged less than 2	• Resolution of current episode of OME	Mean duration of follow-up: 8.8 months Participants did not have OME before the study. The duration of OME prior to first assessment where it was detected is unknown.

Study	Population	Outcomes	Comments
USA	years who had a tracheostomy Age in months, mean (SD)*: 5.6 (3.4) Sex (male/female)*: 34/26 *Data extracted for children who developed OME and had repeat tympanometry assessments only		The diagnosis of OME (type B tympanogram) confirmed by tympanometry. Resolution of OME defined as change from type B to non-B tympanogram
Zeisel 1995 Observational single group (non-comparative) study USA	N=102 (n=57 children with OME) Black infants aged 6-12 months enrolled in participating childcare centres Age in months, mean (SD)*: 8.1 (1.8) Sex (male/female)*: 51/51 * Reported for total study sample only	• Resolution of current episode of OME	Follow-up: 16 months Duration of OME before study is unknown. The diagnosis of OME confirmed by tympanometry (type B tympanogram) and otoscopy but was based on otoscopy when there were discrepant findings. Resolution of OME defined as being free of bilateral effusion for at least 6 consecutive weeks, but tympanometric/otoscopic definition was not reported.
Zielhuis 1990 Observational single group (non-comparative) study Netherlands	N=1328 (n=816 children or n=1631 ears with OME) Children born between 1 September 1982 and 31 August 1983 living in Nijmegen on their 2nd birthday Age in years, mean (SD): NR but study	• Resolution of current episode of OME	Follow-up: 24 months Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) confirmed by tympanometry. Resolution of OME defined as change from type B to non-B tympanogram

Study	Population	Outcomes	Comments
	included children aged 2 years Sex (male/female): NR		

ENT: ear, nose, and throat; NR: not reported; OM: otitis media; OME: otitis media with effusion; SD: standard deviation

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

Summary of the evidence

The evidence was low to very low quality 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 evidence was stratified by duration of OME before the study or follow-up, duration of follow-up, definition of recurrence or resolution used, and unit of analysis (ear or child). None of the studies included children with craniofacial anomalies. In the event of heterogeneity, evidence was subgrouped according to age and country; there was insufficient information reported or variation across studies to subgroup according to the other factors specified in the protocol.

Resolution of current episode of OME

Resolution of OME of <2 weeks duration before follow-up

Resolution of OME of <2 weeks duration before follow-up, defined as change from type B to non-B tympanogram, was 10% (confidence interval 4% to 21%) by 6 months.

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

OME of <1 month duration before follow-up had 72% resolution (undefined; confidence interval 54% to 86%) by 2 months and 90% (confidence interval 72% to 97%) by 5 months.

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

OME of <3 months duration before follow-up had 67% resolution (undefined; confidence interval 46% to 82%) by 3 months.

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

Resolution of OME of >3 months duration before follow-up, defined as change from type B to non-B tympanogram, was 7% (confidence interval 2% to 20%) by 3 months and 29% (17% to 44%) by 6 months.

Resolution of OME of >4 months duration before follow-up

Resolution (undefined) of OME of >4 months duration before follow-up was 47% (confidence interval 35% to 60%) by 3 months.

Resolution of OME of unknown duration before follow-up

At 1 month follow-up, resolution of OME of unknown duration before follow-up was:

- 15% (confidence interval 9% to 24%) when it was defined as change from type B to type A tympanogram,
- 22% (confidence interval 15% to 32%) when it was defined as change from type B to type A or C1 tympanogram,

- 10% (confidence interval 4% to 24%) to 56% (confidence interval 46% to 65%), depending on unit of analysis, when defined as change from type B to non-B tympanogram, and
- 45% (confidence interval 35% to 55%) when it was defined as change from type B or C2 to type A or C1 tympanogram.

Two studies that did not define resolution reported resolution rates of 36% to 66% (depending on unit of analysis).

Resolution of OME, defined as change from type B to non-B tympanogram, was 28% (confidence interval 16% to 43%) to 48% (39% to 57%) by 1.5 months and 30% (confidence interval 18% to 46%) to 69% (59% to 77%) by 2 months (reasons for heterogeneity unclear). One study that did not define resolution reported 78% resolution (confidence interval 70% to 84%) by 2 months. Resolution of OME, defined as changed from type B to non-B tympanogram, was 35% (confidence interval 22% to 51%) to 59% (confidence interval 49% to 67%) by 2.5 months (reasons for heterogeneity unclear).

At 3 months follow-up, resolution of OME was:

- 18% (confidence interval 9% to 34%) in children aged under 4 years and 3% (confidence interval 1% to 10%) in children agreed 4 years and over when defined as a change from type B to type A tympanogram,
- 30% (confidence interval 23% to 38%) in children aged under 4 years and 14% (confidence interval 8% to 23%) in children aged 4 years and over when defined as change from type B to type A or C1 tympanogram,
- 60% (confidence interval 58% to 63%) in children aged under 4 years and 56% (confidence interval 43% to 68%) in children aged 4 years and over when it was defined as change from type B to non-B tympanogram,
- 45% (confidence interval 34% to 58%) in children aged under 6 years and 73% (confidence interval 63% to 81%) in children agreed 6 years and over when it was defined as change from type B to non-B tympanogram,
- 52% (confidence interval 42% to 63%) when it was defined as change from type B or C2 to type A or C1 tympanogram, and
- 37% (confidence interval 18% to 62%) to 93% (confidence interval 88% to 97%), depending on unit of analysis and study design, when it was undefined.

At 4 months and 5 months follow-up, resolution of OME defined as changed from type B to non-B tympanogram was 44% (confidence interval 31% to 58%) to 81% (confidence interval 72% to 88%), depending on unit of analysis and country, and 84% (confidence interval 75% to 90%), respectively. One study that did not define resolution reported 96% resolution (confidence interval 91% to 98%) by 4 months and 97% resolution (confidence interval 92% to 99%) by 5 months.

At 6 months follow-up, resolution of OME was:

- 34% (confidence interval 27% to 42%) in children aged under 4 years and 20% (confidence interval 13% to 29%) in children aged 4 years and over when defined as change from type B to type A tympanogram,
- 42% (confidence interval 36% to 49%) when defined as change from type B to type A or C1 tympanogram, and
- 67% (confidence interval 53% to 78%) to 85% (confidence interval 84% to 87%), depending on country, in children aged under 4 years and 65% (confidence interval 51% to 76%) in children aged 4 years and over when defined as change from type B to non-B tympanogram.

Two studies that did not define resolution reported 68% (confidence interval 57% to 77%) to 98% resolution (confidence interval 93% to 99%), depending on unit of analysis.

At 8 months follow-up, resolution of OME defined as change from type B to non-B tympanogram was 76% (confidence interval 62% to 86%) to 78% (confidence interval 66% to 86%), depending on unit of analysis.

At 9 months follow-up, resolution of OME was:

- 47% (confidence interval 34% to 61%) when defined as change from type B to type A tympanogram,
- 67% (confidence interval 53% to 78%) in children aged under 4 years and 45% (confidence interval 35% to 56%) in children aged 4 years and over when it was defined as change from type B to type A or C1 tympanogram,
- 86% (confidence interval 74% to 93%) to 92% (confidence interval 91% to 93%) in children aged under 4 years (depending on country) and 73% (confidence interval 63% to 82%) in children aged 4 years and over when defined as change from type B to non-B tympanogram, and
- 65% (confidence interval 54% to 75%) when defined as change from type B or C2 to type A or C1 tympanogram.

Resolution of OME, defined as change from type B to non-B tympanogram, at 9 months in a population of children who had tracheostomy for respiratory failure and airway obstruction was 20% (confidence interval 10% to 34%).

At 12 months follow-up, resolution of OME defined as change from type B to non-B tympanogram was 78% (confidence interval 68% to 86%) to 99% (confidence interval 93% to 100%), depending on age, unit of analysis and country.

Resolution of OME defined as change from type B to non-B tympanogram was 97% (confidence interval 96% to 98%) by 15 months, 98% (confidence interval 97% to 98%) by 18 months, 98% (confidence interval 97% to 99%) by 21 months, 99% (confidence interval 98% to 99%) by 24 months, and 83% (confidence interval 70% to 91%) by 27 months.

Recurrence of OME (following spontaneous resolution)

Recurrence of OME defined as change from non-B to type B tympanogram was 8% (confidence interval 3% to 19%) by 6 months and 10% (confidence interval 4% to 21%) by 9 months in children aged under 4 years and 17% (confidence interval 10% to 27%) by 6 months and 28% (confidence interval 19% to 39%) by 9 months in children aged 4 years and over. At 12 months, recurrence of OME defined as change from non-B to type B tympanogram was 8% (confidence interval 3% to 18%) to 35% (confidence interval 26% to 45%), depending on unit of analysis and country.

Recurrence of OME was 7% (confidence interval 0% to 58%) by 3 months, 18% (confidence interval 11% to 28%) by 6 months, and 34% (confidence interval 26% to 42%) by 12 months when the definition of recurrence of OME was unspecified.

There were a number of outcomes in the protocol that were not reported on by any studies, progression to OME with associated hearing loss, time to progression to OME with associated hearing loss, total resolution (no further recurrences) of OME, and time to total resolution of OME.

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 without 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 to OME with associated hearing loss and time to progression to OME with associated hearing loss were prioritised as critical outcomes, as the committee agreed it was important to understand how often children with OME without hearing loss will develop hearing loss. Resolution of current episode of OME, time to resolution of current episode of OME, total resolution (no further recurrences) of OME, time to total resolution of OME and recurrence of OME (following spontaneous resolution) were chosen as important outcomes as they are useful indicators of natural history of OME without 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 to OME with associated hearing loss, time to progression to OME with associated hearing loss, total resolution (no further recurrences) of OME, and time to total resolution of OME.

Benefits and harms

The evidence showed wide variation in resolution rates reported across papers. There was a trend towards greater resolution over longer follow-up periods, but this did not follow the linear pattern that the committee expected, based on their experience. 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 aged under 4 years compared with children aged 4 years and over, 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 type A tympanogram). Further, the committee noted that a large number of the included studies did not specify the duration of the OME before the follow-up period began and as noted above, the committee would expect higher rates of spontaneous resolution as the duration of OME increases; therefore, potential differences in the length of OME before follow-up where this was unknown may also contribute to the heterogeneity across studies.

The available data on recurrence showed a similar pattern to the data on resolution; there was a tendency for greater recurrence rates over longer follow-up periods, but again there was variation in rates reported across papers which may be due to differences in populations included and definitions used. There were lower rates of recurrence in children aged under 4 years compared with those aged 4 years and over which, combined with the evidence for resolution, may suggest that the natural history of OME is better in children aged under 4. However, the committee were not confident in this finding due to the low quality of the evidence.

The committee agreed that the evidence on resolution and recurrence provided some support for the recommendations on information and support (see evidence review N) about providing information to children, parents, and carers about the fluctuating nature of OME, but did not think it was appropriate to provide any additional information about this due to the low quality of, and the heterogeneity in, the evidence. The committee acknowledged that heterogeneity is to 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). However, the evidence available from studies conducted in the UK (Reves 1985; Williamson 1994; Williamson 2009) included small numbers of children with OME and, in two of the studies (Williamson 1994; Williamson 2009), the included children were older than those typically seen in practice, based on the committee's experience. Therefore, consideration of the evidence from the UK specifically also did not provide robust evidence to inform recommendations, and the committee did not make recommendations as they were not sufficiently confident in the findings.

It is not current practice to intervene for OME unless there is an associated hearing loss. The committee discussed that the lack of evidence on progression to OME with associated hearing loss meant that it was not possible to identify which children may develop hearing loss and, as a result, may benefit from targeted recommendations. The committee were aware that OME-related hearing loss can impact development, speech, language and learning in children with OME, and understanding the progression to OME with associated hearing loss will contribute to optimal management and will minimise its harmful impacts. Therefore, the committee agreed that further research was needed on the natural history of OME without hearing loss to identify which children are most likely to progress to OME with associated hearing loss and made a research recommendation (see Appendix K).

Cost effectiveness and resource use

No recommendations were made for OME without hearing loss at presentation in children under 12 years, as the committee reasoned that intervention was only likely to be cost-effective in the presence of hearing loss with a resulting loss in health-related quality of life. The committee did not consider that a lack of recommendations for such children would lead to any substantive change in practice and therefore they did not anticipate a significant resource impact.

Recommendations supported by this evidence review

This evidence review supports the research recommendation on progression, resolution and recurrence of OME with and without hearing loss. Other evidence supporting this recommendation can be found in the evidence review on natural history of OME-related hearing loss (see evidence review D).

References – included studies

Epidemiological

Birch 1984

Birch, L. and Elbrond, O. (1984). Prospective epidemiological investigation of secretory otitis media in children attending day-care centers, Journal for Oto-Rhino-Laryngology and its Related Specialties 46(5), 229-234

Birch 1986

Birch, L. and Elbrond, O. (1986). Prospective epidemiological study of secretory otitis media in children not attending kindergarten, an incidence study, International Journal of Pediatric Otorhinolaryngology 11(2), 183-190

Casselbrant 1985

Casselbrant, M. L., Brostoff, L. M., Cantekin, E. I. et al. (1985). Otitis media with effusion in preschool children, The Laryngoscope 95(4), 428-436

Fiellau-Nikolaisen 1983

Fiellau-Nikolajsen, M. (1983). Epidemiology of secretory otitis media. a descriptive cohort study, The Annals of Otology, Rhinology, and Laryngology 92(2pt1), 172-177

Fiellau-Nikolajsen 1979

Fiellau-Nikolajsen, M. and Lous, J. (1979). Prospective tympanometry in 3-year-old children. a study of the spontaneous course of tympanometry types in a nonselected population, Archives of Otolaryngology (Chicago, Ill.: 1960) 105(8), 461-466

Holm-Jensen 1981

Holm-Jensen, S., Sorensen, C. H., Tos, M. (1981). Repetitive tympanometric screenings in 4-year-old children. seasonal influence on secretory otitis and tubal dysfunction, Journal for Oto-Rhino-Laryngology and its Related Specialties 43(3), 164-174

Hughes 1984

Hughes, K. B. (1984). Management of middle-ear effusions in children, The Journal of Laryngology and Otology 98(7), 677-684

Leach 2008

Leach, A. J., Morris, P. S., Mathews, J. D. (2008). Compared to placebo, long-term antibiotics resolve otitis media with effusion (OME) and prevent acute otitis media with perforation (AOMwiP) in a high-risk population: a randomized controlled trial, BMC Pediatrics 8, 23

Lous 1981

Lous, J. and Fiellau-Nikolajsen, M. (1981). Epidemiology and middle ear effusion and tubal dysfunction. a one-year prospective study comprising monthly tympanometry in 387 non-selected 7-year-old children, International Journal of Pediatric Otorhinolaryngology 3(4), 303-317

Rach 1991

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), 128-132

Reves 1985

Reves, R., Budgett, R., Miller, D. et al. (1985). Study of middle ear disease using tympanometry in general practice, British Medical Journal (Clinical Research Ed.) 290(6486), 1953-1956

Thomsen 1981

Thomsen, J. and Tos, M. (1981). Spontaneous improvement of secretory otitis. a long-term study, Acta Oto-Laryngologica 92(56), 493-499

Tos 1980

Tos, M. (1980). Spontaneous improvement of secretory otitis and impedance screening, Archives of Otolaryngology 106(6), 345-349

Tos 1982

Tos, M., Holm-Jensen, S., Sorensen, C. H. et al. (1982). Spontaneous course and frequency of secretory otitis in 4-year-old children, Archives of otolaryngology (Chicago, Ill.: 1960) 108(1), 4-10

Williamson 1994

Williamson, I. G., Dunleavey, J., Bain, J. et al. (1994). The natural history of otitis media with effusion--a three-year study of the incidence and prevalence of abnormal tympanograms in four South West Hampshire infant and first schools, The Journal of Laryngology and Otology 108(11), 930-934

Williamson 2009

Williamson, I., Benge, S., Barton, S. et al. (2009). Topical intranasal corticosteroids in 4-11 year old children with persistent bilateral otitis media with effusion in primary care: double blind randomised placebo controlled trial, BMJ (Clinical Research Ed.) 339, b4984

Wynings 2022

Wynings, E. M., Jaffal, H., St John, R. et al. (2022). Mechanical ventilation and middle ear effusions among tracheostomy-dependent children, International Journal of Pediatric Otorhinolaryngology 155, 111062

Zeisel 1995

Zeisel, S. A., Roberts, J. E., Gunn, E. B. et al. (1995). Prospective surveillance for otitis media with effusion among black infants in group child care, The Journal of Pediatrics 127(6), 875-880

Zielhuis 1990

Zielhuis, G. A., Rach, G. H., van den Broek, P. (1990). The natural course of otitis media with effusion in preschool children, European Archives of Oto-Rhino-Laryngology 247(4), 215-221

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 without hearing loss at presentation in children under 12 years?

Table 3: Review protocol

Field	Content
PROSPERO registration number	CRD42022341014
Review title	Natural history of OME without hearing loss
Review question	What is the progression, resolution and recurrence (natural history) of OME without hearing loss at presentation in children under 12 years?
Objective	To determine the natural history of OME without 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, without 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 to OME with associated hearing loss • Time to progression to OME with associated hearing loss
Secondary outcomes (important outcomes)	• Resolution of current episode of OME* • Time to resolution of current episode of OME* • Total resolution (no further recurrences) of OME* • Time to total resolution of OME* • Recurrence of OME* (following spontaneous resolution) *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 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

Field	Content
	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.

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

Field	Content	

	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)
	
	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

Field	Content	
	☐	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	☐ / ☑
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	

Field	Content
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=CRD42022341014
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
Keywords	Otitis media with effusion, natural history, progression, resolution, recurrence, hearing loss
Details of existing review of same topic by same authors	None
Current review status	☐ Ongoing

Field	Content	
	☒	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 without 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

1 **Database: Epistemonikos**

2 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

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

5 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]

6 **Database: APA PsycInfo – OVID interface**

7 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"

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

2 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

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

5 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

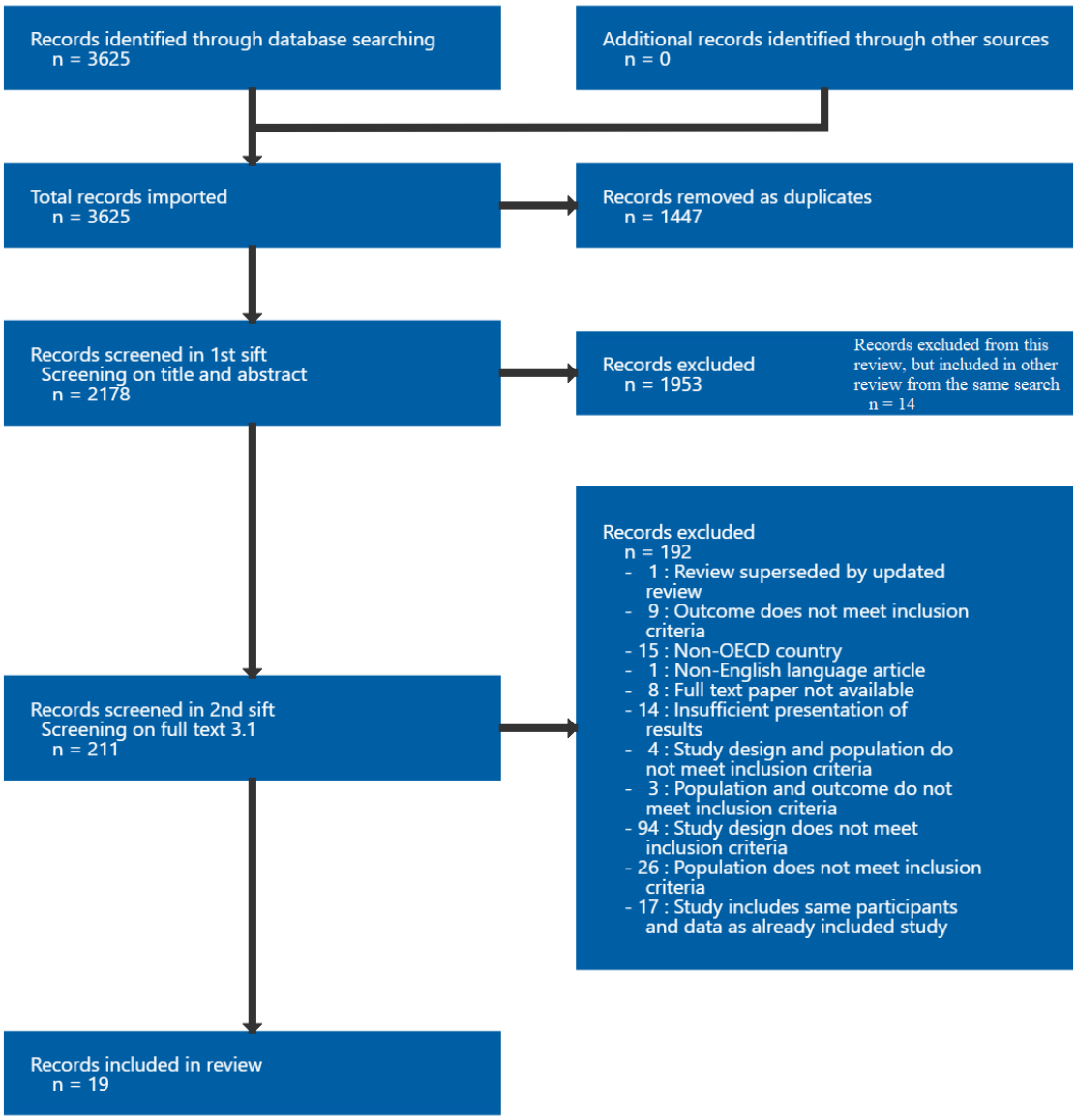
Appendix C Epidemiological evidence study selection

Study selection for: What is the progression, resolution and recurrence (natural history) of OME without 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.

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 without hearing loss at presentation in children under 12 years?

Table 4: Evidence tables

Birch, 1984

Bibliographic Reference	Birch, L; Elbrond, O; Prospective epidemiological investigation of secretory otitis media in children attending day-care centers.; ORL; journal for oto-rhino-laryngology and its related specialties; 1984; vol. 46 (no. 5); 229-34

Study details

Country/ies where study was carried out	Denmark
Study type	Observational single group (non-comparative) study
Study dates	January 1982 - April 1982
Inclusion criteria	Children attending day-care centres
Exclusion criteria	Not reported
Patient characteristics	Mean age in years: 4.3 (reported for total study sample only)
Duration of follow-up	3 months
Sources of funding	Not reported
Sample size	Total study sample (number of children): 373

	Number of ears with OME (number of children not reported): 116
Other information	Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry.
Outcomes	Resolution of current episode of OME (B to non-B tympanogram; number of ears): 4 weeks: 34/116 6 weeks: 56/116 8 weeks: 63/116 10 weeks: 68/116 12 weeks: 78/116

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 *(Sampled from municipality, and potential participants identified from authority records. However, paper reports that municipality is fairly small and restricted to a single 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 (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?	No *(Only age bands reported. No other details reported about the study sample)*

Section	Question	Answer
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?	Yes *(Initial response rate (for participating in the study) was 94%, and data was available for all participants included in the study)*

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

2 **Birch, 1986**

Bibliographic Reference	Birch, L; Elbrond, O; Prospective epidemiological study of secretory otitis media in children not attending kindergarten. An incidence study.; International journal of pediatric otorhinolaryngology; 1986; vol. 11 (no. 2); 183-90

3 **Study details**

Country/ies where study was carried out	Denmark
Study type	Observational single group (non-comparative) study
Study dates	September to December*

	*The authors stated that the study was conducted during the period September to December, but study year was not reported
Inclusion criteria	Children aged between 1 and 7 years, who were exclusively minded at home or in private day care with up to 7 children, or attended a preschool class (a class for 6-year-olds) or school
Exclusion criteria	Children attending day nursery, kindergarten, or municipal day care. No further exclusion criteria reported
Patient characteristics	Total study sample = 210 children. For this review, data extracted for B-tympanogram at 1st examination. Number of children not reported but number of ears with B-tympanogram was 40. Data was from children aged 1 to 5 years. Distribution of B-tympanograms (by ear) by age was as follows: 35% 1 year; 15% 2 years; 12.5% 3 years; 15% 4 years; 22.5% 5 years.
Duration of follow-up	12 weeks
Sources of funding	Not reported
Sample size	40 ears (number of children not reported)
Other information	Duration of OME before the study is unknown.
Outcomes	Resolution of current episode of OME (defined as number of ears with type B tympanograms at first examination but not at follow-up timepoint): 4 weeks: 4/40 ears resolved 6 weeks: 11/40 ears resolved 8 weeks: 12/40 ears resolved 10 weeks: 14/40 ears resolved 12 weeks: 14/40 ears resolved

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 *(Sampled from municipality, and potential participants identified from authority records. However, paper reports that municipality is fairly small and restricted to a single geographical area)*
Participant sampling	Were study participants sampled in an appropriate way?	Unclear *(Paper reports random sampling from the population, but does not provide detail on how sampling was performed, e.g., whether random probabilistic sampling used)*
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?	No *(Only age bands reported. No other details reported about the study sample)*
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)*

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) was 68% and 32% (of total study sample) dropped out during the follow-up period. No reasons for non-response provided, and no comparison of responders versus non-responders)*

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

Casselbrant, 1985

Bibliographic Reference	Casselbrant, M L; Brostoff, L M; Cantekin, E I; Flaherty, M R; Doyle, W J; Bluestone, C D; Fria, T J; Otitis media with effusion in preschool children.; The Laryngoscope; 1985; vol. 95 (no. 4); 428-36

Study details

Country/ies where study was carried out	USA
Study type	Observational single group (non-comparative) study
Study dates	September 1981 - August 1983
Inclusion criteria	Preschool children aged 2-6 years
Exclusion criteria	Children with tympanostomy tubes and sensorineural hearing loss
Patient characteristics	Age range in years*: 2-6 Sex (male/female)*: 81/59 *Reported for total study sample only
Duration of follow-up	2 years

Sources of funding	Not reported
Sample size	Total study sample: 140* *They study had two one-year study periods (n=66 children in the first year and n=37 in the second year), but 37 of the 66 children enrolled in the first year were also observed during the second year, so N=140 was reported as total sample size
Other information	Duration of OME before the study is unknown. The diagnosis of OME was confirmed by tympanometry. The study did not report diagnostic criteria (for example, tympanogram types) for OME or resolution or recurrence of OME.
Outcomes	Resolution of current episode of OME (number of episodes in 134 ears)*: 1 month: 90/137 2 months: 107/137 3 months: 128/137 4 months: 131/137 5 months: 133/137 6 months: 134/137 Recurrence of OME (following spontaneous resolution) (number of ears): 12 months: 45/134 *Data extracted from figure and included multiple episodes per child

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 daycare centre in a small geographical area (a suburb of Pittsburgh))*
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 (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?	No *(Age, gender and ethnic status were reported for the whole sample, but not for those with OME. 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 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?	No *(Initial response rate (for participating in the study) is not reported. 5% (of total study sample) were lost to follow-up, and there were significant differences between those 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

Fiellau-Nikolajsen, 1983

Bibliographic Reference	Fiellau-Nikolajsen, M; Epidemiology of secretory otitis media. A descriptive cohort study.; The Annals of otology, rhinology, and laryngology; 1983; vol. 92 (no. 2pt1); 172-7

1 **Study details**

Country/ies where study was carried out	Denmark
Study type	Observational single group (non-comparative) study
Study dates	1978 - 1979
Inclusion criteria	3-year-old children
Exclusion criteria	Children with grommets in situ or who were going to have grommet surgery before the study period, the tensa defect, or cholesteatoma
Patient characteristics	Age in years: 3
Duration of follow-up	6 months
Sources of funding	Not industry funded
Sample size	Total study sample: 404 Number of children with OME at first examination: 78 Number of children who had at least one episode of OME during 6 months: 166 Number of episodes of OME in 166 children during 6 months: 182

Other information	Duration of OME before the study is unknown. However, some data was reported for children who had developed OME since previous screening assessments; therefore, it was possible to include duration of OME for this data. The diagnosis of OME was confirmed by impedance audiometry (tympanometry) and pneumatic otoscopy. The study did not report diagnostic criteria (for example, tympanogram types) for OME or resolution or recurrence of OME.
Outcomes	Resolution of current episode of OME in children with OME at first examination: 1 month: 28/78 3 months: 46/78 6 months: 53/78 Resolution of current episode of OME in children with OME at second examination: 2 months: 21/29 5 months: 26/29 Resolution of current episode of OME in children with OME at third examination (data from figure): 3 months: 16/24 Recurrence of OME (following spontaneous resolution) (number of children): 6 months: 14/78

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 municipality 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 (particularly for subgroup analyses of interest, i.e., those with OME) were small)*

Section	Question	Answer
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	No *(Age was reported for the whole sample, but not for those with OME. 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 *(Impedance audiometry (including tympanometry) and pneumatic otoscopy 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. 5% (of total study sample) were lost to follow-up, and characteristics of those lost to follow-up not reported)*

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

2 **Fiellau-Nikolajsen, 1979**

Bibliographic Reference	Fiellau-Nikolajsen, M; Lous, J; Prospective tympanometry in 3-year-old children. A study of the spontaneous course of tympanometry types in a nonselected population.; Archives of otolaryngology (Chicago, Ill. : 1960); 1979; vol. 105 (no. 8); 461-6

3 **Study details**

Country/ies where study was carried out	Denmark
Study type	Observational single group (non-comparative) study
Study dates	1976
Inclusion criteria	Children aged 3 years
Exclusion criteria	Not reported
Patient characteristics	Age in years: 3
Duration of follow-up	6 months
Sources of funding	Not industry funded
Sample size	Total study sample (number of children): 504 Number of ears with OME (number of children not reported) at first examination: 91
Other information	Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Classification of tympanometry types was based on middle ear pressure and gradient (A: >-100 mmH2O and >0.1; B: 200 to -400 or inderterminable and ≤0.1; C1: -100 to -199 and >0.1; C2: -200 to -400 and >0.1)
Outcomes	Resolution of current episode of OME (B to A tympanogram; number of ears): 1 month: 14/91 3 months: 22/91 6 months: 32/91

	Resolution of current episode of OME (B to A or C1 tympanogram; number of ears): 1 month: 20/91 3 months: 30/91 6 months: 41/91

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 municipality in a small geographical area)*
Participant sampling	Were study participants sampled in an appropriate way?	Yes *(Almost everyone in the sampling frame is included (96.1% of all children in the municipality born in 1972))*
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?	No *(All participants were 3 years old at 1st test, but no further details reported)*
Coverage bias	Was the data analysis conducted with sufficient coverage of the identified sample?	No *(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) is not reported. 3% (of total study sample) were lost to follow-up, and characteristics of those lost to follow-up not reported)*

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

2 **Holm-Jensen, 1981**

Bibliographic Reference	Holm-Jensen, S; Sorensen, C H; Tos, M; Repetitive tympanometric screenings in 4-year-old children. Seasonal influence on secretory otitis and tubal dysfunction.; ORL; journal for oto-rhino-laryngology and its related specialties; 1981; vol. 43 (no. 3); 164-74

3 **Study details**

Country/ies where study was carried out	Denmark
Study type	Observational single group (non-comparative) study
Study dates	February to August 1979
Inclusion criteria	Healthy children aged 4 years (born on the 1st to the 10th of every month in 1975), living in 1 of 2 Copenhagen counties
Exclusion criteria	Not reported
Patient characteristics	Total study sample = 373 children for first test, 335 children (670 ears) for second test, and 333 children (666 ears) for third test.

	For this review, data extracted for those with B-tympanogram at 1st examination. Number of children not reported but number of ears with B-tympanogram was 92 for 3-month follow-up and 93 for 6-month follow-up. All included children were 4 years old.
Duration of follow-up	6 months
Sources of funding	Not reported
Sample size	92 ears (number of children not reported) at 3-month follow-up 93 ears (number of children not reported) at 6-month follow-up
Other information	Duration of OME before the study is unknown.
Outcomes	Resolution of current episode of OME (defined as number of ears that changed from having a type B tympanogram to a type A or C tympanogram): 3 months: 54/92 (58.8%) ears resolved (3.3% changed to type A, 12% to type C1, and 43.5% to type C2) 6 months: 54/93 (58.1%) ears resolved (15.1% change to type A, 11.8% to type C1, and 31.2% to type C2)

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 not sampled from the population randomly (those born on the 1st to the 10th of every month in 1975 were selected))*

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 with OME) were small)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	No *(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 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 not reported. 10% (of total study sample) failed to attend the 2nd test and 11% (of total study sample) failed to attend the 3rd test. No reasons for non-response provided, and no comparison of responders versus non-responders)*

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

1 **Hughes, 1984**

Bibliographic Reference	Hughes, K B; Management of middle-ear effusions in children.; The Journal of laryngology and otology; 1984; vol. 98 (no. 7); 677-84

2 **Study details**

Country/ies where study was carried out	Germany (the British Army of the Rhine)
Study type	Untreated control arm from comparative experimental study
Study dates	Not reported
Inclusion criteria	Children with OME, normal palatal function and no history of ear, nose or throat surgery
Exclusion criteria	Not reported
Patient characteristics	Not reported
Duration of follow-up	up to 6 months
Sources of funding	Industry funded
Sample size	Total sample size*: 16 *Data from untreated control arm
Other information	Duration of OME before the study is unknown. The diagnosis of OME was confirmed by tympanometry. The study did not report diagnostic criteria (for example, tympanogram types) for OME or resolution or recurrence of OME.

Outcomes	Resolution of current episode of OME (number of children)*: 3 months: 6/16 Recurrence of OME (following spontaneous resolution) (number of children)*: 3 months: 0/6 *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 families in the British Army of the Rhine (BAOR))*
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?	No *(Characteristics of the study subjects (e.g., age and gender) not 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?	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. 13% and 23% (of total study sample) were lost to follow-up at 3 months and 6 months, respectively, and characteristics of those lost to follow-up not reported)*

1 *BAOR: the British Army of the Rhine; JBI: The Joanna Briggs Institute Checklist*

2 **Leach, 2008**

Bibliographic Reference	Leach, AJ; Morris, PS; Mathews, JD; Compared to placebo, long-term antibiotics resolve otitis media with effusion (OME) and prevent acute otitis media with perforation (AOMwiP) in a high-risk population: a randomized controlled trial; BMC pediatrics; 2008; vol. 8; 23

3 **Study details**

Country/ies where study was carried out	Australia
Study type	Untreated control arm from comparative experimental study
Study dates	1996 – 2001
Inclusion criteria	Aboriginal infants aged less than 12 months from three Aboriginal communities with unilateral or bilateral OME
Exclusion criteria	Gestational age less than 34 weeks, chronic infection that needs prophylactic antibiotic therapy, craniofacial abnormalities or immune deficiency syndromes
Patient characteristics	Mean age in months at enrolment*: 3.2 Sex (male/female)*: 30/21

	Children with OME at randomisation*: 49/51 (96%) Children with unilateral dry perforation at randomisation*: 1/51 (2%) Children with resolving acute otitis media at randomisation*: 1/51 (2%) *Data from untreated control arm
Duration of follow-up	24 weeks
Sources of funding	Not industry funded
Sample size	Total sample size*: 51** *Data from untreated control arm **One child had resolving acute otitis media and one child had unilateral dry perforation at randomisation, but they were not excluded from analysis
Other information	Duration of OME before study was less than 2 weeks. The diagnosis of OME was confirmed by tympanometry and otoscopy. OME was defined as type B tympanogram with or without mild bulging or fluid behind an intact tympanic membrane, reduced mobility on pneumatic otoscopy. Normal ear was defined as absence of infection or inflammation, normal mobility on pneumatic otoscopy, and type A, C1 or C2 tympanogram.
Outcomes	Resolution of current episode of OME (number of children)*: 24 weeks: 5/51 *Data from untreated control arm

OME: otitis media with effusion

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 three Aboriginal communities 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?	Yes *(The authors conducted a sample size calculation to determine an adequate sample size)*
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Age, gender, birth weight, and gestational age were reported for those with OME, and the setting was 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?	No *(Initial response rate (for participating in the study) is 67%. 13% (of total*

Section	Question	Answer
		control group) were lost to follow-up or discontinued placebo, and characteristics of those lost to follow-up not reported)

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

2 **Lous, 1981**

Bibliographic Reference	Lous, J; Fiellau-Nikolajsen, M; Epidemiology and middle ear effusion and tubal dysfunction. A one-year prospective study comprising monthly tympanometry in 387 non-selected 7-year-old children.; International journal of pediatric otorhinolaryngology; 1981; vol. 3 (no. 4); 303-17

3 **Study details**

Country/ies where study was carried out	Denmark
Study type	Observational single group (non-comparative) study
Study dates	August 1978 - August 1979
Inclusion criteria	Children from two rural municipalities who started schooling (1st grade) in August 1978
Exclusion criteria	Not reported
Patient characteristics	Age range in years*: 6.5-7.5 Sex (male/female)*: 190/197 Otological treatment during study period*: Adenoidectomy and paracentesis: 1/387 Adenoidectomy alone: 3/387 *Reported for total study sample only

Duration of follow-up	12 months
Sources of funding	Not industry funded
Sample size	Total study sample: 387 Number of children with OME during 12 months: 100 Number of episodes of OME in 100 children during 12 months: 139
Other information	Duration of OME before the study not reported where this was known. The study stated that time of onset of 22/139 episodes of OME is unknown. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Classification of tympanometry types was based on the following criteria: A: pressure >100 mmH2O B: flat curves plus otoadmittance <0.20 millimhos, absolute gradient <0.04 millimhos, and absence of ipsilateral acoustic reflex C: pressure ≤-100 mmH2O (tubal dysfunction)
Outcomes	Resolution of current episode of OME (number of children): 1 month: 56/100 2 months: 69/100 3 months: 73/100 4 months: 81/100 5 months: 84/100 12 months: 99/100 Recurrence of OME (following spontaneous resolution) (number of children): 12 months: 35/100

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 two rural municipalities 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 (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?	No *(Age and gender were reported for the whole sample, but not for those with OME. 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 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. 11% (of total study sample) were lost to follow-up, and characteristics of those lost to follow-up not reported)*

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

2 **Rach, 1991**

Bibliographic Reference	Rach, G H; Zielhuis, G A; van Baarle, P W; van den Broek, P; The effect of treatment with ventilating tubes on language development in preschool children with otitis media with effusion.; Clinical otolaryngology and allied sciences; 1991; vol. 16 (no. 2); 128-32

3 **Study details**

Country/ies where study was carried out	Netherlands
Study type	Untreated control arm from comparative experimental study
Study dates	Not reported
Inclusion criteria	Children with confirmed bilateral OME
Exclusion criteria	Children with congenital ear problems (for example, sensorineural hearing loss) or speech-producing apparatus defects (for example, cleft palate), serious or neurological visual disorders, emotional or mental disorders, chronic diseases, and history of prolonged hospitalisation (≥6 weeks) or chronic otorrhoea
Patient characteristics	Age in years: 2 Children did not have treatments for OME before the study (for example, adenoidectomy, tonsillectomy, antral washout, myringotomy or grommets)
Duration of follow-up	6 months
Sources of funding	Not industry funded
Sample size	Total sample size*: 21

	*Data from untreated control arm
Other information	Duration of OME before the study is 3-6 months in n=7 children and at least 6 months in n=14 children. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry and impedance measurements.
Outcomes	Resolution of current episode of OME (number of ears)*: 3 months: 3/42 6 months: 12/42 *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 small geographical area (Nijmegen))*
Participant sampling	Were study participants sampled in an appropriate way?	Yes *(A complete sample is used (93% of a birth cohort of 2-year-old children participated 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?	Yes *(Characteristics of the study subjects, including age and duration of OME, 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)*

Section	Question	Answer
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?	No *(Initial response rate (for participating in the study) is low (18%), although data is available for all participants.)*

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

Reves, 1985

Bibliographic Reference	Reves, R; Budgett, R; Miller, D; Wadsworth, J; Haines, A; Study of middle ear disease using tympanometry in general practice.; British medical journal (Clinical research ed.); 1985; vol. 290 (no. 6486); 1953-6

Study details

Country/ies where study was carried out	UK
Study type	Observational single group (non-comparative) study
Study dates	November 1983 to February 1984
Inclusion criteria	Children aged 3 months to 6 years, registered at a GP practice in North-West London

Exclusion criteria	Not reported
Patient characteristics	Total study sample = 264 children. For this review, data extracted for B-tympanogram at entry to the study. N=68 children (N=29 children in 1 ear; N=39 children both ears). Data analysed for those without missing data N=64.
Duration of follow-up	Follow-up at least 3 months (longer in 41% of those with OME)
Sources of funding	Not reported
Sample size	N=64 children
Other information	Duration of OME before the study is unknown.
Outcomes	Resolution of current episode of OME (defined as number of ears that changed from having a type B tympanogram to a type A or C tympanogram): 3 months: 29/64 (45.3%) of children showed resolution of OME (29.7% changed to type As or C, and 15.6% to type A)

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 GP practice that covers a deprived population)*
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)*

Section	Question	Answer
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	No *(No demographic 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 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 *(Initial response rate (for participating in the study) was 89% and data was not available for 31% (of total study sample). No reasons for non-response provided, and no comparison of responders versus non-responders)*

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

2 **Thomsen, 1981**

Bibliographic Reference	Thomsen, J; Tos, M; Spontaneous improvement of secretory otitis. A long-term study.; Acta oto-laryngologica; 1981; vol. 92 (no. 56); 493-9

3 **Study details**

Country/ies where study was carried out	Denmark
Study type	Observational single group (non-comparative) study
Study dates	November 1977 to February 1980
Inclusion criteria	Healthy children aged 2 years at the first test (born between the 1st and the 10th of every month in 1976), and living (at the time of the first test) in either of 2 Copenhagen municipalities
Exclusion criteria	Not reported
Patient characteristics	Total study sample = 184 children (368 ears) with complete data for all 6 tests. For total study sample, there were 92 male and 92 female. For this review, data extracted for those with B-tympanogram at 1st examination. Number of children not reported but number of ears with B-tympanogram was 48. All included children were 2 years old at the time of the 1st test and 4 years old at the time of the 6th (final) test.
Duration of follow-up	27 months
Sources of funding	Not reported
Sample size	48 ears (number of children not reported)
Other information	Duration of OME before the study is unknown.
Outcomes	Resolution of current episode of OME (defined as number of ears that changed from having a type B tympanogram to a type A or C tympanogram): 27 months: 40/48 (84%) ears resolved (19% changed to type A, 21% to type C1, and 44% to type C2)

1 *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?	No *(Participants not sampled from the population randomly (those born on the 1st to the 10th of every month in 1976 were selected))*
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?	No *(All participants were 2 years old at 1st test and 4 years old at 6th (and final test), and gender reported for the total sample, 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 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)*

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. 34% (of total study sample) did not have complete data for all 6 tests and were not included in the analysis. No reasons for non-response provided. Paper reports that there were no differences between dropouts and completers but neither data nor statistical analysis reported, and no comparison of initial responders versus non-responders.)*

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

2 **Tos, 1980**

Bibliographic Reference	Tos, M.; Spontaneous improvement of secretory otitis and impedance screening; Archives of Otolaryngology; 1980; vol. 106 (no. 6); 345-349

3 **Study details**

Country/ies where study was carried out	Denmark
Study type	Observational single group (non-comparative) study
Study dates	1977 - 1978
Inclusion criteria	Infants* and 2-year-old children *The study included infant group and children group, but data on outcomes of interest was only reported for the children group.
Exclusion criteria	Not reported
Patient characteristics	Characteristics of children group: Age in years: 2

Duration of follow-up	9 months in children group
Sources of funding	Not reported
Sample size	Children group: Total study sample: 222 Number of ears with OME (number of children not reported) at first examination: 51
Other information	Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Classification of tympanometry types was based on the following criteria (middle ear pressure): A: 0 to -99 mm H2O B: flat curve C1: -100 to -199 mm H2O C2: -200 to -350 mm H2O
Outcomes	Resolution of current episode of OME (B to A tympanogram; number of ears): 3 months: 6/51 6 months: 16/51 9 months: 24/51 Resolution of current episode of OME (B to A or C1 tympanogram; number of ears): 3 months: 13/51 6 months: 24/51 9 months: 34/51 Resolution of current episode of OME (B to non-B tympanogram; number of ears): 3 months: 27/51 6 months: 34/51 9 months: 44/51 Recurrence of OME (following spontaneous resolution) (non-B to B tympanogram; number of ears): 6 months: 4/51

	9 months: 5/51

OME: otitis media with effusion

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 (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?	No *(Age was reported for the whole sample, but not for those with OME. 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 otoscopy 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.)*

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

Tos, 1982

Bibliographic Reference	Tos, M; Holm-Jensen, S; Sorensen, C H; Mogensen, C; Spontaneous course and frequency of secretory otitis in 4-year-old children.; Archives of otolaryngology (Chicago, Ill. : 1960); 1982; vol. 108 (no. 1); 4-10

Study details

Country/ies where study was carried out	Denmark
Study type	Observational single group (non-comparative) study
Study dates	February 1979 – February 1980
Inclusion criteria	Healthy children aged 4 years who were born the first ten days of every month in 1976
Exclusion criteria	Not reported
Patient characteristics	Age in years: 4 Number of children with grommets: 20/373 (5%) Number of ears with grommets: 35/746 (5%)

Duration of follow-up	12 months
Sources of funding	Not reported
Sample size	Total study sample: 373 Number of ears with OME (number of children not reported) at first examination: 87
Other information	Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Classification of tympanometry types was based on the following criteria (middle ear pressure): A: 0 to -99 mm H2O B: flat curve C1: -100 to -199 mm H2O C2: -200 to -350 mm H2O
Outcomes	Resolution of current episode of OME (B to A tympanogram; number of ears): 3 months: 3/87 6 months: 17/87 Resolution of current episode of OME (B to A or C1 tympanogram; number of ears): 3 months: 12/87 6 months: 31/87 9 months: 37/82 Resolution of current episode of OME (B to non-B tympanogram; number of ears): 3 months: 51/87 6 months: 62/87 9 months: 60/82 12 months: 64/82 Recurrence of OME (following spontaneous resolution) (non-B to B tympanogram; number of ears): 6 months: 14/82 9 months: 23/82

	12 months: 27/82

OME: otitis media with effusion

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 2 municipalities in a small geographical area)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants not sampled from the population randomly (Participants born the first 10 days of every month in 1976 were recruited))*
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?	No *(Age reported for whole sample, but not for those with OME. 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 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)*

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. 22 % (of total study sample) were lost to follow-up, and characteristics of those lost to follow-up not reported)*

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

2 **Williamson, 1994**

Bibliographic Reference	Williamson, I G; Dunleavey, J; Bain, J; Robinson, D; The natural history of otitis media with effusion--a three-year study of the incidence and prevalence of abnormal tympanograms in four South West Hampshire infant and first schools.; The Journal of laryngology and otology; 1994; vol. 108 (no. 11); 930-4

3 **Study details**

Country/ies where study was carried out	UK
Study type	Observational single group (non-comparative) study
Study dates	September 1988 to summer term 1991
Inclusion criteria	Children aged 5 to 8 years attending 1 of 4 schools in southwest Hampshire
Exclusion criteria	Not reported
Patient characteristics	Total study sample = 856 children. For this review, data extracted for a sample of 50 children (67 ears) with B-tympanogram at screening in Spring 1990 as this is the only usable data on outcomes of interest.
Duration of follow-up	12 months

Sources of funding	Not reported
Sample size	50 children, 67 ears
Other information	Duration of OME before study is unknown. During the 12-month follow-up period 6/50 children (12% of children, 10.4% of ears) were treated with grommet insertion.
Outcomes	Resolution of current episode of OME (defined as number of children and number of ears with type B tympanograms at screening in Spring 1990 but not at follow-up timepoint): 4 months: 22/50 (44%) children and 35/67 (52%) ears resolved 8 months: 38/50 (76%) children and 52/67 (78%) ears resolved 12 months: 45/50 (90%) children and 61/67 (91%) ears resolved Recurrence of OME, following resolution (defined as number of children and number of ears that had shown clearance followed by recurrence during the 12-month follow-up period): 12 months: 4/45 (9%) children and 5/61 (8%) recurrence

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 schools in a small geographical area (suburban and close to the coast) and the catchment area of the schools included groups with similar sociodemographic characteristics)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants not sampled from the population randomly (children selected for screening from individual class lists in alphabetical order))*
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)*

Section	Question	Answer
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	No *(Only age bands were reported (for whole sample and not for those with OME). 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 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) was 75%. On average there was missing data for 2.6% of children for each screening. No reasons for non-response provided, and no comparison of responders versus non-responders)*

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

2 **Williamson, 2009**

Bibliographic Reference	Williamson, Ian; Benge, Sarah; Barton, Sheila; Petrou, Stavros; Letley, Louise; Fasey, Nicky; Haggard, Mark; Little, Paul; Topical intranasal corticosteroids in 4-11 year old children with persistent bilateral otitis media with effusion in primary care: double blind randomised placebo controlled trial.; BMJ (Clinical research ed.); 2009; vol. 339; b4984

3 **Study details**

Country/ies where study was carried out	UK
Study type	Untreated control arm from comparative experimental study
Study dates	2004 - 2007
Inclusion criteria	Children aged 4-11 years with a history of otitis media and OME confirmed by tympanometry
Exclusion criteria	Children aged less than 4 years with normal tympanogram (i.e., A or C1), large amounts of ear wax, uninterpretable tympanograms, grommets, tympanic membrane perforation, planned ear surgery, frequent or heavy epistaxis, developmental concerns, hypersensitivity to mometasone, risk of recurrent disease (for example, cleft palate, Down's syndrome, primary ciliary dyskinesia, Kartagener's syndrome, and immunodeficiency) or systemic steroid therapy
Patient characteristics	Mean age in months (SD)*: 72.1 (18.6) Sex (male/female)*: 63/49 Children with atopy*: 33/112 Previous treatments for OME*: Grommets inserted >12 months before randomisation: 2/102 Adenoidectomy before randomisation: 2/102 *Data from untreated control arm
Duration of follow-up	9 months
Sources of funding	Not industry funded
Sample size	Total sample size*: 112

	*Data from untreated control arm
Other information	Duration of OME before the study is unknown. The diagnosis of OME (B/B or B/C2 types) was confirmed by tympanometry. Tympanometry types A and C1 were accepted as normal. Classification of tympanometry types was based on the following criteria (middle ear pressure): A: 200 to -1000 daPa B: ≤−400 daPa (flat trace) C1: -100 to -199 daPa C2: -200 to -399 daPa
Outcomes	Resolution of current episode of OME (B or C2 to A or C1 in at least one ear; number of children)*: 1 month: 44/98 3 months: 45/86 9 months: 47/72 *Data from untreated control arm

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?	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?	Yes *(The authors conducted a sample size calculation to determine an adequate sample size)*

Section	Question	Answer
Reporting of characteristics and setting	Were the study subjects and the setting described in detail?	Yes *(Age, gender, ethnicity, and socioeconomic status were reported for those with OME, and the setting was 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?	Yes *(Details reported on those collecting data and training received, and on validity checks (regular calibration of tympanometers and follow-up advice provided))*
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 participants in control arm) were lost to follow-up, and characteristics of those lost to follow-up not reported)*

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

2 **Wynings, 2022**

Bibliographic Reference	Wynings, Erin M; Jaffal, Hussein; St John, Rachel; Johnson, Romaine F; Chorney, Stephen R; Mechanical ventilation and middle ear effusions among tracheostomy-dependent children.; International journal of pediatric otorhinolaryngology; 2022; vol. 155; 111062

3 **Study details**

Country/ies where study was carried out	USA
Study type	Untreated control arm from comparative observational study
Study dates	January 2015 - January 2020
Inclusion criteria	Children aged less than 2 years who had a tracheostomy at Children's Medical Center Dallas
Exclusion criteria	Children with abnormal tympanograms or children obtaining myringotomy with or without grommet before tracheostomy
Patient characteristics	Mean age in months (SD): 5.6 (3.4) Sex (male/female): 34/26 Passed new-born hearing: 36 Tracheostomy indication: Respiratory failure: 43/59 Airway obstruction: 16/59
Duration of follow-up	Mean duration of follow up 8.8 months (duration between two assessments)
Sources of funding	Not reported
Sample size	Total sample size (children who developed OME): 60 Number of children with repeat tympanometry assessments: 41
Other information	Participants did not have OME before the study. The primary outcome of the study was development of middle ear effusion, and this review reported the data on children who developed OME and had repeat tympanometry assessments.

	The duration of OME prior to first assessment where it was detected is unknown. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry.
Outcomes	Resolution of current episode of OME (number of children): 8.8 months: 8/41

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?	No *(Sample taken from a single GP practice that covers a deprived population)*
Participant sampling	Were study participants sampled in an appropriate way?	No *(Participants do not appear to have been sampled from the population randomly (children aged less than 2 years with tracheostomy))*
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?	Yes *(Characteristics of the study subjects, including age, gender, race, ethnicity and comorbidities, 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)*

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?	No *(Initial response rate (for participating in the study) is not reported. Data is not available for 32% (of children with OME) of participants, and no further details reported)*

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

2 **Zeisel, 1995**

Bibliographic Reference	Zeisel, S A; Roberts, J E; Gunn, E B; Riggins, R Jr; Evans, G A; Roush, J; Burchinal, M R; Henderson, F W; Prospective surveillance for otitis media with effusion among black infants in group child care.; The Journal of pediatrics; 1995; vol. 127 (no. 6); 875-80

3 **Study details**

Country/ies where study was carried out	USA
Study type	Observational single group (non-comparative) study
Study dates	Not reported
Inclusion criteria	Healthy black infants aged 6 to 12 months, enrolled in (1 of 9) participating childcare centres
Exclusion criteria	Not reported

Patient characteristics	Total study sample = 102 children. For total study sample, there were 51 male and 51 female, and mean age at first examination was 8.1 months (SD=1.8). For this review, data extracted for those who had at least 4 months of continuous bilateral effusion at some point during the observation period (N=66), minus those who had ventilation tubes inserted (N=6) or were lost to follow-up (N=5), resulting in a sample with complete data for N=57, as this is the only usable data on outcomes of interest.
Duration of follow-up	16 months
Sources of funding	Not industry funded
Sample size	Number of children = 57 (number of ears not reported)
Other information	Duration of OME before study is unknown. The diagnosis of OME confirmed by tympanometry (type B tympanogram) and otoscopy but was based on otoscopy when there were discrepant findings. Resolution of OME defined as being free of bilateral effusion for at least 6 consecutive weeks, but tympanometric/otoscopic definition was not reported.
Outcomes	Resolution of current episode of OME (diagnosis of bilateral effusion based on otoscopic and the tympanometric diagnoses). Sample included children who had at least 4 months of continuous bilateral effusion at some point during the observation period. Resolution defined as spontaneous resolution of bilateral effusion (free of bilateral effusion for at least 6 consecutive weeks): 3 months (following the attainment of the 4-month criterion): 27/57 (47%) children showed spontaneous resolution

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 childcare centres 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 (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?	No *(Mean age, gender and ethnic status were reported for the whole sample, but not for those with OME. 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 *(Condition identified based on otoscopic and the tympanometric diagnoses)*
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Yes *(Details reported on those collecting data and training received, and on validity checks between healthcare professionals, and details given about which of the methods was favoured when there was disagreement between the otoscopic and the tympanometric diagnoses (otoscopic diagnosis was used in analyses))*
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?	No *(Initial response rate (for participating in the study) is not reported. 19% (of total study sample) were lost to follow-up, and there were significant differences between those lost to follow-up and completers in the proportion with bilateral OME (higher percentages in those lost to follow-up in 2 time intervals))*

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

2 **Zielhuis, 1990**

Bibliographic Reference	Zielhuis, G A; Rach, G H; van den Broek, P; The natural course of otitis media with effusion in preschool 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; 1990; vol. 247 (no. 4); 215-21

3 **Study details**

Country/ies where study was carried out	Netherlands
Study type	Observational single group (non-comparative) study
Study dates	Not reported
Inclusion criteria	Children who were born between 1 September 1982 and 31 August 1983 and living in Nijmegen on their 2nd birthday
Exclusion criteria	Not reported
Patient characteristics	Age in years: 2
Duration of follow-up	24 months

Sources of funding	Not industry funded
Sample size	Total study sample: 1328 (n=816 children or n=1631 ears with OME) Number of children who completed all 9 assessments: 609 Number of ears with 9 valid tympanograms: 1217
Other information	Duration of OME before the study is unknown. The diagnosis of OME (type B tympanogram) was confirmed by tympanometry. Children were assessed with tympanometry every 3 months from the age of 2 to 4 years. Classification of tympanometry types was based on the following criteria: A: compliance ≥0.2ml and pressure ≥-99 dPa B: compliance <0.2ml or pressure ≤-400 dPa C1: compliance ≥0.2 ml and pressure between -100 and -199 dPa C2: compliance ≥0.2ml and pressure between -200 and -399 dPa
Outcomes	Time to resolution of current episode of OME (data reported per ear)*: 0 months: Effective number of ears at risk: 1529; Resolution probability: 0% 3 months: Effective number of ears at risk: 559; Resolution probability: 61% 6 months: Effective number of ears at risk: 213; Resolution probability: 84% 9 months: Effective number of ears at risk: 93; Resolution probability: 92% 12 months: Effective number of ears at risk: 55; Resolution probability: 95% 15 months: Effective number of ears at risk: 27; Resolution probability: 97% 18 months: Effective number of ears at risk: 15; Resolution probability: 98% 21 months: Effective number of ears at risk: 6; Resolution probability: 98% 24 months: Effective number of ears at risk: 4; Resolution probability: 99%

	*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.

OME: otitis media with effusion

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 medium-sized city in a small geographical area)*
Participant sampling	Were study participants sampled in an appropriate way?	Yes *(A complete sample used (All children born between 1 September 1982 and 31 August 1983 were enrolled in the study))*
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?	No *(Age was reported whole sample, but not for those with OME. 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 used)*

Section	Question	Answer
Measurement of condition	Was the condition measured in a standard, reliable way for all participants?	Yes *(Details reported on those collecting data and training received, and the condition was measured in the same way for all participants)*
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?	No *(Initial response rate (for participating in the study) is 92%. However, 55% (of total study sample) did not have complete data for all 9 tests. The Kaplan-Meier survival analysis included ears with incomplete follow-up; however, insufficient information was reported about length of follow-up and censoring. No reasons for non-response provided. No comparison of initial responders versus non-responders and no comparison of dropouts versus completers))*

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

2

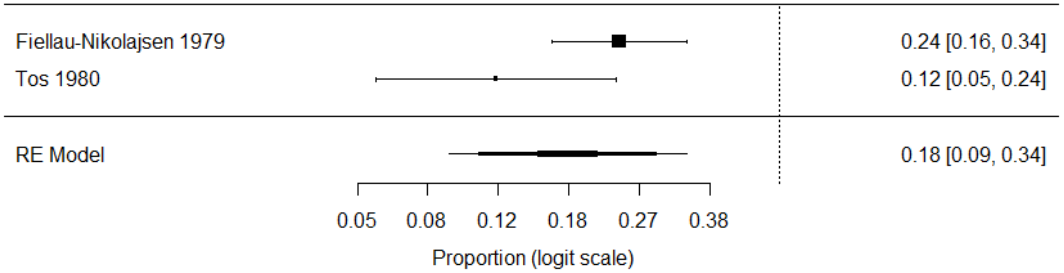
Appendix E Forest plots

Forest plots for review question: What is the progression, resolution and recurrence (natural history) of OME without hearing loss at presentation in children under 12 years?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here; the quality assessment for such outcomes is provided in the GRADE profiles in appendix F.

Resolution of OME of unknown duration before follow-up

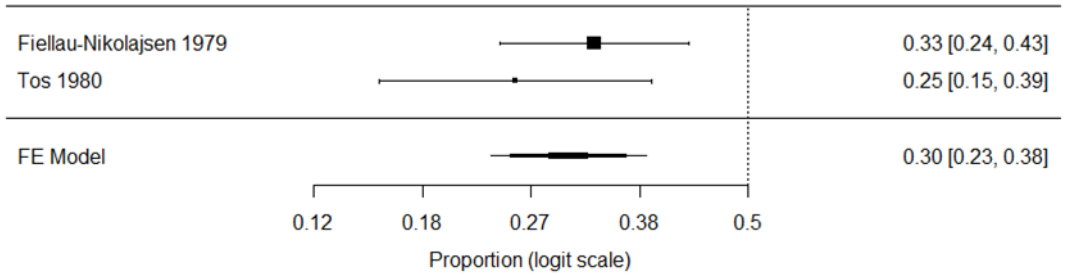
Figure 2: Resolution of OME (defined as change from type B tympanogram to type A tympanogram) at 3 months in children aged under 4 years; unit of analysis=ear



Heterogeneity: I^2 = 67.26%

OME: otitis media with effusion

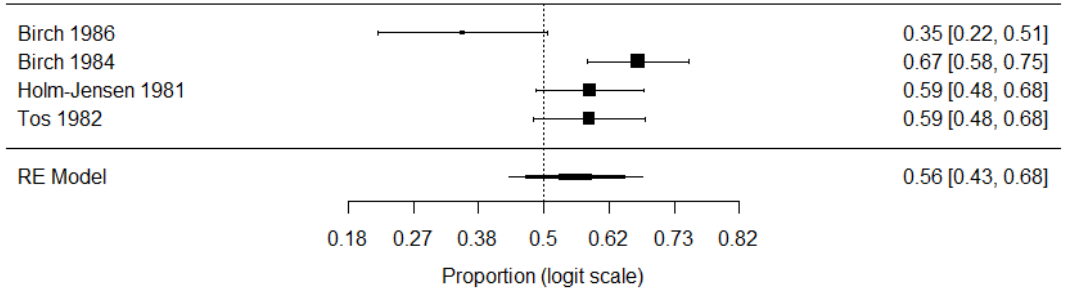
Figure 3: Resolution of OME (defined as change from type B tympanogram to type A or C1 tympanogram) at 3 months in children aged under 4 years; unit of analysis=ear



Heterogeneity: I^2 = 0.00%

OME: otitis media with effusion

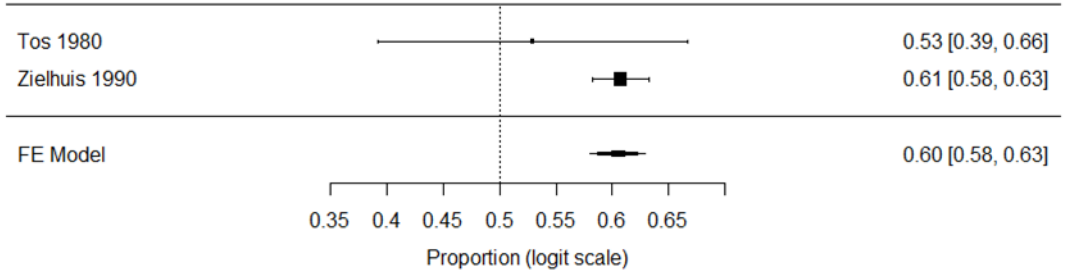
Figure 4: Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 3 months in children aged over 4 years; unit of analysis=ear



Heterogeneity: I^2 = 79.99%

OME: otitis media with effusion

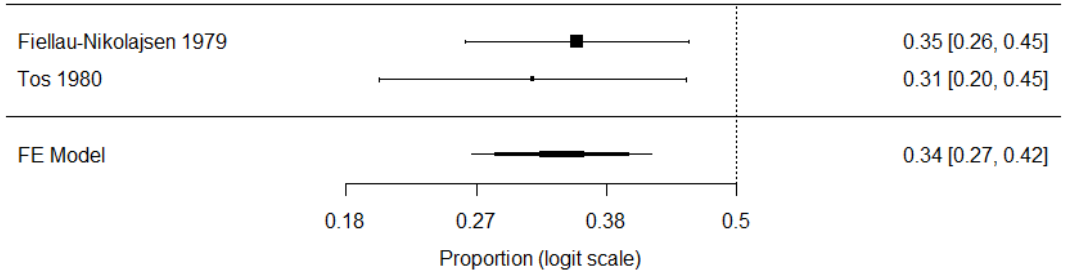
Figure 5: Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 3 months in children aged under 4 years; unit of analysis=ear



Heterogeneity: I^2 = 16.38%

OME: otitis media with effusion

Figure 6: Resolution of OME (defined as change from type B tympanogram to type A tympanogram) at 6 months in children aged under 4 years; unit of analysis=ear

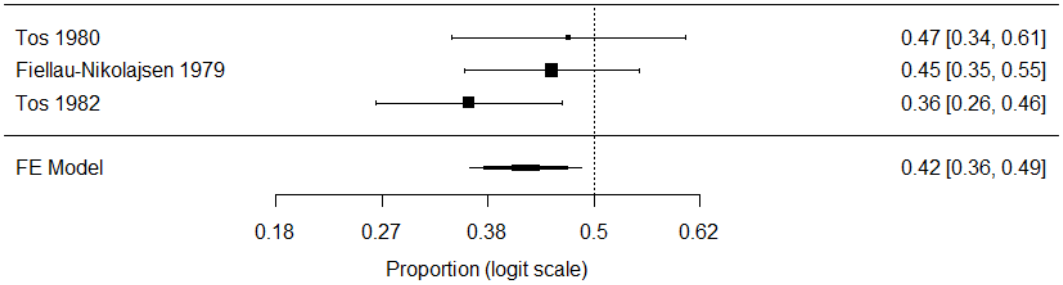


Heterogeneity: I^2 = 0.00%

OME: otitis media with effusion

1

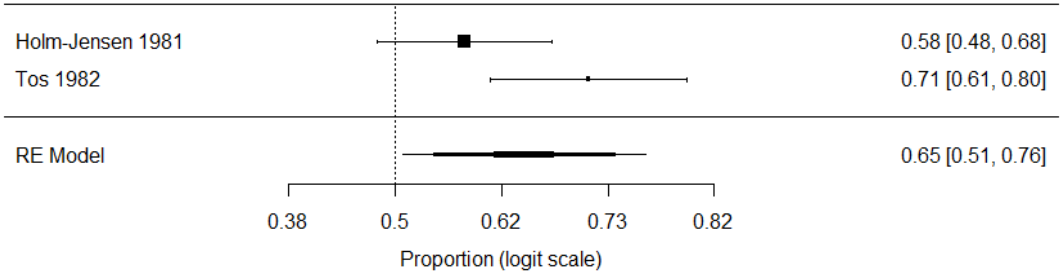
Figure 7: Resolution of OME (defined as change from type B tympanogram to type A or C1 tympanogram) at 6 months; unit of analysis=ear



Heterogeneity: I^2 = 13.85%

OME: otitis media with effusion

Figure 8: Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 6 months in children aged over 4 years; unit of analysis=ear



Heterogeneity: I^2 = 70.48%

OME: otitis media with effusion

2

Appendix F GRADE tables

GRADE tables for review question: What is the progression, resolution and recurrence (natural history) of OME without hearing loss at presentation in children under 12 years?

Table 5: Evidence profile for resolution of OME of <2 weeks 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 non-B tympanogram) at 6 months; unit of analysis=child											
1 (Leach 2008)	untreated control arm from experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/51 (9.8%)	0.10 (0.04 to 0.21)	100 per 1000 (from 40 to 210 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 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 (undefined) at 2 months; unit of analysis=child											
1 (Fiellau-Nikolajsen 1983)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	21/29 (72.4%)	0.72 (0.54 to 0.86)	720 per 1000 (from 540 per 1000 to 860 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 5 months; unit of analysis=child											
1 (Fiellau-Nikolajsen 1983)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	26/29 (89.7%)	0.90 (0.72 to 0.97)	900 per 1000 (from 720 per 1000 to 970 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 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 (undefined) at 3 months; unit of analysis=child											
1 (Fiellau-Nikolajsen 1983)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	16/24 (66.7%)	0.67 (0.46 to 0.82)	670 per 1000 (from 460 per 1000 to 820 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 >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 non-B tympanogram) at 3 months; unit of analysis=ear											
1 (Rach 1991)	untreated control arm from experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/42 (7.1%)	0.07 (0.02 to 0.20)	70 per 1000 (from 20 per 1000 200 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 (Rach 1991)	untreated control arm from experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12/42 (28.6%)	0.29 (0.17 to 0.44)	290 per 1000 (from 170 per 1000 to 440 per 1000)	VERY LOW	IMIPORTANT

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 9: Evidence profile for resolution of OME of >4 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 (undefined) at 3 months; unit of analysis=child											
1 (Zeisel 1995)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	27/57 (47.4%)	0.47 (0.35 to 0.60)	470 per 1000 (from 350 per 1000 to 600 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 10: 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 (defined as change from type B tympanogram to type A tympanogram) at 1 month; unit of analysis=ear											
1 (Fiellau-Nikolajsen 1979)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	14/91 (15.4%)	0.15 (0.09 to 0.24)	150 per 1000 (from 90 per 1000 to 240 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A or C1 tympanogram) at 1 month; unit of analysis=ear											
1 (Fiellau-Nikolajsen 1979)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	20/91 (22.0%)	0.22 (0.15 to 0.32)	220 per 1000 (from 150 per 1000 to 320 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 1 month; unit of analysis=ear											
2 (Birch 1984; Birch 1986)	observational	very serious[1]	very serious inconsistency[3]	no serious indirectness	very serious[2]	none	38/156 (24.4%)	Birch 1984: 0.29 (0.22 to 0.38)	100 to 290 per 1000 (from 40 per 1000 to 380 per 1000)	VERY LOW	IMPORTANT

								Birch 1986: 0.10 (0.04 to 0.24)			
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 1 month; unit of analysis=child											
1 (Lous 1981)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	56/100 (56.0%)	0.56 (0.46 to 0.65)	560 per 1000 (from 460 per 1000 to 650 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B or C2 tympanogram to type A or C1 tympanogram) at 1 month; unit of analysis=child											
1 (Williamson 2009)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	44/98 (44.9%)	0.45 (0.35 to 0.55)	450 per 1000 (from 350 per 1000 to 550 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 1 month; unit of analysis=ear											
1 (Casselbrant 1985)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	90/137 (65.7%)	0.66 (0.57 to 0.73)	660 per 1000 (from 570 per 1000 to 730 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 1 month; unit of analysis=child											
1 (Fiellau-Nikolajsen 1983)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	28/78 (35.9%)	0.36 (0.26 to 0.47)	360 per 1000 (from 260 per 1000 to 470 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 1.5 months; unit of analysis=ear											
2 (Birch 1984; Birch 1986)	observational	very serious[1]	very serious inconsistency[3]	no serious indirectness	very serious[2]	none	67/156 (42.9%)	Birch 1984: 0.48 (0.39 to 0.57) Birch 1986: 0.28 (0.16 to 0.43)	280 to 480 per 1000 (from 160 per 1000 to 570 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 2 months; unit of analysis=ear											
2 (Birch 1984; Birch 1986)	observational	very serious[1]	very serious inconsistency[3]	no serious indirectness	very serious[2]	none	75/156 (48.1%)	Birch 1984: 0.54 (0.45 to 0.63) Birch 1986: 0.30 (0.18 to 0.46)	300 to 540 per 1000 (from 180 per 1000 to 630 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 2 months; unit of analysis=child											

1 (Lous 1981)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	69/100 (69.0%)	0.69 (0.59 to 0.77)	690 per 1000 (from 590 per 1000 to 770 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 2 months; unit of analysis=ear											
1 (Casselbrant 1985)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	107/137 (78.1%)	0.78 (0.70 to 0.84)	780 per 1000 (from 700 per 1000 to 840 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 2.5 months; unit of analysis=ear											
2 (Birch 1984; Birch 1986)	observational	very serious[1]	very serious inconsistency[3]	no serious indirectness	very serious[2]	none	82/156 (52.6%)	Birch 1984: 0.59 (0.49 to 0.67) Birch 1986: 0.35 (0.22 to 0.51)	350 to 590 per 1000 (from 220 per 1000 to 670 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A tympanogram) at 3 months in children aged over 4 years; unit of analysis=ear											
1 (Tos 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/87 (3.4%)	0.03 (0.01 to 0.10)	30 1000 (from 10 per 1000 to 100 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A tympanogram) at 3 months in children aged under 4 years; unit of analysis=ear											
2*	observational	very serious[1]	serious inconsistency[4]	no serious indirectness	very serious[2]	none	28/142 (19.7%)	0.18 (0.09 to 0.34)	180 per 1000 (from 90 per 1000 to 340 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A or C1 tympanogram) at 3 months in children aged over 4 years; unit of analysis=ear											
1 (Tos 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	12/87 (13.8%)	0.14 (0.08 to 0.23)	140 per 1000 (from 80 per 1000 to 230 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A or C1 tympanogram) at 3 months in children aged under 4 years; unit of analysis=ear											
2*	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	43/142 (32.6%)	0.30 (0.23 to 0.38)	300 per 1000 (from 230 per 1000 to 380 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 3 months in children aged over 4 years; unit of analysis=ear											
4*	observational	very serious[1]	serious inconsistency[4]	no serious indirectness	seroius[5]	none	197/335 (58.8%)	0.56 (0.43 to 0.68)	560 per 1000 (from 430 per 1000 to 680 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 3 months in children aged under 4 years; unit of analysis=ear											

2*	observational	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1015/1682 (60.3%)	0.60 (0.58 to 0.63)	600 per 1000 (from 580 per 1000 to 630 per 1000)	LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 3 months in children aged over 6 years; unit of analysis=child											
1 (Lous 1981)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	73/100 (73.0%)	0.73 (0.63 to 0.81)	730 per 1000 (from 630 per 1000 to 810 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 3 months in children aged under 6 years; unit of analysis=child											
1 (Reves 1985)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	29/64 (45.3%)	0.45 (0.34 to 0.58)	450 per 1000 (from 340 per 1000 to 580 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=child											
1 (Williamson 2009)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	45/86 (52.3%)	0.52 (0.42 to 0.63)	520 per 1000 (from 420 per 1000 to 630 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 3 months; unit of analysis=ear											
1 (Casselbrant 1985)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	128/137 (93.4%)	0.93 (0.88 to 0.97)	930 per 1000 (from 880 per 1000 to 970 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 3 months; unit of analysis=child; observational study											
1 (Fiellau-Nikolajsen 1983)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	46/78 (59.0%)	0.59 (0.48 to 0.69)	590 per 1000 (from 480 per 1000 to 690 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 3 months; unit of analysis=child; untreated control arm from experimental study											
1 (Hughes 1984)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/16 (37.5%)	0.37 (0.18 to 0.62)	370 per 1000 (from 180 per 1000 to 620 per 1000)	VERY LOW	IMPORTANT

Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 4 months; unit of analysis=ear											
1 (Williamson 1994)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	35/67 (52.2%)	0.52 (0.40 to 0.64)	520 per 1000 (from 400 per 1000 to 640 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 4 months in children in Denmark; unit of analysis=child											
1 (Lous 1981)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	81/100 (81.0%)	0.81 (0.72 to 0.88)	810 per 1000 (from 720 per 1000 to 880 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 4 months in children in UK; unit of analysis=child											
1 (Williamson 1994)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	22/50 (44.0%)	0.44 (0.31 to 0.58)	440 per 1000 (from 310 per 100 to 580 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 4 months; unit of analysis=ear											
1 (Casselbrant 1985)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	131/137 (95.6%)	0.96 (0.91 to 0.98)	960 per 1000 (from 910 per 1000 to 980 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 5 months; unit of analysis=child											
1 (Lous 1981)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	84/100 (84.0%)	0.84 (0.75 to 0.90)	840 per 1000 (from 750 per 1000 to 900 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 5 months; unit of analysis=ear											
1 (Casselbrant 1985)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	133/137 (97.1%)	0.97 (0.92 to 0.99)	970 per 1000 (from 920 per 1000 to 990 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A tympanogram) at 6 months in children aged over 4 years; unit of analysis=ear											
1 (Tos 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	17/87 (19.5%)	0.20 (0.13 to 0.29)	200 per 1000 (from 130 per 1000 to 290 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A tympanogram) at 6 months in children aged under 4 years; unit of analysis=ear											
2*	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	48/142 (33.8%)	0.34 (0.27 to 0.42)	340 per 1000 (from 270 per 1000 to 420 per 1000)	VERY LOW	IMPORTANT

Resolution of OME (defined as change from type B tympanogram to type A or C1 tympanogram) at 6 months; unit of analysis=ear											
3*	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	96/229 (41.9%)	0.42 (0.36 to 0.49)	420 per 1000 (from 360 per 1000 to 490 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 6 months in children aged over 4 years; unit of analysis=ear											
2*	observational	very serious[1]	serious inconsistency[4]	no serious indirectness	very serious[2]	none	116/180 (64.4%)	0.65 (0.51 to 0.76)	650 per 1000 (from 510 per 1000 to 760 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 6 months in children ages under 4 years in Denmark; unit of analysis=ear											
1 (Tos 1980)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	34/51 (66.7%)	0.67 (0.53 to 0.78)	670 per 1000 (from 530 per 1000 to 780 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 6 months in children aged under 4 years in Netherlands; unit of analysis=ear											
1 (Zielhuis 1990)	observational	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1394/1631 (85.5%)	0.85 (0.84 to 0.87)	850 per 1000 (from 840 per 1000 to 870 per 1000)	LOW	IMPORTANT
Resolution of OME (undefined) at 6 months; unit of analysis=ear											
1 (Casselbrant 1985)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	134/137 (97.8%)	0.98 (0.93 to 0.99)	980 per 1000 (from 930 to 990 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (undefined) at 6 months; unit of analysis=child											
1 (Fiellau-Nikolajsen 1983)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	53/78 (67.9%)	0.68 (0.57 to 0.77)	680 per 1000 (from 570 per 1000 to 770 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 8 months; unit of analysis=ear											
1 (Williamson 1994)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	52/67 (77.6%)	0.78 (0.66 to 0.86)	780 per 1000 (from 660 per 1000 to 860 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 8 months; unit of analysis=child											
1 (Williamson 1994)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	38/50 (76.0%)	0.76 (0.62 to 0.86)	760 per 1000 (from 620 per 1000 to 860 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A tympanogram) at 9 months; unit of analysis=ear											

1 (Tos 1980)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	24/51 (47.1%)	0.47 (0.34 to 0.61)	470 per 1000 (from 340 per 1000 to 610 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A or C1 tympanogram) at 9 months in children aged over 4 years; unit of analysis=ear											
1 (Tos 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	37/82 (45.1%)	0.45 (0.35 to 0.56)	450 per 1000 (from 350 per 1000 to 560 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to type A or C1 tympanogram) at 9 months in children aged under 4 years; unit of analysis=ear											
1 (Tos 1980)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	34/51 (66.7%)	0.67 (0.53 to 0.78)	670 per 1000 (from 530 per 1000 to 780 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 9 months in children aged over 4 years; unit of analysis=ear											
1 (Tos 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	60/82 (733.2%)	0.73 (0.63 to 0.82)	730 per 1000 (from 630 to 820 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 9 months in children aged under 4 years in Denmark; unit of analysis=ear											
1 (Tos 1980)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	44/51 (86.3%)	0.86 (0.74 to 0.93)	860 per 1000 (from 740 per 1000 to 930 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 9 months in children aged under 4 years in Netherlands; unit of analysis=ear											
1 (Zielhuis 1990)	observational	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1502/1631 (92.1%)	0.92 (0.91 to 0.93)	920 per 1000 (from 910 per 1000 to 930 per 1000)	LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 9 months; unit of analysis=child											
1 (Wynings 2022)	untreated control arm from comparative observational study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/41 (19.5%)	0.20 (0.10 to 0.34)	200 per 1000 (from 100 per 1000 to 340 per 1000)	VERY 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 (Williamson 2009)	untreated control arm from	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	47/72 (65.3%)	0.65 (0.54 to 0.75)	650 per 1000 (from 540 per 1000 to 750 per 1000)	VERY LOW	IMPORTANT

	comparative experimental study										
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 12 months in children aged over 4years in Denmark; unit of analysis=ear											
1 (Tos 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	64/82 (78.0%)	0.78 (0.68 to 0.86)	780 per 1000 (from 680 per 1000 to 860 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 12 months in children aged over 4 years in UK; unit of analysis=ear											
1 (Williamson 1994)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	61/67 (91.0%)	0.91 (0.81 to 0.96)	910 per 1000 (from 810 per 1000 to 960 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 12 months in children aged under 4 years; unit of analysis=ear											
1 (Zielhuis 1990)	observational	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1543/1631 (94.6%)	0.95 (0.93 to 0.96)	950 per 1000 (from 930 per 1000 to 960 per 1000)	LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 12 months in children in Denmark; unit of analysis=child											
1 (Lous 1981)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	99/100 (99.0%)	0.99 (0.93 to 1.00)	990 per 1000 (from 930 per 1000 to 1000 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 12 months in children in UK; unit of analysis=child											
1 (Williamson 1994)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	45/50 (90.0%)	0.90 (0.78 to 0.96)	900 per 1000 (from 780 per 1000 to 960 per 1000)	VERY LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 15 months; unit of analysis=ear											
1 (Zielhuis 1990)	observational	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1579/1631 (96.8%)	0.97 (0.96 to 0.98)	970 per 1000 (from 960 per 1000 to 980 per 1000)	LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 18 months; unit of analysis=ear											
1 (Zielhuis 1990)	observational	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1593/1631 (97.7%)	0.98 (0.97 to 0.98)	980 per 1000 (from 970 per 1000 to 980 per 1000)	LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 21 months; unit of analysis=ear											

1 (Zielhuis 1990)	observational	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1602/1631 (98.2%)	0.98 (0.97 to 0.99)	980 per 1000 (from 970 per 1000 to 990 per 1000)	LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 24 months; unit of analysis=ear											
1 (Zielhuis 1990)	observational	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1608/1631 (98.6%)	0.99 (0.98 to 0.99)	990 per 1000 (from 980 per 1000 to 990 per 1000)	LOW	IMPORTANT
Resolution of OME (defined as change from type B tympanogram to non-B tympanogram) at 27 months; unit of analysis=ear											
1 (Thomsen 1981)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	40/48 (83.3%)	0.83 (0.70 to 0.91)	830 per 1000 (from 700 per 1000 to 910 per 1000)	VERY LOW	IMPORTANT

CI: confidence interval; JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion
**See corresponding forest plot*
[1]Very serious risk of bias in the evidence contributing to the outcomes as per JBI
[2]<150 events
[3] Very serious heterogeneity unexplained by subgroup analysis
[4] Serious heterogeneity unexplained by subgroup analysis
[5]<300-≥150 events

Table 11: Evidence profile for recurrence of OME

Quality assessment							No of patients	Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**		**Relative (95% CI)**	**Absolute**		
Recurrence of OME (following spontaneous resolution; undefined) at 3 months; unit of analysis=child											
1 (Hughes 1984)	untreated control arm from comparative experimental study	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/6 (0.0%)	0.07 (0.00 to 0.58)	70 per 1000 (from 0 per 1000 to 580 per 1000)	VERY LOW	IMPORTANT
Recurrence of OME (following spontaneous resolution; defined as change from non-B tympanogram to type B tympanogram) at 6 months in children aged over 4 years; unit of analysis=ear											
1 (Tos 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	14/82 (17.1%)	0.17 (0.10 to 0.27)	170 per 1000 (from 100 per 1000 to 270 per 1000)	VERY LOW	IMPORTANT

Recurrence of OME (following spontaneous resolution; defined as change from non-B tympanogram to type B tympanogram) at 6 months in children aged under 4 years; unit of analysis=ear											
1 (Tos 1980)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/51 (7.8%)	0.08 (0.03 to 0.19)	80 per 1000 (from 30 per 1000 to 190 per 1000)	VERY LOW	IMPORTANT
Recurrence of OME (following spontaneous resolution; undefined) at 6 months; unit of analysis=child											
1 (Fiellau-Nikolajsen 1983)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	14/78 (17.9%)	0.18 (0.11 to 0.28)	180 per 1000 (from 110 per 1000 to 280 per 1000)	VERY LOW	IMPORTANT
Recurrence of OME (following spontaneous resolution; defined as change from non-B tympanogram to type B tympanogram) at 9 months in children aged over 4 years; unit of analysis=ear											
1 (Tos 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	23/82 (28.0%)	0.28 (0.19 to 0.39)	280 per 1000 (from 190 per 1000 to 390 per 1000)	VERY LOW	IMPORTANT
Recurrence of OME (following spontaneous resolution; defined as change from non-B tympanogram to type B tympanogram) at 9 months in children aged under 4 years; unit of analysis=ear											
1 (Tos 1980)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/51 (9.8%)	0.10 (0.04 to 0.21)	100 per 1000 (from 40 per 1000 to 210 per 1000)	VERY LOW	IMPORTANT
Recurrence of OME (following spontaneous resolution; defined as change from non-B tympanogram to type B tympanogram) at 12 months in children in Denmark; unit of analysis=ear											
1 (Tos 1982)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	27/82 (32.9%)	0.33 (0.24 to 0.44)	330 per 1000 (from 240 per 1000 to 440 per 1000)	VERY LOW	IMPORTANT
Recurrence of OME (following spontaneous resolution; defined as change from non-B tympanogram to type B tympanogram) at 12 months in children in UK; unit of analysis=ear											
1 (Williamson 1994)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/61 (8.2%)	0.08 (0.03 to 0.18)	80 per 1000 (from 30 per 1000 to 180 per 1000)	VERY LOW	IMPORTANT
Recurrence of OME (following spontaneous resolution; defined as change from non-B tympanogram to type B tympanogram) at 12 months in children in Denmark; unit of analysis=child											
1 (Lous 1981)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	35/100 (35.0%)	0.35 (0.26 to 0.45)	350 per 1000 (from 260 per 1000 to 450 per 1000)	VERY LOW	IMPORTANT

Recurrence of OME (following spontaneous resolution; defined as change from non-B tympanogram to type B tympanogram) at 12 months in children in UK; unit of analysis=child											
1 (Williamson 1994)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/45 (8.9%)	0.09 (0.03 to 0.21)	90 per 1000 (from 30 per 1000 to 210 per 1000)	VERY LOW	IMPORTANT
Recurrence of OME (following spontaneous resolution; undefined) at 12 months; unit of analysis=ear											
1 (Casselbrant 1985)	observational	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	45/134 (33.6%)	0.34 (0.26 to 0.42)	340 per 1000 (from 260 per 1000 to 420 per 1000)	VERY LOW	IMPORTANT

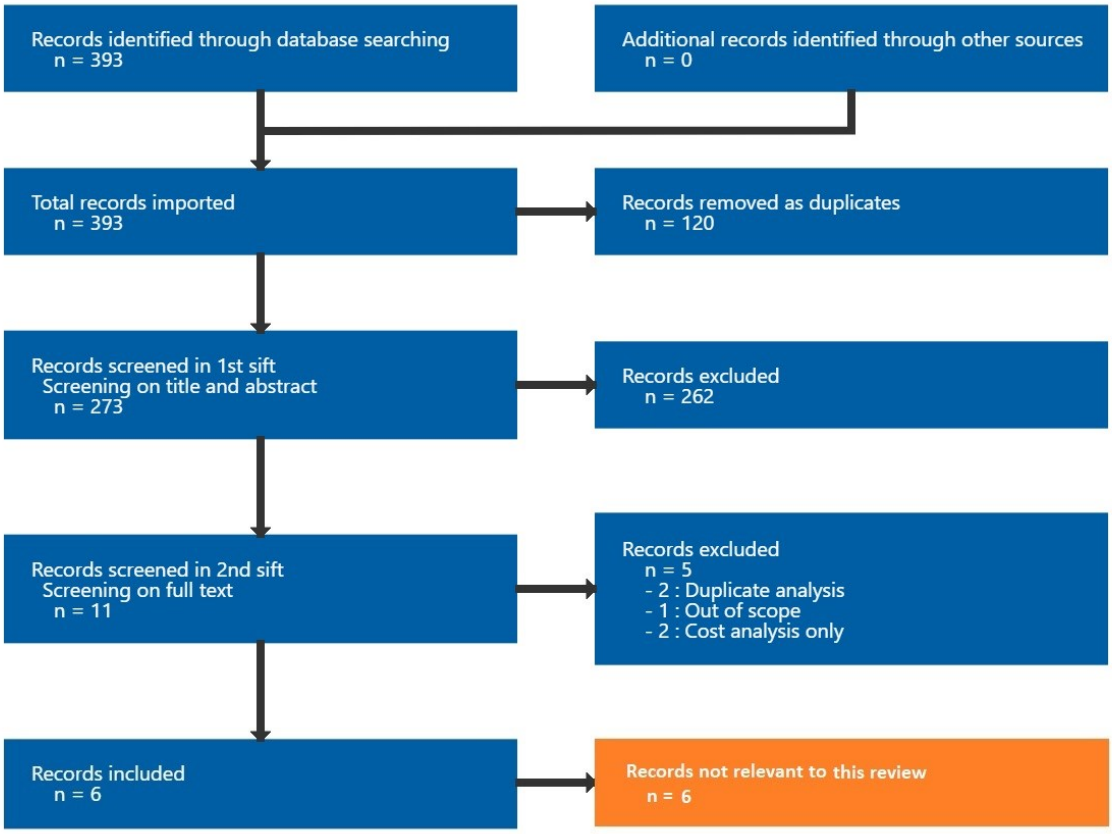
CI: confidence interval; JBI: The Joanna Briggs Institute Checklist; OME: otitis media with effusion
[1]Very serious risk of bias in the evidence contributing to the outcomes as per JBI
[2]<150 events

Appendix G Economic evidence study selection

Study selection for: What is the progression, resolution and recurrence (natural history) of OME without 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 9)

Figure 9: 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 without 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 without 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 without 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=192) and not studies (N=14) 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 12: 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 OME, so is not reporting on natural history*
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 (United States) 165(5): 710-715	- Population does not meet inclusion criteria *This study was conducted in children with OME-related hearing loss, so it is included in the review on natural history of OME-related hearing loss*
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 (2002) Selecting persistent glue ear for referral in general practice: a risk factor approach. The British journal of general practice : the journal of the Royal College of General Practitioners 52(480): 549-53	- Study design does not meet inclusion criteria *The study investigates the risk factors that predict persistence of OME, and no outcomes of interest reported*
Anonymous (2001) Pars tensa and pars flaccida retractions in persistent otitis media with	- Outcome does not meet inclusion criteria

Study	Code [Reason]
effusion. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 22(3): 291-8	*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 effusion and associated hearing loss in children. Part I: clinical trial. Ear, nose, & throat journal 84(9): 567-passim	- Study design does not meet inclusion criteria *Follow-up <3 months*
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 and population does not meet inclusion criteria *Duration of follow-up <3 months, and children with OME-related hearing loss*
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*
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*

Study	Code [Reason]
Bernard, PA, Stenstrom, RJ, Feldman, W et al. (1991) Randomized, controlled trial comparing long-term sulfonamide therapy to ventilation tubes for otitis media with effusion. Pediatrics 88(2): 215-22	- Study design does not meet inclusion criteria *All participants received 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 hypertrophy with otitis media with effusion. American journal of otolaryngology 35(6): 766-70	- Non-OECD country *India*
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.*
Birch, L and Elbrond, O (1987) A prospective epidemiological study of secretory otitis media in young children related to the indoor environment. ORL; journal for oto-rhino-laryngology and its related specialties 49(5): 253-8	- Study includes same participants and data as already included study *Birch 1986*
Blanshard, J D; Maw, A R; Bawden, R (1993) Conservative treatment of otitis media with effusion by autoinflation of the middle ear. Clinical otolaryngology and allied sciences 18(3): 188-92	- Insufficient presentation of results *Only reports the percentage of different tympanogram types at each time point, cannot calculate number who have had a change in tympanogram type.*
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
Boswell, J B and Nienhuys, T G (1996) Patterns of persistent otitis media in the first year of life in aboriginal and non-aboriginal infants. The Annals of otology, rhinology, and laryngology 105(11): 893-900	- Outcome does not meet inclusion criteria *Outcomes of interest not reported*
Brooks, D.N. (1976) Middle ear effusion in children. Journal of Otolaryngology 5(6): 453-458	- Insufficient presentation of results *No usable data on outcomes of interest*
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	- Study design does not meet inclusion criteria *Includes studies with treated control groups. Included studies not checked for relevance as*

Study	Code [Reason]
Cochrane database of systematic reviews: cd001801	*this review has been superseded by ongoing update (which has been checked)*
Buckley, G and Hinton, A (1991) Otitis media with effusion in children shows a progressive resolution with time. Clinical otolaryngology and allied sciences 16(4): 354-7	- Study design does not meet inclusion criteria *39.3% of participants received antibiotics or decongestants, 26.6% had grommet insertion, and 6 children had adenoidectomy, so does not report natural history*
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 is <3 months*
Castagno, Lucio A and Lavinsky, Luiz (2002) Otitis media in children: seasonal changes and socioeconomic level. International journal of pediatric otorhinolaryngology 62(2): 129-34	- Non-OECD country *Brazil*
Chen, Kaitian, Wu, Xuan, Jiang, Guangli et al. (2013) Low dose macrolide administration for long term is effective for otitis media with effusion in children. Auris, nasus, larynx 40(1): 46-50	- Non-OECD country *China*
Chohan, A, Lal, A, Chohan, K et al. (2015) Systematic review and meta-analysis of randomized controlled trials on the role of mometasone in adenoid hypertrophy in children. International journal of pediatric otorhinolaryngology 79(10): 1599-608	- Population does not meet inclusion criteria *Included studies include populations other than OME. Included studies checked for relevance.*
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 and population does not meet inclusion criteria *This study was conducted in children with OME-related hearing loss, and 30% and 12% of participants had grommet insertion and adenoidectomy, respectively, so does not report natural history*
Cooper, Hannah E; Grifa, Ilaria; Bryant, Catriona (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 : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery 47(1): 160-166	- Population does not meet inclusion criteria *This study was conducted in children with OME-related hearing loss, so it is included in the review question on natural history of OME-related hearing loss*
Corwin, M J; Weiner, L B; Daniels, D (1986) Efficacy of oral antibiotics for the treatment of persistent otitis media with effusion. International journal of pediatric otorhinolaryngology 11(2): 109-12	- Study design does not meet inclusion criteria *Follow-up <3 months*
Della Volpe, A, Ricci, G, Ralli, M et al. (2019) The effects of oral supplements with Sambucus nigra, Zinc, Tyndallized Lactobacillus	- Study design does not meet inclusion criteria

Study	Code [Reason]
acidophilus (HA122), Arabinogalactans, vitamin D, vitamin E and vitamin C in otitis media with effusion in children: a randomized controlled trial. European review for medical and pharmacological sciences 23(14): 6360-6370	*Control group were treated with a mucolytic agent and hypertonic solution, 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.*
Dhillon, RS (1988) The middle ear in cleft palate children pre and post palatal closure. Journal of the Royal Society of Medicine 81(12): 710-3	- Study design does not meet inclusion criteria *Participants had myringotomy, so does not report natural history*
Diacova, Svetlana; McDonald, Thomas J; Ababii, Ion (2016) Clinical, functional, and surgical findings in chronic bilateral otitis media with effusion in childhood. Ear, nose, & throat journal 95(8): e31-7	- Full text paper not available
Donaldson, JD, Martin, GF, Maltby, CC et al. (1990) The efficacy of pulse-dosed antibiotic therapy in the management of persistent otitis media with effusion. The Journal of otolaryngology 19(3): 175-8	- Study design does not meet inclusion criteria *All participants received antibiotic treatment for OME, so does not report natural history*
El-Anwar, Mohammad Waheed, Nofal, Ahmad Abdel-Fattah, Khazbak, Alaa Omar et al. (2015) The Efficacy of Nasal Steroids in Treatment of Otitis Media with Effusion: A Comparative Study. International archives of otorhinolaryngology 19(4): 298-301	- Non-OECD country *Egypt*
Fiellau-Nikolajsen, M (1979) Tympanometry in 3-year-old children. Type of care as an epidemiological factor in secretory otitis media and tubal dysfunction in unselected populations of 3-year-old children. ORL; journal for oto-rhino-laryngology and its related specialties 41(4): 193-205	- Study includes same participants and data as already included study *Fiellau-Nikolajsen 1979 and Fiellau-Nikolajsen 1983*
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	- Study includes same participants and data as already included study *Fiellau-Nikolajsen 1979 and Fiellau-Nikolajsen 1983*
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	- Study includes same participants and data as already included study *Fiellau-Nikolajsen 1979*
Fiellau-Nikolajsen, M and Lous, J (1979) Tympanometry in three-year-old children. A cohort study on the prognostic value of	- Study design does not meet inclusion criteria

Study	Code [Reason]
tympanometry and operative findings in middle ear effusion. ORL; journal for oto-rhino-laryngology and its related specialties 41(1): 11-25	*The study investigates correlation between operative findings and the results of pre- and postoperative tympanometry*
Gates, G A, Wachtendorf, C, Holt, G R et al. (1986) Medical treatment of chronic otitis media with effusion (secretory otitis media). Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 94(3): 350-4	- Study design does not meet inclusion criteria *All participants received treatment for OME, so does not report natural history*
Ghedia, Reshma, Ahmed, Jahangir, Navaratnam, Annakan 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	- Population does not meet inclusion criteria *This study was conducted in children with OME-related hearing loss, so it is included in the review question on natural history of OME-related hearing loss*
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*
Giles, M and O'Brien, P (1989) Otitis media and hearing loss in the children of the Ruatoki valley: a continuing public health problem. The New Zealand medical journal 102(865): 160-1	- Study design does not meet inclusion criteria *Unclear if diagnosis of OME was confirmed by tympanometry*
Gluth, Michael B, McDonald, Darren R, Weaver, Amy L et al. (2011) Management of eustachian tube dysfunction with nasal steroid spray: a prospective, randomized, placebo-controlled trial. Archives of otolaryngology--head & neck surgery 137(5): 449-55	- Population does not meet inclusion criteria *Includes adults and children (mean age 41.7 years)*
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*
Gordon, Michael A; Grunstein, Eli; Burton, William B (2004) The effect of the season on otitis media with effusion resolution rates in the New York Metropolitan area. International journal of pediatric otorhinolaryngology 68(2): 191-5	- Study design does not meet inclusion criteria *Participants received antibiotic treatment, so does not report on natural history*
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, but no clear information about the number of participants who had myringotomy, so does not report natural history*

Study	Code [Reason]
Grover Jr., F. (2003) Are nasal steroid sprays effective for otitis media with effusion?. Journal of Family Practice 52(8): 647-649	- Study design does not meet inclusion criteria *Commentary*
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*
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*
Haugeto, O.K.; Schroder, K.E.; Mair, I.W.S. (1981) Secretory otitis media, oral decongestant and antihistamine. Journal of Otolaryngology 10(5): 359-362	- Insufficient presentation of results *No usable data on outcomes of interest*
Hayden, G F, Randall, J E, Randall, J C et al. (1984) Topical phenylephrine for the treatment of middle ear effusion. Archives of otolaryngology (Chicago, Ill. : 1960) 110(8): 512-4	- Study design does not meet inclusion criteria *Follow-up <3 months*
Hemlin, C; Carenfelt, C; Papatziamos, G (1997) Single dose of betamethasone in combined medical treatment of secretory otitis media. The Annals of otology, rhinology, and laryngology 106(5): 359-63	- Study design does not meet inclusion criteria *All children received antibiotics, so does not report on natural history.*
Hogan, S C; Stratford, K J; Moore, D R (1997) Duration and recurrence of otitis media with effusion in children from birth to 3 years: prospective study using monthly otoscopy and tympanometry. BMJ (Clinical research ed.) 314(7077): 350-3	- Insufficient presentation of results *Study reports the probability of changing between different OME states (unilateral, bilateral and no OME) but does not provide sufficient information to calculate the number of people who had resolution. Some data on mean duration of episodes and time between episodes is reported, but no measure of variation (e.g., SD) is reported.*
Homoc, P.; Christensen, R.B.; Bretlau, P. (1996) Prevalence of otitis media in a survey of 591 unselected Greenlandic children. International Journal of Pediatric Otorhinolaryngology 36(3): 215-230	- Non-OECD country *Greenland*
Hsu, G S; Levine, S C; Giebink, G S (1998) Management of otitis media using Agency for	- Study design does not meet inclusion criteria

Study	Code [Reason]
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	*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*
Ingels, K, Rovers, MM, van der Wilt, GJ et al. (2005) Ventilation tubes in infants increase the risk of otorrhoea and antibiotic usage. B-ENT 1(4): 173-6	- Outcome does not meet inclusion criteria *Reports episodes, of and symptoms related to, otorrhea.*
Johnston, Lindsay C, Feldman, Heidi M, Paradise, Jack L et al. (2004) Tympanic membrane abnormalities and hearing levels at the ages of 5 and 6 years in relation to persistent otitis media and tympanostomy tube insertion in the first 3 years of life: a prospective study incorporating a randomized clinical trial. Pediatrics 114(1): e58-67	- Outcome does not meet inclusion criteria *Reports on otomicroscopic and audiometric findings (does not report the number with/without hearing loss) only.*
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*
Karlidağ, T, Kaygusuz, I, Gök, U et al. (2002) The efficacy of combining antibiotic treatment with topical intranasal steroid administration in the treatment of chronic otitis media with effusion. Kulak burun bogaz ihtisas dergisi : KBB [Journal of ear, nose, and throat] 9(4): 257-262	- Full text paper not available
Khan, JA; Marcus, P; Cummings, SW (1981) S-carboxymethylcysteine in otitis media with effusion. (A double-blind study). The Journal of laryngology and otology 95(10): 995-1001	- Study design does not meet inclusion criteria *Follow-up <3 months, and diagnosis of OME was not confirmed by tympanometry*
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)*

Study	Code [Reason]
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	- Population does not meet inclusion criteria *>50% of children had hearing loss. Included in the review on natural history of OME-related hearing loss*
Lambert, PR (1986) Oral steroid therapy for chronic middle ear perfusion: a double-blind crossover study. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 95(2): 193-9	- Study design does not meet inclusion criteria *All participants received antibiotic treatment, so does not report natural history*
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*
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*
Lee, Chang Ho, Yoo, Chan Kee, Hong, Jong Eui et al. (2011) Resolved effusion on myringotomy: a study of dry tap without general anesthesia. International journal of pediatric otorhinolaryngology 75(5): 635-8	- Study design does not meet inclusion criteria *The study included participants with persistent OME who did not respond to medical therapy (proportion not provided) and then had myringotomy, so does not report natural history*
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*

Study	Code [Reason]
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*
Mandel, E M, Casselbrant, M L, Rockette, H E et al. (1996) Efficacy of antimicrobial prophylaxis for recurrent middle ear effusion. The Pediatric infectious disease journal 15(12): 1074-82	- Study design does not meet inclusion criteria *Participants received medical treatment, so does not report natural history*
Marchisio, P, Principi, N, Passali, D et al. (1998) Epidemiology and treatment of otitis media with effusion in children in the first year of primary school. Acta oto-laryngologica 118(4): 557-62	- Insufficient presentation of results *Results for 12-week follow-up not reported separately for the untreated group.*
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 design and population do not meet inclusion criteria *The study investigates the factors that influence the outcome of OME and includes children with OME-related hearing loss*
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. Acta oto-rhino-laryngologica Belgica 48(4): 317-24	- Population does not meet inclusion criteria *Children with OME-related hearing loss*
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	- Population does not meet inclusion criteria *Children with OME-related hearing loss*
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	- Population does not meet inclusion criteria *Children with OME-related hearing loss*
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 (Clinical research ed.) 306(6880): 756-60	- Population does not meet inclusion criteria *Children had hearing loss. Included in review on natural history of OME-related hearing loss.*
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 (London, England) 353(9157): 960-3	- Population does not meet inclusion criteria *Children had hearing loss. Included in the review of natural history of OME-related hearing loss.*

Study	Code [Reason]
Mills, R (1999) Risk factors for chronicity in childhood otitis media with effusion. Clinical otolaryngology and allied sciences 24(4): 343-5	- Study design does not meet inclusion criteria *Participants received treatment for OME, so does not report natural history*
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*
Mohammadi Ardehali, M., Mahdizade Seraj, J., Kiani Asiabar, M. et al. (2008) The possible role of gastroesophageal reflux disease in children suffering from chronic otitis media with effusion. Acta Medica Iranica 46(1): 33-37	- Non-OECD country *Iran*
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*
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): 147-56	- Population does not meet inclusion criteria *Children had hearing loss. Included in the review of natural history of OME-related hearing loss.*
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, 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): 150-3	- Population does not meet inclusion criteria *Children with OME-related hearing loss*
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): 285-9	- Population does not meet inclusion criteria *Children with OME-related hearing loss*
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*
Olson, A L, Klein, S W, Charney, E et al. (1978) Prevention and therapy of serous otitis media by	- Study design does not meet inclusion criteria *Follow-up <3 months*

Study	Code [Reason]
oral decongestant: a double-blind study in pediatric practice. Pediatrics 61(5): 679-84	
Papadakis, H., Christodoulou, P., Volitakis, M. et al. (1996) Otitis media with effusion: Allergic origin and management. Acta Therapeutica 22(1): 37-49	- Study design does not meet inclusion criteria *The study investigates role of allergy in OME, and no outcomes of interest reported.*
Paradise, J L, Dollaghan, C A, Campbell, T F et al. (2000) Language, speech sound production, and cognition in three-year-old children in relation to otitis media in their first three years of life. Pediatrics 105(5): 1119-30	- Study design does not meet inclusion criteria *The study investigates the associations of language, speech sound production and cognition with otitis media*
Paradise, J L, Rockette, H E, Colborn, D K et al. (1997) Otitis media in 2253 Pittsburgh-area infants: prevalence and risk factors during the first two years of life. Pediatrics 99(3): 318-33	- Study design does not meet inclusion criteria *Participants received treatment for otitis media (such as antibiotics and surgery), so does not report natural history*
Paradise, Jack L, Dollaghan, Christine A, Campbell, Thomas F et al. (2003) Otitis media and tympanostomy tube insertion during the first three years of life: developmental outcomes at the age of four years. Pediatrics 112(2): 265-77	- Outcome does not meet inclusion criteria *Reports developmental outcomes only.*
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	- Population and outcome do 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 children with chronic otitis media with effusion. Journal of Audiological Medicine 9(2): 104-117	- Study design does not meet inclusion criteria *Participants received grommets, intra-nasal steroids or decongestants, so does not report natural history*
Parlea, E; Georgescu, M; Calarasu, R (2012) Tympanometry as a predictor factor in the evolution of otitis media with effusion. Journal of medicine and life 5(4): 452-4	- Non-OECD country *Romania*
Parrella, A, Hiller, J et al. (2005) EarPopper (TM) for the treatment of otitis media with effusion in children.	- Full text paper not available
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*
Pedrero-Escalas, M F, Jimenez-Antolin, J, Lassaletta, L et al. (2016) Hospital clinical trial: Homeopathy (Agraphis nutans 5CH, Thuya occidentalis 5CH, Kalium muriaticum 9CH and Arsenicum iodatum 9CH) as adjuvant, in children with otitis media with effusion.	- Study design does not meet inclusion criteria *All participants received medical treatments for OME, so does not report natural history*

Study	Code [Reason]
International journal of pediatric otorhinolaryngology 88: 217-23	
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)*
Portoian-Shuhaiber, S and Cullinan, T R (1984) Middle ear disease assessed by impedance in primary school children in south London. Lancet (London, England) 1(8386): 1111-2	- Study design does not meet inclusion criteria *Follow-up is less than 3 months*
Poulsen, G and Tos, M (1978) Screening tympanometry in newborn infants and during the first six months of life. Scandinavian audiology 7(3): 159-66	- Insufficient presentation of results *No usable data on outcomes of interest*
Poulsen, G and Tos, M (1980) Repetitive tympanometric screenings of two-year-old children. Scandinavian audiology 9(1): 21-8	- Study includes same participants and data as already included study *Tos 1980*
Randolph, C C and Fraser, B (1994) Incidence and progress of middle ear effusion in allergy practice as detected by acoustic otoscope reflectometry. Allergy proceedings : the official journal of regional and state allergy societies 15(3): 157-62	- Population does not meet inclusion criteria *Mean age of participants was 13 years, and duration of follow-up is <3 months*
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. (1975) Tympanometry in secretory otitis media. Scandinavian Audiology 4(2): 83-88	- Study design does not meet inclusion criteria *Participants had myringotomy and ventilation tube surgery, so does not report natural history*
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*

Study	Code [Reason]
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 *The study is about 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*
Roberts, D G, Johnson, C E, Carlin, S A et al. (1995) Resolution of middle ear effusion in newborns. Archives of pediatrics & adolescent medicine 149(8): 873-7	- Study design does not meet inclusion criteria *Duration of follow-up <3 months*
Roberts, Joanne Erwick; Burchinal, Margaret R; Campbell, Frances A (1994) Otitis media in early childhood and patterns of intellectual development and later academic performance. Journal of Pediatric Psychology 19(3): 347-367	- Study design does not meet inclusion criteria *Participants received treatments for OME (such as antibiotics and ventilation tubes), so does not report natural history*
Robinson, P J, Lodge, S, Goligher, J et al. (1993) Secretory otitis media and mastoid air cell development. International journal of pediatric otorhinolaryngology 25(13): 13-8	- Study design does not meet inclusion criteria *Participants had myringotomy, so does not report natural history.*
Roos, K; Håkansson, EG; Holm, S (2001) Effect of recolonisation with "interfering" alpha streptococci on recurrences of acute and secretory otitis media in children: randomised placebo controlled trial. BMJ (Clinical research ed.) 322(7280): 210-2	- Study design does not meet inclusion criteria *All children received antibiotic treatment, so does not report on natural history.*
Rosenfeld, R.M. and Kay, D. (2003) Natural history of untreated otitis media. Laryngoscope 113(10): 1645-1657	- Population does not meet inclusion criteria *Systematic review includes studies of acute otitis media*
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 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	- Study design does not meet inclusion criteria *Control received treatments, including adenoidectomy, antibiotics and nose drops*

Study	Code [Reason]
waiting. Journal of clinical epidemiology 54(8): 789-94	*(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*
Roydhouse, N (1981) Adenoidectomy for otitis media with mucoid effusion. The Annals of otology, rhinology & laryngology. Supplement 89(3pt2): 312-5	- Study design does not meet inclusion criteria *All participants received medical treatments for OME, so does not report natural history*
Sams, C (1998) Review: parental smoking increases risk of recurrent otitis media, middle ear effusion, and tonsillectomy or adenoidectomy in children [commentary on Strachan DP, Cook DG. Parental smoking, middle ear disease and adenotonsillectomy in children. THORAX 1998 Feb;53:50-6]. Evidence Based Nursing: 124-124	- Study design does not meet inclusion criteria *Commentary*
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 >12 years included*
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	- Population does not meet inclusion criteria *OME was not confirmed using tympanometry.*
Schilder, A G, Zielhuis, G A, Haggard, M P et al. (1995) Long-term effects of otitis media with effusion: otomicroscopic findings. The American journal of otology 16(3): 365-72	- Study design does not meet inclusion criteria *Participants received treatments for OME (decongestants, mucolytic, antibiotics, and surgery), so does not report natural history*
Schoem, Scott R; Willard, Alice; Combs, Jerome T (2010) A prospective, randomized, placebo-controlled, double-blind study of montelukast's effect on persistent middle ear effusion. Ear, nose, & throat journal 89(9): 434-7	- Study design does not meet inclusion criteria *Follow-up <3 months*
Schwartz, R H and Rodriguez, W J (1982) Trimethoprim-sulfamethoxazole treatment of persistent otitis media with effusion. Pediatric infectious disease 1(5): 333-5	- Study design and population does not meet inclusion criteria *Children with acute otitis media and OME treated with amoxicillin*

Study	Code [Reason]
Schwartz, R H; Rodriguez, W J; Grundfast, K M (1984) Duration of middle ear effusion after acute otitis media. Pediatric infectious disease 3(3): 204-7	- Study design does not meet inclusion criteria *Participants received antibiotic treatment and myringotomy, so does not report natural history*
Shekelle, P, Takata, G, Chan L, S et al. (2003) Diagnosis, natural history, and late effects of otitis media with effusion.	- Study design does not meet inclusion criteria *Includes diagnostic test accuracy studies. Included studies checked for relevance*
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 model. Journal of Speech, Language, and Hearing Research 43(1): 100-120	- 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.*
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*
Skovbjerg, S, Roos, K, Holm, SE et al. (2009) Spray bacteriotherapy decreases middle ear fluid in children with secretory otitis media. Archives of disease in childhood 94(2): 92-8	- Study design does not meet inclusion criteria *Follow-up period <3 months.*
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.*
Stangerup, S E; Sederberg-Olsen, J; Balle, V (1992) Autoinflation as a treatment of secretory otitis media. A randomized controlled study. Archives of otolaryngology--head & neck surgery 118(2): 149-52	- Study design does not meet inclusion criteria *Participants had adenoidectomy, and grommets insertion, so does not report natural history*
Stangerup, SE; Sederberg-Olsen, J; Balle, VH (1991) Treatment with the Otovent device in tubal dysfunction and secretory otitis media in children. Ugeskrift for laeger 153(43): 3008-3009	- Full text paper not available
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.*
Stenstrom, C and Ingvarsson, L (1995) Late effects on ear disease in otitis-prone children: a	- Population does not meet inclusion criteria *Participants with acute otitis media*

Study	Code [Reason]
long-term follow-up study. Acta oto-laryngologica 115(5): 658-63	
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*
Subarevic, V., Arsovic, N., Simic, R. et al. (2018) Importance of early ventilation tubes insertion in chronic otitis media with effusion in children with congenital cleft palate. Vojnosanitetski Pregled 75(3): 253-259	- Non-OECD country *Serbia*
Swedish Council on Health Technology, Assessment (2008) Tympanostomy Tube Insertion for Otitis Media in Children: A Systematic Review. SBU Systematic Review Summaries	- Population and outcome do not meet inclusion criteria *Systematic review includes studies of acute otitis media. included studies checked for relevance*
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*
Thomsen, J., Sederberg-Olsen, J., Stangerup, S.E. et al. (1988) Long-term antibiotic treatment of children with secretory otitis media: A double-blind placebo-controlled study. Acta Oto-Laryngologica, Supplement 106(449): 49-50	- Study includes same participants and data as already included study *Thomsen 1989*
Thomsen, J, Sederberg-Olsen, J, Balle, V et al. (1989) Antibiotic treatment of children with secretory otitis media. A randomized, double-blind, placebo-controlled study. Archives of otolaryngology--head & neck surgery 115(4): 447-51	- Insufficient presentation of results *No usable data on outcomes of interest*
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	- Population does not meet inclusion criteria

Study	Code [Reason]
inflammations. International Journal of Immunopathology and Pharmacology 29(3): 438-442	*Includes children with OME or a history of recurrent AOM. Proportion of those with OME not reported.*
Torretta, S, Marchisio, P, Rinaldi, V et al. (2017) Endoscopic and clinical benefits of hyaluronic acid in children with chronic adenoiditis and middle ear disease. 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 274(3): 1423-1429	- Population does not meet inclusion criteria *Only 48% of participants had OME, and data not presented separately for those with OME*
Tos, M (1983) Epidemiology and spontaneous improvement of secretory otitis. Acta oto-rhino-laryngologica Belgica 37(1): 31-43	- Study includes same participants and data as already included study *Tos 1980 and Tos 1982*
Tos, M (1979) Frequency of secretory otitis and histology of the normal middle ear mucosa. International journal of pediatric otorhinolaryngology 1(3): 241-8	- Study includes same participants and data as already included study *Tos 1980*
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 already included study *Tos 1980 and Tos 1982*
Tos, M.; Poulsen, G.; Borch, J. (1978) Tympanometry in two-year-old children. Alterations of tympanograms at reevaluation. ORL 40(4): 206-215	- Study includes same participants and data as already included study *Tos 1980*
Tos, M; Holm-Jensen, S; Sorensen, C H (1981) Changes in prevalence of secretory otitis from summer to winter in four-year-old children. The American journal of otology 2(4): 324-7	- Study includes same participants and data as already included study *Tos 1982*
Tos, M, Holm-Jensen, S, Stangerup, S E et al. (1983) Changes in point prevalence of secretory otitis in preschool children. ORL; journal for oto-rhino-laryngology and its related specialties 45(4): 226-34	- Study includes same participants and data as already included study *Tos 1982*
Tos, M and Poulsen, G (1979) Tympanometry in 2-year-old children. Seasonal influence on frequency of secretory otitis and tubal function. ORL; journal for oto-rhino-laryngology and its related specialties 41(1): 1-10	- Study includes same participants and data as already included study *Tos 1980*
Tos, M; Poulsen, G; Borch, J (1978) Tympanometry in 2-year-old children. ORL; journal for oto-rhino-laryngology and its related specialties 40(2): 77-85	- Study includes same participants and data as already included study *Tos 1980*
Tos, M; Stangerup, S E; Andreassen, U K (1985) Size of the mastoid air cells and otitis	- Study design does not meet inclusion criteria *The study investigate association between size of mastoid air cells and OME*

Study	Code [Reason]
media. The Annals of otology, rhinology, and laryngology 94(4pt1): 386-92	
Tos, M, Stangerup, S E, Holm-Jensen, S et al. (1984) Spontaneous course of secretory otitis and changes of the eardrum. Archives of otolaryngology (Chicago, Ill. : 1960) 110(5): 281-9	- Insufficient presentation of results *No usable data on outcomes of interest*
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): 605-11	- Population does not meet inclusion criteria *This study was conducted in children with OME-related hearing loss, so it is included in the review question on natural history of OME-related hearing loss*
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 include an untreated control group, so does not report on natural history.*
van der Merwe, J and Wagenfeld, D J (1987) The negative effects of mucolytics in otitis media with effusion. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde 72(9): 625-6	- Non-OECD country *South Africa*
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
Varricchio, A, De Lucia, A, Varricchio, A M et al. (2017) Sinuclean Nebules treatment in children suffering from otitis media with effusion. International journal of pediatric otorhinolaryngology 94: 30-35	- Study design does not meet inclusion criteria *Follow-up <3 months*
Varsano, I B; Volovitz, B M; Grossman, J E (1989) Effect of naproxen, a prostaglandin inhibitor, on acute otitis media and persistence of middle ear effusion in children. The Annals of otology, rhinology, and laryngology 98(5pt1): 389-92	- Population does not meet inclusion criteria *Children with acute otitis media included*
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	- Population does not meet inclusion criteria

Study	Code [Reason]
acute otitis media and in treating otitis media with effusion. A meta-analytic attempt to resolve the brouhaha. JAMA 270(11): 1344-51	*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*
Williamson, I, Benge, S, Barton, S et al. (2009) A double-blind randomised placebo-controlled trial of topical intranasal corticosteroids in 4- to 11-year-old children with persistent bilateral otitis media with effusion in primary care. Health technology assessment (Winchester, England) 13(37): 1-144	- Study includes same participants and data as already included study *Williamson 2009*
Williamson, Ian, Vennik, Jane, Harnden, Anthony et al. (2015) An open randomised study of autoinflation in 4- to 11-year-old school children with otitis media with effusion in primary care. Health technology assessment (Winchester, England) 19(72): 1-150	- Study design does not meet inclusion criteria *Unclear if the usual care group received intervention of not - examples given were decongestant, information or watchful waiting, but not clear what treatment was actually given.*
Williamson, Ian, Vennik, Jane, Harnden, Anthony et al. (2015) Effect of nasal balloon autoinflation in children with otitis media with effusion in primary care: an open randomized controlled trial. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 187(13): 961-969	- Study design does not meet inclusion criteria *Unclear if the usual care group received intervention of not – no further definition provided.*
Wright, P F, McConnell, K B, Thompson, J M et al. (1985) A longitudinal study of the detection of otitis media in the first two years of life. International journal of pediatric otorhinolaryngology 10(3): 245-52	- Study design does not meet inclusion criteria *The study investigates the diagnostic accuracy of pneumatic otoscopy, electroacoustic immittance, and tympanometry*
Zeisel, S A, Roberts, J E, Neebe, E C et al. (1999) A longitudinal study of otitis media with effusion among 2- to 5-year-old African-American children in child care. Pediatrics 103(1): 15-9	- Insufficient presentation of results *Reports the same participants and outcomes as Zeisel 1995, which is already included. The only additional data is the proportion resolved after 4 months in those had already had OME for at least 4 months in both this study and the previous study (conducted at a younger are); therefore, observations are not independent of already included data*
Zeisel, SA and Roberts, JE (2003) Otitis media in young children with disabilities. Infants & Young Children: An Interdisciplinary Journal of Early Childhood Intervention 16(2): 106-119	- Outcome does not meet inclusion criteria *No outcomes of interest reported*
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*

Study	Code [Reason]
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.*
Zielhuis, G A; Rach, G H; van den Broek, P (1989) Screening for otitis media with effusion in preschool children. Lancet (London, England) 1(8633): 311-4	- Study includes same participants and data as already included study *Zielhuis 1990*
Zielhuis, G A; Rach, G H; Van den Broek, P (1990) The occurrence of otitis media with effusion in Dutch pre-school children. Clinical otolaryngology and allied sciences 15(2): 147-53	- Study includes same participants and data as already included study *Zielhuis 1990*
Zielinski, R. and Zakrzewska, A. (2012) Complaints accompanying hearing loss in children with adenoid hypertrophy and middle ear exudation. Przeglad Pediatryczny 42(4): 195-199	- Full text paper not available

1 *OME: otitis media with effusion*

2 **Excluded economic studies**

3 No economic evidence was identified for this review.

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Appendix K Research recommendations – full details

Research recommendations for review question: What is the progression, resolution and recurrence (natural history) of OME without 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

OME is a common condition, affecting 80% of children at least once. It can cause hearing loss which can impact development, speech, language and learning. Understanding the progression, resolution and recurrence of OME with and without hearing loss will contribute to the best management. However, evidence reviews on natural history of OME without hearing loss and OME-related hearing loss (see evidence review D) showed that there is limited evidence, and robust evidence is needed to inform clear understanding of the natural history and strong recommendations.

K.1.3 Rationale for research recommendation

Table 13: Research recommendation rationale

Importance to 'patients' or the population	OME is a common condition, affecting 80% of children at least once. It can cause hearing loss which can impact development, speech, language and learning. Understanding the progression, resolution and recurrence of OME with and without hearing loss will contribute to best management.
Relevance to NICE guidance	The research is essential to inform future updates of key recommendations regarding the natural history of OME with and without hearing loss.
Relevance to the NHS	Understanding progression resolution and recurrence will inform optimal management of OME, which can reduce burden on NHS services and morbidity related to this common condition.
National priorities	Core20plus 5 in paediatrics priority for reducing health care inequalities. Hearing loss is a main contributor towards childhood disability and lifetime outcomes in education and employment.
Current evidence base	There was limited evidence on the natural history of OME with and without hearing loss, and robust evidence is needed to inform strong recommendations.
Equality considerations	OME is currently not thought to affect sexes differently, but sex disaggregated data may help to capture potential differences in progression, resolution and recurrence of OME between sexes. There are certain conditions where OME is more prevalent such as children with Down's syndrome. Understanding the natural history of OME with and without hearing loss in these populations may contribute to the reduction of health care inequalities at both national and system level.

OME: otitis media with effusion, NHS: National Health Service; NICE: National Institute for Health and Care Excellence

K.1.41 Modified PICO table

2 **Table 14: Research recommendation modified PICO table**

Population	• Children aged 6 months to 12 years with unilateral or bilateral OME with and without hearing loss. • Include all children regardless of any comorbidity such as Down's syndrome or cleft palate. • Clinical diagnosis of OME will be at least confirmed by oto(micro)scopy or tympanometry or both
Intervention	None as it is the natural history of OME
Comparator	None or matched controls without OME
Outcome	• Progression to OME with associated hearing loss • Time to progression to OME with associated hearing loss • Resolution of current episode of OME • Time to resolution of current episode of OME • Total resolution (no further recurrences) of OME • Time to total resolution of OME • Recurrence of OME (following spontaneous resolution) • Progression of OME-related hearing loss (e.g., worsening of hearing loss) • Time to progression of OME-related hearing loss • 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 • Number of episodes of OME, duration and resolution time of each episode. • Number of interventions or treatments • Number of interactions with health care professionals including speech and language therapists, audiologist, educational specialists, clinicians, etc. • Quality of life • Hearing outcomes in short and long term • Educational outcomes
Study design	Observational (epidemiological) single group (non-comparative) study
Timeframe	Long term (over 5 or more years) to fully delineate the natural history of OME with and without hearing loss
Additional information	N/A

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

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