

Otitis media with effusion in under 12s

[G] Evidence reviews for antibiotics

NICE guideline number tbc

Evidence reviews underpinning recommendation 1.5.2 in the NICE guideline

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Draft for consultation

This evidence review was developed by NICE

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1 Antibiotics

2 Review question

3 What is the effectiveness of antibiotics for managing OME in children under 12 years?

4 Introduction

5 The aim of this review is to assess the effectiveness of antibiotics in managing OME in
6 children under 12 years.

7 Summary of the protocol

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

10 Table 1: Summary of the protocol (PICO table)

Population	<p>Inclusion: Children aged 6 months to 12 years with unilateral or bilateral otitis media with effusion (OME).</p> <ul style="list-style-type: none">• If a study includes children aged younger than 6 months and older than 12 years, we will only include the study if the majority of children fit our inclusion criteria or only if the trialists present outcome data by age group.• Include all children regardless of any comorbidity such as Down syndrome or cleft palate• Clinical diagnosis of OME will be confirmed by oto(micro)scopy or tympanometry or both
Intervention	Oral antibiotics of all types and courses of duration
Comparison	<ul style="list-style-type: none">• Oral antibiotics versus placebo;• Oral antibiotics tubes versus no treatment <p>If trial participants have received other treatments, for example, intranasal steroids, oral steroids, mucolytics or decongestants, we will include these trials if both arms of the study received identical treatment.</p> <p>Exclusion:</p> <ul style="list-style-type: none">• We will exclude studies in which one antibiotic is compared with another.• We will exclude studies comparing one dose of an antibiotic to a different dose of the same antibiotic.
Outcome	<p>We will analyse the following outcomes in the review, but we will not use them as a basis for including or excluding studies. We will assess all outcomes in the very short term (< 6 weeks for adverse events), short term (<= 3 months), medium term (> 3 months to <= 1 year) and long term (> 1 year).</p> <p>Critical</p> <ul style="list-style-type: none">• Hearing<ul style="list-style-type: none">○ proportion of children whose hearing has returned to normal;○ mean final hearing threshold (determined for the child or ear, depending on the unit of analysis);○ change in hearing threshold from baseline (determined for the child or ear, depending on the unit of analysis).

- Disease-specific quality of life measured using a validated instrument, for example:
 - OM8-30;
 - Otitis Media-6.
- Adverse events: Anaphylactic reaction
- Important**
- Presence/persistence of OME.
- Adverse events - measured by the number of participants affected.
 - Tympanic membrane changes, such as:
 - atrophy;
 - atelectasis or retraction;
 - persistent perforation
 - myringosclerosis;
 - tympanosclerosis.
 - Patient-related, such as:
 - vomiting;
 - diarrhoea;
 - dry throat;
 - nasal stinging;
 - cough;
 - long-term hearing loss;
 - postsurgical haemorrhage;
 - pain.
- Receptive language skills, measured using a validated scale, for example:
 - Peabody Picture Vocabulary Test – Revised;
 - relevant domains of the Reynell Developmental Language Scales;
 - relevant domains of the Preschool Language Scale (PLS);
 - relevant domains of the Sequenced Inventory of Communication (SCID).
- Speech development, or expressive language skills, measured using a validated scale, for example:
 - Schlichting test;
 - Lexi list;
 - relevant domains of the Reynell Developmental Language Scales;
 - relevant domains of the PLS;
 - relevant domains of the SCID.
- Cognitive development, measured using a validated scale, for example:
 - Griffiths Mental Development Scales;
 - McCarthy General Cognitive Index;
 - Bayley Scales of Infant and Toddler Development.
- Psychosocial outcomes, measured using a validated scale, for example:
 - the Social Skills Scale of the Social Skills Rating System;
 - Child behaviour Checklist;
 - Strengths and Difficulties Questionnaire;
 - Pediatric Symptom Checklist.
- Listening skills, for example, listening to stories and instructions effectively. Given that there are few validated scales to assess listening skills in children with OME, we will include any methods used by trialists.
- Generic health-related quality of life assessed using a validated instrument, for example:
 - EQ-5D;
 - TNO AZL Children's QoL (TACQOL);
 - TNO AZL Pre-school children QoL (TAPQOL);
 - TNO AZL Infant Quality of Life (TAIQOL);

- Infant Toddler Quality of Life Questionnaire (ITQOL);
- Child Health Questionnaire (CHQ).
- Parental stress, measured using a validated scale, for example:
 - Parenting Stress Index.
- Vestibular function:
 - balance;
 - coordination.
- Number of doctor-diagnosed AOM episodes within a specified time frame

1 AOM: acute otitis media; CHQ: Child Health Questionnaire; EQ: EuroQol; OM: otitis media; OME: otitis media with
2 effusion; PLS: Preschool Language Scale; QoL: quality of life; SCID: Sequenced Inventory of Communication;
3 TNO AZL: Netherlands Organisation for Applied Scientific Research Academic Medical Centre

4 For further details see the review protocol in appendix A.

5 **Methods and process**

6 During the development of this guideline, a registered Cochrane protocol was identified
7 which matched the committee's intended PICO's. The Cochrane protocol differed from the
8 committee's intended population in that the Cochrane protocols excluded studies that did not
9 meet their inclusion criteria for trustworthiness (that is, those identified as being potentially
10 'high-risk' using a screening tool developed by Cochrane Pregnancy and Childbirth which
11 included specified criteria to identify studies that are considered sufficiently trustworthy),
12 however no studies were identified that were excluded from the review on these grounds
13 alone.

14 The Cochrane review team completed a review investigating the effectiveness of antibiotics
15 for OME in children (Mulvaney 2023a) during guideline development and presented their
16 results to the committee, who used them to make recommendations. Cochrane's methods
17 are closely aligned to standard NICE methods, minor deviations (summary of findings tables
18 instead of full GRADE tables, defining primary and secondary outcomes as opposed to
19 critical and important, assessing the risk of bias in primary studies using version 1 (as
20 opposed to version 2) of the Cochrane Risk of Bias tool, how clinically important differences
21 are determined, and including countries from a broader range of income categories than the
22 majority of the other reviews in the guideline) relevant to the topic area were highlighted to
23 the committee and taken into account in discussions of the evidence. Where results were
24 reported per ear instead of per child, Cochrane used an assumed intra-cluster correlation
25 coefficient of 0.5 to adjust the sample size. Full details of the Cochrane review, including
26 methods, are available in the review of antibiotics for children with OME, see Mulvaney
27 2023a at <https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents>.

28 We thank the Cochrane ENT Group for their assistance in providing the literature searches
29 and data for review questions relating to Otitis media with effusion in under 12s.

30 Declarations of interest were recorded according to [NICE's conflicts of interest policy](#).

31 **Effectiveness evidence**

32 **Included studies**

33 A Cochrane review (Mulvaney 2023a) including 17 randomised controlled trials (RCTs;
34 Ardehali 2008, Balle 1990, Chen 2013, Endo 1997, Ernston 1985, Healy 1984, Hemlin 1997,
35 Karlidag 2002, Leach 2008, Mandel 1987, Mandel 1991, Marchisio 1998, Møller 1990,
36 Podoshin 1990, Puhakka 1985, Thomsen 1989, van Balen 1996) is considered in this report.
37 This review was used for making recommendations by the committee, as it was considered
38 sufficiently relevant, high quality and up to date.

1 One study included children aged up to 4 years (Leach 2008), and 15 studies included
2 children aged over 4 years (Ardehali 2008; Balle 1990; Chen 2013; Endo 1997; Ernston
3 1985; Healy 1984; Hemlin 1997; Karlidag 2002; Mandel 1987; Mandel 1991; Marchisio 1998;
4 Møller 1990; Podoshin 1990; Puhakka 1985; van Balen 1996). One study did not report the
5 age of the participants (Thomsen 1989). None of the studies reported data on participants'
6 hearing levels at baseline, or whether participants had allergy, previous grommets, cleft
7 palate, or Down's syndrome.

8 The Cochrane review is summarised in Table 2, however full details of the Cochrane review
9 including methods are available in the review of antibiotics for children with OME, see
10 Mulvaney 2023a at [https://www.nice.org.uk/guidance/indevelopment/gid-](https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents)
11 [ng10193/documents](https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents).

12 See the Cochrane review for the literature search strategies, study selection flow charts,
13 forest plots and summary of findings tables, Mulvaney 2023a at
14 <https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents>.

15 Excluded studies

16 See the lists of excluded studies in the Cochrane review with reasons for their exclusions,
17 Mulvaney 2023a at [https://www.nice.org.uk/guidance/indevelopment/gid-](https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents)
18 [ng10193/documents](https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents).

19 Summary of included studies

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

21 **Table 2: Summary of included studies**

Study	Population	Comparison	Outcomes
Mulvaney 2023a Systematic review	Children aged 6 months to 12 years with unilateral or bilateral otitis media with effusion. Number of studies: 16 Number of participants: 2951	Antibiotic vs no treatment 6 trials, N=647 children with OME (Ardehali 2008, Chen 2013, Ernston 1985, Healy 1984, Karlidag 2002, Marchisio 1998) Antibiotic vs placebo 10 trials, N=2304 children with OME (Balle 1990, Endo 1997, Hemlin 1997, Leach 2008, Mandel 1987, Mandel 1991, Møller 1990, Podoshin 1990, Puhakka 1985, Thomsen 1989, van Balen 1996)	Primary: <ul style="list-style-type: none"> Hearing as <ul style="list-style-type: none"> (i) return to normal; or (ii) mean threshold Disease-specific quality of life Anaphylaxis Secondary: <ul style="list-style-type: none"> Persistence of OME Other adverse events: <ul style="list-style-type: none"> (i) ear drum changes; and (ii) patient-related Receptive and expressive language Cognitive development Psychosocial development Listening skills Generic health-related QoL Parental stress Vestibular function Number of episodes of acute otitis media

22 *N: number; OME: otitis media with effusion; QoL: quality of life*

- 1 See the Cochrane review for characteristics of studies tables, Mulvaney 2023a at
- 2 <https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents>.

3 Summary of the evidence

4 The Cochrane review of antibiotics for children with OME investigated 2 comparisons, with
5 the following findings:

- 6 • Comparison 1: Antibiotics versus no treatment. Antibiotics had an important benefit
7 for hearing returned to normal in the very short term and persistence of OME in the
8 short term (all low to very low quality of the evidence according to GRADE criteria).
9 However, when using Cochrane’s MID of 10dBHL for hearing thresholds, there was
10 no important difference between antibiotics and no treatment for final hearing
11 threshold in the short term. There was no evidence of an important difference
12 between antibiotics and no treatment for the other outcome: episodes of acute otitis
13 media (AOM) in the short term (very low quality of the evidence according to GRADE
14 criteria). There was no evidence available for this comparison for any of the other
15 outcomes specified in the protocol
- 16 • Comparison 2: Antibiotics versus placebo. Antibiotics had an important benefit for
17 number of participants with normal hearing (defined as complete improvement in air-
18 bone gap in worst ear; very low quality) in the short-term, and a possible important
19 benefit for ear-drum perforation in the medium term (90% CI: 0.2 to 0.88; very low
20 quality), but had an important harm of the adverse events: itching/ rash and diarrhoea
21 in the short term (low to very low quality), and a possible important harm of the
22 adverse event: ‘gastrointestinal’ in the very short term (90% CI: 1.03 to 2.70;
23 moderate quality of the evidence according to GRADE criteria). There was no
24 important difference or no evidence of an important difference between antibiotics
25 and placebo for the other outcomes: final hearing threshold (speech reception or
26 speech awareness) in the short term; persistence of OME in the short or medium
27 term; adverse events: vomiting, abdominal pain, mild sedation/irritability, or episodes
28 of AOM in the short term (all very low to low quality of the evidence according to
29 GRADE criteria). There was no evidence available for this comparison for any of the
30 other outcomes specified in the protocol.

31 See the Cochrane review for summary of findings tables and full results, including all primary
32 and secondary outcomes and sub-group analyses, Mulvaney 2023a at
33 <https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents>.

34 Economic evidence

35 Included studies

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

38 Economic model

39 No economic modelling was undertaken for this review because the committee agreed that
40 other topics were higher priorities for economic evaluation.

41 The committee’s discussion and interpretation of the evidence

42 The outcomes that matter most

43 The Cochrane protocol’s primary outcomes were hearing, disease-specific quality of life, and
44 anaphylaxis. The committee agreed these outcomes were critical: hearing is a direct
45 measure of any differential effectiveness associated with antibiotics; disease-specific quality

1 of life is a measure of well-being which may capture long-term health-related outcomes
2 associated with the effectiveness of interventions; and anaphylaxis would capture the risk of
3 this serious adverse event which can happen as a result of using antibiotics.

4 All other outcomes listed in the Cochrane protocol (persistence of OME; adverse events
5 (other than anaphylaxis); receptive and expressive language skills; cognitive development;
6 psychosocial development; listening skills; generic health-related quality of life; parental
7 stress; vestibular function; and number of doctor-diagnosed acute otitis media (AOM)
8 episodes) were agreed to be important outcomes by the committee. The committee agreed
9 that presence or persistence of OME after the use of antibiotics directly measures the
10 effectiveness of the intervention, and that adverse events other than anaphylaxis (including
11 harmful ear drum changes such as atrophy, and patient-related complications such as
12 vomiting), that are relatively common when using antibiotics, were important outcomes
13 because they capture the risks associated with the intervention. OME and related hearing
14 loss can be associated with impairment of receptive and expressive language skills, cognitive
15 development, psychosocial outcomes, listening skills, and vestibular function, which could
16 impact on the child's development, and therefore the committee agreed these were important
17 outcomes. The committee also agreed parental stress levels were important in order to
18 capture whether antibiotics are successful at reducing the stress that can be associated with
19 a child having OME, and generic health-related quality of life was important because this
20 would measure the well-being of the child more generally than disease-specific scales. The
21 number of doctor-diagnosed AOM episodes was agreed to be an important outcome
22 because antibiotics may have a protective role for recurrent AOM.

23 **The quality of the evidence**

24 The quality of the evidence was assessed using GRADE methodology and the evidence for
25 outcomes identified in this review ranged from very low to moderate quality, in most cases
26 due to high or moderate risk of bias and/or serious or very serious imprecision. Two
27 outcomes were also downgraded for serious indirectness (for example due to all included
28 children being aged <12 months), and for 1 outcome, there was serious inconsistency.

29 The Cochrane authors noted that the quality of the included studies likely reflected the era
30 these studies were conducted in, because they were run when reporting standards were less
31 defined. Therefore, despite the GRADE findings, Cochrane's qualitative assessment was that
32 the trials were conducted with rigour, and it is therefore unlikely that any newer trials
33 adhering to current reporting standards would have different findings. The committee agreed
34 with this assessment.

35 **Benefits and harms**

36 The committee discussed the fact that there was limited new evidence on the effectiveness
37 of antibiotics, with the latest included trial from 2013. There was evidence that antibiotics had
38 an important benefit in terms of hearing returned to normal and persistence of OME when
39 compared to no treatment, and number of participants with normal hearing when compared
40 to placebo. There was also a possible important benefit in terms of ear-drum perforation
41 when comparing antibiotics to placebo, though the committee agreed there was uncertainty
42 in the importance of the outcome. On the other hand, antibiotics had an important harm of
43 itching/ rash and diarrhoea, and a possible important harm of 'gastrointestinal' adverse
44 events when compared to placebo. The committee discussed the fact that, other than for
45 'gastrointestinal' adverse events (which had moderate quality evidence but uncertainty in the
46 importance of the outcome), the evidence for all of these outcomes was very low to low
47 quality, and some of the evidence was inconsistent; for example, other outcomes related to
48 hearing or persistence of OME showed antibiotics did not have a benefit over placebo, and
49 there was no evidence of a benefit for antibiotics compared to no treatment or placebo for
50 adverse events data for AOM, vomiting, abdominal pain, or mild sedation/irritability-related
51 adverse events.

1 The committee agreed the hearing improvement potentially associated with the use of
2 antibiotics is somewhat trivial. In particular, the hearing improvements classified as important
3 differences in the evidence would not reflect a clinically important difference in practice. The
4 committee were aware, based on their knowledge and experience, that the Uncertainty of
5 Measurement value (the doubt about the results of a measurement) is considered to be
6 about 12dB clinically (with some tests' values up to 20dB), meaning differences in hearing
7 improvement less than this are usually not regarded as clinically important. The committee
8 also discussed the fact that all evidence showing benefits of antibiotic use (including any
9 improvement in hearing gain or resolution of OME) was of low or very low quality, and was
10 inconsistent with other hearing outcomes when comparing antibiotics to placebo, which
11 showed no evidence of an important difference between interventions. Although only oral
12 antibiotics were investigated in the review, the committee agreed it was appropriate to
13 extrapolate the evidence to apply to topical antibiotics as well, based on their knowledge that
14 topical antibiotics tend to be weaker than oral antibiotics, and would therefore likely have
15 even less of an effect on outcomes such as hearing or persistence of OME. The committee
16 agreed that overall, the potential benefits of antibiotics did not outweigh the risks associated
17 with their use, including the potential for adverse events as shown in the data, and increased
18 antibiotic resistance. Given this decision, and the lack of new evidence contributing to the
19 review, the committee agreed antibiotics should not be recommended for children with OME.
20 The committee discussed the fact that long term outcomes were not represented in the data
21 and agreed, based on their knowledge and experience, that these would be unlikely to
22 change recommendations significantly, because the critical period to consider for hearing
23 outcomes is in the short-term. The committee agreed this is because a negative impact on
24 hearing levels even for short periods of time can significantly impact a child's development,
25 and it is therefore important to negate these as soon as possible rather than waiting for
26 spontaneous resolution.

27 In the 2008 guideline on OME there was a single recommendation that stated that the
28 following treatments were not recommended for the management of OME: antibiotics;
29 antihistamines; decongestants; steroids; homeopathy; cranial osteopathy; acupuncture;
30 dietary modification, including probiotics; and massage. When the guideline was updated in
31 2023, review questions were prioritised for antibiotics, antihistamines, decongestants and
32 steroids. An evidence review was not conducted when the guideline was updated in 2023 for
33 homeopathy, cranial osteopathy, acupuncture, dietary modification, including probiotics, and
34 massage. The review performed for the 2008 guideline did not find any [evidence of](#)
35 [effectiveness](#) for homeopathy, cranial osteopathy, acupuncture, dietary modification,
36 including probiotics, and massage, and no new applicable evidence has come to light since
37 then. The committee agreed, based on their experience, that there is still variation in practice
38 and so it was important to continue to advise against using homeopathy, cranial osteopathy,
39 acupuncture, dietary modification, including probiotics, and massage as treatment options as
40 there was a lack of evidence regarding their effectiveness in treating OME in children under
41 12. Therefore, the recommendation on not using homeopathy, cranial osteopathy,
42 acupuncture, dietary modification, including probiotics, and massage was brought forward
43 from the 2008 guideline.

44 **Cost effectiveness and resource use**

45 As no formal economic evaluation was undertaken the committee made a qualitative
46 assessment of the likely cost effectiveness of their recommendations. Given that there was
47 very limited evidence suggesting that antibiotics resulted in significant clinical benefit in
48 addition to some harms the committee considered that the use of antibiotics would not
49 represent a cost-effective use of NHS resources. As antibiotics are not currently
50 recommended for the management of OME, the committees' recommendations will not have
51 a resource impact.

1 Recommendations supported by this evidence review

2 This evidence review supports recommendation 1.5.2.

3 References – included studies

4 Effectiveness

5 Mulvaney 2023a

6 Mulvaney CA, Galbraith K, Webster KE, Rana M, Connolly R, Marom T, Daniel M,
7 Venekamp RP, Schilder AGM, MacKeith S. Antibiotics for otitis media with effusion (OME) in
8 children. Cochrane Database of Systematic Reviews 2023. Art. No.: CD015254. DOI:
9 10.1002/14651858.CD015254.pub2

1 **Appendices**

2 **Appendix A Review protocol**

3 **Review protocol for review question: What is the effectiveness of antibiotics for managing OME in children under 12** 4 **years?**

5 See the Cochrane review protocol, Mulvaney 2023a at <https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents>.

1 Appendix B Literature search strategies

2 Literature search strategies for review question: What is the effectiveness of 3 antibiotics for managing OME in children under 12 years?

4 Clinical

5 See Appendix 1 and Appendix 2 of the Cochrane review, Mulvaney 2023a at
6 <https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents>.

7 Economic literature search strategy

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

10 Database: MEDLINE – OVID interface

11 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"

12 Database: Embase – OVID interface

13 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/

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

ID	Search
#30	{or #21-#29}
#31	#20 or #30
#32	#3 and #31 with Cochrane Library publication date Between Jan 2000 and Apr 2022

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

3 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]

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

5 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

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1 **Appendix C Effectiveness evidence study selection**

2 **Study selection for: What is the effectiveness of antibiotics for managing OME** 3 **in children under 12 years?**

4 See Results of the search – figure 1 from the Cochrane review, Mulvaney 2023a at
5 <https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents>.

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1 **Appendix D Characteristics of studies tables**

2 **Characteristics of studies tables for review question: What is the effectiveness of antibiotics for managing OME in children** 3 **under 12 years?**

4 See the Characteristics of included studies tables from the Cochrane review, Mulvaney 2023a at
5 <https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents>.

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1 **Appendix E Data and analyses tables**

2 **Data and analyses tables for review question: What is the effectiveness of antibiotics for managing OME in children under** 3 **12 years?**

4 See the Data and analyses tables from the Cochrane review, Mulvaney 2023a at [https://www.nice.org.uk/guidance/indevelopment/gid-](https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents)
5 [ng10193/documents](https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents).

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1 **Appendix F Summary of findings tables (or other full modified GRADE tables)**

2 **Summary of findings tables for review question: What is the effectiveness of antibiotics for managing OME in children under** 3 **12 years?**

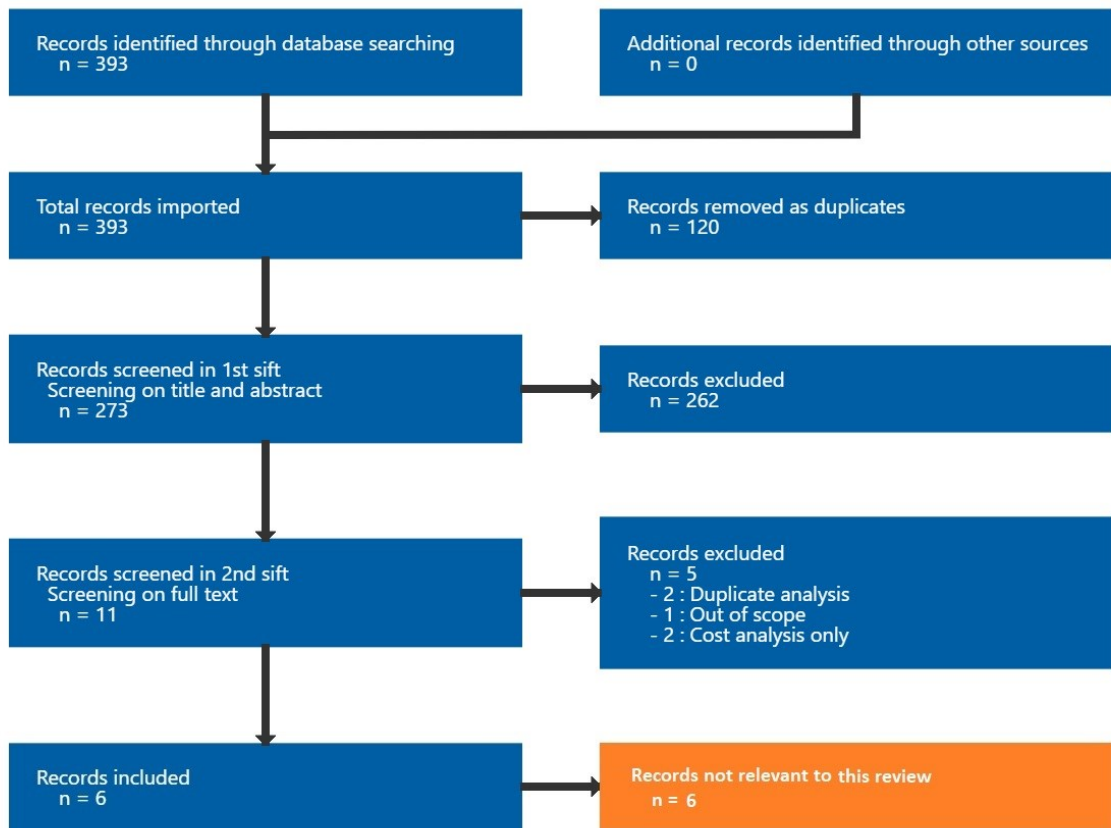
4 See the Summary of findings tables from the Cochrane review, Mulvaney 2023a at [https://www.nice.org.uk/guidance/indevelopment/gid-](https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents)
5 [ng10193/documents](https://www.nice.org.uk/guidance/indevelopment/gid-ng10193/documents).

1 Appendix G Economic evidence study selection

2 Study selection for: What is the effectiveness of antibiotics for managing OME 3 in children under 12 years?

4 A global economic literature search was undertaken for otitis media with effusion in under
5 12s. This covered all 14 review questions in this guideline. As shown in Figure 1 below, no
6 economic studies were identified which were applicable to this review question.

Figure 1: Study selection flow chart



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1 **Appendix H Economic evidence tables**

2 **Economic evidence tables for review question: What is the effectiveness of**
3 **antibiotics for managing OME in children under 12 years?**

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

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1 **Appendix I Economic model**

2 **Economic model for review question: What is the effectiveness of antibiotics**
3 **for managing OME in children under 12 years?**

4 No economic analysis was conducted for this review question.

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1 **Appendix J Excluded studies**

2 **Excluded studies for review question: What is the effectiveness of antibiotics** 3 **for managing OME in children under 12 years?**

4 **Excluded effectiveness studies**

5 See the Characteristics of excluded studies table from the Cochrane review, Mulvaney
6 2023a at <https://www.nice.org.uk/guidance/indevelopment/qid-ng10193/documents>.

7 **Excluded economic studies**

8 No economic evidence was identified for this review.

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1 **Appendix K Research recommendations – full details**

2 **Research recommendations for review question: What is the effectiveness of**
3 **antibiotics for managing OME in children under 12 years?**

4 No research recommendations were made for this review question.
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