National Institute for Health and Care Excellence

Draft for consultation

Otitis media with effusion in under 12s

[B] Evidence reviews for presenting features associated with OME in children

NICE guideline number tbc

Evidence reviews underpinning recommendations 1.2.1 to 1.2.6 in the NICE guideline

March 2023

Draft for consultation

This evidence review was developed by NICE

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Presenting features associated with OME in children

Review question

What presenting features are associated with OME in children under 12 years?

Introduction

The aim of this review is to identify the presenting features that are associated with OME in children under 12 years.

Summary of the protocol

See Table 1 for a summary of the Population, Index tests, Reference standard and Target condition (PIRT) characteristics of this review.

Table 1: Summary of the protocol (PIRT table)

Population	All children under 12 years with suspected otitis media with effusion (OME)
Index tests	Any signs and symptoms (presenting features), alone or in combination, including but not limited to: • Hearing difficulty • Indistinct speech • Poor listening skills • Delayed language development • Ear discomfort or ache • History of recurrent upper respiratory tract infection • History of allergic rhinitis • Rhinorrhoea (nasal discharge) • Behavioural issues (e.g., being withdrawn, head banging, anxiety, frustration) • lack of concentration or attention • Poor educational progress • Poor comprehension • balance difficulties (e.g., clumsiness) • Tinnitus • Hyperacusis • Tiredness/fatigue • Actively socially withdrawn • History of AOM
Reference standard	Diagnosis of OME must be made based on tympanometry with or without otoscopy
Target condition	OME
Outcomes	• Sensitivity • Specificity • Positive predictive value • Negative predictive value

AOM: acute otitis media; 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). In this review, presenting features that cross the low threshold (60%) for sensitivity or specificity are described as moderately sensitive or specific, whereas presenting features that cross the high threshold (90%) for sensitivity or specificity are described as highly sensitive or specific.

The protocol included systematic reviews of cross-sectional diagnostic accuracy studies and primary cross-sectional diagnostic accuracy studies only. However, no studies were identified that aimed to examine the diagnostic test accuracy (DTA) of presenting features. Therefore, we broadened the study design criteria to include studies reporting associations between presenting features and otitis media with effusion (OME). Where sufficient information was presented, data was extracted that allowed for the calculation of DTA outcomes (e.g., sensitivity and specificity); such studies were included in the diagnostic evidence below.

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

Diagnostic evidence

Included studies

Five studies were included: 4 case-control studies (Chantzi 2006; Kwon 2013; Martines 2011; Ralli 2011), and 1 cross-sectional study (Quaranta 2013).

The included studies are summarised in Table 2.

One study (Chantzi 2006) compared children with OME with children attending the ENT department for reasons other than OME with no history of OME and no more than 2 episodes of otitis media (OM) per year; 1 study (Kwon 2013) compared children with OME with children without OME or OM who had undergone blood tests and multiple allergosorbent test – chemiluminescent assay (MAST-CLA) because of ranula, ankyloglossia, preauricular fistula or epistaxis; 1 study (Martines 2011) compared primary school children with OME with those without OME; 1 study (Quaranta 2013) included children with grade 3 or 4 adenoid hypertrophy (and compared those with OME with those without OME; and 1 study (Ralli 2011) compared children with OME for more than 3 months with healthy children with no current or history of OME, and normal otoscopic findings.

Three studies excluded participants with craniofacial anomalies (Chatnzi 2006), suspected head and neck abnormalities (Kwon 2013) or skull-facial malformations (Martines 2011), and 2 studies did not report data on whether any participants had craniofacial anomalies (Quaranta 2013; Ralli 2011).

One study included children with an average age of 4 years (Chantzi 2006), and 4 studies included children with an average age of over 6 years (Kwon 2013, Martines 2011, Quaranta 2013, Ralli 2011).

Only single studies investigated the DTA of the following symptoms, signs, or presenting features: history of adenoidectomy (Chantzi 2006); nasal obstruction (Chantzi 2006); tonsil hypertrophy (Kwon 2013); Immunoglobin E (IgE) sensitisation (Chantzi 2006); any allergic disease (asthma, rhinitis, eczema, or any combination of these) (Chantzi 2006); IgE-mediated asthma (Chantzi 2006); non-allergic rhinitis (Chantzi 2006, Quaranta 2013); infective rhinitis (Quaranta 2013); the combination of allergic rhinitis and infective rhinitis (Quaranta 2013); the combination of non-allergic rhinitis and infective rhinitis (Quaranta 2013); chronic rhinosinusitis (Kwon 2013); IgE-mediated eczema (Chantzi 2006); food

reactions (Chantzi 2006); drug reactions (Chantzi 2006); anaphylaxis (Chantzi 2006); elevated eosinophil count (more than 4%) (Chantzi 2006); urticaria (Chantzi 2006); dyspnoea (Chantzi 2006); wheezing (Chantzi 2006); recurrent cough (Chantzi 2006); rhinorrhoea (Chantzi 2006); paroxysmal sneezing/ nasal itching (Chantzi 2006); snoring (Martines 2011); deleterious sucking habits (Ralli 2011); atypical swallowing (Ralli 2011); history of acute otitis media (AOM) (Martines 2011); history of upper respiratory tract infection (URTI) (Martines 2011); and the combination of allergy and history of URTI (Martines 2011).

The DTA of the following symptoms, signs, or presenting features were investigated by multiple studies, but there was variation in how the features were defined and measured across studies: adenoid hypertrophy (Chantzi 2006; Kwon 2013); atopy (Chantzi 2006; Martines 2011); asthma (Chantzi 2006; Kwon 2013); allergic rhinitis (Chantzi 2006; Kwon 2013; Quaranta 2013) non-allergic rhinitis (Chantzi 2006; Quaranta 2013); eczema/ atopic dermatitis (Chantzi 2006; Kwon 2013); and conjunctivitis (Chantzi 2006; Kwon 2013).

All studies used tympanometry as part of their reference standard. One study (Kwon 2013) used otoscopy in addition to tympanometry to diagnose OME and 1 study (Quaranta 2013) used pure tone audiometry in addition to tympanometry. The remaining 3 studies (Chantzi 2006; Martines 2011; Ralli 2011) used a combination of tympanometry, otoscopy and additional symptoms or medical history to diagnose OME.

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	Index test(s)	Reference standard(s)	Outcomes	Comments
Chantzi 2006 Case-control study Greece	N=168 children with or without OME attending ENT department during the study period OME group: n=88 • Age in years, mean (SD): 4.5 (NR, range: 1-6.7) • Sex (male/female): 56/32 • Craniofacial anomalies: None*	<u>Presenting features:</u> 1. Adenoid hypertrophy 2. History of adenoidectomy 3. Immunoglobin E (IgE) sensitisation 4. Any allergic disease (defined as a positive clinical history of asthma, rhinitis, and/ or eczema) 5. IgE-mediated allergic disease (atopy; defined as the presence of any allergic	Tympanometry (type B or C tympanograms) with otoscopy, clinical symptoms (hearing loss, otalgia, or irritability, 'plugged' feeling or 'popping' in their ears, speech, or behavioural disorders, tinnitus, vertigo) and symptom duration of >1 month or a history of recurrent OME	• Sensitivity • Specificity • PPV • NPV	Control group were children who had no history of or current OME, no frequent (>2 per year) episodes of OM, and no otoscopic findings of OM

Study	Population	Index test(s)	Reference standard(s)	Outcomes	Comments
	Group without OME: n=80 • Age in years, mean (SD): 4.4 (NR, range: 1.3-6.7) • Sex (male/female): 53/27 • Craniofacial anomalies: None* *Study excluded children with craniofacial abnormalities	disease, as above, combined with IgE sensitisation) 6. Dyspnoea 7. Wheezing 8. Recurrent cough 9. Asthma 10. IgE-mediated asthma (defined as asthma combined with IgE sensitisation) 11. Rhinitis 12. Nasal obstruction 13. Rhinorrhoea 14. Paroxysmal sneezing/ nasal itching 15. IgE-mediated allergic rhinitis (defined as rhinitis combined with IgE sensitisation) 16. Conjunctivitis 17. Eczema 18. IgE-mediated eczema (defined as eczema combined with IgE sensitisation) 19. Food reactions 20. Drug reactions 21. Urticaria 22. Anaphylaxis 23. Elevated eosinophil count (>4%)			
Kwon 2013 Case-control study Korea	N=470 children with or without OME OME group: n=370 • Age in years, mean (SD):	<u>Presenting features:</u> 1. Allergic rhinitis 2. Asthma 3. Atopic demartitis 4. Allergic conjunctivitis	Tympanometry (type B or C tympanograms on impedance audiometry) with otoscopy (amber-coloured tympanic membrane on	• Sensitivity • Specificity • PPV • NPV	Control group were children without OME or otitis media, who had undergone blood tests and MAST-CLA because of ranula,

Study	Population	Index test(s)	Reference standard(s)	Outcomes	Comments
	7.5 (NR, range: 2-14) • Sex (male/female): 235/135 • Craniofacial anomalies: none* Group without OME: n=100 • Age in years, mean (SD): 5.9 (NR, range: 3-12) • Sex (male/female): 26/24 (Figure is not correct or incomplete as n=100) • Craniofacial anomalies: none* *Study excluded children with suspected head and neck abnormalities	5. Chronic rhinosinusitis 6. Tonsil hypertrophy 7. Adenoid hypertrophy	otoscopic examination)		ankyloglossia, preauricular fistula or epistaxis
Martines 2011 Case-control study Italy	N=2097 children attending specific primary schools during the study period • Age in years, mean (SD): 9.9 (NR) Children with persistent (≥3 months) OME: n=143 • Age in years, mean (SD): NR. Age: n (%): ○ 5-6 years: 40 (28%) ○ 7-8 years: 32 (22%)	<u>Presenting features:</u> 1. Atopy/ allergy 2. Snoring 3. History of AOM 4. History of upper respiratory tract infection (URTI) 5. Allergy and history of URTI	Tympanometry (presence of B or C tympanograms; absence of ipsilateral acoustic reflex) with otoscopy (documented persistent middle ear effusion for a minimum of 3 months) and a conductive hearing loss greater than 25 dB at any one of the frequencies from 250 Hz through 4 kHz	• Sensitivity • Specificity • PPV • NPV	Control group were children with no OME

Study	Population	Index test(s)	Reference standard(s)	Outcomes	Comments
	○ 9-10 years: 36 (25%) ○ 11-12 years: 20 (14%) ○ 13-14 years: 15 (10%) • Sex (male/female): 43/100 • Craniofacial anomalies: none* Children with no OME: n=1954 • Age in years, mean (SD): NR. Age: n (%): ○ 5-6 years: 270 (14%) ○ 7-8 years: 314 (16%) ○ 9-10 years: 526 (27%) ○ 11-12 years: 368 (19%) ○ 13-14 years: 476 (24%) • Sex (male/female): 889/1065 • Craniofacial anomalies: none* * Study excluded children with skull-facial malformations				
Quaranta 2013 Cross-sectional study Italy	N=81 children with grade 3 or 4 adenoid hypertrophy (choanal obstruction greater than 75%) • Age in years, mean (SD)::	<u>Presenting features:</u> 1. Allergic rhinitis (defined as positive SPT, nasal symptoms due to allergens and	Tympanometry and pure tone audiometry	• Sensitivity • Specificity • PPV • NPV	None

Study	Population	Index test(s)	Reference standard(s)	Outcomes	Comments
	6.9 (NR, range: 4-15) • Sex (male/female): 48/33 • Craniofacial anomalies: NR • OME prevalence (number of children with OME/without OME): 52/29	heterogeneous rhinocytogram) 2. Infective rhinitis (defined as abundant bacteria that could be found in extracellular tissue and inside neutrophils due to phagocytosis) 3. Non-allergic rhinitis (defined as negative SPT and the continuous presence of inflammatory cells in the nasal mucosa independently from the seasonality) 4. Allergic rhinitis and infective rhinitis 5. Non-allergic rhinitis and infective rhinitis			
Ralli 2011 Case-control study Italy	N=125 children with or without OME OME group: n=65 • Age in years, mean (SD): 9.2 (NR) • Sex (male/female): 36/29 • Craniofacial anomalies: NR Healthy control group: N=60 • Age in years, mean (SD):: 9.1 (NR) • Sex (male/female): 38/22	<u>Presenting features:</u> 1. Deleterious sucking habits, such as finger- or dummy-sucking, and bottle feeding (parafunctional sucking habits and mode of mouth breathing were also recorded, though information about recorded this is not reported) 2. Atypical swallowing (defined as lip activity producing strong tension in the perioral	Tympanometry, ENT examination using otoscopy, and medical history	• Sensitivity • Specificity • PPV • NPV	Control group are healthy children with no current or history of OME and normal otoscopic findings

Study	Population	Index test(s)	Reference standard(s)	Outcomes	Comments
	• Craniofacial anomalies: NR	musculature, and/or the tip of the tongue pushed/ placed against the anterior teeth when swallowing)			

AOM: acute otitis media; dB: decibel; ENT: ears, nose and throat; Hz: hertz; IgE: Immunoglobin E; kHz: kilohertz; MAST-CLA: multiple allergosorbent test – chemiluminescent assay; NPV: negative predictive value; NR: not reported; OM: otitis media; OME: otitis media with effusion; PPV: positive predictive value; SD: standard deviation; SPTs: skin prick tests; URTI: upper respiratory tract infection

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

Summary of the evidence

The evidence was very low to high quality. Downgrading of the evidence was due to risk of bias and imprecision. No meta-analyses were possible for any of the index tests as there were insufficient similarities in definitions for and measurement of presenting features between studies, as well as differences in populations and reference standards used.

All the evidence was based on individual signs, symptoms, and presenting features (no multivariate analysis). None of the presenting features examined were both very sensitive and very specific for a diagnosis of OME in children under 12. The majority of presenting features were moderately or very specific, but not sensitive. See table 3 for a summary of the sensitivity, specificity, PPV and NPV for all the presenting features.

Sensitive and specific presenting features

There was variation in the sensitivity and specificity for atopy for a diagnosis of OME, depending on how it was measured. There was evidence that atopy was both moderately sensitive and moderately specific for a diagnosis of OME, when assessed using skin prick tests (SPT). However, there was evidence from a different study that atopy was very specific but not sensitive, when measured using a positive clinical history, SPT and/or CAP-fluoroenzymoimmunoassay (CAP-FEIA).

Sensitive but not specific presenting features

Nasal obstruction was very sensitive but not specific for a diagnosis of OME.

There was evidence that the following presenting features were moderately sensitive, but not specific, for a diagnosis of OME: adenoid hypertrophy, a history of adenoidectomy, rhinorrhoea, and any allergic disease (asthma, rhinitis, eczema, or any combination of these). However, when assessed individually, all the presenting features included under the composite index test 'any allergic disease', (asthma, rhinitis, and eczema) were found to be moderately or very specific but not sensitive. For asthma, the specificity varied depending on how it was measured; it was moderately specific when measured by a physician questionnaire but very specific when measured by multiple allergosorbent test – chemiluminescent assay (MAST-CLA) and medical records.

Specific but not sensitive presenting features

There was evidence that the following presenting features were very specific, but not sensitive, for a diagnosis of OME: IgE-mediated asthma, allergic rhinitis, the combination of allergic rhinitis and infective rhinitis, chronic rhinosinusitis, eczema/ atopic dermatitis, IgE-mediated eczema, food reactions, drug reactions, anaphylaxis, conjunctivitis, wheezing, a history of AOM, and the combination of allergy and a history of URTI.

There was evidence that the following presenting features were moderately specific, but not sensitive, for a diagnosis of OME: Immunoglobin E (IgE) sensitisation, allergic rhinitis, non-allergic rhinitis, infective rhinitis, the combination of non-allergic rhinitis and infective rhinitis, elevated eosinophil count (>4%), urticaria, dyspnoea, paroxysmal sneezing/ nasal itching, snoring, deleterious sucking habits, atypical swallowing, and a history of upper respiratory tract infection.

Not sensitive or specific presenting features

Tonsil hypertrophy and a recurrent cough were neither sensitive nor specific for a diagnosis of OME.

Presenting features with no evidence

No DTA evidence was found for the following signs, symptoms, or presenting features set out in the protocol: hearing difficulty; indistinct speech; poor listening skills; delayed language development; ear discomfort or ache; behavioural issues (such as being withdrawn, head banging, anxiety, frustration); lack of concentration or attention; poor educational progress; poor comprehension; balance difficulties (such as clumsiness); tinnitus; hyperacusis; tiredness/ fatigue; or actively socially withdrawn.

Table 3: Summary of sensitivity, specificity, PPV and NPV for presenting features

	Not sensitive (sensitivity <0.6, i.e. <60%)	**Moderately sensitive (sensitivity ≥0.6 to <0.9, i.e. ≥60% to <90%)**	**Very sensitive (sensitivity ≥0.9, i.e. ≥90%)**
Not specific (specificity <0.6, i.e. <60%)	• Tonsil hypertrophy (PPV: 0.78, NPV: 0.21) • Recurrent cough (PPV: 0.51, NPV: 0.51)	• Adenoid hypertrophy (PPV: 0.52-0.85, NPV: 0.34-0.47) • History of adenoidectomy (PPV: 0.55, NPV: 0.48) • Any allergic disease (PPV: 0.61, NPV: 0.57) • Rhinorrhoea (PPV: 0.58, NPV: 0.55)	• Nasal obstruction (PPV: 0.54, NPV: 0.62)
Moderately specific (specificity ≥0.6 to <0.9, i.e. ≥60% to <90%)	• Asthma (physician questionnaire) (PPV: 0.67, NPV: 0.53) • IgE sensitisation (PPV: 0.70, NPV: 0.53) • Allergic rhinitis (MAST-CLA & medical records) (PPV: 0.89, NPV: 0.26) • Non-allergic rhinitis (PPV: 0.63-0.65, NPV: 0.47-0.53) • Infective rhinitis (PPV: 0.58, NPV: 0.46) • Non-allergic rhinitis and infective rhinitis (PPV: 0.57, NPV: 0.45) • Elevated eosinophil count (PPV: 0.51, NPV: 0.47) • Urticaria (PPV: 0.60, NPV: 0.50) • Dyspnoea (PPV: 0.67, NPV: 0.52) • Paroxysmal sneezing/ nasal itching (PPV: 0.64, NPV: 0.53) • Snoring (PPV: 0.16, NPV: 0.95)	• Atopy (SPT) (PPV: 0.85, NPV: 0.34)	None

	Not sensitive (sensitivity <0.6, i.e. <60%)	Moderately sensitive (sensitivity ≥0.6 to <0.9, i.e. ≥60% to <90%)	Very sensitive (sensitivity ≥0.9, i.e. ≥90%)
	• Deleterious sucking habits (PPV: 0.70, NPV: 0.56) • Atypical swallowing (PPV: 0.67, NPV: 0.58) • History of URTI (PPV: 0.14, NPV: 0.95)		
Very specific (specificity ≥0.9, i.e. ≥90%)	• Atopy (clinical history, SPT…) (PPV: 0.78, NPV: 0.52) • Asthma (MAST-CLA & medical records) (PPV: 0.50, NPV: 0.20) • IgE-mediated asthma (PPV: 0.79, NPV: 0.50) • Allergic rhinitis (physician questionnaire, SPT and/or CAP-FEIA) (PPV: 0.80, NPV: 0.51) • Allergic rhinitis (cytology, SPT and nasal sampling) (PPV: 0.25, NPV: 0.43) • Allergic rhinitis and infective rhinitis (PPV: 1.00, NPV: 0.46) • Chronic rhinosinusitis (PPV: 0.87, NPV: 0.22) • Eczema/ atopic dermatitis (PPV: 0.53-0.81, NPV: 0.20-0.51) • IgE-mediated eczema (PPV: 1.00, NPV: 0.50) • Food reactions (PPV: 0.75, NPV: 0.49) • Drug reactions (PPV: 0.60, NPV: 0.49) • Anaphylaxis (PPV: 1.00, NPV: 0.48) • Conjunctivitis (PPV: 0.45-0.50, NPV: 0.20-0.47) • Wheezing (PPV: 0.83, NPV: 0.54) • History of AOM (PPV: 0.15, NPV: 0.94) • Allergy and history of URTI (PPV: 0.46, NPV: 0.95)	None	None

AOM: acute otitis media; CAP-FEIA: CAP-fluoroenzymoimmunoassay; IgE: Immunoglobin E; PPV: positive predictive value; MAST-CLA: multiple allergosorbent test – chemiluminescent assay; NPV: negative predictive value; SPT: skin-prick test; URTI: upper respiratory tract infection

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

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were selected as critical outcomes as these are commonly used measures of the discriminative ability of index tests and, therefore, provide information about how well different presenting features can discriminate between children with and without OME. The committee considered the impact of true positives (referring children with OME for further investigations that should lead to a diagnosis and management of OME), true negatives (reassuring children who do not have OME and their parents that they are not likely to have OME and not making a referral for further investigations), false positives (referring children without OME for further investigations that are unnecessary) and false negatives (failing to identify children with OME that require further investigations and management of OME) at this point in the pathway (initial recognition) where the aim is to identify when to refer children for further investigation, and noted that false negatives could be particularly impactful. Additionally, the committee agreed further investigations such as tympanometry or otoscopic examination are minimally invasive tests that are unlikely to cause harm in the event of false positives. Therefore, they agreed to prioritise the sensitivity of presenting features over specificity, as index tests with high sensitivity will have a lower false negative rate than those with low sensitivity. The committee considered the positive and negative predictive values as additional information alongside sensitivity and specificity to allow them to understand what the impact of a system that recommended a certain action for all positive or negative test results would be.

The quality of the evidence

The quality of the evidence was assessed using GRADE methodology. The evidence was very low to high quality and downgrading of the evidence was due to risk of bias as per QUADAS-2 (for example, the potential for risk of bias due to case-control methodology, subjective methods of assessment of the presenting feature, or the interval between assessment of the presenting features and diagnosis of OME) and imprecision (95% confidence intervals crossing decision-making thresholds). No meta-analyses were possible for any of the index tests (presenting features), given there was insufficient similarities in terms of the definitions for, and measurement of, the presenting features, the reference standard used (diagnostic criteria for OME), and populations. DTA evidence from the cross-sectional study was all of high to moderate quality and therefore was prioritised in the committee's discussion of the evidence, especially when there was conflicting evidence from studies regarding similar presenting features.

No evidence was found for the following signs, symptoms, or presenting features set out in the protocol: hearing difficulty; indistinct speech; poor listening skills; delayed language development; ear discomfort or ache; behavioural issues (such as being withdrawn, head banging, anxiety, frustration); lack of concentration or attention; poor educational progress; poor comprehension; balance difficulties (such as clumsiness); tinnitus; hyperacusis; tiredness/ fatigue; or actively socially withdrawn.

Benefits and harms

The recommendation about the features that children with OME usually present with was made based on the committee's knowledge and experience, as well as recommendations from the previous NICE guideline on OME (NICE 2008). The committee discussed the lack of evidence on certain signs and symptoms commonly reported by parents, such as behavioural issues, and the fact that all the evidence identified in the literature was on clinical features. The committee agreed it was likely the age of the children in the included studies contributing to the lack of evidence on these presenting features because the participants tended to be over 5 years old, and normally features such as indistinct speech, listening skills, and behavioural issues are identified by parents when children are very young (between 18 months to 3 years). The committee agreed studies looking at older children would have been unlikely to pick up on these types of presenting features. They agreed, based on their knowledge and experience, that these parent-reported factors were usually associated with OME, and should be captured in the recommendations to ensure the recommendations were representative of younger populations and to help raise awareness of the association between such factors and OME among parents, carers, and professionals who are regularly in contact with children, such as teachers. The committee agreed this was important so that people know when to flag concerns about the child or present to services, therefore, facilitating assessment and treatment. As a result, they reviewed the recommendations from the previous NICE guideline on OME about clinical presentation. The committee agreed that hearing difficulties are usually associated with a diagnosis of OME, based on their knowledge and experience that people with OME tend to present with concerns about hearing. The committee agreed that indistinct speech and tinnitus are important presenting features for OME because they can be linked to other symptoms such as nasal obstruction or hearing difficulties, and in their experience are frequently reported by parents. However, indistinct speech only captures speaking quality and not all the elements of speech difficulty that can be indicative of OME, such as not speaking at all. As a result, the committee agreed to include delayed speech development as a potential presenting feature in addition to delayed language development from the original guideline, to capture delays in both receptive and expressive language and phonological elements. The committee agreed that repeated ear infections would not usually be associated with OME, and that instead, in their experience parents and carers of children with OME usually present with concerns about their child having frequent earache (which can sometimes mistakenly be associated with infection). Additionally, intolerance of loud sounds is usually associated with children who have recovered from OME and can now hear more clearly, rather than those who currently have OME. As a result, repeated ear infections and intolerance of loud sounds were removed from the list. The committee also agreed to remove a history of URTI and nasal obstruction from this list to reflect the fact that there was available evidence on these presenting features, and they therefore are covered by the recommendations discussed below. The committee agreed clinicians should suspect OME as a potential diagnosis where there are concerns about these features, but that a stronger recommendation should not be made due to the lack of any evidence on these presenting features.

The recommendation about additional features that can be associated with OME was made based on the committee's knowledge and experience, as well as recommendations from the previous NICE guideline on OME. The committee agreed that some children with OME did present with some of the other features listed in the original guideline, such as poor educational progress and balance difficulties, but in their experience these features were less commonly associated with OME. Some children with OME also present with behavioural problems, such as irritability and frustration, because other symptoms such as pain can manifest as irritability, particularly in very young children who cannot otherwise communicate their discomfort. The committee agreed that parents, carers, and professionals should be aware that these features can be associated with OME, but that they should not have the same priority as the features listed in the recommendation discussed above when considering whether the child has OME. The committee acknowledged that other formal assessments may be considered necessary depending on the features present and potential

differential diagnoses. For example, behavioural issues may prompt a referral for assessment of Autistic spectrum disorders, but this was outside the scope of the current guideline.

The committee assessed the evidence and used it to make recommendations on when clinicians should have a higher suspicion of OME. The committee noted that many of the presenting features identified in the evidence were assessed using tests that are typically performed in secondary care settings, some of which are invasive, such as SPT, blood tests, or other investigations (for example, to confirm adenoid hypertrophy). These features included IgE sensitisation, allergic rhinitis, infective rhinitis, allergic rhinitis with infective rhinitis, non-allergic rhinitis with infective rhinitis, an elevated eosinophil count, atopy, IgE-mediated asthma, chronic rhinosinusitis, IgE-mediated eczema, and allergy and history of URTI. While atypical swallowing was not necessarily assessed using invasive measures in the evidence, it was investigated using specific consideration of the way in which a child swallowed, in a manner which the committee agreed, in their experience, would not normally be assessed at first presentation. Clinicians, especially those in primary care, would be unlikely to conduct these tests at a child's first presentation to services. For this reason, the committee agreed that, although such presenting features might be useful to inform management further down a care pathway, they would not be useful to inform which children at initial presentation may need further assessment for OME and that relying on such tests would cause delays in identifying children. The committee also agreed that tonsil hypertrophy and a recurrent cough should not be used to identify children who require further assessment for OME as the evidence showed these presenting features were neither sensitive nor specific.

The only presenting feature that was at least moderately sensitive and specific was atopy, when assessed using only SPT. However, the committee agreed the very low quality of the evidence, the fact that there was other, better-quality evidence that atopy was very specific, but not sensitive when assessed using clinical history, SPT and/or CAP-FEIA, and blood tests, and the fact that a diagnosis of atopy would require secondary testing meant that atopy could not be relied upon to identify children who require further assessment. Considering the lack of presenting features that are both sensitive and specific, the committee agreed to make two separate sets of recommendations to capture the presenting features which were at least moderately specific but not sensitive, and the presenting features which were at least moderately sensitive but not specific.

The committee agreed the presenting features that are moderately or very specific and were not assessed using invasive measures would allow clinicians to rule in a potential diagnosis of OME. The committee discussed the fact that, in their experience, it is unusual to associate deleterious sucking habits with OME. However, the study investigating this presenting feature indicated that mode of mouth breathing was assessed as part of the criteria for deleterious sucking habits. The committee agreed mouth breathing can be linked to nasal obstruction, which was shown to have high sensitivity in the evidence and, therefore, agreed that deleterious sucking habits should be included as a presenting feature associated with OME but that the definition of this from the evidence should be included in the recommendation to help clinicians understand what this includes. Without adequate sensitivity, the committee agreed that it would not be appropriate for children to be excluded from consideration for further investigations if they did not have these presenting features, because the absence of these features would not rule out a diagnosis of OME. As a result of this and the committee's decision to prioritise sensitivity as the most useful outcome, the committee did not make a stronger recommendation.

The committee assessed the evidence and used it to make recommendations on when OME is less likely to be a potential diagnosis. The committee discussed the presenting features which were found to be moderately or very sensitive, but not specific. They agreed that people with OME usually have nasal obstruction and rhinorrhoea, and these could be useful symptoms to help rule out OME in children who do not present with it. The committee also

agreed that a history of adenoidectomy may indicate a higher risk of OME and therefore could be used as an indication of OME in children. They discussed whether adenoid hypertrophy could be considered a presenting feature because this is not normally something parents report and is usually assessed in secondary care, but agreed the evidence showed that adenoid hypertrophy was moderately sensitive when assessed using either imaging, which would be performed in secondary care, or a standardised physician questionnaire, which could be used in primary care. However, the lack of specificity for these symptoms mean other potential diagnoses could not be dismissed because of their presence. The committee therefore agreed that the presenting features which were highly sensitive should be used as an indication that the child might be less likely to have OME. The committee agreed the low quality of the evidence for the presenting feature 'any allergic disease', as well as the conflicting evidence that the symptoms included under this composite feature (asthma, rhinitis, and/ or eczema) when assessed in isolation were not sensitive, meant that it would be misleading to suggest that the absence of any of these features should make a clinical suspicion of OME less likely and, therefore, did not include this composite feature in the recommendations. However, the committee discussed that the evidence for 'any allergic disease' may suggest that the consideration of multiple presenting features could be more indicative of OME than assessing features in isolation of each other, suggesting that the presence of multiple of the listed presenting features would increase suspicion of OME.

The recommendation about when to refer for formal assessment was made based on the committee's knowledge and experience. The committee agreed that when children and their parents or carers present with any of the features in the recommendations discussed above, the clinician should assess the features, giving additional attention to any of the presenting features for which there was evidence, but also holistically taking into account the presence of multiple presenting features that tend to be associated with OME. For example, if a child presented with behavioural difficulties, and on initial assessment the clinician found the child also had a history of AOM, it would be sensible to suspect the child might have OME. The committee agreed that in a situation where the clinician suspected OME, the child should be referred for formal audiological assessment so OME can be diagnosed. The committee agreed this would start children with suspected OME on the appropriate care pathway, and enable access to treatment and care for children who do have OME and associated hearing loss. For children who do not have OME in whom OME is suspected at initial assessment, or those who have no associated hearing loss, referring for a formal assessment would allow professionals to correctly identify these children and make the appropriate care decisions.

The recommendation about what formal assessment should involve was made based on the committee's knowledge and experience, as well as recommendations from the previous NICE guideline on OME. The committee reviewed the recommendations from the previous NICE guideline on OME (NICE 2008) about formal assessment, and agreed the methods listed to assess OME are, according to their knowledge and expertise, still used in current practice as the gold standard for diagnosis of OME. These assessment methods included clinical examination (including otoscopy and a focus on general upper respiratory health and general developmental status), hearing testing, and tympanometry. The committee agreed these tests should be done in a formal assessment in order to diagnose OME and related hearing loss, as this would enable clinicians to determine the correct treatment pathway for the child. The committee agreed that the recommendations discussed above addressed clinical history-related factors and so did not include these in the list of factors to consider in a formal assessment.

The committee also discussed the recommendation from the previous NICE guideline that co-existing causes of hearing loss should be considered and agreed this is sensible and still a part of standard practice. They agreed that considering whether hearing loss might have causes other than OME would prevent the risk of children with sensorineural, permanent conductive and non-organic hearing loss being overlooked based on the assumption that

their hearing loss in exclusively caused by OME and will therefore be improved by treating OME.

Cost effectiveness and resource use

As no formal economic evaluation was undertaken the committee made a qualitative assessment of the likely cost effectiveness of their recommendations. The purpose of these recommendations is to support early recognition of OME with hearing loss to expedite interventions and management that will improve health related quality of life and educational and developmental outcomes. Most of the recommendations reflect current practice and therefore are not likely to have a significant resource impact. Whilst there are costs associated with better and earlier recognition of OME there are also likely to be offsetting savings and therefore, given the benefits of prompt recognition, the committee considered that their recommendations would represent a cost-effective use of NHS resources.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.2.1 to 1.2.6.

References – included studies

Diagnostic

Chantzi 2006

Chantzi, F M, Kafetzis, D A, Bairamis, T et al. (2006) IgE sensitisation, respiratory allergy symptoms, and heritability independently increase the risk of otitis media with effusion. Allergy 61(3): 332-6

Kwon 2013

Kwon, Chul, Lee, Ho Yun, Kim, Myung Gu et al. (2013) Allergic diseases in children with otitis media with effusion. International journal of pediatric otorhinolaryngology 77(2): 158-61

Martines 2011

Martines, F, Bentivegna, D, Maira, E et al. (2011) Risk factors for otitis media with effusion: case-control study in Sicilian schoolchildren. International journal of pediatric otorhinolaryngology 75(6): 754-9

Quaranta 2013

Quaranta, Nicola, Milella, Claudia, Iannuzzi, Lucia et al. (2013) A study of the role of different forms of chronic rhinitis in the development of otitis media with effusion in children affected by adenoid hypertrophy. International journal of pediatric otorhinolaryngology 77(12): 1980-3

Ralli 2011

Ralli, Giovanni, Ruoppolo, Giovanni, Mora, Renzo et al. (2011) Deleterious sucking habits and atypical swallowing in children with otitis media with effusion. International journal of pediatric otorhinolaryngology 75(10): 1260-4

Appendices

Appendix A Review protocols

Review protocol for review question: What presenting features are associated with OME in children under 12 years?

Table 4: Review protocol

Field	Content
PROSPERO registration number	CRD42022333991
Review title	Presenting features associated with OME in children
Review question	What presenting features are associated with OME in children under 12 years?
Objective	To determine the presenting features that are associated with OME in children under 12 years
Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • Epistemonikos • International Health Technology Assessment (INAHTA) database • MEDLINE & MEDLINE In-Process Searches will be restricted by: • Date limitations: 2000 onwards (see rationale under Section 10) • English language studies • Human studies Other searches: • Inclusion lists of systematic reviews

Field	Content
	• Citation searches of included studies With the agreement of the guideline committee, the searches will be re-run between 6-8 weeks before final submission of the review and further studies retrieved for inclusion. The full search strategies for MEDLINE database will be published in the final review.
Condition or domain being studied	Otitis media with effusion in children under 12 years
Population	Inclusion: All children under 12 years with suspected otitis media with effusion (OME)
Presenting features	Any signs and symptoms (presenting features), alone or in combination, including but not limited to: • Hearing difficulty • Indistinct speech • Poor listening skills • Delayed language development • Ear discomfort or ache • History of recurrent upper respiratory tract infection • History of allergic rhinitis • Rhinorrhoea (nasal discharge) • Behavioural issues (e.g. being withdrawn, head banging, anxiety, frustration) • lack of concentration or attention • Poor educational progress • Poor comprehension • balance difficulties (e.g. clumsiness) • Tinnitus • Hyperacusis • Tiredness/fatigue • Actively socially withdrawn • History of AOM

Field	Content
Reference standard	Diagnosis of OME must be made based on tympanometry with or without otoscopy
Types of study to be included	Include published full-texts: • Systematic reviews of cross-sectional diagnostic accuracy studies • Cross-sectional diagnostic accuracy studies Studies with prospective and retrospective data collection will be included. Two-gate studies will only be included if there are insufficient single-gate studies for a given sign, symptom or combination)
Other exclusion criteria	• Country limitations: OECD high-income countries • Date limitations: 2000 as the 2008 OME guideline has changed practice. However, the committee wanted to capture research leading up to the 2008 guideline also, and not just research conducted afterwards. • Language limitations: studies published not in English-language • Conference abstracts will not be considered.
Context	This guidance will fully update the following NICE guideline: Otitis media with effusion in under 12s: surgery (2008; CG60)
Primary outcomes (critical outcomes)	• Sensitivity • Specificity • Positive predictive value • Negative predictive value
Secondary outcomes (important outcomes)	None
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Dual sifting will be performed on at least 10% of records; 90% agreement is required, if capacity allows it. Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion

Field	Content
	criteria, details of the risk factors, 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 • QUADAS-2 tool for diagnostic accuracy studies The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.

Strategy for data synthesis	Where data is available from two or more studies for the same parameter and is sufficiently consistent, meta-analysis of diagnostic test accuracy will be performed using the metandi and midas applications in STATA/winbugs and Cochrane Review Manager software. Sensitivity, specificity, and the positive and negative predictive values with 95% CIs will be used as outcomes for diagnostic test accuracy. These diagnostic accuracy parameters will be obtained from the studies or calculated by the technical team using data from the studies.
	
	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/
	
	Decision making thresholds:
	• Sensitivity:
	  ○ Very useful test: ≥90%
	  ○ Moderately useful test: ≥60%
	  ○ Not a useful test <60%
	• Specificity:
	  ○ Very useful test: ≥90%
	  ○ Moderately useful test: ≥60%
	  ○ Not a useful test <60%
	
	Decision making thresholds for positive and negative predictive values have not been defined a priori. Imprecision in and importance of positive and negative predictive values will be assessed qualitatively during committee discussions and documented in the committee's discussion and interpretation of the evidence.

Field	Content

Analysis of sub-groups	Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes:
	• Craniofacial anomalies
	  ○ Children with Down's syndrome
	  ○ Children with cleft palate
	  ○ Children with other craniofacial anomalies
	  ○ Children without craniofacial anomalies
	• Age
	  ○ Children <2 years vs ≥2 years
	  ○ Children <4 years vs ≥4 years
	  ○ Children <6 years vs ≥6 years
	• Reference standard
	  ○ Tympanometry alone vs tympanometry with otoscopy
	
	Where evidence is stratified or subgrouped the committee will consider on a case by case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.

Type and method of review	☐ Intervention ☒ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)
Language	English
Country	England

Field	Content		
Anticipated or actual start date	1/05/2022		
Anticipated completion date	23/12/2022		
Stage of review at time of this submission	Review stage	Started	Completed
	Preliminary searches	☑	☑
	Piloting of the study selection process	☑	☑
	Formal screening of search results against eligibility criteria	☑	☑
	Data extraction	☑	☑
	Risk of bias (quality) assessment	☑	☑
	Data analysis	☑	☑
Named contact	**Named contact:** National Guideline Alliance **Named contact e-mail** otitis@nice.org.uk **Organisational affiliation of the review:** National Institute for Health and Care Excellence (NICE) and National Guideline Alliance		
Review team members	National Guideline Alliance		
Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance which receives funding from NICE.		
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.		

Field	Content
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?RecordID=333991
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, presenting features, hearing, diagnosis
Details of existing review of same topic by same authors	None
Current review status	☒ Ongoing ☐ Completed but not published ☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued
Additional information	None
Details of final publication	www.nice.org.uk

AOM: acute otitis media; NICE: National Institute of Health and Care Excellence; OECD: Organisation for Economic Co-operation and Development; OME: otitis media with effusion

Appendix B Literature search strategies

Literature search strategies for review question: What presenting features are associated with OME in children under 12 years?

Database: Medline – OVID interface

Date last searched: 17/05/2022

#	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	exp Hearing Disorders/ or exp Auditory Perception/ or exp Speech Disorders/ or Speech Intelligibility/ or exp Language Development Disorders/ or (exp Otitis/ and exp Recurrence/) or Earache/ or (exp Respiratory Tract Infections/ and exp Recurrence/) or exp Rhinitis, Allergic/ or exp Rhinorrhea/ or Nasal Obstruction/ or exp Child Behavior/ or Attention/ or exp Academic Performance/ or exp Child Development/ or Developmental Disabilities/ or exp Cognition/ or Dizziness/ or Postural Balance/ or exp Vertigo/ or exp Fatigue/
5	(((hearing or listen*) adj2 (abnormal* or affect* or degenerat* or deteriorat* or deficit* or difficult* or disabilit* or disorder* or hard or impair* or los* or muffl* or one side* or partial or poor or problem* or unilateral*)) or deaf* or hypoacus*).ti,ab.
6	((language* or speech* or communicat* or talk*) and (delay* or develop* or behav* or difficult* or indistinct or late or poor or problem*)).ti,ab.
7	(((nose or nasal) adj3 (block* or catarrh* or congest* or discharg* or mucus or running or runny)) or rhinorrh?ea).ti,ab.
8	(((bronchi* or broncho* or laryn* or pharyn* or sinonasal or sinus* or tonsil* or trachea* or upper airway* or upper respirat*) adj3 (infect* or inflam*)) and (chronic or constant or continu* or flar* up or frequen* or history or persist* or periodic* or recur* or regular* or reoccur* or re occur* or repeat* or return* or several)).ti,ab.
9	((bronchit* or bronchiolit* or common cold* or coryza or croup* or epiglott* or flu or grippe or influenza* or laryngit* or laryngotracheobronchit* or laryngotracheit* or parainfluenza* or pharyngit* or rhinit* or rhinopharyngit* or rhinosinusit* or sinusit* or sore throat* or tonsillit* or tracheiti* or tracheobronchit* or URTI*) and (chronic or constant or continu* or flar* up or frequen* or history or persist* or periodic* or recur* or regular* or reoccur* or re occur* or repeat* or return* or several)).ti,ab.
10	(earache* or otalgia or otitis or ((ear? or otic) adj3 (ache* or aching or discomfort* or fluid* or fullness or infect* or inflam* or neuralgi* or pain*))).ti,ab.
11	(((balanc* or vestibul*) adj3 (deteriorat* or difficult* or disorder* or disturb* or equilibrium or impair* or los* or poor or problem*)) or clumsy or clumsiness or dizzy or dizziness or unstead* or vertigo).ti,ab.
12	((child* or baby or babies or boy? or girl? or infan* or juvenile? or kid? or kindergar* or minor or minors or p?ediatric* or prepubert* or pre pubert* or prepubescen* or pre pubescen* or preschool* or pre school* or preteen* or pre teen* or schoolchild* or school age? or toddler* or young) adj5 (attenti* or anxiet* or anxious or behav* or cogniti* or comprehend* or comprehension or concentrat* or delay* or develop* or education* or frustrat* or head bang* or irritab* or progress* or understand* or understood or withdraw*)).ti,ab.
13	(tinnit* or (ear? and (buzz* or ring* or roar* or puls* or click*))).ti,ab.
14	(((auditory or aural or loudness or noise* or sound*) adj3 (discomfort* or dislik* or disturb* or hyper?esthesia* or intoleran* or pain* or perception or recruitment or sensitiv* or uncomfortable)) or hyperacus*).ti,ab.
15	(apath* or drows* or exhaust* or fatigu* or lassitude or letharg* or tired* or sleepy or sleepiness or weary or ((lack* or los*) adj2 (energ* or vital*))).ti,ab.
16	exp "Signs and Symptoms"/ or Symptom Assessment/
17	(complain* or presentation or prevalen* or red flag* or sign or signs or symptom*).ti,ab.
18	((clinical* or physical* or present*) adj3 (aspect* or characteristic* or feature* or finding* or history or manifest* or marker* or suspect* or suspicion*)).ti,ab.
19	or/4-18
20	3 and 19
21	(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.
22	20 not 21
23	limit 22 to english language
24	limit 23 to yr="2000 -Current"

Database: Embase – OVID interface

Date last searched: 17/05/2022

#	Searches
1	exp secretory otitis media/
2	(glue ear or ((middle ear or otitis media) adj2 effusion*) or ome or ((secretory or serous) adj2 otitis media)).ti,ab.
3	1 or 2
4	exp hearing disorder/ or exp hearing/ or exp speech disorder/ or speech intelligibility/ or exp developmental language disorder/ or (exp otitis/ and recurrent disease/) or otalgia/ or (exp respiratory tract infection/ and recurrent disease/) or exp allergic rhinitis/ or exp rhinorrhea/ or nose obstruction/ or exp child behavior/ or exp attention/ or academic achievement/ or child development/ or exp developmental disorder/ or exp cognition/ or dizziness/ or body equilibrium/ or exp vertigo/ or exp fatigue/

#	Searches
5	(((hearing or listen*) adj2 (abnormal* or affect* or degenerat* or deteriorat* or deficit* or difficult* or disabilit* or disorder* or hard or impair* or los* or muffl* or one side* or partial or poor or problem* or unilateral*)) or deaf* or hypoacus*).ti,ab.
6	((language* or speech* or communicat* or talk*) and (delay* or develop* or behav* or difficult* or indistinct or late or poor or problem*)).ti,ab.
7	(((nose or nasal) adj3 (block* or catarrh* or congest* or discharg* or mucus or running or runny)) or rhinorrh?ea).ti,ab.
8	(((bronchi* or broncho* or laryn* or pharyn* or sinonasal or sinus* or tonsil* or trachea* or upper airway* or upper respirat*) adj3 (infect* or inflam*)) and (chronic or constant or continu* or flar* up or frequen* or history or persist* or periodic* or recur* or regular* or reoccur* or re occur* or repeat* or return* or several)).ti,ab.
9	((bronchit* or bronchiolit* or common cold* or coryza or croup* or epiglott* or flu or grippe or influenza* or laryngit* or laryngotracheobronchit* or laryngotracheit* or parainfluenza* or pharyngit* or rhinit* or rhinopharyngit* or rhinosinusit* or sinusit* or sore throat* or tonsillit* or tracheiti* or tracheobronchit* or URTI*) and (chronic or constant or continu* or flar* up or frequen* or history or persist* or periodic* or recur* or regular* or reoccur* or re occur* or repeat* or return* or several)).ti,ab.
10	(earache* or otalgia or otitis or ((ear? or otic) adj3 (ache* or aching or discomfort* or fluid* or fullness or infect* or inflam* or neuralgi* or pain*))).ti,ab.
11	(((balanc* or vestibul*) adj3 (deteriorat* or difficult* or disorder* or disturb* or equilibrium or impair* or los* or poor or problem*)) or clumsy or clumsiness or dizzy or dizziness or unstead* or vertigo).ti,ab.
12	((child* or baby or babies or boy? or girl? or infan* or juvenile? or kid? or kindergar* or minor or minors or p?ediatric* or prepubert* or pre pubert* or prepubescen* or pre pubescen* or preschool* or pre school* or preteen* or pre teen* or schoolchild* or school age? or toddler* or young) adj5 (attenti* or anxiet* or anxious or behav* or cogniti* or comprehend* or comprehension or concentrat* or delay* or develop* or education* or frustrat* or head bang* or irritab* or progress* or understand* or understood or withdraw*)).ti,ab.
13	(tinnit* or (ear? and (buzz* or ring* or roar* or puls* or click*))).ti,ab.
14	(((auditory or aural or loudness or noise* or sound*) adj3 (discomfort* or dislik* or disturb* or hyper?esthesia* or intoleran* or pain* or perception or recruitment or sensitiv* or uncomfortable)) or hyperacus*).ti,ab.
15	(apath* or drows* or exhaust* or fatigu* or lassitude or letharg* or tired* or sleepy or sleepiness or weary or ((lack* or los*) adj2 (energ* or vital*))).ti,ab.
16	symptom assessment/ or clinical feature/ or disease marker/ or exp symptom/
17	(complain* or presentation or prevalen* or red flag* or sign or signs or symptom*).ti,ab.
18	((clinical* or physical* or present*) adj3 (aspect* or characteristic* or feature* or finding* or history or manifest* or marker* or suspect* or suspicion*)).ti,ab.
19	or/4-18
20	3 and 19
21	(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.
22	20 not 21
23	limit 22 to english language
24	limit 23 to yr="2000 -Current"
25	limit 24 to (conference abstract or conference paper or conference review or conference proceeding)
26	24 not 25

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

3 Date last searched: 17/05/2022

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: [Hearing Disorders] explode all trees
#5	MeSH descriptor: [Auditory Perception] explode all trees
#6	MeSH descriptor: [Speech Disorders] explode all trees
#7	MeSH descriptor: [Speech Intelligibility] this term only
#8	MeSH descriptor: [Language Development Disorders] explode all trees
#9	MeSH descriptor: [Earache] this term only
#10	MeSH descriptor: [Rhinitis, Allergic] explode all trees
#11	MeSH descriptor: [Rhinorrhea] explode all trees
#12	MeSH descriptor: [Nasal Obstruction] this term only
#13	MeSH descriptor: [Child Behavior] explode all trees
#14	MeSH descriptor: [Attention] this term only
#15	MeSH descriptor: [Academic Performance] explode all trees
#16	MeSH descriptor: [Child Development] this term only
#17	MeSH descriptor: [Developmental Disabilities] this term only
#18	MeSH descriptor: [Cognition] explode all trees
#19	MeSH descriptor: [Dizziness] this term only
#20	MeSH descriptor: [Postural Balance] this term only
#21	MeSH descriptor: [Vertigo] explode all trees
#22	MeSH descriptor: [Fatigue] explode all trees

ID	Search
#23	{or #4-#22}
#24	MeSH descriptor: [Otitis] explode all trees
#25	MeSH descriptor: [Respiratory Tract Infections] explode all trees
#26	#24 or #25
#27	MeSH descriptor: [Recurrence] this term only
#28	#26 and #27
#29	#23 or #28
#30	(((hearing or listen*) near/2 (abnormal* or affect* or degenerat* or deteriorat* or deficit* or difficult* or disabilit* or disorder* or hard or impair* or los* or muffl* or "one side*" or partial or poor or problem* or unilateral*)) or deaf* or hypoacus*).ti,ab.
#31	((language* or speech* or communicat* or talk*) and (delay* or develop* or behav* or difficult* or indistinct or late or poor or problem*)):ti,ab
#32	(((nose or nasal) near/3 (block* or catarrh* or congest* or discharg* or mucus or running or runny)) or rhinorrh?ea):ti,ab
#33	(((bronchi* or broncho* or laryn* or pharyn* or sinonasal or sinus* or tonsil* or trachea* or "upper airway*" or "upper respirat*") near/3 (infect* or inflam*)) and (chronic or constant or continu* or "flar* up" or frequen* or history or persist* or periodic* or recur* or regular* or reoccur* or "re occur*" or repeat* or return* or several)):ti,ab
#34	((bronchit* or bronchiolit* or "common cold*" or coryza or croup* or epiglott* or flu or grippe or influenza* or laryngit* or laryngotracheobronchit* or laryngotracheit* or parainfluenza* or pharyngit* or rhinit* or rhinopharyngit* or rhinosinusit* or sinusit* or "sore throat*" or tonsillit* or tracheiti* or tracheobronchit* or URTI*) and (chronic or constant or continu* or "flar* up" or frequen* or history or persist* or periodic* or recur* or regular* or reoccur* or "re occur*" or repeat* or return* or several)):ti,ab
#35	(earache* or otalgia or otitis or ((ear? or otic) near/3 (ache* or aching or discomfort* or fluid* or fullness or infect* or inflam* or neuralgi* or pain*))):ti,ab
#36	(((balanc* or vestibul*) near/3 (deteriorat* or difficult* or disorder* or disturb* or equilibrium or impair* or los* or poor or problem*)) or clumsy or clumsiness or dizzy or dizziness or unstead* or vertigo):ti,ab
#37	((child* or baby or babies or boy? or girl? or infan* or juvenile? or kid? or kindergar* or minor or minors or p?ediatric* or prepubert* or "pre pubert*" or prepubescen* or "pre pubescen*" or preschool* or "pre school*" or preteen* or "pre teen*" or schoolchild* or "school age?" or toddler* or young) near/5 (attenti* or anxiet* or anxious or behav* or cogniti* or comprehend* or comprehension or concentrat* or delay* or develop* or education* or frustrat* or "head bang*" or irritab* or progress* or understand* or understood or withdraw*)):ti,ab
#38	(tinnit* or (ear? and (buzz* or ring* or roar* or puls* or click*))):ti,ab
#39	(((auditory or aural or loudness or noise* or sound*) near/3 (discomfort* or dislik* or disturb* or hyper?esthesia* or intoleran* or pain* or perception or recruitment or sensitiv* or uncomfortable)) or hyperacus*):ti,ab
#40	(apath* or drows* or exhaust* or fatigu* or lassitude or letharg* or tired* or sleepy or sleepiness or weary or ((lack* or los*) near/2 (energ* or vital*))):ti,ab
#41	MeSH descriptor: [Signs and Symptoms] explode all trees
#42	MeSH descriptor: [Symptom Assessment] this term only
#43	(complain* or presentation or prevalen* or red flag* or sign or signs or symptom*):ti,ab
#44	((clinical* or physical* or present*) near/3 (aspect* or characteristic* or feature* or finding* or history or manifest* or marker* or suspect* or suspicion*)):ti,ab
#45	{or #29-#44}
#46	#3 and #45
#47	"conference":pt or (clinicaltrials or trialsearch):so
#48	#46 not #47 with Cochrane Library publication date Between Jan 2000 and May 2022

1 **Database: Epistemonikos**

2 Date last searched: 17/05/2022

#	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:(complain* OR presentation OR prevalen* OR "red flag" OR "red flags" OR sign OR signs OR symptom*)) OR abstract:((complain* OR presentation OR prevalen* OR "red flag" OR "red flags" OR sign OR signs OR symptom*))
3	1 AND 2
4	date limit: 2000-

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

5 Date last searched: 17/05/2022

#	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 FROM 2000 TO 2022 AND (English)[Language]

6 **Economic literature search strategy:**

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

Database: MEDLINE – OVID interface

Date last searched: 09/11/2022

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

Database: Embase – OVID interface

Date last searched: 09/11/2022

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

#	Searches
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]

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

7 Date last searched: 09/11/2022

Line	Search for
1	MeSH DESCRIPTOR Otitis Media with Effusion EXPLODE ALL TREES

Line	Search for
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

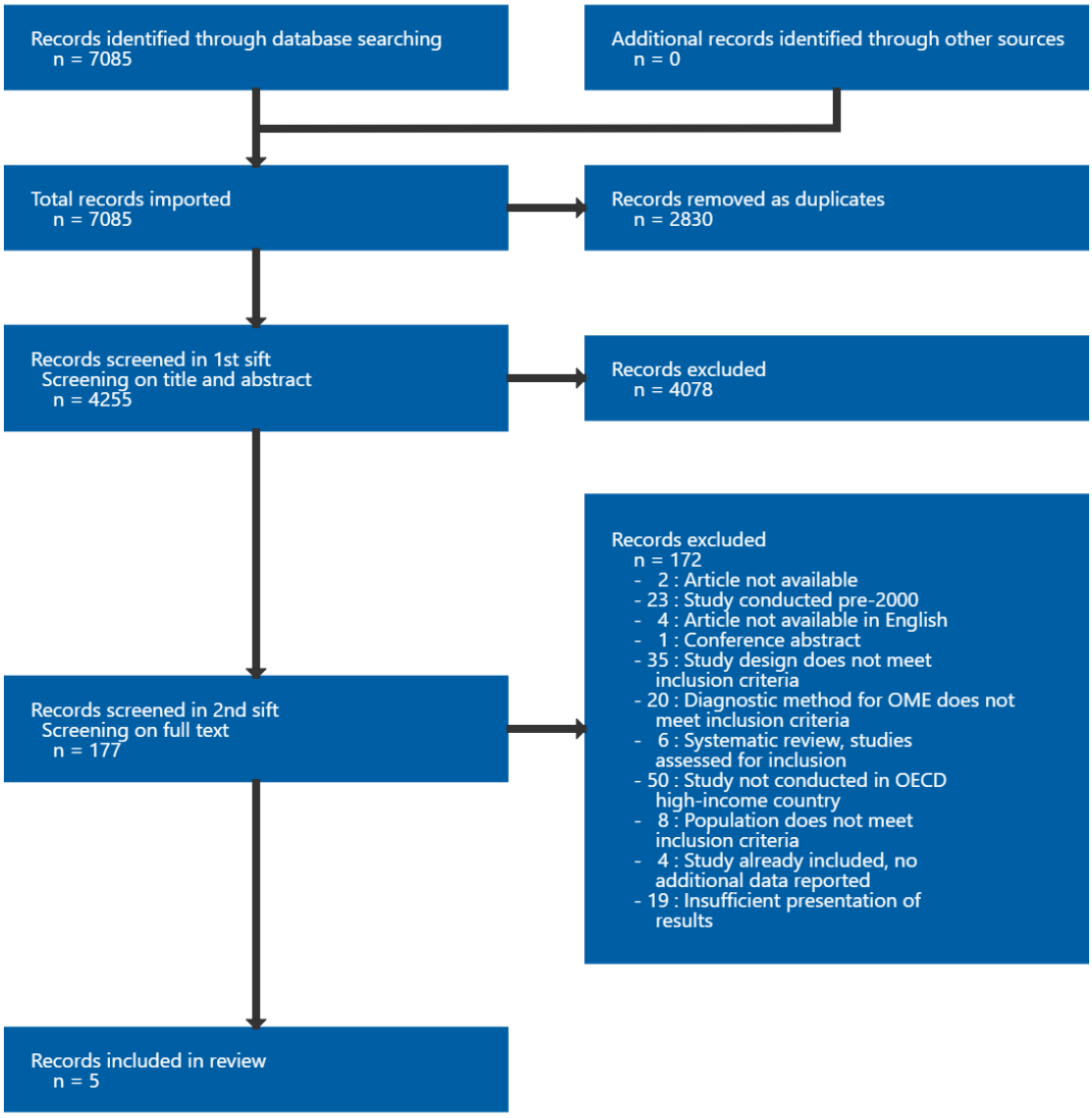
1

2

Appendix C Diagnostic evidence study selection

Study selection for: What presenting features are associated with OME in children under 12 years?

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What presenting features are associated with OME in children under 12 years?

Table 5: Evidence tables

Chantzi, 2006

Bibliographic Reference	Chantzi, F M; Kafetzis, D A; Bairamis, T; Avramidou, C; Paleologou, N; Grimani, I; Apostolopoulos, N; Papadopoulos, N G; IgE sensitisation, respiratory allergy symptoms, and heritability independently increase the risk of otitis media with effusion.; Allergy; 2006; vol. 61 (no. 3); 332-6

Study details

Country/ies where study was carried out	Greece
Study type	Case-control study
Study dates	October 2002 - May 2004
Inclusion criteria	Case group: • Children with OME (diagnosed based on clinical symptoms (hearing loss, otalgia, or irritability, 'plugged' feeling or 'popping' in their ears, speech, or behavioural disorders, tinnitus, vertigo), otoscopy and tympanometry) • Type B or C tympanograms • Symptom duration of >1 month or a history of recurrent OME • Attended the ENT department during the study period Control group: • Attended the ENT department for reasons other than OME during the study period • No history of OME • No frequent (>2 per year) episodes of OM • No otoscopic findings of OM • Type A tympanograms
Exclusion criteria	• AOM • Perforations of the tympanic membrane

	• Craniofacial anomalies • Sensorineural hearing loss • Chronic underlying diseases or under chronic pharmaceutical management (except asthma and anti-asthmatic medication) • Children with underage mothers
Patient characteristics	Whole cohort: N=168 OME group: n=88 • Mean age (range): 4.5 (1-6.7) years • Sex (female/ male): 32/ 56 • Craniofacial anomalies: None Group without OME: n=80 • Mean age (range): 4.4 (1.3-6.7) years • Sex (female/ male): 27/ 53 • Craniofacial anomalies: None
Index test(s)	Presenting features: 1. Adenoid hypertrophy (assessed by a physician using a standardised questionnaire) 2. History of adenoidectomy (assessed by a physician using a standardised questionnaire) 3. Immunoglobin E (IgE) sensitisation (skin-prick tests (SPT) and/or CAP-FEIA to seven locally relevant allergens (grass mix, weed mix, dust mite mix, olive, cat, alternaria, and egg white), using the appropriate positive and negative controls. SPT wheals >3 mm in diameter and greater than the negative control were considered positive. CAP-FEIA >class 2 was considered positive. A blood sample was also obtained in which eosinophil counts and total IgE were assessed) 4. Any allergic disease (defined as a positive clinical history of asthma, rhinitis, eczema, or any combination of these) 5. IgE-mediated allergic disease (atopy) (defined as the presence of any allergic disease, as above, combined with IgE sensitisation) 6. Dyspnoea (assessed by a physician using a standardised questionnaire) 7. Wheezing (assessed by a physician using a standardised questionnaire) 8. Recurrent cough (assessed by a physician using a standardised questionnaire) 9. Asthma (assessed by a physician using a standardized questionnaire and strict clinical definitions) 10. IgE-mediated asthma (defined as asthma combined with IgE sensitisation) 11. Rhinitis (assessed by a physician using a standardized questionnaire and strict clinical definitions)

	12. Nasal obstruction (assessed by a physician using a standardised questionnaire) 13. Rhinorrhoea (assessed by a physician using a standardised questionnaire) 14. Paroxysmal sneezing/ nasal itching (assessed by a physician using a standardised questionnaire) 15. IgE-mediated allergic rhinitis (defined as rhinitis combined with IgE sensitisation) 16. Conjunctivitis (assessed by a physician using a standardized questionnaire and strict clinical definitions) 17. Eczema (assessed by a physician using a standardized questionnaire and strict clinical definitions) 18. IgE-mediated eczema (defined as eczema combined with IgE sensitisation) 19. Food reactions (assessed by a physician using a standardized questionnaire and strict clinical definitions) 20. Drug reactions (assessed by a physician using a standardized questionnaire and strict clinical definitions) 21. Urticaria (assessed by a physician using a standardized questionnaire and strict clinical definitions) 22. Anaphylaxis (assessed by a physician using a standardized questionnaire and strict clinical definitions) 23. Elevated eosinophil count (>4%) (A blood sample was obtained in which eosinophil counts and total IgE were assessed)
Reference standard(s)	Tympanometry (type B or C tympanograms) with otoscopy, clinical symptoms (hearing loss, otalgia, or irritability, 'plugged' feeling or 'popping' in their ears, speech, or behavioural disorders, tinnitus, vertigo) and symptom duration of >1 month or a history of recurrent OME
Duration of follow-up	N/A
Sources of funding	Not reported
Other information	None

AOM: acute otitis media; CAP-FEIA: College of American Pathologists fluorescence enzyme immunoassay; ENT: ears, nose and throat; IgE: 3. Immunoglobin E; N: number; N/A: not applicable; OM: otitis media; OME: otitis media with effusion: SPT: skin-prick tests

Study arms

Reference standard positive (OME group) (N = 88)

Reference standard negative (group without history of/ current OME or frequent OM attending ENT department) (N = 80)

Outcomes

Adenoid hypertrophy

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: adenoid hypertrophy No of events	n = 59	n = 54
Index test negative No adenoid hypertrophy No of events	n = 29	n = 26

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

History of adenoidectomy

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: history of adenoidectomy No of events	n = 6	n = 5
Index test negative No history of adenoidectomy No of events	n = 82	n = 75

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

IgE sensitisation

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: IgE sensitisation No of events	n = 28	n = 12
Index test negative No IgE sensitisation No of events	n = 60	n = 68

ENT: ears, nose and throat; IgE: immunoglobin E; N: number; OM: otitis media; OME: otitis media with effusion

Any allergic disease

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: Any allergic disease No of events	n = 53	n = 34
Index test negative No allergic disease No of events	n = 35	n = 46

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Atopy (IgE-mediated allergic disease)

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: atopy No of events	n = 21	n = 6
Index test negative No atopy No of events	n = 67	n = 74

ENT: ears, nose and throat; IgE: immunoglobin E; N: number; OM: otitis media; OME: otitis media with effusion

Dyspnoea

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: dyspnoea No of events	n = 26	n = 13
Index test negative No dyspnoea No of events	n = 62	n = 67

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Wheezing

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: wheezing No of events	n = 25	n = 5
Index test negative No wheezing No of events	n = 63	n = 75

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Recurrent cough

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: recurrent cough No of events	n = 45	n = 35
Index test negative No recurrent cough No of events	n = 43	n = 45

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Asthma

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: asthma No of events	n = 29	n = 14
Index test negative No asthma No of events	n = 59	n = 66

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

IgE-mediated asthma

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: IgE-mediated asthma No of events	n = 11	n = 3
Index test negative No IgE-mediated asthma No of events	n = 77	n = 77

ENT: ears, nose and throat; IgE: immunoglobin E; N: number; OM: otitis media; OME: otitis media with effusion

Rhinitis

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: rhinitis No of events	n = 37	n = 22
Index test negative No rhinitis No of events	n = 51	n = 58

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Nasal obstruction

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: nasal obstruction No of events	n = 80	n = 67
Index test negative No nasal obstruction No of events	n = 8	n = 13

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Rhinorrhea

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: rhinorrhea No of events	n = 56	n = 41
Index test negative No rhinorrhea No of events	n = 32	n = 39

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Paroxysmal sneezing/ nasal itching

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: paroxysmal sneezing/ nasal itching No of events	n = 35	n = 20
Index test negative No paroxysmal sneezing/ nasal itching No of events	n = 53	n = 60

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

IgE-mediated allergic rhinitis

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: IgE-mediated allergic rhinitis No of events	n = 16	n = 4
Index test negative No IgE-mediated allergic rhinitis No of events	n = 72	n = 76

ENT: ears, nose and throat; IgE: immunoglobin E; N: number; OM: otitis media; OME: otitis media with effusion

Conjunctivitis

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: conjunctivitis No of events	n = 5	n = 6
Index test negative No conjunctivitis No of events	n = 83	n = 74

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Eczema

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: eczema No of events	n = 13	n = 3
Index test negative No eczema No of events	n = 75	n = 77

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

IgE-mediated eczema

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: IgE-mediated eczema No of events	n = 7	n = 0
Index test negative No IgE-mediated eczema No of events	n = 81	n = 80

ENT: ears, nose and throat; IgE: immunoglobin E; N: number; OM: otitis media; OME: otitis media with effusion

Food reactions

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: food reactions No of events	n = 9	n = 3
Index test negative No food reactions No of events	n = 79	n = 77

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Drug reactions

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: drug reactions No of events	n = 12	n = 8
Index test negative No drug reactions No of events	n = 76	n = 72

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Urticaria

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: urticaria No of events	n = 24	n = 16
Index test negative No urticaria No of events	n = 64	n = 64

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Anaphylaxis

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: anaphylaxis No of events	n = 1	n = 0
Index test negative No anaphylaxis No of events	n = 87	n = 80

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Elevated eosinophil count (>4%)

Outcome	Reference standard positive (OME group), N = 88	Reference standard negative (group without history of/ current OME or frequent OM attending ENT department), N = 80
Index test positive Presenting feature: elevated eosinophil count (>4%) No of events	n = 20	n = 19
Index test negative No elevated eosinophil count No of events	n = 68	n = 61

ENT: ears, nose and throat; N: number; OM: otitis media; OME: otitis media with effusion

Critical appraisal - NGA Critical appraisal - QUADAS-2

Section	Question	Answer
Patient selection: risk of bias	Could the selection of patients have introduced bias?	High *(Case-control study. Unclear if selection of patients consecutive or random, plus children with AOM, perforations of the tympanic membrane, sensoneural hearing loss, chronic underlying diseases or under chronic pharmaceutical management (except asthma and antiasthmatic medication) were excluded. It is unclear whether inclusion of children with these comorbidities would have influenced diagnostic test accuracy.)*
Patient selection: applicability	Are there concerns that included patients do not match the review question?	Low
Index tests: risk of bias	Could the conduct or interpretation of the index test have introduced bias?	Low *(Unclear whether study physician collecting data on presenting features was aware of OME diagnosis, however this is unlikely to have influenced results as they were based on strict clinical definitions as referenced in previous literature, plus objective skin-prick tests (SPT) and/or CAP-FEIA to seven locally relevant allergens with pre-specified thresholds.)*
Index tests: applicability	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low

Section	Question	Answer
Reference standard: risk of bias	Could the reference standard, its conduct, or its interpretation have introduced bias?	Low *(Recruitment to study dependent on OME status but it is unclear at what point the reference standard was conducted. No information about whether reference standard was interpreted without knowledge of the index tests; however, reference standard was interpreted according to objective, pre-specified thresholds so unlikely that knowledge of results would introduce bias.)*
Reference standard: applicability	Is there concern that the target condition as defined by the reference standard does not match the review question?	Low
Flow and timing: risk of bias	Could the patient flow have introduced bias?	Unclear *(No information about interval between index tests and reference standard)*

AOM: acute otitis media; CAP-FEIA: College of American Pathologists fluorescence enzyme immunoassay; OME: otitis media with effusion: SPT: skin-prick tests

Kwon, 2013

Bibliographic Reference	Kwon, Chul; Lee, Ho Yun; Kim, Myung Gu; Boo, Sung Hyun; Yeo, Seung Geun; Allergic diseases in children with otitis media with effusion.; International journal of pediatric otorhinolaryngology; 2013; vol. 77 (no. 2); 158-61

Study details

Country/ies where study was carried out	Korea
Study type	Case-control study
Study dates	January 2007 - December 2012
Inclusion criteria	OME group: children aged 1-14 years, diagnosed with OME at ENT clinics Control group: children aged 3-12 years without OME or otitis media, who had undergone blood tests and multiple allergosorbent test – chemiluminescent assay (MAST-CLA) because of ranula (cyst in your mouth caused by a blockage in the salivary gland), ankyloglossia (tongue-tie), preauricular fistula (congenital external ear disease) or epistaxis (nose bleeds)
Exclusion criteria	Children with suspected head and neck abnormalities, congenital or acquired immunodeficiency, or systemic disease

Patient characteristics	Whole cohort: N=470 OME group: n=370 • Mean age (range): 7.5 (2-14) years • Sex (female/male): 135/ 235 • Craniofacial anomaly: not reported (study excluded children with suspected head and neck abnormalities) Group without OME: n=100 • Mean age (range): 6.3* (3-12) years • Sex (female/male): 24/26 (However, it seems that this figure is not correct or incomplete as total number of participants should be 100) • Craniofacial anomaly: not reported (study excluded children with suspected head and neck abnormalities) *Note that in table 1, the mean age of this group is reported as 5.9 years. It is unclear if this is an error.
Index test(s)	Presenting features: Assessed using MAST-CLA and participants' medical records: 1. Allergic rhinitis 2. Asthma 3. Atopic demartitis 4. Allergic conjunctivitis 5. Chronic rhinosinusitis Assessed using imaging: 1. Tonsil hypertrophy 2. Adenoid hypertrophy
Reference standard(s)	Tympanometry (type B or C tympanograms on impedance audiometry) with otoscopy (amber-coloured tympanic membrane on otoscopic examination)

Duration of follow-up	Not reported
Sources of funding	Industry funded
Other information	None

ENT: ears, nose and throat; MAST-CLA: multiple allergosorbent test – chemiluminescent assay; N: number; OME: otitis media with effusion

Study arms

Reference standard positive (OME group) (N = 370)

Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA) (N = 100)

Outcomes

Allergic rhinitis

Outcome	Reference standard positive (OME), N = 370	Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA), N = 100
Index test positive Presenting feature: allergic rhinitis No of events	n = 125	n = 16
Index test negative No allergic rhinitis No of events	n = 245	n = 84

MAST-CLA: multiple allergosorbent test – chemiluminescent assay; N: number; OME: otitis media with effusion

Asthma

Outcome	Reference standard positive (OME), N = 370	Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA), N = 100
Index test positive	n = 8	n = 8

Outcome	Reference standard positive (OME), N = 370	Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA), N = 100
Presenting feature: asthma No of events		
Index test negative No asthma No of events	n = 362	n = 92

MAST-CLA: multiple allergosorbent test – chemiluminescent assay; N: number; OME: otitis media with effusion

Atopic dermatitis

Outcome	Reference standard positive (OME), N = 370	Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA), N = 100
Index test positive Presenting feature: atopic dermatitis No of events	n = 10	n = 9
Index test negative No atopic dermatitis No of events	n = 360	n = 91

MAST-CLA: multiple allergosorbent test – chemiluminescent assay; N: number; OME: otitis media with effusion

Allergic conjunctivitis

Outcome	Reference standard positive (OME), N = 370	Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA), N = 100
Index test positive	n = 2	n = 4

Outcome	Reference standard positive (OME), N = 370	Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA), N = 100
Presenting feature: allergic conjunctivitis No of events		
Index test negative No allergic conjunctivitis No of events	n = 368	n = 96

MAST-CLA: multiple allergosorbent test – chemiluminescent assay; N: number; OME: otitis media with effusion

Chronic rhinosinusitis

Outcome	Reference standard positive (OME), N = 370	Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA), N = 100
Index test positive Presenting feature: chronic rhinosinusitis No of events	n = 27	n = 4
Index test negative No chronic rhinosinusitis No of events	n = 343	n = 96

MAST-CLA: multiple allergosorbent test – chemiluminescent assay; N: number; OME: otitis media with effusion

Tonsillar hypertrophy (grade ≥2)

Outcome	Reference standard positive (OME), N = 370	Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA), N = 100
Index test positive	n = 197	n = 55

Outcome	Reference standard positive (OME), N = 370	Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA), N = 100
Presenting feature: tonsillar hypertrophy No of events		
Index test negative Tonsillar size grade <2 No of events	n = 173	n = 45

MAST-CLA: multiple allergosorbent test – chemiluminescent assay; N: number; OME: otitis media with effusion

Adenoid hypertrophy (grade ≥2)

Outcome	Reference standard positive (OME), N = 370	Reference standard negative (group without OME with symptoms necessitating blood tests MAST-CLA), N = 100
Index test positive Presenting feature: adenoid hypertrophy No of events	n = 264	n = 45
Index test negative Adenoid size grade <2 No of events	n = 106	n = 55

MAST-CLA: multiple allergosorbent test – chemiluminescent assay; N: number; OME: otitis media with effusion

Critical appraisal - NGA Critical appraisal - QUADAS-2

Section	Question	Answer
Patient selection: risk of bias	Could the selection of patients have introduced bias?	High *(Case-control study.)*
Patient selection: applicability	Are there concerns that included patients do not match the review question?	Unclear *(Study included participants up to the age of 14 in the OME group; number of children over the age of 12 not reported)*

Section	Question	Answer
Index tests: risk of bias	Could the conduct or interpretation of the index test have introduced bias?	Low *(Index test is objective so unlikely that knowledge of results would introduce bias.)*
Index tests: applicability	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low
Reference standard: risk of bias	Could the reference standard, its conduct, or its interpretation have introduced bias?	Low *(No information about whether reference standards were interpreted without knowledge of the index tests; however, tests are objective so unlikely that knowledge of results would introduce bias.)*
Reference standard: applicability	Is there concern that the target condition as defined by the reference standard does not match the review question?	Low
Flow and timing: risk of bias	Could the patient flow have introduced bias?	Unclear *(No information about interval between index tests and reference standard)*

OME: otitis media with effusion

Martines, 2011

Bibliographic Reference	Martines, F; Bentivegna, D; Maira, E; Sciacca, V; Martines, E; Risk factors for otitis media with effusion: case-control study in Sicilian schoolchildren.; International journal of pediatric otorhinolaryngology; 2011; vol. 75 (no. 6); 754-9

Study details

Country/ies where study was carried out	Italy
Study type	Case-control study
Study dates	September 2006 - June 2007
Inclusion criteria	Children attending primary schools in the District of Sciacca during the study period
Exclusion criteria	• Skull-facial malformations • Down's syndrome

	• Perforated drums • Ventilation tubes

Patient characteristics	Whole cohort: N=2097
	
	• Mean age (SD): 9.9 (not reported) years
	
	Children with persistent (≥3 months) OME: n=143
	
	• Mean age (SD): not reported
	  ○ 5-6 years: 40
	  ○ 7-8 years: 32
	  ○ 9-10 years: 36
	  ○ 11-12 years: 20
	  ○ 13-14 years: 15*
	• Sex (female/ male): 100/ 43
	• Craniofacial anomalies: not reported (children with skull-facial malformations were excluded)
	
	Children with no OME: n=1954
	
	• Mean age (SD): not reported
	  ○ 5-6 years: 270
	  ○ 7-8 years: 314
	  ○ 9-10 years: 526
	  ○ 11-12 years: 368
	  ○ 13-14 years: 476*
	• Sex (female/ male): 1065/ 889
	• Craniofacial anomalies: not reported (children with skull-facial malformations were excluded)
	
	*Results not presented separately for participants over 12 years of age for any presenting features except atopy

Index test(s)	Presenting features: 1. Atopy/ allergy (skin prick tests for 12 common perennial and seasonal allergens: Alternaria, Aspergillus, Cladosporium, Penicillium, ragweed, grass mix, trees mix, cockroach, dust mites, Dermatophagoides farinae and Dermatophagoides pteronyssinus, and cat and dog epithelium) 2. Snoring (data collected via questionnaire answered by parents)

	3. History of AOM (data collected via questionnaire answered by parents) 4. History of upper respiratory tract infection (URTI) (data collected via questionnaire answered by parents) 5. Allergy and history of URTI
Reference standard(s)	Tympanometry (presence of B or C tympanograms; absence of ipsilateral acoustic reflex) with otoscopy (documented persistent middle ear effusion for a minimum of 3 months) and a conductive hearing loss greater than 25 dB at any one of the frequencies from 0.25 kHz through 4 kHz
Duration of follow-up	N/A
Sources of funding	Industry funded
Other information	Results for degree of hearing loss of children with OME were also reported but these data were not extracted due to the potential for incorporation bias - hearing loss as an index test is part of the reference standard

AOM: acute otitis media; dB: decibels; kHz: kilohertz; N: number; OME: otitis media with effusion; N/A: not applicable; SD: standard deviation; URTI: upper respiratory tract infection

Study arms

Reference standard positive (diagnosed with OME) (N = 143)

Reference standard negative (no OME) (N = 1954)

Outcomes

Atopy

Outcome	Reference standard positive (diagnosed with OME), N = 128	Reference standard negative (no OME), N = 1478
Index test positive Presenting feature: atopy No of events	n = 80	n = 178
Index test negative No atopy No of events	n = 48	n = 1300

N: number; OME: otitis media with effusion

Data only extracted from participants 12 years of age and under

Snoring

Outcome	Reference standard positive (diagnosed with OME), N = 143	Reference standard negative (no OME), N = 1954
Index test positive Presenting feature: snoring No of events	n = 65	n = 347
Index test negative No snoring No of events	n = 78	n = 1607

N: number; OME: otitis media with effusion

History of AOM

Outcome	Reference standard positive (diagnosed with OME), N = 143	Reference standard negative (no OME), N = 1954
Index test positive Presenting feature: history of AOM No of events	n = 14	n = 80
Index test negative No history of AOM No of events	n = 129	n = 1874

AOM: acute otitis media; N: number; OME: otitis media with effusion

History of URTI

Outcome	Reference standard positive (diagnosed with OME), N = 143	Reference standard negative (no OME), N = 1954
Index test positive Presenting feature: history of URTI No of events	n = 57	n = 338
Index test negative No history of URTI No of events	n = 86	n = 1616

N: number; OME: otitis media with effusion; URTI: upper respiratory tract infection

Allergy and history of URTI

Outcome	Reference standard positive (diagnosed with OME), N = 143	Reference standard negative (no OME), N = 1954
Index test positive Presenting feature: allergy and history of URTI No of events	n = 41	n = 48
Index test negative Participant does not have both allergy and history of URTI No of events	n = 102	n = 1906

N: number; OME: otitis media with effusion; URTI: upper respiratory tract infection

Critical appraisal - NGA Critical appraisal - QUADAS-2

Section	Question	Answer
Patient selection: risk of bias	Could the selection of patients have introduced bias?	High *(Case-control study)*

Section	Question	Answer
Patient selection: applicability	Are there concerns that included patients do not match the review question?	Low *(491/ 2097 (23%) of participants are over 12, data not presented separately for these participants)*
Index tests: risk of bias	Could the conduct or interpretation of the index test have introduced bias?	Unclear *(Unclear risk of bias for snoring, history of AOM, history of URTI, and composite index test allergy and history of URTI because data were collected via questionnaires to the children's parents, rather than based on clinical history. It is unclear if results of the index test were interpreted without knowledge of the results of the reference standard, and data collected via questionnaire not sufficiently objective to discount potential for bias. However, low risk of bias for atopy because interpretation of skin prick tests pre-specified using objective thresholds so results for these unlikely to have been influenced by knowledge of reference standard results.)*
Index tests: applicability	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low
Reference standard: risk of bias	Could the reference standard, its conduct, or its interpretation have introduced bias?	Low *(No information about whether reference standard was interpreted without knowledge of the index tests; however, reference standard was interpreted according to objective, pre-specified thresholds so unlikely that knowledge of results would introduce bias.)*
Reference standard: applicability	Is there concern that the target condition as defined by the reference standard does not match the review question?	Low
Flow and timing: risk of bias	Could the patient flow have introduced bias?	High *(Only participants who had abnormal otoscopic results received tympanometry to confirm OME status. Participants who had normal otoscopic results were confirmed to have no OME without confirmation via tympanometry. Additionally, no information is given about the interval between completion of questionnaires and reference standard, although skin prick tests were performed at the same time as the reference standard)*

1 *AOM: acute otitis media; OME: otitis media with effusion; URTI: upper respiratory tract infection*

2

1 Quaranta, 2013

Bibliographic Reference	Quaranta, Nicola; Milella, Claudia; Iannuzzi, Lucia; Gelardi, Matteo; A study of the role of different forms of chronic rhinitis in the development of otitis media with effusion in children affected by adenoid hypertrophy.; International journal of pediatric otorhinolaryngology; 2013; vol. 77 (no. 12); 1980-3

2 Study details

Country/ies where study was carried out	Italy
Study type	Cross-sectional study
Study dates	2009 - 2011
Inclusion criteria	Children aged 4-15 years with grade 3 or 4 adenoid hypertrophy (choanal obstruction greater than 75%)
Exclusion criteria	Not reported
Patient characteristics	Whole cohort: N=81 • Mean age (range): 6.9 (4-15) years • Sex (male/female): 48/33 • Craniofacial anomalies: not reported • OME prevalence (number of children with OME/ without OME): 52/ 29
Index test(s)	Presenting features: 1. Allergic rhinitis (defined as positive skin prick test, nasal symptoms due to allergens and heterogeneous rhinocytogram) 2. Infective rhinitis (defined as abundant bacteria that could be found in extracellular tissue and inside neutrophils due to phagocytosis) 3. Non-allergic rhinitis (defined as negative skin prick test and the continuous presence of inflammatory cells in the nasal mucosa independently from the seasonality) 4. Allergic rhinitis and infective rhinitis 5. Non-allergic rhinitis and infective rhinitis
Reference standard(s)	Tympanometry and pure tone audiometry

Duration of follow-up	N/A
Sources of funding	Not reported
Other information	None

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

Study arms

Reference standard positive (diagnosed with OME and adenoid hypertrophy) (N = 45)

Reference standard negative (diagnosed with adenoid hypertrophy but no OME) (N = 36)

Outcomes

Allergic rhinitis

Outcome	Reference standard positive (diagnosed with OME), N = 45	Reference standard negative (diagnosed with adenoid hypertrophy but no OME), N = 36
Index test positive Presenting feature: allergic rhinitis No of events	1	3
Index test negative No allergic rhinitis No of events	44	33

N: number; OME: otitis media with effusion

Non-allergic rhinitis

Outcome	Reference standard positive (diagnosed with OME), N = 45	Reference standard negative (diagnosed with adenoid hypertrophy but no OME), N = 36
Index test positive Presenting feature: non-allergic rhinitis No of events	11	6
Index test negative No non-allergic rhinitis No of events	34	30

N: number; OME: otitis media with effusion

Infective rhinitis

Outcome	Reference standard positive (diagnosed with OME), N = 45	Reference standard negative (diagnosed with adenoid hypertrophy but no OME), N = 36
Index test positive Presenting feature: infective rhinitis No of events	14	10
Index test negative No infective rhinitis No of events	31	26

N: number; OME: otitis media with effusion

Allergic rhinitis and infective rhinitis

Outcome	Reference standard positive (diagnosed with OME), N = 45	Reference standard negative (diagnosed with adenoid hypertrophy but no OME), N = 36
Index test positive	2	0

Outcome	Reference standard positive (diagnosed with OME), N = 45	Reference standard negative (diagnosed with adenoid hypertrophy but no OME), N = 36
Presenting features: allergic rhinitis and infective rhinitis No of events		
Index test negative No allergic rhinitis and infective rhinitis No of events	43	36

N: number; OME: otitis media with effusion

Non-allergic rhinitis and infective rhinitis

Outcome	Reference standard positive (diagnosed with OME), N = 45	Reference standard negative (diagnosed with adenoid hypertrophy but no OME), N = 36
Index test positive Presenting features: non-allergic rhinitis and infective rhinitis No of events	8	6
Index test negative No non-allergic rhinitis and infective rhinitis No of events	37	30

N: number; OME: otitis media with effusion

Critical appraisal - NGA Critical appraisal - QUADAS-2

Section	Question	Answer
Patient selection: risk of bias	Could the selection of patients have introduced bias?	Low *(Consecutive sample enrolled)*

Section	Question	Answer
Patient selection: applicability	Are there concerns that included patients do not match the review question?	Unclear *(Study included participants up to the age of 15; number of children over the age of 12 not reported)*
Index tests: risk of bias	Could the conduct or interpretation of the index test have introduced bias?	Low *(No information about whether index test was interpreted without knowledge of the reference standard; however, test is objective so unlikely that knowledge of results would introduce bias.)*
Index tests: applicability	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low
Reference standard: risk of bias	Could the reference standard, its conduct, or its interpretation have introduced bias?	Low *(No information about whether reference standards were interpreted without knowledge of the index tests; however, tests are objective so unlikely that knowledge of results would introduce bias)*
Reference standard: applicability	Is there concern that the target condition as defined by the reference standard does not match the review question?	Low
Flow and timing: risk of bias	Could the patient flow have introduced bias?	Unclear *(No information about interval between index tests and reference standards)*

Ralli, 2011

Bibliographic Reference	Ralli, Giovanni; Ruoppolo, Giovanni; Mora, Renzo; Guastini, Luca; Deleterious sucking habits and atypical swallowing in children with otitis media with effusion.; International journal of pediatric otorhinolaryngology; 2011; vol. 75 (no. 10); 1260-4

Study details

Country/ies where study was carried out	Italy
Study type	Case-control study

Study dates	March 2010 - February 2011
Inclusion criteria	OME group: children aged 7-12 years with OME for >3 months Healthy group: children aged 7-12 years with no current or history of OME and normal otoscopic findings Both groups: • Absence of temporomandibular joint disorders • Presence of healthy periodontal ligament, Angle's first molar class, and good dental arch symmetry
Exclusion criteria	• Systemic diseases • Uncooperative behaviour • History of trauma, dental pain, or orthodontic treatment
Patient characteristics	Whole cohort: N=125 OME group: n=65 • Mean age (range): 9.2 (7-12) years • Sex (female/male): 29/ 36 • Craniofacial anomalies: not reported Healthy group: N=60 • Mean age (range): 9.1 (7-12) years • Sex (female/male): 22/ 38 • Craniofacial anomalies: not reported
Index test(s)	Presenting features: 1. Deleterious sucking habits, such as finger- or dummy-sucking, and bottle feeding (assessed though parental interview. Parafunctional sucking habits and mode of mouth breathing were also recorded, though information about who recorded this/ how this was assessed is not reported) 2. Atypical swallowing (defined as lip activity producing strong tension in the perioral musculature, and/or the tip of the tongue pushed/ placed against the anterior teeth when swallowing)

Reference standard(s)	Tympanometry, ENT examination using otoscopy, and medical history
Duration of follow-up	Not reported
Sources of funding	Not industry funded
Other information	None

ENT: ears, nose and throat; N: number; OME: otitis media with effusion

Study arms

Reference standard positive (OME group) (N = 65)

Reference standard negative (healthy group) (N = 60)

Outcomes

Deleterious sucking habits

Outcome	Reference standard positive (OME group), N = 65	Reference standard negative (healthy group), N = 60
Index test positive Presenting feature: deleterious sucking habits No of events	n = 28	n = 12
Index test negative No deleterious sucking habits No of events	n = 37	n = 48

N: number; OME: otitis media with effusion

Atypical swallowing

Outcome	Reference standard positive (OME group), N = 65	Reference standard negative (healthy group), N = 60
Index test positive Presenting feature: atypical swallowing No of events	n = 33	n = 16
Index test negative No atypical swallowing No of events	n = 32	n = 44

N: number; OME: otitis media with effusion

Critical appraisal - NGA Critical appraisal - QUADAS-2

Section	Question	Answer
Patient selection: risk of bias	Could the selection of patients have introduced bias?	High *(Case-control study)*
Patient selection: applicability	Are there concerns that included patients do not match the review question?	Low
Index tests: risk of bias	Could the conduct or interpretation of the index test have introduced bias?	Unclear *(No information about whether index tests were interpreted without knowledge of the reference standard, and tests are somewhat subjective: deleterious sucking habits were assessed through parental interview; it is unclear who assessed atypical swallowing criteria or how they were interpreted)*
Index tests: applicability	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low
Reference standard: risk of bias	Could the reference standard, its conduct, or its interpretation have introduced bias?	Low *(No information about whether reference standards were interpreted without knowledge of the index tests; however, tests are objective so unlikely that knowledge of results would introduce bias)*

Section	Question	Answer
Reference standard: applicability	Is there concern that the target condition as defined by the reference standard does not match the review question?	Low
Flow and timing: risk of bias	Could the patient flow have introduced bias?	Unclear *(No information about interval between index tests and reference standard)*

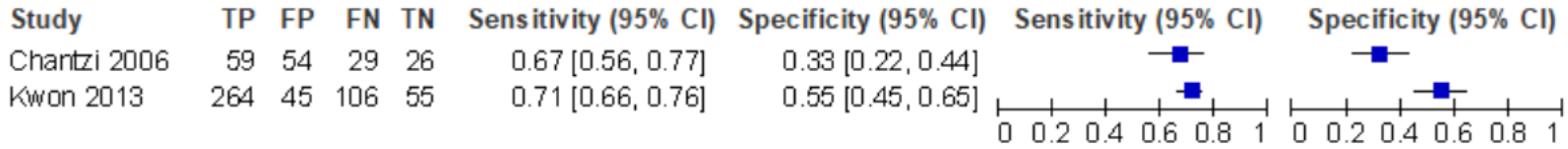
1
2

Appendix E Forest plots

Forest plots for review question: What presenting features are associated with OME in children under 12 years?

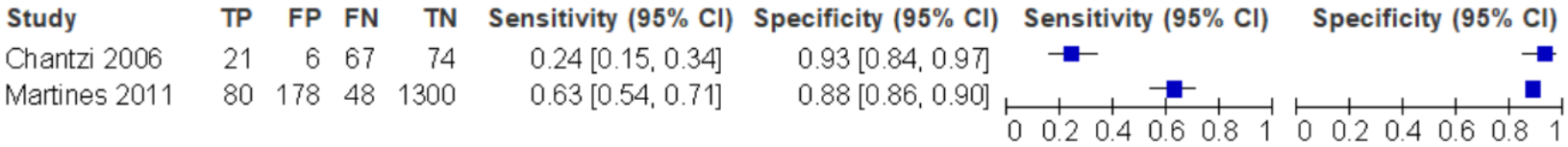
This section includes forest plots only for presenting feature which were investigated by multiple studies. Presenting features from single studies are not presented here; the quality assessment for such outcomes is provided in the GRADE profiles in appendix F.

Figure 2: Adenoid hypertrophy for OME



CI: confidence intervals; FN: false negative; FP: false positive; TN: true negative; TP: true positive

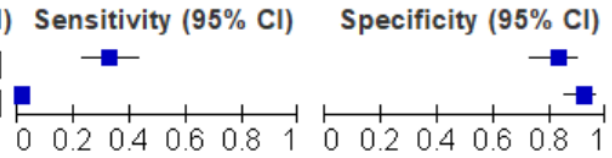
Figure 3: Atopy for OME



CI: confidence intervals; FN: false negative; FP: false positive; TN: true negative; TP: true positive

Figure 4: Asthma for OME

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chantzi 2006	29	14	59	66	0.33 [0.23, 0.44]	0.82 [0.72, 0.90]
Kwon 2013	8	8	362	92	0.02 [0.01, 0.04]	0.92 [0.85, 0.96]

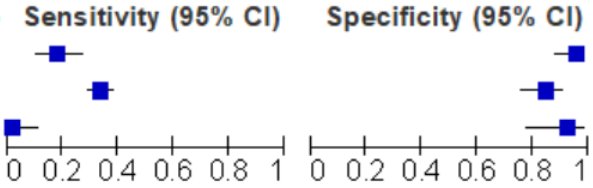


CI: confidence intervals; FN: false negative; FP: false positive; TN: true negative; TP: true positive

1

Figure 5: Allergic rhinitis for OME

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chantzi 2006	16	4	72	76	0.18 [0.11, 0.28]	0.95 [0.88, 0.99]
Kwon 2013	125	16	245	84	0.34 [0.29, 0.39]	0.84 [0.75, 0.91]
Quaranta 2013	1	3	44	33	0.02 [0.00, 0.12]	0.92 [0.78, 0.98]

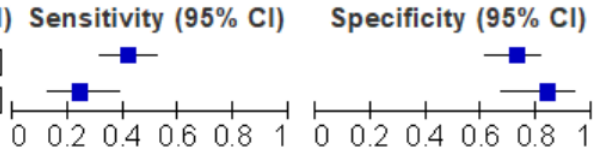


CI: confidence intervals; FN: false negative; FP: false positive; TN: true negative; TP: true positive

2

Figure 6: Non-allergic rhinitis

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chantzi 2006	37	22	51	58	0.42 [0.32, 0.53]	0.72 [0.61, 0.82]
Quaranta 2013	11	6	34	30	0.24 [0.13, 0.40]	0.83 [0.67, 0.94]

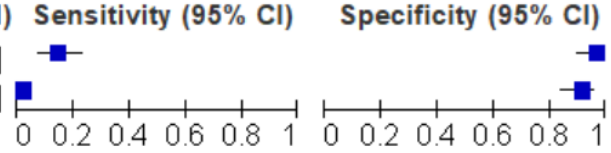


CI: confidence intervals; FN: false negative; FP: false positive; TN: true negative; TP: true positive

3

Figure 7: Eczema/ atopic dermatitis for OME

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chantzi 2006	13	3	75	77	0.15 [0.08, 0.24]	0.96 [0.89, 0.99]
Kwon 2013	10	9	360	91	0.03 [0.01, 0.05]	0.91 [0.84, 0.96]

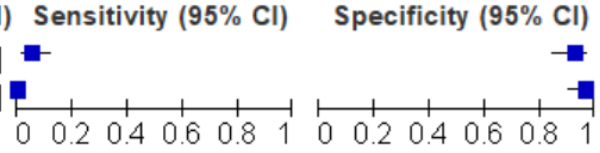


CI: confidence intervals; FN: false negative; FP: false positive; TN: true negative; TP: true positive

1

Figure 8: Conjunctivitis for OME

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chantzi 2006	5	6	83	74	0.06 [0.02, 0.13]	0.93 [0.84, 0.97]
Kwon 2013	2	4	368	96	0.01 [0.00, 0.02]	0.96 [0.90, 0.99]



CI: confidence intervals; FN: false negative; FP: false positive; TN: true negative; TP: true positive

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Appendix F GRADE tables

GRADE tables for diagnostic evidence for review question: What presenting features are associated with OME in children under 12 years?

Table 6: Presenting feature: Adenoid hypertrophy for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.67 (0.56 to 0.77)	Serious[1]	No serious	No serious	Serious[2]	**LOW**	0.52	0.47
			Specificity: 0.33 (0.22 to 0.44)	Serious[1]	No serious	No serious	No serious	**MODERATE**		
Imaging										
1 (Kwon 2013)	Population: Case group: Children with OME Control group: Children without OME/ OM who had undergone blood tests and MAST-CLA because of ranula, ankyloglossia (tongue-tie), preauricular fistula or epistaxis (nose bleeds) Reference standard: Tympanometry (type B or C tympanograms using impedance audiometry) with otoscopy (amber-coloured tympanic membrane)	Whole cohort: N=470 Case group: n=370 Control group: n=100	Sensitivity: 0.71 (0.66 to 0.76)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.85	0.34
			Specificity: 0.55 (0.45 to 0.65)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		

CI: confidence interval; ENT: ears, nose and throat; MAST-CLA: multiple allergosorbent test – chemiluminescent assay; NPV: negative predictive value; OM: otitis media; OME: otitis media with effusion; PPV: positive predictive value

[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

[2] 95% CI crosses 1 decision making threshold

Table 7: Presenting feature: History of adenoidectomy for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.67 (0.56 to 0.77)	Serious[1]	No serious	No serious	Serious[2]	**LOW**	0.55	0.48
			Specificity: 0.33 (0.22 to 0.44)	Serious[1]	No serious	No serious	No serious	**MODERATE**		

	Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms									

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[2] 95% CI crosses 1 decision making threshold

Table 8: Presenting feature: Nasal obstruction for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.91 (0.83 to 0.96)	Serious[1]	No serious	No serious	Serious[2]	**LOW**	0.54	0.62
			Specificity: 0.16 (0.09 to 0.26)	Serious[1]	No serious	No serious	No serious	**MODERATE**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[2] 95% CI crosses 1 decision making threshold

Table 9: Presenting feature: Tonsil hypertrophy for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Imaging										
1 (Kwon 2013)	Population: Case group: Children with OME Control group: Children without OME/ OM who had undergone blood tests and MAST-CLA because of ranula, ankyloglossia (tongue-tie), preauricular fistula or epistaxis (nose bleeds) Reference standard: Tympanometry (type B or C tympanograms using impedance audiometry) with otoscopy (amber-coloured tympanic membrane)	Whole cohort: N=470 Case group: n=370 Control group: n=100	Sensitivity: 0.53 (0.48 to 0.58)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.78	0.21
			Specificity: 0.45 (0.35 to 0.55)	Serious[1]	No serious	No serious	No serious	**MODERATE**		

CI: confidence interval; MAST-CLA: multiple allergosorbent test – chemiluminescent assay; NPV: negative predictive value; OM: otitis media; OME: otitis media with effusion; PPV: positive predictive value
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 10: Presenting feature: Atopy[1] for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV

Positive clinical history, SPT and/or CAP-FEIA, blood tests[2]										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.24 (0.15 to 0.34)	Serious[3]	No serious	No serious	No serious	**MODERATE**	0.78	0.52
			Specificity: 0.93 (0.84 to 0.97)	Serious[3]	No serious	No serious	Serious[4]	**LOW**		
SPT[5]										
1 (Martines 2011)	Population: Case group: Children from selected schools with OME Control group: Children from selected schools without OME Reference standard: Tympanometry (type B or C tympanograms with no stapedial reflex) with otoscopy (≥3 months middle ear effusion), absence of ipsilateral acoustic reflex and conductive hearing loss > 25 dB	Whole cohort: N=2097 Case group: n=143 Control group: n=1954	Sensitivity: 0.63 (0.54 to 0.71)	Very serious[6]	No serious	No serious	Serious[4]	**VERY LOW**	0.85	0.34
			Specificity: 0.88 (0.86 to 0.90)	Very serious[6]	No serious	No serious	Serious[4]	**VERY LOW**		

CAP-FEIA: College of American Pathologists fluorescence enzyme immunoassay; CI: confidence interval; dB: decibel; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value; SPT: skin prick test

[1] Defined as IgE-mediated allergic disease in Chantzi 2006, and atopy/ allergy in Martines 2011

[2] Positive clinical history of asthma, rhinitis, eczema, or any combination of these, plus skin-prick tests (SPT) and/or CAP-FEIA to seven locally relevant allergens (grass mix, weed mix, dust mite mix, olive, cat, alternaria, and egg white). A blood sample was also obtained in which eosinophil counts and total IgE were assessed

[3] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

[4] 95% CI crosses 1 decision making threshold

[5] SPTs for 12 common perennial and seasonal allergens (Alternaria, Aspergillus, Cladosporium, Penicillium, ragweed, grass mix, trees mix, cockroach, dust mites, Dermatophagoides farinae and Dermatophagoides pteronyssinus, and cat and dog epithelium)

[6] Very serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 11: Presenting feature: Immunoglobin E (IgE) sensitisation for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
SPT and/or CAP-FEIA, blood tests[1]										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.32 (0.22 to 0.43)	Serious[2]	No serious	No serious	No serious	**MODERATE**	0.70	0.53
			Specificity: 0.85 (0.75 to 0.92	Serious[2]	No serious	No serious	No serious	**MODERATE**		

CAP-FEIA: College of American Pathologists fluorescence enzyme immunoassay; CI: confidence interval; ENT: ears, nose and throat; IgE: Immunoglobin E; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value; SPT: skin prick test

[1] Skin-prick tests (SPT) and/or CAP-FEIA to seven locally relevant allergens (grass mix, weed mix, dust mite mix, olive, cat, alternaria, and egg white). A blood sample was also obtained in which eosinophil counts and total IgE were assessed

[2] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 12: Presenting feature: Any allergic disease (asthma, rhinitis, eczema, or any combination of these) for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Positive clinical history										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.60 (0.49 to 0.71)	Serious[1]	No serious	No serious	Serious[2]	**LOW**	0.61	0.57
			Specificity: 0.57 (0.46 to 0.68)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value

[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

[2] 95% CI crosses 1 decision making threshold

Table 13: Presenting feature: Asthma for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.33 (0.23 to 0.44)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.67	0.53
			Specificity: 0.82 (0.72 to 0.90)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		
MAST-CLA and medical records										
1 (Kwon 2013)	Population: Case group: Children with OME Control group: Children without OME/ OM who had undergone blood tests and MAST-CLA because of ranula, ankyloglossia (tongue-tie), preauricular fistula or epistaxis (nose bleeds) Reference standard: Tympanometry (type B or C tympanograms using impedance audiometry) with otoscopy (amber-coloured tympanic membrane)	Whole cohort: N=470 Case group: n=370 Control group: n=100	Sensitivity: 0.02 (0.01 to 0.04)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.50	0.20
			Specificity: 0.92 (0.85 to 0.96)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		

CI: confidence interval; ENT: ears, nose and throat; MAST-CLA: multiple allergosorbent test – chemiluminescent assay; NPV: negative predictive value; OM: otitis media; OME: otitis media with effusion; PPV: positive predictive value

[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[2] 95% CI crosses 1 decision making threshold

Table 14: Presenting feature: IgE-mediated asthma for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire, SPT and/or CAP-FEIA, blood tests[1]										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.13 (0.06 to 0.21)	Serious[2]	No serious	No serious	No serious	**MODERATE**	0.79	0.50
			Specificity: 0.96 (0.89 to 0.99)	Serious[2]	No serious	No serious	Serious[3]	**LOW**		

CAP-FEIA: College of American Pathologists fluorescence enzyme immunoassay; CI: confidence interval; ENT: ears, nose and throat; IgE: Immunoglobin E; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value; SPT: skin prick test
[1] Assessed by a physician using a standardised questionnaire and strict clinical definitions, plus skin-prick tests (SPT) and/or CAP-FEIA to seven locally relevant allergens (grass mix, weed mix, dust mite mix, olive, cat, alternaria, and egg white). A blood sample was also obtained in which eosinophil counts and total IgE were assessed
[2] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[3] 95% CI crosses 1 decision making threshold

Table 15: Presenting feature: Allergic rhinitis[1] for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire, SPT and/or CAP-FEIA, blood tests[2]										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.18 (0.11 to 0.28)	Serious[3]	No serious	No serious	No serious	**MODERATE**	0.80	0.51
			Specificity: 0.95 (0.88 to 0.99)	Serious[3]	No serious	No serious	Serious[4]	**LOW**		
MAST-CLA and medical records										
1 (Kwon 2013)	Population: Case group: Children with OME Control group: Children without OME/ OM who had undergone blood tests and MAST-CLA because of ranula, ankyloglossia (tongue-tie), preauricular fistula or epistaxis (nose bleeds) Reference standard: Tympanometry (type B or C tympanograms using impedance audiometry) with otoscopy (amber-coloured tympanic membrane)	Whole cohort: N=470 Case group: n=370 Control group: n=100	Sensitivity: 0.34 (0.29 to 0.39)	Serious[3]	No serious	No serious	No serious	**MODERATE**	0.89	0.26
			Specificity: 0.84 (0.75 to 0.91)	Serious[3]	No serious	No serious	Serious[4]	**LOW**		

Cytology, SPT and nasal sampling[5]										
1 (Quaranta 2013)	Population: Children with grade 3/ 4 adenoid hypertrophy Reference standard: Tympanometry and pure tone audiometry	Whole cohort: N=81 Children with OME: n= 52 Children without OME: n= 29	Sensitivity: 0.02 (0.00 to 0.12)	No serious	No serious	No serious	No serious	**HIGH**	0.25	0.43
			Specificity: 0.92 (0.78 to 0.98)	No serious	No serious	No serious	Serious[4]	**MODERATE**		

CAP-FEIA: College of American Pathologists fluorescence enzyme immunoassay; CI: confidence interval; ENT: ears, nose and throat; MAST-CLA: multiple allergosorbent test – chemiluminescent assay; NPV: negative predictive value; OM: otitis media; OME: otitis media with effusion; PPV: positive predictive value; SPT: skin prick test
[1] Defined as IgE-mediated allergic rhinitis (rhinitis combined with IgE sensitisation) in Chantzi 2006, and allergic rhinitis in Kwon 2013 and Quaranta 2013
[2] Assessed by a physician using a standardised questionnaire and strict clinical definitions, plus skin-prick tests (SPT) and/or CAP-FEIA to seven locally relevant allergens (grass mix, weed mix, dust mite mix, olive, cat, alternaria, and egg white). A blood sample was also obtained in which eosinophil counts and total IgE were assessed
[3] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[4] 95% CI crosses 1 decision making threshold
[5] Positive skin prick test, nasal symptoms due to allergens and heterogeneous rhinocytogram

Table 16: Presenting feature: Non-allergic rhinitis for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.42 (0.32 to 0.53)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.63	0.53
			Specificity: 0.72 (0.61 to 0.82)	Serious[1]	No serious	No serious	No serious	**MODERATE**		
Cytology, SPT and nasal sampling[2]										
1 (Quaranta 2013)	Population: Children with grade 3/ 4 adenoid hypertrophy Reference standard: Tympanometry and pure tone audiometry	Whole cohort: N=81 Children with OME: n= 52 Children without OME: n= 29	Sensitivity: 0.24 (0.13 to 0.40)	No serious	No serious	No serious	No serious	**HIGH**	0.65	0.47
			Specificity: 0.83 (0.67 to 0.94)	No serious	No serious	No serious	Serious[3]	**MODERATE**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value; SPT: skin prick test
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[2] Negative skin prick test and the continuous presence of inflammatory cells in the nasal mucosa independently from the seasonality
[3] 95% CI crosses 1 decision making threshold

Table 17: Presenting feature: Infective rhinitis for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Cytology, SPT and nasal sampling[1]										

1 (Quaranta 2013)	Population: Children with grade 3/ 4 adenoid hypertrophy Reference standard: Tympanometry and pure tone audiometry	Whole cohort: N=81 Children with OME: n= 52 Children without OME: n= 29	Sensitivity: 0.31 (0.18 to 0.47)	No serious	No serious	No serious	No serious	**HIGH**	0.58	0.46
			Specificity: 0.72 (0.55 to 0.86)	No serious	No serious	No serious	Serious[2]	**MODERATE**		

CI: confidence interval; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value; SPT: skin prick test
[1] Assessed using SPT, cytology and nasal sampling, infective rhinitis was diagnosed when there were abundant bacteria that could be found in extracellular tissue and inside neutrophils due to phagocytosis
[2] 95% CI crosses 1 decision making threshold

Table 18: Presenting feature: Allergic rhinitis and infective rhinitis for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Cytology, SPT and nasal sampling[1]										
1 (Quaranta 2013)	Population: Children with grade 3/ 4 adenoid hypertrophy Reference standard: Tympanometry and pure tone audiometry	Whole cohort: N=81 Children with OME: n= 52 Children without OME: n= 29	Sensitivity: 0.04 (0.01 to 0.15)	No serious	No serious	No serious	No serious	**HIGH**	1.00	0.46
			Specificity: 1.00 (0.90 to 1.00)	No serious	No serious	No serious	No serious	**HIGH**		

CI: confidence interval; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value; SPT: skin prick test
[1] Positive skin prick test, nasal symptoms due to allergens and heterogeneous rhinocytogram (allergic rhinitis), plus abundant bacteria that could be found in extracellular tissue and inside neutrophils due to phagocytosis (infective rhinitis)

Table 19: Presenting feature: Non-allergic rhinitis and infective rhinitis for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Cytology, SPT and nasal sampling[1]										
1 (Quaranta 2013)	Population: Children with grade 3/ 4 adenoid hypertrophy Reference standard: Tympanometry and pure tone audiometry	Whole cohort: N=81 Children with OME: n= 52 Children without OME: n= 29	Sensitivity: 0.18 (0.08 to 0.32)	No serious	No serious	No serious	No serious	**HIGH**	0.57	0.45
			Specificity: 0.83 (0.67 to 0.94)	No serious	No serious	No serious	Serious[2]	**MODERATE**		

CI: confidence interval; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value; SPT: skin prick test
[1] Negative skin prick test and the continuous presence of inflammatory cells in the nasal mucosa independently from the seasonality (non-allergic rhinitis), plus abundant bacteria that could be found in extracellular tissue and inside neutrophils due to phagocytosis (infective rhinitis)
[2] 95% CI crosses 1 decision making threshold

Table 20: Presenting feature: Chronic rhinosinusitis for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
MAST-CLA and medical records										

1 (Kwon 2013)	Population: Case group: Children with OME Control group: Children without OME/ OM who had undergone blood tests and MAST-CLA because of ranula, ankyloglossia (tongue-tie), preauricular fistula or epistaxis (nose bleeds) Reference standard: Tympanometry (type B or C tympanograms using impedance audiometry) with otoscopy (amber-coloured tympanic membrane)	Whole cohort: N=470 Case group: n=370 Control group: n=100	Sensitivity: 0.07 (0.05 to 0.10)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.87	0.22
			Specificity: 0.96 (0.90 to 0.99)	Serious[1]	No serious	No serious	No serious	**MODERATE**		

CI: confidence interval; MAST-CLA: multiple allergosorbent test – chemiluminescent assay; NPV: negative predictive value; OM: otitis media; OME: otitis media with effusion; PPV: positive predictive value

[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 21: Presenting feature: Eczema/ atopic dermatitis for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.15 (0.08 to 0.24)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.81	0.51
			Specificity: 0.96 (0.89 to 0.99)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		
MAST-CLA and medical records										
1 (Kwon 2013)	Population: Case group: Children with OME Control group: Children without OME/ OM who had undergone blood tests and MAST-CLA because of ranula, ankyloglossia (tongue-tie), preauricular fistula or epistaxis (nose bleeds) Reference standard: Tympanometry (type B or C tympanograms using impedance audiometry) with otoscopy (amber-coloured tympanic membrane)	Whole cohort: N=470 Case group: n=370 Control group: n=100	Sensitivity: 0.03 (0.01 to 0.05)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.53	0.20
			Specificity: 0.91 (0.84 to 0.96)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		

CI: confidence interval; ENT: ears, nose and throat; MAST-CLA: multiple allergosorbent test – chemiluminescent assay; NPV: negative predictive value; OM: otitis media; OME: otitis media with effusion; PPV: positive predictive value

[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

[2] 95% CI crosses 1 decision making threshold

Table 22: Presenting feature: IgE-mediated eczema for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire, SPT and/or CAP-FEIA, blood tests[1]										

1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.08 (0.03 to 0.16)	Serious[2]	No serious	No serious	No serious	**MODERATE**	1.00	0.50
			Specificity: 1.00 (0.95 to 1.00)	Serious[2]	No serious	No serious	No serious	**MODERATE**		

CAP-FEIA: College of American Pathologists fluorescence enzyme immunoassay; CI: confidence interval; ENT: ears, nose and throat; IgE: Immunoglobin E; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value; SPT: skin prick test

[1] Assessed by a physician using a standardised questionnaire and strict clinical definitions, plus skin-prick tests (SPT) and/or CAP-FEIA to seven locally relevant allergens (grass mix, weed mix, dust mite mix, olive, cat, alternaria, and egg white). A blood sample was also obtained in which eosinophil counts and total IgE were assessed

[2] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 23: Presenting feature: Food reactions for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.10 (0.05 to 0.19)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.75	0.49
			Specificity: 0.96 (0.89 to 0.99)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value

[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

[2] 95% CI crosses 1 decision making threshold

Table 24: Presenting feature: Drug reactions for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.14 (0.07 to 0.23)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.60	0.49
			Specificity: 0.90 (0.81 to 0.96)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[2] 95% CI crosses 1 decision making threshold

Table 25: Presenting feature: Anaphylaxis for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.01 (0.00 to 0.06)	Serious[1]	No serious	No serious	No serious	**MODERATE**	1.00	0.48
			Specificity: 1.00 (0.95 to 1.00)	Serious[1]	No serious	No serious	No serious	**MODERATE**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 26: Presenting feature: Elevated eosinophil count (>4%) for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Blood tests										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.23 (0.14 to 0.33)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.51	0.47
			Specificity: 0.76 (0.65 to 0.85)	Serious[1]	No serious	No serious	No serious	**MODERATE**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 27: Presenting feature: Conjunctivitis[1] for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME	Whole cohort: N=168	Sensitivity: 0.06 (0.02 to 0.13)	Serious[2]	No serious	No serious	No serious	**MODERATE**	0.45	0.47

	Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Case group: n=88 Control group: n=80	Specificity: 0.93 (0.84 to 0.97)	Serious[2]	No serious	No serious	Serious[3]	**LOW**		
MAST-CLA and medical records										
1 (Kwon 2013)	Population: Case group: Children with OME Control group: Children without OME/ OM who had undergone blood tests and MAST-CLA because of ranula, ankyloglossia (tongue-tie), preauricular fistula or epistaxis (nose bleeds) Reference standard: Tympanometry (type B or C tympanograms using impedance audiometry) with otoscopy (amber-coloured tympanic membrane)	Whole cohort: N=470 Case group: n=370 Control group: n=100	Sensitivity: 0.01 (0.00 to 0.02)	Serious[2]	No serious	No serious	No serious	**MODERATE**	0.50	0.20
			Specificity: 0.96 (0.90 to 0.99)	Serious[2]	No serious	No serious	No serious	**MODERATE**		

CI: confidence interval; ENT: ears, nose and throat; MAST-CLA: multiple allergosorbent test – chemiluminescent assay; NPV: negative predictive value; OM: otitis media; OME: otitis media with effusion; PPV: positive predictive value

[1] Defined as conjunctivitis in Chantzi 2006, and allergic conjunctivitis in Kwon 2013

[2] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

[3] 95% CI crosses 1 decision making threshold

Table 28: Presenting feature: Urticaria for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.27 (0.18 to 0.38)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.60	0.50
			Specificity: 0.80 (0.70 to 0.88)	Serious[1]	No serious	No serious	No serious	**MODERATE**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value

[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 29: Presenting feature: Dyspnoea for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population:	Whole cohort: N=168	Sensitivity: 0.30 (0.20 to 0.40)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.67	0.52

	Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Case group: n=88 Control group: n=80	Specificity: 0.84 (0.74 to 0.91)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[2] 95% CI crosses 1 decision making threshold

Table 30: Presenting feature: Wheezing for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.28 (0.19 to 0.39)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.83	0.54
			Specificity: 0.94 (0.86 to 0.98)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[2] 95% CI crosses 1 decision making threshold

Table 31: Presenting feature: Recurrent cough for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.51 (0.40 to 0.62)	Serious[1]	No serious	No serious	Serious[2]	**LOW**	0.51	0.51
			Specificity: 0.51 (0.40 to 0.61)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
1 Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
2 95% CI crosses 1 decision making threshold

Table 32: Presenting feature: Rhinorrhoea for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.64 (0.53 to 0.74)	Serious[1]	No serious	No serious	Serious[2]	**LOW**	0.58	0.55
			Specificity: 0.49 (0.37 to 0.60)	Serious[1]	No serious	No serious	Serious[2]	**LOW**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[2] 95% CI crosses 1 decision making threshold

Table 33: Presenting feature: Paroxysmal sneezing/ nasal itching for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Standardised physician questionnaire										
1 (Chantzi 2006)	Population: Case group: Children with OME Control group: Children with type A tympanograms attending ENT department for other reasons Reference standard: Tympanometry (type B or C tympanograms), otoscopy and clinical symptoms	Whole cohort: N=168 Case group: n=88 Control group: n=80	Sensitivity: 0.40 (0.29 to 0.51)	Serious[1]	No serious	No serious	No serious	**MODERATE**	0.64	0.53
			Specificity: 0.75 (0.64 to 0.84)	Serious[1]	No serious	No serious	No serious	**MODERATE**		

CI: confidence interval; ENT: ears, nose and throat; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 34: Presenting feature: Snoring for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Parent questionnaire										
1 (Martines 2011)	Population: Case group: Children from selected schools with OME Control group: Children from selected schools without OME Reference standard: Tympanometry (type B or C tympanograms with no stapedial reflex) with otoscopy	Whole cohort: N=2097 Case group: n=143 Control group: n=1954	Sensitivity: 0.45 (0.37 to 0.54)	Very serious[1]	No serious	No serious	No serious	**LOW**	0.16	0.95
			Specificity: 0.82 (0.80 to 0.84)	Very serious[1]	No serious	No serious	No serious	**LOW**		

	(≥3 months middle ear effusion), absence of ipsilateral acoustic reflex and conductive hearing loss > 25 dB									

CI: confidence interval; dB: decibel; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Very serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 35: Presenting feature: Deleterious sucking habits for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Parent interview and symptoms[1]										
1 (Ralli 2011)	Population: Case group: Children with OME for >3 months Control group: Children with no current or history of OME and normal otoscopic findings Reference standard: Tympanometry with otoscopy and medical history	Whole cohort: N=125 Case group: n=65 Control group: n=60	Sensitivity: 0.43 (0.31 to 0.56)	Serious[2]	No serious	No serious	No serious	**MODERATE**	0.70	0.56
			Specificity: 0.80 (0.68 to 0.89)	Serious[2]	No serious	No serious	No serious	**MODERATE**		

CI: confidence interval; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Finger- or dummy-sucking and bottle feeding were assessed through parental interview; parafunctional sucking habits and mode of mouth breathing were recorded (information about who recorded these symptoms not given)
[2] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 36: Presenting feature: Atypical swallowing for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Symptoms[1]										
1 (Ralli 2011)	Population: Case group: Children with OME for >3 months Control group: Children with no current or history of OME and normal otoscopic findings Reference standard: Tympanometry with otoscopy and medical history	Whole cohort: N=125 Case group: n=65 Control group: n=60	Sensitivity: 0.51 (0.38 to 0.63)	Serious[2]	No serious	No serious	Serious[3]	**LOW**	0.67	0.58
			Specificity: 0.73 (0.60 to 0.84)	Serious[2]	No serious	No serious	Serious[3]	**LOW**		

CI: confidence interval; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Lip activity producing strong tension in the perioral musculature, and/or the tip of the tongue pushed/placed against the anterior teeth when swallowing
[2] Serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2
[3] 95% CI crosses 1 decision making threshold

Table 37: Presenting feature: History of AOM for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Parent questionnaire										

1 (Martines 2011)	Population: Case group: Children from selected schools with OME Control group: Children from selected schools without OME Reference standard: Tympanometry (type B or C tympanograms with no stapedial reflex) with otoscopy (≥3 months middle ear effusion), absence of ipsilateral acoustic reflex and conductive hearing loss > 25 dB	Whole cohort: N=2097 Case group: n=143 Control group: n=1954	Sensitivity: 0.10 (0.05 to 0.16)	Very serious[1]	No serious	No serious	No serious	**LOW**	0.15	0.94
			Specificity: 0.96 (0.95 to 0.97)	Very serious[1]	No serious	No serious	No serious	**LOW**		

CI: confidence interval; dB: decibel; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value
[1] Very serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 38: Presenting feature: History of upper respiratory tract infection (URTI) for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Parent questionnaire										
1 (Martines 2011)	Population: Case group: Children from selected schools with OME Control group: Children from selected schools without OME Reference standard: Tympanometry (type B or C tympanograms with no stapedial reflex) with otoscopy (≥3 months middle ear effusion), absence of ipsilateral acoustic reflex and conductive hearing loss > 25 dB	Whole cohort: N=2097 Case group: n=143 Control group: n=1954	Sensitivity: 0.10 (0.32 to 0.48)	Very serious[1]	No serious	No serious	No serious	**LOW**	0.14	0.95
			Specificity: 0.83 (0.81 to 0.84)	Very serious[1]	No serious	No serious	No serious	**LOW**		

CI: confidence interval; dB: decibel; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value; URTI: upper respiratory tract infection
[1] Very serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2

Table 39: Presenting feature: Allergy and history of URTI for diagnosis of OME

No of studies	Study details	No of participants	Effect size (95% CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality of evidence	PPV	NPV
Parent questionnaire and SPT[1]										
1 (Martines 2011)	Population: Case group: Children from selected schools with OME Control group: Children from selected schools without OME Reference standard: Tympanometry (type B or C tympanograms with no stapedial reflex) with otoscopy (≥3 months middle ear effusion), absence of ipsilateral acoustic reflex and conductive hearing loss > 25 dB	Whole cohort: N=2097 Case group: n=143 Control group: n=1954	Sensitivity: 0.29 (0.21 to 0.37)	Very serious[2]	No serious	No serious	No serious	**LOW**	0.46	0.95
			Specificity: 0.98 (0.97 to 0.98)	Very serious[2]	No serious	No serious	No serious	**LOW**		

CI: confidence interval; dB: decibel; NPV: negative predictive value; OME: otitis media with effusion; PPV: positive predictive value; SPT: skin prick test; URTI: upper respiratory tract infection
[1] Assessed using a questionnaire answered by parents, plus SPTs for 12 common perennial and seasonal allergens (Alternaria, Aspergillus, Cladosporium, Penicillium, ragweed, grass mix, trees mix, cockroach, dust mites, Dermatophagoides farinae and Dermatophagoides pteronyssinus, and cat and dog epithelium)

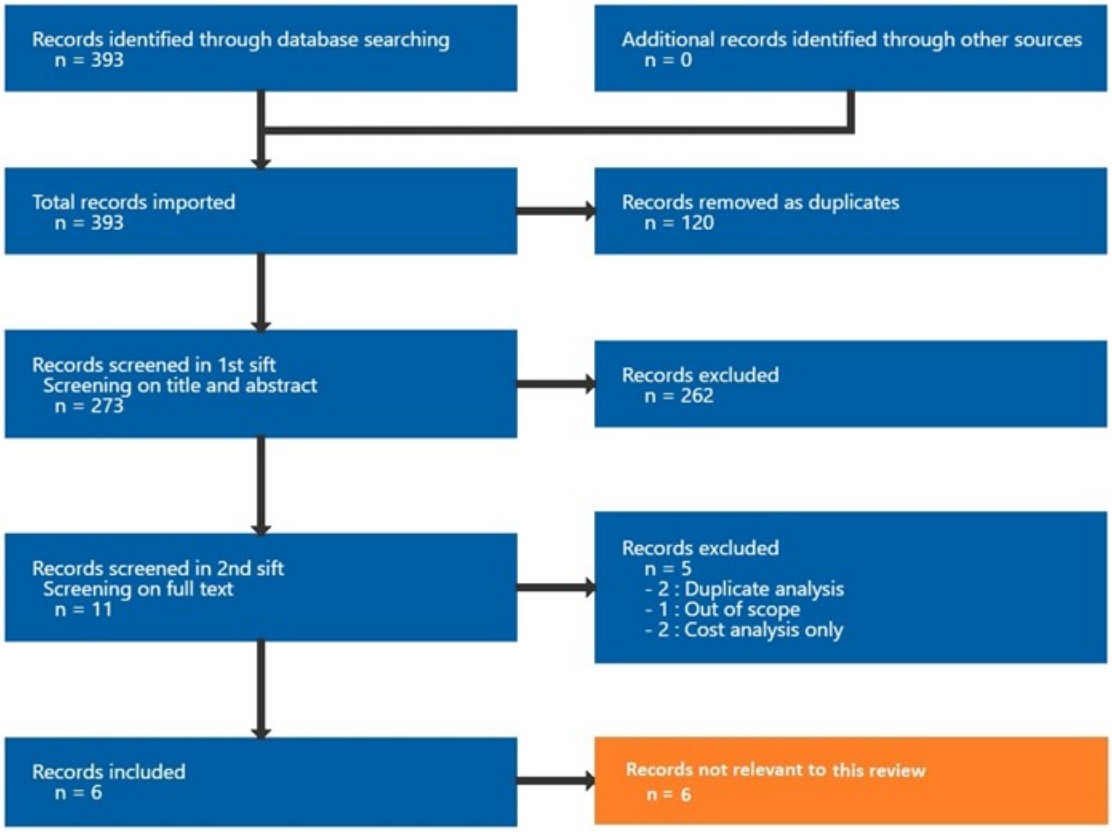
[2] *Very serious risk of bias in the evidence contributing to the outcomes as per QUADAS-2*

Appendix G Economic evidence study selection

Study selection for: What presenting features are associated with OME 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 presenting features are associated with OME 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 presenting features are associated with OME in children under 12 years?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What presenting features are associated with OME in children under 12 years?

Excluded diagnostic studies

Table 40: Excluded studies and reasons for their exclusion

Study	Code [Reason]
Abdullah, Baharudin; Hassan, Shahid; Sidek, Dinsuhaimi (2007) Clinical and audiological profiles in children with chronic otitis media with effusion requiring surgical intervention. The Malaysian journal of medical sciences : MJMS 14(2): 22-7	- Study conducted pre-2000 *Study conducted 1999-2001*
Acke, Frederic R E, De Vriese, Casper, Van Hoecke, Helen et al. (2021) Twelve years of neonatal hearing screening: audiological and etiological results. 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	- Diagnostic method for OME does not meet inclusion criteria *OME diagnosed based on 'etiological investigations' not further defined*
Al Anazy, F.H. (2011) The role of nasal allergy in otitis media with effusion. Bahrain Medical Bulletin 33(1)	- Study not conducted in OECD high-income country *Study conducted in Saudi Arabia*
Al-Saab, Fahad, Manoukian, John J, Al-Sabah, Basel et al. (2008) Linking laryngopharyngeal reflux to otitis media with effusion: pepsinogen study of adenoid tissue and middle ear fluid. Journal of otolaryngology - head & neck surgery = Le Journal d'oto-rhino-laryngologie et de chirurgie cervico-faciale 37(4): 565-71	- Insufficient presentation of results *Continuous data not possible to dichotomise for the sake of converting to diagnostic data*
Al-Salim, Sarah, Tempero, Richard M, Johnson, Hannah et al. (2021) Audiologic Profiles of Children With Otitis Media With Effusion. Ear and hearing 42(5): 1195-1207	- Insufficient presentation of results *Continuous data not possible to dichotomise for the sake of converting to diagnostic data*
Alam, M M, Ali, M I, Habib, M A et al. (2015) Otitis media with effusion in children admitted for adenoidectomy. Mymensingh medical journal : MMJ 24(2): 284-9	- Study not conducted in OECD high-income country *Study conducted in Bangladesh*
Alles, R, Parikh, A, Hawk, L et al. (2001) The prevalence of atopic disorders in children with chronic otitis media with effusion. Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology 12(2): 102-6	- Study conducted pre-2000 *Study conducted over the course of 2 years and was accepted for publication in 2000*

Study	Code [Reason]
AlSarhan, Haider; Mohammed, Ali Abed; T Yaseen, Ehab (2021) Reliability of the otoscopic tympanic membrane findings in the diagnosis of middle ear effusion. JPMA. The Journal of the Pakistan Medical Association 71(Suppl 8): 110-s112	- Study not conducted in OECD high-income country *Conducted in Iraq*
Aqeel-ur-Rehman, H.; Abbasi, A.; Khan, F.A. (2017) Causes of conductive hearing loss in school going children. Medical Forum Monthly 28(7): 130-133	- Study not conducted in OECD high-income country *Conducted in Pakistan*
Aydin, Emine, Tastan, Eren, Aydogan, Filiz et al. (2011) Role of nasopharyngeal reflux in the etiology of otitis media with effusion. Journal of otolaryngology - head & neck surgery = Le Journal d'oto-rhino-laryngologie et de chirurgie cervico-faciale 40(6): 499-503	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Aydogan, Barlas, Kiroglu, Mete, Altintas, Derya et al. (2004) The role of food allergy in otitis media with effusion. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 130(6): 747-50	- Study conducted pre-2000 *Study conducted 1996-1999*
Baggi, Elena, Semino, Margherita, Bianchini, Sonia et al. (2013) Middle ear problems in children hospitalised because of lower respiratory tract infections: a comparison between two cohorts in Burundi and Italy. International journal of pediatric otorhinolaryngology 77(12): 1984-6	- Study design does not meet inclusion criteria *Comparative study on prevalence of OME between two cohorts of children in Burundi and Italy*
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 not conducted in OECD high-income country *Study conducted in India*
Bemanian, Mohammad Hassan, Rezaei, Kazem, Atighechi, Saeid et al. (2020) The Relation of Allergy to Adenoid Hypertrophy and Otitis Media with Effusion: A Cross-sectional Study. Iranian journal of allergy, asthma, and immunology 19(5): 529-533	- Study not conducted in OECD high-income country *Study conducted in Iran*
Boone, Ryan T; Bower, Charles M; Martin, Patti F (2005) Failed newborn hearing screens as presentation for otitis media with effusion in the newborn population. International journal of pediatric otorhinolaryngology 69(3): 393-7	- Study conducted pre-2000 *Study conducted between 1999-2001*
Boudewyns, An, Declau, Frank, Van den Ende, Jenneke et al. (2011) Otitis media with effusion:	- Study design does not meet inclusion criteria *Non-comparative study*

Study	Code [Reason]
an underestimated cause of hearing loss in infants. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 32(5): 799-804	
Braun, T., Dreher, A., Dirr, F. et al. (2012) Pediatric OSAS and otitis media with effusion. HNO 60(3): 216-219	- Article not available in English
Cakabay, Taliye, Ustun Bezgin, Selin, Tarakcioglu, Mahmut Cem et al. (2019) Why do infants pull their ears?. Auris, nasus, larynx 46(5): 803-807	- Study design does not meet inclusion criteria *Non-comparative study: people without symptom (ear-tugging) not included and data for them not reported*
Carr, M M, Poje, C P, Ehrig, D et al. (2001) Incidence of reflux in young children undergoing adenoidectomy. The Laryngoscope 111(12): 2170-2	- Study conducted pre-2000 *Conducted between 1998-2000*
Casselbrant, Margaretha L; Mandel, Ellen M; Doyle, William J (2016) Information on co-morbidities collected by history is useful for assigning Otitis Media risk to children. International journal of pediatric otorhinolaryngology 85: 136-40	- Diagnostic method for OME does not meet inclusion criteria *Criteria for OME "three or more consecutive months of middle ear effusion if bilateral, six consecutive months of effusion if unilateral or three or more episodes of OM lasting for at least two months with at least one episode of OME or tympanostomy tube insertion in the year prior to entry and had not met the criteria for [recurrent acute otitis media]". Diagnostic criteria for OME not further defined*
Caylan, Refik, Bektas, Devrim, Atalay, Cemalettin et al. (2006) Prevalence and risk factors of otitis media with effusion in Trabzon, a city in northeastern Turkey, with an emphasis on the recommendation of OME screening. 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 263(5): 404-8	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Chalishazar, U K and Singh, V (2007) Correlation between a foreign body in the external auditory canal and otitis media with effusion. The Journal of laryngology and otology 121(9): 850-2	- Insufficient presentation of results *Data on the association between a foreign body in the external auditory canal and OME not reported separately from association between a foreign body in the external auditory canal and eustachian tube disorder. Data on other presenting features (previous history of ear complaints, hearing loss) not reported in association with OME.*
Chaudhry, Sadia, Ahmad, Zafar, Khan, Faraz Basharat et al. (2010) Frequency of otitis media in patients of nasal polypi. Journal of Ayub	- Study not conducted in OECD high-income country *Study conducted in Pakistan*

Study	Code [Reason]
Medical College, Abbottabad : JAMC 22(2): 83-5	
Chen, Judy L (2015) Newborn hearing screening may predict Eustachian tube dysfunction. International journal of pediatric otorhinolaryngology 79(12): 2099-103	- Diagnostic method for OME does not meet inclusion criteria *"no otoscopy or tympanometry was performed to confirm middle ear status" p2102*
Cheng, X, Sheng, H, Ma, R et al. (2017) Allergic rhinitis and allergy are risk factors for otitis media with effusion: A meta-analysis. Allergologia et immunopathologia 45(1): 25-32	- Systematic review, studies assessed for inclusion *Non-comparative studies, studies conducted before 2000, and studies from non-OECD high-income countries were included*
Chmielik, J., Chmielik, M., Zajac, B. et al. (2002) Vertigo and dizziness in children - Diagnostic problems. New Medicine 5(2): 67-70	- Article not available
da Costa, Sady Selaimen; Rosito, Leticia Petersen Schmidt; Dornelles, Cristina (2009) Sensorineural hearing loss in patients with chronic otitis media. 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 266(2): 221-4	- Study not conducted in OECD high-income country *Study conducted in Brazil*
Daval, Mary, Picard, Herve, Bequignon, Emilie et al. (2018) Chronic otitis media with effusion in chronic sinusitis with polyps. Ear, nose, & throat journal 97(8): e13-e18	- Population does not meet inclusion criteria *All participants over 15 years of age*
De Schrijver, L, Topsakal, V, Wojciechowski, M et al. (2019) Prevalence and etiology of sensorineural hearing loss in children with down syndrome: A cross-sectional study. International journal of pediatric otorhinolaryngology 116: 168-172	- Insufficient presentation of results *Study investigates etiology of hearing loss in children with down syndrome but no association data for OME reported*
Din, S., Khan, A.R., Khan, N.S. et al. (2005) Management of secretory otitis media in children. Journal of Postgraduate Medical Institute 19(1): 106-110	- Study not conducted in OECD high-income country *Conducted in Pakistan*
Durmaz, Bengul, Abdulmajed, Olkar, Durmaz, Riza et al. (2021) Respiratory viruses in the healthy middle ear and middle ear with otitis media with effusion. Journal of medical virology 93(11): 6140-6147	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Eftekharian, Ali, Sabeti, Shahram, Khajavi, Mahdi et al. (2012) Light microscopic histopathology of adenoid tissue in otitis media with effusion: is there any relation?. International	- Study not conducted in OECD high-income country *Study conducted in Iran*

Study	Code [Reason]
journal of pediatric otorhinolaryngology 76(11): 1598-600	
Engel, J, Anteunis, L, Volovics, A et al. (2000) Predictive value of parent-reported symptoms in the assessment of otitis media with effusion during infancy. Scandinavian journal of primary health care 18(1): 25-9	- Study conducted pre-2000 *Study conducted 1990-1995*
Engel-Yeger, B; Golz, A; Parush, S (2004) Impact of middle ear effusion on balance performance in children. Disability and rehabilitation 26(2): 97-102	- Insufficient presentation of results *Continuous data not possible to dichotomise for the sake of converting to diagnostic data*
Esteves, Sara Duarte Sena, Silva, Ana Pereira da, Coutinho, Miguel Bebiano et al. (2014) Congenital defects of the middle ear--uncommon cause of pediatric hearing loss. Brazilian journal of otorhinolaryngology 80(3): 251-6	- Study design does not meet inclusion criteria *Case series*
Gan, R W C, Daniel, M, Ridley, M et al. (2018) Quality of questionnaires for the assessment of otitis media with effusion in children. Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery 43(2): 572-583	- Study design does not meet inclusion criteria *Non-comparative study*
Gawron, Wojciech; Pospiech, Lucyna; Orendorz-Fraczkowska, Krystyna (2004) An evaluation of postural stability and the effects of middle-ear drainage on vestibulo-spinal reflexes of children with chronic otitis media with effusion. International journal of pediatric otorhinolaryngology 68(9): 1175-9	- Insufficient presentation of results *Continuous data not possible to dichotomise for the sake of converting to diagnostic data*
Gomaa, Mohammed A; Karim, Abdel Rahim Ahmed Abdel; Elsherbeny, Yaser Makram (2014) Role of immunoglobulin E and gastro-esophageal reflux disease in the development of otitis media with effusion. Otolaryngologia polska = The Polish otolaryngology 68(3): 119-23	- Study not conducted in OECD high-income country *Study conducted in Egypt*
Gouma, Panagiota, Mallis, Antonios, Daniilidis, Vasilis et al. (2011) Behavioral trends in young children with conductive hearing loss: a case-control study. 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 268(1): 63-6	- Population does not meet inclusion criteria *Children with an episode of OME in the past 6 weeks were excluded from the study*
Gravel, J S and Wallace, I F (2000) Effects of otitis media with effusion on hearing in the first 3	- Study conducted pre-2000

Study	Code [Reason]
years of life. Journal of speech, language, and hearing research : JSLHR 43(3): 631-44	*Study was conducted during the first 3 years of the lives of participants and was published in 2000*
Gravel, Judith S, Roberts, Joanne E, Roush, Jackson et al. (2006) Early otitis media with effusion, hearing loss, and auditory processes at school age. Ear and hearing 27(4): 353-68	- Study design does not meet inclusion criteria *Non-comparative study*
Grewal, Jeewanjot S, Cohn, Jason E, Burdett, Jacob et al. (2022) Otitis Media and Hearing Loss in Patients With Nonsyndromic Craniosynostosis: A Multicenter Study. The Cleft palate-craniofacial journal : official publication of the American Cleft Palate-Craniofacial Association 59(5): 652-658	- Insufficient presentation of results *Study investigates whether craniosynostosis (congenital defect) is a risk factor for OME. Data are provided regarding presence of other symptoms, but information about the association between OME status and these presenting features are not given*
Han, Honglei and Lv, Qiuping (2018) Characteristics of laryngopharyngeal reflux in patients with chronic otitis media. American journal of otolaryngology 39(5): 493-496	- Study design does not meet inclusion criteria *Non-comparative study*
He, Zhaoping, O'Reilly, Robert C, Bolling, Laura et al. (2007) Detection of gastric pepsin in middle ear fluid of children with otitis media. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 137(1): 59-64	- Diagnostic method for OME does not meet inclusion criteria *OME diagnosed based on clinical history and otoscopic evaluation*
Heo, Kyung Wook; Kim, Min Jae; Lee, Jun Ho (2018) Impact of nasal conditions on chronic otitis media: a cross-sectional study in Koreans. Acta oto-laryngologica 138(2): 116-121	- Diagnostic method for OME does not meet inclusion criteria *Chronic otitis media diagnosed based on "otoscopic or endoscopic examinations" and pure tone audiometry; no data reported for OME*
Hooper, Stephen R, Ashley, Timothy A, Roberts, Joanne E et al. (2006) The relationship of otitis media in early childhood to attention dimensions during the early elementary school years. Journal of developmental and behavioral pediatrics : JDBP 27(4): 281-9	- Study design does not meet inclusion criteria *Non-comparative study*
Humaid, Al-Humaid I, Ashraf, Abou-Halawa S, Masood, Khan A et al. (2014) Prevalence and risk factors of Otitis Media with effusion in school children in Qassim Region of Saudi Arabia. International journal of health sciences 8(4): 325-34	- Study not conducted in OECD high-income country *Study conducted in Saudi Arabia*
Hunter, Lisa L, Davey, Cynthia S, Kohtz, Allison et al. (2007) Hearing screening and middle ear measures in American Indian infants and toddlers. International journal of pediatric otorhinolaryngology 71(9): 1429-38	- Study conducted pre-2000 *Participants (pregnant women) recruited between 1998-2001*

Study	Code [Reason]
Hunter, Lisa L, Prieve, Beth A, Kei, Joseph et al. (2013) Pediatric applications of wideband acoustic immittance measures. Ear and hearing 34suppl1: 36s-42s	- Study design does not meet inclusion criteria *Narrative review*
Huyett, Phillip, Raz, Yael, Hirsch, Barry E et al. (2017) Radiographic Mastoid and Middle Ear Effusions in Intensive Care Unit Subjects. Respiratory care 62(3): 350-356	- Diagnostic method for OME does not meet inclusion criteria *OME diagnosed based on head CT or MRI*
Jang, Chul Ho and Jung, Jae Kwon (2003) Expression of mast cell tryptase in pediatric otitis media with effusion. International journal of pediatric otorhinolaryngology 67(11): 1185-8	- Study design does not meet inclusion criteria *Study compares presence and level of mast cell tryptase concentration in MEE samples from children with and without allergy. Data for children without OME not provided.*
Jastrzebska, I., Gorecka-Tuteja, A., Sladek, M. et al. (2012) Characteristics of laryngopharyngeal reflux as well as of gastroesophageal reflux in children with otitis media with effusion. Pediatria Wspolczesna 14(2): 69-73	- Article not available in English
Jin, Zhe, Cha, Sung Ho, Choi, Yong-Sung et al. (2016) Expression of CXCL4 and aquaporin 3 and 10 mRNAs in patients with otitis media with effusion. International journal of pediatric otorhinolaryngology 81: 33-7	- Study design does not meet inclusion criteria *Study compares culture results of MEE samples from children with OME who are and are not prone to otitis media. Data for children with and without OME not provided*
Jung, Su Young, Kim, Sung Su, Kim, Young Il et al. (2018) Expression of aquaporins mRNAs in patients with otitis media. Acta oto-laryngologica 138(8): 701-707	- Population does not meet inclusion criteria *Participants are adults*
Kaleida, Phillip H (2004) Evidence assessment of the accuracy of methods of diagnosing middle ear effusion in children with otitis media with effusion. The Journal of pediatrics 145(1): 138	- Conference abstract
Karyanta, Mahastini; Satrowiyoto, Siswanto; Wulandari, Dian Paramita (2019) Prevalence Ratio of Otitis Media with Effusion in Laryngopharyngeal Reflux. International journal of otolaryngology 2019: 7460891	- Study not conducted in OECD high-income country *Study conducted in Indonesia*
Keles, Bahar, Ozturk, Kayhan, Gunel, Engin et al. (2004) Pharyngeal reflux in children with chronic otitis media with effusion. Acta oto-laryngologica 124(10): 1178-81	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Khan, A.A., Khan, A.R., Junaid, M. et al. (2020) Enlarged adenoids and allergy in otitis media-an experience at a tertiary care hospital. Journal of Medical Sciences (Peshawar) 28(1): 6-9	- Study not conducted in OECD high-income country *Study conducted in Pakistan*
Khavarghazalani, B., Hosseini Dastgerdi, Z., Gohari, N. et al. (2022) Auditory temporal	- Study not conducted in OECD high-income country

Study	Code [Reason]
processinzg in children with history of recurrent otitis media with effusion. Hearing, Balance and Communication 20(1): 46-51	*Study conducted in Iran*
Khavarghazalani, Bahare, Farahani, Farhad, Emadi, Maryam et al. (2016) Auditory processing abilities in children with chronic otitis media with effusion. Acta oto-laryngologica 136(5): 456-9	- Study not conducted in OECD high-income country *Study conducted in Iran*
Kim, S.K., Park, I.-S., Hong, S.J. et al. (2022) Association Between Pneumonia and Chronic Otitis Media: A Nested Case-Control Study Using a National Health Screening Cohort. International Journal of Infectious Diseases 118: 54-61	- Insufficient presentation of results *Results for OME not presented separately from results for other types of chronic otitis media*
Klaudt, Monte R; Steinbach, William J; Sectish, Theodore C (2003) Clinical considerations in the diagnosis of otitis media. Current allergy and asthma reports 3(4): 313-20	- Study design does not meet inclusion criteria *Narrative review*
Kocyigit, Murat, Cakabay, Taliye, Ortekin, Safiye G et al. (2017) Association Between Endocrine Diseases and Serous Otitis Media in Children. Journal of clinical research in pediatric endocrinology 9(1): 48-51	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Kocyigit, Murat, Ortekin, Safiye Giran, Cakabay, Taliye et al. (2017) Frequency of Serous Otitis Media in Children without Otolaryngological Symptoms. International archives of otorhinolaryngology 21(2): 161-164	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Kolkaila, E A; Emara, A A; Gabr, T A (2015) Vestibular evaluation in children with otitis media with effusion. The Journal of laryngology and otology 129(4): 326-36	- Study not conducted in OECD high-income country *Study conducted in Egypt*
Korres, S, Nikolopoulos, Thomas P, Peraki, E E et al. (2008) Outcomes and efficacy of newborn hearing screening: strengths and weaknesses (success or failure?). The Laryngoscope 118(7): 1253-6	- Study design does not meet inclusion criteria *Study investigates number of children who fail hearing screening tests who have hearing loss. Association with OME not investigated*
Kosmidou, Panagiota, Tzifas, Sotiris, Lygeros, Spyros et al. (2021) Newborn Hearing Screening: Analysing the Effectiveness of Early Detection of Neonatal Hearing Loss in a Hospital in Greece. Cureus 13(11): e19807	- Study design does not meet inclusion criteria *Non-comparative study*
Kostic, Mirjana, Ribaric Jankes, Ksenija, Trotic, Robert et al. (2015) Clinical and audiological findings in children with acute otitis media. Acta oto-laryngologica 135(7): 645-50	- Population does not meet inclusion criteria *Study investigating children with AOM, data on the association between history of AOM and OME not reported*

Study	Code [Reason]
Kreiner-Moller, E, Chawes, B L K, Caye-Thomasen, P et al. (2012) Allergic rhinitis is associated with otitis media with effusion: a birth cohort study. Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology 42(11): 1615-20	- Insufficient presentation of results *Only summary measures (adjusted odds ratios) reported and results not reported sufficiently to convert to diagnostic data*
Krzyzak, Anna, Zagolski, Olaf, Pawelek, Michal et al. (2018) Paediatric otitis media with effusion is connected to deficits in music perception. Logopedics, phoniatrics, vocology 43(1): 42-46	- Insufficient presentation of results *Continuous data not possible to dichotomise for the sake of converting to diagnostic data*
Kubba, Haytham; Swan, Iain R C; Gatehouse, Stuart (2004) How appropriate is the OM6 as a discriminative instrument in children with otitis media?. Archives of otolaryngology--head & neck surgery 130(6): 705-9	- Insufficient presentation of results *Continuous data not possible to dichotomise for the sake of converting to diagnostic data*
Kucur, Cuneyt, Simsek, Eda, Kuduban, Ozan et al. (2015) Prevalence of and risk factors for otitis media with effusion in primary school children: case control study in Erzurum, Turkey. The Turkish journal of pediatrics 57(3): 230-5	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Lack, Gideon; Caulfield, Helen; Penagos, Martin (2011) The link between otitis media with effusion and allergy: a potential role for intranasal corticosteroids. Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology 22(3): 258-66	- Study design does not meet inclusion criteria *Narrative review*
Lechien, Jerome R, Hans, Stephane, Simon, Francois et al. (2021) Association Between Laryngopharyngeal Reflux and Media Otitis: A Systematic Review. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 42(7): e801-e814	- Systematic review, studies assessed for inclusion *Non-comparative studies, studies using diagnostic methods not including tympanometry, and studies investigating participants with other types of OM (not OME) were included*
Leo, G., Piacentini, E., Incorvaia, C. et al. (2007) Sinusitis and Eustachian tube dysfunction in children. Pediatric Allergy and Immunology 18(suppl18): 35-39	- Population does not meet inclusion criteria *Study investigates association between sinusitis and eustachian tube dysfunction, not specifically OME*
Lieu, Judith E C; Muthappan, P Ganesh; Uppaluri, Ravindra (2005) Association of reflux with otitis media in children. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 133(3): 357-61	- Study design does not meet inclusion criteria *Non-comparative study*
Lipson, S., Wang, A., Corcoran, M. et al. (2020) Severe motion sickness in infants and children. European Journal of Paediatric Neurology 28: 176-179	- Diagnostic method for OME does not meet inclusion criteria *Diagnostic criteria for OME not defined; diagnostic results report OME together with*

Study	Code [Reason]
	AOM under 'Eustachian tube dysfunction' ("Eustachian tube dysfunction was defined as either chronic otitis media with effusion for at least 3 consecutive months and/or recurrent acute otitis media with at least 4 or more infections within a year"). Results not presented separately
Lou, Zhengcai (2017) Assessment of laryngopharyngeal reflux and the shape of the Eustachian tube should be considered in chronic rhinosinusitis with nasal polyps and chronic otitis media. 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(12): 4265-4266	- Study design does not meet inclusion criteria *Commentary*
Magliulo, Giuseppe, Iannella, Giannicola, Granata, Guido et al. (2016) Otologic evaluation of patients with primary antibody deficiency. 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 273(11): 3537-3546	- Insufficient presentation of results *Study investigates whether common variable immunodeficiency (CVID) is a risk factor for OME. Data are provided regarding association between OME status and presence of symptoms, but information about what the symptoms are is not given*
Mandour, Y.M., Shendy, M., Ramadan, S.A. et al. (2021) Vitamin d level in children with secretory otitis media. Otorhinolaryngology Clinics 13(1): 18-22	- Study not conducted in OECD high-income country *Study conducted in Egypt*
Maris, M, Wojciechowski, M, Van de Heyning, P et al. (2014) A cross-sectional analysis of otitis media with effusion in children with Down syndrome. European journal of pediatrics 173(10): 1319-25	- Insufficient presentation of results *Data cannot be compared between two groups as both cohorts include children with OME. Number of children with OME in comparison group not reported.*
Marseglia, Gian Luigi, Pagella, Fabio, Caimmi, Davide et al. (2008) Increased risk of otitis media with effusion in allergic children presenting with adenoiditis. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 138(5): 572-5	- Insufficient presentation of results *Study only includes participants presenting with acute upper-airway infection. Results for which participants have acute rhinosinusitis, adenoiditis, or both are reported for the OME group only. Insufficient comparative data to extract for the purpose of converting to diagnostic data because which kind of acute upper-airway infection the non-OME group have is not reported*
Martines, F, Martinciglio, G, Martines, E et al. (2010) The role of atopy in otitis media with effusion among primary school children: audiological investigation. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-	- Reports same study/population as Martines 2011, no additional data reported

Study	Code [Reason]
Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery 267(11): 1673-8	
Martines, Francesco, Bentivegna, Daniela, Di Piazza, Fabiola et al. (2010) The point prevalence of otitis media with effusion among primary school children in Western Sicily. 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 267(5): 709-14	- Reports same study/population as Martines 2011, no additional data reported
Martines, Francesco, Martines, Enrico, Sciacca, Vincenzo et al. (2011) Otitis media with effusion with or without atopy: audiological findings on primary schoolchildren. American journal of otolaryngology 32(6): 601-6	- Reports same study/population as Martines 2011, no additional data reported
McCormick, D P, Baldwin, C D, Klecan-Aker, J S et al. (2001) Association of early bilateral middle ear effusion with language at age 5 years. Ambulatory pediatrics : the official journal of the Ambulatory Pediatric Association 1(2): 87-90	- Study conducted pre-2000 *Study conducted 1984-1989*
McCormick, David P; Johnson, Dale L; Baldwin, Constance D (2006) Early middle ear effusion and school achievement at age seven years. Ambulatory pediatrics : the official journal of the Ambulatory Pediatric Association 6(5): 280-7	- Study conducted pre-2000 *Study conducted 1984-1989*
Melake, Nahla A; Shaker, Ghada H; Salama, Magdy A (2012) Incidence of Helicobacter pylori infection and their clarithromycin-resistant strains in otitis media with effusion regarding phenotypic and genotypic studies. Saudi pharmaceutical journal : SPJ : the official publication of the Saudi Pharmaceutical Society 20(4): 345-53	- Insufficient presentation of results *Study investigates presence of H. pylori in culture results of MEE samples from children with and without OME, but no data reported about presenting features*
Minter, K R, Roberts, J E, Hooper, S R et al. (2001) Early childhood otitis media in relation to children's attention-related behavior in the first six years of life. Pediatrics 107(5): 1037-42	- Study conducted pre-2000
Minto, H. and Hogan, A.D. (2013) Allergic rhinitis is associated with otitis media with effusion: A birth cohort study. Pediatrics 132(suppl1): 29-s30	- Reports same study/population as Kreiner-Moller 2012, no additional data reported
Miura, Mauricio Schreiner; Mascaro, Miguel; Rosenfeld, Richard M (2012) Association between otitis media and gastroesophageal	- Systematic review, studies assessed for inclusion

Study	Code [Reason]
reflux: a systematic review. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 146(3): 345-52	*Studies investigating participants with other types of OM (not OME), and studies from non-OECD high-income countries were included*
Monsanto, Rafael da Costa, Kasemodel, Ana Luiza Papi, Tomaz, Andreza et al. (2018) Current evidence of peripheral vestibular symptoms secondary to otitis media. Annals of medicine 50(5): 391-401	- Systematic review, studies assessed for inclusion *Non-comparative studies, studies conducted before 2000, studies investigating participants with other types of OM (not OME), studies including adults, and studies from non-OECD high-income countries were included*
Morita, Shinya; Suzuki, Masanobu; Iizuka, Keiji (2010) Non-organic hearing loss in childhood. International journal of pediatric otorhinolaryngology 74(5): 441-6	- Diagnostic method for OME does not meet inclusion criteria *Diagnostic criteria for OME not defined*
Nair, Surendran; Kumar, Madhumita; Nair, Prathapan (2012) Role of GERD in children with otitis media with effusion. Indian journal of pediatrics 79(10): 1328-32	- Study not conducted in OECD high-income country *Study conducted in India*
Nery, C de Gois, Buranello, F Stefanato, Pereira, C et al. (2010) Otitis media with effusion and dental occlusion: is there any relationship?. European journal of paediatric dentistry 11(3): 132-6	- Study not conducted in OECD high-income country *Study conducted in Brazil*
Nguyen, Lily H P, Manoukian, John J, Sobol, Steven E et al. (2004) Similar allergic inflammation in the middle ear and the upper airway: evidence linking otitis media with effusion to the united airways concept. The Journal of allergy and clinical immunology 114(5): 1110-5	- Study design does not meet inclusion criteria *Non-comparative study*
Nguyen, Lily H P, Manoukian, John J, Tewfik, Ted L et al. (2004) Evidence of allergic inflammation in the middle ear and nasopharynx in atopic children with otitis media with effusion. The Journal of otolaryngology 33(6): 345-51	- Study design does not meet inclusion criteria *Non-comparative study*
Norhafizah, S; Salina, H; Goh, B S (2020) Prevalence of allergic rhinitis in children with otitis media with effusion. European annals of allergy and clinical immunology 52(3): 121-130	- Study not conducted in OECD high-income country *Study conducted in Malaysia*
O'Reilly, Robert C, He, Zhaoping, Bloedon, Esa et al. (2008) The role of extraesophageal reflux in otitis media in infants and children. The Laryngoscope 118(7part2suppl116): 1-9	- Diagnostic method for OME does not meet inclusion criteria *OME diagnosed based on clinical history and otoscopic evaluation, not tympanometry*
Paradise, J L, Dollaghan, C A, Campbell, T F et al. (2000) Language, speech sound production, and cognition in three-year-old children in	- Study conducted pre-2000 *Study began in 1991*

Study	Code [Reason]
relation to otitis media in their first three years of life. Pediatrics 105(5): 1119-30	
Parietti-Winkler, Cecile, Baumann, Cedric, Gallet, Patrice et al. (2009) Otitis media with effusion as a marker of the inflammatory process associated to nasal polyposis. Rhinology 47(4): 396-9	- Population does not meet inclusion criteria *Adults*
Park, Chul-Won, Han, Jang-Hee, Jeong, Jin-Hyeok et al. (2004) Detection rates of bacteria in chronic otitis media with effusion in children. Journal of Korean medical science 19(5): 735-8	- Study design does not meet inclusion criteria *Non-comparative study*
Parmar, Suchina, Davessar, Jai Lal, Singh, Gurbax et al. (2019) Prevalence of Otitis Media with Effusion in Children with Hearing Loss. Indian journal of otolaryngology and head and neck surgery : official publication of the Association of Otolaryngologists of India 71(suppl2): 1276-1281	- Study not conducted in OECD high-income country *Study conducted in India*
Passali, D., Damiani, V., Passali, G.C. et al. (2005) The impact of persistent allergic rhinitis on the middle ear – Data from the observation of 100 children. Allergy and Clinical Immunology International 17(3): 114-116	- Study design does not meet inclusion criteria *Non-comparative study*
Passali, Desiderio, Passali, Giulio C, Lauriello, Maria et al. (2014) Nasal Allergy and Otitis Media: A real correlation?. Sultan Qaboos University medical journal 14(1): e59-64	- Study design does not meet inclusion criteria *Non-comparative study*
Pavic, Ivan, Babic, Irena, Matijasic, Nusa et al. (2018) Combined multichannel intraluminal impedance-pH monitoring should be used to diagnose reflux-related otitis media with effusion in children. Acta paediatrica (Oslo, Norway : 1992)	- Study design does not meet inclusion criteria *Non-comparative study*
Pereira, Priscila Karla Santana; Azevedo, Marisa Frasson de; Testa, Jose Ricardo (2010) Conductive impairment in newborn who failed the newborn hearing screening. Brazilian journal of otorhinolaryngology 76(3): 347-54	- Study not conducted in OECD high-income country *Study conducted in Brazil*
Petinou, K C, Schwartz, R G, Gravel, J S et al. (2001) A preliminary account of phonological and morphophonological perception in young children with and without otitis media. International journal of language & communication disorders 36(1): 21-42	- Study conducted pre-2000 *Study received for publication in 1999*
Polka, L. and Rvachew, S. (2005) The impact of otitis media with the effusion on infant phonetic perception. Infancy 8(2): 101-117	- Insufficient presentation of results *Continuous data not possible to dichotomise for the sake of converting to diagnostic data*

Study	Code [Reason]
Pucher, B., Szydlowski, J., Sroczynski, J. et al. (2014) The most common reasons for referral to pediatric ENT outpatient clinic in Poznan. Family Medicine and Primary Care Review 16(3): 282-284	- Article not available in English
Rehagen, Sonia Kim; Valente, Maureen; Lieu, Judith E C (2020) Vestibular Screening in Pediatric Patients with Otitis Media. Journal of the American Academy of Audiology 31(3): 209-216	- Diagnostic method for OME does not meet inclusion criteria *OME confirmed through medical charts. No further details given*
Ren, Dong-dong and Wang, Wu-qing (2012) Assessment of middle ear effusion and audiological characteristics in young children with adenoid hypertrophy. Chinese medical journal 125(7): 1276-81	- Study not conducted in OECD high-income country *Study conducted in China*
Revai, Krystal, Patel, Janak A, Grady, James J et al. (2008) Tympanometric findings in young children during upper respiratory tract infections with and without acute otitis media. The Pediatric infectious disease journal 27(4): 292-5	- Study design does not meet inclusion criteria *Non-comparative study*
Rezes, Szilard, Soderlund-Venermo, Maria, Roivainen, Merja et al. (2009) Human bocavirus and rhino-enteroviruses in childhood otitis media with effusion. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology 46(3): 234-7	- Study design does not meet inclusion criteria *Non-comparative study*
Robb, P J and Shahab, R (2001) Infrared transtympanic temperature measurement and otitis media with effusion. International journal of pediatric otorhinolaryngology 59(3): 195-200	- Diagnostic method for OME does not meet inclusion criteria *Diagnostic criteria for OME not defined*
Roberts, J E, Burchinal, M R, Jackson, S C et al. (2000) Otitis media in childhood in relation to preschool language and school readiness skills among black children. Pediatrics 106(4): 725-35	- Study conducted pre-2000 *Article received for publication in 1999*
Roberts, Joanne E; Burchinal, Margaret R; Zeisel, Susan A (2002) Otitis media in early childhood in relation to children's school-age language and academic skills. Pediatrics 110(4): 696-706	- Study conducted pre-2000 *Children enrolled in study pre-2000 (see Roberts 2000 above)*
Roberts, Joanne E; Rosenfeld, Richard M; Zeisel, Susan A (2004) Otitis media and speech and language: a meta-analysis of prospective studies. Pediatrics 113(3pt1): e238-48	- Systematic review, studies assessed for inclusion *Studies conducted before 2000 and studies using diagnostic methods not including tympanometry were included*
Roddey Jr., O.F.; Hoover, H.A.; Earle Jr., R. (2003) Physical examination for otitis media [4]. Pediatric Infectious Disease Journal 22(7): 673	- Study design does not meet inclusion criteria *Commentary*

Study	Code [Reason]
Roditi, Rachel E; Veling, Maria; Shin, Jennifer J (2016) Age: An effect modifier of the association between allergic rhinitis and Otitis media with effusion. The Laryngoscope 126(7): 1687-92	- Diagnostic method for OME does not meet inclusion criteria *Diagnostic criteria for OME not defined*
Rozmanic, Vojko, Velepic, Mitja, Ahel, Vladimir et al. (2002) Prolonged esophageal pH monitoring in the evaluation of gastroesophageal reflux in children with chronic tubotympanal disorders. Journal of pediatric gastroenterology and nutrition 34(3): 278-80	- Diagnostic method for OME does not meet inclusion criteria *OME diagnosed based on medical history and ENT examination*
Sabo, Diane L, Paradise, Jack L, Kurs-Lasky, Marcia et al. (2003) Hearing levels in infants and young children in relation to testing technique, age group, and the presence or absence of middle-ear effusion. Ear and hearing 24(1): 38-47	- Study conducted pre-2000 *Study conducted 1991-1995*
Saes, S.D.O.; Goldberg, T.B.L.; Montovani, J.C. (2005) Secretion of middle ear in infants - Occurrence, recurrence and related factors. Jornal de Pediatria 81(2): 133-138	- Article not available in English
Saki, Nader, Samarbaf Zadeh, Ali Reza, Sheikhpour Jonaky, Reza et al. (2014) The Prevalence Rate of Helicobacter pylori Infection in, Chronic Otitis Media With Effusion Patients. Jundishapur journal of microbiology 7(3): e15694	- Study not conducted in OECD high-income country *Study conducted in Iran*
Samuels, Tina L, Khampang, Pawjai, Espahbodi, Mana et al. (2022) Association of Pepsin With Inflammatory Signaling and Effusion Viscosity in Pediatric Otitis Media. The Laryngoscope 132(2): 470-477	- Diagnostic method for OME does not meet inclusion criteria *Diagnostic criteria for OME not defined*
Sanli, Arif, Tasdemir, Omer, Eken, Mehmet et al. (2014) Prevalence of otitis media with effusion among primary school age-children and etiopathogenic examination. Indian journal of otolaryngology and head and neck surgery : official publication of the Association of Otolaryngologists of India 66(suppl1): 95-8	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Sanyelbhaa Talaat, H.; Hasn Kabel, A.; Qatanani, E. (2009) Paediatric speech intelligibility (PSI) in normal hearing children with history of recurrent otitis media with effusion (OME). Audiological Medicine 7(2): 112-119	- Study not conducted in OECD high-income country *Study conducted in Jordan*
Sarkar, Saurav, Sadhukhan, M, Roychoudhury, A et al. (2010) Otitis media with effusion in children and its correlation with foreign body in the external auditory canal. Indian journal of otolaryngology and head and neck surgery :	- Study not conducted in OECD high-income country *Study conducted in India*

Study	Code [Reason]
official publication of the Association of Otolaryngologists of India 62(4): 346-9	
Serbetcioglu, Bulent, Ugurtay, Ozgur, Kirkim, Gunay et al. (2008) No association between hearing loss due to bilateral otitis media with effusion and Denver-II test results in preschool children. International journal of pediatric otorhinolaryngology 72(2): 215-22	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Shaikh, Nader, Hoberman, Alejandro, Kaleida, Phillip H et al. (2011) Otoscopic signs of otitis media. The Pediatric infectious disease journal 30(10): 822-6	- Diagnostic method for OME does not meet inclusion criteria *Study investigates the association between individual tympanic membrane findings by otoscopists and diagnosis of OME (via myringotomy) in part 1, and diagnostic accuracy of otoscopists according to tympanometric membrane features in part 2*
Shaikh, Nader, Hoberman, Alejandro, Rockette, Howard E et al. (2012) Development of an algorithm for the diagnosis of otitis media. Academic pediatrics 12(3): 214-8	- Diagnostic method for OME does not meet inclusion criteria *Diagnosis of OME not defined (possibly by otoscopy: "We developed a decision tree by using data from a previously conducted cohort study (of pneumococcal colonization) in which a convenience sample […] were followed for one respiratory season via the use of serial pneumatic otoscopic examinations" p215)*
Sharifian, M.R., Mahmoudi, M., Pourmomenarabi, B. et al. (2019) Correlation between allergic rhinitis and otitis media with effusion. Iranian Journal of Otorhinolaryngology 31(4)	- Study not conducted in OECD high-income country *Study conducted in Iran*
Sharma, K.; Mehan, R.; Arora, A. (2015) Clinico-audio-radiological and operative evaluation of otitis media with effusion. Indian Journal of Otology 21(3): 174-178	- Study not conducted in OECD high-income country *Study conducted in India*
Sharma, K, Pannu, M S, Arora, A et al. (2016) Preventive Audiology: Screening for Hearing Impairment in Children Having Recurrent URTI. Indian journal of otolaryngology and head and neck surgery : official publication of the Association of Otolaryngologists of India 68(2): 163-6	- Study not conducted in OECD high-income country *Study conducted in India*
Shin, Il Ho, Park, Dong Choon, Kwon, Chul et al. (2011) Changes in taste function related to obesity and chronic otitis media with effusion. Archives of otolaryngology--head & neck surgery 137(3): 242-6	- Insufficient presentation of results *Continuous data not possible to dichotomise for the sake of converting to diagnostic data*
Shinogami, Masanobu and Ishibashi, Toshio (2004) Presence of human herpesviruses in young children with acute otitis media.	- Study conducted pre-2000 *Conducted between 1999-2001*

Study	Code [Reason]
International journal of pediatric otorhinolaryngology 68(2): 205-10	
Shriberg, L D, Friel-Patti, S, Flipsen, P 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 : JSLHR 43(1): 100-20	- Study conducted pre-2000 *Participants were a subsample from the Dallas Project, conducted in 1990*
Shriberg, Lawrence D, Flipsen, Peter Jr, Kwiatkowski, Joan et al. (2003) A diagnostic marker for speech delay associated with otitis media with effusion: the intelligibility-speech gap. Clinical linguistics & phonetics 17(7): 507-28	- Study conducted pre-2000 *Participants were a subsample from the Dallas Project, conducted in 1990*
Shriberg, Lawrence D, Kent, Raymond D, Karlsson, Heather B et al. (2003) A diagnostic marker for speech delay associated with otitis media with effusion: backing of obstruents. Clinical linguistics & phonetics 17(7): 529-47	- Study conducted pre-2000 *Participants were a subsample from the Dallas Project, conducted in 1990*
Sogebi, Olusola Ayodele; Oyewole, Emmanuel Abayomi; Ogunbanwo, Olatundun (2021) Asymptomatic Otitis Media With Effusion in Children With Adenoid Enlargement. Journal of the National Medical Association 113(2): 158-164	- Study not conducted in OECD high-income country *Study conducted in Nigeria*
Sommerfleck, Patricia Alejandra, Gonzalez Macchi, Maria Emilia, Weinschelbaum, Romina et al. (2016) Balance disorders in childhood: Main etiologies according to age. Usefulness of the video head impulse test. International journal of pediatric otorhinolaryngology 87: 148-53	- Study not conducted in OECD high-income country *Study conducted in Argentina*
Souter, Melanie Anne, Mills, Nicola Anne, Mahadevan, Murali et al. (2009) The prevalence of atopic symptoms in children with otitis media with effusion. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 141(1): 104-7	- Diagnostic method for OME does not meet inclusion criteria *Diagnostic criteria for OME not defined*
Spiric, Sanja, Spiric, Predrag, Vranjes, Dalibor et al. (2011) Effects of changes in dynamic characteristics of the middle ear on transient-evoked otoacoustic emissions. Medicinski pregled 64(910): 439-42	- Study not conducted in OECD high-income country *Study conducted in Bosnia and Herzegovina*
Sridhara, Shankar K and Brietzke, Scott E (2012) The "Spoke Sign": An otoscopic diagnostic aid for detecting otitis media with effusion. Archives of otolaryngology--head & neck surgery 138(11): 1059-63	- Diagnostic method for OME does not meet inclusion criteria *OME diagnosed based on myringotomy as the reference standard*

Study	Code [Reason]
Swanepoel, De Wet; Eikelboom, Robert H; Margolis, Robert H (2014) Tympanometry screening criteria in children ages 5-7 yr. Journal of the American Academy of Audiology 25(10): 927-36	- Study design does not meet inclusion criteria *Non-comparative study*
Takagi, Dai, Nakamaru, Yuji, Maguchi, Shiroh et al. (2002) Otologic manifestations of Wegener's granulomatosis. The Laryngoscope 112(9): 1684-90	- Study conducted pre-2000 *Conducted between 1992-2001*
Tasker, Andrea, Dettmar, Peter W, Panetti, Marguerite et al. (2002) Reflux of gastric juice and glue ear in children. Lancet (London, England) 359(9305): 493	- Study design does not meet inclusion criteria *Non-comparative study*
Tasker, Andrea, Dettmar, Peter W, Panetti, Marguerite et al. (2002) Is gastric reflux a cause of otitis media with effusion in children?. The Laryngoscope 112(11): 1930-4	- Study design does not meet inclusion criteria *Non-comparative study*
Tewfik, Ted L and Mazer, Bruce (2006) The links between allergy and otitis media with effusion. Current opinion in otolaryngology & head and neck surgery 14(3): 187-90	- Study design does not meet inclusion criteria *Narrative review*
Thakur, J S, Chauhan, Ishan, Mohindroo, N K et al. (2013) Otoacoustic Emissions in Otitis Media with Effusion: Do They Carry any Clinical Significance?. Indian journal of otolaryngology and head and neck surgery : official publication of the Association of Otolaryngologists of India 65(1): 29-33	- Study not conducted in OECD high-income country *Study conducted in India*
Timmerman, Angelique; Anteunis, Lucien; Meesters, Cor (2005) First psychometric evaluation of a disease-specific questionnaire for children's behavior related to otitis media with effusion. Psychological reports 97(3): 819-31	- Study design does not meet inclusion criteria *Non-comparative study*
Tozar, Mesut, Comert, Ela, Sencan, Ziya et al. (2020) Video head impulse test in children with otitis media with effusion and dizziness. International journal of pediatric otorhinolaryngology 129: 109783	- Insufficient presentation of results *The comparative groups mean there are insufficient data reported to extract for the purpose of converting to diagnostic data. It is unclear from the text but cohort groups seem to be patients with OME and dizziness vs patients without OME or dizziness: "Group 1 consisted of 30 patients […] who had OME without a history of AOM in the last 3 months and admitted to the clinic with the complaint of dizziness […] Group 2) included 30 healthy children […] who had normal otoscopic and tympanometric evaluation with no history of AOM in the last 3 months"*
Umapathy, Dolores; Alles, Roshini; Scadding, Glenis K (2007) A community based	- Study conducted pre-2000 *Study conducted 1994-1995*

Study	Code [Reason]
questionnaire study on the association between symptoms suggestive of otitis media with effusion, rhinitis and asthma in primary school children. International journal of pediatric otorhinolaryngology 71(5): 705-12	
Ungkanont, Kitirat; Charuluxananan, Somrat; Komoltri, Chulaluk (2010) Association of otoscopic findings and hearing level in pediatric patients with otitis media with effusion. International journal of pediatric otorhinolaryngology 74(9): 1063-6	- Study not conducted in OECD high-income country *Study conducted in Thailand*
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	- Study conducted pre-2000 *Study conducted 1992-1993*
Villa, Priscila Cruvinel and Zanchetta, Sthella (2014) Auditory temporal abilities in children with history of recurrent otitis media in the first years of life and persistent in preschool and school ages. CoDAS 26(6): 494-502	- Population does not meet inclusion criteria *Study group included children with a history of OME but did not report if they currently had OME, or what the diagnostic criteria for OME were: "The criteria for inclusion in these groups were the following: having the occurrence of the first episode of otitis, in the first year of life, documented in medical records, as well as at least four other episodes over a period of 12 months, under the age of three" (all included children were between the ages of 7-10 years)*
Waldron, M N H; Matthews, J N S; Johnson, I J M (2004) The effect of otitis media with effusions on balance in children. Clinical otolaryngology and allied sciences 29(4): 318-20	- Study design does not meet inclusion criteria *Non-comparative study*
Walker, N. and Wigglesworth, G. (2001) The effect of conductive hearing loss on phonological awareness, reading and spelling of urban aboriginal students. Australian and New Zealand Journal of Audiology 23(1): 37-51	- Insufficient presentation of results *Continuous data not possible to dichotomise for the sake of converting to diagnostic data*
Walker, Rebecca E, Bartley, Jim, Flint, David et al. (2017) Determinants of chronic otitis media with effusion in preschool children: a case-control study. BMC pediatrics 17(1): 4	- Population does not meet inclusion criteria *Cases were children "who had a recent medical history of COME and/or signs of COME confirmed by an otorhinolaryngologist during surgery" but study does not report how many in group have current OME at time of study. Additionally, diagnostic criteria for OME not reported*
Wang, Mao-Che and Lee, Guo-She (2007) Vestibular evoked myogenic potentials in middle ear effusion. Acta oto-laryngologica 127(7): 700-4	- Population does not meet inclusion criteria *Participants are adults*
Weichbold, Viktor; Nekahm-Heis, Doris; Welzl-Mueller, Kunigunde (2006) Universal newborn	- Study design does not meet inclusion criteria *Non-comparative study*

Study	Code [Reason]
hearing screening and postnatal hearing loss. Pediatrics 117(4): e631-6	
Worley, G.A. (2000) Sensitivity, specificity and predictive value of tympanometry in predicting a hearing impairment in otitis media with effusion. MRC multi-centre otitis media study group. CME Bulletin Otorhinolaryngology Head and Neck Surgery 4(3): 112-113	- Article not available
Wu, Zeng-Hong, Tang, Yun, Niu, Xun et al. (2021) The Relationship Between Otitis Media With Effusion and Gastroesophageal Reflux Disease: A Meta-analysis. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology 42(3): e245-e253	- Systematic review, studies assessed for inclusion *Studies including adults, and studies from non-OECD high-income countries were included*
Xenellis, John, Paschalidis, John, Georgalas, Christos et al. (2005) Factors influencing the presence of otitis media with effusion 16 months after initial diagnosis in a cohort of school-age children in rural Greece: a prospective study. International journal of pediatric otorhinolaryngology 69(12): 1641-7	- Study design does not meet inclusion criteria *Non-comparative study*
Yeo, Seung Geun, Park, Dong Choon, Eun, Young Gyu et al. (2007) The role of allergic rhinitis in the development of otitis media with effusion: effect on eustachian tube function. American journal of otolaryngology 28(3): 148-52	- Study not conducted in OECD high-income country *Study conducted in India*
Yilmaz, H Baki (2015) Allergic rhinitis in children with adenoidal hypertrophy and otitis media with effusion. American journal of otolaryngology 36(4): 617-8	- Study design does not meet inclusion criteria *Commentary*
Yilmaz, Mustafa Deniz, Aktepe, Orhan, Cetinkol, Yeliz et al. (2005) Does Helicobacter pylori have role in development of otitis media with effusion?. International journal of pediatric otorhinolaryngology 69(6): 745-9	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Yilmaz, Taner, Ceylan, Mehmet, Akyon, Yakut et al. (2006) Helicobacter pylori: a possible association with otitis media with effusion. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery 134(5): 772-7	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Yukkaldiran, Ahmet; Erdogan, Osman; Kaplama, Mehmet Erkan (2021) Neutrophil-lymphocyte and platelet-lymphocyte ratios in otitis media with effusion in children: Diagnostic	- Study not conducted in OECD high-income country *Study conducted in Turkey*

Study	Code [Reason]
role and audiologic correlations. International journal of clinical practice 75(3): e13805	
Yuksel, Fatih, Dogan, Mansur, Karatas, Duran et al. (2013) Gastroesophageal reflux disease in children with chronic otitis media with effusion. The Journal of craniofacial surgery 24(2): 380-3	- Study not conducted in OECD high-income country *Study conducted in Turkey*
Zhao, Fei, Wada, Hiroshi, Koike, Takuji et al. (2003) Transient evoked otoacoustic emissions in patients with middle ear disorders. International journal of audiology 42(3): 117-31	- Diagnostic method for OME does not meet inclusion criteria *The definition/ diagnostic criteria given for OME do not specify whether tympanometry is used: "The middle ear is under negative pressure caused by Eustachian tube dysfunction, resulting in a certain degree of tympanic membrane retraction and fluid in the middle ear cavity" (p 130)*
Zingade, N D and Sanji, R R (2009) The prevalence of otological manifestations in children with cleft palate. Indian journal of otolaryngology and head and neck surgery : official publication of the Association of Otolaryngologists of India 61(3): 218-22	- Study not conducted in OECD high-income country *Study conducted in India*

AOM: acute otitis media; CT: computed tomography; COME: chronic otitis media with effusion; CVID: common variable immunodeficiency; ENT: ear, nose and throat; H. pylori: Helicobacter pylori; MEE: middle ear effusion; MRI: magnetic resonance imaging; OECD: Organisation for Economic Co-operation and Development; OM: otitis media; OME: otitis media with effusion

Excluded economic studies

No economic evidence was identified for this review.

Appendix K Research recommendations – full details

Research recommendations for review question: What presenting features are associated with OME in children under 12 years?

No research recommendations were made for this review question.