Effective Health Care Program

Comparative Effectiveness Review
Number 101

Otitis Media With Effusion: Comparative Effectiveness of Treatments

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Comparative Effectiveness Review

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Otitis Media With Effusion: Comparative Effectiveness of Treatments

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U.S. Department of Health and Human Services
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This report is based on research conducted by the Research Triangle Institute-University of North Carolina at Chapel Hill (RTI-UNC) Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2007-10056-I). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report may be used, in whole or in part, as the basis for development of clinical practice guidelines and other quality enhancement tools, or as a basis for reimbursement and coverage policies. AHRQ or U.S. Department of Health and Human Services endorsement of such derivative products may not be stated or implied.

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an e-mail list to learn about new program products and opportunities for input.

We welcome comments on this systematic review. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

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Key Informants

Key Informants are the end users of research, including patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with experience in making health care decisions. Within the EPC program, the Key Informant role is to provide input into identifying the Key Questions for research that will inform health care decisions. The EPC solicits input from Key Informants when developing questions for systematic review or when identifying high priority research gaps and needed new research. Key Informants are not involved in analyzing the evidence or writing the report and have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism

Key Informants must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals are invited to serve as Key Informants and those who present with potential conflicts may be retained. The Task Order Officer and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Technical Experts comprise a multidisciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes as well as identifying particular studies or databases to search. They are selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicted opinions are common and perceived as health scientific discourse that results in a thoughtful, relevant systematic review. Therefore study questions, design and/or methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and recommend approaches to specific issues as requested by the EPC. Technical Experts do not do analysis of any kind nor contribute to the writing of the report and have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism

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Otitis Media with Effusion: Comparative Effectiveness of Treatments

Structured Abstract

Objectives. To compare benefits and harms of strategies currently in use for managing otitis media with effusion (OME). Treatment for OME may include single approaches alone or combinations of two or more approaches. We compared benefits and harms among these treatments: tympanostomy tubes (TT), myringotomy (myr), adenoidectomy (adenoid), autoinflation (auto), oral or nasal steroids, complementary and alternative medicine (CAM), and watchful waiting (WW). We included comparisons of treatment effectiveness in subgroups of patients with OME, and whether outcome differences were related to factors affecting health care delivery or the receipt of pneumococcal vaccine inoculation.

Data sources. We identified five recent systematic reviews a priori and searched MEDLINE,® Embase,® the Cochrane Library, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL®), from root through August 13, 2012, for additional studies. Eligible studies included randomized controlled trials (RCTs), nonrandomized trials, and cohort studies.

Review methods. Eligible studies included at least two arms comparing the treatments described above. Pairs of reviewers independently selected, extracted data from, and rated the risk of bias of relevant studies; they graded the strength of evidence using established criteria. We incorporated meta-analyses from the earlier reviews and synthesized additional evidence qualitatively.

Results. We identified 59 studies through the earlier reviews and our independent searches. Generally, studies examined interventions in otherwise healthy, noninfant children. We did not find any eligible studies covering CAM. Findings are reported for clinical and functional outcomes, and harms. Variation in length of TT retention corresponded to whether TT were designed to be short versus long term, but variation in TT type was not related to improved OME and hearing outcomes. TT decreased OME for 2 years compared with WW or myr, and improved hearing for 6 months compared with WW. OME resolution was more likely with adenoid than no treatment at 12 months. Adenoid and myr were superior to myr alone in relation to OME and hearing outcomes at 24 months. Adenoid and TT were superior to WW for hearing outcomes at 24 months. Auto was superior to standard treatment at improving OME at 1 month. We found no benefits from oral steroids at 2 months, or topical steroids at 9 months. In relation to functional outcomes, TT and WW did not differ in long-term language, cognitive or academic outcomes. Tympanosclerosis and otorrhea were more common in ears with TT. Adenoid increased the risk of postsurgical hemorrhage. In one study of a subgroup, adults receiving auto were more likely to recover from OME than those in the control group at one month. We found no studies examining the influence of any health care factors on treatment effectiveness.

Conclusions. There is evidence that both TT and adenoid reduce OME and improve hearing in the short term, but both treatments also have associated harms. Large, well-controlled studies could help resolve the risk-benefit ratio by measuring AOM recurrence, functional outcomes, quality of life measures, and long-term outcomes. Finally, additional research is needed to

support treatment decisions in subpopulations, particularly those with comorbidities and those who have received a pneumococcal vaccine inoculation.

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Executive Summary

Background

Definition of Otitis Media With Effusion

Otitis media with effusion (OME) is defined as a collection of fluid in the middle ear without signs or symptoms of acute ear infection.[1] OME has several potential causes. The leading causes include viral upper respiratory infection, acute otitis media (AOM), and chronic dysfunction of the eustachian tube.[2,3] However, other potential explanations include ciliary dysfunction, proliferation of fluid-producing goblet cells, allergy and residual bacterial antigens, and biofilm.[4] More recent research suggests that mucoglycoproteins cause the hearing loss and much of the fluid presence that is the hallmark of OME.[5,6] The presence of fluid in the middle ear decreases tympanic membrane and middle ear function, leading to decreased hearing, a "fullness" sensation in the ear, and occasionally pain from the pressure changes.

Prevalence of Otitis Media With Effusion

OME occurs commonly during childhood, with as many as 90 percent of children (80% of individual ears) having at least one episode of OME by age 10.[7] OME disproportionately affects some subpopulations of children. Those with cleft palate, Down syndrome, and other craniofacial anomalies are at high risk for anatomic causes of OME and compromised function of the eustachian tube.[8] Individuals of American Indian, Alaskan, and Asian backgrounds are believed to be at greater risk,[9] as are children with adenoid hyperplasia. In addition, children with sensorineural hearing loss will likely be more affected by the secondary conductive hearing loss that occurs with OME.

Although rare, OME also occurs in adults. This usually happens after patients develop a severe upper respiratory infection such as sinusitis, severe allergies, or rapid change in air pressure after an airplane flight or a scuba dive. The incidence of prolonged OME in adults is not known, but it is much less common than in children.[10]

Many episodes of OME resolve spontaneously within 3 months, but 30 to 40 percent of children have recurrent episodes, and 5 to 10 percent of cases last more than 1 year.[1,11,12]

Despite the high prevalence of OME, its long-term impact on child developmental outcomes such as speech, language, intelligence, and hearing remains unclear.[7] The near universality of this condition in children and the high expenditures for treating OME (about $4 billion per year in the United States) make this an important topic for a comparative effectiveness review.

Diagnosis of Otitis Media With Effusion

Diagnostically, the core feature of OME is middle ear effusion (MEE), that is, fluid behind the eardrum in the middle ear. Tympanocentesis, which is the removal of fluid from behind the eardrum by using a needle to puncture the tympanic membrane, remains the gold standard for diagnosing MEE and OME. However, because tympanocentesis is an invasive procedure, it is rarely used for diagnosis. Tympanocentesis is not the same as myringotomy, in which the tympanic membrane is punctured to relieve pressure. A variety of supplemental examination techniques assist with identification. The most studied additional diagnostic method is pneumatic otoscopy, which is considered an accurate way to diagnose MEE by trained examiners.[7] To use

this procedure, clinicians blow air through an otoscope, causing movement of the tympanic membrane that they can compare with normal movement of the membrane. Tympanometry is a supplemental diagnostic tool that indirectly measures middle ear pressure and tympanic membrane mobility. A "flat" tympanogram (Type B tympanogram) is consistent with OME. Additionally, children with OME often have a corresponding conductive hearing loss on pure-tone audiometry that measures 25 decibels (dB) or 10 dB above the IW hearing level of children with normal hearing.

Natural History and Treatment

Despite recent practice guidelines and systematic reviews,[8,13-20] the comparative benefits and harms of treatments and treatment strategies for OME are uncertain. The uncertainty stems from a lack of consensus regarding clinical and long-term functional outcomes of OME. Specifically, the authors of the most recent systematic review of the natural history of OME[8] found mixed evidence regarding the impact of OME in early childhood on later developmental outcomes. Although they concluded that children with early OME were at greater risk for temporary conductive hearing loss, they were unable to draw strong conclusions about the effect of early OME on later speech and language development. This lack of strong conclusions means it is not clear whether OME needs to be treated. Second, difficulty predicting the course of recurrence for individual patients, especially those with comorbid conditions, makes clinical decisions difficult. During topic refinement, the RTI-UNC Evidence-based Practice Center (RTI-UNC EPC) considered each of the known treatments in terms of uncertainty within the published literature (including gaps in the evidence), importance to clinicians, outcomes important to patients, and relevance to the U.S. population. Treatments examined in this review are indicated under Key Question 1.

Scope and Key Questions

The RTI-UNC EPC was charged with conducting this review because of the continuing uncertainty about efficacy, effectiveness, and particularly comparative effectiveness, as well as harms, for the included therapies. Providing more up-to-date and comprehensive comparative information will help many stakeholder groups make decisions about when and how to treat patients with this condition. This comparative review includes all interventions currently in use for treating OME—surgical, pharmacological, and nonpharmacological; we excluded antihistamines and decongestants, which have been extensively reviewed previously and demonstrated to have no benefit in this population. Antibiotics are the subject of a recent Cochrane review, and in cooperation with our Technical Expert Panel (TEP), we decided to not duplicate their work. We did not include this review as evidence because it was published in September 2012 after the deadline for including new reports in our review.[21] For the most part, the treatments examined in the review are limited to those therapies that clinical guidelines recommended for managing OME.[20] However, we included several additional comparisons because more recent literature was available. Most notably, we included the findings of a recently published trial that examined adenoidectomy as an initial treatment with concurrent tympanostomy tubes (TT) placement in comparison with TT alone or watchful waiting because of the prominence of this large, carefully designed trial.[22]

The intent of our review was to cover the entire range of individuals who have OME; in particular, we sought evidence specific to populations who have not been examined in past reviews such as adults and children with comorbid conditions such as Down syndrome, cleft

palate, or existing hearing loss. We did not limit the timeframe for outcomes, nor did we exclude any settings.

The EPC addressed five Key Questions (KQs) in this comparative effectiveness review.

KQ 1. What is the comparative effectiveness of the following treatment options (active treatments and watchful waiting) in affecting clinical outcomes or health care utilization in patients with OME? Treatment options include: tympanostomy tubes, myringotomy, oral or topical nasal steroids, autoinflation, complementary and alternative medical procedures, watchful waiting, and variations in surgical technique or procedures.

KQ 2. What is the comparative effectiveness of the different treatment options listed in KQ 1 (active treatments, watchful waiting, and variations in surgical procedures) in improving functional and health-related quality of life outcomes in patients with OME?

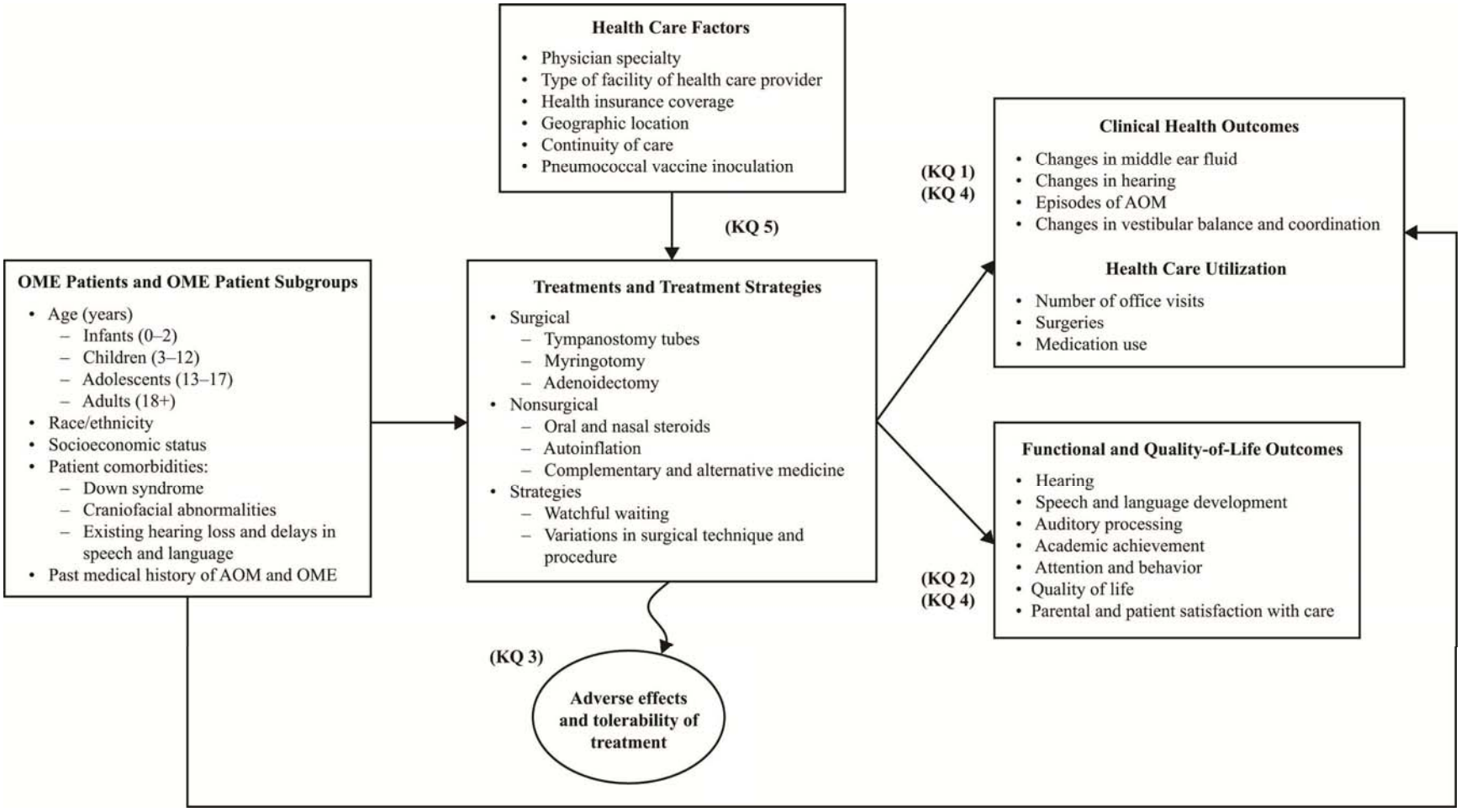
KQ 3. What are the harms or tolerability among the different treatment options?

KQ 4. What are the comparative benefits and harms of treatment options in subgroups of patients with OME?

KQ 5. Is the comparative effectiveness of treatment options related to factors affecting health care delivery or the receipt of pneumococcal vaccine inoculation?

We developed an analytic framework (Figure A) to guide our analysis. The populations of interest are in the box to the far left in the figure; the interventions appear in the middle; and the two sets of outcomes (for KQ 1 and KQ 2 on benefits, and also KQ 4 on important subgroups) appear on the far right. KQ 3 concerns harm (various types of adverse events). Finally, KQ 5 relates to a set of health care delivery or clinical factors (pneumococcal vaccination) that may influence choices of treatments or their clinical and quality-of-life outcomes.

Figure A. Analytic framework for comparisons of interventions for otitis media with effusion



AOM = acute otitis media; KQ = Key Question; OME = otitis media with effusion

Methods

Literature Search Strategy

Search Strategy

Five recently published systematic reviews on comparisons of interest (two on TT, one on adenoidectomy, one on steroids, and one on autoinflation)[13,15-18] were identified during the topic refinement stage of the review. An update of the steroid review[23] was added during peer review. As discussed in our review protocol, The Cochrane Collaboration conducted four of the reviews, and the Swedish Council of Technology in Health Care commissioned the fifth. The reviews covered the following treatment options for OME: TT, adenoidectomy, steroids, and autoinflation.

To avoid duplicating the work of these teams, we used these reviews as a starting point. We included evidence from these systematic reviews plus additional evidence that these reviews did not consider. The additional evidence included: additional outcomes data from studies that were included in the recent reviews but were not the focus of those reviews, observational studies done at any time, newer studies published since the last search dates in those reviews, and studies focusing on populations excluded from the reviews, such as adults with OME or children with Down syndrome or cleft palate, who may be differently affected by OME.

We searched MEDLINE® (via PubMed), Embase,® The Cochrane Library, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL®) to identify studies not included in the systematic reviews. An experienced research librarian used a predefined list of search terms and medical subject headings (MeSH). We reviewed our search strategy with our TEP and incorporated their input into our search strategy. We limited the electronic searches to English-language materials. We completed the initial search on 1/8/2012, and we completed an update during peer review on 8/13/2012.

We searched unpublished and grey literature relevant to the review topic. Methods for identifying grey literature included a review of trial registries. In addition, AHRQ requested Scientific Information Packets (SIPs) from the developers and distributors of the interventions identified in the literature review. We included unpublished studies that met all inclusion criteria and contained enough information on their research methods to permit us to make a standard risk-of-bias assessment of individual studies. Finally, we manually searched reference lists of reviews, including trials and background articles, to look for relevant citations that our searches might have missed and that addressed our KQs. We imported all citations into an electronic database (EndNote® X4).

Inclusion and Exclusion Criteria

We developed inclusion and exclusion criteria with respect to the PICOTS (i.e., populations, interventions, comparators, outcomes, timeframes, and settings) framework. The review included only English-language studies of individuals with OME. We included five systematic reviews that had been determined a priori to fit our PICOTS criteria and the relevant studies included in those reviews; we also retained eligible studies that the earlier reviews had not used, and these included randomized controlled trials (RCTs), nonrandomized controlled trials, and cohort studies. We imposed no other restrictions so that we could consider studies with individuals of any age, racial or ethnic background, or coexisting condition.

The treatments of interest were TT, myringotomy, adenoidectomy, oral or intranasal steroids, autoinflation of the eustachian tube, complementary and alternative medicine (CAM) procedures, watchful waiting, and variations in surgical technique or procedures. With two exceptions, included studies had to compare at least two of these treatments. We considered inactive controls in comparison with steroid treatment and usual care in comparison with autoinflation, based on the Cochrane review inclusion criteria. Based on discussions with our TEP, because the effectiveness of CAM treatments was unknown and there were concerns about the quality of nonrandomized studies, we limited studies of CAM to RCTs.

We specified a broad range of outcomes (see Figure A). We included clinical outcomes such as changes in middle ear fluid, episodes of AOM, and hearing thresholds; use of health care; functional and quality-of-life outcomes such as speech and language development, behavior, and parental satisfaction with care; and harms.

We were interested primarily in treatment outcomes of 3 months or longer, but we included outcomes of less than 3 months. We focused on end-of-intervention results when they were the only endpoint data available, such as in the autoinflation treatment studies.

We did not exclude studies based on geography or the setting of the service provision.

Study Selection

A total of six trained members of the team reviewed article abstracts and full-text articles. First, two members of the team independently reviewed each abstract using the inclusion/exclusion criteria. One reviewer was always a senior member of the review team. If both reviewers agreed that the study did not meet eligibility criteria, we excluded it; otherwise, we included the abstract for full article review. Two members of the team independently reviewed each full-text article. One reviewer was always a senior member of the review team. If both reviewers agreed that a study did not meet eligibility criteria, we excluded it. Each reviewer recorded the primary reason for exclusion. If the reviewers disagreed about whether an article should be excluded or about the primary reason for exclusion, they resolved conflicts by discussion and consensus or by consulting a third member of the team. We screened unpublished studies identified through a grey literature search and review of SIPs using the same title/abstract and full-text review processes.

Data Abstraction

We developed a template for evidence tables for data synthesis using the PICOTS framework. For the five systematic reviews and additional studies that met our inclusion criteria, we abstracted relevant information into these evidence tables: characteristics of study populations, interventions, comparators, settings, study designs, methods, and results. We directly reviewed individual studies included in the systematic reviews to capture additional outcomes data that were not the focus of the earlier reviews and to determine the availability of subgroup analyses not included in the reviews.

Six trained members of the team participated in the data abstraction. One of the reviewers initially abstracted the relevant data from each included article using Microsoft Excel® software and a second more senior member of the team reviewed each data abstraction against the original article for completeness and accuracy.

Risk-of-Bias Assessment

The risk-of-bias assessment was conducted using two tools, one appropriate for trials based on the Cochrane risk-of-bias tool[24] and modified by our EPC to be used to evaluate observational studies (including instructions to reviewers that some questions concerning trial study design would be considered not applicable) and AMSTAR (assessment of multiple systematic reviews),[25] appropriate for systematic reviews. We did not reevaluate the risk of bias of the studies included in the previous systematic reviews,[13,15-18,23] but the original review study authors had determined these studies to be of low or medium risk of bias.

Two independent reviewers rated the risk of bias for each study. Disagreements between the two reviewers were resolved by discussion and consensus or by consulting a third member of the team. Results of this assessment were summarized in a rating of low, medium, or high risk of bias. High risk-of-bias studies were those that had at least one major issue that had the potential to cause significant bias and might invalidate the results.

Data Synthesis

Across all included studies, the populations, interventions, and outcome measures in the additional data were heterogeneous and did not lend themselves to a pooled analysis beyond what was currently available in the meta-analyses from the five earlier systematic reviews. Because we determined that additional quantitative analyses were not necessary or appropriate, we did all analyses qualitatively. Evidence used in the synthesis included the results from the earlier meta-analyses, additional data from individual studies contained in those systematic reviews, and data from the articles added from our own searches.

Strength of the Body of Evidence

We graded the strength of evidence based on the guidance established for the Agency for Healthcare Research and Quality Effective Health Care Program EPCs conducting comparative effectiveness reviews, as detailed in the paper by Owens and colleagues.[26] The EPC approach incorporates four key domains: risk of bias, consistency, directness, and precision of the evidence. The overall grade for strength of evidence is based on the scores for the four domains and reflects the strength of the body of evidence to answer the KQs on the comparative effectiveness, efficacy, and harms of the treatments and treatment strategies covered in this review.

A grade of high strength of evidence indicates that we have high confidence that the evidence reflects the true effect. Moderate strength of evidence implies that we have moderate confidence that the evidence reflects the true effect. Low strength or evidence suggests that we have low confidence that the evidence reflects the true effect. Insufficient strength of evidence signifies either that evidence is completely unavailable or that it does not permit estimation of an effect. Typically, evidence from just one study was considered insufficient to permit confidence in the estimation of an effect. Exceptions were single study bodies of evidence consisting of a relatively larger, low risk of bias trial, particularly if it showed a large magnitude of effect.

Two reviewers assessed each domain independently and assigned an overall grade for each treatment comparison for each key outcome listed in the framework. They resolved any conflicts through consensus discussion. If they did not reach consensus, the team brought in a third party to settle the conflict.

Applicability

We assessed the applicability of individual studies as well as the body of evidence. For individual studies, we examined factors that may limit applicability based on the PICOTS structure such as population characteristics, intervention characteristics, and comparators. We abstracted key characteristics of applicability into the evidence tables. During data synthesis, we assessed the applicability of the body of evidence using the abstracted characteristics. KQ 4 includes a detailed analysis of intervention effectiveness in population subgroups.

Results

This section is organized by KQ and then grouped by intervention comparison. The summaries of evidence findings are presented in Tables A–D by KQ. The full report contains summary tables. Appendix C contains evidence tables for included studies, and Appendix F has the strength of evidence grades for the main outcomes of each KQ. Except where otherwise noted, across KQs, the studies we included were limited to otherwise healthy children.

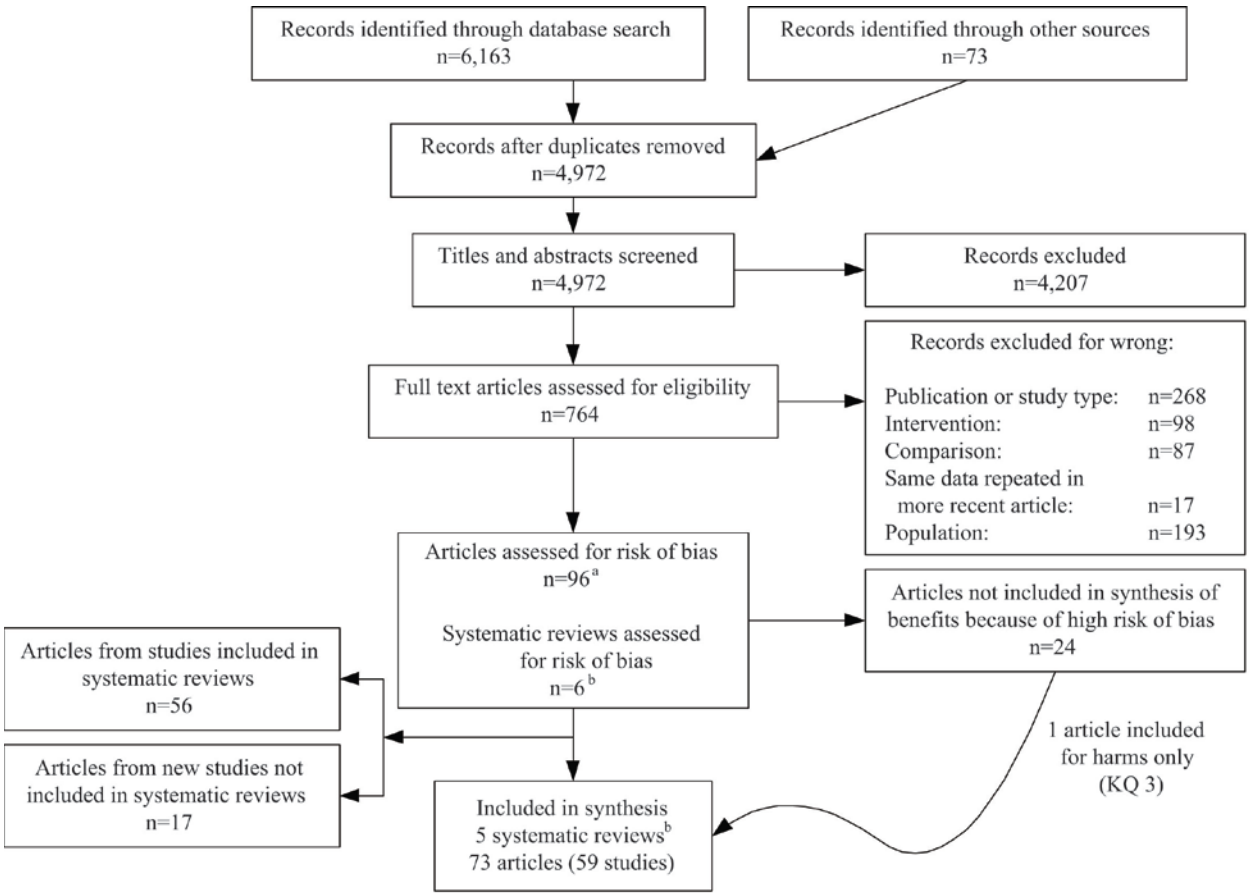
Literature Searches

We identified a total of 4,967 unduplicated citations and determined that 764 met criteria for full-text review (Figure B). We excluded 668 full-text articles based on our inclusion criteria and before risk-of-bias assessment. There were a total of 73 full-text articles, detailing 59 studies and five systematic reviews. Of the 59 studies, 42 studies were included in one of the five systematic reviews, and we included 17 additional studies. Of the 59 studies included in this review, 49 were RCTs (33 by person, 12 by ear, and 4 by person and ear), 6 were nonrandomized control trials (1 by person and 5 by ear), and 4 were cohort studies. Of the 17 articles not included in one of the five systematic reviews, we assessed 15 as medium risk of bias, 1 as low risk of bias and 1 as high risk of bias. Of the five included systematic reviews, four were limited to RCTs. We assessed four systematic reviews as low risk of bias and one as medium risk of bias.

We recorded the reason that each excluded full-text publication failed to satisfy the eligibility criteria and compiled a comprehensive list of such studies (Appendix B of the full report).

We did not include 23 high-risk-of-bias studies in our analyses (Appendix C of the full report). Virtually all lacked information on any baseline patient characteristics; of particular concern, unknown differences between groups based on age or time with OME could invalidate outcomes. Other serious concerns were a lack of control for selective concurrent treatment and lack of control for confounders in cohort studies.

Figure B. Disposition of articles on otitis media with effusion



[a]We accepted the risk of bias assessment conducted by the review authors for the studies included in one of the 5 earlier systematic reviews (56 articles). We conducted our own risk of bias assessment for 17 new articles not included in one of those reviews.
[b]One of the 5 included systematic reviews was updated during our peer review period. We reviewed both the original report and the update.

Key Question 1. Comparative Effectiveness: Clinical Outcomes or Health Care Utilization

All but four of the 59 studies included in this review examined clinical outcomes. Thirty one studies and 12 meta-analyses examined signs and symptoms of OME. Thirty studies and six meta-analyses examined hearing as an outcome. Only three studies examined subsequent AOM as an outcome. No studies reported use of health services or balance outcomes. A description of the treatment comparisons and comparative effectiveness follows.

Tympanostomy Tube Comparisons

Six individually located studies[27-32] and eight studies[33-40] from one systematic review[13] addressed comparisons of TT. These studies compared different types of tubes (e.g., design, materials, size), approaches to insertion, or topical prophylaxis therapies. All comparisons were made between ears of the same individual.

Ten[27-31,33-37] of the 14 studies provided evidence for KQ 1; the other four provided evidence only for harms. Of these 10 studies, 7 were RCTs. Length of tube retention was higher in the longer term TT. Other TT comparisons and endpoints differed across studies. Because of sparse data, the diversity of comparisons, and inconsistent findings, the evidence is insufficient for comparisons of other design features or for hearing outcomes.

Tympanostomy Tubes Versus Watchful Waiting/Myringotomy

Two individual studies[41,42] and two systematic reviews[13,15] addressed comparisons between RCTs of TTs with either myringotomy or watchful waiting. The Browning et al.[15] systematic review reviewed 10 studies;[43-52] 7 were in comparison with watchful waiting or delayed treatment,[43-45,48,50-52] 2 were in comparison with myringotomy in the control ear,[46,49] and 1[47] included both myringotomy and watchful waiting arms. The Hellstrom et al.[13] systematic review included six of the studies that were in the Browning review; in addition, data on hearing outcomes from Gates et al. (1989)[53] were reported only in the Hellstrom review. We included as a companion study the Medical Research Council Trial of Alternative Regimens in Glue Ear Treatment (MRC TARGET)[22] that was a recently published version of the preliminary data included in the Browning review.[44] We also present additional reports of later followup of the cohorts of Maw and colleagues (1999),[43] Rovers and colleagues (2000),[45] and Paradise and colleagues (2001).[48]

TT placement decreased time with middle ear effusion by 32 percent compared with watchful waiting or delayed treatment (high strength of evidence) and up to 42 percent in comparison with myringotomy (moderate strength of evidence) at 1 year after surgery. Compared with watchful waiting or myringotomy (data combined), there was a 13 percent reduction through 2 years after surgery (moderate strength of evidence). Evidence was insufficient for longer followup. TT improved hearing through 9 months after surgery compared with watchful waiting (3–6 months: 8.8 dB; 6–9 months: 4.2 dB) (high strength of evidence); TT improved hearing by 10 dB at 4 to 6 months after surgery in comparison with watchful waiting or myringotomy (data combined) (high strength of evidence). Thereafter the differences in hearing became attenuated and were not significant at either 7 to 12 months compared with watchful waiting or myringotomy (low strength of evidence) or 12 to 18 months after surgery compared with watchful waiting (low strength of evidence). Evidence was insufficient for longer time periods and for other clinical outcomes or health utilization.

Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy or Adenoidectomy Alone

Seven individually located studies[54-60] and four studies[53,61-63] reported in the Hellstrom review examined outcomes in relation to TT plus adenoidectomy as compared with myringotomy plus adenoidectomy or adenoidectomy alone. We included another report[64] that was a followup study to the Bonding and Tos report (1985)[61] included in the Hellstrom review. Four of the studies compared TT in one ear with an ear that received no surgery, in children who all had had adenoidectomies. Three studies (four articles)[59,61,63,64] compared ear outcomes between ears with TT and ears with myringotomy, among children who all had had adenoidectomies. The other four studies[53,57,58,60] compared TT with myringotomy among children who all had had adenoidectomies.

Two small studies found that TT conferred no additional benefit to adenoidectomy alone for reducing the recurrence of OME (insufficient strength of evidence); three studies comparing TT

and adenoidectomy with myringotomy and adenoidectomy produced mixed results (insufficient strength of evidence). Five of six studies failed to find a difference in hearing at various endpoints between TT and myringotomy among children who had also received adenoidectomies (low strength of evidence). We found mixed results for hearing when comparing TT with watchful waiting in children who also received adenoidectomies (insufficient strength of evidence).

Myringotomy Comparisons

Only one RCT compared two different procedures for myringotomy on both middle ear and hearing outcomes.[65] The two procedures were radio frequency myringotomy with mitomycin C, a topical chemotherapeutic agent and radio frequency myringotomy alone. A majority of individuals in each arm received adenoidectomy (73% and 67%, respectively). There was insufficient evidence for concluding superiority of either myringotomy procedure for OME signs and symptoms or hearing outcomes.

Myringotomy Plus Adenoidectomy Comparisons

One retrospective cohort study compared two different procedures for myringotomy.[66] The comparison was between laser myringotomy and cold knife myringotomy. In both groups all individuals received an adenoidectomy. The evidence is insufficient for determining superiority for either myringotomy approach for OME signs and symptoms. No study examined hearing or any other clinical outcome.

Adenoidectomy Versus Other Interventions

Eight RCTs provided all the evidence for adenoidectomy in comparison to TT, myringotomy, watchful waiting, or no surgery among patients with OME. Seven of the RCTs were included in the Cochrane review by van den Aadweg et al.[16,46,49-51,67-69] and the eighth was the newly published MRC TARGET trial.[22] The trials examined adenoidectomy with and without myringotomy versus nonsurgical treatment or myringotomy only; adenoidectomy with unilateral TT versus a unilateral TT only (comparison by ears); adenoidectomy with bilateral TT versus bilateral TT only; and adenoidectomy plus TT versus watchful waiting.

Adenoidectomy was superior to no treatment for resolution of OME at both 6 months (risk difference of 0.27 [95% CI, 0.13 to 0.42] measured through otoscopy and 0.22 [95% CI, 0.12 to 0.32] as measured through tympanometry; high strength of evidence) and 12 months postsurgery (risk difference of 0.29 [95% CI, 0.19 to 0.39] through tympanometry; high strength of evidence). Adenoidectomy was superior to no treatment for hearing in one study at 6 months but not at 12 months; in a second study, no differences were detected between adenoidectomy and no treatment (insufficient strength of evidence for mixed findings). One single study found that adenoidectomy and myringotomy were superior to myringotomy alone for reducing time with effusion ($p<0.001$).and improving hearing at 24 months (better ear standard mean difference of -0.66 [95% CI, -0.93 to -0.40]; low strength of evidence). Because results were mixed, the evidence was insufficient for determining the effectiveness of adenoidectomy when added to TT in relation to effusion or hearing (insufficient strength of evidence). Hearing outcomes were superior with adenoidectomy and TT compared with watchful waiting at 24 months (low strength of evidence). There was insufficient evidence to determine the effectiveness of adenoidectomy compared with other treatments for recurrence of AOM.

Oral or Topical Nasal Steroids

The included evidence consisted of one systematic review conducted by The Cochrane Collaboration,[18] that was updated while we were conducting our review,[23] that examined oral steroids and topical intranasal steroids. The update review includes the studies included in the earlier review, nine RCTs of oral steroids[70-78] and three RCTs of topical intranasal steroids,[79,80] and adds one recent RCT conducted by Williamson et al.[80,81] All studies were in comparison with placebo controls; some of the oral steroid studies included antibiotics in both arms. All studies examined signs and symptoms of OME and hearing.

Results of a meta-analysis[18] comparing oral steroids with controls did not show differences in middle ear effusion at 1–2 months post treatment (low strength of evidence); nor did a meta-analysis comparing oral steroids with control along with adjunct antibiotics (moderate strength of evidence). Due to limited data, evidence was insufficient for determining the effectiveness of oral steroids with and without antibiotics for OME signs and symptoms at followup beyond 3 or more months. Topical intranasal steroids did not show differences in cure rate at various followup points with antibiotics (insufficient strength of evidence) or without antibiotics (low strength of evidence). The evidence was insufficient for determining the effectiveness of oral steroids with and without antibiotics for hearing at any time point. The RCT by Williamson et al.[80,81] comparing intranasal steroids with controls did not find differences in OME cure rate or in hearing at one or more months post treatment (low strength of evidence). There was insufficient evidence for comparing either oral or topical intranasal steroids with controls for any other clinical outcomes.

Autoinflation

One Cochrane review conducted by Perera et al.[17] summarized evidence from six RCTs of any form of autoinflation, a technique designed to increase pressure in the oropharynx forcing open the eustachian tube though a nasal balloon or other process. The review included five studies with children[82-86] and one study with adults, 16–75 years of age.[87] All studies were in comparison with no autoinflation, and other treatments (e.g., antibiotics, analgesics) were permitted as long as they were given equally to both arms. Meta-analyses comparing autoinflation with controls found an improvement in OME at 1 month or less, post treatment (low strength of evidence). Evidence was insufficient for drawing conclusions regarding improvements in OME at longer time periods or for other clinical outcomes, including hearing.

Key Question 2. Comparative Effectiveness: Functional Outcomes or Quality of Life

Only a subset of the treatment comparisons reported functional or quality of life outcomes. These include TT versus watchful waiting, TT plus adenoidectomy versus myringotomy plus adenoidectomy, and steroids versus control. In general, there were no differences between the treatments. The studies included to address KQ 2 are described under KQ 1.

Tympanostomy Tubes Versus Watchful Waiting/Myringotomy

Meta-analyses reported by Browning et al.[15] did not find any differences in language development at 6 and 9 months post treatment between TT and watchful waiting (moderate strength of evidence for no differences). With one exception, studies examining children during preschool and elementary school years failed to find a difference in language skills. In the one

exception where a difference favoring TT was reported, the investigators used a teacher rating of children's language; this difference disappeared at 8 years of age when they used a direct assessment of language (low strength of evidence for no difference). We did not find differences between TT and watchful waiting in any RCTs reporting cognitive development, academic achievement or quality of life at any time point (all low strength of evidence for no difference). Studies reported mixed findings for behavior outcomes at less than 1 year (insufficient strength of evidence); three studies reporting behavior at more than 1 year reported no difference (low strength of evidence). No studies comparing TT with myringotomy reported on functional or quality of life outcomes (insufficient strength of evidence).

Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy

One study comparing TTs plus adenoidectomy with myringotomy plus adenoidectomy reported quality of life outcomes.[60] The two groups did not differ at any time point (insufficient strength of evidence). Strength of evidence was insufficient for all speech/language, cognitive, and behavioral outcomes because there were no studies including these outcomes.

Oral or Topical Nasal Steroids

Two studies comparing steroids to control (three reports)[79-81] examined functional outcomes. In one small study, patients receiving intranasal steroids plus oral antibiotics did not differ in parents' assessment of their children's symptoms from patients receiving placebo plus antibiotics (insufficient strength of evidence); nor did patients receiving intranasal steroids differ from controls in parent reported hearing outcomes (low strength of evidence). No studies comparing topical or oral steroids to control examined any other functional outcomes (insufficient strength of evidence).

Key Question 3. Harms or Tolerability

Six of the treatment comparisons included in the review reported on harms. These included comparisons between different types of TT, TT versus watchful waiting/myringotomy, TT plus adenoidectomy versus myringotomy plus adenoidectomy/adenoidectomy alone, steroids, and autoinflation. Only a limited range of harms was included for any comparison. Few significant differences in harms were reported.

Tympanostomy Tube Comparisons

We reviewed nine studies that reported on otorrhea.[27-32,37-39] Otorrhea rates differed by TT type, with placement of longer term TT related to a higher probability of otorrhea (low strength of evidence). For other harms such as perforation, cholesteatoma, occlusion, tympanosclerosis, and the presence of granulation tissue, the evidence was too limited to determine a direction of effect (insufficient strength of evidence).

Tympanostomy Tubes Versus Watchful Waiting/Myringotomy

We reviewed nine studies that compared side effects for TT with side effects for watchful waiting or myringotomy.[57,64,88-94] Otorrhea and tympanosclerosis occurred more frequently in ears that had TT than watchful waiting or myringotomy (low strength of evidence). Evidence was insufficient for other harms due to either conflicting results or data reported in only a single study.

Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy/Adenoidectomy Alone

We reviewed nine studies that examined harms.[33-35,48,53,95-98] These included repeat TTs, otorrhea, perforation, and tympanosclerosis or myringosclerosis. The risk of tympanosclerosis was higher with TT than myringotomy or no surgery in addition to adenoidectomy (moderate strength of evidence). Results for other harms were either mixed, were reported in single studies, or were lacking precision (insufficient strength of evidence).

Adenoidectomy

Only two studies (three articles)[22,46,53] reported harms. In both studies, there was one report of a postoperative hemorrhage following adenoidectomy (low strength of evidence). Evidence was insufficient for other harms.

Oral or Topical Nasal Steroids

Evidence for harms of steroids comes from the systematic review and its update.[28,29] A meta-analysis of two RCTs in the updated review[29] comparing oral steroids plus antibiotics with control plus antibiotics reported no difference in mild to moderate adverse events at 2 weeks to 6 months. A second RCT[31,99] found no significant differences in mild adverse harms such as stinging nose, nose bleed, dry throat, or cough between those receiving nasal steroids and those receiving placebo control (low strength of evidence). Evidence concerning serious harms was sparse for either nasal or oral steroids (insufficient strength of evidence).

Autoinflation

None of the studies that compared autoinflation to control[17] provided quantitative information on rates of serious or mild harms, only verbal statements indicating there were few harms noted (insufficient strength of evidence).

Key Question 4. Comparative Effectiveness of Interventions for Subgroups of Patients

One of the explicit goals of this review was to examine treatment options for subgroups of patients including individuals defined by age groups and subpopulations at greater risk for OME such as individuals of American Indian, Alaskan, and Asian backgrounds and individuals with cleft palate, Down syndrome, and other craniofacial anomalies. Our search found very few studies of any subgroups that met our inclusion criteria. Two treatment comparisons examined comparative effectiveness of interventions for subgroups of patients—TT plus adenoidectomy versus myringotomy plus adenoidectomy/adenoidectomy alone and autoinflation.

Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy or Adenoidectomy Alone

One study[60] included children with sleep apnea and OME. The study did not find differences in hearing thresholds between children who received TT plus adenoidectomy and children who received myringotomy plus adenoidectomy (insufficient strength of evidence). Quality of life scores were measured in only one study (insufficient strength of evidence).

Autoinflation

One study[87] included in the systematic review of autoinflation[17] included adults 16 to 75 years of age. The autoinflation group was significantly more likely to experience a complete recovery than those in the control group at the end of treatment and 50 days later (low strength of evidence).

Key Question 5. Comparative Effectiveness by Health Care Factors

No included studies or systematic reviews examined effectiveness of intervention comparisons by any health care factors.

Discussion

Key Findings and Strength of Evidence

Key Question 1. Comparative Effectiveness: Clinical Outcomes or Health Care Utilization

Table A summarizes the strength of evidence for comparative effectiveness of treatments on clinical outcomes. We are able to draw some conclusions regarding surgical treatments.

We examined several design, placement, and material features of TTs. Longer acting TT such as Goode T-tubes and Paparella tubes were retained longer than shorter acting Shah and Shepard TTs; No other TT features were associated with clinical outcomes.

Compared with watchful waiting, TT decreased the number of children with MEE at 1 year after surgery (high strength of evidence); compared with myringotomy, TT decreased time with effusion at 1-year followup (moderate strength of evidence). TTs continued to improve MEE at 2-year followup (moderate strength of evidence), but the effect washed out thereafter. TT also improved hearing relative to watchful waiting or myringotomy, but the effect was shorter in duration, not lasting beyond 9 months after treatment (high strength of evidence). We found only limited evidence for drawing conclusions about the relative benefits of TT for other clinical outcomes such as OME recurrence or episodes of AOM.

We examined the evidence for whether TT or myringotomy differentially improved clinical outcomes when they were added to adenoidectomy. Based on finding no differences in hearing at any time point in five studies, we concluded that hearing outcomes do not differ (low strength of evidence); evidence was insufficient for all other clinical outcomes. However, TT plus adenoidectomy improved hearing at 3 to 24 months compared with watchful waiting (low strength of evidence). Adenoidectomy is superior to no treatment for improving the likelihood of OME resolution at 6 and 12 months after surgery (high strength of evidence). Adenoidectomy plus myringotomy was superior to myringotomy alone at 2 years after surgery for improving OME resolution and hearing (low strength of evidence). Evidence was insufficient for other outcomes. Evidence was also insufficient for comparisons between different approaches to myringotomy with and without adenoidectomy because of the limited number of studies.

We have reached some conclusions for nonsurgical interventions. Oral steroids do not offer any improvements in OME at 1 to 2 months after treatment (low strength of evidence). Similarly, oral steroids with antibiotics do not provide improvements in OME at 1 to 2 months (moderate strength of evidence). A recent study (low risk of bias) provided additional evidence that OME and hearing outcomes were not improved through the use of topical intranasal steroids through 9

months after treatment. These findings support the current clinical practice guidelines that recommend against the use of oral and intranasal steroids in treating OME in children. Although autoinflation improved MEE at less than 1 month after treatment (low strength of evidence), evidence was insufficient for reaching conclusions for other outcomes, largely because outcomes across studies testing autoinflation were not measured at consistent lengths of followup or through consistent measures.

Table A. Strength of evidence for interventions to improve clinical outcomes

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
TT vs. watchful waiting, delayed treatment, or myringotomy	MA of 3 RCTs (N=574)	TT had less persistent middle ear effusion at 1 year compared with watchful waiting or delayed treatment: 32% less time (95% CI, 17% to 48%).	High for benefit
	2 studies (N=294)	TT had less time with effusion through 1 year compared with myringotomy.	Moderate for benefit
	MA of 3 RCTs (N=426)	TT had less persistent middle ear effusion at 2 years compared with watchful waiting or myringotomy: 13% less time (95% CI, 8% to 17%).	Moderate for benefit
	MA of 3 RCTs (N=523) + 1 RCT (N=248)	TT had better measured hearing for up to 9 months than watchful waiting. MA results: -4.20dB (95% CI, -4.00 to -2.39).	High for benefit
	MA of 3 RCTs (by ears) (N=230)	TT had better measured hearing for up to 6 months than watchful waiting or myringotomy: -10.08 (95% CI, -19.12 to -1.05).	High for benefit
	MA of 3 RCTs (by ears) (N=234)	No difference between TT and watchful waiting or myringotomy in measured hearing at 7-12 months: -5.18dB (95% CI, -10.43 to 0.07).	Low for no difference
	MA of 2 RCTs (N=328); MA of 2 RCTs (N=283)	No difference between TT and watchful waiting in measured hearing at 12 months: -0.41dB (95% CI, -2.37 to 1.54) and 18 months -0.02 dB (95% CI, -3.22 to 3.18).	Low for no difference
TT + adenoidectomy vs. myringotomy + adenoidectomy	6 studies: 3 RCTs by person (N=431); 2 RCTs (by ears) (N=338); 1 NRCT (by ears) (N=193)	No difference in measured hearing between groups at 6 and 12 months and at more than 3 years.	Low for no difference
Adenoidectomy vs. no treatment	MA of 2 RCTs (by ears) (N=153); MA of 3 RCTs (by ears) (N=297)	Adenoidectomy had better OME resolution than no treatment at 6 months. The risk difference was 0.27 (95% CI, 0.13 to 0.42) measured through otoscopy and 0.22 (95% CI, 0.12 to 0.32) measured through tympanometry.	High for benefit
	MA of 3 RCTs (by ears) (N=298)	Adenoidectomy had better OME resolution than no treatment at 12 months. The risk difference was 0.29 (95% CI, 0.19 to 0.39).	High for benefit
Adenoidectomy + myringotomy vs. myringotomy	1 RCT (N=237)	Adenoidectomy and myringotomy had less mean time with effusion than myringotomy alone at 24 months: -0.76 standard mean difference (95% CI, -1.02 to -0.49).	Low for benefit
	1 RCT (N=237)	Adenoidectomy and myringotomy had better hearing than with myringotomy alone at 24 months measured as standard mean difference time with hearing level ≥ 20: worse ear: -0.65 (95% CI, -0.91 to -0.39); better ear: -0.66 (95% CI, -0.93 to -0.40).	Low for benefit
TT + adenoidectomy vs. WW	1 study (n = 250)	TT plus adenoidectomy improved hearing at 3 to 24 months.	Low for benefit
Oral steroids vs. controls	MA of 3 RCTs (N=106)	No difference in persisting OME at 1-2 months (no antibiotics provided in either group): OR=0.55 (95% CI, 0.21 to 1.48).	Low for no difference

Table A. Strength of evidence for interventions to improve clinical outcomes (continued)

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
Oral steroids + antibiotics vs. controls + antibiotics	MA of 3 RCTs (N=243)	No difference in persisting OME at 1-2 months (antibiotics provided to both groups): OR=0.75 (95% CI, 0.45 to 1.27).	Moderate for no difference
Topical intranasal steroids vs. controls	1 RCT (N=217)	No difference in OME cure rates at 1, 3, and 9 months.	Low for no difference
	1 RCT (N=217)	No difference in hearing loss at 3 and 9 months.	Low for no difference
Autoinflation vs. controls	MA of 2 RCTs (N=185)	Improvement in OME at ≤1month: RR=3.84 (tympanometry change C2 to C1 or A) and RR=2.72 (tympanometry change B to C1 or A).	Low for benefit

CI = confidence intervals; dB = decibels; MA = meta-analysis; NRCT = non-randomized controlled trial; N = number; OME= otitis media with effusion; OR = odds ratio; RCT = randomized controlled trial; RR = risk ratio; TT = tympanostomy tubes; vs. = versus

Key Question 2. Health-Related Quality of Life and Functional Outcomes

Table B summarizes the strength of evidence for health-related quality of life and functional outcomes. We found only limited evidence regarding these outcomes. Language comprehension and language expression outcomes at 6 to 9 months were not significantly better among children with OME who received TT than among those who were limited to watchful waiting or delayed treatment (moderate strength of evidence). Results for cognitive development, behavioral competence, and academic achievement were similar; outcomes from TT versus watchful waiting or delayed treatment at various followup times did not differ (low strength of evidence). Evidence was insufficient to reach conclusions related to differences in either behavioral outcomes or quality of life for this treatment comparison.

Quality of life outcomes were measured in one small study comparing TT and adenoidectomy versus myringotomy and adenoidectomy, but we considered the evidence to be insufficient to reach conclusions. Topical steroids do not improve parent-reported hearing difficulties of their children at up to 9 months (low strength of evidence). However, evidence was insufficient to reach conclusions about other quality of life outcomes for oral steroids.

Table B. Health-related quality of life and functional status

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
TT vs. watchful waiting or delayed treatment	MA of 3 RCTs (N=394) and 2 RCTs (N=503) MA of 3 RCTs (N=393) and 2 RCTs (N=503)	No difference in language comprehension at 6 to 9 months post-intervention (mean difference, 0.09; 95% CI, -0.21 to 0.39) or at preschool and elementary school age. No difference in language expression at 6 to 9 months post-intervention (mean difference, 0.03; 95% CI, -0.41 to 0.49) or at preschool and elementary school age.	Moderate for no difference
	2 RCTs (N=503)	No difference in cognitive development at 9 months post-intervention or at preschool and elementary school age.	Low for no difference
	3 RCTs (N=710)	No difference in behavior at 1 year or more.	Low for no difference
	2 RCTs (N=503)	No difference in academic achievement at elementary school age.	Low for no difference
Intranasal steroids vs. controls	1 study (N=144)	No difference in parent-reported hearing difficulties at 3 and 9 months or in median days with hearing loss at 3 months.	Low for no difference

CI = confidence interval; MA = meta-analysis; N = number; RCT = randomized controlled trial; TT = tympanostomy tubes; vs. = versus

Key Question 3. Harms Associated With Interventions To Treat Otitis Media With Effusion

Table C summarizes the OME interventions on which we had low, moderate, or high strength of evidence about safety and harms. In relation to TT, we considered concerns such as otorrhea, tympanosclerosis, cholesteatoma, or surgical complications. In relation to steroid treatment, we considered problems such as diarrhea and nasal stinging.

Otorrhea was more common among ears with TT than those without (low strength of evidence), especially for those TT designed to stay in longer. Tympanosclerosis was more common in children who had TT than those who were actively monitored or who had myringotomy (low strength of evidence). Likewise, tympanosclerosis was more common when TT were added to adenoidectomy than for adenoidectomy alone or with myringotomy (moderate strength of evidence). Additionally, the risk of post-surgical hemorrhage, although rare, was associated with adenoidectomy, not any other comparison treatments.

We concluded that mild adverse events are not significantly higher with topical nasal steroids than with placebo (low strength of evidence). However, evidence was insufficient to reach conclusions related to oral steroids and serious adverse events from oral or topical steroids. Evidence was also insufficient concerning the surgical risks from the insertion of TT or those from myringotomy procedures with adenoidectomy.

Table C. Strength of evidence for harms of interventions

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
TT vs. TT	1 RCT (N=30 ears); 2 observational studies (N=779 ears)	Otorrhea occurred more frequently in ears with longer-term TT than in ears with shorter-term TT after 1 year or more.	Moderate for harms of longer-term TT
TT vs. watchful waiting or myringotomy	5 studies (N=1,129)	Tympanosclerosis occurred more frequently in ears that had TT, based on examinations after the TT had been extruded.	Moderate for harms of TT
	4 studies (N=960)	Otorrhea occurred more frequently in ears with TT.	Low for harms of TT
TT plus adenoidectomy vs. adenoidectomy alone or with myringotomy	3 studies (N=485)	Tympanosclerosis occurred more frequently in ears with TT than ears with only adenoidectomy or myringotomy.	Moderate for harms of TT
Adenoidectomy vs. other treatments	2 studies (N=739)	Although rare, adenoidectomy increased the risk of postsurgical hemorrhage.	Low for harms of adenoidectomy
Oral nasal steroids vs. control	5 studies (N=637)	No difference in mild adverse events such as vomiting and diarrhea.	Low for no difference
Topical nasal steroids vs. control	2 studies (N=215)	No difference in mild adverse events such as nasal stinging, dry throat, and cough.	Low for no difference

N = number; NR = not reported; SR = systematic review; TT = tympanostomy tubes; vs. = versus

KQ 4. Outcomes for Important Patient Subgroups

Table D provides the limited evidence we found for patient subgroups. Although we attempted to examine treatment effectiveness or harms for key subgroups characterized by clinical variables (e.g., cleft palate, Down syndrome, or sensorineural hearing loss) or sociodemographic factors (such as age), we could not identify studies that covered most of our subgroups of interest.

One study examined children with sleep apnea and OME, and one examined adults with OME. Among children with sleep apnea, all of whom had adenoidectomy to treat that condition, the addition of TT or myringotomy did not differ significantly in terms of any measured outcomes (insufficient strength of evidence). The study of autoinflation in one systematic review[17] found differences in rates of recovery between those receiving autoinflation and those who were in the control group. Individuals in the autoinflation group were significantly more likely to experience a complete recovery than those in the control group at both the end of treatment ($p<0.001$) and at 50 days after treatment ($p<0.001$). Similarly, the ears of the participants receiving autoinflation had better recovery rates than control ears at both time points ($p<0.001$). Strength of evidence was low for benefit.

Table D. Strength of evidence for subgroups

Intervention and Comparator	Number of Studies (Sample sizes)	Subgroup and Results	Strength of Evidence
Autoinflation vs. control	1 RCT (N=396 ears)	Adults (16–75) with OME: differences between groups in composite measure of recovery (otoscopy, tympanometry, audiometry) at end of tx and 50 days after tx.	Low for benefit (one study)

OME = otitis media with effusion; tx = treatment; RCT = randomized control trial

Key Question 5. Health Care Factors

No studies examined issues related to health insurance coverage, physician specialty, type of facility of the provider, geographic location of patients, presence or absence of continuity of care, or prior use of pneumococcal virus inoculation. Evidence is thus insufficient for all such factors.

Applicability

This review was intended to apply to individuals with OME of all ages. Findings about all interventions are likely to be applicable to otherwise healthy children other than infants. In some cases, study authors did not provide sufficient information on age of the target population (e.g., provided only the average age without providing the age range) or included a wide age range of children, rendering it difficult to ascertain applicability of the tested intervention to specific age groups. The evidence base is clearly limited for adults and for infant children, and it is virtually nonexistent for children with major coexisting or congenital conditions, such as those with cleft palate, Down syndrome, and sensorineural hearing loss, who may be disproportionately affected by OME.

We provided evidence on all the commonly used treatments for OME, including TT, myringotomy, adenoidectomy and watchful waiting; we also examined outcomes from use of steroids upon the advice of our TEP, even though they are not recommended in current U.S. guidelines. We also provided evidence for autoinflation, an alternative noninvasive treatment strategy. We note the limitation in the evidence that not all studies comparing TT to other surgical or non-surgical treatments provided information regarding the type of TT used, limiting conclusions that can be made at this level of specificity. We also sought to include CAM procedures, but no RCTs met our inclusion criteria.

We did not limit the outcomes of interest. However, the bulk of the literature concerned reductions in OME and measured hearing. Only a few studies included quality-of-life outcomes, and none included satisfaction with care. Included studies were limited to head-to-head comparisons that collected a variety of harms, but they were not uniformly collected in all studies. We recognize that other study designs may have expanded our identification of possible harms. We did not limit the time frame for followup but were most interested in outcomes 3 months or more following treatment. Studies were conducted in clinical settings. They generally included populations from the United States and Western Europe, but a few studies were conducted in other countries including Egypt, Iran, and Japan.

Research Gaps

Research gaps in treatments for OME exist in several areas. We recommend the following for improving the research base.

The first area is to expand research in subgroups that were targeted in this review but for whom no evidence could be amassed. These groups include infants and toddlers who are developmentally vulnerable for language acquisition and for whom a mild conductive hearing loss over a shorter period of time may be more detrimental than for older children. Children with craniofacial anomalies such as cleft palate and other developmental disorders including Down syndrome and sensorineural hearing loss have not been a part of most treatment studies. When we did find studies on children with comorbid conditions, we excluded them for reasons such as having no valid comparison group (e.g., case series with no comparator) or data combined with

children with acute AOM. Additionally, only limited research is available on treatment effectiveness in adults; we could identify only one study about treatments for adults.

The second area is to examine treatments that have heretofore not been subjected to rigorous research methods. For instance, despite the interest in CAM treatments, the lack of carefully designed investigations of these treatments is clear. While insertion of TT remains a common procedure, we have little evidence regarding different types of TT or routines for insertion. An ongoing Swedish trial plans to enroll a large cohort of children in an RCT comparing different TT; results from this trial may be able to provide the needed evidence regarding which TT are more (or less) beneficial. Some researchers are designing treatments to counteract the otological effects of gastroesophageal reflux disease; further research of promising treatments is welcome.

Methods deficiencies constitute a third gap. Measures are not uniform; investigators do not report on reoccurrence of AOM and functional outcomes; time points for collecting outcomes differ; and baseline measures are not always provided. Pain or discomfort resulting from OME was not measured in any studies. Studies do not routinely document effect sizes and many researchers fail to report their statistical power calculations of the sample size needed to find an effect (the RCTs of Williamson et al., the MRC, and Paradise et al. being notable exceptions). Missing data are often not addressed, and even if attrition is acknowledged, statistical procedures are rarely used to correct for this problem. We encourage investigators to give far more attention to their methods in the service of greatly improving the literature base.

Conclusions

Overall, we found a small and uneven body of evidence across treatment comparisons and outcomes. Compared with watchful waiting or myringotomy, we found strong and consistent evidence that TT decreased effusion and improved hearing over a short period but did not affect longer-term speech, language, or other functional outcomes. However, we found weaker evidence that TT placement also increases the rate of side effects such as otorrhea and tympanosclerosis. Although adenoidectomy decreases the number of children with OME in the short term relative to watchful waiting, less is known about its long-term effects particularly with respect to functional outcomes. Steroids were not found to provide a benefit. Additional research and better methods are needed to develop a comprehensive evidence base to support decisionmaking among the various treatment options, particularly in subpopulations defined by age and coexisting conditions.

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Introduction

Background

Otitis media with effusion (OME) is defined as a collection of fluid in the middle ear (effusion) without signs or symptoms of acute ear infection.[1] OME has been known by a variety of terms including serous otitis media, chronic otitis media, secretory otitis media, nonsuppurative otitis media, mucoid otitis media, or fluid in the middle ear.[1] This condition occurs commonly during childhood; as many as 90 percent of children will have at least one episode of OME by age 10.[2] Many episodes are short-term and transient; they do not recur or recur infrequently. However, for some children, OME recurs frequently or lasts for a prolonged period of time.[3]

Despite the high prevalence of OME, its long-term impact on child developmental outcomes such as speech, language, intelligence, and hearing remains unclear. An Agency for Healthcare Research and Quality systematic review examining the natural history of OME[2] concluded that children with OME in the first 3 years of life had a higher risk of conductive hearing loss at 6 to 10 years of age. However, the authors found no evidence of an impact of early OME on speech, language, or verbal intelligence and found insufficient evidence to establish the possibility of important effects on development.

Determining the necessity of treatment has been difficult because of OME's uncertain effects on clinical and functional outcomes. Yet, many individuals with OME are treated: annual costs of treating OME in the United States are estimated at $4 billion.[2] The near universality of this condition in children and the high expenditures for treating OME make this an important topic. This review was not designed to examine the question of whether one should treat OME but rather to compare the effectiveness of the range of treatments for OME.

Anatomy and Cause of Otitis Media With Effusion

The physiologic changes that lead to OME begin with dysfunction of the eustachian tube. Normally this tube aerates the middle ear by connecting it to the nasopharynx. The function of the eustachian tube becomes evident during atmospheric ascent or descent. The pressure sensation one experiences when taking off in an airplane comes from middle ear barometric pressure changes. The "popping" of the ear is actually the opening of the orifice to the eustachian tube in the nasopharynx and equalization of pressure between atmospheric pressure and the barometric pressure in the middle ear.

The pathophysiology of OME is still unclear. The traditional teaching has been that OME develops when a negative pressure develops in the middle ear relative to atmospheric pressure and then exudative or transudative fluid accumulates because of that pressure.[4] However, various other potential explanations involve ciliary dysfunction, proliferation of fluid producing goblet cells, allergy and residual bacterial antigens, and biofilm.[5] The presence of fluid in the middle ear decreases tympanic membrane and middle ear function, leading to decreased hearing, a sensation of fullness in the ear, and occasionally pain from the pressure changes.

In addition to chronic dysfunction of the eustachian tube, the leading causes for OME are viral upper respiratory infection and acute otitis media (AOM).[6,7] Several predisposing environmental factors are associated with an increased risk of developing OME: exposure to secondhand smoke, child care attendance, and environmentally induced allergies.[8]

Populations With Otitis Media With Effusion

OME is typically considered a childhood affliction. In fact, although OME usually resolves spontaneously within 3 months, 30 to 40 percent of children have recurrent episodes and 5 to 10 percent of episodes last more than 1 year.[1,3,9]

Some subpopulations of children are at greater risk of having episodes of OME. Those with cleft palate, Down syndrome, and other craniofacial anomalies are at high risk for anatomic causes of OME and decreased function of the eustachian tube.[10] Individuals of American Indian, Alaskan, and Asian backgrounds are believed to be at greater risk,[11] as are children with adenoid hyperplasia. In addition, children with existing hearing loss can experience further reduction in hearing because of secondary conductive hearing loss that occurs with OME.

Although rare, OME can also occur in adults, usually after patients develop a severe upper respiratory infection such as sinusitis, severe allergies, or rapid change in air pressure (after a plane flight or a scuba dive). The incidence of prolonged OME in adults is not known, but it is much less common than in children.[12]

Symptoms of Otitis Media With Effusion

OME can be associated with discomfort from pressure changes and a feeling of fullness in the ear. Individuals with OME are also prone to episodes of AOM. Temporary hearing loss is common among OME patients. This hearing loss is often mild and transient (i.e., worsened or with hearing threshold elevated by a mild hearing loss of about 10 decibels [dB]), but in some cases moderate and prolonged hearing loss can occur.[13] Children with OME that leads to chronic eustachian tube dysfunction are at risk for structural damage of the tympanic membrane.[14] Because protracted hearing loss in young children may delay or permanently change their communication skills and may lead to behavioral and educational difficulties,[15] clinicians and others are concerned about the possible role of OME on these outcomes.

Diagnosis of Otitis Media With Effusion

The core feature of OME is middle ear effusion (MEE)—i.e., fluid behind the eardrum in the middle ear space over a period of time, commonly 3 or more months. Tympanocentesis, use of a needle to puncture the tympanic membrane to allow for confirmation, drainage, and examination of fluid, is the gold standard for diagnosing MEE associated with OME. However, because tympanocentesis is an invasive procedure, it is rarely used for diagnosis. Instead, pneumatic otoscopy is the most reliable and readily available diagnostic method; in this technique, clinicians blow air through the otoscope, attempting to cause movement of the tympanic membrane.[2] Any decreased movement when fluid is present behind the tympanic membrane can be identified through comparison to normal membrane movement. Additionally, bubbles seen behind the tympanic membrane assures that MEE is present.[15] Tympanometry is a diagnostic tool that indirectly measures middle ear pressure and tympanic membrane mobility. This procedure is performed with an inexpensive, handheld tool and can be performed more easily than otoscopy on children who are resisting examination. The accuracy of tympanometry is similar to pneumatic otoscopy.[16] A “flat” tympanogram (Type B tympanogram) is consistent with OME.

OME often has a corresponding conductive hearing loss as measured by pure-tone audiometry. Hearing is generally measured across the speech range, and for young children normal hearing is considered to be no worse than 15 dB (the measure of loudness needed to

respond to a sound).[17] In contrast, the average hearing levels for ears with OME often measure at 25 dB, with about 20 percent exceeding 35 dB, (considered a moderate hearing loss).[1]

OME is distinguished from AOM by the lack of acute symptoms or signs of inflammation.[15] OME should not have purulent fluid or redness on examination of the ear, as found with AOM. Another distinguishing feature between AOM and OME is the appearance of the tympanic membrane, which usually bulges with AOM and is typically retracted or neutral with OME.

Treatments and Treatment Strategies That Were Addressed in This Review: Rationale for Inclusion

During the topic refinement phase of the project, we looked at each of the following treatments in terms of uncertainty within the published literature (including gaps in the evidence), clinical importance, patient important outcomes, and relevance to the U.S. population. The interventions described below fall into one of four treatment types noted in Table 1—surgical interventions, nonpharmacologic physician interventions, pharmacotherapies, and complementary and alternative medicine (CAM) interventions. As explained more thoroughly in the Methods chapter, we have adopted specific criteria for including or excluding types of studies for the different kinds of therapies; we briefly mention the included study types below.

Table 1. Treatments for otitis media with effusion, with presumed mechanism of action

Type of Intervention	Treatment	Description	Presumed Mechanism of Action
Surgical	Tympanocentesis (or paracentesis)	A needle is used to aspirate fluid from the middle ear.	Initial relief of fluid may improve conductive hearing loss and may not recur. Considered the gold standard for diagnosis.
	Myringotomy	After anesthesia, a small incision or perforation is made in the tympanic membrane.	Air enters the middle ear and pressure to equalize with atmospheric pressure. The hole in the tympanic membrane lasts for only a short time—i.e., is open from 1 to 10 days for standard procedure.[18]
	Tympanostomy tube placement	After anesthesia (general anesthesia in children, can be topical anesthesia in adults) myringotomy is done in the tympanic membrane and a thin tube is inserted through the tympanic membrane.	Placement of the tube allows aeration of the middle ear, equalization of pressure in the middle ear, and drainage of fluid from the middle ear. Hearing and symptoms can improve allowing time for underlying eustachian tube dysfunction to resolve.
	Adenoidectomy	After general anesthesia, the adenoids are excised from the posterior pharynx. The overlying tonsils can also be removed at the same time.	The eustachian tube opens in the posterior pharynx in close proximity to the adenoids, and the potential benefit of removal is that the eustachian tube function may improve thereby resolving OME.
Other treatment strategies	Variations in surgical technique and procedures	Clinicians may use different or possibly newer approaches or devices.	Same as those of the original or parent surgical intervention.

Table 1. Treatments for otitis media with effusion, with presumed mechanism of action (continued)

Type of Intervention	Treatment	Description	Presumed Mechanism of Action
Nonsurgical physical interventions	Autoinflation of the eustachian tube	Using either a closed mouth and valsalva maneuver or blowing against pressure in a device against a closed glottis, the intraoral cavity pressure is increased.	Increased intraoral pressure above the eustachian tube or middle ear pressure opens the eustachian tube into the oropharynx. Each time the procedure is repeated, it allows intermittent aeration of the middle ear and can mitigate abnormal eustachian tube function until function returns to normal.
	Hearing aids	A small electronic device that amplifies sound, worn behind the ear (children and adults) or placed into the external ear canal (adults).	This device overcomes the conductive hearing loss associated with middle ear effusion. Since hearing deficit is one of the concerning effects of OME, improving hearing may eliminate adverse effects of OME.
Pharmacological interventions	Nasal and oral steroids	Anti-inflammatory medications are applied either topically (through the nose) or systemically.	Decreased inflammation at the site of eustachian tube orifice in the posterior pharynx or in the middle ear may improve function.
	Antihistamines	Antihistamines are used to dampen inflammatory response	See above for nasal or oral steroids.
	Decongestants	Either topical or systemic medications are used to decrease edema of mucous membranes.	Decreased swelling at or near eustachian tube orifice may improve function.
	Antibiotics and antimicrobials	Medications that kill or stop duplication of infectious agents such as bacteria are used.	Bacterial infections may precede OME or develop during an episode of OME. Antibiotic treatment may treat infection that is not evident by clinical examination and decrease inflammation to allow more rapid resolution of eustachian tube dysfunction.
Complementary and alternative therapies	Including, but not limited to dietary amendments and osteopathic manipulation	Varies by treatment.	Varies by treatment.
Watchful waiting		Sometimes referred to as active observation, this choice involves delaying treatment while monitoring patient progress. It contrasts with immediately administering a treatment.	Not directly applicable.

OME = otitis media with effusion

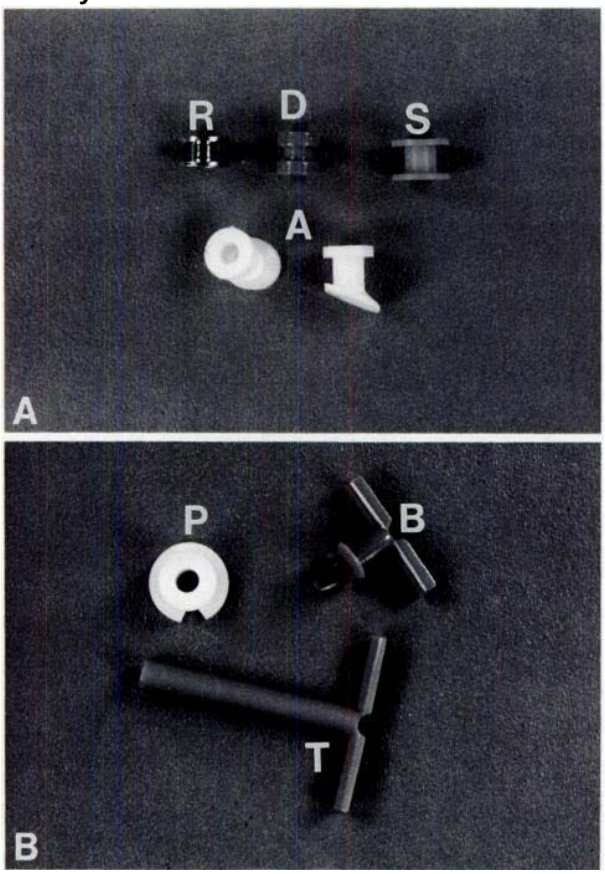
The set of treatments examined in the review are generally limited to those that are recommended in clinical guidelines for managing OME.[15] The guidelines do not recommend adenoidectomy as an initial procedure for OME unless a specific indication for it exists, but we included studies of it as a first-line procedure because a recent large trial was specifically undertaken to compare adenoidectomy and tubes.[19] Nor do recent guidelines recommend the use of myringotomy alone. However, we included studies of it as a standalone treatment (with and without adenoidectomy) because we found some studies with laser-assisted myringotomy and myringotomy using radiofrequency that were not evaluated in the practice guidelines. The guidelines also do not recommend treatment with steroids but a large trial was also recently completed related to treatment with topical intranasal steroids[20] In addition, we included studies of CAM procedure(s) in our search. Notably, the clinical guidelines did not have any

recommendation for CAM because of a lack of studies, particularly randomized trials. On the recommendation of our Technical Expert Panel (TEP), we searched for studies that may have been published in the time since the guidelines were published. Each treatment we included in this review is discussed in turn.

The benefits and harms of **tympanostomy tubes** (TT) for managing OME in children have been addressed by two recent systematic reviews identified during our topic refinement.[21,22] They include a 2010 Cochrane review of 11 randomized controlled trials (RCTs)[22] of otherwise healthy children and a 2011 systematic review, commissioned by the Swedish Council on Technology Assessment in Health Care,[21] of 10 RCTs. For this review, we began with evidence from these systematic reviews limited to patients with OME and searched for additional evidence.

TT can be broadly separated into short-term and long-term tube types based on the length of time they can be expected to remain in the ear without extrusion. The length that TT stay in the tympanic membrane is related to tube length and design.[23,24] Tubes are designed to stay in the tympanic membrane for as little as 6 months, to over 2 years.[23] Figure 1 presents pictures of common TT types based on average retention time.

Figure 1. Short-term tympanostomy tubes: R, Reuter-Bobbin; D,Donaldson; S, Sheehy; A, Armstrong (2 views). B. Long-term tympanostomy tubes: P, Paparella II; T, Goode t-tube; B, butterfly



Source: Isaacson G, Rosenfeld RM. Care of the child with tympanostomy tubes: A visual guide for the pediatrician. Pediatrics 1994 Jun:93(6):924-929.[24]

A growing body of literature examines variations in TT-related surgical techniques and procedures for treating patients with OME. The 2011 Swedish systematic review[21] considered various characteristics of tube design and surgical procedures. We searched for other relevant studies comparing TT materials, designs, and surgical procedures.

As indicated above, the most recent guidelines for treating OME do not recommend the use of **myringotomy** alone,[15] but more recent literature suggests that laser-assisted myringotomy or radio frequency myringotomy may be a useful alternative to myringotomy plus TT because it may allow for aeration of the ear for a longer time than would myringotomy alone. These recent studies suggest that it may provide a treatment with fewer complications for selected subgroups of children and adults.[25-28] Because no systematic reviews have addressed the effectiveness of myringotomy alone, we searched for relevant RCTs and observational studies examining myringotomy alone as a treatment strategy for OME in otherwise healthy children, special populations of children, and adults.

Adenoidectomy as a treatment for OME in children was also reviewed in a 2010 Cochrane review.[29] The review included seven RCTs comparing adenoidectomy (with or without TT) and nonsurgical management or TT only; studies involved children up to 18 years of age with followup of 6 months or longer, and study populations were not limited to otherwise healthy children. We searched for additional evidence. One additional study (i.e. TARGET)[19] that compared adenoidectomy plus TT with TT alone and with watchful waiting was published and so included in the current review. Preliminary data from this study was included in The Cochrane Review of TT[22] but not in the adenoidectomy systematic review.[29]

The technique of **autoinflation** has been used as a therapy for OME. The goal of autoinflation is to use either a Valsalva maneuver or external device to equalize middle ear and nasopharyngeal pressure, transiently opening the eustachian tube. A 2006 Cochrane review included six RCTs examining the use of autoinflation versus no treatment for hearing loss associated with OME.[30] Studies included children and adults. We began with this review and searched for additional evidence.

The benefits and harms of **oral and topical nasal steroids** in treating children with OME and hearing loss were the focus of a 2010 Cochrane review that was updated in 2011.[31,32] The review was limited to RCTs of either steroid use alone or in combination with another agent such as antibiotics; it included special populations of children of interest to our current review. Current guidelines developed by both the United Kingdom's National Collaborating Centre for Women's and Children's Health (2008)[10] and the American Academy of Pediatrics (2004)[15] recommend against using oral or topical nasal steroids in treating children with OME. In consultation with our TEP, we concluded that newly identified studies should be integrated with those previously identified through the Cochrane review, because the newly integrated studies may result in conclusions different from those of the earlier review.[31] We conducted a completely new search to identify studies pertaining to adults, because we did not find an existing review focusing on this population.

Very little literature addressed **CAM interventions** to treat patients with OME. The book "Evidence-Based Otitis Media"[33] lists treatments and supportive studies for at least two CAM approaches: physical manipulation and restricted diets. Based on the recommendations of our TEP that little is known about the efficacy of CAM treatment for OME, in the current review we only searched for RCTs of CAM interventions.

Watchful waiting, or active observation as it also has been called, is the process of regular review and followup of the child, including assessments of hearing, development, and

educational progress. We examined this as a treatment strategy, distinct from "no treatment." Watchful waiting has not been the focus of a systematic review, although it has been a comparator in RCTs in systematic reviews focusing on other interventions. Current clinical practice guidelines recommend that watchful waiting be employed for 3 months and possibly longer, prior to initiating treatment in otherwise healthy children.[10,15]

We considered whether to exclude studies reporting outcomes by ears, rather than by subjects. Omitting studies reporting results by ears is reasonable and appropriate when (1) the treatment involved is systemic or (2) outcomes are measures of the patient's overall function, such as academic achievement, speech production, language development, or quality of life. We included ear-specific treatments or outcomes such as hearing thresholds or presence of fluid in the current review.

Treatments That Were Not Addressed in This Review: Rationale for Exclusion

Hearing aids are not used as a treatment option for OME in the United States. According to a 2008 National Collaborating Centre for Women's and Children's Health of the National Institute for Health and Clinical Excellence (NICE) guideline,[10] no high-quality comparative studies have evaluated the effectiveness of hearing aids to other interventions for treating OME. Furthermore, we did not find any comparative studies on hearing aids during topic refinement, and our Key Informants did not consider hearing aids of clinical relevance in the context of OME treatment in the United States. Hearing aids, therefore, were not included in the current review.

Using **antihistamines and decongestants** for treating children with OME has been extensively studied in primary RCTs and summarized in recent systematic reviews[34,35] and clinical practice guidelines.[10,15] A Cochrane review of OME for use of these medications in children identified 16 RCTs that included more than 1,800 subjects.[34] High-quality evidence of multiple short- and long-term outcomes repeatedly and unequivocally demonstrated no benefit for use of these medications over placebo for treating OME. Additionally, the reviewed studies found evidence of side effects and harms with the use of these medications. We see no reason to believe that these findings will change with future advances in the medication class or causes of OME. We, therefore, decided to exclude antihistamines and decongestants from the current review as a treatment that is definitively not effective and likely harmful.

Conflicting evidence exists regarding the effectiveness and utility of antimicrobials including **antibiotics** for treating patients with OME.[10,15,35] They are not recommended in current U.S. guidelines.[15] A Cochrane review on the use of antibiotics for the treatment of OME in children was started in 2011 and was published after the period of updating our search.[36] We did not duplicate their efforts and have excluded antibiotics from the current comparative review.

Scope and Key Questions

Scope

This review is designed to address the comparative effectiveness of the interventions described above for all individuals with OME. We were especially interested in examining effectiveness in subpopulations based on age, including adults and in special populations such as individuals with craniofacial abnormalities, Down syndrome, and existing hearing loss. We targeted impacts of these treatments on clinical outcomes, functional and quality-of-life

outcomes, health care utilization, and harms. Both short-term and long-term studies were included. We did not limit the setting where these treatments occurred.

We conducted this review (nominated by an adult patient) because of the continuing uncertainty about efficacy, effectiveness, and particularly comparative effectiveness, as well as harms, for the included therapies. This uncertainty leaves clinicians, patients, and families (e.g., parents of younger children) facing considerable dilemmas about choosing appropriate interventions, given patient characteristics and preferences. OME is a common condition and more up-to-date and comprehensive comparative information will be helpful to many stakeholder groups in making decisions about when and how to treat this condition. We also were mindful of the need to provide this information for populations not otherwise included in past reviews such as adults and children with special conditions such as Down syndrome, cleft palate, or existing hearing loss.

Thus, we aimed to provide useful information for clinical decisionmaking and policymaking. Of particular concern, as reflected in our Key Questions (KQs), were issues such as weighing benefits and harms for patients, appropriate interventions for particular population subgroups, and considering the applicability of evidence to primary versus specialty practice.

Key Questions

We addressed five KQs in this comparative effectiveness review.

KQ 1. What is the comparative effectiveness of the following treatment options (active treatments and watchful waiting) in affecting clinical outcomes or health care utilization in patients with OME?

Treatment options include:

a. Tympanostomy tubes,
b. Adenoidectomy,
c. Myringotomy,
d. Oral or topical nasal steroids,
e. Autoinflation,
f. Complementary and alternative medical procedures,
g. Watchful waiting,
h. Variations in surgical technique or procedure.

Clinical outcomes include changes in:

a. OME signs (middle ear fluid) and symptoms (fullness in ear), objective hearing thresholds,
b. Episodes of acute otitis media, and
c. Vestibular function such as balance and coordination.

KQ 2. What is the comparative effectiveness of the different treatment options listed in KQ 1 (active treatments, watchful waiting, and variations in surgical procedures) in improving functional and health-related quality-of-life outcomes in patients with OME?

These outcomes include:

a. Perceived hearing level (i.e., patient or parent-reported hearing problems)

b. Speech and language development,
c. Auditory processing,
d. Academic achievement,
e. Attention and behavioral outcomes,
f. Health-related quality of life, and
g. Patient and parent satisfaction with care.

KQ 3. What are the harms or tolerability among the different treatment options?

KQ 4. What are the comparative benefits and harms of treatment options in subgroups of patients with OME?

Subgroups include:

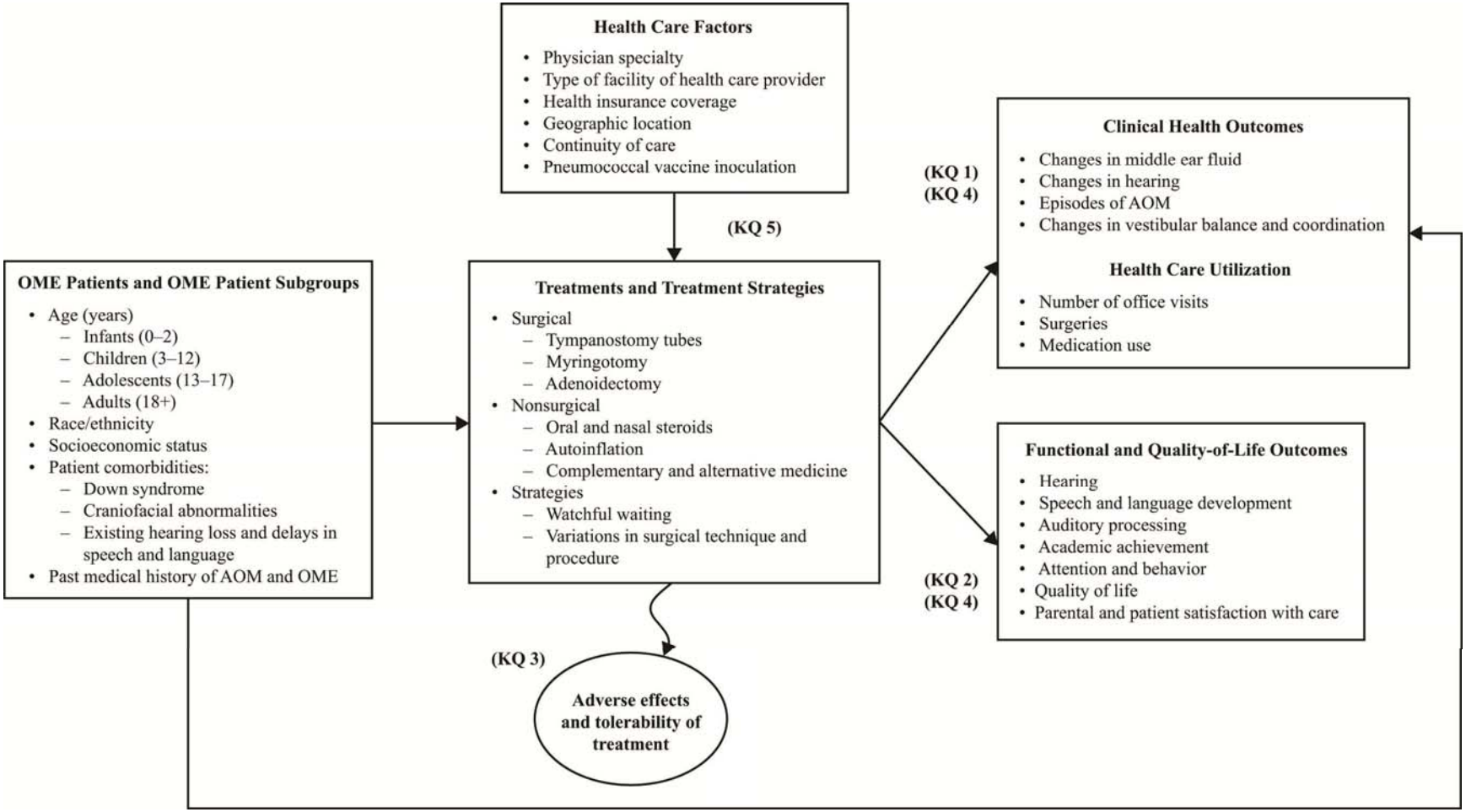
a. Patients of different age groups,
b. Patients of different racial or ethnic backgrounds,
c. Patients in different socioeconomic status groups,
d. Patients with comorbidities such as craniofacial abnormalities (e.g., cleft palate), Down syndrome, and existing speech, language and hearing problems, and
e. Patients with a medical history of AOM or OME (with and without clinical hearing loss or other problems).

KQ 5. Is the comparative effectiveness of treatment options affected by any of the following factors:

a. Health insurance coverage,
b. Physician specialty,
c. Type of facility of the treatment provider,
d. Geographic location,
e. Continuity of care, or
f. Prior inoculation with the pneumococcal vaccine?

Figure 2 gives the analytic framework for this review. The populations of interest are in the box to the far left; the interventions appear in the middle; and the two sets of outcomes (for KQ 1 and KQ 2 on benefits, and also KQ 4 on important subgroups) appear on the far right. KQ 3 concerns harm (various types of adverse events). Finally, KQ 5 relates to a set of health care delivery or clinical factors (pneumococcal vaccination) that may influence choices of treatments or their clinical and quality-of-life outcomes.

Figure 2. Analytic framework for review of treatments of otitis media with effusion



AOM = acute otitis media; KQ = Key Question; OME = otitis media with effusion

Organization of This Report

In the remainder of this report, the second chapter documents our methods, and the third chapter presents our key findings and data synthesis for all five KQs. Chapter 4 discusses findings in the light of ongoing debate and what is already known about therapy for patients with OME, discusses the limitations of the evidence base and this review, identifies gaps in the evidence, and suggests a future research agenda to fill those gaps.

The main report has several appendixes, as follows: Appendix A, search strategies; Appendix B, list of studies excluded at full-text review with reasons for exclusion; Appendix C, evidence tables; Appendix D, abstract and full-text forms; Appendix E, risk-of-bias tables; Appendix F, strength of evidence tables; Appendix G, glossary; and Appendix H, acronyms list.

Methods

The Evidence-based Practice Center (EPC) conducted this review using the research methods described in the Agency for Healthcare Research and Quality (AHRQ) "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[37] Further, we used the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Statement as a guide to ensure transparent reporting.[38]

Topic Refinement and Protocol Review

The EPC developed this topic and Key Questions (KQs) through a public process. The topic was nominated through an online public forum and subsequently developed and refined by a team at the RTI-UNC EPC with input from Key Informants in the field. AHRQ posted KQs for public comment (11/17/2011). We incorporated public comments and guidance from a Technical Expert Panel (TEP) into the final research protocol, which was also posted on the AHRQ Web site (3/20/2012).

Literature Search Strategy

Search Strategy

During topic refinement, the EPC identified five recently published systematic reviews with results on comparisons of interest for otitis media with effusion (OME) that were conducted either by the Cochrane Collaboration or commissioned by a national governmental agency. The Cochrane Collaboration conducted four of these;[22,29-31] the Swedish Council on Technology Assessment in Health Care commissioned the fifth.[21] These reviews covered the following OME-related treatment topics: autoinflation, oral and topical steroids, tympanostomy tubes (TT), and adenoidectomy. One additional Cochrane review, updating the earlier oral and topical steroids report, was identified during the update search.[32]

To avoid repeating or duplicating the work of these other systematic review teams, we limited our search, review, and analysis for each of our KQs to evidence that these systematic reviews included plus evidence from other reports that these recent reviews would not have considered. These additional elements of our review include observational studies, nonrandomized trials, trials published since the last search dates in those reviews, studies focusing on populations excluded from the reviews, such as adults with OME or children with Down syndrome or cleft palate, who may be differently affected by OME and outcomes excluded from the reviews.

We conducted focused searches of MEDLINE® (via PubMed), Embase, CINAHL (nursing and allied health database) and the Cochrane Library. An experienced research librarian used a predefined list of search terms and medical subject headings (MeSH). The librarian completed the first search on 1/8/2012 and conducted an update search on 8/13/2012, during peer review. We limited searches to studies published in English, given limited resources. The complete search strategies, including specific limitations used for each database, are presented in Appendix A.[39]

We searched unpublished and grey literature relevant to the review topic. Methods for identifying grey literature included a review of trial registries, specifically ClinicalTrials.gov, Health Services Research Projects in Progress (www.nlm.nih.gov/hsrproj/), and the European Union Clinical Trials Register (https://www.clinicaltrialsregister.eu/). Further, AHRQ requested

Scientific Information Packets (SIPs) from the developers and distributors of the interventions identified in the literature review. SIPs allow an opportunity for the intervention developers and distributors to provide the EPC with both published and unpublished data that they believe should be considered for the review. We included unpublished studies that met all inclusion criteria and contained enough information on their research methods to permit us to make a standard risk-of-bias assessment of individual studies.

Lastly, we searched reference lists of review articles that were pertinent but did not meet inclusion criteria for studies that we should consider for inclusion in this review.

Inclusion and Exclusion Criteria

Table 2 outlines the population, intervention, comparators, outcomes, timing, and settings (PICOTS) that define the major inclusion criteria for studies in this review. In the following sections we provide additional detail related to each of these domains as needed.

Table 2. Inclusion and exclusion criteria for studies of otitis media with effusion

Domain	Description
Population	All individuals with OME. Subpopulations include infants; adults; individuals from different racial/ethnic backgrounds; and special populations of any age including individuals with craniofacial abnormalities (e.g., cleft palate), Down syndrome, existing hearing loss, delays in speech and language, or a history of AOM or OME.
Interventions	• Surgical interventions: tympanostomy tubes (also referred to as pressure equalization tubes, grommets and ventilation tubes), myringotomy (also referred to as paracentesis), and adenoidectomy with or without myringotomy. • Pharmacological treatments: oral or topical nasal steroids. • Nonpharmacological and nonsurgical treatments or treatment strategies: watchful waiting, complementary and alternative medicine procedures, and autoinflation of the eustachian tube.
Comparator	• Different combinations of the above interventions and strategies. These include head-to-head comparisons of one or more treatments, treatment strategies (e.g., watchful waiting/delayed treatment vs. early treatment), or surgical procedures and techniques (e.g., one type of tympanostomy tube or procedure vs. another or different adjunct therapies to enhance the main intervention). We considered inactive controls in comparison with steroid treatment and usual care in comparison with autoinflation, based on the Cochrane Review inclusion criteria. We considered head-to-head trial evidence and observational study data.
Outcomes	• Clinical outcomes: changes in middle ear fluid, episodes of AOM, hearing thresholds, vestibular function (i.e., balance and coordination). • Health care utilization: number of office visits, number of surgeries, and medication use. • Functional and quality-of-life outcomes: hearing, auditory processing, speech and language development, cognitive functioning, academic achievement, attention and behavior, quality of life, and parental satisfaction with care. • Harms: all reported harms for each treatment option.
Timing	• Shorter studies looking at outcomes 0 to less than 3 months postintervention. • Longer studies looking at outcomes past 3 months and into adolescence or adulthood.
Setting	Studies conducted in the United States or internationally. Interventions provided in primary care offices where the patient is seen by a pediatrician, family physician, or nurse practitioner; subspecialist physician offices where the patient is seen by an otolaryngologist; surgical settings within a hospital or outpatient clinic; emergency departments; and craniofacial treatment centers.

AOM = acute otitis media; OME = otitis media with effusion

Population

The population of interest for this review included individuals with OME, defined as a collection of fluid in the middle ear without signs or symptoms of ear infection. Patients had to have OME at the time of the intervention or randomization. We excluded studies that focused on

the interventions of interest, such as TTs or myringotomy, but did not isolate results for individuals with only OME, because we could not measure the results in the OME population. Most commonly, studies with a mix of participants also included individuals with acute otitis media (AOM). For the same reason, we also excluded studies that focused on subpopulations of interest, such as adults or children with craniofacial abnormalities, if participants did not all have a diagnosis of OME.

Interventions

Interventions were limited to the surgical, pharmaceutical, and nonpharmaceutical listed in Table 2. Interventions could include a combination of these interventions, such as adenoidectomy and TT. Interventions could also include adjunct therapy, such as topical substances to reduce the harms from TT.

Comparators

All studies included in this review had to have at least two groups. Acceptable comparisons included one of the other treatment comparisons included in the review, except that for steroid treatment, we included placebo or nonintervention controls because these were the only comparison studies available. Autoinflation treatment was considered in comparison with treatment without autoinflation with the addition of usual care treatments, provided they were administered equally in both arms.

Studies that included adjunct therapies that were not the focus of the review, such as antibiotic treatment, were included if those therapeutic modalities were provided similarly to all study groups.

Outcomes

Study outcomes were categorized as clinical (KQ 1), functional (KQ 2), and harms (KQ 3), corresponding to our KQs. Clinical outcomes were grouped as OME signs and symptoms, objective hearing, AOM, vestibular function such as balance and coordination, and use of health care services. Functional outcomes were grouped as perceived hearing ability, speech, language, and cognitive development, behavior, quality of life, and satisfaction with care. Potential harms differed across interventions (i.e., surgical, pharmaceutical, device).

Timing

We included studies reporting outcomes of fewer than 3 months and 3 months or longer including some studies with only end-of-intervention results.

Setting

We did not exclude studies based on geography or the setting of service provision.

Study Designs

Table 3 describes the study design inclusion criteria developed for this report.

Table 3. Study inclusion criteria for review of otitis media with effusion

Category	Criteria for Inclusion
Study design	Meta-analyses, systematic reviews conducted by the Cochrane Collaboration or commissioned by a national governmental agency that were identified during topic refinement and during the update search, RCTs, and nonrandomized controlled trials, prospective and retrospective cohort studies, and case-control studies not included in one of these five systematic reviews.
Study duration	Unlimited.
By ear or by subject studies	Studies could separate groups by subject or by ear. For studies by ear to be considered RCTs, they needed to randomize by ear. Studies that analyzed results by ear and created groups by distinguishing between left ear and right ear are considered nonrandomized controlled trials.
Sample size	Unlimited.
Study location	Unlimited.
Time of publication	Because some of the treatment options of interest have been comprehensively addressed in recent Cochrane or national government-commissioned systematic reviews, we searched only for RCTs not included in the reviews and observational studies published at any time, when a treatment had been addressed in a review from one of these two types of sources. The following summarizes our search strategy for each included treatment option and population of interest. We searched from 1948 forward for: • All treatments not addressed in one of the identified systematic reviews (namely comparisons of myringotomy). • Nonrandomized and observational studies across treatment options. • Studies concerning adults and subpopulations of interest (particularly children with comorbidities such as Down syndrome and craniofacial abnormalities), across treatment options. • RCTs of complementary and alternative medicine. • RCTs of treatments not covered in recent systematic reviews including: o Tympanostomy tubes vs. tympanostomy tubes (one review): last search April 2007 o Tympanostomy tubes vs. nonsurgical interventions (two reviews): last search April 2007 o Adenoidectomy with or without myringotomy (one review): last search March 2008 o Oral and topical nasal steroids (one review that was updated): last search August 2010 o Autoinflation (one review): last search August 2005 In relation to otherwise healthy children, who would not be considered as members of subpopulations of interest because of comorbidities, we included relevant evidence from each of the recent systematic reviews relevant to our KQs and searched for other RCT literature not included in the reviews.
Language of publication	Given the volume of literature on this topic, we limited our search to publications in the English language.

KQs = Key Questions; RCT = randomized controlled trial

Study Selection

Six trained members of the research team reviewed article abstracts. Two of the members of the research team independently reviewed all titles and abstracts produced by the searches to determine study eligibility against predefined inclusion and exclusion criteria. Studies marked for possible inclusion by either reviewer underwent a full-text review. Each full-text article was again independently reviewed by two members of the team to determine if it met inclusion criteria. If both reviewers agreed that a study did not meet the eligibility criteria, it was excluded; each reviewer recorded the primary reason for exclusion. If the reviewers disagreed, they resolved conflicts by discussion and consensus or by consulting a third member of the review team. The full-text review form reviewers used is reproduced in Appendix B.

The project coordinator tracked results of the abstract and full-text reviews in an EndNote database (EndNote® X4). Appendix B contains a complete list of studies excluded during the full-text review, denoted by their primary reason for exclusion.

We screened unpublished studies identified through grey literature search and review of SIPs using the same title/abstract and full-text review processes.

Data Extraction

We developed a template for evidence tables for data synthesis using the PICOTS framework. For the systematic reviews and additional studies that met inclusion criteria, we abstracted relevant information into these evidence tables using Microsoft Excel. We abstracted characteristics of study populations, interventions, comparators, settings, study designs, methods, and results. Data from studies included in the systematic reviews were abstracted as they were presented in the review, although we did refer to the original article to obtain additional information for clarification purposes, to determine if additional data concerning subgroup analyses and outcomes of interest, including harms, were contained in any of the studies and not reported in the systematic review results. Six trained members of the team participated in the data abstraction. One of the reviewers initially abstracted the relevant data from each included article and a second senior member of the team reviewed each data abstraction against the original article for completeness and accuracy.

Risk-of-Bias Assessment

For each included systematic review and additional study identified, we assessed the potential for selection bias, performance bias, attrition bias, detection bias, and outcome reporting bias using instruments that our EPC previously used successfully (Appendix tables E-1 through E-5). The risk-of-bias assessment was conducted using two tools, one appropriate for trials based on the Cochrane risk- of-bias tool[40] and modified by our EPC to be used to also evaluate observational studies (including instructions to reviewers that some questions concerning trial study design would be considered not applicable) and AMSTAR,[41] appropriate for systematic reviews. We did not reevaluate the risk of bias of the individual studies included in the five systematic reviews and relied on the original authors' assessments. In each systematic review, the authors had concluded that all included studies were not high risk of bias. Two independent reviewers rated the risk of bias for each systematic review and each study not included in one of the previous systematic reviews. Disagreements between the two reviewers were resolved by discussion and consensus or by consulting a third member of the team.

Results of this assessment are summarized by a rating of low, medium, or high risk of bias. In general, a study with a low risk of bias has a strong design (adequate randomization and allocation concealment if a trial and controls for concurrent treatments), measures outcomes appropriately including whether there was blinding of the patient and provider (if possible) and outcome assessor, uses appropriate statistical and analytical methods, and reports low attrition. Studies with a medium risk of bias are those that do not meet all criteria required for low risk of bias but do not have flaws that are likely to cause major bias. Studies with a high risk of bias include those with at least one major issue that has the potential to cause significant bias and thus might invalidate the results. Examples of flaws leading to a high risk-of-bias rating include different application of inclusion/exclusion criteria between groups, substantial differences in groups at baseline, high overall attrition, or differential attrition across study conditions, lack of control for concurrent treatment or among cohort studies, lack of control for critical potential

confounding, either through design or statistical analyses. A high risk-of-bias rating was assigned to studies in which the critical information needed to make that assessment was not reported or was unclear. To maintain a focus on interpretable evidence, we opted to not include studies with a high risk in the synthesis of benefits findings in the Results chapter of this review. However, we included high risk-of-bias studies in our evidence for harms. We list each study rated as high risk of bias, reconciled reviewer responses to each question in the risk-of-bias instrument, and the main reasons we gave it that rating in Appendix E.

Data Synthesis

Across all included studies, the populations, interventions, and outcome measures in the additional data were heterogeneous and did not lend themselves to a pooled analysis. They also did not lend themselves to updating the meta-analyses from the five earlier systematic reviews. Thus, we did all analyses qualitatively, based on our reasoned judgment of similarities in measurement of interventions and outcomes, and homogeneity of patient populations. Evidence used in the synthesis included the results from the earlier meta-analyses and additional data from individual studies as presented in the systematic reviews and in the original articles, and data from the articles included from our own searches.

Strength of the Body of Evidence

In the key points section we present the strength of evidence for each comparison and overarching outcome (e.g., OME signs and symptoms, measured hearing) as specified for each KQ. We graded the strength of evidence based on the guidance established for the AHRQ Effective Health Care Program EPCs conducting comparative effectiveness reviews, as detailed in the paper by Owens and colleagues.[37] The EPC approach incorporates four key domains: risk of bias, consistency, directness, and precision of the evidence.

- Risk of bias is determined according to the "degree to which the included studies for a given outcome or comparison have a high likelihood of adequate protection against bias." It is graded as high, medium, or low.
- Consistency is the "degree to which reported effect sizes from included studies appear to have the same direction of effect." Each body of evidence is graded as consistent or inconsistent. Consistency cannot be assessed when a body of evidence has only a single study (unknown or not applicable).
- Directness is determined based on "whether the evidence links the interventions directly to health outcomes." It is graded direct or indirect. In this review, most of the included measures are direct.
- Lastly, precision is determined according to "the degree of certainty surrounding an effect estimate" for each outcome separately. "Precise" indicates a clinically useful conclusion that is statistically significant, and "imprecise" indicates that no conclusion can be drawn as to whether either treatment is superior or whether the treatments are equivalent.

The overall grades for strength of evidence, based on the scores for the above domains, are described in Table 4. Grades reflect the strength of the body of evidence to answer the KQs on the comparative effectiveness, efficacy, and harms of the interventions in this review for each key outcome.

Table 4. Definitions of the grades of overall strength of evidence

Grade	Definition
High	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of the effect and may change the estimate.
Low	Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate.
Insufficient	Evidence either is unavailable or does not permit estimation of an effect.

Source: Owens et al., 2010[37]

Two reviewers assessed each domain independently and also assigned an overall grade for intervention comparisons for each key outcome; they resolved any conflicts through consensus discussion. If they did not reach consensus, the team brought in a third party to settle the conflict. Typically, evidence from just one study was considered insufficient to permit confidence in the estimation of an effect. Exceptions were single study bodies of evidence consisting of a relatively large, low risk of bias trial, particularly if it showed a large magnitude of effect.

Applicability

We assessed the applicability both of individual studies and of the body of evidence. For individual studies, we examined factors that may limit applicability based on the PICOTS structure. Examples of characteristics examined include:

- Population
  - Narrow eligibility criteria, or exclusion of patients with comorbidities;
  - Large differences between demographics of the study population and community patients.
- Intervention
  - Intensity and delivery of interventions that may not be feasible for routine use;
  - Highly selected intervention team or level of training/proficiency not widely available.
- Comparators
  - Comparison group that does not represent an available alternative treatment.

Such factors may be associated with heterogeneity of treatment effect and may lessen our ability to generalize the effectiveness of an intervention to use in everyday practice. We abstracted key characteristics of applicability into evidence tables.

During data synthesis, we assessed the applicability of the body of evidence using the abstracted characteristics. KQ 4 includes an analysis of intervention effectiveness in population subgroups.

Peer Review and Public Commentary

Experts in OME, specifically clinicians and researchers specializing in ear, nose, and throat treatment, pediatrics, and audiology, and evidence-based interventions, were invited to provide external peer review of the draft comparative effectiveness review. AHRQ and an Associate Editor also provided comments. The draft report was posted on the AHRQ Web site for 4 weeks to elicit public comment. We responded to all reviewer comments and noted any resulting revisions to the text in the "Disposition of Comments Report." This disposition report will be made available 3 months after the final comparative effectiveness revew is posted on the AHRQ Web site.

Results

Introduction

This chapter first presents the results of our literature searches. We then discuss the findings of our analyses for each Key Question (KQ) in turn; we address the following as relevant to the KQs, in this order:

- Surgical procedures, specifically:
  - tympanostomy tubes (TT), comparisons of different types or insertion approaches
  - TT versus myringotomy or nonsurgical interventions (delayed treatment or watchful waiting);
  - TT plus adenoidectomy versus myringotomy plus adenoidectomy or adenoidectomy alone;
  - myringotomy versus myringotomy, comparison of different approaches, various combinations of myringotomy plus adenoidectomy;
  - adenoidectomy versus nonsurgical interventions or TT; and
  - pharmacological interventions, specifically, oral or topical nasal steroids
- Nonpharmacological interventions, specifically, autoinflation
- Other treatment strategies, specifically delayed treatment or watchful waiting are presented in comparison with other treatment approaches above.

We did not find any randomized controlled trial (RCT) evidence concerning complementary or alternative medicine (CAM) treatments or procedures; therefore, this intervention will not be discussed further.

We describe all included studies for each treatment comparison at the beginning of the results for KQ 1. Because virtually all studies are included in KQ 1, we did not repeat the description of studies for other KQs. Exceptions are of the specifically identified studies in these tables included in the review solely for evidence of harms (KQ 3).[43-45] We then present key points along with grades for strength of evidence for major comparisons and outcomes, followed by text and tables providing a more detailed synthesis of the included studies. When no studies reported on categories of outcomes, we note this finding in key points and do not repeat it in detailed synthesis.

We present all of the relevant results from meta-analyses that were conducted in the recent Cochrane reviews as part of our evidence. Because of the heterogeneity of populations, interventions, or outcomes in the newly included studies and because all of the included earlier reviews were recently completed, we did not find any additional bodies of information that lent themselves to quantitative synthesis. As a result, all results new to this systematic review are based on qualitative "narrative" synthesis.

In summary tables that describe included studies, we specify not only study type (e.g., RCT, nonrandomized trial, or observational study) but also whether the arms of the study were determined by ear or by participant. Evidence tables for included studies are provided in Appendix C and include the risk-of-bias assessments for each of the included studies and systematic reviews.

We included in these analyses only studies that we had rated as low or medium risk of bias, except for KQ 3 (harms) where two studies (in three articles) with high risk of bias were included.[43-45] Studies rated high risk of bias are listed in Appendix E together with the principal reason(s) for that rating.

We did not include in our analysis 24 articles concerning benefits of treatment that we evaluated as high risk of bias because we believed that they would not provide reliable estimates in our qualitative synthesis and could detract from the findings in the more methodologically rigorous studies. Three RCTs[46-48] were determined to have a high risk of bias because participants received co-interventions that were either not accounted for in the analysis or because they received interventions included in comparison arms. Seven nonrandomized controlled trials[43,44,49-53] were determined to have a high risk of bias for similar reasons as the RCTs and/or because baseline characteristics of participants were not adequately reported to determine that the study arms were comparable. Similarly, 14 cohort studies[26,45,54-65] inadequately reported baseline characteristics to evaluate selection bias and did not control for potential confounding; and one case control study[66] inadequately reported patient characteristics and inclusion/exclusion criteria so that we were unable to determine if outcome differences were due to the procedures that patients received or patient characteristics.

Detailed strength of evidence tables are presented in Appendix F. The final strength of evidence grades for the most critical findings are presented in this chapter. A description of procedures for measuring hearing, language, and quality-of-life measures is found in Table 5.

Table 5. Description of procedures/measures of hearing, language and quality of life related to OME

Method of Measurement and Example Indices	Description	Range/Meaning of Possible Scores	Improvement Indication
Hearing Measures: Pure-tone audiometry (PTA)	PTA is a behavioral test used to measure hearing sensitivity. Pure-tone thresholds (PTTs) or hearing levels (HLs) indicate the softest sound audible to an individual at least 50% of the time. Results are often averaged over different frequency levels. A modified form is sweep audiometry.	Normal hearing is age dependent: 15 dB for young children, 20 dB for children through early adolescence; and 25 dB for older adolescents and adults. The least intense audible sound is 0 dB. A sound 10 times more powerful is 10 dB, a sound 100 times more powerful than 0 dB is 20 dB, and a sound 1,000 greater is 30 dB. A 10 dB increase from 35 to 45 is much larger than a threshold increase from 15 dB to 25 dB.	Reduction in PTA HLs
Hearing Measures: Air-Bone Gap (ABG)	A method of diagnosing conductive hearing loss. It is the difference in audiometric hearing thresholds using bone conduction and air conduction.	The degree of conductive hearing loss is represented by difference in audiometric hearing thresholds using bone conduction in which sound transmission bypasses the middle ear and air conduction. Greater ABGs indicate greater hearing loss.	Reductions in ABGs
Hearing Measures: Sweep audiometry	A modified form of pure tone audiometry.	Same interpretation as PTA.	Same as PTA
Hearing Measures: Speech Recognition Threshold (SRT)	The speech recognition threshold is the softest level at which speech is understood.	Scores are given in dBs and have the same meaning as pure tone hearing levels.	Reduction in SRTs

Table 5. Description of procedures/measures of hearing, language and quality of life related to OME (continued)

Method of Measurement and Example Indices	Description	Range/Meaning of Possible Scores	Improvement Indication
Speech and Language: Receptive language	Receptive language measures how one understands language.	Usually provided as a standard score that has been normed on a representative sample.	Increases in standard scores
Speech and Language: Expressive language	Expressive language measures how one produces language.	Usually provided as a standard score that has been normed on a representative sample.	Increases in standard scores
Quality of Life: Otitis Media 6 (OM-6)	Parent-reported scale measuring effects of OME on quality of life.	1-7, higher scores associated with poorer quality of life.	Decreases

dB = decibels; OME = otitis media with effusion

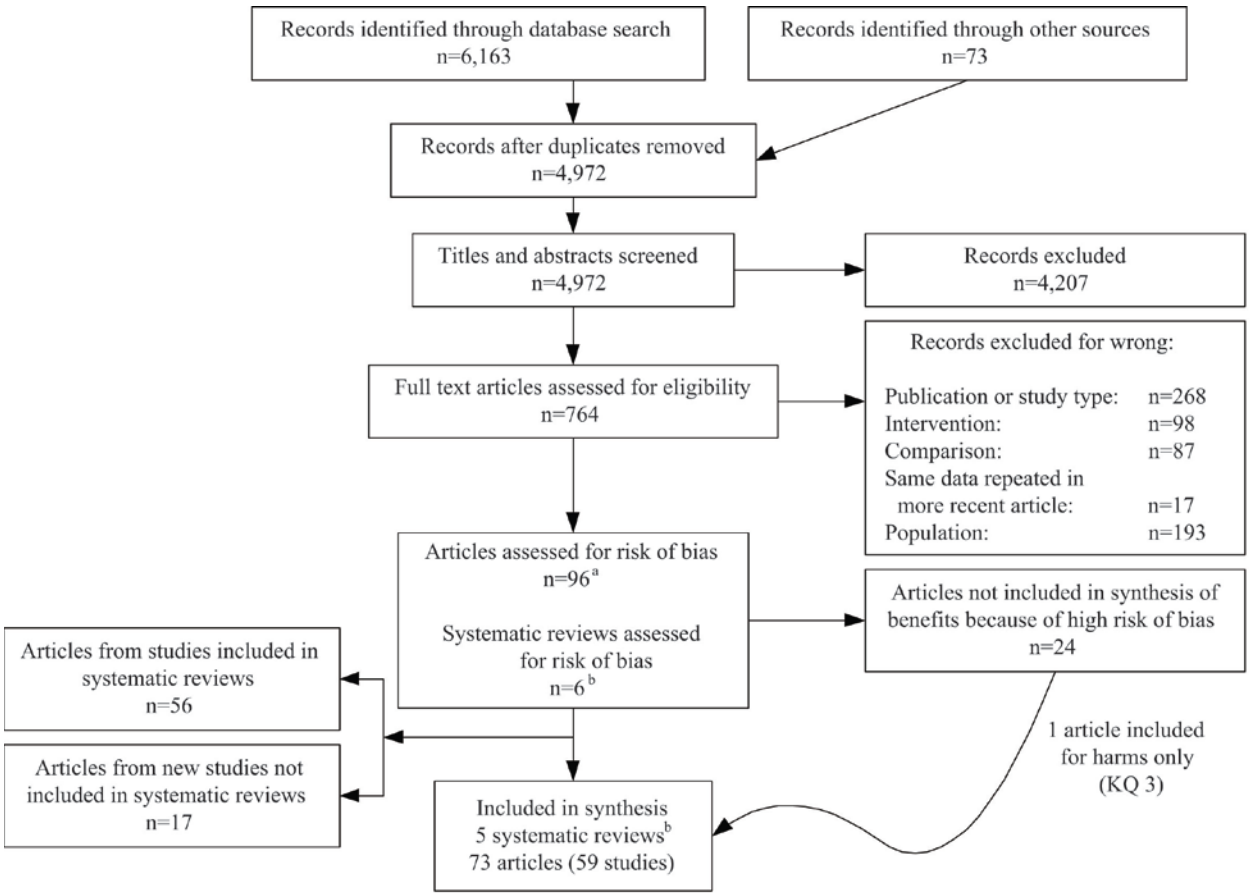
Results of Literature Searches

Figure 3 presents our literature search results. Initial literature searches completed on February 28, 2012, and updated on August 13, 2012, for the current report identified 4,967 unduplicated citations. Appendix A provides a list of all search terms used and the results of each literature search.

After applying our eligibility and exclusion criteria to titles and abstracts of all identified citations, 764 citations for full-text review remained. We reapplied our inclusion criteria and excluded 663 of these articles from further review before risk-of-bias assessment. Appendix B provides a list of excluded studies and reasons for exclusion at the full-text stage.

Of the 102 publications included after full-text review (96 articles and five systematic reviews [one systematic review was updated and so was included as 2 reports]), we dropped 24 articles from further analysis of benefits because of their high risk of bias but included 1 of these articles in our assessment of harms. Thus, we included a total of 73 articles (reporting on 59 studies) and data from 5 systematic reviews in qualitative synthesis; including 17 newly identified articles (reporting on 17 studies) and 56 articles identified in the earlier reviews (reporting on 42 studies). Evidence tables for these articles and systematic reviews are provided in Appendix C and risk-of-bias assessments for the newly identified articles can be found in Appendix D. Risk-of-bias assessments are also provided for the 24 high risk-of-bias studies in Appendix E.

Figure 3. Disposition of articles on otitis media with effusion



[a]We accepted the risk of bias assessment conducted by the review authors for the studies included in one of the 5 earlier systematic reviews (56 articles). We conducted our own risk of bias assessment for 17 new articles not included in one of those reviews.
[b]One of the 5 included systematic reviews was updated during our peer review period. We reviewed both the original report and the update.

Of the 59 studies included in this review, 49 were RCTs (33 by person, 12 by ear, 4 by person and ear), six were nonrandomized control trials (one by person and five by ear), and four were cohort studies. Of the 17 articles not included in one of the five systematic reviews, we assessed 15 as medium risk of bias, one as low risk of bias and one as high risk of bias. Of the five included systematic reviews, four were limited to RCTs. We assessed four systematic reviews as low risk of bias and one as medium risk of bias (Appendix E, Table E-3 presents details of these assessment).

A study by Paradise et al. was cited as evidence in two of the systematic reviews[21,22] and is included as evidence within our review.[67-74] This seminal study concerning TT for otitis media with effusion (OME) merits specific mention here because it was very influential. Investigators enrolled infants from birth to 2 months of age from a variety of clinical settings around Pittsburgh, Pennsylvania. The randomized subjects, who were from lower socioeconomic status backgrounds than the general population[68] and mainly were African American or White, were recruited from both urban and rural areas.[70] The study excluded children with other comorbid risk factors such as prematurity, being small for gestational age, serious illness, major congenital

anomaly, or maternal limitations that may preclude their children from participating in the study. The study enrolled more than 6,000 subjects who were followed to determine if they met the criteria for OME. Once children were enrolled in the study, the investigators followed the sample to evaluate middle ear effusion (MEE) at least monthly using validated pneumatic otoscopy. Children were eligible for randomization if they had: bilateral OME for >90 days, unilateral OME for >135 days, or a more prolonged intermittent presence of OME up until age 3 years; and hearing thresholds less than 40dB (decibels).

Of those followed, 588 became eligible for randomization, and 429 were randomized and included in the study. The investigators randomized participants to either immediate or delayed TT insertion., By the time they received TT, the immediate treatment group had already had 3 months of OME and the delayed group had 9 months of OME (3 months prior to being randomized, followed by 6 months of delay) for bilateral effusion and 12 total months for unilateral OME (3 months prior to being randomized, followed by 9 months of delay). Children in the delayed group could get TT placement more quickly if parents preferred or if other clinical indications existed. Average age at randomization was 15 months. The analysis and interpretation of results were complicated by some of the early treatment group and a large number of the delayed group not receiving treatment. By 3 years of age, 83 percent of the early treatment group and 39 percent of the delayed treatment group had received TT.[68] The study followed children until they were between 11 and 13 years of age with little attrition. Outcomes included clinical findings such as effusion and hearing and also functional outcomes such as developmental status and school performance.

KQ 1. Comparative Effectiveness of Interventions: Clinical Outcomes or Health Care Utilization

Surgical Interventions: Tympanostomy Tube Comparisons

Description of Studies

The included evidence about comparisons of different types of TT consisted of 14 studies, (eight studies from a recent systematic review by Hellstrom et al.[21] and six additional studies). These are indicated in Table 6. All studies compared groups by "ears," so that the participant acted as his or her own comparison, although one study also randomized by person. In some studies, the choice of ear that received a particular treatment was randomized and these are considered RCTs; in others, the choice of ear was based on "left" versus "right" ear or other criteria and these studies are considered nonrandomized trials if they meet other trial criteria.

Of the TT comparison studies included in the Hellstrom systematic review, five studies provide evidence for KQ 1.[75-79] Three additional TT comparison studies in the Hellstrom review were limited to harms and are discussed in relation to KQ 3.[80-82] We identified six additional studies; five of these provide evidence for KQ 1.[83-87] One other TT comparison study provides evidence for harms only.[45]

Of the 10 studies that provided evidence for KQ 1, seven are RCTs; four of these were included in the Hellstrom review[75-78] and we identified three additional studies.[83,85,87] Hellstrom included one nonrandomized controlled trial,[79] and we identified a second.[84] One observational study was a retrospective medical record review.[86]

Table 6. Characteristics of studies: Tympanostomy tube comparisons

Study, Study Type, Country	Arm N Randomized	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Followup	Age (Range)	Risk of Bias
Wielinga et al.,1990[83] RCT by ear Ireland	G1: Goode Silicon tube (N=15) G2: Teflon Armstrong tube (N=15)	Otoscopy, PTA, tympanometry	≤ 6 months	Include: OME, 6 months unsuccessful treatment with standard decongestive meds; mucoid secretion	Mean: 6.8 years	Male mean: 7 years Female mean: 6 years	Medium
Abdullah et al., 1994[84] NRCT by ear England	G1: Trimmed high-grade silicone Shah permavent tube (N=25) G2: Polyethylene Shah tube (N=25)	NR	NR	Include: Age 3-10 years, de novo MEE Exclude: History of significant AOM	29 months	Mean: 6 years (3-10 years)	Medium
Licameli et al., 2008[85] RCT by ear United States	G1: Phophoryl-choline-coated fluoroplastic Armstrong tube (N=70) G2: Uncoated fluoroplastic Armstrong tube (N=70)	NR	3-4 months	Include: OME with 3-4 months medical management Exclude: Prior TT	24 months	Mean: 19 months (8-51 months)	Medium
Iwaki et al., 1998[86] Observational by ear Japan	G1: Teflon Shepard tube (N=75) G2: Silicone Goode-T tube (N=39) G3: Silicone Paparella II tube (N=106)	Audiometry, tympanometry and clinical history	6 months	Include: 25 dB air-bone gap conductive HL, failed politerization and unsuccessful conservative management, retracted and glue-colored TM Exclude: children with craniofacial problems	24 months	Mean: G1: 6.2 G2: 6.2 G3: 5.8 (3-12 years)	Medium
Ovesen et al., 2000[87] RCT by person and by ear Demark	G1: TT[a] + N-acetylcysteine instilled (N=37) G2: TT[a] + placebo vehicle (N=38)	Otiomicroscopic examinations including tympanometry	3 months	Include: OME, pressure <200mmHg Exclude: Recent antibiotics or AOM at time of surgery	39 months	Mean: 38 months (1-7 years)	Medium

Table 6. Characteristics of studies: Tympanostomy tube comparisons (continued)

Study, Study Type, Country	Arm N Randomized	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Followup	Age (Range)	Risk of Bias
Slack et al., 1987[45b] Retrospective cohort by ear	G1: Shepard TT (N=214) G2: Shah TT (N=70) G3: Paparella TT (N=275)	NR	NR	Include: Children < 16 years old; TT inserted for OME in 1983	Until extrusion or end of study period	Children < 16 years old	High
Hellstrom et al., 2011[21] Systematic Review Hampal et al., 1991,[75] Heaton et al.,1991,[76] Hern and Jonathan, 1999,[77] Youngs and Gartland, 1988,[78] Pearson et al., 1996,[79] Kinsella et al., 1994,[80b] Salam and Cable, 1993,[81b] and Hampton and Adams, 1996[82b]	Arms differ across 9 studies (arms appear in Table 7 and Table 31) (N=828 participants)	Varies by study	Minimum of 3 months	Include: RCTs (individual or ear), NRCTs, and cohort studies published between 1966 and 2007 of effectiveness of TT on hearing, language development, QOL and of complications	Various	Children or adolescents, one study included an unknown mix of adults and children[79]	Medium

AOM = acute otitis media; dB = decibels; G = group; HL= hearing loss; MEE = middle ear effusion; mmHg = millimeters of mercury; mos = months; N = number; NR = not reported; NRCT = nonrandomized controlled trial; OME = otitis media with effusion; PTA = pure-tone audiometry; QOL = quality of life; RCT = randomized controlled trial; TM = tympanic membrane; TT = tympanostomy tubes; tx = treatment [a]Tympanostomy tube type not specified.
[b]Study included for harms (KQ 3) only.

TT comparisons included tube design (shape or size), materials, and routes or techniques for insertion. TT are often categorized by length of time they can be expected to stay in place—broadly speaking, short- or long-term. Short term tubes have an average extrusion time of 8 months to 16 months while long-term tubes have average extrusion rates from 18 months to 3 years or until they are removed by a surgeon.[24,88,89] Virtually all evidence is limited to children and only one study identified that a portion of the sample included children less than 1 year of age.[85]

Key Points

We found that variation in length of retention corresponded to whether TT were designed to be short versus long-term. Evidence for other comparisons was sparse: tube size and material, approach to insertion, and topical prophylaxis therapies.

OME recurrence was inconsistently associated with length of retention (insufficient strength of evidence). No studies compared OME recurrence based on other design features (strength of evidence insufficient because of no evidence).

Hearing outcomes did not differ between short- and long-term TT in two studies (strength of evidence insufficient because of sparse and imprecise data).

No studies compared vestibular outcomes, or health care service use as a function of type of TT or routes or techniques in their insertion (strength of evidence insufficient because there are no studies).

Detailed Synthesis

Types of TT were compared in relation to clinical outcomes including tube retention time, OME recurrence, and hearing (Table 7). Included studies compare outcomes based on TT design TT material, and TT placement position and technique.

Table 7. Clinical outcomes: Tympanostomy tube comparisons

Study	Arm (N Randomized)	Study Duration Until Outcome Measurement (N Analyzed if Reported)	Tube Retention (% Retained Unless Otherwise Noted)	OME Recurrence	Measured Hearing
Wielinga and Smyth, 1990[83]	G1: Goode Silicon tube (N=15) G2: Teflon Armstrong tube (N=15)	NA	Mean months (range): G1: 52.5 (5-88) G2:17.5 (1-56) p=NR	NR	Mean hearing loss: G1: 14dB G2: 11dB p=NR
		Year 1	G1: 93 G2: 67 p=NS	NR	NR
		Year 2	G1: 80 G2: 13 p<0.05	NR	NR
		Year 3	G1: 73 G2: 7 p<0.05	NR	NR
		Year 4	G1: 53 G2: 7 p<0.05	NR	NR
		Year 5	G1: 33 G2: 0 p=NS	NR	NR
		Years 6 and 7	G1: 27 G2: 0 p=NS	NR	NR
Abdullah et al., 1994[84]	G1: Trimmed high grade silicone Shah permavent tube (N=25) G2: Polyethylene Shah tube (N=25)	Month 12 (N=25)	G1: 100 G2: 56 p=NR	NR	NR
		Month 29 (N=17)	G1: 71[a] G2: 18[a] p=NR	G1: 6%[a] G2: 53% p=NR	NR
Licameli et al., 2008[85]	G1: Phophoryl-choline-coated fluoroplastic Armstrong tube (N=70) G2: Uncoated fluoroplastic Armstrong tube (N=70)	Year 2	G1: 21 G2: 28 p=0.84	NR	NR
Iwaki et al., 1998[86]	G1: Teflon Shepard tube (N=75) G2: Silicone Goode-T tube (N=39) G3: Silicone Paparella II tube (N=106)	Seen at 1-3 month intervals postsurgery and at 1-3 month post- tube removal or extrusion	Mean months: G1: 5.9 G2: 10.7 G3: 15.1 p=NR	NR	NR
		24 months	G1: 9.3 G2: 20.5 G3: 50 p=NR	G1: 40% G2: 28.2% G3: 17.0% p<0.01	NR

Table 7. Clinical outcomes: Tympanostomy tube comparisons (continued)

Study	Arm (N Randomized)	Study Duration Until Outcome Measurement (N Analyzed if Reported)	Tube Retention (% Retained Unless Otherwise Noted)	OME Recurrence	Measured Hearing
Ovesen et al., 2000[87]	G1: TT[b] + N-acetylcysteine instilled (N=37) G2: TT[b] + placebo vehicle (N=38)	Mean months (range): 16.5[a] (11 to 39)	Mean months: G1: 9 G2: 7 p>0.14	Total # episodes G1:15 G2: 25 p=NR Persistent OME: G1: 13.5% G2: 37% p<0.025 Recurrence at single examination postextrusion: G1: 16% G2: 13% p=NR	NR
Hellstrom et al., 2011[21] Systematic Review	1 RCT (by ear) Hampal et al., 1991[75] G1: Shah tube (N=116 ears) G2: Mini-Shah (N=116 ears)	Year 1 (N=91)	G1: 70% G2: 6% p<0.001	G1: 7% G2: 18% p<0.05	Mean threshold at 1 year: (N=64) G1:17.5 dB G2:18.4 dB p=0.34 Mean threshold at 2 years: (N=69) G1: 17.2 dB G2: 17.1 dB p=NS
	1 RCT (by ear) Heaton, et al., 1991[76] G1: Shepard tube G2:Sheehy tube (Total=292 ears)	21-36 months (N=124)	G1: 8% G2: 24%[a] p<0.001	G1:38 (29%) G2:28 (21%)[a] p = NS	NR
	1 RCT (by ear) Heaton, et al., 1991[76] (second study analysis combines TT types) G1: Anteroinferior placement of TT in TM (N=191 ears) G2: Posteroinferior placement of TT in TM (N=71 ears)	1-12 months post-TT extrusion	G1 remaining *in situ* longer than G2 whichever TT was used p=0.002 Shepard: G1: 9% vs. G2: 6% Sheehy: G1: 29% vs. G2: 8%	NR	NR

Table 7. Clinical outcomes: Tympanostomy tube comparisons (continued)

Study	Arm (N Randomized)	Study Duration Until Outcome Measurement (N Analyzed if Reported)	Tube Retention (% Retained Unless Otherwise Noted)	OME Recurrence	Measured Hearing
Hellstrom et al., 2011[21] (continued)	1 RCT (by ear) Hern and Jonathan, 1999[77] G1: Shah TT placed in anterosuperior quadrant (N=54 ears) G2: Shah TT placed anteroinferior quadrant (N=54 ears)	3-26 months until extrusion	Mean months: G1: 12.7 months G2: 13.7 months Diff: 1 (95% CI, -2.96 to 0.96)	NR	NR
	1 RCT (by ear) Youngs and Gartland, 1988[78] Companion: McRae, et al.,1989[90] G1: Shah Teflon tube + aspiration before placement (N=55 ears) G2: Shah Teflon tube (no aspiration) (N=55 ears)	1 month (N=53)	G1: 98% G2: 98%		Audiometric improvement at the 5% level: (N=51) G1 vs. G2: no difference
		3 months	G1: 46 (90%) G2: 47 (92%) p=1.0	NR	Audiometric improvement at the 5% level: (N=51) G1 vs. G2: no difference
		6 months	G1: 39 (76%) G2: 41 (80%) p=0.71	NR	NR
		12 months	G1: 24 (47%) G2: 21 (41%) p=0.71	NR	NR
		18 months	G1: 4 (7.8%) G2: 3 (5.8%) p=1.0	NR	NR
		3 months	G1: 143 (96%) G2: 143 (96%) p=NS[a]	Bilateral effusion[a] G1: 5 (5.4%) G2 10 (10.9%)	Hearing gain (N=165) G1: 13.6 dB G2: 12.9 dB p=NS
	1 NRCT (by person) Pearson et al., 1996[79] G1: Teflon Shah TT + steroid/abx otic drops postoperatively G2: Teflon Shah TT (N=165)	3 months	G1: 143 (96%) G2: 143 (96%) p=NS[a]	Bilateral effusion[a] G1: 5 (5.4%) G2 10 (10.9%)	Hearing gain (N=165) G1: 13.6 dB G2: 12.9 dB p=NS

abx= antibiotic; CI = confidence interval; dB = decibel; Diff = difference; G = group; N = number; NA = not applicable; NR = not reported; NRCT = nonrandomized controlled trial; NS = not significant; OME = otitis media with effusion; RCT = randomized controlled trial; TM = tympanic membrane; TT = tympanostomy tube; vs. = versus

[a]Calculated by investigator.

[b]Tympanostomy tube type not specified.

Tube Retention and OME Recurrence

We identified five studies that compared outcomes based on TT design. Three of these studies compared long-term with short-term TT types. Wielinga et al. compared silicon Goode-T tubes (considered long-term TT) and Teflon Armstrong TT (considered short-term TT) and demonstrated that the average retention of the Goode-T tubes was longer, an average of 52 months (range: 5-88 months) while the Teflon Armstrong TT were retained an average of 17 months (range: 1-56 months). Another RCT compared Sheehy TT (considered long term) and Shepard TT (considered short term).[76] The Sheehy TT were retained significantly longer than the Shepard TT; at up to 36 months, 24 percent of ears retained the Sheehy TT, as did 8 percent of ears with the Shepard. An observational study also compared TT types considered long term (Goode-T tubes and Paparella II tubes) and short term (Shepard Teflon tubes).[86] The Paparella II TT was retained for 15 months, the Goode-T tubes were retained for almost 11 months, and the Shepard TT were retained for six months. Statistical differences were not reported in this study.

An RCT of 116 participants compared two types of Shah TT, the standard Shah and the mini-Shah; the standard Shah TT had significantly longer retention; at 1 year, 70 percent of those with the Shah retained their TT and 6 percent of those with the mini-Shah.[75] A second comparison of Shah TT demonstrated that at 29-month followup, silicone permavent tubes had a 71 percent retention rate as contrasted with an 18 percent rate for the polyethylene Shah tubes.[84]

Four studies examined TT retention based on TT placement technique or position. One small study (N=54) compared anteroinferior versus anterosuperior placement location of Shah (short acting) TT and found that it did not affect length of time that the TT stayed in place (mean months: 12.7 vs. 13.7).[77] In contrast, in a second larger study of Shepard and Sheehy TT (N=292 ears) anteroinferior placement was retained longer than anterosuperior placement.[76]

N-acetylcysteine infused at the time of insertion was not found to change retention time.[87] A second study reported that infusion of steroid and antibiotic combined otic drops infused at the time of surgery did not change retention rate at 3 months.[79]

One study compared extrusion rates based on material of the TT, Armstrong TT (considered short term), with and without phosphorylcholine-coated fluoroplastic. Rates did not differ appreciably at 2-year followup (21% vs. 28%, respectively, p=0.84).[85]

OME recurrence was inconsistently associated with length of retention. Two studies reported a higher rate of OME recurrence in the TT that had a shorter retention: mini-Shah TT (18%) versus Shah (7%),[75] and Shepard (40%) versus Goode-T (28%) versus Paperella (17%).[86] One study[76] that reported a difference in retention rates, did not find a reduction in OME recurrence associated with longer lasting TT. Another study[83] with differences in retention rates did not examine OME recurrence. Results were measured at different end points and generally, the samples were small.

Measured Hearing

Two studies compared hearing outcomes based on TT design. Hampal et al.[75] found no differences between Shah and mini-Shah TT in hearing thresholds at 1 and 2 years after placement.[75] Similarly, Wielenga and Smith compared short-term (Armstrong) and long-term (Goode-T) TT, and found no differences in mean hearing loss.[83]

Two studies examined hearing outcomes by technique of tube insertion. Youngs and Gartland (1988) failed to find a difference in hearing outcomes based on aspiration before TT placement.[78] Similarly, infusion of steroid and antibiotic drops at the time of TT placement did not change hearing outcomes at up to 30 months after placement.[79]

Surgical Interventions: Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Description of Studies

The evidence consisted of 12 studies, all of which were RCTs (Table 8). Two recent systematic reviews, one of which was a Cochrane review by Browning et al.[22] included 10 studies and the second was by Hellstrom et al.,[21] which included six of the studies in the Browning review (three additional reports of later followup of studies included in Browning review). We identified two additional studies through our search.[91,92] We also found later published results of the Medical Research Council (MRC) Trial of Alternative Regimens in Glue Ear Treatment (TARGET) study. The study's preliminary findings were included in the Browning review.[19] We also present outcomes in this section that were reported in later follow-up papers of Paradise and colleagues but were not discussed in either the Browning or the Hellstrom reviews.

Table 8. Characteristics of studies: Tympanostomy tubes versus watchful waiting or myringotomy

Study, Study Type Country	Arm (N Randomized)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Study Followup	Age	Risk of Bias
Browning et al., 2010[22] Systematic Review Maw et al.,1999,[93] MRC TARGET, 2001 and 2012,[19] Rovers et al., 2000,[94] Gates et al., 1987,[95] Mandel et al., 1992,[96] Paradise et al., 2001,[68] Black et al., 1990,[97] Dempster et al.,1993,[98] Maw and Herod, 1986,[99] and Rach et al., 1991[100]	Arms differ across comparisons: 10 trials (1,728 participants)	Combination of otoscopy (including pneumatic and microscopic), tympanometry and audiometry	NR	Include: RCTs of short-term TT; randomization could be by child or by ear Exclude: Observational studies or NRCTs; studies including adenoidectomy (unless the adenoidectomy arms could be excluded)	Child: 6-9 and 12 months Ear: 4-6, 7-12 months	1 to12 years	Low

Table 8. Characteristics of studies: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study, Study Type Country	Arm (N Randomized)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Study Followup	Age	Risk of Bias
Koopman et al., 2004[91] RCT by ear Amsterdam	G1: Donaldson or Goode TT + cold knife myringotomy (N=208) G2: Laser myringotomy (N=208)	Binocular otoscopy tympanometry and audiometry	3 months	Include: Bilateral OME; <11 years; 3 months of hearing problem per parent report Exclude: Unilateral OME; uncooperative; clinically admitted patients; asymmetric perceptive HL; previously operated ears with other than myringotomy or TT	6 months	<11 years	Medium
Mandel et al., 1989[92] RCT, clustered first by HL United States	Without significant HL G1: Myringotomy (N=27) G2: Myringotomy + Armstrong TT (N=30) G3: No surgery (N=29) With significant HL G4: Myringotomy (N=12) G5: Myringotomy + Armstrong TT (N=11)	Tympanometry and middle ear muscle reflex testing	2 months and medical treatment	Include: MEE ≥2 months duration persisting after a 14 day course of antimicrobial and pseudoephedrine Exclude: craniofacial malformations; systemic illnesses; history of ear surgery	3 years	7 months to 12 years	Medium

G = group; HL= hearing loss; MEE = middle ear effusion; MRC = Medical Research Counsel; N = number; NR = not reported; NRCTs = nonrandomized controlled trials; OME = otitis media with effusion; RCT = randomized controlled trial; TARGET = Trial of Alternative Regimens in Glue Ear Treatment; TT = tympanostomy tubes; yrs = years

Watchful waiting, also known as active monitoring, is defined as a period of time in which no surgery is performed; the patient's condition is monitored at specified periods; if the OME or sequelae worsen, treatment could be initiated. Delayed treatment with TT was the strategy used in the RCT of Paradise et al., 2001[68] and was defined as providing TT after a delay of 6 months for bilateral OME and 9 months for unilateral OME if the effusion persisted.

The Browning et al. review summarized 10 RCTs of TT in treating children with OME; seven of which were in comparison with watchful waiting or delayed treatment[68,93,94,98-101] and two were in comparison with myringotomy in the control ear;[95,97] Mandel[96] examined both

myringotomy and watchful waiting (separately) in relation to TT. While Hellstrom[21] reviewed six RCTs comparing TT with watchful waiting or myringotomy that were all included in the Browning et al. review, data on hearing outcomes from Gates et al., 1989[102] were only reported in the Hellstrom review.[21]

We identified two additional studies that compared TT placement with either myringotomy and/or watchful waiting.[91,92] Mandel[92] compared 3-year outcomes in children who received TT, myringotomy or no surgery as well as outcomes in a small group of children with conductive hearing loss who received either TT or myringotomy. Koopman et al. examined children who received TT and laser myringotomy in randomized ears, following the children through 6 months post-treatment.[91]

All of these 12 RCTs were of children, most of whom were younger than 12 years of age but older than 1 year (except for the Paradise et al., 2001 study where participants could have been as young as 3 months). None of the studies included children with any medical conditions such as cleft palate or Down syndrome.

Key Points

- Meta-analyses found that TT placement was associated with less time with MEE compared with watchful waiting or delayed treatment, at 1 year (32% less time) (strength of evidence high), less time with MEE compared with myringotomy at 1 year (42% less time) (strength of evidence moderate), and less time with MEE compared with watchful waiting or myringotomy at 2 years (13% less time) (strength of evidence moderate) (Table 9). Evidence was only available based on one small study comparing TT with either myringotomy or watchful waiting at 3 years post-treatment (insufficient strength of evidence).
- In relation to improved hearing, comparing TT placement with watchful waiting, a meta-analysis of three studies combined with qualitative synthesis of one additional study showed improved hearing with TT in comparison with watchful waiting at up to 9 months post-treatment. Strength of evidence is high.
- No significant differences in hearing between TT and watchful waiting were detected in two meta-analyses at longer followup of 12 and 18 months post-treatment; Strength of evidence is moderate.
- Based on a meta-analysis of three studies with ears randomized, TT placement improved hearing up to 6 months followup in relation to a comparison group of watchful waiting or myringotomy (Strength of evidence is high).
- No significant differences in hearing between TT placement and watchful waiting or myringotomy were detected at longer followup of 7 to 12 months after treatment, based on a meta-analysis of three studies by ear (Strength of evidence is low).
- One small RCT comparing TT and myringotomy examined differences in hearing at 24 months post-treatment (Strength of evidence is insufficient).
- Only one small RCT examined acute otitis media (AOM) outcomes. Strength of evidence is insufficient.
- We found no evidence concerning vestibular or health care use outcomes. Strength of evidence is insufficient.

Table 9. Strength of evidence for KQ 1: Clinical outcomes and health care utilization

Treatment Comparison	OME Signs and Symptoms	Objective Hearing	AOM	Balance	Health Care Utilization
TT vs. watchful waiting	**High** 1 MA (3 ,574) 32% less time with TT at 1 year **Insufficient** 1, 119 No difference at 3 years	**High** 1 MA (3, 523); 1, 248 Better hearing with TT at 3-6 months of 8.8 dB and 6-9 months of 4.2 dB **Low** 1 MA (2, 328), 1 MA (2, 283) 1, 248 No difference in hearing, by child, at 12, 18, and average of 12, 18, and 24 months **Insufficient** 1, 281 No difference at 5 years of age **Insufficient** One study by ear (N=72) at 24 months	**Insufficient** 1 study	**Insufficient** (No studies)	**Insufficient** (No studies)
TT vs. myringotomy	**Moderate** 2, 294 Up to 42% less time with MEE through 1 year **Insufficient** 1 study at 2 and 3 years		NR	NR	NR
TT vs. WW or myringotomy	**Moderate** 1 MA (3, 426) 13% less time with TT at 2 years	**High** 1 MA (3, 230 ears) Better hearing with TT at 4-6 months of 10 dB **Low** 1 MA (3, 232 ears) No difference at 7-12 months **Insufficient** 1 study at 24 months	NR	NR	NR

MEE = middle ear effusion; myr = myringotomy; OME = otitis media with effusion; TT = tympanostomy tubes; WW = watchful waiting

Detailed Synthesis

Duration of Middle Ear Effusion

Two meta-analyses conducted by Browning et al., 2010[22] and two additional single studies (Koopman et al., 2004[91] and Mandel et al., 1989[92]) found superior results concerning MEE with TT compared with myringotomy, watchful waiting, and/or delayed tubes measured at different endpoints, with either ears or participants randomized (Table 10).

Table 10. Clinical outcomes: Tympanostomy tubes versus watchful waiting or myringotomy

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion/ AOM	OME Recurrence/ Ventilation	Measured Hearing
Browning et al., 2010[22]	MA:3 studies Maw et al.,1999[93] MRC TARGET, 2001[103] Rovers et al., 2000[94] (N=523)	6-9 months	NR	NR	Bilateral TT vs. WW: Mean Diff: - 4.20 (95% CI, -6.00 to -2.39) (favors tube)
	MA: 3 studies Mandel et al., 1992[96] Paradise et al., 2001[68] Rovers, 2000[94] (N=574)	12 months	Bilateral TT vs. delayed treatment or WW: Mean diff: -0.32 (95% CI, -0.48 to -0.17) (favors tube)	NR	NR
	MA: 2 studies MRC TARGET, 2001[103] Rovers et al., 2000[94] (N=328)	12 months	NR	NR	Bilateral TT vs. WW: Mean Diff - 0.41 (95% CI, -2.37, 1.54)
	MA: 2 studies Maw et al.,1999[93] MRC TARGET, 2001[103] (N=283)	18 months	NR	NR	Bilateral TT vs. WW Mean Diff: -0.02 (95% CI, -3.22, 3.18)
	MA: 3 studies Gates et al., 1987[95] Mandel et al., 1992[96] Paradise et al., 2001[68] (N=426)	2 years	Billateral TT vs. myringotomy, delayed treatment or WW: Mean diff: -0.13 (95% CI, -0.17, -0.08) (favors TT)	NR	NR
	1 study MRC TARGET, 2012[19] TT (N=126) WW (N=122)	3-6 months average	NR	NR	Bilateral TT vs. WW Mean diff=- 8.8 dB (95% CI, -7.1 to -10.5) (favors tube)
		12, 18, 24 months average	NR	NR	Bilateral TT vs. WW Mean diff= -0.7 dB (statistics not reported)
		3 months to 2 years average	NR	NR	Bilateral TT vs. WW Mean diff = 2.9 dB (statistics not reported)
	1 study Johnston, et al., 2004[104] G1: Early TT (N=147) G2: Late TT (N=134)	5-6 years of age			Early TT vs. Late TT Left Ear: G1 = 6.2 G2 = 5.5 Mean Diff=-0.7, p=0.13 Right Ear G1: 6.2 G2: 6.0 Mean Diff = -.0.2 p=0.80

Table 10. Clinical outcomes: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion/ AOM	OME Recurrence/ Ventilation	Measured Hearing
Browning et al., 2010[22] (continued)	MA: 3 studies Black et al., 1990,[97] Dempster et al.,1993,[98] and Maw and Herod, 1986[99] (N=230 ears)	4 to 6 months	NR	NR	Unilateral TT vs. WW (2 studies) or myringotomy (1 study): Mean Diff: -10.08 (95% CI, -19.12, to -1.05) (favors tube)
	MA: 3 studies Black et al., 1990[97] Dempster et al.,1993[98] Maw and Herod, 1986[99] (N=234 ears)	7 to 12 months	NR	NR	Unilateral TT vs. WW (2 studies) or myringotomy (1 study): Mean Diff: -5.18 (95% CI, -10.43, 0.07)
	1 study (by ears) Black et al, 1990[97] Unilateral TT: (N=74) Myringotomy: (N=37) No surgery: (N=37)	24 months	NR	NR	Unilateral TT vs. myringotomy: Mean Diff: -3.4 (95% CI, -1.1 to 8.0) Unilateral TT vs. no surgery: Mean Diff: -0.5 (95% CI, -3.7 to 4.6)
Koopman et al., 2004[91]	G1: Donaldson or Goode TT + cold knife myringotomy (N=208) G2: Laser myringotomy (N=208)	1 month	Absence of effusion G1: 87.4% G2: 46.6%	NR	NR
		2 months	G1: 81.9% G2: 35.5%	NR	NR
		3 months	G1: 81.5% G2: 38.6%	NR	NR
		4 months	G1: 75.5% G2: 41.6%	NR	NR
		5 months	G1: 68.5% G2: 39.1%	NR	NR
		6 months	G1: 70.7% G2: 39.1% all p<0.001[a]	NR	NR
Mandel et al., 1989[92]	Without significant HL G1: Myringotomy G2 :Myringotomy + Armstrong TT G3: WW With significant conductive HL G4: Myringotomy G5: Myringotomy + Armstrong TT	2 months	NR	NR	SRT in dB Right ear G1: 18.5 G2: 16.2 G3: 6.2 G4: 22.0 G5: 5.5
		1 year	% Time with OME G1: 56.6% G2:16.4% G3: 56.3% G4: 56.7% G5: 9.8% G1 or G3 vs. G2: p<0.001 G4 vs. G5: p<0.001	NR	

Table 10. Clinical outcomes: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion/ AOM	OME Recurrence/ Ventilation	Measured Hearing
Mandel et al., 1989[92] (continued)		2 years	G1: 35.2% G2: 20.4% G3: 28.2% G4: 39.9% G5: 28.3% p=NS	NR	NR
	(N=93)	3 years	G1: 25.5% G2: 25.0% G3: 19.2% G4: 14.4% G5: 30.3% p=NS AOM Episodes/ person-year G1: 0.58 G2: 0. 18 G3: 0.38 G4: 0.31 G5: 0.41 G2 reported to have fewer episodes than G1 or G3	NR	NR

AOM = acute otitis media; CI = confidence interval; dB= decibels; Diff = difference; G = group; HL = hearing loss; MA = meta-analysis; MRC = Medical Research Council; N = number; NR = not reported; NS = not significant; OME = otitis media with effusion; SRT = speech related threshold; TARGET = Trial of Alternative Regimens in Glue Ear Treatment; TT = tympanostomy tube; WW = watchful waiting; vs.= versus

[a]p values calculated by investigators.

One meta-analysis of three studies conducted by Browning et al., 2010[22] found that bilateral TT reduced time with effusion compared with watchful waiting/delayed TT placement. The reduction was 32 percent at 1 year post-treatment (95% CI, 17% to 48%). A study by Mandel et al., 1989[92] similarly found that TT were superior to watchful waiting at 1 year post-treatment (40 percentage point difference).

Two studies found that TT were superior to myringotomy alone. Koopman et al., 2004[91] reported superiority through 6 months post-treatment (42 percentage point difference), and Mandel reported superiority through 1 year post-treatment (40 percentage point difference).[92] These studies were not included with the meta-analysis because their comparisons or time frame were different than those in the meta-analysis of the Browning et al., 2010 systematic review.

A second meta-analysis reported in Browning et al.[22] examined time with MEE at 2 years post-treatment in children with TT compared with children who had myringotomy, delayed TT, or no surgery; findings showed a difference of 13 percent favoring the TT group (95% CI, 8% to 17%). Mandel et al., 1989,[92] who examined TT in comparison to myringotomy and watchful waiting separately, reported a difference between TT and both myringotomy and watchful waiting at 1 year but no statistically significant difference in time with OME at either 2 or 3 years post-treatment. The percentage of time with effusion declined over time in the watchful waiting and myringotomy groups but increased in the TT group so that by 3 years, the time was similar across the three groups.

Measured Hearing

Five meta-analyses presented in the Browning et al. review (2010)[22] and data from four individual studies[19,92,97,104] reported hearing outcomes. These analyses compared TT with watchful waiting, delayed TT, and/or myringotomy.

One meta-analysis of 3 studies reported in Browning showed a significant improvement in hearing in the TT arm compared with watchful waiting at 6–9 months of -4.2 dB (95% CI, -6.00 to -2.39). However, results of two meta-analyses at 12 and 18 months did not find that TT were superior to watchful waiting (12 months: -0.41 dB [95% CI, -2.37 to 1.54]; 18 months: -0.02 dB [95% CI, -3.22 to 3.18]). Results reported in the MRC TARGET study (2012)[19] also provide evidence of an early advantage for TT in comparison with watchful waiting (3- and 6-month average followup: 8.8 dB [95% CI, 7.1 to 10.5]) that did not persist at later followup of up to 24 months (statistics not reported). Johnston et al.,[104] reporting data from the Paradise and colleagues RCT, did not find differences in hearing between children who received early TT and those who received late TT when they were between 5 to 6 years of age (TT insertion ranged from 3 months of age to 3 years of age) (left ear: -0.7 dB, p=0.13; right ear: -0.2 dB, p=0.80).

Two meta-analyses included three studies randomized by ear that compared TT with either watchful waiting or with myringotomy (combined) at 4 to 6 months and at 7 to 12 months. Only the MA at 4 to 6 months found an advantage for TT (-10.18 dB [95% CI, -19.12 to -1.05]). At 7 to 12 months the advantage disappeared (-5.18 dB [95% CI, -10.43 to 0.07]). In addition, another study randomized by ear (Black et al., 1990[97]) failed to find differences between TT and either myringotomy (3.4 dB [95% CI, -1.1 to 8.0]) or watchful waiting (0.5 dB [95% CI, -3.7 to 4.6)] at 24 month followup.

Recurrent AOM

After 3 years of observation, even though rates in all groups were low, children who had received TT had fewer episodes per person year of AOM after placement (0.18) compared with children with myringotomy alone (0.58) and those who had not had surgery (0.38).[92]

Surgical Interventions: Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy or Adenoidectomy Alone

Description of Studies

The evidence comparing the effectiveness of TT with myringotomy or no surgery when added to adenoidectomy was contained in 11 studies (Table 11). Hellstrom et al.[21] included four studies in which the participants in both arms received adenoidectomy and one arm also received TT.[105,102,106,107] Another report (Tos and Stangerup [1989][108]) that was a followup to the Bonding and Tos (1985) study[105] reported in Hellstrom was also included.

We identified an additional seven studies[109-115] The studies were all of children. Although one study included children as young as 1 year of age, most studies included children who were at least 3 years of age.

Four of the 11 studies (12 reports) compared outcomes by ears in which one ear received TT and the other ear received no surgery, among children who all had adenoidectomies.[106,109-111] Three studies (four articles) compared outcomes by ears with TT with ears with myringotomy, among children who all had adenoidectomies.[105,107,108,114] Of these, Maw and Bawden[107] included participants who had received either adenotonsillectomy or adenoidectomy; in this study, children were randomized to adenoidectomy/adenotonsillectomy or not prior to randomizing ears

to a unilateral TT or no TT. Four studies randomized children (in contrast to ears) to TT or myringotomy; all participants also had adenoidectomies.[102,111,112,115] No studies included children with comorbid conditions. Length of study followup generally ranged from 2 days to 12 months. However, one study followed patients for 10 years.[107]

Table 11. Characteristics of studies: Tympanostomy tubes and adenoidectomy versus watchful waiting or myringotomy and adenoidectomy or adenoidectomy alone

Study, Study Type, Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Study Followup	Age (range)	Risk of Bias
Brown et al., 1978[109] RCT by ear Wales	G1: Shepard TT + adenoidectomy (N=55) G2: Adenoidectomy (N=55)	Medical history, Otoscopy, Audiometry	Not specified	Not specified	48 hrs, 3, 6, 9, 12 months, 5 years	4-10 years	Medium
Austin, 1994[110] NRCT by ear United States	G1: TT[a] + adenoidectomy (N=31) G2: Adenoidectomy (N=31)	Audiometry	Not specified	Include: OME; Indication for adeno-tonsillectomy; resistant to ENT or pediatric management	3 months	NR	Medium
Lildholdt, 1979[111] NRCT by ear Denmark	G1:Donaldson TT+ adenoidectomy (N=91) G2: Adenoidectomy (N=91)	Tympanometry and audiometry	Not specified	Include: Bilateral OME; minimal between ear difference in pressure and hearing Exclude: Previous ear surgery	Until extrusion, 8 months	Mean: 4 years (1-10 years)	Medium
D'Eredita and Shah, 2006[112] RCT by person Italy	G1: Shah mini TT + adenoidectomy (N=15) G2: CDLM + adenoidectomy (N=15)	Tympanometry	3 months	Include: OME for 3 months Exclude: History of prior surgery, craniofacial syndrome, MR or cognitive disorder	12 months	Mean: 4 years (2-6 years)	Medium
Popova et al., 2010[113] RCT by person Bulgaria	G1: Donaldson TT + adenoidectomy (N=42) G2: Myringotomy + adenoidectomy (N=36)	Pneumatic otoscopy and tympanometry	3 months	Include: OME for 3 months; conductive HL >20 dB Excluded: Previous ear or throat surgery; craniofacial syndromes; destructive middle ear disease; conductive HL attributed to destructive middle ear changes; sensorineural HL	12 months	Mean: G1: 60 months G2: 61 months	Medium

Table 11. Characteristics of studies: Tympanostomy tubes and adenoidectomy versus watchful waiting or myringotomy and adenoidectomy or adenoidectomy alone (continued)

Study, Study Type, Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Study Followup	Age (range)	Risk of Bias
Shishegar and Hobhoghi, 2007[114] RCT by ear Iran	G1: Shepard TT + adenoidectomy (n=30) G2: Myringotomy + adenoidectomy (N=30)	Otoscopy, tympanometry, audiometry	Not specified	Include: OME unresponsive to medical therapy Exclude: Prior ear surgery or adenoidectomy; cleft palate; perforated TM	6 months	4-8 years	Medium
Vlastos et al., 2011[115] RCT by person Greece	G1: Shepard TT + adenoidectomy (N=25) G2: Adenoidectomy + myringotomy (N=27)	Otoscopy, tympanometry, pure tone audiometry	Not specified	Include: Bilateral OME; scheduled for adenoidectomy due to sleep apnea; >3 yrs age Excluded: chronic OME; previous ear surgery; language delays; behavioral problems; anatomic changes	12 months	Mean: G1: 4.6 years (3-7 years) G2: 4.4 years (3-7 years)	Medium
Hellstrom et al., 2011[21] Systematic Review Gates et al., 1989 [102] Lildholdt, 1983[106] Bonding, 1985[105] Maw, 1994[107]	Arms differ across comparisons (Arms appear in tables 13 and 33 ,) 4 studies (N=1,054 participants)	Varies by study	Minimum of 3 months	Include: RCTs (individual or ear), NRCTs, and cohort studies published between 1966 and 2007 of TT effectiveness on hearing, QOL, language development, and complications	Various	Children or adolescents	Medium

CDLM = Contact diode laser myringotomy dB = decibel; ENT = ear, nose, and throat; G = group; HL = hearing loss; hrs = hours; MR = mental retardation; N = number; NR = not reported; NRCT = nonrandomized controlled trial; OME = otitis media with effusion; QOL = quality of life; RCT = randomized controlled trial; TM = tympanic membrane; TT = tympanostomy tubes; yrs = years[a]Tympanostomy tube type not specified.

Key Points

- Two studies found that TT confer no additional benefit for limiting OME recurrence to that obtained by adenoidectomy alone (strength of evidence insufficient) (Table 12).
- The evidence that TT and adenoidectomy reduce OME recurrence in comparison with myringotomy and adenoidectomy is mixed. One RCT found no difference in recurrence rate with the addition of TT, but two studies found that OME recurred later with TT plus adenoidectomy compared with myringotomy plus adenoidectomy. Strength of evidence is insufficient for mixed findings.
- Findings from four studies are mixed concerning whether TT and adenoidectomy improve hearing in comparison to adenoidectomy alone beyond 3 weeks post-treatment. Strength of evidence is insufficient for mixed results.

- Five of six studies did not find that TT plus adenoidectomy was superior to myringotomy plus adenoidectomy for hearing outcomes. Strength of evidence is low for no difference.
- Only one small RCT examined AOM, and no difference was found between TT and adenoidectomy and myringotomy and adenoidectomy. Strength of evidence is insufficient.
- Evidence was insufficient for vestibular outcomes and health care service use because we found no studies.

Table 12. Strength of evidence for KQ 1: Clinical outcomes and health care utilization

Treatment Comparison	OME Recurrence/ Ventilation	AOM	Measured Hearing
TT+ adenoidectomy vs. Adenoidectomy alone	**Insufficient** No difference, two small studies	**Insufficient** (No studies)	**Insufficient** Mixed results
TT+ adenoidectomy vs. Myringotomy + adenoidectomy	**Insufficient** Mixed results	**Insufficient** Single study No difference	**Low** No difference (6 mos, 12 mos and >3 years)

mos = months; TT = tympanostomy tubes; yrs = years

Detailed Synthesis

Recurrence of Middle Ear Effusion

Six studies[102,106,107,109,112,113] examined MEE or ventilation as an outcome (Table 13). The two studies[106,109] that compared TT added to adenoidectomy in comparison with no ear surgery found no significant difference in OME recurrence at follow-up points from 48 hours to 5 years. Later data were shown in figures only.

Results were mixed comparing TT with myringotomy, when added to adenoidectomy. One small study[113] (N=78) comparing TT with myringotomy found similar and nonsignificant OME recurrence at 12 months post-surgery. Over a 2-year period, Gates et al. (1989)[102] found recurrence an average of 148 days later in children with TT and adenoidectomy compared with children with myringotomy and adenoidectomy ($p< 0.0001$) but the percentage of time with effusion was similar between the two groups. In another small study (N=30), D'Eredita and Shah[112] found that ears with TT remained ventilated, on average, 2.8 months longer than those that received myringotomy ($p<0.001$), when all children received adenoidectomy.

Table 13. Clinical outcomes: Tympanostomy tubes plus adenoidectomy versus watchful waiting or myringotomy plus adenoidectomy or adenoidectomy alone

Study	Arm (N randomized)	Study Duration Until Outcome Measurement	OME Recurrence/ Ventilation	AOM	Measured Hearing
Brown et al., 1978[109]	G1: Shepard TT + adenoidectomy (N=55) G2: Adenoidectomy (N=55)	48 hours	G1: 2% G2: 4% p=NS	NR	PTA G1: 8.9 dB G2: 24.7 dB (significant but no p-value reported)
		3 months	NR	NR	G1: 11.4 dB G2: 16.6 dB (significant but no p-value reported)
		5 years	NR	NR	G1: 17 dB G2: 14 dB p=NR
Austin, 1994[110]	G1: TT[a] + adenoidectomy (N=31) G2: Adenoidectomy (N=31)	1-3 months	NR	NR	Air-bone gap G1: 13.2 G2: 14.4 p>0.1 Mean improvement in Air-bone gap G1:16 dB G2: 12.2 dB p>0.1 Mean difference: 1.9 dB in hearing between ears p=NS
Lildholdt, 1979[111]	G1:Donaldson TT+ adenoidectomy (N=91) G2: Adenoidectomy (N=91	3-18 months	NR	NR	Mean HL at 3 months G1: 5.5 dB G2: 6.1 dB at 6 months G1: 8.8 dB G2: 7.6 dB at 9 months G1: 4.9 dB G2: 7.3 dB at 12 months G1: 8.2 dB G2: 5.0 dB at 15 months G1: 4.7 dB G2: 4.1 dB at 18 months G1: 8.8 dB G2: 2.4 dB All p's=NS

Table 13. Clinical outcomes: Tympanostomy tubes plus adenoidectomy versus watchful waiting or myringotomy plus adenoidectomy or adenoidectomy alone (continued)

Study	Arm (N randomized)	Study Duration Until Outcome Measurement	OME Recurrence/ Ventilation	AOM	Measured Hearing
D'Eredita and Shah, 2006[112]	G1: Shah mini + adenoidectomy (N=15) G2: CDLM + adenoidectomy (N=15)	NA	Middle ear ventilation maintained G1: 6.3 months G2: 3.5 months p<0.001	NR	NR
		3 months	Number ears ventilated (%) G1: 30 (100) G2: 11 (36.6) p=NR	NR	NR
Popova et al., 2010[113]	G1: Donaldson TT + adenoidectomy (N=42) G2: Myringotomy + adenoidectomy (N=36)	1 month	NR	NR	PTA G1: 13.9 dB G2: 14.1 dB p=0.83
		6 months	NR	NR	G1: 7.6 dB G2: 8.0 dB p=0.68
		12 months	OME recurrence G1: 10% G2:14% p=0.547	# episodes ≥ 1 G1: 28% G2: 25% p=NR	G1: 5.5 dB G2: 6.3 dB p=0.24
Shishegar and Hobhoghi, 2007[114]	G1: Shepard TT + adenoidectomy (N=30) G2: Myringotomy + adenoidectomy (N=30)	1 month	NR	NR	Air-bone gap improvement G1: 17.47 dB G2: 16.04 dB p=NS Mean SRT hearing threshold G1: 18.3 dB G2: 17 dB p=NS
		6 months	NR	NR	Air-bone gap improvement G1:17.62 dB G2: 16.25 dB p=NS Means SRT Hearing threshold G1: 19.3 dB G2: 17.16 dB p=NS

Table 13. Clinical outcomes: Tympanostomy tubes plus adenoidectomy versus watchful waiting or myringotomy plus adenoidectomy or adenoidectomy alone (continued)

Study	Arm (N randomized)	Study Duration Until Outcome Measurement	OME Recurrence/ Ventilation	AOM	Measured Hearing
Vlastos et al., 2011[115]	G1: Shepard TT + adenoidectomy (N=25) G2: Myringotomy + adenoidectomy (N=27)	6 months	NR	NR	Change in hearing G1: -7.41 dB G2: -4.06 dB Mean HL change, dB 3.35 (95% CI, -6.64 to 10.35)
		12 months	NR	NR	Change in hearing: G1: -8.06 dB G2: -7.40 dB Mean HL change, dB: 0.66(95% CI, -6.82 to 8.15)
Hellstrom et al., 2011[21] Systematic Review	1 NRCT (by ears) 2 articles Bonding, 1985[105] Companion Study: Tos and Strangerup, 1989[108] G1: Adenoidectomy + Donaldson TT (N=146) G2: Myringotomy + adenoidectomy (N=146)	While grommet functioning (N=224 children)	NR	NR	% with hearing threshold > 20 dB G1:4 G2: 31 p<0.01
		2-3 years	NR	NR	Mean hearing threshold, PTA G1: 15.0 dB G2: 14.7 dB p=NR Mean gain after treatment : G1: 14.5 dB G2: 13.1 dB p=NR
		6-7 years	NR	NR	Mean hearing threshold, PTA G1: 11.7 dB G2: 11.1 dB p=NR Mean gain after treatment G1: 3.3 dB G2: 3.6 dB
	1 RCT Gates et al., 1989[102] G1: Adenoidectomy + TT[a] (N=125) G2: Adenoidectomy + myringotomy (N=130)	2 years	Days until recurrence G1: 240 ±22 G2: 92 ±33 p<0.0001 Time with effusion G1: 0.258 ±0.212 G2: 0.302 ±0.250 p=0.2364	NR	Proportion of time with hearing threshold >20 dB (better ear) G1: 0.065 G2: 0.078 p=0.5042

Table 13. Clinical outcomes: Tympanostomy tubes plus adenoidectomy versus watchful waiting or myringotomy plus adenoidectomy or adenoidectomy alone (continued)

Study	Arm (N randomized)	Study Duration Until Outcome Measurement	OME Recurrence/ Ventilation	AOM	Measured Hearing
Hellstrom et al., 2011[21] (continued)	1 RCT (by ear) Lildholdt, 1983[106] G1: Donaldson TT + adenoidectomy (N=150 ears) G2:Adenoidectomy (N=150 ears)	3 weeks	NR	NR	Hearing loss: PTA Data shown in figures only p<0.001 favoring TT ear
		5 years	Flat tympanogram G1: NR G2: NR p=NS	NR	Hearing loss: PTA Data shown in figures only p=NS
	1 RCT (by person and ear) Maw, 1994[107] G1:Shepard TT + Adenoidectomy/ adenotonsillectomy (N=139) G2: Adenoidectomy/ adenotonsillectomy alone (N=139)	6/12 months-10 years	% without MEE at 6/12 mos G1: 88.4 G2: 50.9 at 1 years G1: 78.1 G2: 60.1 at 2 years G1: 78.3 G2: 66.7 at 3 years G1: 89.8 G2: 79.8 at 4 years G1: 89.4 G2: 87.7 at 5 years G1: 91.9 G2: 82 at 7 years G1: 92.7 G2: 92.9 at 10 years G1: 95.4 G2: 90.9 all p's=NR		Mean hearing loss, dB at 6/12 mos G1: 17.6 G2: 21.3 G1: 19.1 G2: 20.9 G1: 18.1 G2: 20.0 G1: 17.3 G2: 17.0 G1: 17.5 G2: 16.6 G1: 16.4 G2: 17.0 G1: 14.7 G2: 14.6 all p's=NR

AOM = acute otitis media; CDLM = contact diode laser for myringotomy; dB = decibel; G = group; HL = hearing level; MEE = middle ear effusion; mos = months; N = number; NA = not applicable; NR = not reported; NRCT = nonrandomized controlled trial; NS = not significant; OME = otitis media with effusion; PTA = pure tone average; RCT = Randomized controlled trial; SRT = speech reception threshold; TT = tympanostomy tubes

[a]Tympanostomy tube type not specified.

Measured Hearing

Hearing outcomes were examined by all studies but D'Eredita and Shah.[112] Two[110,111] of the four studies comparing TT plus adenoidectomy with adenoidectomy alone did not find that TT added any benefit to hearing that was not obtained by adenoidectomy alone at a number of follow-up points, from 1 to 18 months. Two other studies found that TT conferred a benefit when added to adenoidectomy at 48 hours and 3 months postsurgery[109] and at 3 weeks postsurgery.[106] Neither of the latter two studies found a benefit at 5-year followup.

In the three studies (four reports)[105,107,108,114] that compared TT to myringotomy by ears, only the Bonding and Tos (1985)[105] study found that TT conferred an advantage, but only during the period in which the grommets were intact (4% of ears with hearing threshold greater than 20 dB vs. 31%). None of the three studies[102,113,115] that examined children (in contrast to ears) randomized to either TT or myringotomy along with adenoidectomy found a benefit for TT; followup in these studies occurred between 1 month and 2 years and outcomes were typically similar in both arms.

Acute Otitis Media

Only one small RCT examined whether TT plus adenoidectomy were superior to myringotomy plus adenoidectomy for developing AOM. Popova et al. (2010)[113] reported that at 12-month followup approximately one-quarter of each group developed one or more cases of AOM following treatment.

Surgical Interventions: Myringotomy Comparisons

Description of Studies

The included evidence consisted of one RCT by Ragab[116] (Table 14). This study was designed to compare two different procedures for myringotomy; namely, radio frequency myringotomy with mitomycin C, a topical chemotherapeutic agent, in comparison to radio frequency myringotomy alone. In this trial, a subset of individuals received an adenoidectomy (73% and 67% respectively by arm). Followup was short term.

Table 14. Characteristics of studies: Myringotomy comparisons

Study, Study Type, Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Study Follow-up	Age in Years	Risk of Bias
Ragab, 2005[116] RCT Egypt	G1: Radiofrequency myringotomy + Mitomycin C (N=30) 73% had adenoidectomy G2: Radiofrequency myringotomy (no Mitomycin C) (N=30) 67% had adenoidectomy	History, pneumatic otoscopy and tympanometry	NR	Include: Patients undergoing surgery for OME	3 months	Mean G1: 4.8 G2: 5.2	Medium

G = group; N = number; NR = not reported; OME = otitis media with effusion; RCT = randomized control trial

Key Points

One small RCT comparing approaches to myringotomy found a significant difference in resolution of OME favoring myringotomy with mitomycin C but no significant differences in hearing improvement. Based on one small study, the strength of evidence is insufficient.

Detailed Synthesis

OME Signs and Symptoms Outcomes

Ragab[116] examined resolution of middle ear effusion and reported a significant difference favoring radio frequency myringotomy with mitomycin C at 3 months ($p<0.01$) (Table 15). This study did not present data on either OME recurrence or AOM.

Table 15. Clinical outcomes: Myringotomy comparisons

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/Time With Effusion	Patency	Measured Hearing
Ragab, 2005[116]	G1: Radiofrequency myringotomy + mitomycin C (N=30) G2: Radiofrequency myringotomy (no mitomycin C) (N=30)	3 months	Resolution of OME G1: 59% G2: 28% p<0.01	G1: 5.3 weeks G2: 3.5 weeks p<0.01	Air-bone gap Improvement: G1: 12 dB G2: 10 dB p=NS

dB = decibel; G = group; N = number; NS = not significant; OME = otitis media with effusion

Hearing Outcomes

Both myringotomy with and without mitomycin C groups demonstrated a significant air-bone gap improvement 3 months postsurgery compared with presurgery but no significant difference in improvement was observed in air-bone gap improvement rates between the two groups.[116]

Surgical Interventions: Myringotomy With Adenoidectomy Comparisons

Description of Studies

One retrospective cohort study compared two different procedures for myringotomy—namely, laser myringotomy with cold knife myringotomy (Table 16).[117] In both arms, all participants received an adenoidectomy. Patients included children older than 4 years of age who had refractory OME or children of any age who needed a second TT insertion.

Table 16. Characteristics of studies: Myringotomy with adenoidectomy

Study, Study Type, Country	Arm (N)	Inclusion/ Exclusion Criteria	Length of Followup	Age in Years (Range)	Risk of Bias
Szeremeta et al., 2000[117] Retrospective cohort USA	G1: Laser myringotomy + adenoidectomy (N=29) G2: Cold knife myringotomy + adenoidectomy (N=35)	Include: Children >4 yrs with refractory OME or children any age with a need for a second tube; spring operations	Mean time in months (range) G1: 16.6 (6–27) G2: 20.2 (12–48)	Mean: G1: 6.5 (2.74 to 12.52) G2: 7.4 (3.86 to 5.34)	Medium

G = group; N = number; OME = otitis media with effusion; USA = United States of America; yrs = years

Key Points

A particular approach to myringotomy (laser vs. cold knife) among patients who had also all received adenoidectomy displayed mixed findings in relation to clinical outcomes in an evidence base consisting of one study. The study did not find that laser myringotomy was superior to cold knife myringotomy in the percentage of patients with OME but did find it superior in relation to the intermediate outcome of patency of ears (open hole based on myringotomy), postoperatively. Based on one small study, the evidence is graded as insufficient.

This one study evidence base did not report any other clinical or health care utilization outcomes such as AOM, balance, or use of health care services.

Detailed Synthesis

Outcomes focused on the percentage of ears with MEE and patency of ears at the first postsurgery visit (Table 17). Laser myringotomy with adenoidectomy did not differ from cold knife myringotomy with adenoidectomy in the percentage of ears presenting with MEE at followup. However, the authors reported a significant difference in the percentage of ears that were patent at the first postoperative visit, favoring laser myringotomy with adenoidectomy ($p<0.01$).

Table 17. Clinical outcomes: Myringotomy with adenoidectomy comparisons

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/Time With Effusion	OME Recurrence or Ventilation
Szeremeta et al., 2000[117]	G1: Laser myringotomy + adenoidectomy (N=29) G2: Cold knife myringotomy + adenoidectomy (N=35)	Within 50 days	MEE G1: 10.3% G2: 17.1% p>0.1	Patency G1: 20.5% G2: 0% p<0.01

G = group; MEE = middle ear effusion; N = number; OME = otitis media with effusion

Surgical Interventions: Adenoidectomy Versus Other Interventions

Description of Studies

The evidence comparing the effectiveness of adenoidectomy to other interventions was included in a recent Cochrane review by van den Aardweg et al.[29] and a newly published TARGET study conducted by the MRC Multicentre Otitis Media Study Group (2012)[19] (Table 18). Included studies were all RCTs of children (1 to 15 years of age) with persistent or recurrent OME lasting at least 3 months, who were followed for 6 months or more. We included seven of the studies summarized in the Cochrane review that were limited to OME patients (N=1,103).[95,97-99,118-120] Treatment comparisons included: adenoidectomy with and without myringotomy versus nonsurgical treatment, myringotomy or watchful waiting only; adenoidectomy with unilateral TT versus a unilateral TT only; and adenoidectomy with bilateral TT versus bilateral TT only.

Table 18. Characteristics of studies: Adenoidectomy versus other interventions

Study, Study Type, Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Study Followup	Age Range	Risk of Bias
van den Aardweg et al., 2010[29] Systematic review 7 RCTs included in analysis: Dempster et al., 1993,[98] Black et al., 1990,[97] Maw and Herod, 1986,[99] and Fiellau-Nikolajsen et al., 1980,[118] RCT: Gates et al, 1987,[95] Roydhouse et al., 1980,[120] and Casselbrant et al., 2009[119]	Arms differ across comparisons: 7 RCTs (1,103 participants) (Arms appear in tables 20 and 34)	Various criteria including clinical judgment, otoscopy, tympanometry, pure tone thresholds	Various	Include: RCTs of adenoidectomy for OME compared with nonsurgical tx or TT alone; children ≤18 yrs of age Exclude: Quasi randomized trials (e.g., allocation by DOB or record number)	At least 6 months	2-14 yrs	Low
MRC TARGET, 2012[19] RCT UK	G1: Ad + myr + bilateral Shepard TT G2: Myr + bilateral Shepard TT G3: WW (N=376)	On 2 visits, 3 mos. apart: a bilateral B+B or B+C2 tympanogram combination and better ear HL ≥20 dB HL averaged across 0.5, 1,2, and 4 kHz and air-bone gap >10 dB	3 months	Include: A bilateral B+B or B+C2 tympanogram combination and better ear HL ≥20 dB HL averaged across 0.5, 1,2, and 4 kHz and air-bone gap >10 dB, on 2 visits, 3 months apart HL >40 dB HL could choose to not be randomized	3, 6, 12, 18, and 24 months	3.25 to 6.75 years at first visit	Medium

Ad = adenoidectomy; dB = decibels; DOB = date of birth; HL = hearing level; kHz = kilohertz; mos = months; MRC = Medical Research Council; myr = myringotomy; N = number; RCT = randomized controlled trial; TARGET = Trial of Alternative Regimens in Glue Ear Treatment; TT = tympanostomy tubes; tx = treatment; UK = United Kingdom; ww = watchful waiting; yrs = years

Key Points

- Adenoidectomy was superior to no treatment in resolving OME at both 6 months and 12 months followup, based on evidence from meta-analyses of studies by ear (Table 19).[29] At 6 months, the risk difference was 0.27 (95% CI, 0.13 to 0.42), measured through otoscopy and 0.22 (95% CI, 0.12 to 0.32) measured through tympanometry. At 12 months the risk difference was 0.29 (95% CI, 0.19 to 0.39). High strength of evidence.

- Resolution of OME and hearing were superior with adenoidectomy and myringotomy at 24 months in one large study (N=237) compared with myringotomy alone. Low strength of evidence.
- Results of studies using varied effusion outcome measures (time with effusion and percentage of patients with effusion) that examined whether the addition of adenoidectomy to TT was superior to TT alone after 1 to 3 years were mixed. Strength of evidence is insufficient for mixed results.
- Measured hearing levels were mixed in the adenoidectomy group compared with no treatment. Insufficient strength of evidence.
- Measured hearing was superior with adenoidectomy and TT compared with watchful waiting at all follow-up visits between 3 to 6 months and 2 years in one study (N=250). Low strength of evidence.
- Measured hearing outcomes at 6-month followup were similar in three studies measuring differences between adenoidectomy and TT groups and TT only groups. However, by 1 year followup, results were mixed in the adenoidectomy and TT group compared with the TT-only group in two studies. Strength of evidence is insufficient for mixed results.
- Evidence was insufficient to determine the comparative effectiveness of adenoidectomy versus no treatment or TT in relation to vestibular function and health services-related outcomes.

Table 19. Strength of evidence for KQ 1: Clinical outcomes and health care utilization

Treatment Comparison	OME Signs and Symptoms	Objective Hearing	AOM	Balance	Health Care Utilization
Adenoidectomy vs. no treatment	**High** OME resolution favors adenoidectomy vs. no treatment 2 MA at 6 mos (2,153) (3, 297), 1 MA at 12 mos (3, 298)	**Insufficient** Mixed results (2, 221)	**Insufficient** No studies	**Insufficient** No studies	**Insufficient** No studies
Adenoidectomy plus myringotomy vs. myringotomy	**Low** Mean time with effusion favors adenoidectomy+ myringotomy over myringotomy alone at 24 mos (1, 237)	**Low** Hearing favors adenoidectomy+ myringotomy over myringotomy alone at 24 mos (1, 237)	**Insufficient** No studies	**Insufficient** No studies	**Insufficient** No studies
Adenoidectomy plus TT vs. TT	**Insufficient** Mixed results (3, 538)	**Insufficient** Mixed results (4, 683)	**Insufficient** One study	**Insufficient** No studies	**Insufficient** No studies
Adenoidectomy plus TT vs. WW	**Insufficient** No studies	**Low** Hearing favors adenoidectomy+TT over WW at 3 to 24 mos (1, 250)	**Insufficient** No studies	**Insufficient** No studies	**Insufficient** No studies

AOM = acute otitis media; OME = otitis media with effusion; mos = months; MA = meta-analysis; TT = tympanostomy tubes; vs. = versus; WW = watchful waiting

Detailed Synthesis

OME Signs and Symptoms Outcomes

OME resolution was superior in the adenoidectomy group compared with no treatment in three meta-analyses conducted by van den Aardweg et al. that compared unoperated ears in

patients with unilateral TT, both at 6 months based on otoscopy (risk difference=0.27, based on 2 studies) and tympanometry (risk difference=0.22, based on three studies) and at 12 months based on tympanometry (risk difference=0.29, based on three studies) (Table 20).[29] In a single study, Gates et al. also found that the mean time with effusion over a 24-month period was significantly lower in the adenoidectomy and myringotomy group compared with the myringotomy-only group (SMD=-0.76) and that the mean time to recurrence of effusion was almost twice as long in the adenoidectomy and myringotomy group compared with the myringotomy-only group, 92 and 54 days, respectively.[95]

OME-related outcomes were better in adenoidectomy and TT groups compared with TT alone, in two of three studies. Roydhouse et al. found that, among patients with adenoidectomies and TT, 18 percent had MEE at the end of year 1 and 15 percent at the end of year 2.[120] In contrast, among patients who had only TT, effusion was present in 23 percent at the end of year 1 and 18 percent at the end of year 2, but risk differences were not significant at either time point. In a second study, Gates et al. found that the mean time with effusion over a 2-year period was 26 percent of visits among patients with adenoidectomies and TT and 35 percent of visits among patients with only TT (SMD: -0.40 [95% CI, -0.65 to -0.15]).[95] In a third small study by Casselbrant et al., mean time with effusion was higher in the adenoidectomy plus TT arm at 18 and 36 months, but differences were small and not statistically significant.[119]

Table 20. Clinical outcomes: Adenoidectomy versus other interventions

Study	Arm (N)	Study Duration Until Outcome Measurement	MEE/ Time With Effusion	OME Resolution	AOM	Measured Hearing
van den Aardweg et al., 2010[29]	RCT (by person and ear): Dempster et al., 1993[98] G1: Adenoidectomy G2: Control (N=72)	6 months	NR	Included in MA	NR	Mean hearing level (dB) (95% CI) G1: 18.0 G2: 21.1 SMD: -0.25 (-0.71 to 0.22)
		12 months	NR	Otoscopy G1: 54% G2: 37% Risk diff: 17% (95% CI, -6% to 40%)	NR	G1; 15.6 G2: 18.4 SMD: -0.29 (-0.76 to 0.17)
	RCT: Black et al., 1990 (by person and ear)[97] G1: Adenoidectomy G2: Control (N=149)	6 months	NR	NR	NR	Diff in change in mean dB: 4.3 (1.4 to 9.9)
		12 months	NR	NR	NR	Diff in chance in mean dB: 4.3 (-3.1 to 11.6)
	MA: 2 RCTs (by ears): Dempster et al., 1993[98] Maw and Herod, 1986[99] G1: Adenoidectomy G2: No treatment (N =153)	6 months	NR	Otoscopy G1: 49% G2: 21% Risk diff: 0.27 (95% CI, 0.13 to 0.42)	NR	NR

Table 20. Clinical outcomes: Adenoidectomy versus other interventions (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	MEE/ Time With Effusion	OME Resolution	AOM	Measured Hearing
van den Aardweg et al., 2010[29] (continued)	MA: 3 RCTs (by ears): Dempster et al., 1993[98] Black et al., 1990[97] Maw and Herod, 1986[99] G1: Adenoidectomy G2: No treatment (N =297)	6 months	NR	Tympanometry G1: 39% G2: 17% Risk diff: 0.22 (95% CI, 0.12 to 0.32)	NR	NR
	MA: 3 RCTs (by ears): Dempster et al., 1993[98] Maw and Herod, 1986[99] Black et al., 1990[97] G1: Adenoidectomy G2: No treatment (N=298)	12 months	NR	Tympanometry G1: 47% G2: 20% Risk diff: 0.29 (95% CI, 0.19 to 0.39)	NR	NR
	RCT: Fiellau-Nikolajsen et al., 1980[118] G1: Adenoidectomy + Myringotomy G2: Myringotomy (N=42)	6 months	NR	Normal ears (Type A tympanogram) G1: 68% G2: 52% Risk diff: 15% (95% CI, -5% to 46%)	NR	NR
	RCT: Gates et al, 1987[95]; Gates et al., 1989[102] G1: Adenoidectomy + myringotomy G2: Myringotomy G3: Adenoidectomy + Shepard TT G4: Shepard TT (N=491) Gates (cont.)	24 months (ITT)	Median days to first recurrence of effusion G1: 92 (±33) G2: 54 (±2) (p<0.0007) G3: 240 (±22) G4: 222 (±11) (p=0.2314) Mean time with effusion G1: 0.302 G2: 0.491 SMD: -0.76 (95% CI, -1.02 to -0.49)	NR	NR	Mean time HL ≥20 dB better ear G1: 0.078 G2: 0.186 SMD: -0.66 (95% CI, -0.93 to -0.40) Mean time HL ≥20 dB worse ear G1: 0.220 G2: 0.375 SMD: -0.65 (95% CI, -0.91 to -0.39) Mean time HL ≥20 dB better ear G3: 0.065 G4: 0.101 SMD: -0.23 (95% CI, -0.48 to 0.02)
			G3: 0.258 G4: 0.349 SMD: -0.40 (95% CI, -0.65 to -0.15)			Mean time HL ≥20 dB worse ear G3: 0.224 G4: 0.304 SMD: -0.35 (95% CI, -0.60 to -0.11)

Table 20. Clinical outcomes: Adenoidectomy versus other interventions (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	MEE/ Time With Effusion	OME Resolution	AOM	Measured Hearing
van den Aardweg et al., 2010[29] (continued)	RCT: Maw and Herod, 1986[99] G1: Adenoidectomy + unilateral Shepard TT G2: Unilateral Shepard TT (N=103)	6 months	NR	Presented in MA	NR	Mean hearing level (dB) (SD) G1: 16.4 (8.03) G2: 17.5 (9.79) (p=NS)
		12 months	NR	Presented in MA	NR	Mean hearing level (dB) (SD) G1: 16.4 (8.03) G2: 17.5 (8.61) (p=NS)
	RCT: Black et al., 1990[97] G1: Adenoidectomy+ myringotomy + unilateral Shepard TT G2: Myringotomy + unilateral Shepard TT (N=72)	6 months	NR	NR	NR	Diff in change in mean dB: 2.1 (95% CI, -2.6 to 6.8)
		12 months	NR	NR	NR	Diff in change in mean dB: 2.4 (95% CI, -2.7 to 7.6)
	RCT: Roydhouse, 1980[120] G1: Adenoidectomy + bilateral TT G2: Bilateral TT (N = 95)	12 months	% with effusion G1: 18% G2: 23% Risk diff: -5% (95% CI, -8% to 17%)	NR	NR	NR
		24 months	G1: 15% G2: 18% Risk diff: -3% (95% CI, -10% to 15%)		NR	NR
	RCT: Casselbrant et al., 2009[119] G1: Adenoidectomy + myringotomy + bilateral Teflon Armstrong TT G2: Myringotomy + bilateral Teflon Armstrong TT (N=62)	18 months (ITT)	Mean time with effusion G1: 18% G2: 12% Diff G1 vs. G2: 6% (95% CI, -12 to 24)	NR	>1 episode G1: 27% G2: 23% Diff G1 vs. G2: (p=0.58)	NR

Table 20. Clinical outcomes: Adenoidectomy versus other interventions (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	MEE/ Time With Effusion	OME Resolution	AOM	Measured Hearing
van den Aardweg et al., 2010[29] (continued)	Casselbrant et al., 2009[119]	36 months (ITT)	Mean time with effusion G1: 21% G2: 19% Diff G1 vs. G2: 2% (95% CI, -19 to 23)	NR	# episodes G1: 7 G2: 6 Risk diff: 5% (95% CI, -22 to 32) >1 episode G1: 58% G2: 55% Diff G1 vs. G2: (p=0.77) # episodes G1: 17 G2: 21 Risk diff: -18% (95% CI, -37 to 1)	NR
MRC TARGET, 2012[19]	G1: Adenoidectomy + myringotomy + bilateral Shepard TT G2: Myringotomy + bilateral Shepard TT G3: WW (N=376)	3- and 6-month visit (ITT) (N at 3 mos=332)	NR	NR	NR	Mean hearing levels: G1: 14.6 (95% CI, 13.6 to 15.7) G2: 15.9 (95% CI, 14.8 to 17.0) G3: 24.7 (95% CI, 23.3 to 26.1) Diff TES G1 vs. G3: 1.50 (p<0.05) G1 vs. G2: 0.23 (p=NS)
		12-, 18-, and 24-mo visit (ITT) (N at 12 mos=323)	NR	NR	NR	G1: 15.9 (95% CI, 14.9 to 17.0) G2: 20.1 (95% CI, 19.0 to 21.2) G3: 19.4 (95% CI, 18.3 to 20.5) Diff TES G1 vs. G3: 0.55 (p<0.05) G1 vs. G2: 0.69 (p<0.05)

Table 20. Clinical outcomes: Adenoidectomy versus other interventions (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	MEE/ Time With Effusion	OME Resolution	AOM	Measured Hearing
MRC TARGET, 2012[19] (continued)		2-year combined average (ITT) (N at 24 mos=321)	NR	NR	NR	G1: 15.5 (95% CI, 14.5 to 16.4) G2: 18.5 (95% CI, 17.6 to 19.5) G3: 21.4 (95% CI, 20.4 to 22.4) Diff TES G1 vs. G3: 1.11 (p<0.05) G1 vs. G2: 0.61 (p<0.05)

Ad = adenoidectomy; AOM = acute otitis media; bil = bilateral; CI = confidence interval; dB = decibel; diff = difference; G = group; HL = hearing level; ITT = intent to treat; MA = meta-analysis; mos = months; MEE = middle ear effusion; MRC = Medical Research Council; myr = myringotomy; N = number; NR = not reported; NS = not significant; OME = otitis media with effusion; RCT = randomized controlled trial; SD = standard deviation; SMD = standard mean difference; TARGET = Trial of Alternative Regimens in Glue Ear Treatment; TES = treatment effect size; TT = tympanostomy tubes; vs. = versus; ww = watchful waiting

Hearing Outcomes

Hearing measures differed across two RCTs that measured outcomes by ears but the directon of the results was consistent. Comparing adenoidectomy alone with no treatment at 6-month followup, one study found significantly larger improvement in hearing outcomes in the adenoidectomy group (4.3dB).[97] A second study found better mean hearing levels in the adenoidectomy group
(SMD = -0.25) but the results were not statistically significant.[98] Studies continued to find different results in the two groups at 12-month followup but in both studies the differences were not statistically significant.

The larger TARGET study found significantly better hearing in the adenoidectomy, myringotomy, and TT arm compared with the watchful waiting arm at 3- to 6-month followup, 12- to 24-month followup, and overall for the 24-month combined average (mean hearing levels of 15.5 dB compared with 21.4 dB).[19]

Three studies compared hearing outcomes for patients who received adenoidectomy and TT with those that received TT alone. At 6-month followup, outcomes were similar in the two groups and not significantly different.[19,97,99] At 12 months, Black et al.[97] and Maw and Herod[99] studies, comparing one ear in each patient, continued to find differences between groups to be small and not statistically significant. In contrast, the TARGET study, randomized by child, found significantly better hearing outcomes in the adenoidectomy group.[19] The mean hearing level at 12 to 24 months was 15.9 dB in adenoidectomy and TT patients and 20.1 dB in TT-only patients.

Other Outcomes

Episodes of AOM were measured in one study included in the systematic review and they were similar at 18 or 36 months.[119] No studies measured vestibular function.

Pharmaceutical Interventions: Oral or Topical Nasal Steroids

Description of Studies

The included evidence consisted of one recent Cochrane review[31] which was updated[32] during the period of this review. The update includes one more recent trial, conducted by Williamson et al.[20,121] (Table 21). The Cochrane review summarized evidence from nine RCTs of oral steroids and three RCTs of topical intranasal steroids, excluding studies limited to ears (rather than children). The Williamson et al. study with topical intranasal steroids was conducted by the UK Health Technology Assessment Programme, and published as a report[20] and peer-reviewed manuscript.[121] All studies were in comparison with placebo controls and some of the oral steroid studies included antibiotics in both arms. All studies included participants 14 years of age and younger. The studies in the Cochrane review did not exclude children with comorbidities, except for the Williamson et al. study which excluded children with Down syndrome, cleft palate, and other comorbidities (Table 21). The studies in the Cochrane review included 1 week and 1- to 6-month followup; except for the Williamson RCT which also included 9-month followup. Both the original review and the update were assessed as low risk of bias.

Table 21. Characteristics of studies: Oral or topical nasal steroids

Study, Study Type, Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Followup	Age Range	Risk of Bias
Thomas et al., 2006[31] Systematic review International 11 RCTs included in analysis: Giebink et al., 1990,[122] Macknin et al., 1985[123] Niederman et al., 1984,[124] Mandel et al., 2002,[125] Podoshin et al., 1990,[126] Tracy et al., 1998,[127] Hemlin et al., 1997,[128] Williamson et al., 2010,[121] Schwartz et al., 1980,[129] Lambert, 1986,[130] Berman et al., 1990,[131] and Shapiro et al., 1982[132]	Arms differ across comparisons: 11 trials (728 participants)	OME determined by: A. Air-bone gap of 10 dB or more + 2 or more of: otomicroscopy, pneumatic otoscopy, tympanometry (type B or C2) B. 2 or more of: otomicroscopy, pneumatic otoscopy, tympanometry (type B or C2) C. 1 of otoscopy alone or tympanometry (type B or C2) D. Poorly or not defined Significant hearing loss defined by: A. Pure-tone audiometry hearing loss of >20 dB at 2 or more times within 3 months (e.g., mean of 500, 1,000, and 2,000 Hz hearing loss bilaterally) B. Defined, but less strict than A C. Uncertain or not defined	NR	Include: RCTs of oral and topical intranasal steroids, including studies using non-intervention controls with adequate blinding of outcome assessor. Exclude: Observational studies, studies reporting outcomes only with ears as unit of analysis; studies (or data from arms of studies) comparing steroid + additional treatment vs. treatment with placebo + placebo because effect of steroid could not be isolated. However, studies with antibiotic co-intervention were included, if identical in both arms.	1-2, and 6 months	0-14 yrs	Low

Table 21. Characteristics of studies: Oral or topical nasal steroids (continued)

Study, Study Type, Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Followup	Age Range	Risk of Bias
Simpson et al.,2011[32] Systematic review update of Thomas et al., 2006[31] 11 RCTs included in Thomas et al., 2006[31] plus Williamson et al., 2009[20]	Arms differs across comparisons: 12 trials (945 participants)	Same criterion as Thomas et al.,2006[31]	NR	Same criterion as Thomas et al., 2006[31] except additional study Williamson et al. 2009[20] Excluded: cleft palate, Down syndrome, primary ciliary dyskinesia	1-3 wks, 1-3 months, 6 months, 9 months	0-12 yrs	Low

dB = decibel; Hz = Hertz; mos = months; NR = not reported; OME = otitis media with effusion; RCT = randomized control trial; vs. = versus; wks= weeks; yrs = years

Key Points

- Meta-analyses comparing oral steroids and controls (N=106) did not show differences in MEE at 1- or 2-month followup (low strength of evidence) (Table 22).
- Meta-analyses comparing oral steroids and controls (N=243) (with oral antibiotic adjunctive therapy) did not show differences in MEE at 1- or 2-month followup (medium strength of evidence).
- We found insufficient evidence comparing oral steroids with controls (with or without oral antibiotic adjunctive therapy) at 3 months or longer for any hearing outcomes.
- Patients receiving topical intranasal steroids did not differ from controls in cure rates or hearing loss at 3-month or longer followup, based on results from one low risk-of-bias study (low strength of evidence).
- No studies reported on AOM or other clinical or health care use outcomes (insufficient evidence).

Table 22. Strength of evidence: Clinical outcomes and health care utilization

Comparison	OME Signs And Symptoms	Measured Hearing
Oral steroids vs. control (1-2 months)	**Low** Persisting OME: no difference MA, 3, 106	**Insufficient** Hearing gain: no diff 1, 49
Oral steroids + antibiotic vs. control + antibiotic (1-2 months)	**Moderate** Persisting OME: no difference MA, 2, 243	**Insufficient** No studies
Topical intranasal steroid vs. control (1, 3, and 9 or more months)	**Low** Cure rate: no diff 1, 217	**Low** Hearing loss: no diff 1, 217
Topical intranasal steroid + antibiotic vs. control + antibiotic (3 or more months)	**Insufficient** Persisting OME (6 months): no diff 1, 59	**Insufficient** No studies
Oral steroids vs. control (3 months)	**Insufficient** No studies	**Insufficient** Hearing gain: no difference 1, 49
Oral steroids + antibiotic vs. control + antibiotic (6 or more months)	**Insufficient** Persisting: No diff 1, 15	**Insufficient** No study

diff = difference; MA = meta-analysis; OME = otitis media with effusion; RCT = randomized control trial; vs. = versus; wks = weeks; yrs = years

Detailed Synthesis

OME Signs and Symptoms Outcomes

The Cochrane reviews[31,32] presented results on outcomes related to MEE through two measures: persisting OME and cure rates as measured by a flat tympanogram (Table 23). The reviews found oral steroids plus antibiotics to be superior to placebo plus antibiotics at less than one month, based on a meta-analysis of five studies, Risk Ratio (RR): 1.99 (95% CI, 1.14 to 3.49) (N=409). In contrast, one study that did not include antibiotics found no difference at 3 weeks, RR: 0.64 (95% CI, 0.31 to 1.31).[132] We found no differences in any treatment comparisons at any end points of longer duration. At 1- to 2-month followup, the systematic review found no difference between oral steroids versus controls in relation to persisting OME, RR=1.54 (95% CI, 0.76 to 3.14) based on a meta-analysis of three studies (N=106) or similarly for oral steroids versus controls, when both arms also received antibiotic treatment, RR=1.44 (95% CI, 0.97 to 2.13), based on a meta-analysis of three studies (N=231).[32] The Williamson et al. study also found no significant difference in cure rates in topical steroids versus controls at 1 month, controlling for season, age, atrophy, and clinical severity, RR=0.97 (95% CI, 0.74 to 1.26) (N=194).

Table 23. Clinical outcomes: Oral or topical nasal steroids

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion	Measured Hearing
Thomas et al., 2006[31] Systematic review Simpson, et al., 2011[32] Update systematic review	MA of 5 RCTs: Oral steroid plus antibiotic vs. control plus antibiotic (N=409) Berman et al., 1990,[131] Hemlin et al., 1997,[128] Lambert et al., 1986,[130] Mandel et al., 2002,[125] Schwartz et al., 1980[129]	7-28 days	OME resolution RR: 1.99 (95% CI 1.14 to 3.49)	NR
	MA of 3 RCTs: Oral steroid vs. control Giebink et al., 1990,[122] Macknin et al., 1985,[123] Niederman et al., 1984[124] (N=106)	1-2 months 4-6 weeks	Persisting OME Peto OR: 0.55 (95% CI, 0.21 to 1.48) OME resolution [a] RR:1.54 (95% CI 0.76 to 3.14)	NR
Thomas et al., 2006[31] Systematic review (continued)	1 RCT: Macknin et al., 1985[123] Oral steroid vs. control (N=49)	1-2 months	NR	Hearing gain by at least 10 dB in either ear OR: 1.47 (95% CI, 0.39 to 5.57) (baseline: NR) Hearing not improved by at least 10 dB in either ear RR: 1.09 (95% CI, 0.80 to 1.49) [a]
	MA: 2 RCTs: Mandel et al., 2002[125] Podoshin et al., 1990[126] Oral steroids + antibiotic vs. control + antibiotic (N=243) (N=231) [a]	1-2 months	Persisting OME Peto OR: 0.75 (95% CI, 0.45 to 1.27) OME resolution [a] RR: 1.44 (95% CI, 0.97 to 2.13)	NR
	1 RCT [a] Podoshin et al., 1990[126] Oral steroid + antibiotic vs. control + antibiotic (N=99)	2 months	NR	Hearing loss through assessment of air-bone gap (at least some conductive loss) [a] G1: 60% G2: 60% RR:1.01 (95% CI, 0.73 to 1.40)
	1 RCT [a] Shapiro et al., 1982[132] Intranasal steroid vs. control	3 weeks	OME resolution: RR: 0.64 (95% CI, 0.31 to 1.31)	NR
	1 RCT: Tracy et al., 1998[127] Intranasal steroid + antibiotic vs. placebo + antibiotic or antibiotic alone (N=59)	3 months	Persisting OME OR: 0.72 (95% CI, 0.21 to 2.44) OME resolution [a] RR: 1.26 (95% CI, 0.54 to 2.96)	NR

Table 23. Clinical outcomes: Oral or topical nasal steroids (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion	Measured Hearing
Thomas et al., 2006[31] Systematic review (continued)	1 RCT: Hemlin et al., 1997[128] Oral steroid + antibiotic vs. control + antibiotic (N=15)	6 months	Persisting OME OR: 0.15 (95% CI, 0.00 to 7.80)	NR
	1 RCT: Williamson et al., 2010[121] Williamson et al., 2009[20] Intranasal steroid vs. control (N=141)	1-6 months	NR	Audiometry failing on ≥ 2 out of 5 frequencies in both ears [a] RR: 1.17 (95% CI, 0.87 to 1.58)
	Williamson et al., 2010[121] Williamson et al., 2009[20] Intranasal steroid vs. control G1: 96 G2: 98	1 month	Cure rate[b] Diff in OR (adj): 0.934 (0.498 to 1.751) Diff in RR (adj): 0.97 (0.74 to 1.26)	NR
	Williamson et al., 2010[121] Williamson et al., 2009[20] Intranasal steroid vs. control G1: 86 G2: 86	3 months	Diff in OR (adj): 1.451 (0.742 to 2.838) Diff in relative risk(adj): 1.23 (0.84 to 1.80) OME resolution [a] RR 1.11 (95% CI, 0.85 to 1.46)	Pass/fail criteria on sweep audiometry (fail at 2 or more frequencies at 25 dB in the better ear): G1: 52/83 (63%) G2: 47/81 (58%) Hearing loss from tympanograms, median days (IQR) G1: 19.43 (14.64-1.21) G2: 21.15 (14.86-0.94) WMD: 0.0 (95% CI, 4.51 to 4.51 [a] Baseline hearing G1: 30.97 (23.8-32.65) G2: 30.94(24.03-32.21)
	Williamson et al., 2010[121] Williamson et al., 2009[20] Intranasal steroid vs. control G1: 72 G2: 72	9 months	Diff in OR (adj): 0.822 (0.387 to 1.746) Diff in relative risk (adj): 0.90 (0.58 to 1.41) OME resolution [a] RR: 0.85 (95% CI, 0.65 to 1.11)	Pass/fail criteria on sweep audiometry (fail at 2 or more frequencies at 25 dB in the better ear): G1: 44/74 (59%) G2: 34/67 (51%) Audiometery failing on ≥ 2 out of 5 frequencies in both ears)[a] RR: 1.17 (0.87 to 1.58) Hearing loss from tympanograms, median (IQR) G1:19.56(14.88-0.84) G2: 17.89 (14.11-3.55)

adj = adjusted; CI = confidence interval; dB = decibel; diff = difference; G = group; IQR = interquartile range; MA = meta-analysis; N = number; NR = not reported; OME = otitis media with effusion; OR = odds ratio; RCT = randomized controlled trial; RR = risk Ratio; vs. = versus; WMD = weighted mean difference

[a]Denotes information from update review, Simpson, et al., 2011.[32]

[b]Determined by A or C1 tympanogram in at least 1 ear; adjusted results (OR and RR) controlling for season, age, atrophy, and clinical severity score.

At 3-month followup, in two studies, MEE, as measured by OME resolution,was superior with intranasal steroids but results were not statistically significant. Tracy et al. included antibiotics in both arms in one small RCT, RR= 1.26 (95% CI, 0.54 to 2.96) (N=59).[127] We also found small nonsignificant differences in cure rates based on evidence from the larger Williamson et al. study, RR=1.11 (95% CI, 0.85 to 1.46) (N=172).[32] At 6-month followup, persisting OME did not differ significantly between patients receiving oral steroid treatment plus antibiotic and controls plus antibiotic, based on evidence from one trial (N=15).[128] At 9-month followup, OME resolution did not differ between topical steroids and control, based on the Williamson et al. study, RR=0.85 (95% CI, 0.65 to 1.11) (N=144).[32,121]

Hearing Outcomes

Hearing did not differ between topical steroid and control groups, as measured at 3 and 9 months through audiometry and tympanometry based on one low risk-of-bias study (Table 23).[20] We did not find evidence related to hearing outcomes based on oral steroid treatment at 3 months or later.[31]

Other Outcomes

We found no evidence on other clinical outcomes, including OME episodes of AOM or vestibular function.

Nonpharmaceutical Interventions: Autoinflation

Description of Studies

The evidence consisted of one recent Cochrane review by Perera et al.[30] (Table 24) summarizing evidence from six RCTs of any form of autoinflation, a technique designed to increase oropharyngeal pressure via a nasal balloon or other process. Two different types of autoinflation devices were reviewed. One required the patient to actively inflate a balloon type device, whereas the other was a passive device in which the air was delivered into the nose while the patient swallowed. The review included five studies with children 3–12 years of age (Arick and Silman, 2005;[133] Blanshard et al., 1993;[134] Brooker et al., 1992;[135] Fraser et al.,1977;[136] Stangerup and Tos, 1992[137]) and one study of adults, 16–75 years of age Lesinskas, 2003.[138] All studies were in comparison to no autoinflation. Other treatments (e.g., analgesics, antibiotics) were permitted as long as they were provided equally to both arms. The Cochrane review included one study with an end point of 4 weeks post-treatment,[133] one study at the end of treatment and 50 days post-treatment[138] and one study at the end of treatment and approximately 2 weeks, 6 weeks, and 10 weeks post-treatment.[137] The other three trials recorded outcomes only at the end of treatment, the length of which differed.[134-136]

Table 24. Characteristics of studies: Autoinflation

Study, Study Type, Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Study Followup	Age Range	Risk of Bias
Perera et al., 2009[30] Systematic review International 6 RCT's Arick & Silman, 2005,[133] Blanshard et al., 1993[134] Brooker et al., 1992;[135] Fraser et al.,1977,[136] Lesinskas 2003, and Stangerup and Tos, 1992[137]	Autoinflation vs. control:6 trials (602 participants)	Tympanometry (type B or C2), either alone or in combination with simple or pneumatic otoscopy or audiometry	Various	Include: RCTs; any form of autoinflation; other treatments had to be given to both arms	3 trials: at end of treatment 1 trial: 4 wks post-treatment 1 trial: 2 mos 1 trial: 3 mos	3-16 yrs (5 studies) 16-75 yrs (1 study)	Medium

mos = months; RCT = randomized controlled trial; wks = weeks; yrs = years; vs.= versus

Key Points

- Based on two meta-analyses of two studies,[134,137] included in the Perera et. al systematic review,[30] autoinflation improved middle ear status as measured by tympanometry in the short term (e.g., a month or less from treatment initiation) (low strength of evidence). Autoinflation did not show improvement in tympanometry at more than 1 month from treatment (insufficient strength of evidence) (Table 25).
- Groups receiving autoinflation did not differ significantly from controls in measured hearing (pure tone audiometry [PTA]) at either the end of treatment or 4 weeks after treatment (insufficient strength of evidence).
- No included studies reported on AOM, balance, or use of health care services (insufficient strength of evidence).

Table 25. Strength of evidence for KQ 1: Autoinflation

Comparison (G1 vs. G2)	OME Signs and Symptoms	Objective Hearing
Autoinflation vs. Control	Low Two MA (2; 185) Improvement in tympanogram with autoinflation at $\leq$ 1 mo Insufficient One MA (2: 185) no difference in improvement in tympanogram at > 1 mo	Insufficient One MA (2: 125) No difference in HL improvement using PTA Insufficient One MA (2:179) No difference in average HL using PTA (4 wks post-tx and end of tx)

mo = month; MA = meta-analysis; HL = hearing level; PTA = pure tone audiometry; tx = treatment

Detailed Synthesis

OME Signs and Symptoms Outcomes

The systematic review[30] presented results on improvement in middle ear status as measured with tympanometry (Table 26). Several of the trials reported improvement in tympanometric classification at different time points; in some studies, the outcomes were measured during the period of time that treatment was administered. The results were presented for different classifications at different time points. No study in the review reported on OME recurrence.

In one meta-analysis of three studies,[134,135,137] the systematic review reported that, at 1 month or less, the autoinflation group did not have significant improvement from a B classification (a flat tracing usually indicative of the presence of middle ear fluid) at baseline, or C2 (highly negative curve, which is usually indicative of an abnormality) to a C1 classification (a moderately negative curve indicative as normal) or a tympanometric classification of A (considered to be normal).

Using data from two of the three trials included in the meta-analysis,[134,137] the systematic review authors reported two additional meta-analysis subanalyses in which baseline tympanogram classifications were more narrowly combined. They found that autoinflation significantly improved middle ear status relative to no treatment in children with a baseline B classification (presence of middle ear fluid) and in children with a baseline C2 classification (negative pressure, indicative of abnormality) at followup of 1 month or less. However, in the meta-analysis of trials that examined ears at more than 1 month from treatment initiation, Perera et al. found no difference between autoinflation patients and controls in rates of improvement in tympanometry (i.e., from B or C2 classifications indicating presence of fluid or an abnormal to C1 or A classifications, indicating as normal middle ear status).[30]

Table 26. Clinical outcomes: Autoinflation

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion	Measured Hearing
Perera et al., 2009[30]	MA: 3 studies Blanshard et al., 1993[134] Brooker et al., 1992;[135] Stangerup and Tos, 1992[137] (N=225) MA: 2 studies Blanshard et al., 1993;[134] and Stangerup and Tos, 1992[137] (N=185) MA: 2 studies Blanshard et al., 1993[134] and Stangerup and Tos, 1992[137] (N=185)	≤1 month	Tympanometry improvement B or C2 to C1 or A: RR: 1.65 (95% CI, 0.49 to 5.56) B to C1 or A RR: 2.71 (95% CI, 1.43 to 5.12) C2 to C1 or A RR: 3.84 (95% CI, 1.94 to 7.59)	NR
	MA: 2 studies Blanshard et al., 1993[134] and Stangerup and Tos, 1992[137] (N=185)	>1 month	B or C2 to C1 or A: RR 1.89 (95% CI, 0.77 to 4.67)	NR
	MA: 2 studies Blanshard et al., 1993[134] and Stangerup and Tos, 1992[137] (N=125)	End of treatment (3 weeks in 1 study and 3 months in the other study)	NR	Improvement in HL ≥10 dB measured by PTA RR 0.80 (95% CI, 0.22 to 2.88)
	MA 2 studies Arick and Silman, 2005[133] and Fraser et al.,1977[136] (N=179)	End of treatment in 1 study (6 weeks) and 4 weeks after treatment in the other study	NR	Average HL measured by PTA Weighted Mean Diff 7.02 (95% CI, -6.92 to 20.96)

CI= confidence interval; dB = decibel; Diff = difference; HL = hearing level; MA = meta-analysis; NR = not reported; N = number; PTA = pure tone average; RR = relative risk

Hearing Outcomes

Two meta-analyses examined hearing outcomes. In one, change in hearing level was measured by PTA of greater than 10 dB; in the second, the average hearing level was the outcome.[30] The first meta-analysis failed to find a difference between the autoinflation and control groups in change in hearing level either at the end of treatment or at 3 months post-treatment [RR= 0.80 (95% CI, 0.22 to 2.88)]. In the second meta-analysis, hearing levels at the end of 6 weeks of treatment or at 4 weeks post-treatment did not differ in the autoinflation and control groups (weighted mean difference = 7.02 [95% CI, -6.92 to 20.96]).

Other Outcomes

Other relevant outcomes, such as episodes of AOM, OME recurrence, or vestibular function were not discussed as a function of treatment.

KQ 2. Comparative Effectiveness of Interventions: Functional and Quality-of-Life Outcomes

Surgical Interventions: Tympanostomy Tube Comparisons

No studies reported on functional or quality-of-life outcomes.

Surgical Interventions: Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Key Points

- With one exception, children receiving TT did not display better language comprehension or expression than children who received active monitoring (Table 27). The one finding of superior performance with TT relied on teacher assessment at 4½ years of age. Failure to find differences between those receiving TT and those receiving watchful waiting were observed in a meta-analysis with data collected at 6 to 9 months followup as well as during preschool and the later elementary school years. Strength of evidence is moderate for no effect.
- Two RCTs did not find any differences between TT and watchful waiting on measures of cognitive development at 9 months followup and throughout the elementary school years (low strength of evidence).
- Children with early TT did not exceed children who received delayed treatment on any measure of academic achievement in 2 studies (low strength of evidence).
- In the only study to examine phonological or auditory processing, children with early TT did not differ from children with late TT (insufficient strength of evidence).
- One of two studies found that children with TT displayed better behavior than children receiving watchful waiting at less than 1 year followup (insufficient strength of evidence for mixed findings). Three studies found no differences in behavioral competence between TT and watchful waiting at time points from 1 year to 11 years of age (low strength of evidence for no difference).
- Only one investigation examined quality of life; researchers did not find differences between TT and watchful waiting (insufficient strength of evidence).

Table 27. Strength of evidence for KQ 2: Tympanostomy tubes versus watchful waiting or myringotomy

Treatment Comparison	Speech/ Language	Cognitive Development	Academic Achievement	Behavior	Quality of Life
TT vs. watchful waiting 6 to 9 months	**Moderate** No difference MA: 3, 394; Study: 1, 160	**Low** No difference Study: 1,160	**Insufficient** No studies	**Insufficient** Mixed results Studies: 2, 358	**Insufficient** No difference Study: 1, 176
TT vs. watchful waiting 1 year or more	**Low** No difference Study: 1, 393	**Low** No difference Studies 2: 553	**Low** No difference Studies 2, 499	**Low** No difference Studies: 3, 716	**Insufficient** No difference Study: 1 Study: 1, 176
TT vs. Myringotomy	**Insufficient** No studies	**Insufficient** No studies	**Insufficient** No studies	**Insufficient** No studies	**Insufficient** No studies

MA = meta-analysis; TT = tympanostomy tubes; vs. = versus

Detailed Synthesis

The evidence for functional and quality-of-life outcomes of TT as compared with either myringotomy or watchful waiting is found in two systematic reviews,[21,22] and more extensively in individual reports for three of the included studies[68,93,140] (seven reports) (Table 28). Outcomes include language and cognitive skills, behavior, phonological processing, and academic performance.

Speech/Language and Cognitive Outcomes

Browning et al.[22] performed meta-analysis of three studies[93,94,100] measuring differences in language comprehension and language expression at 6–9 months post-treatment between TT and watchful waiting groups and found no significant difference (mean difference=0.09 [95% CI, -0.21 to 0.39] and mean difference=0.03 [95% CI, -0.41 to 0.49], for language comprehension and expression respectively). Individual studies provided similar evidence that TT were not associated with better language outcomes. In several reports, Paradise and colleagues[68,69] failed to find a difference in children's receptive language skills between those who had received early TT and those who had received late TT at either 3 years of age (mean difference = 0, 95% CI, -2.8 to 2.8) or 6 years of age (mean difference = 0; 95% CI,-3.6 to 3.2). Hall and colleagues[141] who followed the sample in Maw et al.[93] found significant differences in teacher assessment of language at 4½ years of age favoring TT (adjusted OR, 3.45; 95% CI: 1.42 to 8.39), but the benefit disappeared at 8 years of age, based on a standardized test (language comprehension: adjusted OR, 1.58; 95% CI, 0.59 to 4.25; oral expression: adjusted OR, 2.1; 95% CI, 0.78 to 5.65), controlling for age, gender, maternal education, housing, and mother's parity.

Two individual studies, one by Paradise and colleagues and one by Maw and colleagues (in four articles), reported on cognitive development.[68,69,93,141] No differences were observed between TT and watchful waiting/late TT at any time point from 9 months post-surgery (mean difference, 1.3; 95% CI, -2.58 to 7.04)[93]; 3 years of age (mean difference, 2.0; 95% CI, -4.1 to 1.1)[68]; 6 years of age (mean difference, 0; 95% CI, -3.0 to 2.5)[69]; to 8 years of age (OR, 2.39; 95% CI, 0.85 to 6.76).[141]

Table 28. Functional and health-related quality-of-life outcomes: Tympanostomy tubes versus watchful waiting or myringotomy

Study	Arm (N)	Study Duration Until Outcome Measurement	Speech/Language Cognitive Development	Academic Achievement	Phonological Processing/ Auditory Processing	Behavior	Quality of Life
Browning et al., 2010[22]	MA:3 RCTs (N=394) Maw et al., 1999[93] Rach et al., 1991[100] Rovers et al., 2000[94]	6-9 months	Language Comprehension, Bilateral TT vs. WW: Mean Difference 0.09 (95% CI, -0.21, 0.39)	NR	NR	NR	NR
	MA: 3 RCT (N=393) Maw et al., 1999[93] Rach et al., 1991[100] Rovers et al., 2000[94]	6-9 months	Language Expression TT vs. WW: Mean Difference 0.03 (95% CI, -0.42, 0.49)	NR	NR	NR	NR
	1 RCT by child Maw et al., 1999[93] (N=160) Companions: Wilks et al., 2000[142] Hall et al., 2009[141]	9 months	Griffiths Mental Development Mean Cognitive Index TT vs. WW 106.5 vs. 104.2 (95% CI, -2·58 to 7·04) (p=ns)	NR	NR	Richman Behavioral Scale, % with Problems (N=152) TT vs. WW 30% vs. 47% (95% CI, -33% to –2%) p=0.031 (favors tx)	NR
		18 months (N=152) Mean age 4.5 years	NR	NR	NR	24% vs. 20% (95% CI, -10% to 19%) p=0.66	NR
		7 years of age (N=108)	NR	NR	NR	SDQ, Teacher Report[a] Total Score OR: 2.05 (95% CI, 0.62 to 6.70) p=0.237	NR

Table 28. Functional and health-related quality-of-life outcomes: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Speech/Language Cognitive Development	Academic Achievement	Phonological Processing/ Auditory Processing	Behavior	Quality of Life
Browning et al., 2010[22] (continued)	1 RCT by child Maw et al., 1999[93] (N=160) Companions: Wilks et al., 2000[142] Hall et al., 2009[141] (continued)	8 years of age (N=108)	Language Comprehension[a] Total Score TT vs. WW OR: 1.58 (95% CI, 0.59 to 4.25) p=0.366 Oral Expression[a] Total Score TT vs. WW OR: 2.10 (95% CI, 0.78 to 5.65 p=0.143 WISC-III[a] Total Score TT vs. WW OR: 2.39 (95% CI, 0.85 to 6.76) p=0.100	Reading TT vs. WW OR: 1.57 (95% CI, 0.72 to 3.43) Writing OR: 0.597 (95% CI, 2.05 to 0.92) Mathematics OR: 0.618 (95% CI, 1.71 to 0.77)	NR	NR	NR
	1 RCT (by child) Paradise et al., 2001[68] (N=393)	3 years of age	PPVT-R Early Tubes vs. Late Tubes 92 vs. 92 (95% CI, -2.8 to 2.8) McCarthy Mental Development Mean General Cognitive Index Early Tubes vs. Late Tubes 99 vs. 101 (95% CI, -4.1 to 1.1)	NR	NR	CBCL (Parent) Mean Total Problem Score Early Tubes vs. Late Tubes 50 vs. 49 (95% CI, -0.6 to 3.4)	NR

Table 28. Functional and health-related quality-of-life outcomes: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Speech/Language Cognitive Development	Academic Achievement	Phonological Processing/ Auditory Processing	Behavior	Quality of Life
Browning et al., 2010[22] (continued)	Paradise et al., 2005[69] (N=395)	6 years of age	PPVT-R Early Tubes vs. Late Tubes 94 vs. 94 (95% CI, -3.6 to 3.2) WISC-R Early Tubes vs. Late Tubes 98 v. 98 (95% CI, -3.0 to 2.5)	NR	SCAN Test Early Tubes vs. Late Tubes 95 vs. 94 (95% CI, -4.6 to 1.5)	CBCL (Parent) Early Tubes vs. Late Tubes 49 vs. 48 95% CI, -1.5 to 2.7)	NR
	Paradise et al., 2007[67] (N=391)	9-11 years of age	NR	WJRMT Word Identification Early Tubes vs. Late Tubes 98 vs. 99 (95% CI, -3.2 to 1.3) WJRMT Passage Comprehension Early Tubes vs. Late Tubes 98 vs. 99 (95% CI, -3.2 to 1.2) W-J III Spelling Early Tubes vs. Late Tubes 96 vs. 97 (95% CI, -3.9 to 2.0) WJ III Writing Early Tubes vs. Late Tubes 104 vs. 105 (95% CI, -4.1 to 1.7)	CTPP Elision Subtest Early Tubes vs. Late Tubes 8.6 vs. 8.7 (95% CI, -0.9 to 0.7) Children's HNT (noise tested from the front Early Tubes vs. Late Tubes -0.4 vs. -0.6 (95% CI, -0.06 vs. 0.58)	CBCL (Parent) Early Tubes vs. Late Tubes 51 vs. 49 (95% CI, 0.2 to 4.8)	NR

Table 28. Functional and health-related quality-of-life outcomes: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Speech/Language Cognitive Development	Academic Achievement	Phonological Processing/ Auditory Processing	Behavior	Quality of Life
Browning et al., 2010[22] (continued)	1 RCT (by child) Rovers et al., 2001[140] (N=176)	6 months	NR	NR	NR	The Erickson child Mean scores TT vs. WW Affection 4.4 vs. 4.6 Avoidance 6.3 vs. 6.5 Compliance 5.1 vs. 5.2 Negativism 6.6 vs. 6.7 Reliance 6.5 vs. 6.7 MANOVA Hotelling Trace p=0.19	The TAIQOL Mean scores TT vs. WW Vitality 3.3 vs. 3.3 Appetite 5.0 vs. 4.7 Communication G1: 6.7 vs. 5.8 Motoric 4.4 vs. 4.4 Social 3.5 vs. 3.5 Anxiety 4.3 vs. 4.1 Aggression 11.9 vs. 11.1 Eating 3.3 vs. 3.5 Sleeping 6.8 vs. 6.6 MANOVA Hotelling Trace p=0.22

Table 28. Functional and health-related quality-of-life outcomes: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Speech/Language Cognitive Development	Academic Achievement	Phonological Processing/ Auditory Processing	Behavior	Quality of Life
Browning et al., 2010[22] (continued)		12 months (N=165)	NR	NR	NR	Affection 4.5 vs. 4.9 Avoidance 6.5 vs. 6.9 Compliance 5.2 vs. 5.6 Negativism 6.6 vs. 6.9 Reliance 6.6 vs. 6.8 MANOVA Hotelling Trace p=0.38	Vitality 3.1 vs.3.2 Appetite 5.3 vs.4.9 Communication 5.9 vs.5.6 Motoric 4.2 vs.4.2 Social 3.5 vs. 3.5 Anxiety 4.6 vs. 4.3 Aggression 11.8 vs.11.5 Eating 3.3 vs. 3.4 Sleeping 6.4 vs. 6.4 MANOVA Hotelling Trace p=0.94

CBCL = Child Behavior Checklist; CI = confidence interval; CTPP = Comprehensive Test of Phonological Processing; HNT = Hearing in Noise Test; MA = meta-analysis; MANOVA = Multivariate analysis of variance; N = number; NR = not reported; ns = not sufficient; OR = odds ratio; PPVT-R = Peabody Picture Vocabulary Test, Revised; RCT = randomized controlled trial; SDQ = Strengths and Difficulties Questionnaire; TAIQOL = TNO-AZL Infant Quality of Life; TT = tympanostomy tubes; tx = treatment; vs. = versus; W-J III = Woodcock-Johnson III Tests of Achievement; WISC-III = Wechsler Intelligence Scale for Children, Third edition; WISC-R = Wechsler Intelligence Scale for Children, Revised; WJRMT = Woodcock-Johnson Reading Mastery Test –Revised; WW = watchful waiting

[a]Analyses adjusted for age, gender, maternal education, housing and mother's parity.

Academic Achievement

Two studies examined whether children with TT had better academic achievement scores than children who received delayed treatment.[67,141] Followup was at age 8 in the Hall et al. (2009) study and at ages 9 to 11 in the Paradise et al. (2007) study. Neither study reported differences in reading (overall reading; adjusted OR, 1.57; 95% CI, 0.72 to 3.43[141]; passage comprehension: mean difference, 1.0; 95% CI, 3.2 to 1.2,[67] spelling: mean difference, 1.0; 95% CI, -3.9 to 2.0[67]; mathematics: adjusted OR, 2.05; 95% CI, 0.92 to 4.58,[141] or writing: adjusted OR, 1.71; 95% CI, 0.77 to 3.81;[141] mean difference, 1.0; 95% CI, -4.0 to 1.7[67]).

Phonological and Auditory Processing

Only the Paradise and colleagues study[67,69] examined phonological and auditory processing. The investigators failed to find a difference between children's performance on measures of phonological and auditory processing at either 6 years of age (mean difference = 1.0 [95% CI, -4.6 to 1.5]) or 9 to 11 years of age (Elision subtest: mean difference = 0.0 [95% CI, -0.9 to 0.7]; Children's Hearing in Noise Test: mean difference = 0.2 [95% CI, -0.06 to 0.58]).

Behavioral Competence

Three studies (seven reports)[67-69,140-143] examined behavioral competence comparing TT with watchful waiting. Aside from the Wilks et al. study[142] in which children with TT displayed fewer behavior problems (30%) than those in the watchful waiting condition (47%) (95% CI, -33% to -2%) p=0.031, no other differences between TT and watchful waiting or delayed TT were detected.

Quality of Life

Rovers et al.[140] was the only investigator to include a measure of quality of life. Using the TNO-AZL Infant Quality of Life (TAIQOL) (a health-related quality-of-life measure for 1- to 4-year-olds), they did not find a difference in any of the subscales measured at either 6 months (MANOVA, Hotelling's trace p=0.19) or 12 months post-treatment (MANOVA, Hotelling's trace p=0.22).

Surgical Interventions: Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy or Adenoidectomy Alone

Key Findings

- One small study examined differences in quality-of-life between children receiving adenoidectomy and TT and those receiving adenoidectomy and myringotomy. Strength of evidence was insufficient.
- Strength of evidence was insufficient for all speech/language, cognitive and behavioral outcomes because these outcomes were not examined in any study.

Detailed Synthesis

Only one small study (N=52) evaluated differences in quality-of-life outcomes between children receiving TT and adenoidectomy and those receiving myringotomy and adenoidectomy[115] (Table 29). Although only TT group improved from baseline, the difference between the two groups was not significant.[115]

Table 29. Functional and health-related quality-of-life outcomes: Tympanostomy tubes plus adenoidectomy versus myringotomy plus adenoidectomy or adenoidectomy alone

Study	Arm (N)	Study Duration Until Outcome Measurement	Speech/ Language Cognitive Development	Quality of Life
Vlastos et al., 2011[115]	G1: Shepard TT + adenoidectomy (N=25) G2: Myringotomy + adenoidectomy (N=27)	6 months	NR	OM-6 Score Score G1: 1.88 G2: 2.04 Mean Difference: -.0.16 (95% CI, -0.43 to 0.10) Change from Baseline G1: -0.38 G2: -0.00 Mean change: -0.38 (95% CI, -0.65 to -0.10)
		12 months	NR	Score G1: 1.84 G2: 2.04 Mean Difference: -0.20 (95% CI, -.0.57 to 0.17) Change from Baseline G1: -0.32 G2: 0.01 Mean change: -0.23 (95% CI, -0.76 to 0.11)

CI = confidence interval; G = group; N = number; NR = not reported; OM-6 = Otitis Media-6; TT = tympanostomy tubes

Surgical Interventions: Myringotomy Comparisons

Key Findings

We found no evidence examining functional outcomes or health-related quality of life.

Surgical Interventions: Myringotomy Plus Adenoidectomy Comparisons

Key Findings

We found no evidence examining functional outcomes or health-related quality of life.

Surgical Interventions: Adenoidectomy Versus Other Interventions

Key Findings

We found no evidence examining functional outcomes or health-related quality of life.

Pharmaceutical Interventions: Oral or Topical Nasal Steroids

Key Points

- Patients receiving topical intranasal steroids versus controls did not differ on the quality-of-life outcome of reported hearing at 3 months (insufficient evidence, one small study).

- Patients receiving topical intranasal steroids versus controls, both receiving antibiotics, did not differ at 3 months on a quality-of-life symptom score (low strength of evidence, one study).
- No study reported on quality-of-life outcomes for oral steroids versus controls (with or without antibiotics) or oral steroids plus antibiotics versus controls (insufficient evidence).
- No study reported on speech or language outcomes, cognitive development, or behavioral outcomes (insufficient evidence).

Detailed Synthesis

Topical nasal steroids did not differ from controls in relation to symptom scores in one small study that included antibiotics in both arms (N=39)[31] (Table 30). The larger Williamson et al. study comparing nasal steroids to control without the addition of antibiotics did not find significant differences between groups in parent-reported hearing difficulties or days with hearing loss; rates and confidence intervals were similar in both arms.[20]

Table 30. Functional and health-related quality-of-life outcomes: Oral or topical nasal steroids

Study	Arm (N)	Study Duration Until Outcome Measurement	Quality of Life
Thomas et al., 2010[31]	1 RCT: Tracy et al., 1998[127] Topical intranasal steroid + antibiotic vs. control + antibiotic or antibiotic alone (N=39)	3 months	Symptom score Weighted mean diff: -4.50 (95% CI, -10.28 to 1.28)
Williamson et al., 2010[121,b] Williamson et al., 2009[20]	Baseline: (N=196) G1: Topical intranasal steroid (N=86) G2:Control (N=86)	Baseline: G1: 6.06 (2.83-8.57) G2: 5.88 (2.33-7.60) 3 months	Parent-reported hearing difficulties, median (IQR) G1: 5.54 (0.90-8.43) G2: 3.92 (0.90-7.60) (p=NS)[a]
	G1: 72 G2: 72	9 months	G1: 2.33 (0.21 to 7.60) G2: 2.33 (0.42-6.60) (p=NS)[a]
	G1: 86 G2: 86	3 months	Days with hearing loss, median (IQR) G1: 4 (0 to 24.5) G2: 4 (0 to 18.5) p=0.45

CI = confidence interval; IQR = interquartile range; mos = months; N = number; NS = not significant; vs. = versus
[a]Calculated by authors.
[b]Study included in Simpson et al. systematic revidew update, 2011.[31]

Nonpharmaceutical Interventions: Autoinflation

Key Findings

We found no evidence examining functional outcomes or health-related quality of life.

KQ 3. Harms or Tolerability

Surgical Interventions: Tympanostomy Tube Comparisons

Key Points

- Otorrhea rates differed by TT type; placement of longer-term TT are related to a higher probability of otorrhea (low strength of evidence).
- For other side effects, such as perforation, tympanosclerosis, atrophy, cholesteatoma, or granulation, evidence was either not available at all (no studies) or too sparse in too few studies with similar intervention comparisons to determine a direction of effect (insufficient evidence).

Detailed Synthesis

We identified 13 studies that compared side effects by type of TT or insertion technique (Table 31). The systematic review by Hellstrom et al.[21] included seven studies; 5 RCTs (2 of which were reported in 2 articles)[75,76,78,81,82,90,144] and 2 nonrandomized controlled trials.[79,80] We identified 6 additional studies: 3 RCTs,[83,85,87] 1 nonrandomized controlled trial,[84] and 2 cohort studies.[45,86]

Otorrhea

Otorrhea was the most frequently studied harm in the included studies. Similar to our benefits analysis for KQ 1, we examined harms in relation to TT design (short or long term retention), placement technique, and material.

Otorrhea rates were found to vary by type of TT inserted. Based on one RCT and two observational studies, longer-term TT had higher otorrhea rates; Goode-T made with silicon (longer term) versus Armstrong made with Teflon,[83] Paparella (longer term) versus Shepard and Shah tubes at 12, 24, and 30 months after placement[45] and Paparella versus Shepard TT at 24 months.[86] However, the studies did not report otorrhea rates per day that the TT were in place; thus, it is unclear if the design of long-term TT increased otorrhea or if this result was solely because the TT were in place for a longer time.

Otorrhea rates were lower in subjects who got N-acetylcysteine at the time of insertion.[87] Ottorhea rates were also lower at 2 weeks post-TT insertion after infusion of benesol-N.[81] The technique of touching by the surgeon versus not touching during TT insertion did not change otorrhea rates.[80] Two studies of topical antibiotics at the time of TT insertion found decreased rates of otorrhea (data not provided).[79,81]

Abdullah (1990) and Licamelli (2008) studied otorrhea differences based on TT material, and found no significant difference based on silicon versus polyethylene[84] or phosphorylcholine coating of Armstrong tubes.[85] Heaton et al found no differences based on anterior versus posterior placement.[76]

Table 31. Treatment harms or tolerability: Tympanostomy tube comparison studies

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes	Otorrhea/ Occlusion/ Granulation	Perforation/ Atelectasis/ Retraction	Cholesteatoma/ Tympanosclerosis
Wielinga et al., 1990[83] RCT by ear	G1: Goode Silicon tube (N=15) G2: Teflon Armstrong tube (N=15)	Over 7 year period	G1: 20% G2: 47%	Otorrhea G1: 20% G2: 13% Occlusion G1: 20% G2: 40% Granulation G1: 1 ear (6%) G2: 1 ear (6%)	Perforation G1: 6% G2: 6%	Cholesteatoma G1: 0% G2: 0%
Abdullah et al., 1994[84] NRCT by ear	G1: Trimmed high grade silicone Shah permavent tube (N=25) G2: Polyethylene Shah tube (N=25)	24-29 months	G1: 0 G2: 5.8%	Otorrhea G1: (0%) G2: 2 ears: (8%)	Perforation G1: 0% G2: 4%	Tympanosclerosis G1: 7 ears G2: 11 ears None in both ears: 2 children
Licameli et al., 2008[85] RCT by ear	G1: Phosphorylcholine-coated fluoroplastic Armstrong tube (N=70) G2: Uncoated fluoroplastic Armstrong tube (N=70)	24 months	NR	Otorrhea G1: 8.7% G2: 7.5% p=0.74 Occlusion G1: 10.3% G2: 13.4 p=0.53 Granulation G1: 4.4% G2: 6.0% p=0.66	Perforation G1: 4.0% G2: 0% p=0.24	NR

Table 31. Treatment harms or tolerability: Tympanostomy tube comparison studies (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes	Otorrhea/ Occlusion/ Granulation	Perforation/ Atelectasis/ Retraction	Cholesteatoma/ Tympanosclerosis
Iwaki et al., 1998[86] Retrospective cohort by ear	G1: Teflon Shepard tube (N=75 ears) G2: Silicone Goode-T tube (N=39 ears) G3: Silicone Paparella II tube (N=106 ears)	12 to 24 months	NR	Otorrhea G1: 9 ears (12%)[a] G2: 14 ears (36%)[a] G3: 40 ears (38%)[a] G2 or G3 vs. G1 diff p<0.01 Granulation G1: 0 ears G2: 0 ears G3: 8 ears (7.5%) G1 vs. G3: p<0.05	Perforation G1: 0% G2: 7.7% G3: 10.4% G1 vs. G2: p<0.05 G1 vs. G3: p<0.01 Atelectasis G1: 0% G2: 1 ear (2.6%) G3:2 ears (1.9%) p=NR Retraction G1: 12% G2: 10.2% G3: 6.6% p=NR	Cholesteatoma G1: 1.3% G2: 0% G3: 0% p=NS
Slack, Gardner, and Chatfield, 1987[45] Retrospective cohort by ear	G1: Shepard tube (N=214) G2: Shah tube (N=70) G3: Paparella tube (N=275)	12 to 24 mos	NR	Otorrhea G1: 5.7% G2: 5.6% G3: 40% G1 vs. G3: p<0.001 G2 vs. G3: p<0.001	NR	NR
Ovesen et al., 2000[87] RCT by person and by ear	G1: TT[a] + N-acetylcysteine instilled in one ear (N=37 ears) G2: TT[a] + placebo vehicle in one ear (N=38 ears) G3 (contralateral ear): TT[a] (N=75)	29 mos	G1: 5 ears (14%) G2: 14 ears (37%) G3: 24 ears (32%) 3-way diff: p<0.025	Otorrhea G1: 24% G2: 13% G3: 16% p>0.15	NR	NR

Table 31. Treatment harms or tolerability: Tympanostomy tube comparison studies (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes	Otorrhea/ Occlusion/ Granulation	Perforation/ Atelectasis/ Retraction	Cholesteatoma/ Tympanosclerosis
Hellstrom et al., 2011[21]	NRCT Pearson et al., 1996[79] (N=165) G1: Teflon Shah TT + steroid/abx otic drops postoperatively G2: Teflon Shah TT	3 mos	NR	Otorrhea G1:0 G2:2	NR	NR
	NRCT (by ear) Kinsella et al., 1994[80] G1: Shepard TT, no-touch technique (N=60) G2: Shepard TT, touch technique (N=60)	7-10 days post-operation	NR	Otorrhea G1: 1.67% G2: 1.67%	NR	NR
	RCT (by ear) Hampal et al., 1991[75] G1: Shah TT (N=105 ears) G2: Mini-shah TT (N=105 ears) Companion: Dingle et al., 1993[144]	1 year	G1:0 G2: 0	NR	NR	Tympanosclerosis G1: 40% G2: 23% p<0.01
		2 years (N=92)	14/92 children underwent surgery for recurrent OME; NR by group.	NR	NR	Tympanosclerosis (grades 1-4) G1: 19 of 39 ears G2: 38 of 39 ears

Table 31. Treatment harms or tolerability: Tympanostomy tube comparison studies (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes	Otorrhea/ Occlusion/ Granulation	Perforation/ Atelectasis/ Retraction	Cholesteatoma/ Tympanosclerosis
Hellstrom et al., 2011[21] (continued)	RCT by ear Heaton et al., 1991[76] G1: Shepard TT (N=131) G2: Sheehy TT (N=129)	15-36 months	NR		Perforation G1: 2% G2: 1% p=NS	Cholesteatoma G1: 27% G2: 30% p=NS Tympanosclerosis G1: 28%[a] G2: 31%[a] p=NS
	G1: Anterior placement of Shepard TT in TM (N=96 ears) G2: Posterior placement of Shepard TT in TM (N=35 ears) G3: Anterior placement of Sheehy TT in TM (N=95 ears) G4: Posterior placement of Sheehy TT in TM (N=34 ears)	15-36 months	NR	Otorrhea G1: 5 ears G2: 2 ears G3: 9 ears G4: 3 ears	NR	Tympanosclerosis G1: 31 ears G2: 6 ears G3: 31 ears G4: 9 ears
	RCT, by ear Salam and Cable, 1993[81] G1:Sheehy collar (N=162) G2: Sheehy collar plus betnesol-N drops (N=162)	2 weeks	NR	Otorrhea G1: 8.6% G2: 1.9% p<0.01 Occlusion G1: 4.3% G2: 1.9% p>0.005	NR	NR

Table 31. Treatment harms or tolerability: Tympanostomy tube comparison studies (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes	Otorrhea/ Occlusion/ Granulation	Perforation/ Atelectasis/ Retraction	Cholesteatoma/ Tympanosclerosis
Hellstrom et al., 2011[21] (continued)	RCT, by ear Hampton and Adams, 1996[82] G1: Armstrong TT placed anteriorly (N=109) G2: Armstrong TT placed posteriorly (N=109)	3-29 months	NR	NR	Perforation G1: 1.8% G2: 3.7% p>0.05	NR
		1 month	NR	Occlusion G1: 3 G2: 4 p=0.85	NR	NR
	1 RCT (by ear) 2 articles Youngs and Gartland,1988[78] Companion: McRae, et al.,1989[90] G1: Shah Teflon plus aspiration (N=53) G2: Shah Teflon no aspiration (N=53)	3 months	NR	Occlusion G1: 7 G2: 4 p=0.72	NR	NR
		24 months (N=76 ears)	NR	NR	NR	Tympanosclerosis G1: 66%[a] G2: 47%[a] p<0.05

diff = difference; G = group; mos = months; N = number; NR = not reported; NRCT = nonrandomized controlled trial; NS = not sufficient; RCT = randomized controlled trial; TM = tympanic membrane; TT = tympanostomy tubes; vs. = versus

[a]Calculated by reviewer.

Repeat Tube Placement

In one small trial (N=30), patients who received Teflon Armstrong tubes (shorter term) were more likely to undergo repeat TT placement than those receiving the silicone Goode-T tube (47% vs. 20%, respectively).[83] Patients who received N-acetylcysteine at the time of TT insertion, compared with placebo or the contralateral ear were also less likely to have repeat TT placement.[87]

Other Harms

Other side effects and potential harms found in studies included risk of cholesteatoma, occlusion, rate of tympanosclerosis, and presence of granulation tissue. Groups did not differ significantly in cholesteatoma formation by tube type.[76,83,86] Results were mixed in three studies examining occlusion rates.[78,83,85]

In relation to tympanosclerosis, standard Shah TT had higher tympanosclerosis rates than mini-Shah TT, but the standard Shah also had higher retention rates.[144] Abdullah et al. found a possible increased rate of tympanosclerosis for polyethylene Shah TT compared with silicone permavent Shah TT (65% vs. 41%, no p value reported).[84] Aspiration prior to TT placement increased the tympanosclerosis rate in one study over 24 months ($p<0.05$).[90] Finally, Iwaki et al. demonstrated higher rates of granulation tissue at 24 months for silicone Paparella TT compared with either Goode-T silicone or Teflon Shepard TT (7.5%, 0%, 0% respectively, $p<0.05$).[86]

Surgical Interventions: Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Key Points

- Otorrhea and tympanosclerosis were found to occur more frequently in ears with TT (strength of evidence moderate).
- Evidence was insufficient for all other side effects or harms.

Detailed Synthesis

We identified nine studies that compared side effects by treatment (Table 32). Seven studies[19,96,98,102,104,140,145] were discussed in at least one of the two systematic reviews. We included two additional studies[91,92] (Table 32).

Otorrhea/AOM/Otalgia

Otorrhea occurs with a perforated tympanic membrane or an in-place TT, so that outcome is unlikely to occur with watchful waiting.[91,92,140] Higher rates of otorrhea were found in TT arms at 6 months.[140] Mandel et al. found a higher rate of otorrhea at 1 year in the TT arm, compared with the myringotomy and no surgery arms but similar rates by 3 years in one study.[96] They found higher rates in the TT group at 3 years in an earlier study.[92]

Tympanosclerosis

Tympanosclerosis rates were higher in the TT groups in three studies in subsequent examinations after the tubes had been extruded.[19,98,145]

Table 32. Harms or tolerability: Tympanostomy tubes versus watchful waiting or myringotomy

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes/ Treatment Failure	Otorrhea/ AOM/ Otalgia	Atrophy	Tympanosclerosis/ Myringosclerosis	Perforation	Cholesteatoma	Granulation
Browning et al., 2010[22]	1 RCT by ear Dempster et al., 1993[98] (N=78 ears)	1 year	NR	NR	NR	TT vs. none 11 ears vs. 1 ear	NR	NR	NR
	1 RCT by child MRC Target, 2012[19] (N=248)	24 months	NR	NR	NR	TT vs. WW 20% vs. 0%	Any perforation: 8 of 635 ears with TT. Lasting perforations: 6 of 635	NR	NR
	1 RCT Rovers, 2000[140] (N=187)	6 months	NR	Otorrhea TT vs. WW 49% (95% CI, 39% to 60%) vs. 10% (95% CI, 4% to 16%)	NR	NR	NR	NR	NR
	1 RCT Gates, 1989[102] (N=236) G1: Myr G2: TT	NR	G1:31.8% G2 20.2% p=0.004[a]	AOM TT vs. non-tubed 27% vs. 11%	NR	NR	G1: 3% G2: 2.2%	G1: 3% G2: 2.2%	NR
				Otorrhea G1: 22% G2: 29%	NR	NR	G1: 0 G2: 0	G1: 0 G2: 0	NR
Hellstrom et al., 2011[21]	1 RCT by ear Maw and Bawden[145] (N=400 ears) G1: TT G2: no TT	12 mos	NR	NR	G1: 5.6% G2: 0.5% Atelectasis G1: 3.7% G2: 4.2% Attic retraction: G1: 0.9% G2: 2.9%	G1: 14% G2: 7.5% p=NR	NR	NR	NR

Table 32. Harms or tolerability: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes/ Treatment Failure	Otorrhea/ AOM/ Otalgia	Atrophy	Tympanosclerosis/ Myringosclerosis	Perforation	Cholesteatoma	Granulation
Hellstrom et al., 2011[21] (continued)	1 RCT Johnston, 2004[104] G1: Early TT (N=147) G2: Late TT (N=134)	F/U at 5/6 years of age	NR	NR	TT worse in G1 RR: 17.4	TT worse in G1 RR diff: 24.5	NR	NR	NR
	1 RCT Mandel[96] (N=111)	3 years	NR	1 year TT: 0.58 Myr: 0.17 No surg: 0.28 p=0.01 3 years TT: 0.36 Myr: 0.29 No surg: 0.29		NR	TT: 12 ears	Myr arm: 2 children	NR
Koopman et al., 2004[91]	G1: TT + cold knife Myr (N=208) G2: Laser Myr (N=208)	NR	NR	Otorrhea G1 more often than G2 p=0.0020 Otalgia without inflammation G1: 1 G2: 0	NR	NR	NR	NR	NR

Table 32. Harms or tolerability: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes/ Treatment Failure	Otorrhea/ AOM/ Otalgia	Atrophy	Tympanosclerosis/ Myringosclerosis	Perforation	Cholesteatoma	Granulation
Mandel et al., 1989[92]	Without "significant" hearing loss G1: Myr G2: Myr + TT G3: No surgery With "significant" hearing loss G4: Myr G5: Myr + TT	NR	Tx failure: G1: 0.53 G2: 0 G3: 0.59 G4: 0.75 G5: 0 p=NS	Otorrhea episodes/ person yr G1: 0.15 G2: 0.41 G3: 0.23 G4: 0.34 G5: 0.61 In non-TT groups this is tx failures received TT	NR	NR	NR	G3: 1 ear	NR

AOM = acute otitis media; CI = confidence interval; Myr = myringotomy; NR = not reported; NS = not significant RR = relative risk; TT = tympanostomy tubes; tx = treatment; RR= risk ratio; vs. = versus; WW = watchful waiting; yr = year

[a]Calculated by reviewer.

Atrophy

Three studies evaluated atrophy subsequent to TT versus myringotomy or watchful waiting and results were mixed. TT were associated with higher rates of atrophy in two studies[104,145] and no different in a third study.[96]

Other Harms

Three studies evaluated perforation following TT insertion in comparison with myringotomy or no treatment. In all studies, TT were associated with low rates of perforation.[19,92,102] Similarly, Gates et al. found a low and comparable rate of cholesteatoma in the TT and myringotomy arms.[102]

Surgical Interventions: Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy or Adenoidectomy Alone

Key Points

- The risk of tympanosclerosis was higher in patients receiving TT than in patients receiving myringotomy or no surgery in addition to adenoidectomy (strength of evidence was moderate).
- The evidence for otorrhea was insufficient because of inadequate data to perform statistical difference tests.
- Evidence for repeat tubes and perforation was insufficient because of conflicting results or inadequate data to perform statistical difference tests.

Detailed Synthesis

The evidence for harms related to TT in comparison with myringotomy or no surgery when added to adenoidectomy is based on six studies we identified [109,111-115] plus three[102,105,106] that were in the Hellstrom review.[21] All but two[109,111] compared TT with myringotomy. Harms included repeat TT, otorrhea, perforation, and tympanosclerosis (Table 33).

Tympanosclerosis

Three studies contributed to the evidence for tympanosclerosis for TT in comparison to myringotomy or no surgery (Table 33).[105,108,109,111] Later followups[43,108] of the Bonding and Tos cohort[105] also contributed to the evidence. One study (three reports)[43,105,108] examined TT plus adenoidectomy in comparison with myringotomy plus adenoidectomy. Results indicate that ears with TT had a significantly higher rate of tympanosclerosis than did ears with myringotomy from 3 years postsurgery to 25 years postsurgery, with differences as great as 46 percent ($p<.001$) at 6 to 7 years post-treatment. Brown[109] and Lildholdt[106] compared tympanosclerosis in tubed ears and ears without surgery. Both found a higher rate of about 40% in tubed ears at 5-year followup, although only Brown provided a significance test ($p<.05$).

Table 33. Harms or tolerability: Tympanostomy tubes plus adenoidectomy versus myringotomy plus adenoidectomy or adenoidectomy alone

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes/ Treatment Failure	Otorrhea	Perforation	Tympanosclerosis
Brown et al., 1978[109]	G1: TT + AD (N=55) G2: AD (N=55)	5 yrs.	NR	NR	NR	G1: N=23 G2: N=0 p<0.05
Lildholdt, 1979[111]	G1: TT+ AD (N=91 ears) G2: AD (N=91 ears)	18 mos	G1: 14% (reinsertion) G2: 0.6% (later insertion)	NR	NR	NR
D'Eredita and Shah, 2006[112]	G1: CDLM + AD (N=15 ears) G2: TT + AD (N=15 ears)	30 days	NR	Otorrhea G1: 0% G2: 26.7% p=NR	NR	NR
		2 months	NR	G1: 2 reports	NR	NR
		3 months	NR	G2: 4 reports	NR	NR
		1 year	NR		G1: 0 G2: 6.7% p=NR	
Popova et al., 2010[113]	G1: Donaldson TT + adenoidectomy (N=42) G2: Myr + adenoidectomy (N=36)	NR	NR	G1: 40% G2: 0 Diff=.40 (95% CI, 0.252 to 0.548)[a]	NR	NR
Shishegar and Hobhoghi, 2007[114]	G1: Shepard TT + adenoidectomy (N=30 ears) G2: Myr + AD (N=30 ears)	>6 months	NR	G1: 27% G2: 7%	NR	NR
Vlastos et al., 2011[115]	G1: Shepard TT + adenoidectomy (N=25) G2: Myr + adenoidectomy (N=27)	12 mos	G1: 0 G2: 20% (TT in nonTT group)	G1: 0 G2: 0	G1: 0 G2: 0	NR
Hellstrom, 2011	NRCT by ear, Bonding & Tos 1985[105]	3 yrs.	NR	NR	G1: 3.1% G2: 2.1%	G!: 48% G2:19% p<0.001
	Companions Tos and Stangerup, 1989[108]	6-7 yrs	NR	NR	NR	G1: 59% G2: 13% p<0.05
	Caye-Thomasen, et al., 2008[43] G1: Adenoidectomy + Donaldson TT	25 yrs G1: (N=146) G2 (N=146)				G1:50% G2: 20% p<0.001

Table 33. Harms or tolerability: Tympanostomy tubes plus adenoidectomy versus myringotomy plus adenoidectomy or adenoidectomy alone (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes/ Treatment Failure	Otorrhea	Perforation	Tympanosclerosis
Hellstrom, 2011 (continued)	G2: Adenoidectomy + Myr (N=224, 193 analyzed)					
	NRCT by ear Lildholt, 1983[106] G1: Donaldson TT +adenoidectomy (N=150) G2: Adenoidectomy (N=150)	5 yrs		G1: 2-10% G2: 0%		G1: 47% G2: 8.7%
	RCT by person Gates, 1989[102] G1: AD+Myr (N=130) G2: AD+TT (N=125)	2 years	G1: 13.1% G2: 13.6% p=.932			

AD = adenoidectomy; CDLM = Contact diode laser myringotomy; G = group; Myr = myringotomy; mos = months; NRCT = nonrandomized controlled trial; RCT = randomized controlled trial; TT = tympanostomy tubes
[a]Calculated by investigators.

Otorrhea

Five studies,[57,106,113-115] three of which were assigned by ears, examined otorrhea. In the four studies in which ears received myringotomy,[57,113-115] rates of otorrhea in the tubed ears were between 0% and 40%, with no to low rates in the ears with myringotomy. However, statistical differences were only calculated for the Popova et al., 2010[113] sample where TT was associated with a higher rate of otorrhea (Diff = .40, [95% CI, 0.252 to 0.548]). In the one study in which comparison ears received no surgery,[106] the rate of otorrhea was 10 percent in tubed ears compared with no episodes in the ears with no surgery.

Perforation

Three studies[57,105,115] examined perforation in tubed ears compared with ears with myringotomy. At 1 year post-treatment, D'Eredita and Shah, 2006[112] found one case in the ear with TT as compared with none in the ear with myringotomy only. Similarly, Vlastos and colleagues, 2011[115] found no cases in either ears with TT or ears with myringotomy. Lildholdt, 1983[106] found rates of 3.1 percent in tubed ears as compared with 2.1 percent in ears with myringotomy at 3 years post-treatment.

Repeat Tubes or Treatment Failure

Three studies[102,111,115] evaluated the need for repeat TT or treatment failure. Vlastos et al. demonstrated that 20 percent of children who initially had adenoidectomy without TT eventually had a TT placed. However, neither Lildholt et al. nor Gates et al. found statistically significant

differences in reoperation rates in ears that received no intervention or myringotomy, respectively, compared with TT when adenoidectomy was performed.

Surgical Interventions: Myringotomy Comparisons

Key Points

- We found no evidence examining harms or tolerability.

Surgical Interventions: Myringotomy Plus Adenoidectomy Comparisons

Key Points

- We found no evidence examining harms or tolerability.

Surgical Interventions: Adenoidectomy Versus Other Interventions

Key Points

- In two studies, one child experienced postoperative hemorrhage following adenoidectomy.[19,95,102] Strength of evidence is low.
- Based on evidence from one study; 0.8 percent of operated ears had lasting perforations and 20 percent had tympanosclerosis.[19] Strength of evidence is insufficient.

Detailed Synthesis

Harms from adenoidectomy surgery were rare in the included evidence. Two studies reported that one patient hemorrhaged as a result of the surgery (Table 34).[19,95,102]

Table 34. Treatment harms: Adenoidectomy versus other interventions

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes/ Treatment Failure	Otorrhea, Perforation	Tympanosclerosis/ Other Harms
RCT: Paradise et al., 1990[74a]	G1: Adenoidectomy G2: No treatment (N=99)		Of 125 who received adenoidectomy, none developed anesthetic complications Mean # of TT/subject (range) procedure Year 1 G1: 0.13 (0-1) G2: 0.29 (0-1) Year 2 G1: 0.13 (0-2) G2: 0.26 (0-2) Year 3 G1: 0.08 (0-1) G2: 0.13 (0-1)	Otorrhea, Mean #/subject (range) Year 1 G1: 0.13 (0-1) G2: 0.13 (0-2) Year 2 G1: 0.09 (0-1) G2: 0.14 (0-1) Year 3 G1: 0.05 (0-1) G2: 0.07 (0-1)	

Table 34. Treatment harms: Adenoidectomy versus other interventions (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes/ Treatment Failure	Otorrhea, Perforation	Tympanosclerosis/ Other Harms
RCT: Casselbrant et al., 2009[119]	G1: Adenoidectomy+ myr + bilateral TT G2: Myr + bilateral TT (18 mos: N=44) (36 mos: N=39)			Otorrhea,1 or more episodes: 0-18 mos: G1: 41% G2:36% Diff G1 vs. G2: p = 0.59 0-36 mos: G1: 47% G2:45% Diff G1 vs. G2: p = 0.59	
RCT: Gates et al., 1987[95] Companion Gates et al., 1989[102]	G1: Myr (N=107) G2: Bilateral Shepard TT (N=129) G3: Adenoidectomy + Myr (N=130) G4: Adenoidectomy + Bilateral Shepard TT (N=125)		Surgical retreatments: G1: 46% G2: 24% G3: 12% G4: 11% p = 0.001	Otorrhea, 1 or more episodes: G1: 22% G2: 29% G3: 19% G4: 24% p = 0.009	1 patient bled after adenoidectomy surgery, no other adenoidectomy complications, no deaths
MRC TARGET, 2012[19]	G1: Adenoidectomy + Myr + Bilateral Shepard TT G2: Myr + bilateral Shepard TT G3: WW (N = 376)			Perforation 5 of 635 ears may have lasting perforations, based on observed followup.	Tympanosclerosis 20% in operated ears vs. 0% in unoperated Other, hemorrhage 1 adenoidectomy post-operative hemorrhage (0.6%)

G = group; Myr = myringotomy; mos = months; NRCT = nonrandomized controlled trial; RCT = randomized controlled trial; TARGET = Trial of Alternative Regimens in Glue Ear Treatment; TT = tympanostomy tubes; vs. = versus; WW = watchful waiting

Pharmaceutical Interventions: Oral or Topical Nasal Steroids

Key Points

- Groups did not differ significantly in mild adverse events such as nasal stinging (low strength of evidence).
- Evidence concerning serious harms was sparse (insufficient strength of evidence).

Detailed Synthesis

The earlier systematic review focusing on steroid treatment for OME found no serious or lasting harms reported in five studies of oral steroids and two studies of topical steroids (Table 35).[31] The review update found no difference in mild to moderate adverse events in a meta-analysis of two RCTs comparing oral steroids plus antibiotics versus control plus antibiotics, at 2 weeks to 6 months, RR=1.34 (95% CI, 0.84 to 2.14) (N=255).[32] The Williamson et al. study

found no significant difference at 3 months between the topical steroid group and control in relation to stinging nose, nose bleed, dry throat, or cough.[20,121]

Table 35. Treatment harms or tolerability: Oral or topical nasal steroids

Study	Arm (N)	Study Duration Until Outcome Measurement	Serious Or Lasting Harm Outcomes	Mild Adverse Outcomes
Thomas et al., 2010[31] Systematic review International	NR	Variable	No serious or lasting harms reported in 5 studies of oral steroids or 2 studies of topical intranasal steroids.	Some studies mentioned mild adverse outcomes: vomiting, diarrhea, dermatitis, transient nasal stinging, and epistaxis.
Simpson et al., 2011[32] Systematic review Update of Thomas et al.,2010[31]	MA: 2 RCTs Oral steroids plus antibiotic vs. control plus antibiotic Hemlin et al., 1997[128] Mandel et al., 2002[125] (N=255)	2 weeks to 6 months		Mild to moderate adverse events RR: 1.34 (95% CI, 0.84 to 2.14)
	1 RCT: Giebink et al, 1990[122] Oral steroid vs. control (N=76)			"No significant hematologic complications." 1 prednisone patient was neutropenic 2 weeks after randomization, not leukopenic, remained well.14/18 prednisone-treated patients had depressed cortisol values; of these, 7 had normal values between 2 and 4 days of stopping treatment, 1 normal values at day 14, and 6 normal values at days 17-36 post-treatment.
	1 RCT: Niederman et al., 1984[124] Oral steroid vs. control (N=22)	5 weeks	No significant adverse effects were seen in any study participant.	
	1 RCT: Hemlin et al., 1997[128] G1: Oral steroid plus antibiotic G2: Control plus antibiotic (N=140)			Dermatitis G1: 1.7% G2: 0.0% Diarrhea G1: 6.7% G2: 3.3% Loose stools G1: 3.3% G2: 3.3% Vomiting G1: 1.7% G2: 4.9% Stomach pain G1: 3.3% G2: 3.3% Gastroenteritis G1: 0/0% G2: 1.7%

Table 35. Treatment harms or tolerability: Oral or topical nasal steroids (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Serious Or Lasting Harm Outcomes	Mild Adverse Outcomes
Simpson et al., 2011[32] (continued)	Mandel et al., 2002[125] G1: Oral steroid plus antibiotic G2: Control plus antibiotic (N=144)			Hyperactivity G1: N=10 G2: N=6 Increased appetite G1: N=8 G2: N=4 Vomiting G1: N=3 G2: N=2 Diarrhea G1: N=4 G2: N=1 Irritability G1: N=1 G2: N=2 Abdominal discomfort G1: N=1 G2: N=2 Hives G1: N=0 G2: N=1 Other rash G1: N=4 G2: N=2
	1 RCT[a] Shapiro et al., 1982[132] Intranasal steroid vs. Control			No sig declining trend for cortisol levels of steroid versus placebo patients (p=0.55) and overall differences in cortisol levels from initiation to conclusion were not statistically sig for inter- or intra-group variation.
	1 RCT[a] Williamson et al., 2010[121] Williamson et al., 2009[20] G1: 9/85 (11%) G2: 9/85 (11%) G1: 10/86 (12%) G2: 6/84 (7%) G1: 10/85 (12%) G2: 7/83 (8%) G1: 19/86 (22%) G2: 11/83 (13%)	3 months		Stinging nose: RR: 1.00 (95% CI, 0.42 to 2.40 Nose bleed: RR: 1.63 (95% CI, 0.62 to 4.28) Dry throat: RR:1.40 (95% CI, 0.56 to 3.49) Cough: RR: 1.67 (95% CI, 0.85 to 3.29) Any adverse event: RR: 1.26 (95% CI, 0.80 to 1.99)

CI= confidence interval; G = group; MA = meta-analysis; N = number; NR = not reported; RCT = randomized control trial; RR = relative risk; sig = significant; vs. = versus

[a]Denotes information from update review, Simpson, et al. 2011.[32]

Nonpharmaceutical: Autoinflation

Key Points

- No quantitative information on rates of serious or mild harms was provided (insufficient strength of evidence).

Detailed Synthesis

The systematic review stated that no serious or lasting harms were reported in the six studies of autoinflation, but no data were provided (Table 36).[30] It reported that, in one trial, a patient stopped treatment because of pain.[30]

Table 36. Treatment harms or tolerability: Autoinflation

Study	Arm (N)	Study Duration Until Outcome Measurement	Serious or Lasting Harms	Mild Adverse Outcomes
Perera et al., 2009[30]	NR	Variable	None of the studies included in the review demonstrated a significant difference in the incidence of side effects between the control or intervention groups.	One trial in the systematic review reported that "that one patient stopped the treatment due to the pain caused by the procedure."

N = number; NR = not reported

KQ 4. Comparative Effectiveness of Interventions for Subgroups of Patients

One of the explicit goals of this review was to examine treatment options for subgroups of patients including individuals defined by age groups; adults were of particular interest. Our search found very few studies of any subgroups that met our inclusion criteria. We found one study of adults examining autoinflation and one study of children with sleep apnea who received TT or myringotomy. Other subpopulations of interest included those groups at greater risk for OME such as individuals of American Indian, Alaskan, and Asian backgrounds, individuals with cleft palate, Down syndrome, and other craniofacial anomalies. We had no success in finding studies specific to these groups that met our inclusion criteria. Although we did find OME treatment studies for individuals with cleft palate, the studies did not provide data on pretreatment diagnosis of OME using validated procedures.

Surgical Interventions: Tympanostomy Tube Comparisons

Key Points

No studies reported on patient subgroups. Strength of evidence is insufficient.

Surgical Interventions: Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Key Points

No studies reported on patient subgroups. Strength of evidence is insufficient.

Surgical Interventions: Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy or Adenoidectomy Alone

Key Points

A single study evaluated subgroups of patients (strength of evidence is insufficient).

Detailed Synthesis

One study of children with sleep apnea and OME[115] did not find important differences in hearing thresholds after placement of TT or myringotomy (see Tables 13 and 29). Among this group of children who had adenoidectomies for sleep apnea and also had OME, quality of life did not change at 12 months between TT or myringotomy groups. At 6 months, results were mixed with some measures improving more quickly in the TT group, while on other measures TT and myringotomy were the same.[115] Twenty percent of the children who initially received a myringotomy eventually also received TT.[115] We were unable to compare this rate with other identified studies.

Surgical Interventions: Myringotomy Comparisons

Key Points

- The one study examining differences in myringotomy procedures did not examine the comparative effectiveness of the two approaches within subgroups of patients. Evidence is insufficient.

Surgical Interventions: Myringotomy With Adenoidectomy Comparisons

Key Points

No studies of these interventions reported on patient subgroups. Evidence is insufficient.

Surgical Interventions: Adenoidectomy Versus Other Interventions

Key Points

No studies of these interventions reported on patient subgroups. Evidence is insufficient.

Pharmaceutical Interventions: Oral or Topical Nasal Steroids

Key Points

No studies of these interventions reported on patient subgroups. Evidence is insufficient.

Nonpharmaceutical Interventions: Autoinflation

Key Points

- A subgroup of adults who received autoinflation had better middle ear effusion outcomes than controls at end of treatment and 50 days after treatment (Low strength of evidence, one study).

Detailed Synthesis

One study in the Cochrane review on autoinflation,[30] Lesinskas, 2003,[138] included adults (Table 37).[138] The treatment intervention was a BD Politzer device used twice a day for 10 days, with or without antibiotics. The control group received equal care except for the intervention. Followup and adherence were 100 percent. The outcome measure was a composite measure of recovery from OME based on pneumo-otoscopy, tympanometry, and audiometry. Individuals in the autoinflation group were significantly more likely to experience a complete recovery than those in the control group at both the end of treatment ($p<0.001$) and at 50 days after treatment ($p<0.001$). Similarly, the ears of the participants receiving autoinflation had better recovery rates than control ears at both time points ($p<0.001$).

Table 37. Comparative effectiveness for adults: Autoinflation

Study	Arm (N)	Study Duration Until Outcome Measurement	Composite Measure of Recovery
Perera et al., 2009[30]	1 RCT Lesinskas, 2003[138] Autoinflation vs. control (n=198)	End of treatment (10 weeks)	Individuals: 50.6% vs. 3.8% Ears: 49.2% vs. 3.9% (p<0.001) (favors autoinflation)
		50 days after treatment	Individuals: 55.2% vs. 11% Ears: 57.8% vs. 11.8% (p<0.001) (favors autoinflation)

OME = otitis media with effusion; vs. = versus

KQ 5. Comparative Effectiveness by Health Care Factors

Key Points

No included studies for any intervention comparisons examined effectiveness by any health care factors.

Discussion

Key Findings and Strength of Evidence

This systematic review addressed the comparative effectiveness of treatments for otitis media with effusion (OME). OME is characterized by eustachian tube dysfunction, the accumulation of fluid in the middle ear; the condition most commonly affects children. Health care providers have been particularly concerned when fluid persists for a relatively long period of time (e.g., 3 months or more) and when the problem reduces hearing because it may result in functional limitations and have long-term sequelae.

Various approaches have been studied for treating OME. Sometimes investigators used a single treatment alone; sometimes they combined two or more approaches. In this review, we focused on the following interventions and comparisons among them: surgical procedures (tympanostomy tubes [TT], myringotomy, and adenoidectomy); nonpharmacological interventions (autoinflation); pharmacological interventions (oral or nasal steroids); complementary and alternative medicine approaches (CAM); and other treatment strategies (watchful waiting and delayed treatment). The effectiveness of these interventions has generally been studied in pediatric samples that included a wide range of ages.

The focus of this review was to compare the relative benefits and harms of these treatment approaches overall and then specifically in particular subpopulations of interest that may be particularly affected by OME (e.g., children with preexisting hearing limitations, craniofacial abnormalities, or Down syndrome) or for whom little is known (adults). As discussed in the introduction, we did not consider hearing aids, antihistamines and decongestants, or antibiotics.

Overview

Overall, the evidence included five recent systematic reviews, relevant studies identified in those reviews, and additional studies discovered through our searches. These totaled 49 randomized controlled trials (RCTs), six nonrandomized trials (e.g., studies comparing left and right ears), and four observational studies. By treatment comparison, the literature included the following:

- Surgical approaches:
    - TT compared by type of tube or procedure approach;
    - TT versus myringotomy or nonsurgical interventions (delayed treatment or watchful waiting);
    - TT plus adenoidectomy versus myringotomy plus adenoidectomy;
    - TT plus adenoidectomy versus adenoidectomy;
    - Myringotomy versus myringotomy, comparison of different approaches, and various combinations of myringotomy plus adenoidectomy; and
    - Adenoidectomy versus nonsurgical interventions or myringotomy.
- Pharmacological interventions, specifically oral and topical nasal steroids.
- Nonpharmacological interventions, specifically, autoinflation.

We had no studies meeting inclusion criteria on any CAM interventions.

We restricted our review to treatments for OME. Although clinicians use many of these treatments for patients with recurrent acute otitis media (AOM), we included only studies from which we could obtain evidence for purely OME populations. We did not restrict inclusion by

other coexisting conditions beyond AOM or disease processes that produce OME (e.g., allergies) as long as the participants had OME.

Although we had hoped to be able to provide evidence for these and other subpopulations, the review pertains mainly to typically developing children. The majority of children included in studies were older than 2 years, which may limit the applicability of the results to some treatments, such as TT, which are routinely used with infants. We were unable to find studies on individuals with cleft palate or sensorineural hearing loss that met our inclusion criteria. The studies available on individuals with cleft palate did not diagnose OME unambiguously before treatment. We found only one study that targeted individuals 16 to 75 years of age.

We tried to examine a broad range of clinical, functional, and quality-of-life outcomes and harms of treatment. Although most of the studies examined middle ear status (e.g., presence of effusion or recurrence of OME) and many examined hearing, some included harms of treatment. Only a handful, however, included measures of speech, language, behavior, or quality of life. No study examined vestibular function or health care utilization. Thus, our statements about evidence are limited primarily to middle ear status, hearing, and harms.

We summarize the strength of evidence for benefits of interventions, comparisons, and outcomes on which we had studies of at least low or medium risk of bias. We included studies with high risk of bias only for harms. Strength of evidence grades are developed from ratings on four domains: overall risk of bias, directness of the evidence or the comparisons, consistency, and precision of estimates.[37] We did not evaluate other strength of evidence domains (e.g., magnitude of effect, dose-response relationships). Strength of evidence can have one of four grades—high, moderate, low, or insufficient. Insufficient evidence arises when we had no studies addressing the particular topic; when we had only a single small study; when available studies were sufficiently inconsistent, indirect, or imprecise as to preclude drawing any conclusions; or when differences in treatments appear to show no difference among studies that may be underpowered or clinical thresholds for minimal differences have not been established.

Key Question 1. Clinical Outcomes

For this Key Question (KQ), we sought evidence on the effectiveness of surgical and other interventions on a range of clinical outcomes, including recurrent middle ear effusion, recurrent AOM, and measured hearing. As noted, we had no studies that reported on vestibular function or use of health care services.

Table 38 summarizes the OME interventions on which we had low, moderate, or high strength of evidence for clinical outcomes.

Table 38. Strength of evidence for interventions to improve clinical outcomes

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
TT vs. watchful waiting, delayed treatment, or myringotomy	MA of 3 RCTs (N=574)	TT decreased persistent middle ear effusion at 1 year compared with watchful waiting or delayed treatment: 32% less time (95% CI, 17% to 48%).	High for benefit
	2 studies (N=294)	TT less time with effusion through 1 year compared with myringotomy.	Moderate for benefit
	MA of 3 RCTs (N=426)	TT decreased persistent middle ear effusion at 2 years compared with watchful waiting or myringotomy: 13% less time (95% CI, 8% to 17%).	Moderate for benefit
	MA of 3 RCTs (N=523) + 1 RCT (N=248)	TT had better measured hearing for up to 9 months than watchful waiting. MA results: -4.20dB (95% CI, -4.00 to -2.39).	High for benefit
	MA of 3 RCTs (by ears) (N=230)	TT better measured hearing for up to 6 months than watchful waiting or myringotomy: -10.08 (95% CI, -19.12 to -1.05).	High for benefit
	MA of 3 RCTs (by ears) (N=234)	No difference between TT and watchful waiting or myringotomy in measured hearing at 7-12 months: -5.18dB (95% CI, -10.43 to 0.07).	Low for no difference
	MA of 2 RCTs (N=328); MA of 2 RCTs (N=283)	No difference between TT and watchful waiting in measured hearing at 12 months: -0.41dB (95% CI, -2.37 to 1.54) and 18 months -0.02 dB (95% CI, -3.22 to 3.18).	Low for no difference
TT + adenoidectomy vs. myringotomy + adenoidectomy	6 studies: 3 RCTs by person (N=431); 2 RCTs (by ears) (N=338); 1 NRCT (by ears) (N=193)	No difference in measured hearing between groups at 6 and 12 months and at more than 3 years.	Low for no difference
TT + adenoidectomy vs. WW	1 study (n = 250)	TT plus adenoidectomy improved hearing at 3 to 24 mos compared to WW.	Low for benefit
Adenoidectomy vs. no treatment	MA of 2 RCTs (by ears) (N=153); MA of 3 RCTs (by ears) (N=297)	Adenoidectomy produced better OME resolution than no treatment at 6 months. The risk difference was 0.27 (95% CI, 0.13 to 0.42) measured through otoscopy and 0.22 (95% CI, 0.12 to 0.32) measured through tympanometry.	High for benefit
	MA of 3 RCTs (by ears) (N=298)	Adenoidectomy produced better OME resolution than no treatment at 12 months. The risk difference was 0.29 (95% CI, 0.19 to 0.39).	High for benefit
Adenoidectomy + myringotomy vs. myringotomy	1 RCT (N=237)	Adenoidectomy and myringotomy produced less mean time with effusion than myringotomy alone at 24 months: -0.76 standard mean difference (95% CI, -1.02 to -0.49).	Low for benefit
	1 RCT (N=237)	Adenoidectomy and myringotomy produced better hearing than myringotomy alone at 24 months, measured as standard mean difference time with hearing level ≥ 20: worse ear: -0.65 (95% CI, -0.91 to -0.39); better ear: -0.66 (95% CI, -0.93 to -0.40).	Low for benefit
Oral steroids vs. controls	MA of 3 RCTs (N=106)	No difference in persisting OME at 1-2 months (no antibiotics provided in either group): OR=0.55 (95% CI, 0.21 to 1.48).	Low for no difference
Oral steroids + antibiotics vs. controls + antibiotics	MA of 3 RCTs (N=243)	No difference in persisting OME at 1-2 months (antibiotics provided to both groups): OR=0.75 (95% CI, 0.45 to 1.27).	Moderate for no difference

Table 38. Strength of evidence for interventions to improve clinical outcomes (continued)

Topical intranasal steroids vs. controls	1 RCT (N=217)	No difference in OME cure rates at 1, 3, and 9 months.	Low for no difference
	1 RCT (N=217)	No difference in hearing loss at 3 and 9 months.	Low for no difference
Autoinflation vs. controls	MA of 2 RCTs (N=185)	Improvement seen in OME at ≤1month: RR=3.84 (tympanometry change C2 to C1 or A) and RR=2.72 (tympanometry change B to C1 or A).	Low for benefit

CI = confidence intervals; dB = decibels; NRCT = non-randomized controlled trial; MA = meta-analysis; N = number; OME = otitis media with effusion; OR = odds ratio; RCT = randomized controlled trial; RR = risk ratio; TT = tympanostomy tubes; vs. = versus

Evidence concerning clinical outcome comparisons of TT based on tube design differed in retention length. For example, TT that are considered longer acting, such as Goode T-tubes and Paparella tube designs, were retained longer than other tubes such as Shah and Shepard. OME recurrence at 1 year or longer was higher in shorter term TT. We found insufficient evidence to demonstrate differences in clinical outcomes based on placement technique or TT material. TT design, placement technique, or material did not affect hearing outcomes.

We found that TT are more likely to decrease the time with persistent middle ear effusion lasting more than 1 year (high strength of evidence) and 2 years (moderate strength of evidence) compared with watchful waiting or delayed treatment. Hearing, the more critical and patient-centered clinical outcome, was found to be superior with TT as well, but for a shorter period of time, up to 9 months (high strength of evidence). Shorter time periods may be more important for the youngest children (younger than 3 years of age) who are still developing their speech and language skills, but results were not available specifically for this age group.

At increasingly longer periods over which outcomes were measured, hearing differences between groups became smaller and not significantly different. These findings are based on various analyses: (1) meta-analysis results comparing TT with watchful waiting or myringotomy over 7 to 12 months, measured by ears (low strength of evidence for no difference); and (2) based on meta-analyses comparing TT with just watchful waiting over 12 and 18 months, measured by child (low strength of evidence for no difference). We found limited evidence comparing TT to either watchful waiting or myringotomy in relation to OME recurrence, ear ventilation, or episodes of AOM; thus, we are unable to comment on these outcomes.

We examined whether TT or myringotomy are more likely to improve clinical outcomes when one or the other is added to adenoidectomy. We found no differences in hearing outcomes at any time points measured in five studies. Because of this consistent finding, we concluded that the strength of evidence was low for no difference.

We compared adenoidectomy with other treatments options, either alone or with concomitant myringotomy or TT. Adenoidectomy was superior to no treatment in relation to improving the probability of OME resolution at 6 months and 1-year followup (strength of evidence high). We found mixed results in relation to hearing outcomes for this comparison. The combination of adenoidectomy and myringotomy was superior to myringotomy alone in relation to time with effusion and hearing outcomes at 24 months, based on one RCT (strength of evidence low).

From these findings, our review suggests that adenoidectomy alone or in combination with myringotomy or TT is superior to watchful waiting, myringotomy or no treatment. Given the similarity of hearing outcomes when TT or myringotomy are added to adenoidectomy, our findings also suggest that it remains unclear whether additional benefit is obtained from the myringotomy procedure. We found some evidence that adding adenoidectomy to TT may

provide further benefit (above and beyond TT only), but we found no evidence comparing adenoidectomy alone with TT alone.

For nonsurgical interventions, we found evidence that oral steroids provide no short-term improvements in OME (at 1 to 2 months) either with the addition of antibiotics (moderate for no difference) or without antibiotics (low for no difference). One new low risk-of-bias study provided additional evidence that use of topical intranasal steroids does not improve OME and hearing outcomes at 9 months (low for no difference). These findings support the current American Academy of Pediatrics guidelines against the use of oral and intranasal steroids in treating OME in children.[146]

Evidence concerning clinical outcomes related to autoinflation found improvement in relation to middle ear effusion at 1 month or less (low strength of evidence); evidence was insufficient, however, for evaluating lengthier followup periods or in relation to hearing outcomes.

As described above, many interventions were compared with watchful waiting and, in some cases, with myringotomy. OME is different from many other medical diagnoses because nearly all cases of OME will resolve with time with no intervention. Therefore, the question for many interventions becomes whether shortening patients' time with effusion improves other important outcomes. We found evidence that surgical interventions decrease time with effusion compared with watchful waiting and that TT improves hearing in the short term. However, KQ 2 considers whether these short-term improvements in clinically measurable outcomes improve developmental and functional outcomes; that this could be the case is plausible in physiological terms.

Key Question 2. Health-Related Quality of Life and Functional Outcomes

For KQ 2, we sought evidence of the effectiveness of the various interventions to improve quality of life, subjective hearing, speech and language development, or behavior. Of the evidence meeting our inclusion criteria for the review overall, only a small number of studies included data on these outcomes. Evidence was limited to the following intervention comparisons: TT versus watchful waiting or delayed treatment, TT plus adenoidectomy versus myringotomy plus adenoidectomy, and topical intranasal steroids versus control.

Table 39 summarizes the OME interventions on which we had low, moderate, or high strength of evidence for clinical outcomes.

Table 39. Strength of evidence for interventions to improve health-related quality of life and functional status

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
TT vs. watchful waiting or delayed treatment	MA of 3 RCTs (N=394) and 2 RCTs (N=503)	No difference in language comprehension at 6 to 9 months post-intervention (mean difference, 0.09; 95% CI, -0.21 to 0.39) or at preschool and elementary school age.	Moderate for no difference
	MA of 3 RCTs (N=393) and 2 RCTs (N=503)	No difference in language expression at 6 to 9 months post-intervention (mean difference, 0.03; 95% CI, -0.41 to 0.49) or at preschool and elementary school age.	
	2 RCTs (N=503)	No difference in cognitive development at 9 months post-intervention or at preschool and elementary school age.	Low for no difference
	2 RCTs (N=503)	No difference in academic achievement at elementary school age.	Low for no difference
Intranasal steroids vs. controls	1 study (N=144)	No difference in parent-reported hearing difficulties at 3 and 9 months or in median days with hearing loss at 3 months.	Low for no difference

CI = confidence interval; MA = meta-analysis; N = number; RCT = randomized controlled trial; TT = tympanostomy tubes; vs. = versus

Language comprehension and language expression were not significantly better among children who received TT than among those who participated in watchful waiting or delayed treatment at various followup points, including 6 to 9 months post-treatment, during preschool, and at the later elementary school years (ages 3, 6, and 8) (strength of evidence moderate). Cognitive development results were similar (strength of evidence low for no difference). These findings correspond to the conclusions that clinical hearing outcomes were not superior in the TT group after both shorter and longer periods of followup. Delayed TT treatment did not negatively affect academic achievement when measured at later elementary school years. Evidence was insufficient to reach conclusions related to differences in behavioral or quality-of-life outcomes for this treatment comparison.

One small study comparing TT and adenoidectomy versus myringotomy and adenoidectomy measured quality-of-life outcomes. Therefore, we considered this evidence to be insufficient to reach conclusions.

Parents' report of their children's hearing difficulties did not differ in one low risk-of-bias study comparing intranasal steroids and controls (low strength of evidence for no difference).

Key Question 3. Harms Associated With Interventions To Treat Otitis Media With Effusion

We sought evidence of the potential harms or side effects that may occur with various treatment options. We considered such concerns as otorrhea, atrophy, tympanosclerosis, cholesteatoma, tissue granulation, and surgical complications. Specifically, in relation to TT we considered otorrhea and perforation, and in relation to steroid treatment such problems as diarrhea and nasal stinging. Table 40 summarizes the OME interventions on which we had low, moderate, or high strength of evidence for harms outcomes.

Table 40. Strength of evidence for harms or tolerability of interventions

Intervention and Comparator	Number of Studies (Sample Sizes)	Outcome and Results	Strength of Evidence
TT vs. TT	1 RCT (N=30 ears), 2 observational studies (N=779 ears)	Otorrhea occurred more frequently in ears with longer-term TT than in ears with shorter-term TT after 1 year or more.	Low for harms of longer-term TT
TT vs. watchful waiting or myringotomy	5 studies (N=1129)	Tympanosclerosis occurred more frequently in ears that had TT, based on examinations after the TT had been extruded.	Moderate for harms of TT
	4 studies (N=960)	Otorrhea occurred more frequently in ears with TT.	Moderate for harms of TT
TT plus adenoidectomy vs. adenoidectomy alone or with myringotomy	3 studies (N=485)	Tympanosclerosis occurred more frequently in ears with TT than ears with only adenoidectomy or with myringotomy.	Moderate for harms of TT
Adenoidectomy vs. other treatments	2 studies (N=739)	Although rare, adenoidectomy increased the risk of post-surgical hemorrhage.	Low for harms of adenoidectomy
Oral steroids vs. control	5 studies (N = 637)	No difference in mild adverse events such as nausea and diarrhea.	Low for no difference
Topical nasal steroids vs. control	2 RCT (N=225)	No difference in mild adverse events such as nasal stinging, dry throat, and cough.	Low for no difference

N = number; NR = not reported; RCT = randomized controlled trial; SR = systematic review; TT = tympanostomy tubes; vs. = versus

Otorrhea was more common among ears with TT (strength of evidence moderate) and was more common for TT that were intended to stay in ears for a longer period of time (strength of evidence low). We found consistent evidence that tympanosclerosis was more common in children who had TT than in those who were actively monitored or who had myringotomy; these results pertained whether or not the children had an adenoidectomy (strength of evidence moderate).

We found limited evidence of differences in hemorrhage from adenoidectomy (strength of evidence low). We found insufficient evidence about surgical risks from insertion of TT or myringotomy procedures. Note, however, that the studies were not powered to detect rare but potentially serious events, such as harms from either anesthesia or the surgical procedures themselves.

The systematic review concerning nasal steroids found few mild adverse events in the studies they reviewed.[121] Similarly, one new study found no differences between groups in relation to stinging nose, nose bleed, dry throat, or cough.[20] We concluded, therefore, that mild adverse events are not significantly higher through the use of topical nasal steroids (low for no difference). However, evidence was insufficient to reach conclusions related to mild adverse events from oral steroids or to serious adverse events from oral or topical steroids.

Key Question 4. Outcomes for Important Patient Subgroups

We attempted to differentiate treatment effectiveness or harms for key subgroups characterized by clinical or sociodemographic factors (such as age). For example, clinicians often treat children with preexisting hearing deficiencies, Down syndrome, or cleft palate differently than they would manage children who do not have such coexisting or congenital conditions and are otherwise following a typical development trajectory. Despite the important clinical and social questions that arise for children or adults in such subgroups, we could not identify studies that included most of our subgroups of interest.

Two studies examined different subgroups—children with sleep apnea and adults with OME. Vlastos et al. performed a study specifically with children with sleep apnea and OME. Among children with sleep apnea, all of whom had adenoidectomy to treat that condition, we found insufficient evidence to reach conclusions in terms of any measured outcomes.[115] A study of autoinflation that was included in a systematic review[30] found differences in rates of recovery among adults between those receiving autoinflation and those who were in the control group (low strength of evidence).

Key Question 5. Health Care Factors

We found no studies that examined issues related to health insurance coverage, physician specialty, type of facility of the provider, geographic location of patients, presence or absence of continuity of care, or prior use of pneumococcal virus inoculation. Evidence is thus insufficient for all such considerations.

Findings in Relation to What Is Already Known

The preponderance of the evidence included in this systematic review was obtained from recently completed reviews. Four of these reviews (including one update) were conducted by the Cochrane Collaboration[22,29-31,34,147] and the fifth was sponsored by the Swedish government.[21] We sought to determine whether the inclusion of non-RCT evidence (excluded from the Cochrane reviews) and newer trials would affect their findings. We also sought to obtain answers to questions not addressed in these reviews; these included the comparative effectiveness of different approaches to myringotomy, use of CAM therapies in treating OME, and the value of watchful waiting. Last, we sought evidence concerning populations not addressed in these reviews, such as findings specific to very young children, adults (an adult nominated the review), and children at greater risk for hearing deficiencies or developmental delays because of preexisting conditions.

Overall, we found few new studies that had not been included in the earlier reviews. We initially found one new RCT (low risk of bias) concerning topical steroid treatment,[20,121] but this study was incorporated into a Cochrane review update while we were completing this review.[32] We also found one large multicenter study comparing adenoidectomy, TT, and watchful waiting and have incorporated those findings.[19]

Thus, new evidence from nonrandomized trials and observational studies did not add appreciably to our understanding of these treatment comparisons. Nor were we able to uncover virtually any evidence regarding special populations. For those reasons, our conclusions are largely a compilation of those that have been made in the previous systematic reviews, supplemented with additional findings that we abstracted directly from the studies included in those reviews.

Implications for Clinical and Policy Decisionmaking

The evidence from this review largely compiles and reconsiders in one document many of the findings that recent systematic reviews of treatments for OME have provided. We did not find evidence to refute the conclusions in current guidance concerning the lack of effectiveness of oral and intranasal steroids as treatment for OME; evidence included a recently conducted large RCT that found intranasal steroids to not be effective.[20,121]

TT are apparently effective in reducing effusion and in improving hearing compared with watchful waiting; nevertheless, their effect is limited, no doubt a consequence of the fact that effusion often resolves even if untreated. We found these results even though, by definition, many subjects in watchful waiting arms eventually received TT. However, questions remain on at least two points: (1) longer term TT outcomes did not generally adjust for whether the TT were still in place at the time of outcome assessments, and (2) criteria for watchful waiting groups receiving TT was discretionary, based on clinical judgment, rather than a priori criteria. TT designed to be retained in the ear for a longer period were more effective in relation to OME recurrence, but they also were related to a higher risk of some side effects. We did not find evidence about which routines for insertion are more beneficial for reducing fluid and mitigating harms and whether outcomes differ for younger versus older individuals. We still do not know for what age child it is most deleterious for fluid to remain untreated. Nor do we know whether subpopulations of children with cleft palate or Down syndrome need to follow a treatment course different from treatment that typically developing children might receive.

Overall, children with TT placement for OME lasting greater than 3 months are more likely to have resolution of middle ear effusion for up to 2 years after the procedure. We noted a similar difference for hearing loss up to 6 months after tube placement. This difference and the physiological and developmental plausibility that the hearing loss could worsen speech and language outcomes in either the short or the long term has driven clinicians to intervene on prolonged OME. Because, in the longer term, effusions resolve in the vast majority of patients without any intervention, a key clinical decision concerns the length of time that mild to moderate hearing loss needs to be present to have an important negative impact; similarly, how these outcomes may differ for individuals at different developmental stages and ages remains a crucial unanswered question. The series of studies by Paradise et al. suggests that delaying TT insertion for 9 to 12 months after OME develops with mild hearing loss does not worsen long-term functional outcomes compared with providing earlier insertion.

Many primary care providers refer patients with prolonged effusion (commonly considered to be 3 months or more) and mild to moderate hearing loss to otolaryngologists for placement of TT. However, our synthesis of the available studies found no evidence of differences in long-term functional outcomes or quality of life between subjects who had TT placement and those who had only watchful waiting for OME.

Currently, many children with craniofacial syndromes or underlying hearing loss have TT placed either prophylactically (e.g., for patients with cleft palate) or at a very low threshold of time that effusion is present. We found no evidence specific to these populations to either support or refute those practices.

Adenoidectomy alone is an effective treatment for middle ear effusion relative to myringotomy. Some evidence suggests that the combination of adenoidectomy and TT provides better outcomes than TT alone. However, surgery for adenoidectomy is more invasive and raises concern that it may threaten more serious complications than TT, but we found limited evidence describing or quantifying the risk.

For clinical questions that have insufficient evidence to provide confident answers, clinicians will need to continue to rely on the recommendations in clinical practice guidelines, clinician experience and expert opinion, and individual patient- and family-level shared decisionmaking.

Applicability

As noted, during the review process we systematically abstracted key factors that may affect the applicability of the evidence base. We identified these key factors a priori, defining applicability as "the extent to which the effects observed in published studies are likely to reflect the expected results when a specific intervention is applied to the population of interest under real-world conditions."[148]

Population

Findings about all interventions are likely to be applicable in otherwise healthy children beyond infancy. However, the evidence base is limited for adults and for infants. In some cases, study authors did not provide sufficient information on age of the target population (e.g., provided only the average age without providing the age range) rendering it difficult to ascertain the applicability of the tested intervention. It is also limited for children with major coexisting or congenital conditions who may be at risk of having OME for longer periods of time, such as those with cleft palate or Down syndrome, and for those who may be more sensitive to hearing loss, such as those with preexisting hearing loss. Despite our goal of examining outcomes in young children, adults, and individuals with coexisting conditions, we were unable to find sufficient, if indeed any, studies on these populations. Thus, we cannot draw conclusions about whether the relative efficacy of treatment comparisons will be similar for these groups.

Intervention and Comparators

We present evidence on all of the commonly used treatments for OME, including TT, myringotomy, adenoidectomy, and watchful waiting/delayed treatment. We present evidence on oral and intranasal steroids because, although not currently recommended in major guidelines or approved by the U.S. Food and Drug Administration for treating children with OME, our Technical Expert Panel believed that these pharmaceutical agents are still a commonly used intervention. We also include autoinflation, because, although this procedure is not typically used in the United States, it offers an alternative noninvasive treatment strategy for older children and adults. We had planned to include complementary and alternative medicine (CAM) but were unable to find any studies that met our criteria; thus, we have no evidence regarding the effectiveness of these treatments. Similarly, we planned to examine the prior use of pneumococcal virus inoculation as a moderator of the treatments for OME, but we did not find any studies. It should be noted that not all studies comparing TT to other surgical or non-surgical treatments provided information regarding the type of TT used, limiting conclusions that can be made about those comparisons.

Outcomes

We did not limit the outcomes of interest but rather took a broad view of what kinds of benefits might occur with the treatments. We targeted clinical health outcomes, functional outcomes and quality of life, health care utilization, and harms. However, the bulk of the literature examined only whether the interventions reduced OME or improved hearing. A few studies examined language development and behavior problems, and a few of the RCTs examined quality-of-life outcomes. No studies focused on parental and patient satisfaction with care or heath care utilization. Thus, we can say little or nothing about these other important

outcomes. Nor did studies uniformly examine harms, and when they did, there was not a standard set of harms measured, even for the same treatment.

We acknowledge the central role that continued effusion and hearing play in these functional outcomes, yet the broad range of outcomes is important in its own right. Moreover, investigators chose different measures to index many of these outcomes (e.g., quality of life), so even when we had two or more studies reporting an outcome, we could not perform quantitative summaries.

Our lack of evidence in these areas parallels the conclusions reported in the previous AHRQ systematic review[2] of long term effects of OME—chiefly that failure to reach conclusions about effects of OME on long-term speech and language can be attributed at least in part to lack of uniformity in instrumentation as well as in when the outcomes were measured. Most of the investigators examined outcomes at a set followup point post intervention. In contrast, the large RCT of Paradise and colleagues[68] collected outcome data at defined ages of children making integration with the rest of the literature difficult.

Timeframes

Studies varied in their length of followup periods. Many included studies measured results between 3 and 12 months following treatment; the longest was 10 to 12 years. However, for some comparisons, such as differences between types of TT and autoinflation and controls, followup was generally shorter. Overall, for any given comparison, time frames were rarely uniform, making cross-study integration difficult if not impossible.

Settings

Studies were conducted in clinical settings and generally included populations from the United States and European countries. A few studies were conducted in developing countries (e.g., Bulgaria) and in non-Western countries (e.g., Egypt, Iran, Japan).

Limitations of the Review Process

As noted previously, we constrained our synthesis of benefits to trials or other studies with either low or medium risk of bias. Given the limitations of the included studies and their applicability to other contexts, however, including high-risk-of-bias studies for benefits would likely have increased the pool of evidence but without providing more actionable evidence. By contrast, we included harms evidence from high-risk-of-bias studies because some harms, such as otorrhea and surgical complications, could not have occurred without the procedure.

Other possible limitations of the review process included our reliance on results from existing systematic reviews and our restriction to including only articles written in English. Use of the systematic reviews meant that we accepted the authors' assessments of risk of bias and their methodology for conducting meta-analyses. All authors documented how they classified studies and conducted meta-analyses. In all cases they appeared to use appropriate and reliable methods for determining bias and performing syntheses. Given the large literature base in English, we felt that we would have captured most of the eligible studies with this restriction. Although the Cochrane reviews did not limit their searches to English, all of their studies were, in fact, published in English. Thus, we do not believe that the evidence base of this review had serious omissions.

At the outset of the review, we established that we would only include head-to-head trials, including active monitoring. We recognize that by excluding single arm studies, we may have eliminated studies that examined important outcomes, particularly harms.

Limitations of the Evidence Base

Our decision to restrict studies to those that examined treatments in individuals with OME limited the overall evidence base. Many studes indicated only that the participants had otitis media; the published articles typically either did not give information about the type of OME or included a mixed sample of individuals with AOM and OME. When investigators analyzed the OME samples separately, we included the study, but this was the exception rather than the rule. Thus, the body of research we included was restricted because of the lack of specificity in populations covered in published articles.

The evidence base was further restricted by a lack of studies with low risk of bias (i.e., good internal validity). Overall, we rated only 1 of the 17 new studies included in our analysis as low risk of bias. Some of the major reasons we rated studies as medium (rather than low) risk of bias included the following: (1) RCTs lacked information regarding randomization or blinding of outcome assessors and providers, and (2) the studies had high rates of attrition. Overall, the more rigorous studies had been previously identified in the systematic reviews that we included in our review.

Evidence about managing patients with OME is further confounded by a variety of methodological deficiencies. Not all studies provided detailed information about co-interventions. Although some investigators indicated how many patients received a supplementary treatment, they didn't analyze the data separately by these treatments. Studies employed a wide range of criteria for diagnostic inclusion and a wide variety of outcomes measures; they also gave only scant descriptions of how those measures were obtained. Even when outcome measures were similar, we often encountered variations in when investigators collected the data and how the data were reported. Differences in outcome measures and timing of data collection made additional quantitative synthesis impossible. Investigators did not routinely indicate important details about the treatment (e.g., type of TT used and how long the TT remained in place). These details are critical for understanding the generalizability of the findings

Most studies included a wide range of children (2 to 14 years of age) but did not include infants. Children age 6 or older who experience OME are likely to be at different risk for negative impacts than those who experience OME as infants or very young children; however, based on the study and followup by Paradise and colleagues (2001)[68] this concern may not be warranted. Nevertheless, we were not able to draw firm conclusions about the relative benefit of treatments as a function of age; only Paradise et al. (2001)[68] and Rovers et al. (2000)[140] recruited infants. Including all children in studies may mask the benefits of treatment of individuals at varying ages.

Aside from several exceptions—notably, studies by Paradise and colleagues[8] and Black and colleagues[97]—most investigators did not conduct a power analysis. Without such information, we could not determine with confidence whether a failure to find differences in individual studies was because the study was underpowered. We suspect that power was low for many of these studies, given the relatively small and heterogeneous samples.

Research Gaps

Given the severe limitations of the evidence base, with gaps both in study topics (interventions, appropriate outcomes, relevant populations) and in methods, we have several recommendations for future directions.

Gaps in Subgroups Studied

Additional research needs to determine the appropriate criteria and waiting period before surgical intervention with children. Analyses by Paradise et al. suggest that mild hearing loss in preschool children for periods of up to 9 to 12 months does not affect subsequent speech or language outcomes. Whether toddlers are able to tolerate the same degree of hearing loss without risk to their language development is not known.

A hearing loss of any degree creates a barrier to full access to the auditory signal. Thus, infants and toddlers who are learning the rules that govern language comprehension and production may be more vulnerable to any hearing loss that OME may impose. Research on infant speech perception and later outcomes has demonstrated that babies who were able to distinguish between the two simple vowels /i/ (tea) and /u/ (two) at 6 months of age had larger vocabularies when they were 18 and 24 months of age than did babies who could not make those distinctions. Because early vocabulary development is a strong predictor of academic achievement, these clinical considerations about OME are important and warrant more extensive investigation.[149]

In many instances children younger than 2 years of age are underrepresented in studies; even when they are included, investigators often do not present their results by appropriate age groups. We recommend that RCTs that include children at these highly vulnerable ages examine effects of OME on morphosyntactical development (0 to 36 months) and report their results partitioned by age groups that reflect developmental vulnerability.

Evidence about the impact of interventions for OME in at-risk subpopulations is virtually nonexistent. Children with a variety of developmental or sensory delays are usually excluded from studies investigating treatment outcomes for OME; this decision often eliminates children on the autism disorder spectrum and children with Down syndrome, permanent sensorineural or conductive hearing loss, craniofacial anomalies affecting eustachian tube function such as cleft palate, and ciliary dyskinesia. All these subgroups are at risk for developing speech and language problems because of these comorbidities; adding a 15 to 20 dB hearing loss because of OME increases their vulnerability. Although RCTs may not always be feasible because of ethical concerns or because of the relatively low incidence of these conditions, carefully controlled nonrandomized or observational studies can be conducted, and are very much needed, to guide management of OME in these subgroups.

Despite the high prevalence of OME in children with cleft palate,[150,151] we found no evidence on treatment of OME in this population that met our inclusion criteria. Studies were excluded mainly because TT placement occurred prophylactically during other craniofacial surgery and was not limited to children with diagnoses of OME. A recent 2009 systematic review, conducted by Ponduri and colleagues,[152] assessed evidence on OME-related symptoms and hearing, speech, and language outcomes in children with cleft palate who received early placement of TT. Only three of the studies in their report were limited to children who were diagnosed with OME at the time of initial assessment.[153-155] We did not include these studies in our review because they were wrong population (included children with suppurative otitis media), wrong study design (case

series, no comparator), and wrong publication type (the study was not available in English), respectively.

We identified one ongoing study with adult participants. The Children's Hospital of Pittsburgh, in collaboration with The National Institute on Deafness and Other Communication Disorders (NIDCD) and the University of Pittsburgh, is currently conducting an observational study of adults who have received TT for treatment of chronic OME or eustachian tube function (or both).[156] The investigators plan to examine both standard and study-designed eustachian tube function tests that may facilitate the development and use of new medical or surgical treatments to improve eustachian tube function and outcomes associated with middle ear diseases.

Gaps in Outcomes Measured (Benefits or Harms)

As indicated previously, outcomes were limited mainly to resolution of OME and hearing. These outcomes can be easily measured, but we do not know to what extent they are correlated with functional outcomes such as speech and language development or quality of life. We found little evidence concerning cycles of episodes of AOM and OME; thus, we could not determine whether episodes or length of time with OME were related to a greater likelihood of new or recurrent episodes of AOM. Also, we found no information on how treatment choice during one OME episode affected later use of health care services. We believe that one area for future research is to establish whether treatments can affect these health and health care outcomes.

For instance, we had targeted auditory processing as an outcome of interest because research has demonstrated that OME can affect skills such as binaural auditory perception[157] and speech recognition in noise.[149,158] Presumably, these skills affect children's ability to attend to instruction in noisy classrooms. One small study by Hall et al.[159] found that TT can improve one measure of auditory processing, but the recovery period is protracted. Hearing is necessary for auditory processing, but even when hearing returns to normal, auditory perception can still be impaired. This study was not a trial and included only a small number of children. The only trial that reported on auditory processing was by Paradise and colleagues; they found no differences between their early and delayed tube groups among children 6 to 9 years of age.[67,69] Replication of this work with new samples of children with more serious middle ear disease would be extremely useful to increase our confidence in these findings.

No study examined either use of health care services or parent satisfaction with care. Whether any of these treatments reduce time spent at the physician's office (by children and their parents, or adult patients, or both) or lower any costs associated with loss of productivity is not known. Anecdotally, we know that parents often request TT because they hope that this intervention will reduce the time that their children are ill and in pain. The unexamined issue is whether receiving TT or other treatment options affects these outcomes. Proxy reporting on child functional status, including baseline conditions and outcomes important to parents could provide additional criteria for deciding between alternative treatment options.

Although recurrent AOM is an important outcome, and one of the reasons for treating OME, this outcome was reported in few studies. We recommend that future research include recurrence of AOM as an outcome. It is important to know whether an OME treatment shows reductions in AOM, even if hearing and functional outcomes do not show an effect.

We had few conclusions with regard to harms, in part because the evidence base was so limited. Future studies should aim to examine a uniform body of harms for all patients. Some of the treatment complications are rare (e.g., cholesteatoma, complications from adenoidectomy

surgery), making it even more important that both trials and observational studies make a concerted effort to measure these problems and side effects.

Gaps in Interventions

This review provided little evidence regarding different types of TT or routines for insertion. An ongoing Swedish trial plans to enroll 400 children between the ages of 1 and 10 years in an RCT comparing complications from four types of TT, two different materials, and two different shapes.[160] The comparisons described are the Shepard tube (double flanged, Fluoroplastic) versus Donaldson tube (double flanged, silicone); Straight tube (single flanged, Fluoroplastic) versus Armstrong (single flanged, silicone); Armstrong (single flanged, silicone) versus Donaldson tube (double flanged, silicone); and Straight tube (single flanged, Fluoroplastic) versus Shepard tube (double flanged, Fluoroplastic). Outcomes include time to complete expulsion of the TT from the tympanic membrane and various harms, including persistent tympanic membrane perforation, need for TT extraction, pain leading to health care contact, tube-related ear infection, obstruction of the TT, and presence of myringosclerosis. The trial will include both children with recurrent AOM (RAOM) and OME, but presentation of the results (i.e., complications in OME and RAOM reported separately) could inform best practices in TT choice for children with OME. Although this study will likely make an important contribution to the literature about complications as a function of TT design, it is unfortunate that neither hearing nor functional outcomes will be examined.

Despite increasing interest by the public in alternatives to surgical interventions or traditional medical management, an exhaustive review of the literature failed to identify any RCTs regarding CAM treatments. The need for carefully conducted investigations of CAM interventions, including dietary modifications, seems clear. We identified an ongoing and potentially promising RCT that addresses the benefit of dietary modification in treating patients with OME.[161] The study, being conducted at the University of Missouri-Columbia, hopes to provide evidence that standard treatment options for chronic OME in children should involve food allergy assessment and, when indicated, subsequent dietary modifications in addition to standard surgical procedures. Additionally, these investigators are seeking evidence to assess whether adenoidectomy is of added benefit in a treatment course of surgical intervention and dietary modification. Investigators plan to measure recurrence of OME in two treatment groups: (1) bilateral myringotomy with TT in conjunction with food allergy testing and management and (2) bilateral myringotomy with TT in conjunction with adenoidectomy and food allergy testing and management. The incidence of recurrent OME episodes in all trial groups will be recorded at 3-month intervals until TT expulsion, with a further year of followup evaluations at 3-month intervals. At the time of this report, this study is listed as recruiting.[160]

Several studies have found high pepsin or pepsinogen, a component of stomach fluid, in the middle ear fluid of children with chronic middle ear fluid. Some researchers believe that gastroesophageal reflux disease (GERD) may be a cause of OME.[162] We identified two unpublished trials that evaluate treating children with OME with proton pump inhibitors (PPIs, i.e., antireflux medications). One study of chronic OME is listed as completed,[161] with December 2009 reported as the final data collection date for the primary outcome measure(s); we were unable to identify any related publications, however, and to the best of our ability do not know of any publications on the outcomes of this study. An ongoing pilot study of anti-acid treatment for children and adolescents with OME lists the completion date for data collection of primary outcome measures as April 2012. Although the primary goal of this study is to collect data for

calculating sample size and recruitment rates required for a larger clinical trial, the secondary outcomes could potentially be of particular interest to the field; these outcomes include degree of hearing improvement, complications of OME (e.g., recurrent OME, surgery) and side effects of the PPI lansoprazole. The larger clinical trial that is set to follow could provide a clearer picture of the role that gastric reflux might play in OME and could inform treatment decisions, although recent evidence of risks associated with PPI use in children will need to be incorporated into treatment decisions.[163]

A prospective cohort study, ongoing since 2006, in children 3 to 6 years of age who underwent TT insertion for chronic OME aims to determine whether eustachian tube function tests and gas exchange tests can be used to predict successfully whether a child who has TT will redevelop the disease after the TT either becomes nonfunctional or is expelled.[164] The investigators state that the results of their study will be used to support or contest components of existing models of middle ear pressure regulation and to develop test protocols for risk assignments of disease recurrence in individual ears after TT become nonfunctioning or are extruded.

Many cases of OME start after episodes of AOM. Additionally, sinus and pharyngeal infections can further eustachian tube dysfunction and contribute to OME. Vaccines to prevent pneumococcal disease can decrease the frequency of AOM[165] and might be able to decrease episodes of sinusitis and pharyngitis in the future. As rates of vaccination increase, the character of OME may change because bacterial infections will be less likely to play a role in the disease process. The use of vaccines to prevent OME was outside the scope of this review, but it holds promise for decreasing the rate of OME in children.

Deficiencies in Methods

Meta-analyses can strengthen the power for finding effects when trials have, individually, only a limited number of events. However, in many cases, differences in the methods used in these studies hamper or even preclude meta-analysis. This fact underscores the need for high-quality (low risk of bias), sufficiently powered RCTs comparing different TT types and comparing TT insertion with other interventions, utilizing a uniformly agreed-upon set of outcomes. Vastly different outcome measures and outcome assessment times limit the studies that can be (or ought to be) included in systematic reviews, which in turn delays reaching definitive conclusions about efficacy, effectiveness, and harms. If investigators in this field could agree about outcomes to be included in their investigations, then those conducting systematic review on the topic could pursue more and stronger quantitative analyses. At a minimum, uniform time points for outcome assessments and consistency in measures of hearing would make the task of combining research easier.

Conclusions

Overall, a small and uneven body of evidence showed that TT decreased effusion and improved hearing over a short period of time relative to myringotomy alone, watchful waiting, or delayed treatment. However, hearing and effusion did not differ over longer time periods, and differences were not found in speech, language, and functional outcomes. Less is known about long-term outcomes of adenoidectomy, particularly with respect to functional outcomes. Steroids were not found to provide additional benefit. More research is needed to develop a sufficient evidence base to support treatment decisions, particularly in subpopulations defined by age and coexisting conditions.

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Appendix A. Search Strategy

PubMed:

Search Jan. 8, 2012

Search	Query	Items found
#1	Search "Otitis Media with Effusion"[Mesh]	4535
#2	Search "Ear, Middle/secretion"[Mesh]	101
#3	Search "glue ear"[tiab]	251
#4	Search "otitis media"[tiab]	15150
#5	Search middle ear effusion*	1609
#6	Search (OME[tiab] OR SOM[tiab]) AND (otitis[tiab] OR ear*[tiab])	1463
#7	Search "nonsuppurative otitis"[tiab]	0
#8	Search "serous otitis"[tiab]	610
#9	Search "secretory otitis"[tiab]	940
#10	Search "adhesive otitis"[tiab]	165
#11	Search "exudative otitis"[tiab]	89
#12	Search (mucoid*[tiab] AND otitis[tiab]) OR (mucous[tiab] AND otitis[tiab]) OR (sero-muco*[tiab] AND otitis[tiab]) OR (sero[tiab] OR muco[tiab] AND otitis[tiab]) OR (otitis[tiab] AND serosa[tiab])	412
#13	Search (mucoid*[tiab] AND middle[tiab] AND ear*[tiab]) OR (mucous[tiab] AND middle[tiab] AND ear*[tiab]) OR (seromuc*[tiab] AND middle[tiab] AND ear*[tiab])	462
#14	Search #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13	17356
#15	Search "Steroids"[Mesh] OR oral steroid*	653912
#16	Search nasal*[tiab] AND (topical steroid*[tiab])	213
#17	Search "Anti-Bacterial Agents"[Mesh] OR antibiotic*	367969
#18	Search "ear popper"[tiab] OR manual therap*[tiab]	965
#19	Search autoinflation[tiab]	49
#20	Search pressure equalization tube*[tiab]	58
#21	Search "Adenoidectomy"[Mesh] OR adenoidectom*[tiab]	3873
#22	Search "Middle Ear Ventilation"[Mesh] OR tympanostomy[tiab] OR ((middle[tiab] AND (ear*[tiab] OR tympanic[tiab])) AND tube*[tiab])	4130
#23	Search grommet*[tiab]	445
#24	Search ventilation tube*[tiab]	777
#25	Search "Tonsillectomy"[Mesh] OR tonsillectomy[tiab]	8554
#26	Search "Leukotriene Antagonists/therapeutic use"[Mesh] OR "Leukotriene Antagonists" [Pharmacological Action]	4042
#27	Search "Acetates/therapeutic use"[Mesh]	2774
#28	Search "Quinolines/therapeutic use"[Mesh]	35055
#29	Search "Combined Modality Therapy"[Mesh] OR combined modality therap*[tiab]	177569
#30	Search myringotomy[tiab]	1061
#31	Search "Otologic Surgical Procedures"[Mesh]	13165
#32	Search "Phosphorylcholine/administration and dosage"[Mesh] OR "Phosphorylcholine/therapeutic use"[Mesh]	412
#33	Search "Watchful Waiting"[Mesh] OR watchful waiting*[tiab]	1517
#34	Search tubulation[tiab]	257
#35	Search #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #31 or #32 or #33 or #34	1231827
#36	Search #14 and #35	6961
#37	Search #36 or #30	7507
#38	Search #37 Limits: Humans	6659
#39	Search "Randomized Controlled Trial"[Publication Type] OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]	398253
#40	Search #38 and #39	602
#41	Search #38 Limits: Controlled Clinical Trial	70

Search	Query	Items found
#42	Search #38 AND "Controlled Clinical Trials as Topic"[Mesh]	134
#43	Search #40 or #41 or #42	763
#44	Search #38 AND systematic[sb]	258
#45	Search #38 Limits: Meta-Analysis	55
#46	Search #44 or #45	258
#47	Search ("Case-Control Studies"[MeSH] OR "Cohort Studies"[MeSH] OR "Epidemiologic Studies"[MeSH] OR "Cross-Sectional Studies"[MeSH] OR "Organizational Case Studies"[MeSH] OR "Cross-Over Studies"[MeSH] OR "Follow-Up Studies"[MeSH] OR "Seroepidemiologic Studies"[MeSH] OR "Multicenter Study"[Publication Type] OR “Multicenter Studies as Topic”[MeSH] OR "Evaluation Studies"[Publication Type] OR “Evaluation Studies as Topic”[MeSH])	2315890
#48	Search #38 and #47	2603
#49	Search #38 and harms	5
#50	Search #43 or #46 or #48 or #49 **ALL STUDY TYPES GATHERED EXCEPT LIT REVIEWS, SAVED SEPARATELY.**	2939
#51	Search #38 Limits: Review	979
#52	Search #51 not #46 **THE LIT. REVIEWS.**	851

Cochrane Library:

Search Jan. 8, 2012

ID	Search	Hits
#1	"Otitis Media with Effusion" OR "otitis media" OR "middle ear secretion" OR "Ear, Middle/secretion" OR "glue ear" OR middle ear effusion* OR OME OR SOM OR (otitis AND ear) OR (otitis AND ears) OR "nonsuppurative otitis" OR "serous otitis" OR "secretory otitis" OR "adhesive otitis" OR "exudative otitis" OR (mucoid AND otitis) OR (mucous AND otitis) OR (sero-muco* AND otitis) OR ((sero OR muco) AND otitis) OR (otitis AND serosa) OR (mucoid AND middle AND ear*) OR (mucous AND middle AND ear*) OR (seromuc* AND middle AND ear*)	2221
#2	"Steroids" OR oral steroid* OR (nasal* AND topical steroid*) OR "Anti-Bacterial Agents" OR antibiotic* OR "ear popper" OR manual therap* OR pressure equalization tube* OR adenoidectom* OR "Middle Ear Ventilation" OR tympanostomy OR (middle AND ear*AND tube*) OR (middle AND tympanic* AND tube*) OR grommet* OR ventilation tube* OR tonsillectomy OR "Leukotriene Antagonists/therapeutic use" OR "Leukotriene Antagonists" OR acetate* OR quinolone* OR phosphorylcholine OR combined modality therap* OR "Otologic Surgical Procedures" OR watchful waiting* OR tabulation OR autoinflation	50759
#3	(#1 AND #2)	1023
#4	(#3 OR myringotomy)	1119
#5	"Randomized Controlled Trial" OR "Single-Blind Method" OR "Double-Blind Method" OR "Random Allocation" OR "Controlled Clinical Trial" OR "Controlled Clinical Trials as Topic" OR (control* AND trial)	689256
#6	(#4 AND #5)	1067
#7	("Case-Control Studies"[MeSH] OR "Cohort Studies"[MeSH] OR "Epidemiologic Studies"[MeSH] OR "Cross-Sectional Studies"[MeSH] OR "Organizational Case Studies"[MeSH] OR "Cross-Over Studies"[MeSH] OR "Follow-Up Studies"[MeSH] OR "Seroepidemiologic Studies"[MeSH] OR "Multicenter Study"[Publication Type] OR "Multicenter Studies as Topic"[MeSH] OR "Evaluation Studies"[Publication Type] OR "Evaluation Studies as Topic"[MeSH])	120400
#8	(#4 AND #7)	308
#9	(#4)	172
#10	(#6 OR #8 OR #9)	1119

Embase:

Search Jan. 8, 2012

No.	Query	Results
#1	'otitis media with effusion'/exp OR 'otitis media with effusion' OR 'otitis media'/exp OR 'otitis media' OR 'middle ear secretion' OR 'ear, middle/secretion' OR 'glue ear'/exp OR 'glue ear' OR middle AND ('ear'/exp OR ear) AND effusion* OR ome OR som OR ('otitis'/exp OR otitis AND ('ear'/exp OR ear)) OR ('otitis'/exp OR otitis AND ears) OR 'nonsuppurative otitis' OR 'serous otitis'/exp OR 'serous otitis' OR 'secretory otitis' OR 'adhesive otitis' OR 'exudative otitis' OR (mucoid AND ('otitis'/exp OR otitis)) OR (mucous AND ('otitis'/exp OR otitis)) OR ('otitis'/exp OR otitis AND ('serosa'/exp OR serosa)) OR (mucoid AND middle AND ('ear'/exp OR ear)) OR (mucous AND middle AND ('ear'/exp OR ear)) AND [humans]/lim AND ([embase]/lim OR [embase classic]/lim) Bottom of Form Bottom of Form	23,677
#2	'steroids'/exp OR steroids OR 'oral'/exp OR oral AND steroid* OR (nasal* AND ('topical'/exp OR topical) AND ('steroid'/exp OR steroid)) OR 'antibacterial agents' OR 'anti-bacterial agents' OR antibiotic* OR autoinflation OR 'ear popper' OR manual AND ('therapy'/exp OR therapy) OR 'pressure'/exp OR pressure AND equalization AND ('tube'/exp OR tube) OR 'adenoidectomy'/exp OR adenoidectomy OR 'middle ear ventilation'/exp OR 'middle ear ventilation' OR tympanostomy OR (middle AND ('ear'/exp OR ear) AND ('tube'/exp OR tube)) OR (middle AND tympanic* AND tube*) OR grommet* OR 'ventilation'/exp OR ventilation AND ('tube'/exp OR tube) OR 'tonsillectomy'/exp OR tonsillectomy OR 'leukotriene antagonists/therapeutic use' OR 'leukotriene antagonists'/exp OR 'acetate'/exp OR acetate OR quinolone* OR 'phosphorylcholine'/exp OR phosphorylcholine OR combined AND modality AND ('therapy'/exp OR therapy) OR 'otologic surgical procedures'/exp OR 'otologic surgical procedures' OR watchful AND waiting OR tubulation AND [humans]/lim AND ([embase]/lim OR [embase classic]/lim)	1,730
#3	#1 AND #2	96
#4	'myringotomy'/exp OR myringotomy AND [humans]/lim AND ([embase]/lim OR [embase classic]/lim)	1,989
#5	#3 OR #4	2,056
#6	#5 AND [review]/lim	264
#7	'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'random allocation'	333,668
#8	#5 AND #7	140
#9	'controlled clinical trial'/exp OR 'controlled clinical trial (topic)'/exp	421,718
#10	#5 AND #9	162
#11	'follow up'/exp	602,436
#12	#5 AND #11	194
#13	'systematic review'/exp OR 'meta analysis'/exp	85,928
#14	#5 AND #13	36
#15	'case control study'/exp OR 'cohort analysis'/exp OR 'epidemiological study' OR 'cross-sectional study'/exp OR 'organizational case study' OR 'crossover procedure'/exp OR 'seroepidemiologic study' OR 'epidemiology'/exp OR 'multicenter study'/exp OR 'multicenter study (topic)'/exp OR 'evaluation research'/exp	1,850,275
#16	#5 AND #15	286
#17	#5 AND harms	1
#18	#8 OR #10 OR #12 OR #14 OR #16 OR #17	4571
#19	#18 NOT #6	499

CINAHL:

Search Jan. 8, 2012

#	Query	Limiters/Expanders	Last Run Via	Results
S35	S34 NOT S8	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	126
S34	S14 or S16 or S18 or S20 or S32 or S33	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	126
S33	S6 AND harms	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1
S32	S6 AND S31	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	93
S31	S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	228629
S30	(MH "Evaluation Research+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	16072
S29	(MH "Multicenter Studies")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	5343
S28	(MH "Seroprevalence Studies")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	295
S27	(MH "Crossover Design")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	6732
S26	"organizational case studies"	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3
S25	(MH "Cross Sectional Studies")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	45985
S24	(MH "Epidemiological Research")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	17482
S23	(MH "Prospective Studies+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	124579
S22	(MH "Case Control Studies+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	25256
S21	(MH "Observational Methods+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	11878
S20	S6 and S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	8
S19	(MH "Meta Analysis")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	11090
S18	S6 and S17	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	7

#	Query	Limiters/Expanders	Last Run Via	Results
S17	(MH "Systematic Review")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	9517
S16	S6 and S15	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	33
S15	"controlled clinical trial" OR (MH "Clinical Trials+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	100728
S14	S6 and S13	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	22
S13	S9 or S10 or S11 or S12	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	46815
S12	(MH "Random Assignment")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	26792
S11	(MH "Double-Blind Studies")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	17004
S10	(MH "Single-Blind Studies")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	4748
S9	(MH "Randomized Controlled Trials")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	7500
S8	S6 and S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	9
S7	(MH "Literature Review+")	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	12381
S6	S5	Limiters - Human Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	243
S5	S3 or S4	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1475
S4	TX myringotomy	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	297
S3	S1 and S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	1237
S2	TX "Histamine Antagonists" OR antihistamine* OR "Steroids" OR oral steroid* OR (nasal* AND topical steroid*) OR "Anti-Bacterial Agents" OR antibiotic* OR complementary medicine* OR alternative medicine* OR complementary therap* OR alternative therap* OR "ear popper" OR manual therap* OR pressure equalization tube* OR adenoidectom* OR "Middle Ear Ventilation" OR tympanostomy OR (middle AND ear*AND	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	96206

#	Query	Limiters/Expanders	Last Run Via	Results
	tube*) OR (middle AND tympanic* AND tube*) OR grommet* OR ventilation tube* OR tonsillectomy OR "Leukotriene Antagonists/therapeutic use" OR "Leukotriene Antagonists" OR acetate* OR quinolone* OR phosphorylcholine OR combined modality therap* OR "Otologic Surgical Procedures" OR watchful waiting* OR tubulation			
S1	TX "Otitis Media with Effusion" OR "otitis media" OR "middle ear secretion" OR "Ear, Middle/secretion" OR "glue ear" OR middle ear effusion* OR OME OR SOM OR (otitis AND ear) OR (otitis AND ears) OR "nonsuppurative otitis" OR "serous otitis" OR "secretory otitis" OR "adhesive otitis" OR "exudative otitis" OR (mucoid AND otitis) OR (mucous AND otitis) OR (sero-muco* AND otitis) OR (sero AND otitis) OR (sero AND muco*) OR (otitis AND serosa) OR (mucoid AND middle AND ear*) OR (mucous AND middle AND ear*) OR (seromuc* AND middle AND ear*)	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	Interface - EBSCOhost Search Screen - Advanced Search Database - CINAHL with Full Text	3096

PubMed supplemental search for CAM:

Search Feb 28, 2012

Search	Query	Items found
#1	Search "Otitis Media with Effusion"[Mesh]	4555
#2	Search "Ear, Middle/secretion"[Mesh]	101
#3	Search "glue ear"[tiab]	251
#4	Search "otitis media"[tiab]	15224
#5	Search middle ear effusion*	1614
#6	Search (OME[tiab] OR SOM[tiab]) AND (otitis[tiab] OR ear*[tiab])	1471
#7	Search "serous otitis"[tiab]	612
#8	Search "secretory otitis"[tiab]	941
#9	Search "adhesive otitis"[tiab]	166
#10	Search "exudative otitis"[tiab]	89
#11	Search (mucoid*[tiab] AND otitis[tiab]) OR (mucous[tiab] AND otitis[tiab]) OR (sero-muco*[tiab] AND otitis[tiab]) OR (sero[tiab] OR muco[tiab] AND otitis[tiab]) OR (otitis[tiab] AND serosa[tiab])	414
#12	Search (mucoid*[tiab] AND middle[tiab] AND ear*[tiab]) OR (mucous[tiab] AND middle[tiab] AND ear*[tiab]) OR (seromuc*[tiab] AND middle[tiab] AND ear*[tiab])	463
#13	Search "nonsuppurative otitis"[tiab]	0
#14	Search #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12	17439
#15	Search "Complementary Therapies"[Mesh]	155090
#16	Search "Diet, Sodium-Restricted"[Mesh]	5155
#17	Search "Diet, Protein-Restricted"[Mesh]	1621
#18	Search "Diet, Carbohydrate-Restricted"[Mesh]	558
#19	Search "Diet, Fat-Restricted"[Mesh]	2350
#20	Search "Dairy Products"[Mesh]	66432
#21	Search dairy OR milk OR cream Or cheese OR butter	130562
#22	Search #15 or #16 or #17 or #18 or #19 or #20 or #21	294555
#23	Search #14 and #22	230
#24	Search #23 Limits: Humans	201
#25	Search "Randomized Controlled Trial"[Publication Type] OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]	401536
#26	Search #24 and #25	17

Cochrane Library supplemental search for CAM:

Search Feb 28, 2012

ID	Search	Hits
#1	"Otitis Media with Effusion" OR "otitis media" OR "middle ear secretion" OR "Ear, Middle/secretion" OR "glue ear" OR middle ear effusion* OR OME OR SOM OR (otitis AND ear) OR (otitis AND ears) OR "nonsuppurative otitis" OR "serous otitis" OR "secretory otitis" OR "adhesive otitis" OR "exudative otitis" OR (mucoid AND otitis) OR (mucous AND otitis) OR (sero-muco* AND otitis) OR ((sero OR muco) AND otitis) OR (otitis AND serosa) OR (mucoid AND middle AND ear*) OR (mucous AND middle AND ear*) OR (seromuc* AND middle AND ear*)	2292
#2	MeSH descriptor **Complementary Therapies** explode all trees	11569
#3	MeSH descriptor **Diet, Sodium-Restricted** explode all trees	456
#4	MeSH descriptor **Diet, Protein-Restricted** explode all trees	145
#5	MeSH descriptor **Diet, Fat-Restricted** explode all trees	643
#6	MeSH descriptor **Diet, Carbohydrate-Restricted** explode all trees	128
#7	MeSH descriptor **Dairy Products** explode all trees	2342
#8	dairy OR milk OR cream Or cheese OR butter	9224
#9	(#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)	22097
#10	(#1 AND #9)	86
#11	"Randomized Controlled Trial" OR "Single-Blind Method" OR "Double-Blind Method" OR "Random Allocation" OR "Controlled Clinical Trial" OR "Controlled Clinical Trials as Topic" OR (control* AND trial)	698608
#12	(#10 AND #11)	86

EMBASE supplemental search for CAM:

Search Feb 28, 2012

No.	Query	Results
#1	'otitis media with effusion'/exp OR 'otitis media with effusion' OR 'otitis media'/exp OR 'otitis media' OR 'middle ear secretion' OR 'ear, middle/secretion' OR 'glue ear'/exp OR 'glue ear' OR middle AND ('ear'/exp OR ear) AND effusion* OR ome OR som OR ('otitis'/exp OR otitis AND ('ear'/exp OR ear)) OR ('otitis'/exp OR otitis AND ears) OR 'nonsuppurative otitis' OR 'serous otitis'/exp OR 'serous otitis' OR 'secretory otitis' OR 'adhesive otitis' OR 'exudative otitis' OR (mucoid AND ('otitis'/exp OR otitis)) OR (mucous AND ('otitis'/exp OR otitis)) OR ('otitis'/exp OR otitis AND ('serosa'/exp OR serosa)) OR (mucoid AND middle AND ('ear'/exp OR ear)) OR (mucous AND middle AND ('ear'/exp OR ear)) AND [humans]/lim AND ([embase]/lim OR [embase classic]/lim)	23,921
#2	'alternative medicine'/exp	28,963
#3	'sodium restriction'/exp	7,519
#4	'protein restriction'/exp	5,671
#5	'low carbohydrate diet'/exp	1,083
#6	'low fat diet'/exp	5, 811
#7	'dairy product'/exp	74,303
#8	dairy OR 'milk'/exp OR 'cream'/exp OR 'cheese'/exp OR 'butter'/exp AND ([embase]/lim OR [embase classic]/lim)	63,357
#9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	140,00
#10	#1 AND #9	129
#11	'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'random allocation'/exp AND ([embase]/lim OR [embase classic]/lim)	278.009
#12	#10 AND #11	6

CINAHL supplemental search for CAM:

Search Feb 28, 2012

#	Query	Limiters/Expanders	Results
S17	S11 and S16	Search modes - Boolean/Phrase	
S16	S12 or S13 or S14 or S15	Search modes - Boolean/Phrase	47751
S15	(MH "Random Assignment")	Search modes - Boolean/Phrase	27104
S14	(MH "Double-Blind Studies")	Search modes - Boolean/Phrase	17138
S13	(MH "Single-Blind Studies")	Search modes - Boolean/Phrase	4834
S12	(MH "Randomized Controlled Trials")	Search modes - Boolean/Phrase	8205
S11	S1 and S10	Search modes - Boolean/Phrase	465
S10	S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9	Search modes - Boolean/Phrase	122594
S9	TX dairy OR milk OR cream Or cheese OR butter	Search modes - Boolean/Phrase	33567
S8	(MH "Dairy Products+")	Search modes - Boolean/Phrase	2989
S7	(MH "Dietary Proteins+")	Search modes - Boolean/Phrase	3917
S6	(MH "Diet, Low Carbohydrate")	Search modes - Boolean/Phrase	266
S5	(MH "Diet, Fat-Restricted")	Search modes - Boolean/Phrase	1304
S4	(MH "Restricted Diet+")	Search modes - Boolean/Phrase	5270
S3	(MH "Diet, Sodium-Restricted")	Search modes - Boolean/Phrase	593
S2	(MH "Alternative Therapies+")	Search modes - Boolean/Phrase	84028
S1	TX "Otitis Media with Effusion" OR "otitis media" OR "middle ear secretion" OR "Ear, Middle/secretion" OR "glue ear" OR middle ear effusion* OR OME OR SOM OR (otitis AND ear) OR (otitis AND ears) OR "nonsuppurative otitis" OR "serous otitis" OR "secretory otitis" OR "adhesive otitis" OR "exudative otitis" OR (mucoid AND otitis) OR (mucous AND otitis) OR (sero-muco* AND otitis) OR (sero AND otitis) OR (sero AND muco*) OR (otitis AND serosa) OR (mucoid AND middle AND ear*) OR (mucous AND middle AN ...	Limiters - Exclude MEDLINE records Search modes - Boolean/Phrase	3118

Embase: Update

Search August 13, 2012

No.	Query	Results
#1	'otitis media with effusion'/exp OR 'otitis media with effusion' OR 'otitis media'/exp OR 'otitis media' OR 'middle ear secretion' OR 'ear, middle/secretion' OR 'glue ear'/exp OR 'glue ear' OR middle AND ('ear'/exp OR ear) AND effusion* OR ome OR som OR ('otitis'/exp OR otitis AND ('ear'/exp OR ear)) OR ('otitis'/exp OR otitis AND ears) OR 'nonsuppurative otitis' OR 'serous otitis'/exp OR 'serous otitis' OR 'secretory otitis' OR 'adhesive otitis' OR 'exudative otitis' OR (mucoid AND ('otitis'/exp OR otitis)) OR (mucous AND ('otitis'/exp OR otitis)) OR ('otitis'/exp OR otitis AND ('serosa'/exp OR serosa)) OR (mucoid AND middle AND ('ear'/exp OR ear)) OR (mucous AND middle AND ('ear'/exp OR ear)) AND [humans]/lim AND ([embase]/lim OR [embase classic]/lim)	24,807
#2	'steroids'/exp OR steroids OR 'oral'/exp OR oral AND steroid* OR (nasal* AND ('topical'/exp OR topical) AND ('steroid'/exp OR steroid)) OR 'antibacterial agents' OR 'anti-bacterial agents' OR antibiotic* OR autoinflation OR 'ear popper' OR manual AND ('therapy'/exp OR therapy) OR 'pressure'/exp OR pressure AND equalization AND ('tube'/exp OR tube) OR 'adenoidectomy'/exp OR adenoidectomy OR 'middle ear ventilation'/exp OR 'middle ear ventilation' OR tympanostomy OR (middle AND ('ear'/exp OR ear) AND ('tube'/exp OR tube)) OR (middle AND tympanic* AND tube*) OR grommet* OR 'ventilation'/exp OR ventilation AND ('tube'/exp OR tube) OR 'tonsillectomy'/exp OR tonsillectomy OR 'leukotriene antagonists/therapeutic use' OR 'leukotriene antagonists'/exp OR 'acetate'/exp OR acetate OR quinolone* OR 'phosphorylcholine'/exp OR phosphorylcholine OR combined AND modality AND ('therapy'/exp OR therapy) OR 'otologic surgical procedures'/exp OR 'otologic surgical procedures' OR watchful AND waiting OR tubulation AND [humans]/lim AND ([embase]/lim OR [embase classic]/lim)	1916
#3	#1 AND #2	100
#4	'myringotomy' OR 'myringotomy'/exp OR myringotomy AND [humans]/lim AND ([embase]/lim OR [embase classic]/lim)	2095
#5	#3 OR #4	2165
#7	'alternative medicine'/exp OR 'sodium restriction'/exp OR 'protein restriction'/exp OR 'low carbohydrate diet'/exp OR 'low fat diet'/exp OR 'dairy product'/exp OR dairy OR 'milk'/exp OR 'cream'/exp OR 'cheese'/exp OR 'butter'/exp	161970
#8	#1 AND #7	140
#9	#5 OR #8	2299
#10	#9 AND [review]/lim	330
#11	#10 AND [humans]/lim AND ([embase]/lim OR [embase classic]/lim) AND [8-12-2011]/sd NOT [13-8-2012]/sd	23
#12	'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'random allocation'/exp	399,085
#13	#9 AND #12	152
#14	'controlled clinical trial'/exp OR 'controlled clinical trial (topic)'/exp	445,547
#15	#9 AND #14	178
#16	'follow up'/exp	655852
#17	#9 AND #16	209
#18	'systematic review'/exp OR 'meta analysis'/exp	95329
#19	#9 AND #18	44
#20	'case control study'/exp OR 'cohort analysis'/exp OR 'epidemiological study' OR 'cross-sectional study'/exp OR 'organizational case study' OR 'crossover procedure'/exp OR 'seroepidemiologic study' OR 'epidemiology'/exp OR 'multicenter study'/exp OR 'multicenter study (topic)'/exp OR 'evaluation research'/exp	1,979,394
#21	#9 AND #20	324
#22	#9 AND harms	1

No.	Query	Results
#23	#13 OR #15 OR #17 OR #19 OR #21 OR #22	641
#24	#23 AND [humans]/lim AND [8-12-2011]/sd NOT [13-8-2012]/sd	41
#25	#11 NOT #24	16

CINAHLUpdate:

Search Aug 13, 2012

#	Query	Limiters/Expanders	Results
S47	S26 or S28 or S30 or S32 or S33 or S44 or S45	Limiters - Published Date from: 20111201-20121231 Search modes - Boolean/Phrase	7
S46	S26 or S28 or S30 or S32 or S33 or S44 or S45	Search modes - Boolean/Phrase	354
S45	S17 AND harms	Search modes - Boolean/Phrase	2
S44	S17 and S43	Search modes - Boolean/Phrase	255
S43	S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42	Search modes - Boolean/Phrase	243768
S42	(MH "Evaluation Research+")	Search modes - Boolean/Phrase	16705
S41	(MH "Multicenter Studies")	Search modes - Boolean/Phrase	5959
S40	(MH "Seroprevalence Studies")	Search modes - Boolean/Phrase	307
S39	(MH "Crossover Design")	Search modes - Boolean/Phrase	7226
S38	"organizational case studies"	Search modes - Boolean/Phrase	3
S37	(MH "Cross Sectional Studies")	Search modes - Boolean/Phrase	49996
S36	(MH "Epidemiological Research")	Search modes - Boolean/Phrase	18031
S35	(MH "Prospective Studies+")	Search modes - Boolean/Phrase	133542
S34	(MH "Case Control Studies+")	Search modes - Boolean/Phrase	26734
S33	S17 AND (MH "Observational Methods+")	Search modes - Boolean/Phrase	4
S32	S17 and S31	Search modes - Boolean/Phrase	21
S31	(MH "Meta Analysis")	Search modes - Boolean/Phrase	11747
S30	S17 and S29	Search modes - Boolean/Phrase	10
S29	(MH "Systematic Review")	Search modes - Boolean/Phrase	10937
S28	S17 and S27	Search modes - Boolean/Phrase	132
S27	"controlled clinical trial" OR (MH "Clinical Trials+")	Search modes - Boolean/Phrase	106932
S26	S17 and S25	Search modes - Boolean/Phrase	77
S25	S21 or S22 or S23 or S24	Search modes - Boolean/Phrase	50882
S24	(MH "Random Assignment")	Search modes - Boolean/Phrase	27917
S23	(MH "Double-Blind Studies")	Search modes - Boolean/Phrase	17853
S22	(MH "Single-Blind Studies")	Search modes - Boolean/Phrase	5117
S21	(MH "Randomized Controlled Trials")	Search modes - Boolean/Phrase	10402
S20	S17 and S18	Limiters - Published Date from: 20111201-20121231 Search modes - Boolean/Phrase	0
S19	S17 and S18	Search modes - Boolean/Phrase	15
S18	(MH "Literature Review+")	Search modes - Boolean/Phrase	13858
S17	S16	Limiters - Human Search modes - Boolean/Phrase	618
S16	S5 or S15	Search modes - Boolean/Phrase	1543
S15	S1 and S14	Search modes - Boolean/Phrase	155
S14	S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13	Search modes - Boolean/Phrase	108145
S13	TX dairy OR milk OR cream Or cheese OR butter	Search modes - Boolean/Phrase	14534
S12	(MH "Dairy Products+")	Search modes - Boolean/Phrase	3124
S11	(MH "Dietary Proteins+")	Search modes - Boolean/Phrase	4086
S10	(MH "Diet, Low Carbohydrate")	Search modes - Boolean/Phrase	289
S9	(MH "Diet, Fat-Restricted")	Search modes - Boolean/Phrase	1337
S8	(MH "Restricted Diet+")	Search modes - Boolean/Phrase	5458
S7	(MH "Diet, Sodium-Restricted")	Search modes - Boolean/Phrase	620
S6	(MH "Alternative Therapies+")	Search modes - Boolean/Phrase	87068

S5	S3 OR S4	Search modes - Boolean/Phrase	1472
S4	TX myringotomy	Search modes - Boolean/Phrase	306
S3	S1 AND S2	Search modes - Boolean/Phrase	1262
S2	TX "Histamine Antagonists" OR antihistamine* OR "Steroids" OR oral steroid* OR (nasal* AND topical steroid*) OR "Anti-Bacterial Agents" OR antibiotic* OR complementary medicine* OR alternative medicine* OR complementary therap* OR alternative therap* OR "ear popper" OR manual therap* OR pressure equalization tube* OR adenoidectom* OR "Middle Ear Ventilation" OR tympanostomy OR (middle AND ear*AND tube*) OR (middle AND tympanic* AND tube*) OR grommet* OR ventilation tube* OR tonsillectomy OR "Leukotriene Antagonists/therapeutic use" OR "Leukotriene Antagonists" OR acetate* OR quinolone* OR phosphorylcholine OR combined modality therap* OR "Otologic Surgical Procedures" OR watchful waiting* OR tubulation	Search modes - Boolean/Phrase	69123
S1	TX "Otitis Media with Effusion" OR "otitis media" OR "middle ear secretion" OR "Ear, Middle/secretion" OR "glue ear" OR middle ear effusion* OR OME OR SOM OR (otitis AND ear) OR (otitis AND ears) OR "nonsuppurative otitis" OR "serous otitis" OR "secretory otitis" OR "adhesive otitis" OR "exudative otitis" OR (mucoid AND otitis) OR (mucous AND otitis) OR (sero-muco* AND otitis) OR (sero AND otitis) OR (sero AND muco*) OR (otitis AND serosa) OR (mucoid AND middle AND ear*) OR (mucous AND middle AND ear*) OR (seromuc* AND middle AND ear*)	Search modes - Boolean/Phrase	3498

Cochrane Library Update: August 13, 2012

Current Search History

ID	Search	Hits
#1	"Otitis Media with Effusion" OR "otitis media" OR "middle ear secretion" OR "Ear, Middle/secretion" OR "glue ear" OR middle ear effusion* OR OME OR SOM OR (otitis AND ear) OR (otitis AND ears) OR "nonsuppurative otitis" OR "serous otitis" OR "secretory otitis" OR "adhesive otitis" OR "exudative otitis" OR (mucoid AND otitis) OR (mucous AND otitis) OR (sero-muco* AND otitis) OR ((sero OR muco) AND otitis) OR (otitis AND serosa) OR (mucoid AND middle AND ear*) OR (mucous AND middle AND ear*) OR (seromuc* AND middle AND ear*)	2327
#2	"Steroids" OR oral steroid* OR (nasal* AND topical steroid*) OR "Anti-Bacterial Agents" OR antibiotic* OR "ear popper" OR manual therap* OR pressure equalization tube* OR adenoidectom* OR "Middle Ear Ventilation" OR tympanostomy OR (middle AND ear*AND tube*) OR (middle AND tympanic* AND tube*) OR grommet* OR ventilation tube* OR tonsillectomy OR "Leukotriene Antagonists/therapeutic use" OR "Leukotriene Antagonists" OR acetate* OR quinolone* OR phosphorylcholine OR combined modality therap* OR "Otologic Surgical Procedures" OR watchful waiting* OR tabulation OR autoinflation	52955
#3	MeSH descriptor **Complementary Therapies** explode all trees	11802
#4	MeSH descriptor **Diet, Sodium-Restricted** explode all trees	461
#5	MeSH descriptor **Diet, Protein-Restricted** explode all trees	145
#6	MeSH descriptor **Diet, Fat-Restricted** explode all trees	648
#7	MeSH descriptor **Diet, Carbohydrate-Restricted** explode all trees	131
#8	MeSH descriptor **Dairy Products** explode all trees	2375
#9	dairy OR milk OR cream OR cheese OR butter	9329
#10	(#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9)	72917
#11	(#1 AND #10)	1142
#12	(#11 OR myringotomy)	1243
#13	Method" OR "Random Allocation" OR "Controlled Clinical Trial" OR "Controlled Clinical Trials as Topic" OR (control* AND trial)	718613
#14	(#12 AND #13)	1225
#15	("Case-Control Studies"[MeSH] OR "Cohort Studies"[MeSH] OR "Epidemiologic Studies"[MeSH] OR "Cross-Sectional Studies"[MeSH] OR "Organizational Case Studies"[MeSH] OR "Cross-Over Studies"[MeSH] OR "Follow-Up Studies"[MeSH] OR "Seroepidemiologic Studies"[MeSH] OR "Multicenter Study"[Publication Type] OR "Multicenter Studies as Topic"[MeSH] OR "Evaluation Studies"[Publication Type] OR "Evaluation Studies as Topic"[MeSH])	125753
#16	(#12 AND #15)	372
#17	(#12), from 2011 to 2012	139
#18	(#14 OR #16 OR #17)	1226
#19	(#18), from 2011 to 2012	139

PubMed Update: August 13, 2012

Search	Query	Items found
#1	Search "Otitis Media with Effusion"[Mesh]	4594
#2	Search "Ear, Middle/secretion"[Mesh]	101
#3	Search "glue ear"[tiab]	252
#4	Search "otitis media"[tiab]	15500
#5	Search middle ear effusion*	1633
#6	Search (OME[tiab] OR SOM[tiab]) AND (otitis[tiab] OR ear*[tiab])	1507
#7	Search "nonsuppurative otitis"[tiab]	0
#8	Search "serous otitis"[tiab]	616
#9	Search "secretory otitis"[tiab]	945
#10	Search "adhesive otitis"[tiab]	168
#11	Search "exudative otitis"[tiab]	92
#12	Search (mucoid*[tiab] AND otitis[tiab]) OR (mucous[tiab] AND otitis[tiab]) OR (sero-muco*[tiab] AND otitis[tiab]) OR (sero[tiab] OR muco[tiab] AND otitis[tiab]) OR (otitis[tiab] AND serosa[tiab])	420
#13	Search (mucoid*[tiab] AND middle[tiab] AND ear*[tiab]) OR (mucous[tiab] AND middle[tiab] AND ear*[tiab]) OR (seromuc*[tiab] AND middle[tiab] AND ear*[tiab])	469
#14	Search #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13	17740
#15	Search "Steroids"[Mesh] OR oral steroid*	665533
#16	Search nasal*[tiab] AND (topical steroid*[tiab])	226
#17	Search "Anti-Bacterial Agents"[Mesh] OR antibiotic*	379785
#18	Search "ear popper"[tiab] OR manual therap*[tiab]	1042
#19	Search autoinflation[tiab]	50
#20	Search pressure equalization tube*[tiab]	58
#21	Search "Adenoidectomy"[Mesh] OR adenoidectom*[tiab]	3977
#22	Search "Middle Ear Ventilation"[Mesh] OR tympanostomy[tiab] OR ((middle[tiab] AND (ear*[tiab] OR tympanic[tiab])) AND tube*[tiab])	4226
#23	Search grommet*[tiab]	448
#24	Search ventilation tube*[tiab]	807
#25	Search "Tonsillectomy"[Mesh] OR tonsillectomy[tiab]	8769
#26	Search "Leukotriene Antagonists/therapeutic use"[Mesh] OR "Leukotriene Antagonists" [Pharmacological Action]	4122
#27	Search "Acetates/therapeutic use"[Mesh]	2860
#28	Search "Quinolines/therapeutic use"[Mesh]	36041
#29	Search "Combined Modality Therapy"[Mesh] OR combined modality therap*[tiab]	183840
#30	Search myringotomy[tiab]	1085
#31	Search "Otologic Surgical Procedures"[Mesh]	13612
#32	Search "Phosphorylcholine/administration and dosage"[Mesh] OR "Phosphorylcholine/therapeutic use"[Mesh]	438
#33	Search "Watchful Waiting"[Mesh] OR watchful waiting*[tiab]	1729
#34	Search tubulation[tiab]	272
#35	Search "Complementary Therapies"[Mesh]	159794
#36	Search "Diet, Sodium-Restricted"[Mesh]	5207
#37	Search "Diet, Protein-Restricted"[Mesh]	1671
#38	Search "Diet, Carbohydrate-Restricted"[Mesh]	600
#39	Search "Diet, Fat-Restricted"[Mesh]	2439
#40	Search "Dairy Products"[Mesh]	67792
#41	Search dairy OR milk OR cream Or cheese OR butter	134103
#42	Search #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41	1540392
#43	Search #14 and #42	7300
#44	Search #43 or #30	7858
#45	Search #43 or #30 Filters: Humans	6955
#46	Search "Randomized Controlled Trial"[Publication Type] OR "Single-Blind Method"[MeSH] OR	412868

Search	Query	Items found
	"Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]	
#47	Search #45 and #46	617
#48	Search #43 or #30 Filters: Humans; Controlled Clinical Trial	72
#49	Search #45 AND "Controlled Clinical Trials as Topic"[Mesh]	142
#50	Search #47 or #48 or #49	786
#51	Search #45 AND systematic[sb]	273
#52	Search #43 or #30 Filters: Humans; Meta-Analysis	58
#53	Search #51 or #52	273
#54	Search ("Case-Control Studies"[MeSH] OR "Cohort Studies"[MeSH] OR "Epidemiologic Studies"[MeSH] OR "Cross-Sectional Studies"[MeSH] OR "Organizational Case Studies"[MeSH] OR "Cross-Over Studies"[MeSH] OR "Follow-Up Studies"[MeSH] OR "Seroepidemiologic Studies"[MeSH] OR "Multicenter Study"[Publication Type] OR “Multicenter Studies as Topic”[MeSH] OR "Evaluation Studies"[Publication Type] OR “Evaluation Studies as Topic”[MeSH])	2420779
#55	Search #45 and #54	2719
#56	Search #45 AND harms	5
#57	Search #50 or #53 or #55 or #56	3072
#58	Search #57 AND (2011/06/12:2012/13/08[edat])	72
#59	Search #43 or #30 Filters: Humans; Review	1028
#60	Search #59 AND (2011/06/12:2012/13/08[edat])	15

Appendix B. Excluded Studies

Wrong Publication, Study Type, or Unavailable in English

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Appendix C. Evidence Tables

Evidence Table 1. Study characteristics

First author's last name, Year Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
Abdullah et al., 1994[1]	NRCT	25
United Kingdom	G1: Trimmed high-grade silicone shah permavent TT	Unilateral by ear
Large ENT Hospital	G2: Polyethylene conventional Shah TT	NR
NR		In cohort: G1: 25 G2: 25 Analyzed (12 mo): G1: 25 G2: 25 Analyzed (29 mo): G1: 17 G2: 17
Austin, 1994[2]	Parallel RCT	62
United States	G1: TT + adenoidectomy G2: Adenoidectomy	Unilateral by ear
Teaching hospital		NR
NR		Randomized: G1: 31 G2: 31 Analyzed: G1: 31 G2: 31

Evidence Table 1. Study characteristics (continued)

First author's last name, Year Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
Brown et al., 1978[3]	Parallel RCT	55 (110 ears)
Wales	G1: TT+ adenoidectomy G2: Adenoidectomy	By ear
University Hospital of Wales		NR
NR		Randomized: G1: 55 G2: 55 Analyzed: G1: 55 G2: 55 (Over 5 years, no attrition was reported)
D'Eredità and Shah, 2006[4]	Parallel RCT	30
Italy	G1: Contact diode laser for myringotomy G2: Myringotomy + TT	By person (but outcomes reported by ear)
Tertiary care pediatric instituion		≥ 3 months
NR		Randomized :30 (60 ears) G1: 15 (30 ears) G2: 15 (30 ears) Analyzed: 30 (60 ears) G1: 15 (30 ears) G2: 15 (30 ears)

Evidence Table 1. Study characteristics (continued)

First author's last name, Year Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
Iwaki et al., 1998[5]	Retrospective cohort	137 (220 ears)
Japan	G1: Shepard grommet tube G2: Silicone Goode-T tube	By ear
Academic hospital	G3: Silicone Paperella type II tube	NR
NR		Received intervention: 220 G1: 75 G2: 39 G3: 106 Analyzed:220 G1:75 G2:39 G3: 106 Adenoidectomy was performed at time of tube placement in 69 patients (50.4%) however distribution across treatment arms is NR.
Koopman et al., 2004[6]	Parallel RCT	208 (416 ears)
Netherlands	G1: Laser myringotomy G2: TT insertion with cold knife myringotomy	By ear
7 Dutch hospitals		NR
The Sophia Fondation for Medical Research and the Revolving Fund Sophia Children's Hospital, Erasmus Medical Center, Rotterdam, Theia Foundation, and Silver Cross Company.		Randomized: G1: 208 G2: 208 Analyzed: G1: 208 G2: 208

Evidence Table 1. Study characteristics (continued)

First author's last name, Year Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
Licameli et al., 2008[7]	Parallel RCT	70
United States	G1: Phophorulcholine-coated fluroplastic Armstrong tubes	By ear
Academic clinic	G2: Uncoated fluroplastic Armstrong tubes	3-4 months
GYRUS Inc.		Randomized: G1: 70 G2: 70 Analyzed: G1: 70 G2: 70
Lildholdt. 1979[8]	NRCT	91 (182 ears)
Denmark	G1: TT + adenoidectomy G2: Adenoidectomy	By ear
Vejle Hospital		Randomized at surgery; wait period NR
NR		Randomized: G1: 91 ears G2: 91 ears Analyzed: G1: 91 ears G2: 91 ears

Evidence Table 1. Study characteristics (continued)

First author's last name, Year Trial Name Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
Mandel et al., 1989[9]	Cluster RCT	109
United States University of Pittsburgh Medical Center Bureau of Maternal and Child Health and the NIH	Without significant hearing loss (HL) G1: Myringotomy G2: Myringotomy + Armstrong TT G3: No surgery Without significant hearing loss (HL) G4: Myringotomy G5: Myringotomy + Armstrong TT	Children were randomized by group. One set of children (86) had no sig hearing loss nor defined symptoms. This cluster was randomized to one of the three groups. A second cluster had significant hearing loss and was assigned to G4 or G5 MEE of at least 2 months duration. Time from then NR Randomized: Without significant HL G1: 27 G2: 30 G3:29 With Significant HL: G4: 12 G5: 11 Analyzed: 93 (85.3%) analyzed at end of 3 yr study G1: 26 of 27 G2: 27 of 30 G3: 25

Evidence Table 1. Study characteristics

First author's last name, Year Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
McRae et al.,1989[10]	Parallel RCT	110
United Kingdom	G1: Shah TT+ aspiration prior to tube placement G2: Shah TT without aspiration	By ear
Hospital	prior to tube placement	NR
NR		Randomized: G1: 55 G2: 55 Analyzed: 38 participants total
Ovesen et al., 2000[11]	Parallel RCT	150
Denmark	G1: TT + N-acetylcysteine after insertion of tubes G2: TT + placebo after insertion of tubes	By ear
University hospital	G3: TT in contralateral ear, exclusively	3 months
NR		Randomized: G1: 37 G2: 38 G3: 75 Analyzed: G1: 37 G2: 38 G3: 75

Evidence Table 1. Study characteristics

First author's last name, Year Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
Popova et al., 2010[12]	Parallel RCT	90
Bulgaria	G1: TT + myringotomy + adenoidectomy G2: Adenoidectomy + myringotomy	By person
Academic ENT Clinic		3 months
No funding source		Randomized: 90 G1: NR G2: NR Analyzed: 78 G1: NR G2: NR
Ragab, 2005[13]	Parallel RCT	60 (120 ears)
Egypt	G1: Radiofrequency tympanostomy + Mitomycin C G2: Radiofrequency tympanostomy (no mitomycin C)	By person
University hospital		NR
NR		Randomized: G1: 30 G2: 30 Analyzed: G1: 30 G2: 30

Evidence Table 1. Study characteristics (continued)

First author's last name, Year Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
Shishegar and Hoghoghi, 2007[14]	Parallel RCT	30 children; 60 ears
Iran	G1: Adenoidectomy + myringotomy G2: Adenoidectomy + myringotomy + TT	By ear
Hospital		NR
NR		Randomized: 60 ears G1: 30 G2: 30 Analyzed: (Unclear; assume same as randomized) G1:30 G2:30
Slack et al., 1987[15]	Retrospective cohort	463 individuals (708 ears)
UK	G1: Shepard tube G2: Shah tube G3: Paprella tube G4: Goode tube G5: Reuter Bobbin tube G6: Unknown or other tube types	By ear NA Received Intervention: 708 ears Analyzed: 654 ears G1: 214 G2:70 G3: 275 G4: 4 G5: 28 G6: 63
Hospital		
NR		

Evidence Table 1. Study characteristics (continued)

First author's last name, Year Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
Szeremeta et al., 2000[16] USA University Hospital NR	Retrospective cohort G1: Laser myringotomy (laser) + adenoidectomy G2: Incisional myringotomy + adenoidectomy	64 children 117 ears By person and by ear NR Population G1: 29 (51 ears) G2: 35 (66 ears) Analyzed: G1: 23 (39 ears) G2: 26 (48 ears)
Tos and Stangerup, 1989[17] Denmark University Hospital NR	Nonrandomized control trial G1: TT + adenoidectomy G2: Myringotomy + adenoidectomy	224 By ear >3 months Randomized: G1: 224 (ears) G2: 224 (ears) Analyzed: (at age 2-3) G1: 193 G2: 193 Analyzed: (at age 6-7) G1:146 G2:146

Evidence Table 1. Study characteristics (continued)

First author's last name, Year Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
Vlastos et al., 2011[18]	Parallel RCT	52
Greece	G1: Adenoidectomy + TT G2: Adenoidectomy + myringotomy	Bilateral by person
University Hospital		NR
NR		Randomized: G1: 25 G2: 27 Analyzed for primary outcome (6 mo): G1: 22 G2: 23 Analyzed for primary outcome (12 mo): G1: 20 G2: 21
Wielinga et al., 1990[19]	Parallel RCT	30
Northern Ireland	G1: Armstrong T-tube G2: Goode tube	Unilateral by ear
University hospital		6 months
NR		Randomized: G1: 15 G2: 15 Analyzed: G1: 15 (ears) G2: 15

Evidence Table 1. Study characteristics (continued)

First author's last name, Year Country Setting Funding Source	Study Design	**Overall Sample Size** **Formation of Groups** **Wait Period Between Diagnosis and Randomization** **Group Sample Sizes** **Other Information**
Williamson et al., 2009[20] Williamson et al., 2009[21] UK Research Medical Council General Practice Research Framework practices throughout the UK Government	Parallel RCT G1: Mometasone furoate nasal spray G2: Placebo spray	217 By person Yr 1: 3 mos of active monitoring if fairled the first screening (B/B or B/C2) and were invited into main study if failed a second time. After that, children with history of bilateral tympanometric failure randomized after first failed screen Randomized: G1: 105 G2: 112 Analyzed: 201 (93%) at 1 months 182 (84%) at 3 months 158 (73%) at 9 months

Evidence Table 2. Populations

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Popova et al., 2010[12]	Age Overall: G1: 60 months G2: 61 months Criteria for Diagnosis Tympanometry (interacoustics AT-235h) - Type B tympanograms with fulid level on otoscopy. Pneumatic otoscopy by validated otoscopist. Inclusion • 2007-2009 • Documented bilateral middle effusion for >3 months • 20 db conductive hearing loss Exclusion • Previous myringotomy (+/- TT) • Previous adenoidectomy or tonsillectomy • Hx of ear surgery • Cleft palate • Down's syndrome • Congenital malformation of ear • Cholesteatoma or chronic mastoiditis • Perforation of TM • Conductive hearing loss due to destructive changes in ME • Sensoneural hearing loss	Baseline Tympanometry NR Baseline Hearing or Hearing Loss (500-4000 Hz) Overall: G1: 31.4 dB G2: 32.3 dB ns p=0.39 Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female Overall: G1: 45 G2: 44 Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Williamson et al., 2009;[20] Williamson et al., 2009[21]	Age Range: 4-11 yrs old Mean months (SD), (range) G1: 73.3 (20.2) (49-129) G2: 72.1 (18.6) (48-125) Criteria for Diagnosis Tympanometry Inclusion • Dx of bilateral OME by a nurse • In the first yr of study children positive screening entered a 3 month period of watchful waiting. • In yr 2 the protocol was changed and children with histories of bilateral tympanic failure were allowed to be randomized at the first failed screen (50:50). Exclusion • Tympanometry screen passed • Large amounts of wax • Uninterpretable tympanogram • Children with cleft palate • Down syndrome • Primary ciliary dyskinesia • Karteagner's syndrom • Immuniodeficiency states • TTs or tympanic perforation • Frequent or heavy epistaxis • Hypersensitivity to mometasone • Hx of steriod use in previous 3 months • Children under 4 yrs	Baseline Tympanometry Type C2 (middle ear pressure −200 to −399) n=54 Type B (middle ear pressure ≤−400) n=88 Baseline Hearing or Hearing Loss Scale: Sweep audiometry at 25 dB (pass/fail) All enrolled children failed audiometric screen Other Baseline Symptoms NR Baseline Relevant Comorbidities History, No. (%) Adenoidectomy: 51 (24.5) Tonsillectomy: 23 (11.1) Cleft palate: 17 (8.2) Grommets 49 (23.6) Allergies: 7 (3.4) Baseline % Female G1: 48 G2: 68 Baseline % Nonwhite G1: 3 G2: 4	Insured Status NHS England Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Licameli et al., 2008[7]	Age Mean months, (range) Overall: 19 (8-51) Criteria for Diagnosis Not specified Inclusion • 3-4 months of medical management for OME prior to randomization Exclusion • Previous TT	Baseline Tympanometry NR Baseline Hearing or Hearing Loss NR Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female Overall: 35.7 Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Ragab, 2005[13]	Age G1: 4.8 yr G2: 5.2 yr Criteria for Diagnosis Hx, pneumo-otoscopic exam, and tympanograms Inclusion • Nov 2002-Jan 2004 patients undergoing surgery for OME Exclusion • NR	Baseline Tympanometry NR Baseline Hearing or Hearing Loss Air Bone Gap: G1: 24.7 dB G2: 24.1 dB Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female NR Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Koopman et al., 2004[6]	Age Children aged < 11 yrs Criteria for Diagnosis Binocular otoscopy in combination with Type B tympanogram or pure tone audiometry used for diagnosis. Bilateral tympanogram Type C1 or C2 (Jerger) considered to support diagnosis of OME. If child was too young or failed at audiometric testing, diagnosis based solely on otoscopic findings and hx Inclusion • Children aged less than 11 years • Impaired hearing noticed by parents during at least 3 successive months • Bilateral OME Exclusion • Unilateral OME • Ear effusions without fever, otalgia, or otorrhea • Poorly cooperative children • Clinically admitted patients • Asymmetric perceptive hearing loss (HL) • Previously operated ears with other than myringotomy or ventialation tubes	Baseline Tympanometry Type B: 362 ears (172 bilaterally) C1: 5 ears C2: 18 (3 bilateral) ears Baseline Hearing or Hearing Loss Mean duration of hearing loss (months [range]) Overall: 6 [3-12] PTAs NR # of children referred for TT because of hearing loss NR Other Baseline Symptoms NR Baseline Relevant Comorbidities No. (%) History of: Adenoidectomy: 51 (24.5) Tonsillectomy: 23 (11.1) Cleft palate: 17 (8.2) Ever grommets 49 (23.6) Allergies: 7 (3.4) Baseline % Female Overall: 48.1 Baseline % Nonwhite Overall: 18.3 Mediterranean: 7.7 Black: 6.3 Asian: 1.9 Other: 2.4	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Ovesen et al., 2000[11]	Age Mean (range) Overall: 38 months (1-7 yrs) Criteria for Diagnosis Otomicroscopical exam, tympanometry (middle ear pressure < 200 mm H2O) Inclusion • Children undergoing TT insertion bilaterally for the first time due to OME Exclusion • Patients with antibiotics within 1 month of surgery • Patients with other diseases • Patients with AOM at time of surgery	Baseline Tympanometry NR Baseline Hearing or Hearing Loss NR Other Baseline Symptoms NR Baseline Relevant Comorbidities Generally excluded Baseline % Female Overall: 36 Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Wielinga et al., 1990[19]	Age Mean, yrs Males: 7 Females: 6 Criteria for Diagnosis Otoscopy, pure tone audiometry, tympanometry Inclusion • Bilateral OME • 6 months of unsuccessfull treatment with standard decongestive medications • Mucoid secretion aspiration Exclusion • NR	Baseline Tympanometry NR Baseline Hearing or Hearing Loss Airconduction thresholds >20 dB G1: 13 G2: 11 Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female Overall: 40 Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Mandel et al., 1989[9]	Age Overall: 7 mos -12 yrs Groups without hearing loss, by age grp G1: 7-23 mos n=6 ; 2-5 yrs n=14; 6-12 yrs n=7 G2: 7-23 mos n=8 ; 2-5 yrs n=17; 6-12 yrs n=5 G3: 7-23 mos; n=7; 2-5 yrs n=17; 6-12 yrs n=5 Groups with hearing loss, by age grp G4: 7-23 mos n=7; 2-5 yrs n= 3; 6-12 yrs n=2 G5: 7-23 mos n=6; 2-5 yrs n=4; 6-12 yrs n =1 Criteria for Diagnosis Validated otoscopy, tympanometry, middle-ear muscle reflex testing Inclusion • Children between 7 mos and 12 yrs of age • Documented MEE of at least 2 mos duration persisting after at least one 14 day course of antimicrobial drug and pseudoephedine hydrochloride-chlorpheniramine maleate syrup. Exclusion • Craniofacial malformations • Down syndrome • Systemic illness such as asthma, cystic fibrosis or diabetes • Seizure disorder	Baseline Tympanometry Acoustic reflex thresholds were estimated for1000 Hz tone ipsilaterally and contralaterally. Baseline Hearing or Hearing Loss Audiologic procedures depended upon age. • < 2.5 yrs: were tested in sound field using a head turn response. Speech awareness thresholds and minimum response levels for warbled pure tones were estimated for these children. • 2.5 – 5 yrs: were tested with play audiometry. • > 5 yrs: traditional clinical protocol was used for chidren older. Bilateral thresholds under earphones from 500 to 4000 Hertz were obtained. • SRT for each ear were obtained using age appropriate responses (picture, id or word rep) Other Baseline Symptoms Significant hearing loss for randomization: pure tone avg of >20 dB bilaterallyu or >40 dB unilaterally or a speech awareness threshold >20 dB above the age-appropriate level or otalgia or vertigo unresponsive to medical treatment among those who do not have hearing or speech deficiencies. Baseline Relevant Comorbidities Otalgia or vertigo Baseline % Female Overall: 33	Insured Status NR Study Population Broadly Applicable? Yes Comments Participants were divided into 2 groups: those with "signifcant" hearing loss (defined arbitrarily as a pure-tone average of >20 dB bilaterally or >40 dB unilaterally, or a speech awareness threshold >20 dB above the age appropriate level) or symptoms consisting of otalgia or vertigo unresponsive to medical treatment, and those who had none of these findings. Within these groups, the subjects were stratified according to age.

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Mandel et al., 1989[9]	• History of tonsillectomy, adenoidectomy, or TT insertion • Structual middle-ear abnormality such as tympanic membrane perforation or adhesive OM; cholesteatoma; sensorineural hearing loss or conductive loss not attributable to MEE; severe upper airway obstruction; AOM; or purulent rhinitis.	Baseline % Nonwhite Overall Black: 25.7	

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
McRae et al.,1989[10]	Age Mean, years (range) Overall: 5.8 Range: (2.3 -10) Criteria for Diagnosis Otoscopy and impedance audiometry Inclusion • Children at head of waiting list for bilateral myringotomy and ventilation tube insertion Exclusion • Subsequent surgery in study duration	Baseline Tympanometry NR Baseline Hearing or Hearing Loss NR Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female Overall: 34 Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Lildholdt 1979[8]	Age Mean years (range) Overall: 4 (1-10) Criteria for Diagnosis Bilateral middle ear pressure below -150mm H20. If audiogram was possible a maximum 15dB diff at 500, 1000, 2,000 Hz Inclusion • Not clearly specified Exclusion • Previous use of TT, recurrent acute supperative OM, unequal involvemnt of ears, congenital defects such as cleft palate	Baseline Tympanometry Bilateral middle ear pressure below -150mm H20. Baseline Hearing or Hearing Loss Overall: If audiogram was possible a a maximum 15dB diff at 500, 1000, 2,000 Hz Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female G1: 41 G2: 41 Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? No

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Brown et al., 1978[3]	Age Range overall, years: 4 to 10 Criteria for Diagnosis Hx, otoscopy and pure tone audiometry Inclusion • Not specified Exclusion • Not specified	Baseline Tympanometry NR Baseline Hearing or Hearing Loss Pure tome audiometry at 500, 1000, 2000, 4000 Hz G1: 25 dB G2: 23.1 dB Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female NR Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? No Comments The subject population is very marginally described.

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Szeremeta et al., 2000[16]	Age Mean years, (range) G1: 6.52 (2.74 - 12.52) G2: 7.37 (3.86 - 5.34) Criteria for Diagnosis NR Inclusion • Children > 4 years with refractory OME or 2nd middle ear intubation • Spring operations Exclusion • NR	Baseline Tympanometry NR Baseline Hearing or Hearing Loss NR Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female NR Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Iwaki et al., 1998[5]	Age Overall: range 3-12 yrs Mean, years G1: 6.2 G2: 6.5 G3: 5.8 Criteria for Diagnosis NR Inclusion • Continuous conductive hearing loss with over 25 dB air-bone gap • ≥ 6 months resistance to conservative thearpy with medication and politzerization • Retracted and glue-colored tympanic membrane with type B tympanogram Exclusion • Craniofacial problems such as cleft palate	Baseline Tympanometry NR Baseline Hearing or Hearing Loss NR Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female Overall:38 Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Austin, 1994[2]	Age NR Criteria for Diagnosis NR Inclusion • Indication for adenotonsillectomy and OME, Resistant to ENT or pediatric management Exclusion • NR	Baseline Tympanometry NR Baseline Hearing or Hearing Loss Air-Bone Gap G1: 29.9 dB G2: 26.6 dB Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female NR Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? No Comments Regarding applicability: Not enough information on the sample so it is hard to generalize.

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Abdullah et al., 1994[1]	Age Mean years (range) Overall: 6 (3-10) Criteria for Diagnosis Inclusion • De novo OME Exclusion • No significant hx of AOM • No evidence of tympanosclerosis	Baseline Tympanometry NR Baseline Hearing or Hearing Loss NR Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female Overall: 36 Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Tos and Stangerup, 1989[17]	Age 5 years (no range reported) this is not the baseline age of the initial population, but average age of the 146 people in the study conducted in 1984 Criteria for Diagnosis NR Inclusion • Bilateral OME Exclusion • NR	Baseline Tympanometry NR Baseline Hearing or Hearing Loss Specify Scale (mean of 250, 1000, 4000 Hz) (250 Hz) G1: 21.7 G2: 19.6 (1000 Hz) G1: 23 G2: 20.4 (4000 Hz) G1: 22.8 G2: 20.5 (Mean) G1: 22.5 G2: 20.2 Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female Overall: NR for baseline cohort; for participants of 1984 study, Overall: 40% Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Slack et al., 1987[22]	Age < 16 years Criteria for Diagnosis NR Inclusion • Children <16 years old • TT inserted for OME in 1983 Exclusion • NR	Baseline Tympanometry NR Baseline Hearing or Hearing Loss NR Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female NR Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Shishegar and Hoghoghi, 2007[14]	Age Range, years Overall: 4-8 Criteria for Diagnosis Physical examinations; otoscopoy, audiometry, tympanometry Inclusion • Not specified Exclusion • Hx of prior adenotonsillectomy, tympanostomy tube iplacement, dry middle ear, cleft palate, and perforated tympanic membrane	Baseline Tympanometry NR Baseline Hearing or Hearing Loss Mean pure tone averages in decibels hearing level (db HL) at 500, 1,000 and 2, 000 HZ) G1: 25.1 db HL G2: 26.3 db HL Mean ears difference, dB (SD): 1.15 (3.25) Decreased hearing level: 30/30 patients Preoperatively 27 of 30 participants had hearing loss Mean speech Reception Threshold (SRT) Mean paired ear as difference (SD): 0.83 dB (5.105) G1: 24.8 G2: 25.6 95%CI=NR p=NR Other Baseline Symptoms N (%): Nasal obstruction and snoring: 26 (87) Recurrent otitis media: 24 (80) Serious otitis media 19 (63) History of allergy: 4 (13) Smoking in parents: 10 (33) Allergic signs: 10 (33) Adenoid enlargement 23 (77) Turbinate hypertrophy: 13 (43) Septal deviation: 5 (17)	Insured Status NR Study Population Broadly Applicable? No Comments Unrepresentative comorbidities, but study says "no significant differences in clinical and demographic variables among treatment groups preoperatively."

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Shishegar and Hoghoghi, 2007[14] (continued)		Baseline Relevant Comorbidities NR Baseline % Female Overall: 37 (11/30 children) G1: 37 G2: 37 Baseline % Nonwhite NA	

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
D'Eredità and Shah, 2006[4]	Age Mean years (range) Overall: 3.7 (2-6) G1:3.8 (2-6) G2:3.6 (2-6) Criteria for Diagnosis Tympanometry Inclusion • OME for at least 3 months duration Exclusion • Hx of prior middle ear surgery or PE tube insertion or previous pharyngeal surgery • Cleft palate, Down syndrome or other syndrome involving the head and neck • Mental retardation or other known cognitive or psychiatric disorder	Baseline Tympanometry NR Baseline Hearing or Hearing Loss NR Other Baseline Symptoms NR Baseline Relevant Comorbidities NR Baseline % Female G1: 47 G2: 47 Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes Comments Total followup was 12 months with post-op evaluations at day 10, 20, 30, 40, 60, and 80 and mo 3,4,6,8, and 12

Evidence Table 2. Populations (continued)

Author, Year	Age Criteria for Diagnosing OME Inclusion Criteria Exclusion Criteria	**Baseline Tympanometry** **Baseline Hearing or Hearing Loss** **Other Baseline Symptoms** **Baseline Relevant Comorbidities** **Baseline % Female** **Baseline % Nonwhite**	**Insured Status** **Study Population Broadly Applicable?** **Comments**
Vlastos et al., 2011[18]	Age Mean years (range) G1: 4.6 (3-7) G2: 4.4 (3-7) Criteria for Diagnosis Otoscopy ,tympanometry, pure tone audiometry Inclusion • > 3 yrs • Scheduled adenoidectomy due to sleep-disordered breathing • Presence of bilateral OME (the presence of an opaque or thickened tympanic mem- brane, air–fluid level, or bubbles, or the inability to visualise the incudostapedial joint, were considered signs of OME • Type B tympanogram (compliance <0.2ml). • Audiogram with an air–bone gap of 20 dB or a hearing loss of 30 dB but no more than 55 dB in at least one frequency in both ears. Exclusion • No signs of effusion at time of myringotomy • Children with chronic otitis media • Structural changes (e.g. tympanic membrane retraction pockets, ossicular chain erosion or cholesteatoma • Previous ear surgery • Language delays • Behavioural problems	Baseline Tympanometry NR Baseline Hearing or Hearing Loss Mean hearing losses at 250, 500, 1000, 2000 and 4000 Hz (range) G1: 31.2 dB (21-39) G2: 32.7 dB (27-37) Other Baseline Symptoms OM-6 Score G1: 2.2 G2: 2.0 Obstructive Sleep Disorders -6 (OSD-6) G1: 3.3 G2: 3.4 Ears with mucoid fluid G1: 68% G2: 61% Baseline Relevant Comorbidities Generally excluded Baseline % Female G1: 44 G2: 44 Baseline % Nonwhite NR	Insured Status NR Study Population Broadly Applicable? Yes

- Syndromes

Evidence Table 3. Interventions

Author, Year	Group 1 Intervention Specification Co-intervention(s):	Group 2 Intervention specification Co-intervention(s):	Group 3 Intervention specification Co-intervention(s):	Comments
Abdullah et al., 1994[1]	Trimmed high-grade silicone shah permavent TT	Polyethylene conventional Shah TT	NA	
Austin, 1994[2]	TT+ adenoidectomy Flared polyethylene TT inserted into random ear Tonsillectomy	Adenoidectomy Tonsillectomy	NA	
Brown et al., 1978[3]	TT+ adneoidectomy	Adenoidectomy	NA	
D'Eredità and Shah, 2006[4]	Myringotomy using Contact diode laser + Adenoidectomy CDLM was performed on both TMs in the antero-inferior quadrant. Laser settings were 2 W power, 0.5 s pulse duration, with 5 pulses in the contact mode. The resultant myringotomy measured 2.5 mm.	Myringotomy + TT	NA	

Evidence Table 3. Interventions (continued)

Author, Year	Group 1 Intervention Specification Co-intervention(s):	Group 2 Intervention specification Co-intervention(s):	Group 3 Intervention specification Co-intervention(s):	Comments
Iwaki et al., 1998[5]	Shepard grommet tube Adenoidectomy performed in those with mouth breathing and hyponasality and found to have hypertrophic adenoids; treatment with antibiotics if sinusitis present.	Silicone Good-T tube Adenoidectomy performed in those with mouth breathing and hyponasality and found to have hypertrophic adenoids; treatment with antibiotics if sinusitis present	Silicone Paperella type II tube Adenoidectomy performed in those with mouth breathing and hyponasality and found to have hypertrophic adenoids; treatment with antibiotics if sinusitis present	Adenoidectomy was performed at time of tube placement in 69 patients (50.4%) however distribution across treatment arms is NR.
Koopman et al., 2004[6]	Laser myringotomy Power setting varied from 7-20 W; diameter of circulm. ar perforation : 1.8-2.6 mm. Fluid not aspirated. No antibiotics given. Children in whom adenoidectomy was indicated underwent this procedure using a sharp curette according to guidelines. Otorrhea persisting for more than 1 week treated by eardrops of dexamethasone/framycetine/gramicidin or ofloxacin; otorrhea with fever treated with amoxicillin oral antibiotics.	TT inserted using cold-knife myringotomy A Donaldson tube was used but in the case of OME with atelectasis of the middle ear, a Goode-T tube was inserted. Children in whom adenoidectomy was indicated underwent this procedure using a sharp curette according to guidelines. Otorrhea persisting for more than 1 week treated by eardrops ofdexamethasone/framycetine/gramicidin or ofloxacin; otorrhea with fever treated with amoxicillin oral antibiotics.	NA	Children who underwent andenoidectomy as a combined procedure: 97; Adenoidectomy + tonsillectomy: 1

Evidence Table 3. Interventions (continued)

Author, Year	Group 1 Intervention Specification Co-intervention(s):	Group 2 Intervention specification Co-intervention(s):	Group 3 Intervention specification Co-intervention(s):	Comments
Licameli et al., 2008[7]	Phophorylcholine coated fluroplastic Armstrong TT	Uncoated fluroplastic Armstrong TT	NA	
Lildholdt, 1979[8]	TT + Adenoidectomy If effusion was present, it was suctioned and a teflon coated Donaldson tube was palced anterially in TM	Adenoidectomy	NA	
Mandel et al., 1989[9]	Myringotomy In children without "significant" hearing loss	Myringotomy + Armstrong TT In children without "significant" hearing loss	Watchful waiting In children without "significant" hearing loss	G4: Myringotomy In children with significant hearing loss G5: Myringotomy + Armstrong TT In children with significant hearing loss

Evidence Table 3. Interventions (continued)

Author, Year	Group 1 Intervention Specification Co-Interventions	Group 2 Intervention specification Co-intervention(s):	Group 3 Intervention specification Co-intervention(s)	Comments
McRae et al.,1989[10]	Shah TT+ aspiration prior to TT placement After myringotomy, glue was aspirated from the selected side using a microsucker.	Shah TT without aspiration prior to tube placement	NA	
Ovesen et al., 2000[11]	TT + application of 0.5 ml of a Mucomyst solution 20 mg/ml in one ear after insertion of tubes	TT + application of 0.5 ml of a placebo in one ear	TT in contralateral ear, exclusively	
Popova et al., 2010[12]	Fluroplastic Donaldson grommet + adenoidectomy	Myringotomy + adenoidectomy	NA	

Evidence Table 3. Interventions (continued)

Author, Year	Group 1 Intervention Specification Co-intervention(s):	Group 2 Intervention specification Co-intervention(s):	Group 3 Intervention specification Co-intervention(s):	Comments
Ragab, 2005[13]	Radiofrequency myringotomy + Mitomycin C Topical mitomycin was applied to the tympanic membrane before radiofrequency tympanostomy. Mitomycin C application was performed using a saturated (not dripping) Gelfoam piece soaked in 0.4 mg/ml of mito- mycin C placed over the tympanic membrane for 10 minutes. The myringotomy (2–3 mm in diameter) was placed in the anteroinferior segment of the tympanic membrane. Adenoidectomy in 26 patients (87%)	Radiofrequency myringotomy + Mitomycin C The myringotomy (2–3 mm in diameter) was placed in the anteroinferior segment of the tympanic membrane. Adenoidectomy in 29 patients (97%)	NA	
Shishegar and Hoghoghi, 2007[14]	Adenoidectomy + myringotomy Ten day courses of ammoxicillin therapy (75 mg/day in 3 doses) prescribed for all patients post-operatively	Adenoidectomy + myringotomy + TT Ten day courses of ammoxicillin therapy (75 mg/day in 3 doses) prescribed for all patients post-operatively	NA	

Evidence Table 3. Interventions (continued)

Author, Year	Group 1 Intervention Specification Co-intervention(s):	Group 2 Intervention specification Co-intervention(s):	Group 3 Intervention specification Co-intervention(s):	Comments
Slack et al., 1987[22]	Shepard tube	Shah tube	Paprella tube	G4: Goode tubes G5: Reuter Bobbin tubes G6: Unknown or other tube type
Szeremeta et al., 2000[16]	Laser Myringotomy + adenoidectomy Using CO2 laser	Incisional, cold knife Myringotomy + adenoidectomy	NA	
Tos and Stangerup, 1989[17]	Right sided -Donaldson type TT + adenoidectomy Evaculation of MEE	Myringotomy + adenoidectomy Evaculation of ME effucion		
Vlastos et al., 2011[18]	Shepard type TT + adenoidectomy Cold steel tonsillectomy	Myringotomy + adenoidectomy Cold steel tonsillectomy		
Wielinga et al., 1990[19]	Teflon bevelled Armstrong TT 1.15 mm internal diameter and 7.5 mm length TT were used	Silicon Goode TT		
Williamson et al., 2009[20] Williamson et al., 2009[21]	Mometasone furoate nasal spray Nasal spray with 140, 50 um doses of mometesone to be administered once per day for 1 month. Total time taking steroid was 3 mos. Support call from staff	Placebo	NA	

Evidence Table 4. Benefits KQ 1 and 2, Part 1

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
Abdullah et al., 1994[1]	Recurrence of OME: G1: 1/17 = 5.9% G2: 9/17 = 52.9%	NR	NR	NR	NR	NR
Austin, 1994[2]		NR	NR	NR	Air Bone Gap G1: 13.2 G2: 14.4 Mean Improvement in Air-Bone Gap G1:16 dB G2: 12.2 dB p >0.1 Mean Difference Between tx: 1.9 dB	NR
Brown et al., 1978[3]	NR		At 5 years, no "significant difference" in fluid level between groups		Preoperative HL G1: 25 dB G2: 23.1 dB 48 hr Postoperative HL G1: 8.9 dB G2: 24.7 dB 3 month Postoperative HL G1: 11.4dB G2: 16.6 dB 5 yr Postoperative HL G1: 17 dB G2: 14 dB	NR

Evidence Table 4. Benefits KQ 1 and 2, Part 1 (continued)

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
D'Eredità and Shah, 2006[4]			Middle ear ventilation: mean G1: 3.5 mos G2: 6.3 mos (95% CI): NR p = 0.001 Still ventilated 3 mo followup: G1: 11 ears, 36.6% G2: 30 ears, 100%		"Normal in both groups at 1 year followup"	
Iwaki et al., 1998[5]	OME healed, n (%) G1: 45 (60%) G2: 25 (64.1%) G3: 77 (72.6%) OME recurrence, n (%) G1: 30 (40%) G2: 11 (28.2%) G3: 18 (17%) G3 vs. G1, P < 0.01 OME recurrence with adenoidectomy G1: 20 (40%) G2: 5 (36%) G3: 12 (24%) OME recurrence without adenoidectomy G1: 8 (35%) G2: 7 (32%) G3: 8 (17%)	NR	NR	NR	NR	NR

Evidence Table 4. Benefits KQ 1 and 2, Part 1 (continued)

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
Koopman et al., 2004[6]	Success rate defined as the absence of effusion or otorrhea documented by binocular otoscopy. 1 month: G1: 46.6% G2: 87.4 % 2 months: G1: 35.5% G2: 81.9% 3 months: G1: 37.1% G2: 81.5% 4 months: G1: 38.6 % G2: 75.5% 5 months: G1: 41.6% G2: 68.5% 6 months: G1: 39.1% G2: 70.7% Positive influence on success rate: Adenoidectomy: p=0.006	NR	NR	NR	NR	NR

Evidence Table 4. Benefits KQ 1 and 2, Part 1 (continued)

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
Licameli et al., 2008[7]	NR	NR	NR	NR	NR	NR
Mandel et al., 1989[9]	MEE (OME and AOM) Year 1: Subjects entering without sig hearing loss or symptoms in G1 (M) and 3 (WW): 56% of the time G2 (MandT): 16.4% Diff: (P<.001). Those entering with sig hearing loss or symptoms G4 (M): 57% G5 (M and T): 9.8%. Diff: (P<.001) YR 2: G1: 35.2 G2: 20.4 G3:28.2 G4: 39.9 G5: 28.3 YR 3: G1: 25.5 G2: 25.0 G3:19.2 G4: 14.4 G5: 30.3 G1, 2, 4 may have had tx failure and gotten TT, mostly YR 2 and 3	AOM (episodes/ person-year) w/o sig HL G1: 0.58 G2: 0. 18 G3: 0.38 With sigHL G4: 0.31 G5: 0.41		NR	Speech-recognition threshold (dB) of right ear, during 3-yr study G1: Functional TT: 5.1 (2.9) Intact TM, no MEE: 7.4 (3.8) Intact TM, MEE: 17.5 (4.7) G2: Functional TT: 4.8 (2.5) Intact TM, no MEE: 6.2 (3.8) Intact TM, MEE: 19.0 (8.7) G3: Functional TT: 5.9 (3.1) Intact TM, no MEE: 7.1 (4.5) Intact TM, MEE: 21.3 (5.7) G4: Functional TT: 5.8 (3.6) Intact TM, no MEE: 7.9 (3.7) Intact TM, MEE: 20.9 (8.7) G5: Functional TT: 6.8 (3.5) Intact TM, no MEE: 5.6 (4.0) Intact TM, MEE: 26.3 (7.7)	NR

Evidence Table 4. Benefits KQ 1 and 2, Part 1 (continued)

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
McRae et al.,1989[10]	NR	NR	NR	NR	NR	NR
Ovesen et al., 2000[11]	Recurrence of OME: G1:15/37 G2: 25/38 G3: 52/75	No. of episodes G1:0/37 G2: 5/38 G3: 16/75	NR	NR	NR	NR
Popova et al., 2010[12]	12 mo Mean Between-group difference 4% (95% CI): p = 0.547	Mean Between-group difference 3% (95% CI):	NR	NR	1 mo post op. 50-4000 hz Mean Between-group difference: 0 .2 (95% CI): p = 0.83 6 mo post op. 50-4000 hz Mean Between-group difference 0.4 (95% CI): p = 0.68 12 mo post op. 50-4000 hz Mean Between-group difference .0.8 (95% CI): p = 0.24	NR
Ragab, 2005[13]	Resolution G1: 59% G2: 28% p < 0.01	NR		NR	Air Bone Gap Improvement from pre-op: G1: 12 dB G2: 10 dB p=NS Both groups improved from pre-op p<0.01)	NR

Evidence Table 4. Benefits KQ 1 and 2, Part 1 (continued)

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
Shishegar and Hoghoghi, 2007[14]	NR	NR	No. (%) of pts with fluid in ears: G1: 24 (80%) G2: 24 (80%) Fluid content of patients ears and No. (%) of patients in each group: Serous fluid: G1: 8 (33%) G2: 8 (33%) Mucoid fluid: G1: 14 (58%) G2: 14 (58%) Purulent fluid: G1: 2 (9%) G2: 2 (9%)	NR	Air-bone gap (pure tone average) at 1 month: Mean difference between G1 and G2: 1.43 db Improvement from baseline: G1: 16.04 db G2: 17.47 db 95%Cis: NR p=NR; NS (not sig) at 6 mos.: Mean difference between G1 and G2: 1.37 db G1: 16.5 db G2: 17.62 db 95% CIs NR p=NS Mean SRT: at 1 month: Mean difference between G1 and G2: 1.83 dB G1: 17 db HL G2: 18.3 db HL 95%CIs: NR p=NS at 6 mos.: Mean difference between G1 and G2: 2.16 db G1: 17.16 db HL G2: 19.33 db HL 95% CIs: NR p=NS	NR

Evidence Table 4. Benefits KQ 1 and 2, Part 1 (continued)

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
Slack et al., 1987[22]	NR	NR	NR	NR	NR	NR
Szeremeta et al., 2000[16]	NR	NR	At post post-op visit Me G1: 4/39 G2: 7/41 p = 0.365	NR	NR	NR
Tos and Stangerup, 1989[17]	NR	NR	NR	NR	(Mean 250-4000 Hz) Total Gain 1977-1984 Mean between-group difference: 0.6 (Db) P=NS G1 Mean Change from Baseline: 17.8 (dB) G2 Mean Change from Baseline: 16.7 (dB) data is also broken out by frequency and years	NR
Vlastos et al., 2011[18]	NR	NR	NR	NR	Change in Hearing (6 mo) G1: -7.41 G2: -4.06 Mean HL Change 3.35 dB (95% CI -6.64 to 10.35) Change in Hearing at 12 mos G1: -8.06 dB G2: -7.40 dB Mean HL Change 0.66 dB(95% CI -6.82 to 8.15)	NR

Evidence Table 4. Benefits KQ 1 and 2, Part 1 (continued)

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
Wielinga et al., 1990[19]	Resolution: G1: 53% G2: 80%	NR	NR	NR	Mean Hearing Loss: G1: 11 dB G2: 14 dB	NR
Williamson et al., 2009[20]	Cure rate (A or C1 tympanogram in at least 1 ear) adjusted results (OR and RR) controlling for season, age, atrophy, and clinical severity score 1 mo. G1: 39/96 (41%) G2: 44/98 (45%) Diff in OR (adj): 0.934 (0.498 to 1.751) Diff in RR (adj): 0.97 (0.74 to 1.26) 3 mos. G1: 50/86 (58%) G2: 44/86 (52%) Diff in OR (adj): 1.451 (0.742 to 2.838) Diff in RR (adj): 1.23 (0.84 to 1.80) 9 mos G1: 40/72 (56%) G2: 47/72 (65%) Diff in OR (adj): 0.822 (0.387 to 1.746) Diff in RR (adj): 0.90 (0.58 to 1.41)	NR	NR	NR	Pass/Fail Criteria on sweep audiometry (fail at 2 or more frequencies at 25 dB in the better ear) 3 mos. failure G1: 52/83 (63%) G2: 47/81 = 58% (63%) At 9 mos failure G1: 44/74 (59%) G2: 34/67 (51%) Hearing loss from tympanograms, median (IQR) at baseline G1: 30.97 (23.8-32.65) G2: 30.94(24.03-2.21) at 3 months G1: 19.43 (14.64-1.21) G2: 21.15 (14.86-0.94)	NR

Evidence Table 4. Benefits KQ 1 and 2, Part 1 (continued)

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
Williamson et al., 2009;[20] (continued)					At 9 months G1:19.56(14.88-0.84) G2: 17.89 (14.11-3.55) Reported hearing difficulties, median(IQR) at baseline G1: 6.06 (2.83-8.57) G2: 5.88 (2.33-7.60) at 3 months G1: 5.54 (0.90-8.43) G2: 3.92 (0.90-7.60) at 9 months G1: 2.33 (0.21 to 7.60) G2: 2.33 (0.42-6.60) Days with hearing loss, median (IQR) At 3 months G1: 4 (0 to 24.5) G2: 4 (0 to 18.5) p=0.45	

Evidence Table 4. Benefits KQ 1 and 2, Part 1 (continued)

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
Williamson et al., 2009[21]	OME resolution at 1 month OR, unadj (95%CI): 0.84 (0.475 to 1.484) OR, adj (95%CI): 0.934 (0.498 to 1.751) at 3 months OR, unadj (95%CI): 1.265 (0.693 to 2.311) OR, adj (95%CI): 1.451 (0.742 to 2.838) at 9 months OR, unadj (95%CI): 0.665 (0.34 to 1.302) OR, adj (95%CI): 0.822 (0.387 to 1.746)	NR	NR	NR	Audiometry faiiing, % at baseline G1: 69.6 G2: 74.5 at 3 months G1: 62.7 G2: 58.0 at 9 months G1: 59.5 G2: 50.7 Hearing loss from tympanograms, median (IQR) at baseline G1: 30.97 (23.8-32.65) G2: 30.94(24.03-2.21) at 3 months G1: 19.43 (14.64-1.21) G2: 21.15 (14.86-0.94) at 9 months G1:19.56(14.88-0.84) G2: 17.89 (14.11-3.55)	NA

Evidence Table 4. Benefits KQ 1 and 2, Part 1 (continued)

Author, Year	OME	AOM	Middle Ear Fluid	Other Ear Symptoms (Fullness)	Hearing (Specify Test)	Speech and Language Development (Speech Discrimination, Acoustic Reflex, Static Acoustic Impedance)
Williamson et al., 2009[21] (continued)					Reported hearing difficulties, median(IQR) at baseline G1: 6.06 (2.83-8.57) G2: 5.88 (2.33-7.60) at 3 months G1: 5.54 (0.90-8.43) G2: 3.92 (0.90-7.60) at 9 months G1: 2.33 (0.21 to 7.60) G2: 2.33 (0.42-6.60) Days with hearing loss, median (IQR) at 3 months G1: 4 (0 to 24.5) G2: 4 (0 to 18.5) p=0.45	
[8]	NR	NR	No significant difference between groups in middle ear pressure	NR	No significant difference between groups at entry into the study or at various points post treatment	NR

Evidence Table 5. Benefits KQ 1 and 2, Part 2

Author, Year	Auditory Processing	Cognition (Tests of Ability)	Academic Achievement and School-based functioning	Quality of Life	Behavior and Attention	Balance and Coordination	Comments
Abdullah et al., 1994[1]	NR	NR	NR	NR	NR	NR	
Austin, 1994[2]	NR	NR	NR	NR	NR	NR	
Brown et al., 1978[3]	NR	NR	NR	NR	NR	NR	
D'Eredità and Shah, 2006[4]							
Iwaki et al., 1998[5]	NR	NR	NR	NR	NR	NR	
Koopman et al., 2004[6]	NR	NR	NR	NR	NR	NR	
Licameli et al., 2008[7]	nr	nr	nr	nr	nr	nr	
Mandel et al., 1989[9]	NR	NR	NR	NR	NR	NR	
McRae et al.,1989[10]	NR	NR	NR	NR	NR	NR	
Ovesen et al., 2000[11]	NR	NR	NR	NR	NR	NR	Time tube remained functional G1: 9 mo G2: 7 mo G3: 8 mo p>0.1367
Popova et al., 2010[12]	NR	NR	NR	NR	NR	NR	

Evidence Table 5. Benefits KQ 1 and 2, Part 2 (continued)

Author, Year	Auditory Processing	Cognition (Tests of Ability)	Academic Achievement and School-based functioning	Quality of Life	Behavior and Attention	Balance and Coordination	Comments
Ragab, 2005[13]	NR	NR	NR	NR	NR	NR	Tympanostomy closure week 1: G1: 3.3 G2: 0 Closure week 2: G1: 11.7 G2: 1.7 Closure week 3: G1: 60 G2: 15 Closure week 4: G1: 90 G2:41.7 Closure week 6: G1: 100 G2:83.3 Closure week 8: G1: G2:100
Shishegar and Hoghoghi, 2007[14]	NR	NR	NR	NR	NR	NR	
Slack et al., 1987[22]	NR	NR	NR	NR	NR	NR	
Szeremeta et al., 2000[16]	NR	NR	NR	NR	NR	NR	Patency of myringotomy at first post-op visit: G1: 8/39 20% G2: 0/48 0% P < 0.01
Tos and Stangerup, 1989[17]	NR	NR	NR	NR	NR	NR	

Evidence Table 5. Benefits KQ 1 and 2, Part 2 (continued)

Author, Year	Auditory Processing	Cognition (Tests of Ability)	Academic Achievement and School-based functioning	Quality of Life	Behavior and Attention	Balance and Coordination	Comments
Vlastos et al., 2011[18]	NR	NR	NR	OM-6 Score (6 mo) G1: 1.88 G2: 2.04 Mean Difference: -.0.16 (95% CI: -0.43 to 0.10) Change from Baseline G1: -0.38 G2: -0.00 mean change: -0.38 (95% CI -0.65 to -0.10) OM-6 Score (12 mo) G1: 1.84 G2: 2.04 Mean Difference: -0.20 (95% CI: -.0.57 to 0.17)	NR	NR	
Wielinga et al., 1990[19]	NR	NR	NR	NR	NR	NR	
Williamson et al., 2009[20]	NR	NR	NR	NR	NR	NR	
Williamson et al., 2009[21]	NA	NA	NA	OM8-30 total score (results in figure 5) at baseline p=0.33 at 3 months p=0.55 at 9 months p=0.77	NA	NA	
[8]	NR	NR	NR	NR	NR	NR	

Evidence Table 6. Subgroup analysis, Part 1

Author, Year	Subgroup Analysis? Subgroup Analyzed	Outcomes reported for OME?	Outcome reported for AOM?	Outcomes reported for Middle Ear Fluid?	Outcomes reported for Other ear symptoms?	Outcomes reported for Hearing?
Abdullah et al., 1994[1]	No NA	No	No	No	No	No
Austin, 1994[2]	No NA	No	No	No	No	No
Brown et al., 1978[3]	No NA	No	No	No	No	No
D'Eredità and Shah, 2006[4]	No No	No	No	No	No	No
Iwaki et al., 1998[5]	Yes NA	No	No	No	No	No
Koopman et al., 2004[6]	No NA	No	No	No	No	No
Licameli et al., 2008[7]	No NA	No	No	No	No	No
Mandel et al., 1989[9]	No NA	No	No	No	No	No
McRae et al.,1989[10]	No NA	No	No	No	No	No
Ovesen et al., 2000[11]	No NA	No	No	No	No	No
Popova et al., 2010[12]	No NA	No	No	No	No	No

Evidence Table 6. Subgroup analysis, Part 1 (continued)

Author, Year	Subgroup Analysis? Subgroup Analyzed	Outcomes reported for OME?	Outcome reported for AOM?	Outcomes reported for Middle Ear Fluid?	Outcomes reported for Other ear symptoms?	Outcomes reported for Hearing?
Ragab, 2005[13]	Yes Those with adenoidectomy G1: 26 (87%) G2: 29 (97%)	Yes	No	No	No	No
Shishegar and Hoghoghi, 2007[14]	No NA	No	No	No	No	No
Slack et al., 1987[15]	No No	No	No	No	No	No
Szeremeta et al., 2000[16]	No NA	No	No	No	No	No
Tos and Stangerup, 1989[17]	No NA	No	No	No	No	No
Vlastos et al., 2011[18]	No NA	No	No	No	No	No
Wielinga et al., 1990[19]	No NA	No	No	No	No	No
Williamson et al., 2009[20, 21]	Yes Age: 4-6.49 years vs. 6.5+ years	Yes	No	No	No	No

Evidence Table 7. Subgroup analysis, Part 2

Author, Year	Subgroup Analysis? Subgroup Analyzed	Speech and Language Development outcomes?	Balance and Coordination outcomes?	Auditory Processing outcomes?	Cognition outcomes?	Academic Achievement and School-based functioning outcomes?	Quality of Life outcomes?	Behavior and Attention Outcomes?	Comments
Abdullah et al., 1994[1]	No NA	No	No	No	No	No	No	No	
Austin, 1994[2]	No NA	No	No	No	No	No	No	No	
Brown et al., 1978[3]	No NA	No	No	No	No	No	No	No	
D'Eredità and Shah, 2006[4]	No No	No	No	No	No	No	No	No	
Iwaki et al., 1998[5]	yes NA	No	No	No	No	No	No	No	
Koopman et al., 2004[6]	No NA	No	No	No	No	No	No	No	
Licameli et al., 2008[7]	No NA	No	No	No	No	No	No	No	
Mandel et al., 1989[9]	No NA	No	No	No	No	No	No	No	
McRae et al.,1989[10]	No NA	No	No	No	No	No	No	No	

Evidence Table 7. Subgroup analysis, Part 2 (continued)

Author, Year	Subgroup Analysis? Subgroup Analyzed	Speech and Language Development outcomes?	Balance and Coordination outcomes?	Auditory Processing outcomes?	Cognition outcomes?	Academic Achievement and School-based functioning outcomes?	Quality of Life outcomes?	Behavior and Attention Outcomes?	Comments
Ovesen et al., 2000[11]	No NA	No	No	No	No	No	No	No	All other scales of Erickson and TAQOL were ns
Popova et al., 2010[12]	No NA	No	No	No	No	No	No	No	
Ragab, 2005[13]	Yes Those with adenoidectomy G1: 26 (87%) G2: 29 (97%)	No	No	No	No	No	No	No	Resolution of OME (in those with Adenoidectomy) G1: 72% G2: 34% P < .01 in G1 (Not clear who the comparison is with, may be with the 3 who didn't receive adenoidectomy)
Shishegar and Hoghoghi, 2007[14]	No. NA	No	No	No	No	No	No	No	
Slack et al., 1987[15]	No No	No	No	No	No	No	No	No	
Szeremeta et al., 2000[16]	No NA	No	No	No	No	No	No	No	
Tos and Stangerup, 1989[17]	No NA	No	No	No	No	No	No	No	
Vlastos et al., 2011[18]	No NA	No	No	No	No	No	No	No	

Evidence Table 7. Subgroup analysis, Part 2 (continued)

Author, Year	Subgroup Analysis? Subgroup Analyzed	Speech and Language Development outcomes?	Balance and Coordination outcomes?	Auditory Processing outcomes?	Cognition outcomes?	Academic Achievement and School-based functioning outcomes?	Quality of Life outcomes?	Behavior and Attention Outcomes?	Comments
Wielinga et al., 1990[19]	No NA	No	No	No	No	No	No	No	
Williamson et al., 2009[23, 24]	yes age: 4-6.49 years vs. 6.5+ years	No	No	No	No	No	Yes	No	OME outcome measure: risk estimate for tympanometric cure Qualilty of Life measure: RESP score on OM8-30 questionaire
[8]	No NA	No	No	No	No	No	No	No	

Evidence Table 8. Harms, Part 1

Author, Year	Overall adverse events?	Withdrawals Due to Adverse Events	Segmental Atrophy	Tympanosclerosis	Otorrhea	Long Term Hearing impact if From PE Tube	Sedation
Abdullah et al., 1994[1]	Yes	NR	NR	Present G1: 15/17 = 88% G2:15/17 = 88% Worse: G1: 2/17 = 12% G2: 8/17 = 47%	At least one episode of otorrhea G1: 0/17 = 0% G2: 3/17 18%	NR	NR
Austin, 1994[2]	No	NR	NR	NR	NR	NR	NR
Brown et al., 1978[3]	Yes	NR	NR	G1: 23 G2: 0	NR	NR	NR
D'Eredità and Shah, 2006[4]	Yes	NR	NR	NR	G1: 2 at 2mos G2: 4 at 30 days and 3mos	NR	NR
Iwaki et al., 1998[5]	Yes	NR	NR	NR	Simple Otorrhea G1: 7 (9.3%) G2: 13 (33.3%) G3: 39 (36.8%) G2 vs. G1, P<0.01 G3 vs. G1, P<0.01 Chronic Otorrhea G1: 2 (2.7%) G2: 1 (2.6%) G3: 1 (0.9%) ns	NR	NR
Koopman et al., 2004[6]	Yes	55 children (26%) quit the study; Lost to f/u: 41 Failures: 14	NR	NR	Otorrhea occurred more frequently on the tube side than on the laser side: p=0.002. (By-group differences NR)	NR	NR
Licameli et al., 2008[7]	Yes	NR	NR	NR	G1: 8.7% G2: 7.5% p=0.742	NR	NR

Evidence Table 8. Harms, Part 1 (continued)

Author, Year	Overall adverse events?	Withdrawals Due to Adverse Events	Segmental Atrophy	Tympanosclerosis	Otorrhea	Long Term Hearing impact if From PE Tube	Sedation
Lildholdt, T., 1979[8]	Yes	NR	NR	G1: 3 cases ofbleeding after several months, tube partially extruded, and granulation present. These had significant scarring. G2:	NR	NR	NR
Mandel et al., 1989[9]	Yes	NR	NR	NR	G1: 0.15 G2: 0.41 G3: 0.23 G4: 0.34 G5: 0.61 In non-TT groups this would be limited to tx failures who got tubes	NR	NR
McRae et al.,1989[10]	Yes	NR	NR	Specify: 24 mos. Bilateral: 17 G1: 8 G2: 1 p=0.045	nr	NR	NR
Ovesen et al., 2000[11]	Yes	NR	NR	Nr	G1: 24% G2: 19% G3: 13% p>0.15	NR	NR
Popova et al., 2010[12]	Yes	NR	NR	NR	G1: 40% G2: 0%	NR	NR
Ragab, 2005[13]	Yes	NR	NR	NR	G1: 1 (may have AOM) G2: 0	NR	NR

Evidence Table 8. Harms, Part 1 (continued)

Author, Year	Overall adverse events?	Withdrawals Due to Adverse Events	Segmental Atrophy	Tympanosclerosis	Otorrhea	Long Term Hearing impact if From PE Tube	Sedation
Shishegar and Hoghoghi, 2007[14]	Yes	NA	NA	NA	Otorrhea G1: 7% G2: 27%	NR	NR
Slack et al., 1987[15]	Yes	NR	NR	NR	Otorrhea at any time: G1: 12 (5.7%) G2: 4 (5.6%) G3: 110 (40%) G4: 3 (NR) G5: 1 (3.6%) G6: 5 (7.9%) G3 vs. G1, P<0.001 G3 vs. G2, P<0.001	NR	NR
Szeremeta et al., 2000[16]	No	NR	NR	NR	NR	NR	NR
Tos and Stangerup, 1989[17]	Yes	NR	NR	G1: 59% G2: 13%	NR	Reported in benefits	NR
Evidence Vlastos et al., 2011[18]	No	No	NR	NR	NR	NR	NR
Wielinga et al., 1990[19]	Yes	NR	NR	NR	G:1: 20% G2: 13%	NR	NR
Williamson et al., 2009[23]	Yes	NR	NR	NR	NR	NR	NR
Williamson et al., 2009[24]	No	NR	NR	NR	NR	NR	NR

Evidence Table 9. Harms, Part 2

Author, Year	Overall adverse events?	Withdrawals Due to Adverse Events	Procedure Related Harm	Cholesteatoma	Tubes in nontube Group or Repeated Tube	Other Adverse Effects
Abdullah et al., 1994[1]	Yes	NR	NR	NR	NR	Otalgia G1: 0/17 = 0% G2: 1/17 = 6% residual perforation G1: 0/17 = 0% G2: 1/17 = 6%
Austin, 1994[2]	no	NR	nr	NR	NR	
Brown et al., 1978[3]	Yes	NR	nr	NR	NR	Retracted TM G1: 10/55 G2: 9/55
D'Eredità and Shah, 2006[4]	Yes	NR	NR	NR	NR	Perforation: G1: 0 G2: 1 at 1 year

Evidence Table 9. Harms, Part 2 (continued)

Author, Year	Overall adverse events?	Withdrawals Due to Adverse Events	Procedure Related Harm	Cholesteatoma	Tubes in Nontube Group or Repeated Tube	Other Adverse Effects
Iwaki et al., 1998[5]	Yes	NR	Specify: G1: G2:	G1: 1 (1.3%) G2: 0 (0%) G3: 0 (0%) na	NR	Perforation, n (%) G1: 0 (0%) G2: 3 (7.7%) G3: 11 (10.4%) G2 vs. G1, p<0.05 G3 vs. G1, p<0.01 Granulation: G1: 0 (0%) G2: 0 (0%) G3: 8 (7.5%) G3 vs. G1, p<0.05 Retraction: G1: 9 (12.0%) G2: 4 (10.2%) G3: 7 (6.6%) Atelactasis G1: 0 (0%) G2: 1 (2.6%) G3: 2 (1.9%) Adhesion G1: 1 (1.3%) G2: 0 (0%) G3: 4 (3.8%) Deep dimple G1: 1 (1.3%) G2: 2 (5.1%) G3: 6 (5.7%)

Evidence Table 9. Harms, Part 2 (continued)

Author, Year	Overall adverse events?	Withdrawals Due to Adverse Events	Procedure Related Harm	Cholesteatoma	Tubes in Nontube Group or Repeated Tube	Other Adverse Effects
Koopman et al., 2004[6]	Yes	55 children (26%) quit the study; Lost to f/u: 41 Failures: 14	NR	NR	NR	Otalgia without inflammation: G1: 1 G2: 0 Epidemeral pearl of tympanic membrane: G1: 1 G2: 0
Licameli et al., 2008[7]	Yes	NR	NR	NR	NR	Granulation G1: 4.4% G2: 6.0% p=0.662 Perforation G1: 4% G2: 0 p=0.235 Occulusion G1: 10.3% G2: 13.4% p=0.530 Extrusion G1: 79.0 G2: 72 p=0.841
Lildholdt, T., 1979[8]	Yes	NR	NR	NR	G1: 13 G2: 6	G1: 25% of ears with tubes showed discharge with avg duration of 13 days.
Mandel et al., 1989[9]	Yes	NR	NR	G3: Cholesteoma in 1 ear	NR	Tx failure: G1: 0.53 G2: 0 G3: 0.59 G4: 0.75 G5: 0
McRae et al.,1989[10]	Yes	NR	NR	NR	NR	NR

Evidence Table 9. Harms, Part 2 (continued)

Author, Year	Overall adverse events?	Withdrawals Due to Adverse Events	Procedure Related Harm	Cholesteatoma	Tubes in Nontube Group or Repeated Tube	Other Adverse Effects
Ovesen et al., 2000[11]	Yes	NR	NR	NR	Repeat tubes: G1: 6/37 G2: 20/38 G3: 32/75	NR
Popova et al., 2010[12]	Yes	NR	NR	NR	NR	NR
Ragab, 2005[13]	Yes	NR	NR	NR	NR	NR
Shishegar and Hoghoghi, 2007[14]	Yes	NA	NR	NR	NR	Over 6 mos. Percentage of TT occluded, resulting in non-functional state: 17%
Slack et al., 1987[15]	Yes	NR	NR	NR	NR	Tubes needing removal due to persistent otorrhoea G1: 0 (0%) G2: 2 (3%) G3: 17 (6%) G4: 0 (0%) G5: 1 (4%) G6: 0 (0%) G3 significantly worse than all other tubes combined, p<0.01; G1 significantly better, p<0.02
Szeremeta et al., 2000[16]	No	NR	NR	NR	NR	NR
Tos and Stangerup, 1989[17]	Yes	NR	NR	NR	NR	NR
Vlastos et al., 2011[18]	No	No	NR	NR	G2: 20% (tubes in non tube group)	NR

Evidence Table 9. Harms, Part 2 (continued)

Author, Year	Overall adverse events?	Withdrawals Due to Adverse Events	Procedure Related Harm	Cholesteatoma	Tubes in Nontube Group or Repeated Tube	Other Adverse Effects
Wielinga et al., 1990[19]	Yes	NR	NR	G1: 0 G2: 0	Repeat tube: G1: 47% G2: 20%	Peritubal Granulation: G1: 7% G2: 7% Blockage: G1: 40% G2: 20% Permanent Perforation: G1: 7% G2: 7%
Williamson et al., 2009[20] and Williamson, 2009[21]	Yes	NR	NR	NR	NR	At 1 mo G1: • stinging nose 9/96 • nose bleed 8/97 • dry throat 13/96 • cough 23/97 G2: 10/102 • nose bleed 7/101 • dry throat 14/102 • cough 19/102 At 3 mos G1: • stinging nose 9/85 • nose bleed 10/86 • dry throat 10/85 • cough 19/867 G2: • stinging nose 9/85 • nose bleed 10/86 • dry throat 7/83 • cough 11/83 • Overall: No significant adverse outcomes reported

Evidence Table 10. Study risk of bias: All studies

Author, Year Study Design	Was Allocation Concealment Generated Adequately? Was the Allocation of Treatment Adequately Concealed?	Did the Strategy for Recruiting Participants into the Study Differ Across Study Groups? Are Baseline Characteristics Similar Between Groups? If not, did the Analysis Control for Differences?	Were Cases and Controls (G1 and G2) Selected Appropriately?	Were Providers Blinded to the Intervention or Exposure Status of Participants?
Popova et al., 2010[12] Parallel RCT	Unclear or NR Unclear or NR	No Yes NA	NA No	No
Austin, 1994[2] NRCT	NA NA	No Yes NA	NA Unclear or NR	Unclear or NR
Brown et al., 1978[3] Parallel RCT	Unclear or NR Unclear or NR	Unclear or NR Yes Yes	Yes NA	NA
D'Eredità and Shah, 2006[4] Parallel RCT	Unclear or NR Unclear or NR	Unclear or NR Unclear or NR No	NA NA	NA
Iwaki et al., 1998[5] Retrospective cohort	NA NA	No Unclear or NR No	NA NA	NA
Koopman et al., 2004[6] Parallel RCT	Yes Yes	No Yes NA	NA Unclear or NR	Unclear or NR
Licameli et al., 2008[7] Parallel RCT	Unclear or NR Unclear or NR	No Yes	Yes Unclear or NR	Unclear or NR
Mandel et al., 1989[9] Cluster RCT	Unclear or NR Unclear or NR	Unclear or NR Yes Yes	NA No	No
McRae et al.,1989[10] Parallel RCT	Yes Unclear or NR	No Yes NA	NA Unclear or NR	Unclear or NR
Ovesen et al., 2000[11] Parallel RCT	Yes Unclear or NR	NA NA NA	NA NA	NA
Popova et al., 2010[12] Parallel RCT	Unclear or NR Unclear or NR	No Yes NA	NA No	No

Evidence Table 11. Systematic reviews

Author, Year Country Funding Study Design	Abstraction Form
Browning et al., 2010[1] Denmark: Arhus University, Arhus University Research Foundation, University of Southern Denmark, The Foundation for Research in General Practice and the Health Care System; and UK National Institute for Health Research Cochrane Review Incentive Scheme Systematic review	**Number of Patients** 1728 in 10 studies of children with OME **Aims of Review** To assess the effectivness of grommet insertion compared with myringotmy or non-surgical treatment in children with OME **Studies Included in Analysis or Review** 10 studies, Maw 1979-86[2], Black, 1990[3], Dempster 1993[4], Gates 1987[5], Rach 1991[6], Mandel 1992[7], Maw 1999[8], Rovers 2000[9], MRC: TARGET 2001[10], Paradise 2001[11] **Characteristics of Included Studies** RCTs 1. Unilateral tubes vs. no surgery OR myringotomy 2. Bilaterial tubes vs. no surgery OR myringotomy Could have short doses of anagesics or antibiotics for AOM in pre-randomization period or decongestants **Criteria for diagnosing OME** OME had to be diagnosed objectively using a combination of otoscopy (pneumatic and microscopic), tympanometry and audiometry **Setting(s):** Referral population, largely to otolaryngology clinics in academic medical centers **Characteristics of Included Populations** Children 1-12 years with bilateral OME **Characteristics of Interventions** • Black 1990: TT vs. myringotomy (adenoidectomy group not included in this review) • Dempster 1993: unilateral TT vs. WW (adenoidectomy not included) • Gates 1987: bilateral myringotomy vs. bilateral TT vs. bilateral myringotomy and adenoidectomy vs. bilateral TT and adenoidectomy • Mandel 1992: bilateral TT vs. bilateral myringotomy vs. no surgery • Maw 1986:Adenotonsillectomy and unliteral TT vs. adenoidectomy and unilateral TT vs. unilateral TT vs. WW • Maw 1999: bilateral TT vs. WW • MRC: TARGET 2001: WW vs. bilateral TT vs. bilateral TT plus adenoidectomy • Paradise 2001: bilateral TT early vs. WW and bilateral TT delayed • Rach 1991: bilateral TT vs. WW • Rovers 2000: bilateral TT vs. WW

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Browning et al., 2010[1] (continued)	**Main Results** Hearing in dB: Negative result: better in tube group • By child, 3 months (1 study) (N=215) Bilateral tubes vs. watchful waiting: Mean Difference -11.9 (95% CI, -9.6 to -14.2) • By child, 6 to 9 months (MA:3 studies) (N=523) Bilateral tubes vs. watchful waiting: Mean Difference - 4.20 (95% CI, -6.00 to -2.39) • By child 12 months (MA: 2 studies) (N=328) Bilateral tubes vs. watchful waiting: Mean Difference - 0.41 (95% CI, -2.37 to 1.54) • By child 18 mos (MA: 2 studies) N=283 Bilateral tubes vs. watchful waiting: Mean Difference -0.02 [-3.22 to 3.18] • By ear, 4 to 6 months (MA: 3 studies) (N=230 ears) Unilateral tubes vs. watchful waiting (2 studies) or myringotomy (1 study): Mean Difference -10.08 (95% CI, -19.12 to -1.05) • By ear, 7 to 12 months (MA: 3 studies) (N=234 ears) Unilateral tubes vs. watchful waiting (2 studies) or myringotomy (1 study): Mean Difference -5.18 (95% CI, -10.43 to 0.07) • By ear, 24 months (1 study) (N=72 ears) Unilateral tubes vs. myringotomy: Mean Difference -2.1 (95% CI, 2.6 to -6.8) Time (proportion) with effusion: Negative result better in tube group • First year (MA: 3 studies) (N=574) Bilateral TT vs. myringotomy, delayed treatment or watchful waiting: Mean difference -0.32 (95% CI, -0.48 to -0.17) • First two years (MA: 3 studies) (N=426) Bilateral TT vs. delayed treatment or watchful waiting: Mean difference -0.13 (95% CI, -0.17 to -0.08) • 1 study 3 mos (N=215) Bilateral TT vs. WW: Mean Diff: -11.9 (95% CI, -9.6 to -14.2) (favors TT) • 1 study 24 mos (N= 72 ears) Unilateral TT vs. myringotomy: Mean Diff: -2.1 (95% CI, 2.6 to -6.8) (favors TT) Language: Positive result: better in tube group • Language Comprehension, 6 to 9 months (MA: 3 studies) (N=394) • Bilateral tubes vs. watchful waiting: Mean Difference 0.09 (95% CI, -0.21 to 0.39) • Language Expression, 6 to 9 months (MA: 3 studies) (N=393) • Bilateral tubes vs. watchful waiting: Mean Difference 0.03 (95% CI, -0.42 to 0.49) Cognitive Development • 1 study (N = 160) 9 mos Griffiths Mental Development Mean Cognitive Index TT vs. WW 106.5 vs. 104.2 (95% CI, -2.58 to 7.04) p=.36 • 1 study (N=393) 3 yrs McCarthy Mental Development Mean General Cognitive Index TT vs. WW 99 vs. 101 (95% CI, -4.1 to 1.1) Behavior

	• 1 study (N=393) 3 yrs Child Behavior Checklist Mean Total Problem Score TT vs. WW 50 vs. 99 (95% CI, -0.6 to 3.4)

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Browning et al., 2010[1] (continued)	<u>Quality of Life:</u> • Rovers 2001: (N=176) 6 mos The TAIQOL Mean scores in domains • 6 mos Vitality 3.3 vs. 3.3 Appetite 5.0 vs. 4.7 Communication G1: 6.7 vs. 5.8 Motoric 4.4 vs. 4.4 Social 3.5 vs. 3.5 Anxiety • 4.3 vs. 4.1 Aggression 11.9 vs. 11.1 Eating 3.3 vs. 3.5 Sleeping 6.8 vs. 6.6 MANOVA Hotelling Trace (p=0.22) • 12 mos Vitality 3.1 vs.3.2 Appetite 5.3 vs.4.9 Communication 5.9 vs.5.6 Motoric 4.2 vs.4.2 Social 3.5 vs. 3.5 • Anxiety 4.6 vs. 4.3 Aggression 11.8 vs.11.5 Eating 3.3 vs. 3.4 Sleeping 6.4 vs. 6.4 MANOVA Hotelling Trace (p=0.94) **Adverse Events** • Tympanosclerosis by ear, 1 year (1 study) (N=78): • Unilateral tube vs. watchful waiting: 38% vs. 1% • Tympanosclerosis by child, 24 months (1 study) (N=248): • Bilateral tubes vs. watchful waiting: 27% vs. 0 • Otorrhoea, 6 months (1 study (N=187)): • Tubed ears vs. non-tubed ears 49% (95% CI, 39%, 60%) vs. 10% (95% CI, 4%, 16%) • Perforation and otorrhoea, 24 months (1 study) (N=248): • Perforation: <1 % • Otorrhoea: 2% • AOM (1 study) (n=236): • Tubed vs. non-tubed 27% vs. 11%

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Hellstrom, 2011[12] Swedish Council on Technology Assessment in Health Care - A governmental Authority Systematic Review	**Number of Patients** 3218 **Aims of Review** The aim of this review was to study the evidence for effectiveness of VT treatment in SOM (i.e., OME) and rAOM as well as the effect of VT material, the different procedures, and their benefits and complications. Note: only studies of participants with OME are included here. Studies with mixed populations were not included unless OME results were stratified. 24 articles in which OME was the focus and there was a comparator of interest: Rovers 2000[9]; Rovers 2001[13]; Paradise 2003[14]; Maw 1999[8]; Maw 1986[2]; Maw 1994[15]; Dempster 1993[4]; Gates 1989; Wilks 2000; Hampal 1991; Dingle 1993; Heaton 1991; Hern 1999; Hampton 1996; Pearson 1996; Salam 1993; Youngs 1988; Kinsella 1994; Bonding 1985; Lildholdt 1983; Mandel 1992; Maw 1994b **Characteristics of Included Studies** OME studies included RCTs (individual or ear), nonrandomized controlled trials, and cohort studies published between 1966 and 2007 of efficacy of tubes on hearing, language development, and quality of life; tube design effects on functioning and complications; tube routines for insertion effects on functioning and complications; prophylaxis and treatment of tube otorrhea; complications and sequelae after tube insertion. **Criteria for diagnosing OME:** Specified only that had to meet international criteria for OME and have OME present for 3 months. Based on methods of underlying studies, OME had to be diagnosed objectively using a combination of otoscopy (pneumatic and microscopic), tympanometry and audiometry **Setting(s):** Referral population, largely to otolaryngology clinics in academic medical centers **Characteristics of Included Populations** Children or adolescents with long-term OME defined as a painless inflammation with effusion in the middle ear with impaired hearing for at least 3 months

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Hellstrom, 2011[12] (continued)	**Characteristics of Interventions** Interventions included trials of: • Efficacy of tubes vs. watchful waiting (late tubes) or myringotomy on hearing, language development, and quality of life: Rovers 2000, Rovers 2001, Paradise, 2003; Maw 1999, Maw 1986; Maw 1994; Dempster 1993; Gates 1989; Wilks 2000 • Tube design effects on functioning and complications: Hampal 1991 (mini shah vs. Shah), Dingle 1993 (Mini Shah vs. Shah); Heaton 1991 (Shepard vs. Sheehy) • Tube routines for insertion effects on functioning and complications (all randomized ears): Heaton 1991 (anterior/inferior vs. posterior/inferior placement), Hern 1999 (anterior/superior vs. anterior/inferior placement), Hampton 1996 (anterior vs. posterior), Pearson 1996 (otic drops preop vs. no drops), Salam 1993 (otic drops preop vs. no drops), Youngs 1988 (aspiration vs. no aspiration), Kinsella 1994 (touch with surgeon gloves vs. non touch) • Prophylaxis and treatment of tube otorrhea (ears randomized): Salam 1993 (otitic drops vs. no drops) Complications and sequelae after tube insertion: • Gates 1989 (Tubes vs. myringotomy vs. adenoidectomy + tubes vs. adenoidectomy + myringotomy), Bonding 1985 (tubes right ear vs. myringotomy left ear), Lildholdt 1983 (tubes vs. control -ears randomized)., Mandel 1992 (tubes vs. myringotomy vs. no tx), Maw 1994 (tube vs. no tube - ears randomized) **Main Results** For tubes vs. watchful waiting, outcomes in hearing and language devleopment were reported in the Browning review (same studies). **Behavior** • 1 study Richman Graham Behavioral Scale • Richman Behavioral Scale % with Problems9 mos: TT vs. WW 30% vs. 47% (95% CI, -33% to –2%) (p=0.031) (favors tx) • 18 mos: TT vs. WW 24% vs. 20% (95% CI, -10% to 19%) (p=0.66) Note: Outcomes varied as to whether they were collected during the treatment or after **Adverse Events** Tubes vs. myringotomy or combination treatment, antibiotics, or watchful waiting/control Perforation • Gates 1989 - Tubes -2.4% vs. myringotomy - 3% vs. adenoidectomy + tubes - 0% vs. adenoidectomy + myringotomy - 0 every 6 weeks for 2 years (no statistical test done) • Mandel 1992 - tubes vs. myringotomy vs. control monthly for 3 years - tubes 5.6% Atrophy • Bonding 1985 tubes vs. myringotomy 1-3 years, n.s. • Lildholdt 1983 - tubes worse than control every 3-6 mos. for 5 yrs. 13% vs. 1.3% • Maw 1994 tubes worse than control 5 years RR 80%, 10 years RR 80%

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Hellstrom, 2011[12] (continued)	Myringosclerosis • Bonding 1985 - tubes worse than myringotomy 1-3 yrs p<.001 • Lildholdt 1983 - tubes worse than control every 3-6 mos. for 5 yrs 33% vs. 6.7% Granulation • Lildholdt tubes worse than control every 3-6 mos for 5 yrs 4% vs. 0% Cholesteatoma • Mandel 1992 tubes vs. myringotomy vs. no surgery - monthly for 3 yrs no surgery 5% Other abnormalities Tube design effects on functioning and complications: • Hampal 1991 - Shah better than mini Shah in situ 52 wks p<.001, reccurence of OME p<.05 • Dingle 1993 Mini Shah better than Shah tympanosclerosis 2 year p<.001 Heaton 1991 - Sheehy better than Shephard for retention time 15-36 mos p<.0001, complication rate 15-30 mos p=NS Tube routines for insertion effects on functioning and complications: Placement • Heaton 1991 - anterior/inferior better than posterior/inferior placement function time 15-36 mos. p=.002 • Hern 1999 - anterior/superior vs. anterior/inferior placement function time 26 mos p=NS. • Hampton 1996 anterior vs.n posterior placement perforation rate 6 wks to 29 mos p=NS Drops • Pearson 1996 - otic drops preop vs. no drops tube patency rate 3 mos p=NS • Salam 1993 otic drops preop vs. no drops obstruction 2 wks n.s., drops better otorrhea p<.01 Other • Youngs 1988 aspiration vs. no aspiration patency 3 mos., p=NS • Kinsella 1994 - touch with surgeon gloves vs. non touch otorrhea 7-10 days p=NS **Comments** • Very difficult to ascertain what kind of statistical test was carried out and not all rates are listed • Can't use their conclusions for adverse events since they combined studies of rAOM along with OME

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Perera et al., 2009[16] University medical Center Oxford, UK Systematic Review	**Number of Patients** 404 in 5 studies of children; 198 adults in 1 study. Total of 602 participants **Aims of Review** To determine the effects of autoinflation in adults an children with OME. **Studies Included in Analysis or Review** 6, 5 of which were for children and 1 of adults. Children: Brooker 1992; Stangerup 1992; Blanshard 1993; Fraser 1977; Arick 2005. Adults: Lesinskas 2003 **Characteristics of Included Studies** RCTs. (excluding any form of quasi-experimental trials) 1. Any form of autoinflation vs. no autoinflation; other treatments (e.g., analgesics, antiobiotics, decongestants) were permitted as long as given equally to the two groups. 2. Comparison could not include another OME treatment **Criteria for diagnosing OME:** OME diagnosis needed to include tympanometery **Setting(s):** **Characteristics of Included Populations** • Children and adults with unilateral or bilateral OME and a clinical diagnosis by a primary care physician or specialist using tympanomerty including: • Arick (2005): 94 children age 4-11 at least 2 month history of MEE and associated hearing loss; absence of enlarged adenoids, AOM or other ear abnormalities at pretest. • Blanshard (1993): 85 children aged 3-10 with bilateral OME using tympanometry on waiting list for tubes. • Brooker (1992): 40 children aged 3 to 10 with unilateral or bilateral OME diagnosed by otoscopy, audiometry and tympanometry referred to ENT. • Fraser (1977): 85 children aged 3 to 12 with bilateral OME using tympanometry. • Lesinskas (2003): 198 adults aged 16 to 75 with unilateral or bilateral OME diagnosed by tympanometry and PTA. • Stangerup (1992): 100 children aged 3 to 10 unilateral or bilateral OME for at least 3 mos. diagnosed by tympanometry **Characteristics of Interventions** Any form of autoinflation vs. no autoinflation with other treatments permitted as long as these were provided equally in the 2 groups. • Arick (2005): Modified Politzer (ear popper) device for 7 weeks twice daily alternating nostrils • Blanshard (1993): Otovent (inflating a baloon) 3 times a day for 3 months • Brooker (1992): Carnival balloon 3 times a day for 3 weeks

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Perera et al., 2009[16] (continued)	• Fraser (1977): Carnival blower for 6 weeks; factorial design in which autoinflation, Dimotapp Elixir (i.e., an antihistamine and nasal decongestant), Ephedrine nose drops,were assigned so that each individual received one of eight combinations of all three treatments (or control). The group receiving autoinflation with those who had not received autoinflation were similar in respect to the proportion of individuals who received the antihistamine and nose drops. • Lesinskas (2003): Politzer inflation 2 times a day for 10 days, with or without oral antibiotics; all patients were prescribed nasal decongestants • Stangerup (1992): Otovent 3 times a day for 2 weeks, extended to 4 weeks in those with persistent OME • Brooker (1992): Carnival balloon 3 times a day for 3 weeks • Fraser (1977): Carnival blower for 6 weeks; factorial design in which autoinflation, Dimotapp Elixir (i.e., an antihistamine and nasal decongestant), Ephedrine nose drops,were assigned so that each individual received one of eight combinations of all three treatments (or control). The group receiving autoinflation with those who had not received autoinflation were similar in respect to the proportion of individuals who received the antihistamine and nose drops. • Lesinskas (2003): Politzer inflation 2 times a day for 10 days, with or without oral antibiotics; all patients were prescribed nasal decongestants • Stangerup (1992): Otovent 3 times a day for 2 weeks, extended to 4 weeks in those with persistent OME **Main Results** Tympanometry Improvement ≤ 1 month • 3 studies (Blanchard, Brooker, Stangerup): B or C2 to C1 or A RR: 1.65 (95% CI, 0.49 to 5.56) • 2 studies (Blanshard, Stangerup): B to C1 or A RR: 2.71 (95% CI, 1.43 to 5.12) • 2 studies (Blanshard, Stangerup) C2 to C1 or A RR: 3.84 (95% CI, 1.94 to 7.59) Tympanometry improvement > 1 month • 2 studies (Blanshard, Stangerup): B1 or C2 to C1 or A RR 1.89 (95% CI, 0.77 to 4,67) Mean change in middle ear pressure • 1 study (Fraser): Autoinflation: 12..7 vs. No Autoinflation: 53.3, p = NS. Mean change in middle ear compliance • 1 study (Frase) Autoinflation: 0.052 vs. No Autoinflation: 0.064, p = NS. Pure tone threshold average improvement > 10 dB (250 Hz to 2000 Hz) • 2 studies discrete outcome (Blanchard, Brooker) RR 0.80 (95% CI, 0.22 to 2.88) • 2 studies continuous outcome (Arick, Fraser) Weighted Mean Diff 7.02 (95% CI, -6.92 to 20.96) Composite improvement in either tympanometry or audiometry (≤ 1 month) • 4 studies (Blanshard, Brooker, Lesinskas, Stangerup,): RR 2.47 (95% CI, 0.93 to 6.58) Composite improvement in either tympanometry or audiometry (> 1 month) • 4 studies (Arick, Blanshard, Lesinskas, Stangerup): RR 2.20 (95% CI, 1.71 to 2.82) Improvement in composite by intervention (≤ 1 month) Otovent or blower + balloon • 3 studies (Blanshard, Brooker, Stangerup) Risk Ratio 1.65 (95% CI, 0.49 to 5.55) •

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Perera et al., 2009[16] (continued)	Improvement in composite by intervention (≤ 1 month) Politzer • 1 study (Lesinskas): Risk Ratio 7.07 (95% CI, 3.70 to 13.51) Improvement in composite by intervention (> 1 month) Otovent or blower + balloon • 2 studies (Blanshard, Stangerup) Risk Ratio 1.89 (95% CI, 0.77 to 4.67) Improvement in composite by intervention (> 1 month) Politzer • 2 studies (Arick, Lesinskas): Risk Ratio 2.25 (95% CI, 1.67 to 3.04) Adults 16-75 yrs • 1 study (Lesinskas), improvement in composite (pneumo-otoscopy, tympanometry, pure tone audiometry) by ears o End of tx: autoinflation vs. control 49.2% vs.9% (p<.001) o 50 days post tx: autoinflation vs. control 57.8% vs. 11.8% (p<.001) **Adverse Events** "No studies demonstrated a significant difference in the incidence of side effects between control or intervention group" AOM • 1 study (Blanchard) stratified by compliance: Control 44%, Low Compliance 30%, High Compliance 36% • 1 study (Stangerup): 2 week Autoinflation 2%, Control 5.5%; 1 month Autoinflation 0%, Control 6.6%; 2 month Autoinflation 9.1%, Control 5.3%; 3 months Autoinflation 9.1%, Control 4.1% URTI • 1 study (Blanshard) stratified by compliance: Control 23%, Low Compliance 61%, High Compliance 32%

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Simpson, 2011[17] Department of Primary Care and Public Health, Cardiff University, UK.; Wales School of Primary Care Research, UK.; The National Institute For Social Care and Health Research All-Wales (NISCHR) Last search: August 2010	**Number of Patients** 945 in 12 studies **Aims of Review** To examine the evidence for treating children with hearing loss associated with OME with systemic or topical intranasal steroids. **Studies Included in Analysis or Review** • Oral steroids: Schwartz 1980[18]; Niederman 1984[19]; Macknin 1985[20]; Lambert 1986[21]; Berman 1990[22]; Giebink 1990[23]; Podoshin 1990[24]; Hemlin 1997[25]; Mandel 2002[26] • Topical intranasal steroids: Shapiro 1982[27]; Tracy 1998[28]; Williamson 2009[29, 30] **Characteristics of Included Studies** Include: • RCTs of oral and topical intranasal steroids. either alone or in combination with another agent such as an oral antibiotic. • Publications in abstract form only; uncontrolled, non-randomised or retrospective studies; and studies reporting outcomes by ears (rather than children). **Criteria for diagnosing OME** A. Air-bone gap of 10 dB or more + 2 or more of: otomicroscopy, pneumatic otoscopy, tympanometry (type B or C2) B. 2 or more of: otomiscroscopy, pneumatic otoscopy, tympanometry (type B or C2) C. 1 of otoscopy alone or tympanometry (type B or C2) D. Poorly or not defined Significant hearing loss defined by: A. Pure-tone audiometry hearing loss of >20 dB at 2 or more times within 3 mos (for example, mean of 500, 1000, and 2000 Hz hearing loss bilaterally) B. Defined, but less strict than A C. Uncertain or not defined **Setting(s):** International; Hospital (secondary or tertiary care) or general practice (primary care) Recruited from the otitis clinic, Departments of Otolaryngology or otolaryngology clinics, hospital based pediatric practices, research centers, private clinics, a hospital and medical centre-based Ambulatory Care Clinic, a Children's Orthopedic Hospital and Medical Centre, a Medical Centre-based pediatric Chronic Ear Clinic and general practices

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Simpson, 2011[17] (continued)	**Characteristics of Included Populations** Children up to the age 12 with the exception of 3 included studies, 2 of which included up to age 14 and one included up to age 15. Berman, 1990: 68 children, 6 months to 5.4 years of age with effusion t for at least 6 weeks and all had 2 previous rounds of antibiotics Giebink, 1990: 76 children, 10 months to 7.9 years of age with continuous OME for at least 8 weeks and at least 3 episodes within previous 18 months. All completed a course of antibiotic therapy for most recent acute OM. Hemlin, 1997: 142 children , 2 to 12 years of age with effusion for at least 3 months Lambert, 1986: 60 children, 2 to 15 years of age with effusion for at least 2 months Macknin, 1985: 49 children, 6 months to 14 years of age enrolled 6 weeks after initial presentation with acute OM and completing 10 day course of antibotic therpay Mandel, 2002: 144 children, 1 to 9 years of age with effusion for at least 2 months Niederman, 1984: 26 children, 2 to 14 years of age with effusion present for 8 weeks Podoshin, 1990: 150 children 3 to 8 years of age with previsouly untreated OME that was present for at least 2 months Schwartz, 1980: 41 children, 1.2 to 10 years of age with effusions present for 3 weeks weeks despite previous antibiotics and/or decongestant treatment Shapiro, 1982: 45 children, 2 to 10 years of age, persistent Eustachian tube dysfunction (documented with abnormal tympanometry) due to allergic rhinitis which failed to respond to 4 weeks of oral antihistamine and decongestants Tracy, 1998: 61 children (military-dependent population)aged from 3 to 11 years with persistent middle ear effusion for at least 3 months and a minimum of 3 episodes of AOM within past 6 months or 4 episodes within the past year Williamson, 2009: 217 children aged 4 to 11 years with 1 or more episodes of otitis media or ear-related problems in previous 12 months. (33% received active monitoring for 3 months prior to randomization). **Characteristics of Interventions** Systemic or topical intranasal steroid compared with control (placebo or non-intervention control). Additional therapy could include antibiotics if it was the same in both arms. **Main Results** <u>OME Resolution</u> Oral Steroids vs. control • MA: 3 studies[19, 20, 23]: OME resolution (4 to 6 weeks): RR:1.54 (95% CI, 0.76 to 3.14) Oral steroids + antibiotic vs. control + antibiotic • MA: 2 studies[24, 26]: OME resolution (1-2 months): RR:1.44 (95% CI, 0.97 to 2.13) Intranasal steroid + antibiotic vs. placebo + antibiotic or antibiotic alone • 1 study[28]: OME resolution (3 months): RR: 1.26 (95% CI, 0.54 to 2.96) Intranasal steroid vs. control • 1 study[29, 30]: OME resolution (3 months) RR 1.11 (95% CI, 0.85 to 1.46); (9 months): RR: 0.85 (95% CI, 0.65 to 1.11)

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Simpson, 2011[17] (continued)	Measured Hearing Oral Steroids vs. control • 1 study[20]: Hearing not improved by at least 10 dB in either ear (6 weeks): RR:1.09 (95% CI, 0.80 to 1.49) Oral steroids + antibiotic vs. control + antibiotic • 1 study[24]: Hearing loss (at least some conductive loss) (2 months): RR:1.01 (95% CI, 0.73 to 1.40) Intranasal steroid vs. control • 1 study[29, 30]: Audiometry failing on ≥ 2 out of 5 frequencies in both ears (1-6 months): RR: 1.17 (95% CI, 0.87 to 1.58) Adverse effects Oral steroids + antibiotics vs. control + antibiotic • MA: 2 studies[25, 26]: Mild to moderate adverse effects (2 wks to 6 months): RR: 1.34 (95% CI, 0.84 to 2.14) Intranasal steroid vs. control • 1 study[29, 30]: Minor adverse effects (3 months): RR: 1.26 (95% CI, 0.80 to 1.99) Intranasal steroids + antibiotics vs. control + antibiotics • 1 study[28]: 2 symptom score (3 months): Mean difference:4.5 (95% CI, -10.28 to 1.28), favors treatment group

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Thomas et al., 2006[31] University of Wales College of Medicine, NHS Wales Office for Research and Development for Health Nd Social, UK Systematic review: Last search January 2006	**Number of Patients** 862 in 11 studies **Aims of Review** To examine evidence for or against treating children with hearing loss associated with OME with systemic or topical intranasal steroids. **Studies Included in Analysis or Review** • Oral steroids: Schwartz, et al., 1980[18]; Niederman 1984[19]; Macknin 1985[20]; Lambert 1986[21]; Berman 1990[22]; Giebink 1990[23]; Podoshin 1990[24]; Hemlin 1997[25]; Mandel 2000[26] Topical intranasal steroids: Shaprio 1982[27]; Tracy 1998[28] **Characteristics of Included Studies** Include: • RCTs of oral and topical intranasal steroids. RCTs that included non-intervention controls included with adequate blinding of outcome assessor. • Include if same co-interventions occuring in all groups. • 3 Studies had steroids without antibiotics as intervention, 7 studies used antibiotics in both control and intervention groups Exclude: • Observational studies, studies reporting outcomes only with ears as unit of analysis; studies (or data from arms of studies) comparing steroid + additional treatment vs. treatment with placebo + placebo because effect of steroid could not be isolated. **Criteria for diagnosing OME:** Diagnosis of OME defined by: A. Air-bone gap of 10 dB or more + 2 or more of: otomicroscopy, pneumatic otoscopy, tympanometry (type B or C2) B. 2 or more of: otomiscroscopy, pneumatic otoscopy, tympanometry (type B or C2) C. 1 of otoscopy alone or tympanometry (type B or C2) D. Poorly or not defined Sig hearing loss defined by: A. Pure-tone audiometry hearing loss of >20 dB at 2 or more times within 3 mos (for example, mean of 500, 1000, and 2000 Hz hearing loss bilaterally) B. Defined, but less strict than A C. Uncertain or not defined

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Thomas et al., 2006[31] (continued)	**Setting(s):** International; Hospital (secondary or tertiary care) or general practice (primary care) Recruited from the otitis clinic, Departments of Otolaryngology or otolaryngology clinics, hospital based pediatric practices, research centers, private clinics, a hospital and medical centre-based Ambulatory Care Clinic, a Children's Orthopedic Hospital and Medical Centre, a Medical Centre-based pediatric Chronic Ear Clinic and general practices **Characteristics of Included Populations** Children up to the age 12 Berman, 1990: 68 children, 6 months to 5.4 years of age with effusion t for at least 6 weeks and all had 2 previous rounds of antibiotics Giebink, 1990: 76 children, 10 months to 7.9 years of age with continuous OME for at least 8 weeks and at least 3 episodes within previous 18 months. All completed a course of antibiotic therapy for most recent acute OM. Hemlin, 1997: 142 children , 2 to 12 years of age with effusion for at least 3 months Lambert, 1986: 60 children, 2 to 15 years of age with effusion for at least 2 months Macknin, 1985: 49 children, 6 months to 14 years of age enrolled 6 weeks after initial presentation with acute OM and completing 10 day course of antibotic therpay Mandel, 2002: 144 children, 1 to 9 years of age with effusion for at least 2 months Niederman, 1984: 26 children, 2 to 14 years of age with effusion present for 8 weeks Podoshin, 1990: 150 children 3 to 8 years of age with previsouly untreated OME that was present for at least 2 months Schwartz, 1980: 41 children, 1.2 to 10 years of age with effusions present for 3 weeks weeks despite previous antibiotics and/or decongestant treatment Shapiro, 1982: 45 children, 2 to 10 years of age, persistent Eustachian tube dysfunction (documented with abnormal tympanometry) due to allergic rhinitis which failed to respond to 4 weeks of oral antihistamine and decongestants Tracy, 1998: 61 children (military-dependent population)aged from 3 to 11 years with persistent middle ear effusion for at least 3 months and a minimum of 3 episodes of AOM within past 6 months or 4 episodes within the past year **Characteristics of Interventions** Systemic or topical intranasal steroid compared with control (placebo or non-intervention control). Additional therapy could include antibiotics if it was the same in both arms.

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
Thomas et al., 2006[31] (continued)	**Main Results** Persisting OME (1-2 mos) Oral steroids vs. control MA: 3 studies (N =106) Peto OR: 0.55 (95% CI, 0.21 to 1.48) (favors tx) Oral steroids + antibiotic vs. control + antibiotic MA: 3 studies (N=243) Peto OR: 0.75 (95% CI, 0.45 to 1.27) Persisting OME (3 mos) Topical intranasal steroid + oral antibiotic vs. control + antibiotic or antibiotic alone 1 study (Tracy 1998) (N=59) Peto OR: 0.72 (95% CI, 0.21 to 2.44) (favors tx) Persisting OME (6 mos) Oral steroids + antibiotic vs. control + antibiotic 1 study (Hemlin 1997) (N=15) Peto OR: 0.15 (95% CI, 0.00 to 7.80) (favors tx) Symptom score (3 mos) Topical intranasal steroid + oral antibiotic vs. control + antibiotic or antibiotic alone 1 study (Tracy 1998) (N=39) Peto OR: -4.50 (95% CI, -10.28 to 1.28) (favors tx) Hearing gain by at least 10 dB (1-2 mos) Oral steroids vs. control 1 study (N=49) Peto OR: 1.47 (95% CI, 0.39 to 5.57) (favors tx) **Adverse Events** No serious or lasting adverse effects reported in 5 studies on oral steroids mentioning adverse events (Niederman, Berman, Giebink, Hemlin, Mandel) or 2 studies on topical (Shapiro, Tracy). Other studies mentioned mild possible adverse effects, such as vomiting, diarrhea, dermatitis, transient nasal stinging and epistaxis.

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form

van den Aardweg et al., 2010[32] University medical Center Utrecht, Netherlands; Systematic review	**Number of Patients** 1177 in 7 studies of OME patients **Aims of Review** To assess the effectiveness of adenoidectomy vs. non-surgical management or TTs in children with OM **Studies Included in Analysis or Review** 14, of these, 7 limited to children with OME and 7 either a combination of OME and AOM or AOM alone OME only studies: • Gates 1987[5]; Filleau-Nikolajsen 1980[33]; Dempster 1993[4]; Black 1990[3] ; Maw 1986[2]; Casselbrant 2009[34]; Roydhouse 1980[35] **Characteristics of Included Studies** RCTs (excluding quasi-randomized trials) allocation by date of birth or record number; followup of at least 6 months **Criteria for diagnosing OME:** OME had to be diagnosed objectively using a combination of otoscopy (pneumatic and microscopic), tympanometry and audiometry **Setting(s):** Referral population, largely to otolaryngology clinics in academic medical centers **Characteristics of Included Populations** Children up to 18 years of age with OM including: • Black (1990): 149 children aged 4-9 with bilateral OME • Casselbrant (2009): 98 children 24-47 mos, with a history of bilateral middle ear effusion for at least 3 mos, unilateral for 6 mos or longer or unilateral for 3 mos after extrusion of a TT, unresponsive to recent antibiotic • Dempster (1993): 78 children aged 3-12 with bilateral OME associated with hearing loss • Fiellau-Nikolajsen (1980): 42 children aged 3 with persistent or recurrent OME • Gates (1987): 491 children aged 4-8 with persistent bilateral OME • Maw (1986): 150 children aged 2-9 with persistent bilateral OME • Roydhouse (1980): 169 children aged 2-14 with persistent OME

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding	Abstraction Form

Study Design	
van den Aardweg et al., 2010[32] (continued)	**Characteristics of Interventions** • Black (1990): Adenoidectomy with bilaterial myringotomy vs. adenoidectomy with a unilateral TT vs. bilateral myringomoty vs. unilateral TT • Casselbrant (2009): myringotomy and TT vs. adenoidectomy, myringotomy and TT vs. adenoidectomy and myringotomy • Dempster (1993): adenoidectomy and unilateral TT vs. unilateral TT • Fiellau-Nikolajsen (1980): myringotomy and adenoidectomy vs. myringotomy • Gates (1987): bilateral myringotomy vs. TT vs. bilateral myringotomy and adenoidectomy vs. TT and adenoidectomy • Maw (1986): Adenotonsillectomy and unliteral TT vs. adenoidectomy and unilateral TT vs. unilateral TT • Roydhouse (1980): TT and adenoidectomy vs. TT vs. control **Main Results** • <u>Mean time with Effusion (SD)</u> • 1 study (Gates, 1987) (N=237) • Adenoid + Myr: 0.302 (0.250); Myr only: 0.491 (0.252) SMD: -0.76 (95% CI, -1.02 to -0.49) • 1 study (Gates, 1987) (N=254) • Adenoid + TT: 0.258 (0.212); TT only: 0.349 (0.235) SMD: -0.40 (95% CI, -0.65 to -0.15) • 1 study during first 18 mos (Casselbrant, 2009) (N=62) • Adenoid + Myr + TT: 18%; Myr + TT: 12% Diff: 6% (95% CI, -12 to 24) 1 study during first 36 mos (Casselbrant, 2009) (N=62) • Adenoid + Myr + TT: 21%; Myr + TT: 19% • Diff: 2% (95% CI, -19 to 23) <u>Type A tympanogram (normal ears) at 6 mos</u> • 1 study (Fiellau-Nikolajsen, 1980) (N=88) • Adenoid + Myr: 68%; Myr: 52% Risk diff: 15% (95% CI, -5% to 46%) <u>Resolution of OME at 6 mos based on otoscopy</u> • (MA: 2 studies) (N=153) • Adenoid + unilateral TT: 35 of 72 (49%); Unilateral TT: 17 of 81 (21%) Risk diff: 0.27 (95% CI, 0.13 to 0.42) <u>Resolution of OME at 6 mos based on tympanometry</u> • (MA: 3 studies) (N=297) • Adenoid + unilateral TT: 56 of 144 (39%); Unilateral TT: 26 of 153 (17%) • Risk diff: 0.22 (95% CI, 0.12 to 0.32)

Evidence Table 11. Systematic reviews (continued)

Author, Year Country Funding Study Design	Abstraction Form
van den Aardweg et al., 2010[32] (continued)	Resolution of OME at 12 mos based on tympanometry • (MA: 3 studies) (N=298) • Adenoid + unilateral TT: 68 of 143 (47%); Unilateral TT: 31 of 155 (20%) Risk diff: 0.29 (95% CI, 0.19 to 0.39) Resolution of OME at 12 mos based on otoscopy • (Dempster, 1993) (N=72) • Adenoid: 54%; No intervention: 37% Risk diff: 17% (95% CI, -6% to 40%) • (Maw, 1986) (N=81) • Adenoid: 69.4%; No intervention: 27.7% Risk diff: 42% (95% CI, 22% to 62%) Percentage of ears with effusion at 12 mos • 1 study (Roydhouse, 1980) (N=95) • Adenoid + TT: 18%; TT: 23% • Risk diff: -5% (95% CI, -8% to 17%) Percentage of ears with effusion at 24 mos • 1 study (Roydhouse, 1980) (N=95) • Adenoid + TT: 15% • TT: 18% • Risk diff: -3% (95% CI, -10% to 15%) Episodes of AOM at 18 mos. • 1 study (Casselbrant, 2009) (N=44) • Adenoid + Myr + TT: 7 • Myr + TT: 6 • Risk diff: 5% (95% CI, -22 to 32) Episodes of AOM at 36 mos. • 1 study (Casselbrant, 2009) (N=39) • Adenoid + Myr + TT: 17 • Myr + TT: 21 • Risk diff: -18% (95% CI, -37 to 1) Hearing loss (air conduction measured in dB HL) at 6 mos • (Dempster, 1993) (N=72) • Adenoid (mean): 18.0 (13.0) • No intervention (mean): 21.1 (11.7) • SMD: -0.25 dB (95% CI, -0.71 to 0.22) • (Maw, 1986) (N=81)

Evidence Table 11. Systematic reviews(continued)

Author, Year Country Funding Study Design	Abstraction Form
van den Aardweg, 2010[32] (continued)	• Adenoid (mean): 20.4 (11.27) • No intervention (mean): 36.5 (11.87) • SMD: -1.37 (95% CI, -1.87 to -0.88) <u>Hearing loss (air conduction measured in dB HL) at 12 mos</u> • 1 study (Dempster, 1993) (N=72) • Adenoid (mean): 15.6 (8.4) • No intervention (mean): 18.4 (10.6) • SMD: -0.29 (95% CI, -0.76 to 0.17) • 1 study (Maw, 1986) (N=81) • Adenoid (mean): 19.7 (10.36) • No intervention (mean): 27.4 (12.13) • SMD: -0.67 (95% CI, -1.12 to -0.22) <u>Change in mean audiometry scores (dB) at 6 mos</u> • 1 study (Black 1990) (N=149) • Diff adenoid vs. no adenoid: 4.3 (95% CI, 1.4 to 9.9) <u>Change in mean audiomtry scores (dB) at 12 mos</u> • 1 study (Black 1990) (N=149) • Diff adenoid vs. no adenoid: 4.3 (95% CI, -3.1 to 11.6) <u>Mean time with hearing loss >20 dB better ear (SD)</u> • 1 study (Gates, 1987) (N=237) • Myr + Adenoid: 0.078 (0.13) • Myr only: 0.186 (0.195)+M3 • 1 study (Gates, 1987) (N=254) • Adenoid + TT: 0.065 (0.116) • TT only: 0.101 (0.141) • SMD: -0.23 (95% CI, -0.48 to 0.02)1 study (Gates, 1987) (N=237) • Myr + Adenoid: 0.220 (0.239) • Myr only: 0.375 (0.253) • SMD: -0.65 (95% CI, -0.91 to -0.39) • 1 study (Gates, 1987) (N=254) • Adenoid + TT: 0.224 (0.221) • TT only: 0.304 (0.227) SMD: -0.35 (95% CI, -0.60 to -0.11)

Abbreviations: Adenoid = adenoidectomy; AOM = acute otitis media; CI = confidence interval; dB = decibels; Diff = difference; ENT = Ear = Nose and Throat; Health Nd = __;HL = hearing level; Hz = Hertz; MA = meta-analysis; MANOVA = Multivariate analysis of variance; MEE = middle ear effusion; mos = months; MRC = Medical Research Council; Myr = myringotomy; N = number; NHS = National Health Service; NS = not significant; OM = otitis media; OME = otitis media with effusion ;OR = odds ratio; preop =

preoperative; PTA = pure tone audiometry; rAOM = recurrent acute otitis media; RCT = randomized controlled trial; RR = relative risk; SMD = standard mean difference; SOM = secretory otitis media; TAIQOL = TNO-AZL Infant Quality of Life; TARGET = Trial of Alternative Regimens in Glue Ear Treatment; TT = tympanostomy tubes; tx = treatment; UK = United Kingdom; URTI = upper respiratory tract infection; vs. = versus; VT = ventilation tube; wks = weeks; WW = watchful waiting; yrs = years

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Appendix D. Abstract and Full-Text Forms

The following are lists of fields used in the abstract and full text review forms. Please see the Evidence Tables (Appendix C) for fields used in the data abstraction forms.

Table D1. Abstract review form fields

REF ID
Author
Year
Title
Abstract
Is the publication original research and available in full text form (NOT editorials, letters, non-systematic reviews, abstract only material)? If no, X1.
Is the publication a controlled trial (randomized or non-randomized), a systematic review or meta-analysis, a cohort study (prospective or retrospective) or a case/control study? If no, X2.
Does the study present information in relation to a population with OME ? If no, X3.
Does the study present information in relation to an intervention of interest? If no, X4.
Does the study compare at least two of the interventions of interest? If no, X5.
Is the study published in the English language? If no X6.
Have met all previous inclusion criteria. Do any of the studies fall into the following categories (place appropriate X code)? Adenoidectomy for OME with a publication date before 2008? If yes, X7. Autoinflation for OME with a publication date before 2005? If yes, X8. Steroids for OME with a publication date before 2005? If yes, X9. Tympanostomy tubes for OME with a publication date before 2006? If yes, X10 Observational and case control studies for CAM? If yes, X11.
Background? (To suggest an abstract that would otherwise be excluded from the review for use as background information, mark it with BKG, along with EXC and the exclusion number/code. Use BKG judiciously!)
Comments: Please include a comment if you included an abstract, but did so do to a lack of clarity within the abstract. Explain why you think the FT will reveal that the study should be excluded.

Table D2. Full text review form fields

Ref ID
Authors
Year
Title
Is the publication original research and available in English and in full text form (NOT editorials, letters, non-systematic reviews, abstract only material)?
Is the publication a controlled trial (randomized or non-randomized), a cohort study (prospective or retrospective) or a case/control study?
Does the study present information in relation to a population with OME? Is the population being treated For OME (i.e., not a prevention study). If the population is mixed are the results stratified? Is the OME population a non-cancer population (i.e., not OME secondary to nasopharyngeal carcinoma)?
Does the study present information in relation to an intervention of interest (autoinflation, myringotomy, adenoidectomy, tympanostomy tubes, steroids, topical or nasal steroids, watchful waiting, variations in surgical techniques, or CAM)
Does the study compare at least two interventions listed above?
Adenoidectomy for OME: RCT of children with a publication date of 2008 or later?
Autoinflation for OME: RCT of children with with a publication date of 2005 or later?
Steroids for OME with a publication date of 2005 or later?
Tympanostomy Tubes for OME:RCT of children with a publication date of 2006 or later?
Randomized and non-randomized trials for CAM?
Comments
Does the study belong to a set of Companion Studies? (Yes/No)
Include citations of any Companion Studies here

AMSTAR: Risk of bias assessment for systematic reviews

1. Was an 'a priori' design provided?
The research question and inclusion criteria should be established before the conduct of the review.

☐ Yes
☐ No
☐ Can't answer
☐ Notapplicable

2. Was there duplicate study selection and data extraction?
There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.

☐ Yes
☐ No
☐ Can't answer
☐ Not applicable

3. Was a comprehensive literature search performed?
At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.

☐ Yes
☐ No
☐ Can'tanswer
☐ Not applicable

4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?
The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.

☐ Yes
☐ No
☐ Can't answer
☐ Not applicable

5. Was a list of studies (included and excluded) provided?
A list of included and excluded studies should be provided.

☐ Yes
☐ No
☐ Can't answer
☐ Not applicable

6. Were the characteristics of the included studies provided?
In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.

☐ Yes
☐ No
☐ Can't answer
☐ Not applicable

7. Was the scientific quality of the included studies assessed and documented?
'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.

☐ Yes
☐ No
☐ Can't answer
☐ Not applicable

8. Was the scientific quality of the included studies used appropriately in formulating conclusions?
The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.

☐ Yes
☐ No
☐ Can't answer
☐ Not applicable

9. Were the methods used to combine the findings of studies appropriate?
For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).

☐ Yes
☐ No
☐ Can't answer
☐ Not applicable

10. Was the likelihood of publication bias assessed?
An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).

☐ Yes
☐ No
☐ Can't answer
☐ Not applicable

11. Was the conflict of interest stated?
Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

☐ Yes
☐ No
☐ Can't answer
☐ Not applicable

Appendix E. Risk-of-Bias Tables

Table E-1. Risk of bias: RCTs and NRCTs

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Abdullah, et al., 1994[1] **Study design** NRCT	**Randomization adequate?** NA **Allocation concealment adequate?** NA **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Unclear or NR **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** No **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Austin, 1994[2] **Study design** NRCT	**Randomization adequate?** NA **Allocation concealment adequate?** NA **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Unclear or NR **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Unclear or NR	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Brown et al., 1978[3] **Study design** Parallel RCT	**Randomization adequate?** Unclear or NR **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** Unclear or NR **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** Yes	**Providers masked?** NA **Patients masked?** NA **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** NA	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** Unclear or NR	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Yes **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year D'Eredità and Shah, 2006[4] **Study design** Parallel RCT	**Randomization adequate?** Unclear or NR **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** Unclear or NR **Groups similar at baseline?** Unclear or NR **If not, did the analysis control for differences?** No	**Providers masked?** NA **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Unclear or NR **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Koopman, et al., 2004[5] **Study design** Parallel RCT	**Randomization adequate?** Yes **Allocation concealment adequate?** Yes **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** Unclear or NR **Patients masked?** Yes **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Yes **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** NA	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Unclear or NR	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Yes **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Unclear or NR	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Licameli, et al., 2008[6] **Study design** Parallel RCT	**Randomization adequate?** Unclear or NR **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** **NA**	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Yes **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** NA	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** No **Health outcome measures equal, valid and reliable?** NA **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Lildholdt, 1979[7] **Study design** NRCT	**Randomization adequate?** No **Allocation concealment adequate?** No **Strategy for recruiting participants differ across study groups?** Unclear or NR **Groups similar at baseline?** Unclear or NR **If not, did the analysis control for differences?** **NA**	**Providers masked?** No **Patients masked?** No **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Unclear or NR **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** Cannot determine	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Unclear or NR	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Mandel, et al., 1989[8] **Study design** Cluster RCT	**Randomization adequate?** Unclear or NR **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** Unclear or NR **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** Yes	**Providers masked?** No **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Yes **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** Yes	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Yes **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year McRae, et al.,1989[9] **Study design** Parallel RCT	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Yes **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** NA	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** No **Health outcome measures equal, valid and reliable?** NA **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Ovesen, et al., 2000[10] **Study design** Parallel RCT	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** NA **Groups similar at baseline?** NA **If not, did the analysis control for differences?** NA	**Providers masked?** NA **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Unclear or NR **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** No **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Popova, et al., 2010[11] **Study design** Parallel RCT	**Randomization adequate?** Unclear or NR **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** No **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Yes **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** NA	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Unclear or NR **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Ragab, 2005[12] **Study design** Parallel RCT	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** No **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Yes **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** Yes	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Unclear or NR	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** No **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Shishegar and Hoghoghi, 2007[13] **Study design** Parallel RCT	**Randomization adequate?** Unclear or NR **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** Unclear or NR **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** Cannot determine	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Unclear or NR	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Tos and Stangerup, 1989[14] **Study design** NRCT	**Randomization adequate?** NA **Allocation concealment adequate?** NA **Strategy for recruiting participants differ across study groups?** NA **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** No **Patients masked?** No **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Yes **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Vlastos, et al., 2011[15] **Study design** Parallel RCT	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Yes **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** Yes	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** No **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Wielinga, et al., 1990[16] **Study design** Parallel RCT	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Unclear or NR **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Yes **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-1. Risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Williamson, et al., 2009;[17] Williamson, et al., 2009[18] **Study design** Parallel RCT	**Randomization adequate?** Yes **Allocation concealment adequate?** Yes **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Yes **If not, did the analysis control for differences?** NA	**Providers masked?** Yes **Patients masked?** Yes **Outcome assessors masked?** Yes **Any impact from a concurrent intervention or exposure ruled out?** Yes **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** Partial (some variables were taken into account)	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Yes **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Low

Table E-2. Risk of bias: Observational

Identifiers	Groups	Masked Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Szeremeta et al., 2000[19] **Study design** Retrospective cohort	**Recruitment strategy differ across groups?** Unclear or NR **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** No	**Outcome assessors blinded to the intervention or exposure status of participants?** Unclear or NR **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Yes **Time of followup or time period between intervention/exposure equal in both groups?** Yes **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** No **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** Medium

Table E-2. Risk of bias: Observational (continued)

Identifiers	Groups	Masked Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Slack et al., 1987[20] **Study design** Retrospective cohort	**Recruitment strategy differ across groups?** No **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** No	**Outcome assessors blinded to the intervention or exposure status of participants?** Unclear or NR **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** Partial (some variables were taken into account)	**Maintain fidelity to the protocol?** Yes **Time of followup or time period between intervention/exposure equal in both groups?** NA **I/E criteria equally applied in both groups?** NA **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** NA **Health outcome measures equal, valid and reliable?** NA **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-2. Risk of bias: Observational (continued)

Identifiers	Groups	Masked Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Iwaki et al., 1998[21] **Study design** Retrospective cohort	**Recruitment strategy differ across groups?** No **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** No	**Outcome assessors blinded to the intervention or exposure status of participants?** Unclear or NR **Any impact from a concurrent intervention or exposure status ruled out?** Yes **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** Partial (some variables were taken into account)	**Maintain fidelity to the protocol?** Unclear or NR **Time of followup or time period between intervention/exposure equal in both groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** Medium

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22]

Author, Year Country Funding Study Design	Risk of Bias Review
Browning, 2010[23] Cochrane Collaboration Systematic review	**1. Was an 'a priori' design provided?** The research question and inclusion criteria should be established before the conduct of the review. YES **2. Was there duplicate study selection and data extraction?** There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. YES **3. Was a comprehensive literature search performed?** At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. YES **4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?** The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. YES **5. Was a list of studies (included and excluded) provided?** A list of included and excluded studies should be provided. YES **6. Were the characteristics of the included studies provided?** In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. YES **7. Was the scientific quality of the included studies assessed and documented?** 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other

	types of studies alternative items will be relevant. YES **8. Was the scientific quality of the included studies used appropriately in formulating conclusions?** The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. YES

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
Browning, 2010[23] (continued)	**9. Were the methods used to combine the findings of studies appropriate?** For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?). YES **10. Was the likelihood of publication bias assessed?** An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test). YES **11. Was the conflict of interest stated?** Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. YES **Risk of Bias?** Low

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
van den Aardweg, 2010[24] Cochrane Collaboration Systematic review	**1. Was an 'a priori' design provided?** The research question and inclusion criteria should be established before the conduct of the review. YES **2. Was there duplicate study selection and data extraction?** There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. YES **3. Was a comprehensive literature search performed?** At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. YES **4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?** The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. YES **5. Was a list of studies (included and excluded) provided?** A list of included and excluded studies should be provided. YES **6. Were the characteristics of the included studies provided?** In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. YES **7. Was the scientific quality of the included studies assessed and documented?** 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other

	types of studies alternative items will be relevant. YES **8. Was the scientific quality of the included studies used appropriately in formulating conclusions?** The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. YES

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
van den Aardweg, 2010[24] (continued)	**9. Were the methods used to combine the findings of studies appropriate?** For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?). YES **10. Was the likelihood of publication bias assessed?** An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test). YES **11. Was the conflict of interest stated?** Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. YES **Risk of Bias?** Low

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
Perera, 2009[25] Cochrane Collaboration Systematic Review	**1. Was an 'a priori' design provided?** The research question and inclusion criteria should be established before the conduct of the review. YES **2. Was there duplicate study selection and data extraction?** There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. YES **3. Was a comprehensive literature search performed?** At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. YES **4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?** The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. YES **5. Was a list of studies (included and excluded) provided?** A list of included and excluded studies should be provided. YES **6. Were the characteristics of the included studies provided?** In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. YES **7. Was the scientific quality of the included studies assessed and documented?** 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other

	types of studies alternative items will be relevant. YES **8. Was the scientific quality of the included studies used appropriately in formulating conclusions?** The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. YES

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
Perera, 2009[25] (continued)	**9. Were the methods used to combine the findings of studies appropriate?** For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?). YES **10. Was the likelihood of publication bias assessed?** An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test). YES **11. Was the conflict of interest stated?** Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. YES **Risk of Bias?** Low

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
Thomas, 2010[26] Cochrane Collaboration Systematic review	**1. Was an 'a priori' design provided?** The research question and inclusion criteria should be established before the conduct of the review. YES **2. Was there duplicate study selection and data extraction?** There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. YES **3. Was a comprehensive literature search performed?** At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. YES **4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?** The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. YES **5. Was a list of studies (included and excluded) provided?** A list of included and excluded studies should be provided. YES **6. Were the characteristics of the included studies provided?** In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. YES **7. Was the scientific quality of the included studies assessed and documented?** 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other

	types of studies alternative items will be relevant. YES **8. Was the scientific quality of the included studies used appropriately in formulating conclusions?** The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. YES

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
Thomas, 2010[26] (continued)	**9. Were the methods used to combine the findings of studies appropriate?** For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?). YES **10. Was the likelihood of publication bias assessed?** An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test). YES **11. Was the conflict of interest stated?** Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. YES **Risk of Bias?** Low

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
Hellstrom, 2011[27] Swedish Council on Technology Assessment in Health Care Systematic Review	**1. Was an 'a priori' design provided?** The research question and inclusion criteria should be established before the conduct of the review. YES **2. Was there duplicate study selection and data extraction?** There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. YES **3. Was a comprehensive literature search performed?** At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. YES **4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?** The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. YES **5. Was a list of studies (included and excluded) provided?** A list of included and excluded studies should be provided. NO **6. Were the characteristics of the included studies provided?** In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. YES **7. Was the scientific quality of the included studies assessed and documented?** 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other

	types of studies alternative items will be relevant. YES **8. Was the scientific quality of the included studies used appropriately in formulating conclusions?** The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. YES

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
Hellstrom, 2011[27] (continued)	**9. Were the methods used to combine the findings of studies appropriate?** For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?). NOT APPLICABLE **10. Was the likelihood of publication bias assessed?** An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test). NO **11. Was the conflict of interest stated?** Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. YES **Risk of Bias?** Moderate

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
Simpson, 2011[28] Cochrane Collaboration Systematic review	**1. Was an 'a priori' design provided?** The research question and inclusion criteria should be established before the conduct of the review. YES **2. Was there duplicate study selection and data extraction?** There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. YES **3. Was a comprehensive literature search performed?** At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. YES **4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?** The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. YES **5. Was a list of studies (included and excluded) provided?** A list of included and excluded studies should be provided. YES **6. Were the characteristics of the included studies provided?** In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. YES **7. Was the scientific quality of the included studies assessed and documented?** 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other

	types of studies alternative items will be relevant. YES **8. Was the scientific quality of the included studies used appropriately in formulating conclusions?** The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. YES

Table E-3. Risk of bias of systematic reviews using AMSTAR questions[22] (continued)

Author, Year Country Funding Study Design	Risk of Bias Review
Simpson, 2011[28] (continued)	**9. Were the methods used to combine the findings of studies appropriate?** For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?). YES **10. Was the likelihood of publication bias assessed?** An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test). YES **11. Was the conflict of interest stated?** Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. YES **Risk of Bias?** Low

Table E-4. High risk of bias: RCTs and NRCTs

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Black et al., 1986[29] **Study Design** Parallel RCT	**Randomization adequate?** Unclear or NR **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** No **If not, did the analysis control for differences?** No	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** Unclear or NR **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unclear or NR **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** This report from this study discusses outcome differences between adenoidectomy and non-adenoidectomy by ear. Hearing levels are measured but some ears had TT and/or myringotomy as well. The analysis does not control for the co-intervention and therefore we are required to assume that it had the same effect in both groups. Some children also had repeat surgery. The comparison becomes adenoidectomy and either (nothing, myringotomy, TT) vs. (nothing, myringotomy, or TT). This is too varied to include in a meaningful way in our analysis. A different report on this study (Black et al., 1990)[30] has been included in the analysis.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NR = not reported; RCT = randomized controlled trial; TT = tympanostomy tubes.

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Gates et al., 1988[31] **Study Design** Prospective cohort (RCT reanalysed by treatment actually received-some received treatment other than original assignment)	**Randomization adequate?** NA **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** Yes **Groups similar at baseline?** Unclear or NR **If not, did the analysis control for differences?** Unclear or NR	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** Partial	**Maintain fidelity to the protocol?** No **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** Analyzed by treatment received (27 subjects chose a treatment other than their assigned one), rather than by assigned treatment. The analysis focuses on differences in outcomes based on adenoid size and does not control for potential confounding that could have been caused by patients not being analysed by their original randomization group.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NR = not reported; RCT = randomized controlled trial

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Gibson et al., 1996[32] **Study Design** Prospective cohort (subset of participants in RCT)	**Randomization adequate?** No **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Unclear or NR **If not, did the analysis control for differences?** NA	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** Yes **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Unclear or NR	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** This study considers a subset of patients from the aborginal cohort that was studied. There are no details about the subset of patients that were enrolled in this portion of a larger study, or the subgroups within the RCT. The primary focus of the analysis was on the nasal cytology and does not have data relevant for this review.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NR = not reported; RCT = randomized controlled trial

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Honjo et al., 1992[33] **Study Design** NRCT	**Randomization adequate?** Unknown **Allocation concealment adequate?** Unknown **Strategy for recruiting participants differ across study groups?** Unknown **Groups similar at baseline?** Yes, in some characteristics **If not, did the analysis control for differences?** No	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Unclear or NR **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Unknown **All outcomes pre-specified? All pre-specified outcomes reported?** Unknown	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Unclear or NR **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** Authors defend randomization with similarity in age, sex, and initial hearing but because the groups are not the same size, they could not have been randomized appropriately. The difference in the size of the two groups at baseline is not explained. There is no description of any comorbidities that the children may have had and no description of the study methods that would have protected the study from various risks of bias.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NR = not reported; NRCT = nonrandomized controlled trial

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Ruckley and Blair, 1988[34] **Study Design** Parallel RCT	**Randomization adequate?** No **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Unclear or NR **If not, did the analysis control for differences?** No	**Providers masked?** No **Patients masked?** Unclear or NR **Outcome assessors masked?** No **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Unclear or NR **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** No **Health outcome measures equal, valid and reliable?** No **Harms outcome measures equal, valid and reliable?** No	**Risk of Bias** High **Notes Explaining Risk of Bias** Baseline characteristics not reported although some outcomes were reported pre-operatively; ITT analysis not conducted; additional myringotomy was performed on some of the patients and not clear how this had an impact the results. Hearing outcomes not provided for both full arms but exclude from one of the arms patients with OME recurrence.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NR = not reported; OME = otitis media with effusion; RCT = randomized controlled trial

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Yagi, 1977[35] **Study Design** Parallel RCT	**Randomization adequate?** Unclear or NR **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Unclear or NR **If not, did the analysis control for differences?** No	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** Unclear or NR **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unclear or NR **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Unclear or NR **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** No patient characteristics reported. Many in both groups had further surgeries that were not controlled in the analysis, including 1/3 in the adenoidectomy group also receiving TT and the comparison treatment is adenoidectomy and TT.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NR = not reported; RCT = randomized controlled trial; TT = tympanostomy tubes

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Caye-Thomasen et al., 2008[36] Companion: Tos, Bonding and Poulsen, 1983[37] **Study Design** NRCT	**Randomization adequate?** No **Allocation concealment adequate?** Unknown **Strategy for recruiting participants differ across study groups?** Unknown **Groups similar at baseline?** Unknown **If not, did the analysis control for differences?** No	**Providers masked?** Unknown **Patients masked?** Unclear or NR **Outcome assessors masked?** Unknown **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Unclear or NR **Maintain fidelity to the protocol?** Yes **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Yes **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** High **Notes Explaining Risk of Bias** Baseline characteristics are not reported adequately. Loss to followup was 50%, and while authors report that remaining participant's charateristics were the same as the orignial cohorts, they do not provide any other information.Of the total myringotomy arm, 21% had a tube inserted. Analysis was conducted on participants that did not have second tube inserted (tube arm) or any tube inserted (myringotomy arm). Because the authors do not report whether the characteristics of these subsamples of the two arms are comparable and do not control for any potential confounding, the results are included for harms only.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NR = not reported; NRCT = nonrandomized controlled trial

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Karlan et al., 1980[38] **Study Design** NRCT (by ear)	**Randomization adequate?** NA **Allocation concealment adequate?** NA **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** NA **If not, did the analysis control for differences?** No	**Providers masked?** NA **Patients masked?** NA **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** NA **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Unclear or NR **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** NR **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** High **Notes Explaining Risk of Bias** No baseline characteristics of participants reported; by ear analysis, infection outcome not defined; potental confounders not taken into account. The analysis considered differences in infection rate by tube type (by ears), follow-up was not similar for all participants and possible differences between the ears were not considered.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NR = not reported; NRCT = nonrandomized controlled trial

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Moller,et al., 1992[39] **Study Design** NRCT	**Randomization adequate?** No **Allocation concealment adequate?** No **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Unknown **If not, did the analysis control for differences?** No	**Providers masked?** No **Patients masked?** No **Outcome assessors masked?** No **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Yes **Followup the same between the groups?** No **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** High **Notes Explaining Risk of Bias** Patients enrolled at different times but compared to completed patient groups from other times. Some comparisons by ear, some by subject and comparisons were mixed between ear and subject. Unable to disentangle issues of time and comparisons being made.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NRCT = nonrandomized controlled trial

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Tatar et al., 2006[40] **Study Design** NRCT	**Randomization adequate?** Unclear or NR **Allocation concealment adequate?** Unclear or NR **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Unclear or NR **If not, did the analysis control for differences?** No	**Providers masked?** Yes **Patients masked?** Unclear or NR **Outcome assessors masked?** Yes **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Unknown **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** Unclear or NR	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Unclear or NR **Health outcome measures equal, valid and reliable?** No **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** High **Notes Explaining Risk of Bias** There are no patient characteristics. It is unknown the extent to which the results are impacted by differences across individuals. The study includes no health outcomes.It is examining the biosurface of two different types of tubes after they have been exuded or removed from the ear.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NR = not reported; NRCT = nonrandomized controlled trial

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Tos, Bonding and Poulsen, 1983[37] Companion: Caye-Thomasen et al., 2008[36] **Study Design** NRCT	**Randomization adequate?** No **Allocation concealment adequate?** Unknown **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Unclear or NR **If not, did the analysis control for differences?** No	**Providers masked?** Unclear or NR **Patients masked?** Unclear or NR **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unclear or NR **Followup the same between the groups?** Unknown **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** NR **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** High **Notes Explaining Risk of Bias** Treatment assignment was not done in randomized fashion, no baseline characteristics reported to know if the characteristics of the groups were the same and there was no control for confounding. Outcomes were measured at different times. However, because the authors only report on harms and not benefits, the results are included in the analysis.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NR = not reported; NRCT = nonrandomized controlled trial

Table E-4. High risk of bias: RCTs and NRCTs (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Zakirullah et al., 2001[41] **Study Design** NRCT	**Randomization adequate?** NA **Allocation concealment adequate?** No **Strategy for recruiting participants differ across study groups?** Unknown **Groups similar at baseline?** Unknown **If not, did the analysis control for differences?** No	**Providers masked?** Unclear or NR **Patients masked?** No **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** Unclear or NR **ITT analysis?** No **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unknown **Followup the same between the groups?** Unclear or NR **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** Unknown	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** Unclear or NR **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** High **Notes Explaining Risk of Bias** Patients were selected into treatment groups based on unexplained clinical differences and length of follow-up differed across groups. Because 120 patients were divided into 9 groups, each of the groups was very small. No control for confounders that could have been related to outcome differences.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NR = not reported; NRCT = nonrandomized controlled trial

Table E-5. High risk of bias: Observational

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Bozkurt and Calguner, 2004[42] **Study Design** Prospective cohort	**Recruitment strategy differ across groups?** Unknown **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** No	**Outcome assessors blinded to the intervention or exposure status of participants?** Unclear or NR **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unclear or NR **Time of followup or time period between intervention/exposure equal in both groups?** Yes **I/E criteria equally applied in both groups?** Unknown **All outcomes pre-specified? All pre-specified outcomes reported?** Unknown	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** Unclear or NR **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** Retrospective comparison group - all tubes had been extruded by time study was done. No patient characteristics are provided other than age. Refers to SOM as an infection in discussion and so not confident this study is about OME rather than AOM. Data not provided on all participants. Unclear to what extent analysis is of ears compared to people.

Abbreviations: AOM = acute otitis media; I/E = inclusion/exclusion; NA = not applicable; NR = not reported; OME = otitis media with effusion; SOM = secretory otitis media

Table E-5. High risk of bias: Observational (continued)

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year D'Eredita, 2004[43] **Study Design** Prospective cohort	**Recruitment strategy differ across groups?** No **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** Unclear or NR	**Outcome assessors blinded to the intervention or exposure status of participants?** Unclear or NR **Any impact from a concurrent intervention or exposure status ruled out?** Unclear or NR **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Unclear or NR **Time of followup or time period between intervention/exposure equal in both groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Unclear or NR	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** Unclear or NR **Health outcome measures equal, valid and reliable?** Unclear or NR **Harms outcome measures equal, valid and reliable?** Unclear or NR	**Risk of Bias** High **Notes Explaining Risk of Bias** Very small sample size. Information about subjects is extremely limited. The outcome of presence or absence of sclerosis of the TM was determined by visual assessment by one individual. Time period of outcome evaluation not specific and specific data on hearing or dysfunction of the TT.

Abbreviations: I/E = inclusion/exclusion; NR = not reported; TM = tympanic membrane; TT = tympanostomy tubes

Table E-5. High risk of bias: Observational (continued)

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Hassmann et al., 2004[44] **Study Design** Prospective cohort	**Recruitment strategy differ across groups?** Yes **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** No	**Outcome assessors blinded to the intervention or exposure status of participants?** No **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Unclear or NR **Time of followup or time period between intervention/exposure equal in both groups?** No **I/E criteria equally applied in both groups?** NA **All outcomes pre-specified? All pre-specified outcomes reported?** NA	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** Yes **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** Comparison groups taken from different time periods; followup period was 2 yrs in one arm but ~1 year in the 2 other arms. The groups have children of different ages. Some in each group received adnoidectomy so concurrent treatment was not controlled. TT group based on consistency of fluid and so different characteristics than myringotomy alone group resulting in groups not being

	comparable.

Abbreviations: I/E = inclusion/exclusion; NA = not applicable; NR = not reported; TT = tympanostomy tubes

Table E-5. High risk of bias: Observational (continued)

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Hornigold et al., 2008[45] **Study Design** Prospective cohort	**Recruitment strategy differ across groups?** No **Baseline characteristics similar between groups?** Yes **If not, did the analysis control for differences?** NA	**Outcome assessors blinded to the intervention or exposure status of participants?** No **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** NA **Time of followup or time period between intervention/exposure equal in both groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Unclear or NR	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** Yes **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** High **Notes Explaining Risk of Bias** Descriptive analysis of 7 participants from original sample of 150 children, after 20 years. No statistical analysis and sample too small to control for any intervening confounders.

Abbreviations: I/E = inclusion/exclusion; NA = not applicable; NR = not reported

Table E-5. High risk of bias: Observational (continued)

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Katz et al., 1995[46] **Study Design** Retrospective cohort	**Recruitment strategy differ across groups?** NA **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** No	**Outcome assessors blinded to the intervention or exposure status of participants?** Unclear or NR **Any impact from a concurrent intervention or exposure status ruled out?** Unclear or NR **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unclear or NR **Time of followup or time period between intervention/exposure equal in both groups?** NA **I/E criteria equally applied in both groups?** No **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** I/E criteria and outcomes not pre-defined; no baseline characteristics reported; study seems to be more of an exploratory analysis that measured hearing outcomes based on identifiable medical records at 6 to 12 months. Study did not control or identify any differences in groups that received different treatment options.

Abbreviations: I/E = inclusion/exclusion; NA = not applicable; NR = not reported

Table E-5. High risk of bias: Observational (continued)

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Marshak et al., 1980[47] **Study Design** Retrospective cohort	**Recruitment strategy differ across groups?** No **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** No	**Outcome assessors blinded to the intervention or exposure status of participants?** Unclear or NR **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unclear or NR **Time of followup or time period between intervention/exposure equal in both groups?** NA **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** Unclear or NR **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** Similarity of groups based on age distribution only; otherwise no other baseline characteristics reported.Groups developed based on chart review of treatment received rather than also controlling for patient characteristics. Outcome is a composite measure of hearing and fluid and results for each of these outcomes is not provided.

Abbreviations: I/E = inclusion/exclusion; NA = not applicable; NR = not reported

Table E-5. High risk of bias: Observational (continued)

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Matt et al., 1991[48] **Study Design** Retrospective cohort	**Recruitment strategy differ across groups?** Unclear or NR **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** No	**Outcome assessors blinded to the intervention or exposure status of participants?** No **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Yes **Time of followup or time period between intervention/exposure equal in both groups?** No **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** NA **Health outcome measures equal, valid and reliable?** Unclear or NR **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** High **Notes Explaining Risk of Bias** No characteristics of the groups were reported. Participants in one of the TT groups had more severe disease at baseline and had previous procedures done on the TM. Additionally, the outcomes were reported from different date ranges at the two institutions and within groups, followup period varied widely.

Abbreviations: I/E = inclusion/exclusion; NA = not applicable; NR = not reported; TM = tympanic membrane; TT = tympanostomy tubes

Table E-5. High risk of bias: Observational (continued)

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Robinson, 1987[49] **Study Design** Retrospective cohort	**Recruitment strategy differ across groups?** NA **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** NA	**Outcome assessors blinded to the intervention or exposure status of participants?** No **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unclear or NR **Time of followup or time period between intervention/exposure equal in both groups?** NA **I/E criteria equally applied in both groups?** No **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** NA **Health outcome measures equal, valid and reliable?** Unclear or NR **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** Unclear if this is a within person comparison or a comparison between ears with some individuals having 2 ears in same condition. Some of the patients had tumors in addition to OME. The population included teens and adults and there were no controls for comorbidities

Abbreviations: I/E = inclusion/exclusion; NA = not applicable; NR = not reported; OME = otitis media with effusion

Table E-5. High risk of bias: Observational

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Siegel and Chandra, 2002[50] **Study Design** Prospective cohort	**Randomization adequate?** NA **Allocation concealment adequate?** NA **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Unknown **If not, did the analysis control for differences?** No	**Providers masked?** No **Patients masked?** No **Outcome assessors masked?** Unclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** NA **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unclear or NA **Followup the same between the groups?** Yes **I/E criteria equally applied in both groups?** No **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** Group assignment chosen by parent; statistically significant age difference between groups and no other characteristics reported. Outcome is statisfaction with various treatment options but patients are self selected into one that they choose and so it is not possible to disentangle difference between the procedures from differences between the participants.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NR = not reported

Table E-5. High risk of bias: Observational

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Slack, et al., 1987[20] **Study design** Retrospective cohort	**Recruitment strategy differ across groups?** Yes **Baseline characteristics similar between groups?** Unknown, NR **If not, did the analysis control for differences?** No	**Outcome assessors blinded to the intervention or exposure status of participants?** No **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unknown **Time of followup or time period between intervention/exposure equal in both groups?** Yes **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Unknown	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** NA **Health outcome measures equal, valid and reliable?** NA **Harms outcome measures equal, valid and reliable?** Yes	**Risk of bias** High **Notes explaining risk of bias** This study examines differences in otorrhea rates by TT type. No data is provided about participant characteristics, except that they had OME. One type of TT was found to have a much higher rate. As stated by the authors, it's possible that the group of patients who were given that type of TT had more long standing disease. We assume (authors did not say) if any of the patients also received adenoidectomies. Study included in harms analysis.

Abbreviations: I/E = inclusion/exclusion; NA = not applicable; NR = not reported; OME = otitis media with effusion; TT = tympanostomy tubes

Table E-5. High risk of bias: Observational

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Smyth et al., 1982[51] **Study design** Retrospective cohort	**Recruitment strategy differ across groups?** NR **Baseline characteristics similar between groups?** Unknown **If not, did the analysis control for differences?** No, analysis by ears and by participant	**Outcome assessors blinded to the intervention or exposure status of participants?** No **Any impact from a concurrent intervention or exposure status ruled out?** No, more than 1/3 of children also had adenoidectomy **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unknown **Time of followup or time period between intervention/exposure equal in both groups?** No **I/E criteria equally applied in both groups?** Unknown **All outcomes pre-specified? All pre-specified outcomes reported?** Unknown	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** Attrition unknown **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?**	**Risk of bias** High **Notes explaining risk of bias** This study combined data from an NRCT to chart records to compare outcomes by TT type. However, the study did not control for potential differences between the children in the samples and a sizable percentage had a concurrent intervention. This is not controlled for in the analysis and the study does not report the percentage in each group. Possible baseline differences between participants receiving different types of TTs are not controlled for as well.

Table E-5. High risk of bias: Observational (continued)

Identifiers	Groups	Masked and Statistical Analysis	Miscellaneous	Outcomes	Risk of Bias
Author, Year Strachan et al., 1996[52] **Study Design** Retrospective cohort	**Recruitment strategy differ across groups?** Unknown **Baseline characteristics similar between groups?** Unclear or NR **If not, did the analysis control for differences?** No	**Outcome assessors blinded to the intervention or exposure status of participants?** Unclear or NR **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unclear or NR **Time of followup or time period between intervention/exposure equal in both groups?** Unknown **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** Unclear or NR **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** NA	**Risk of Bias** High **Notes Explaining Risk of Bias** Matching between cases and controls only by age; I/E criteria not defined or pre-specifed and so not possible to determine why differences were observed between groups. Followup time varied within each group.

Abbreviations: I/E = inclusion/exclusion; NA = not applicable; NR = not reported

Table E-5. High risk of bias: Observational (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Yaman et al., 2010[53] **Study Design** Retrospective cohort	**Randomization adequate?** NA **Allocation concealment adequate?** NA **Strategy for recruiting participants differ across study groups?** No **Groups similar at baseline?** Unclear or NR **If not, did the analysis control for differences?** No	**Providers masked?** NA **Patients masked?** NA **Outcome assessors masked?** Nnclear or NR **Any impact from a concurrent intervention or exposure ruled out?** No **ITT analysis?** NA **Does design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No	**Maintain fidelity to the protocol?** Unclear or NR **Followup the same between the groups?** NA **I/E criteria equally applied in both groups?** Yes **All outcomes pre-specified? All pre-specified outcomes reported?** Yes	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately?** NA **Health outcome measures equal, valid and reliable?** NR **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** High **Notes Explaining Risk of Bias** No baseline characteristics reported besides diagnosis and sex; potential confounding factors not accounted for in analysis. The analysis includes both children that had tubes in one ear and myringotomy in the other (used as their own control) and children who had just myringotomy or just tubes. Because of this, there is unknown confounding in the analysis. Analysis is conducted after different lengths of time in different groups.

Abbreviations: I/E = inclusion/exclusion; ITT = intent to treat; NA = not applicable; NR = not reported

Table E-5. High risk of bias: Observational (continued)

Identifiers	Randomization Groups	Masked Statistical Analysis	Miscellaneous	Outcomes and Attritions	Risk of Bias
Author, Year Zanetti et al., 2005[54] **Study Design** Case control	**Recruitment strategy differ across groups?** Unclear or NR **Baseline characteristics similar between groups?** NA **If not, did the analysis control for differences?** NA	**Outcome assessors blinded to the intervention or exposure status of participants?** Unclear or NR **Any impact from a concurrent intervention or exposure status ruled out?** No **Design and/or analysis account for confounding and modifying variables through matching, stratification, multivariate analysis, or other approaches?** No (Not accounted for or not identified)	**Maintain fidelity to the protocol?** Yes **Time of followup or time period between intervention/exposure equal in both groups?** Yes **I/E criteria equally applied in both groups?** Unclear or NR **All outcomes pre-specified? All pre-specified outcomes reported?** No	**If overall attrition was ≥20% or differential attrition ≥15%, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?** NA **Health outcome measures equal, valid and reliable?** Yes **Harms outcome measures equal, valid and reliable?** Yes	**Risk of Bias** High **Notes Explaining Risk of Bias** No characteristics about the case controls, or how they were chosen are reported. I/E criteria were not discussed and therefore could not determine if differences in outcomes were due to the different procedures or patient characteristics.

Abbreviations: I/E = inclusion/exclusion; NA = not applicable; NR = not reported

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Appendix F. Detailed Strength of Evidence Tables

Key Question 1

Clinical Outcomes

Tympanostomy Tubes Versus Other Tympanostomy Tube or Variation in Tympanostomy Tube Insertion Technique

Table F-1. Detailed strength of evidence grading table, tube retention

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT v. TT + N-acetylcysteine addition, mean time	1; 75	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study, no difference
Shah Teflon tube +aspiration v. shah Teflon tube no aspiration, 3-24 mo	1; 55	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study, no difference
Permavent silicone Shah v. polyethelyne Shah, TT, 1 yr	1; 25	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study, no difference
Goode silicon TT v. Teflon Armstrong TT, 1 yr	1; 15	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study, no difference
Phosphorylcholine -coated fluoroplastic Armstrong TT v. uncoated Armstrong TT, 2 yrs	1; 70	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study, no difference
Goode silicon TT v. Teflon Armstrong TT, 3-5 yrs	1; 15	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study,

Abbreviations: TT = tympanostomy tubes; v. = versus.

Table F-2. Detailed strength of evidence grading table, OME recurrence

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Shorter-term v longer-term TT, recurrence of OME	4, 747	Medium	Consistent	Direct	Imprecise	Low, OME recurrence higher in shorter-term TT after one year
Shah v. mini-shah tube	1, 116	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study, Shah better
Teflon Shepard TT vs. silicone Goode TT vs. Silicone Paparella TT	1; 220	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single observational study, silicone best
Permavent silicone Shah v. polyethelyne Shah	1; 25	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study, statistical difference not reported

Abbreviations: MEE, middle ear effusion; TT, tympanostomy tubes; yr, year.

Table F-3. Detailed strength of evidence grading table, measured hearing

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Goode silicon TT v. Teflon Armstrong TT, mean hearing loss, mean time	1; 15	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single study, statistical difference not reported

Abbreviations: TT = tympanostomy tubes; v. = versus.

Table F-4. Detailed strength of evidence grading table, AOM

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT vs. TT	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: TT = tympanostomy tubes; vs. = versus.

Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Table F-5. Detailed strength of evidence grading table, middle ear effusion and time with effusion

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT vs. WW or delayed treatment, Time with MEE or OME,1 yr,	MA 3, 574 1 study, 119	Medium	Consistent	Direct	Precise	High 32% less time with MEE, sig less % time with OME, favors TT
TT vs. myr, Time with MEE, 1 yr	2 studies, 294	Medium	Consistent	Direct	Imprecise	Low for benefit, favoring TT
TT vs. WW or myr, Time with MEE or OME, 2 yrs	MA:3, 426	Medium	Consistent	Direct	Precise	Moderate 13% less time with MEE, MA favors TT
TT, Time with OME, 3 yrs	1 study, 119	Medium	Unknown, 1 study	Direct	Imprecise	Insufficient, one study found no diff

Abbreviations: MEE = middle ear effusion; myr = myringotomyTT = tympanostomy tubes; WW = watchful waiting; yr = year.

Table F-6. Detailed strength of evidence grading table, OME recurrence and ventilation

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: MEE, middle ear effusion; TT, tympanostomy tubes

Table F-7. Detailed strength of evidence grading table, AOM

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT, episodes/ person yr, 3 yrs	1, 119	Medium	Unknown, single study	Direct	Imprecise	Insufficient: one study found no diff

Abbreviations: TT = tympanostomy tubes.

Table F-8. Detailed strength of evidence grading table, measured hearing

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT, Hearing Levels by ear, 4-6 mos	MA: 3, 230 ears	Medium	Consistent	Direct	Precise	High, 10.1 dB better with TT
TT, Hearing Levels by child, up to 9 mos	MA: 3, 523 Study:1, 248	Medium	Consistent	Direct	Precise	High 4.2 dB better with TT
TT, Hearing levels by ear, 7-12 mos	MA: 3, 234	Medium	Consistent	Direct	Imprecise	Low, no difference -5.18 (95% CI, -10.43 to 0.07)
TT, Hearing Levels by child, 12 mos	MA: 2, 328	Medium	Inconsistent	Direct	Precise	Low, no difference -0.41 dB (95% CI, -2.37 to 1.54)
TT, Hearing Levels by child, 18 mos	MA: 2, 283	Medium	Inconsistent	Direct	Precise	Low, no difference -0.02 dB (95% CI, -3.22 to 3.18)
TT, Hearing Levels by ear, 24 mos	1 study, 72 ears	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study, no difference

Abbreviations: TT = tympanostomy tubes; v. = versus.

Tympanostomy Tubes and Adenoidectomy Versus Myringotomy and Adenoidectomy or Adenoidectomy Alone

Table F-9. Detailed strength of evidence grading table, reoccurrence of middle ear effusion

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+adeno v. myring + adeno, Time with MEE or OME, 1 yrs	1;42	Medium	Unknown, single study	Direct	Imprecise	Insufficient, no difference
TT+adeno v adeno, Time with MEE or OME,5 yr,	1; 55	Medium	Unknown, single study	Direct	Imprecise	Insufficient, no difference

Abbreviations: MEE, middle ear effusion; TT, tympanostomy tubes; yr, year

Table F-10. Detailed strength of evidence grading table, Ventilation maintained

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+adeno v. laser myro+adeno, episodes/ person yr, 3 mo	1; 15	Medium	Unknown, single study	Direct	Imprecise	Insufficient, one small study favoring TT

Abbreviations: TT, tympanostomy tubes; yr, year.

Table F-11. Detailed strength of evidence grading table, AOM

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+adeno, episodes/ person yr, 3 yrs	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: TT, tympanostomy tubes; yr, year.

Table F-12. Detailed strength of evidence grading table, measured hearing

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+adeno v. adeno, Hearing Levels, 3 mos	1; 55	Medium	Unknown, single study	Direct	Imprecise	Insufficient, one small study favoring TT
TT+adeno v. myring +adeno, Hearing Levels, 6 mos, 12 mo and >3 years	6 studies: 3 RCTs by person (N=431) 2 RCTs (by ears) (N=338) 1 NRCT (by ears) (N=193)3, 160	Medium	Consistent	Direct	Imprecise	Low, no difference
TT+adeno v. myring +adeno, Hearing levels,12 mo	2;130	Medium	Consistent	Direct	Imprecise	Insufficient, no difference in 2 small studies
TT+adeno v. myring+adeno, Hearing Levels, 2 years	1, 146	Medium	Unknown, single study	Direct	Imprecise	Insufficient, no difference in 1 small study
TT+adenoid v. myring+adeno/ adenoid alone, Hearing Levels >3 years	2; 201	Medium	Consistent	Direct	Imprecise	Low, no difference

Abbreviations: TT, tympanostomy tubes; yr, year.

Myringotom Comparisons

Table F-13. Detailed strength of evidence grading table, resolution of OME

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy + Mitomycin C vs. myringotomy, resolution of OME	1, 60	Medium	Unknown, single study	Direct	Imprecise	Insufficient

Table F-14. Detailed strength of evidence grading table, OME recurrence and ventilation

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy + Mitomycin C vs. myringotomy	No studies	NA	NA	NA	NA	Insufficient, no evidence

Table F-15. Detailed strength of evidence grading table, AOM

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy + Mitomycin C vs. myringotomy	No studies	NA	NA	NA	NA	Insufficient, no evidence

Table F-16. Detailed strength of evidence grading table, measured hearing

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy + Mitomycin C vs. myringotomy, air-bone gap improvement (3mos)	1, 60	Medium	Unknown, single study	Direct	Imprecise	Insufficient, no difference, one small study

Myringotomy and Adenoidectomy Comparisons

Table F-17. Detailed strength of evidence grading table, middle ear effusion

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy (laser) with adenoidectomy vs. Myringotomy (cold knife) with adenoidectomy, % with middle ear effusion, post-op	1, 87 ears*	Medium	Unknown, single study	Direct	Imprecise	Insufficient, no difference, one small study

* number analyzed

Table F-18. Detailed strength of evidence grading table, OME recurrence and ventilation

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy (laser) with adenoidectomy vs. Myringotomy (cold knife) with adenoidectomy, patency of ears, post-op	1, 87 ears*	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single smallstudy

*number analyzed

Table F-19. Detailed strength of evidence grading table, AOM

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy (laser) with adenoidectomy vs. Myringotomy (cold knife) with adenoidectomy	No studies	NA	NA	NA	NA	Insufficient, no evidence

Table F-20. Detailed strength of evidence grading table, measured hearing

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy (laser) with adenoidectomy vs. Myringotomy (cold knife) with adenoidectomy	No studies	NA	NA	NA	NA	Insufficient, no evidence

Adenoidectomy Versus Other Interventions

Table F-21. Detailed strength of evidence grading table, middle ear effusion and time with effusion

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Adenoidectomy (+unilateral TT) vs no treatment, OME resolution 6 mos	MA otoscopy:2, 153 MA tympanometry: MA: 3, 297	Medium	Consistent	Direct	Precise	High Otoscopy: Risk Diff: 0.27 Tympanometry: Risk diff: 0.22
Adenoidectomy (+ unilateral TT), OME resolution by tympanometry), 12 mos	MA: 3, 298	Medium	Consistent	Direct	Precise	High Risk diff: 0.29
Adenoidectomy+ myringotomy vs. myringotomy, 2 years	1 study (N=237)	Medium	Unknown, single study	Direct	Precise	Low, less time with effusion in adenoidectomy arm

Table F-22. Detailed strength of evidence grading table, measured hearing

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Adenoidectomy vs no intervention, Change in hearing level, 6 mos, 12 mos	2 studies (N=302)	Medium	Inconsistent	Direct	Imprecise	Insufficient, mixed results
Adenoidectomy+ myringotomy vs. myringotomy, 2 years	1 study (N=237)	Medium	Unknown, single study	Direct	Precise	Low, less time with reduced hearing in adenoidectomy arm

Steroids Versus Control

Table F-23. Detailed strength of evidence grading table, middle ear effusion and time with effusion

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Oral, 1-2 mo, persisting	MA 3, 106	Medium	Consistent	Direct	Imprecise	Low: no difference
Oral (+antibiotic), 1-2 mo, persisting	MA 3, 243	Medium	Consistent	Direct	Precise	Moderate: no difference
Topical, 1-2 mo	No studies	NA	NA	NA	NA	Insufficient: no evidence
Topical, cure rate, 3 & 9 mo	1, 217	Low	Unknown, single study	Direct	Precise	Low: no difference
Topical (+antibiotic),	1, 59	Medium	Unknown, single study	Direct	Imprecise	Insufficient: no difference

persisting, 6 mo						
Oral (+antibiotic), persisting, 6 mo	1, 15	Medium	Unknown, single study	Direct	Imprecise	Insufficient: no difference

Table F-24. Detailed strength of evidence grading table, OME recurrence and ventilation

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Topical	No studies	NA	NA	NA	NA	Insufficient: no evidence
Oral	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable.

Table F-25. Detailed strength of evidence grading table, AOM

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Topical	No studies	NA	NA	NA	NA	Insufficient: no evidence
Oral	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable.

Table F-26. Detailed strength of evidence grading table, measured hearing

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Topical, 1-2 mo	No studies	NA	NA	NA	NA	Insufficient: no evidence
Topical,> 3 mo	1, 217	Medium	Unknown, single study	Direct	Precise	Low: no difference
Oral, 1-2 mo	1, 49	Low	Unknown, single study	Direct	Imprecise	Insufficient: no difference
Oral, 3+ mo	No studies	NA	NA	NA	NA	Insufficient: no evidence

Autoinflation Versus Control

Table F-27. Detailed strength of evidence grading table, middle ear effusion and time with effusion

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Autoinflation, improvement in tympanogram ≤ 1 mo	MA:2, 185	Medium	Consistent	Direct	Precise	Low, > improvement with autoinflation RR: 2.71
Autoinflation, improvement in tympanogram > 1 mo	MA:2, 185	Medium	Consistent	Direct	Imprecise	Insufficient, no difference
Autoinflation, (3 wks and 3 mos)	No studies	NA	NA	NA	NA	Insufficient, no evidence
Autoinflation, 4 wks post tx and end of tx	No studies	NA	NA	NA	NA	Insufficient, no evidence

Abbreviations: NA = not applicable.

Table F-28. Detailed strength of evidence grading table, OME recurrence and ventilation

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Autoinflation	No studies	NA	NA	NA	NA	Insufficient, no evidence

Abbreviations: NA = not applicable.

Table F-29. Detailed strength of evidence grading table, AOM

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Autoinflation	No studies	NA	NA	NA	NA	Insufficient, no evidence

Abbreviations: NA = not applicable.

Table F-30. Detailed strength of evidence grading table, measured hearing

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Autoinflation, ≤ 1 mo	No studies	NA	NA	NA	NA	Insufficient, no evidence
Autoinflation, >1 mo	No studies	NA	NA	NA	NA	Insufficient, no evidence
Autoinflation, end of tx improvement in PTA, post tx (3 wks and 3 mos)	MA:2, 125	Medium	Inconsistent	Direct	Imprecise	Insufficient, no difference
Autoinflation, PTA, 4 wks post tx and end of tx	MA 2, 179	Medium	Inconsistent	Direct	Imprecise	Insufficient, no difference

Abbreviations: Mo, month; PTA, pure tone average; tx, treatment; wks, weeks.

Key Question 2

Functional Outcomes

Tympanostomy Tubes Versus Other Tympanostomy Tube or Variation in Tympanostomy Tube Insertion Technique

Table F-31. Detailed strength of evidence grading table, speech, language and cognitive development

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT vs. TT	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: mos = months; NA = not applicable; TT = tympanostomy tubes; vs. = versus.

Table F-32. Detailed strength of evidence grading table, behavior

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT vs. TT	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: TT = tympanostomy tubes; vs. = versus.

Table F-33. Detailed strength of evidence grading table, quality-of-life

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT vs. TT	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable; TT = tympanostomy tubes; vs. = versus.

Table F-34. Detailed strength of evidence grading table, satisfaction with care

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT vs. TT	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable; TT = tympanostomy tubes; vs. = versus.

Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Table F-35. Detailed strength of evidence grading table, speech, language and cognitive development

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT, Language Comprehension, 6-9 mos or at preschool and elementary school age	MA: 3, 394 + 2 RCT, 503	Medium	Inconsistent	Direct	Precise	Moderate, no difference
TT, Language Expression, 6-9 mos	MA:3, 393	Low	Inconsistent	Direct	Precise	Low, no difference
TT, Cognitive Development, 9 mos	2 RCTs, 503	Medium	Consistent	Direct	Imprecise	Low, no difference
TT, Academic Achievement, elementary school age	2 RCTs, 503	Medium	Consistent	Direct	Imprecise	Low, no difference
TT, Cognitive Development, 3 yrs	1 study, 393	Low	Unknown, single study	Direct	Precise	Insufficient, no difference

Abbreviations: mos = months; TT = tympanostomy tubes; yrs = years.

Table F-36. Detailed strength of evidence grading table, behavior

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT, Behavior, 6, 12 mos	1 study, 176, 165	Low	Unknown, single study	Direct	Imprecise	Insufficient, no difference
TT, Behavior, 9, 12 mos	1 study, 182	Medium	Unknown, single study	Direct	Imprecise	Insufficient, conflicting evidence
TT, Behavior. 3 yrs	1 study, 393	Low	Unknown, single study	Direct	Imprecise	Insufficient, no difference

Abbreviations: mos = months; TT = tympanostomy tubes; yrs = years.

Table F-37. Detailed strength of evidence grading table, quality-of-life

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT, Quality of Life, 6, 12 mos	1, 176, 165	Low	Unknown, single study	Direct	Imprecise	Insufficient: no difference

Abbreviations: mos = months; TT = tympanostomy tubes.

Table F-38. Detailed strength of evidence grading table, satisfaction with care

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable; TT = tympanostomy tubes.

Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy or Adenoidectomy Alone

Table F-39. Detailed strength of evidence grading table, speech, language and cognitive development

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+adeno	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable; TT = tympanostomy tubes.

Table F-40. Detailed strength of evidence grading table, behavior

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+adeno,	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: adeno = adenoidectomy; NA = not applicable; TT, tympanostomy tubes.

Table F-41. Detailed strength of evidence grading table, quality-of-life

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+adeno vs. myring+adeno, quality of Life, 6 mos	1; 52	Medium	Unknown, single study	Direct	Precise	Insufficient: no difference
TT+adeno v. myring+adeno, Quality of Life, 12 mos	1, 52	Medium	Unknown, single study	Direct	Precise	Insufficient: no difference

Abbreviations: adeno = adenoidectomy; myring = myringotomy; mos, months; TT, tympanostomy tubes.

Table F-42. Detailed strength of evidence grading table, satisfaction with care

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+adeno	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: adeno = adenoidectomy; NA = not applicable.

Myringotomy Comparisons

Table F-43. Detailed strength of evidence grading table, all functional outcomes

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy + Mitomycin C vs. myringotomy	No studies	NA	NA	NA	NA	Insufficient, no evidence

Abbreviations: NA = not applicable; vs. = versus.

Myringotomy With Adenoidectomy Comparisons

Table F-44. Detailed strength of evidence grading table, all functional outcomes

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy (laser) with adenoidectomy vs. Myringotomy (cold knife) with adenoidectomy	No studies	NA	NA	NA	NA	Insufficient, no evidence

Abbreviations: NA = not applicable; vs. = versus.

Adenoidectomy Versus Other Interventions

Table F-45. Detailed strength of evidence grading table, speech, language and cognitive development

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Adenoidectomy	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable.

Table F-46. Detailed strength of evidence grading table, behavior

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Adenoidectomy	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable.

Table F-47. Detailed strength of evidence grading table, quality-of-life

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Adenoidectomy	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable.

Table F-48. Detailed strength of evidence grading table, satisfaction with care

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Adenoidectomy	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable.

Steroids Versus Control

Table F-49. Detailed strength of evidence grading table, speech, language and cognitive development

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Topical vs control, 3 and 9 mos	1, 144	Medium	Unknown, 1 study	Direct	Imprecise	No difference in parent-reported hearing difficulties
Oral	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: Mos = months; NA = not applicable; vs. = versus.

Table F-50. Detailed strength of evidence grading table, behavior

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Topical	No studies	NA	NA	NA	NA	Insufficient: no evidence
Oral	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable.

Table F-51. Detailed strength of evidence grading table, quality-of-life

Intervention, time to outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Topical, <3 mos	1, 39	Medium	Unknown, single study	Direct	Imprecise	Insufficient: no difference
Topical, ≥3 mos	1, 144	Low	Unknown, single study	Direct	Imprecise	Low, no difference
Oral	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: mos = months; NA = not applicable

Table F-52. Detailed strength of evidence grading table, satisfaction with care

Intervention, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Topical	No studies	NA	NA	NA	NA	Insufficient: no evidence
Oral	No studies	NA	NA	NA	NA	Insufficient: no evidence

Abbreviations: NA = not applicable.

Autoinflation Versus Control

Table F. 53. Detailed strength of evidence grading table, all measures

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Autoinflation, any time period	No studies	NA	NA	NA	NA	Insufficient, no evidence

Abbreviations: NA = not applicable.

Key Question 3

Harms or Tolerability

Tympanostomy Tubes Versus Other Tympanostomy Tube or Variation in Tympanostomy Tube Insertion Technique

Table F-54. Detailed strength of evidence grading table, harms

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Goode silicon TT v. Teflon Armstrong TT, Repeat TT; repeat TT placement	1; 15	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single mall study
TT v. TT + NAC addition, repeat tube placement, 29 mo; repeat TT placement	1; 75	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study
TT v TT, otorrhea	1 RCT, 30 ears; 2 obs, 779 ears	Medium	Consistent	Direct	Imprecise	Low for harms from longer-term TT
TT v TT, perforation	3; 305	Medium	Inconsistent	Direct	Imprecise	Insufficient, mixed results
TT v TT, cholesteatoma	2; 235	Medium	Inconsistent	Direct	Imprecise	Insufficient, no difference
TT v TT, tympanosclerosis	3; 196	Medium	Inconsistent	Direct	Imprecise	Insufficient, mixed results
TT v TT, Occlusion	1; 70	Medium	Unknown, single study	Direct	Imprecise	Insufficient, single small study
TT v TT, Granulation	2; 290	Medium	Inconsistent	Direct	Imprecise	Insufficient, mixed results

Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Table F-55. Detailed strength of evidence grading table, harms

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT, Tx Failure, 3 yrs	1 study, 109	Medium	Unknown, single study	Direct	Imprecise	Insufficient, no difference
TT, Otorrhea, various	4 studies, 960	Medium	Consistent	Direct	Imprecise	Low, higher in TT group
TT, Atrophy, various	4 studies, 1024	Medium	Inconsistent	Direct	Imprecise	Insufficient, mixed results
TT, Perforation, various	3 studies, 466	Medium	Consistent	Direct	Imprecise	Insufficient, mixed results
TT, Tympanosclerosis, various	5 studies, 1129	Medium	Consistent	Direct	Imprecise	Low, higher in TT group
TT, Cholesteatoma, various	2 studies, 220	Medium	Consistent	Direct	Imprecise	Insufficient, no difference
Time with granulation	1 study, 150	Medium	Unknown, single study	Direct	Imprecise	Insufficient, 1 study

Tympanostomy Tubes and Adenoidectomy Versus Myringotomy and Adenoidectomy or Adenoidectomy Alone

Table F-56. Detailed strength of evidence grading table, harms

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+adeno, Tx Failure, 3 yrs	1; 25	Medium	Unknown, single study	Direct	Precise	Insufficient, single studies
TT+adeno v. myring+adeno, Otorrhea, various	3; 87	Medium	Inconsistent	Direct	Precise	Insufficient, mixed results
TT+adeno, Atrophy, Various	No studies	NA	NA	NA	NA	Insufficient: no evidence
TT+adeno v. myring+adeno, Perforation, Various	1; 15	Medium	Unknown, single study	Direct	Imprecise	Insufficient; no difference
TT+adeno v. adeno alone or with myring, Tympanosclerosis, various	3; 485	Medium	Consistent	Direct	Imprecise	Low, rates higher in TT group
TT+adeno, Cholesteatoma, various	No studies	NA	NA	NA	NA	Insufficient: no evidence
Granulation	No studies	NA	NA	NA	NA	Insufficient: no evidence

Myringotomy Comparisons

Table F-57. Detailed strength of evidence grading table, all harms

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy + Mitomycin C vs. myringotomy	No studies	NA	NA	NA	NA	Insufficient, no evidence

Myringotomy With Adenoidectomy Comparisons

Table F-58. Detailed strength of evidence grading table, all harms

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy (laser) with adenoidectomy vs. Myringotomy (cold knife) with adenoidectomy	No studies	NA	NA	NA	NA	Insufficient, no evidence

Adenoidectomy Versus Other Interventions

Table F-59. Detailed strength of evidence grading table, harms

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Adenoidectomy vs. other treatments	2, 739	Medium	Consistent	Direct	Imprecise	Rare but possible chance of post-surgical hemorrhage.

Steroids Versus Control

Table F-60. Detailed strength of evidence grading table, harms

Intervention, outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Topical, serious	3, 323	Medium	Consistent	Direct	Imprecise	Insufficient No events
Oral, serious	5, subjects: NR	Medium	Consistent	Direct	Imprecise	Insufficient No events
Topical, mild	1, 170	Medium	Unknown, single study	Direct	Imprecise	Low, no difference
Oral, mild	2, subjects: NR	Low	Consistent	Direct	Imprecise	Insufficient: no difference

Autoinflation Versus Control

Table F-61. Detailed strength of evidence grading table, harms

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Autoinflation	No studies	NA	NA	NA	NA	Insufficient, no evidence

Key Question 4

Patient Subgroups

Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy or Adenoidectomy Alone

Table F-62. Detailed strength of evidence grading table, sleep apnea

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+ adenoid v. myrin + adenoid, hearing, 6,12 mos.	1, 52	Medium	Unknown, single study	Direct	Imprecise	Insufficient, no difference, one small study
TT+ adenoid v. myrin + adenoid, quality of life, 6,12 mos.	1, 52	Medium	Unknown, single study	Direct	Imprecise	Insufficient, mixed findings, one small study

Autoinflation Versus Control

Table F-63. Detailed strength of evidence grading table, adults

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Autoinflation, improvement in middle ear status end of tx. 50 days post tx	1, 198	Medium	Unknown, single study	Direct	Imprecise	Low Magnitude of difference 44 to 47%

Key Question 5

Health Care Factors

Tympanostomy Tubes Versus Other Tympanostomy Tube or Variation in Tympanostomy Tube Insertion Technique

Table F-64. Detailed strength of evidence grading table, health care factors

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT vs. TT	No studies	NA	NA	NA	NA	Insufficient: no evidence

Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Table F-65. Detailed strength of evidence grading table, health care factors

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT	No studies	NA	NA	NA	NA	Insufficient: no evidence

Tympanostomy Tubes and Adenoidectomy Versus Adenoidectomy Alone or With Other Intervention

Table F-66. Detailed strength of evidence grading table, health care factors

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
TT+adeno	No studies	NA	NA	NA	NA	Insufficient: no evidence

Myringotomy Comparisons

Table F-67. Detailed strength of evidence grading table, all heath care factors

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy + Mitomycin C vs. myringotomy	No studies	NA	NA	NA	NA	Insufficient, no evidence

Myringotomy and Adenoidectomy Comparisons

Table F-68. Detailed strength of evidence grading table, all heath care factors

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Myringotomy (laser) with adenoidectomy vs. Myringotomy (cold knife) with adenoidectomy	No studies	NA	NA	NA	NA	Insufficient, no evidence

Adenoidectomy Versus Other Interventions

Table F-69. Detailed strength of evidence grading table, health care factors

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Adenoidectomy	No studies	NA	NA	NA	NA	Insufficient: no evidence

Steroids Versus Control

Table F-70. Detailed strength of evidence grading table, health care factors

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Topical	No studies	NA	NA	NA	NA	Insufficient: no evidence
Oral	No studies	NA	NA	NA	NA	Insufficient: no evidence

Autoinflation Versus Control

Table F-71. Detailed strength of evidence grading table, all outcomes

Intervention, Outcome, Time to Outcome	Number of Studies; Subjects	Risk of Bias	Consistency	Directness	Precision	Strength of Evidence Grade Magnitude of Effect
Autoinflation, any time period	No studies	NA	NA	NA	NA	Insufficient, no evidence

Appendix G. Glossary

Acute otitis media: An acute infection of the middle ear that can be viral and/or bacterial in origin.

Audiometry: The testing of hearing ability that includes determination of the hearing levels, ability to discriminate between various sound intensities, ability to distinguish speech from background noise and other aspects. Pure tone audiometry and impedance audiometry (tympanometry) are two of the commonly used tests for audiometric evaluation.

Autoinflation: A technique whereby the Eustachian tube (the tube that connects the middle ear and the back of the nose) is reopened by raising pressure in the nose. This can be achieved by forced exhalation with closed mouth and nose, blowing up a balloon through each nostril or using an anesthetic mask. The aim is to introduce air into the middle ear, via the Eustachian tube, equalizing the pressures and allowing better drainage of the fluid.

Myringotomy: A surgical procedure in which an incision is made in the tympanic membrane. It may be performed as a single procedure or as a preparation for insertion of a tympanostomy tube.

Otitis media with effusion: A collection of fluid in the middle ear without signs or symptoms of ear infection.

Otoscopy: The clinical examination of the ear canal and tympanic membrane, usually by means of a hand-held auriscope (also known as an otoscope) providing illumination and magnification. Sometimes an attachment is used that permits insufflation of air into the ear canal so that the mobility of the tympanic membrane can be assessed, and this is known as pneumatic otoscopy.

Tympanogram: A curve showing the transmission of energy through the middle ear at various air pressures in the external auditory canal. It gives a crude but objective assessment of conductive hearing loss, and various middle ear disorders yield distinctive patterns of tympanogram:

- **Tympanogram A:** a symmetrical triangular graph with its peak at zero pressure level represents normal middle ear function.
- **Tympanogram B:** a flat line on the graph represents the middle ear space filled with fluid, restricting movement of the tympanic membrane under the externally applied pressure.
- **Tympanogram C:** this pattern is found when there is a reduction of middle ear pressure relative to the air pressure in the external auditory canal, which causes inward retraction of the tympanic membrane; the graph shows the shift of the tympanographic peak into the negative value range, but it is of a normal shape.

Tympanometry: Also known as impedance audiometry, the test measures how readily the middle ear system (the tympanic membrane and the middle ear ossicles) can be set into vibration with a change of air pressure in the external auditory canal. In the normal ear, maximum sound transmission occurs when the air pressure within the middle ear space is the same as the atmospheric pressure, that is, equal to the air pressure in the external auditory canal.

Watchful waiting: Watchful waiting or active observation, as it has more recently been called, is the process of regular review and followup of the child, including assessments of hearing, development, and educational progress.

Appendix H. Acronyms

ABG, Air-Bone Gap
AHRQ, Agency for Healthcare Research and Quality
AOM, acute otitis media
CAM, complementary and alternative medicine
CI, confidence interval
CINAHL, Cumulative Index to Nursing and Allied Health Literature
CDLM, contact diode laser for myringotomy
CER, comparative effectiveness review
CT, computed tomography
dB, decibals
EHC, effective health care
EMBASE, Excerpta Medica Database
ENT, Ear, Nose and Throat
EPC, Evidence-based practice center
FU, follow-up
G, group
HL, hearing level
KQ, key question
MA, meta-analysis
MEE, middle ear effusion
MeSH, medical subject headings
mos, months
MA, meta-analysis
NA, not applicable
NICE, National Institute for Health and Clinical Excellence
NIDCD, National Institute on Deafness and Other Communication Disorders
NRCT, nonrandomized controlled trial
NR, not reported
ns, not significant
OME, otitis media with effusion
PE, pressure equalization
PICOTS, populations, interventions, comparators, outcomes, timeframes, and settings
PRISMA, Preferred Reporting Items for Systematic Review and Meta-analyses
PTA, pure-tone audiometry
RCT, randomized controlled trial
RR, relative risk
SIP, scientific information packet
SOE, strength of evidence
SR, systematic review
SRT, speech recognition threshold
TEP, technical expert panel
TM, tympanic membrane
TT, tympanostomy tubes
VT, ventilation tube
WW, watchful waiting