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Number XX

Otitis Media With Effusion: Comparative Effectiveness of Treatments

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Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children's Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting comparative effectiveness reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

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 are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see http://www.effectivehealthcare.ahrq.gov/reference/purpose.cfm

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input from are essential to the Effective Health Care Program. Please visit the Web site (http://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. Comparative Effectiveness Reviews will be updated regularly.

We welcome comments on this CER. 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 e-mail to epc@ahrq.hhs.gov.

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The investigators deeply appreciate the considerable support, commitment, and contributions of the EPC team staff at <NAME>. We express our gratitude to the following individuals for their contributions to this project: <NAME, degrees>

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.

Key Informants

To be completed after peer review.

Technical Expert Panel

Technical Experts comprise a multi-disciplinary 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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Peer Reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. Peer review comments on the preliminary draft of the report are considered by the EPC in preparation of the final draft of the report. Peer Reviewers do not participate in writing or editing of the final report or other products. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual reviewers. The dispositions of the peer review comments are documented and will, for CERs and Technical briefs, be published three months after the publication of the Evidence report.

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Otitis Media with Effusion: Comparative Effectiveness of Treatments

Structured Abstract

Objectives. To compare benefits and harms currently in use for treating otitis media with effusion (OME). Treatment for OME may include single approaches alone or combinations of two or more approaches. We focused on the following interventions and comparisons among them: surgical (tympanostomy tubes, myringotomy, and adenoidectomy); nonpharmacological interventions (autoinflation); pharmacological (oral or nasal steroids); complementary and alternative medicine (CAM); and other treatment strategies (watchful waiting).

Data Sources. We identified five recent systematic reviews during topic refinement. We searched MEDLINE,® EMBASE,® the Cochrane Library, the Cumulative Index to Nursing and Allied Health Literature (CINAHL®), from root through January 8, 2012 for additional studies. We identified additional studies from reference lists and experts.

Review Methods. Two people independently selected, extracted data from, and rated the risk of bias of relevant studies. We incorporated meta-analyses from the earlier reviews. Because of clinical heterogeneity, insufficient numbers of similar studies, or insufficient or variation in outcome reporting, we synthesized the additional data qualitatively. Two reviewers graded the strength of evidence (SOE) using established criteria.

Results. We identified five systematic reviews and 20 additional studies meeting our inclusion criteria. Generally, studies examined interventions in non-infant pediatric populations. We found no evidence on CAM. Clinical outcomes (KQ 1) included OME signs and symptoms, measured hearing, episodes of acute otitis media (AOM) and vestibular function. We found high SOE that tympanostomy tubes decrease the presence of middle ear effusion in comparison to watchful waiting or myringotomy, for up to 2 years, and improve hearing for up to 9 months (moderate SOE). Hearing levels were no longer better with tympanostomy tubes between 7 to 12 months post surgery (measured by ears) (low SOE) and at 12 and 18 months post surgery (measured by child) (moderate SOE). OME was more likely to resolve in children after adenoidectomy than in those with no treatment at 6 and 12 month followup (high SOE). We found no differences in hearing at various time points for up to three years between tympanostomy tubes (with adenoidectomy) and myringotomy (with adenoidectomy) or between topical steroids and controls at three and nine months followup (low SOE). We found no evidence concerning vestibular function or health care utilization and only one small study examining AOM outcomes (insufficient SOE). Functional outcomes included speech and language comprehension, behavior and quality of life. We found low SOE for no difference in language comprehension and expression at 6 to 9 months followup between tympanostomy tubes and myringotomy. In relation to harms (KQ3), tympanosclerosis and otorrhea were more common in ears with tympanostomy tubes (low SOE). All evidence was insufficient comparing types of tympanostomy tubes and approaches to myringotomy. We were unable to disentangle results related to watchful waiting from myringotomy. Evidence on subgroups (KQ4) was limited to one study of children with sleep apnea and one of adults. We found no evidence on the comparative effective of interventions by any health care factors (KQ5).

Conclusions. Overall, we found uneven bodies of evidence across treatment comparisons and outcomes. Compared with watchful waiting or myringotomy alone, tympanostomy tubes decreased effusion through at least 2 years of followup and improved hearing through at least 6 months but tubes do not differ from these other treatments thereafter. However, tube placement also increases the rate of multiple side effects such as otorrhea and tympanosclerosis. There was not sufficient evidence to resolve this trade-off using functional outcomes, quality of life or long term outcomes. Nor was there evidence for determining which kind of tubes or tube routines might provide the best risk benefit ratio. However, there is evidence that adenoidectomy and myringotomy improve effusion and hearing more rapidly than myringotomy alone through 2 years post surgery. Tubes do not add any benefit to adenoidectomy in comparison to adenoidectomy plus myringotomy, and placement of tubes increases side effects. Additional research is needed to develop a sufficient evidence base to support treatment decisions, particularly in subpopulations.

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Executive Summary

Background

Definition of OME

Otitis media with effusion (OME) is defined as a collection of fluid in the middle ear without signs or symptoms of ear infection.[1] It has been thought that OME develops when negative pressure develops in the middle ear relative to atmospheric pressure and then fluid accumulates because of that pressure.[2] However, various other potential explanations include ciliary dysfunction, proliferation of fluid producing goblet cells, allergy and residual bacterial antigens, and biofilm.[3] The presence of fluid in the middle ear then 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 OME

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.[4] Some subpopulations of children are disproportionately affected by OME. 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.[5] Individuals of American Indian, Alaskan, and Asian backgrounds are believed to be at greater risk,[6] 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 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.[7]

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, 8, 9]

Diagnosis of OME

Diagnostically, the core feature of OME is middle ear effusion (MEE)—i.e., sticky or thick 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. 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.[4] To use this procedure, clinicians blow air through the otoscope, causing movement of the tympanic membrane that they can then 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.

Types of Treatments

Given the natural history of OME including spontaneous resolution in most patients over time, clinical decisions are complicated. Despite recent practice guidelines and systematic reviews,[5, 10-17] the comparative benefits and harms of treatments and treatment strategies for OME are uncertain. Surgical procedures, medications, and alternative treatments have all been used to treat OME.

During topic refinement, The Evidence-based Practice Center (EPC) considered each of the known 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 set of treatments examined in this review are indicated under Key Question 1.

Scope and Key Questions

The 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 be helpful to many stakeholder groups in making decisions about when and how to treat this condition. This comparative review includes all interventions currently in use for treating OME—surgical, pharmacological, and nonpharmacological—except antibiotics, antihistamines and decongestants which have been extensively reviewed previously and demonstrated to have no benefit in this population.

The intent of the review was to cover the entire range of individuals who have OME, including populations who have not been examined in past reviews such as adults and children with special 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.

KQ1: 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 (CAM) procedures, watchful waiting, and variations in surgical technique or procedures

KQ2: What is the comparative effectiveness of the different treatment options listed in KQ1 (active treatments, watchful waiting, and variations in surgical procedures) in improving functional and health-related quality of life outcomes in patients with OME?

KQ3: What are the harms or tolerability among the different treatment options?

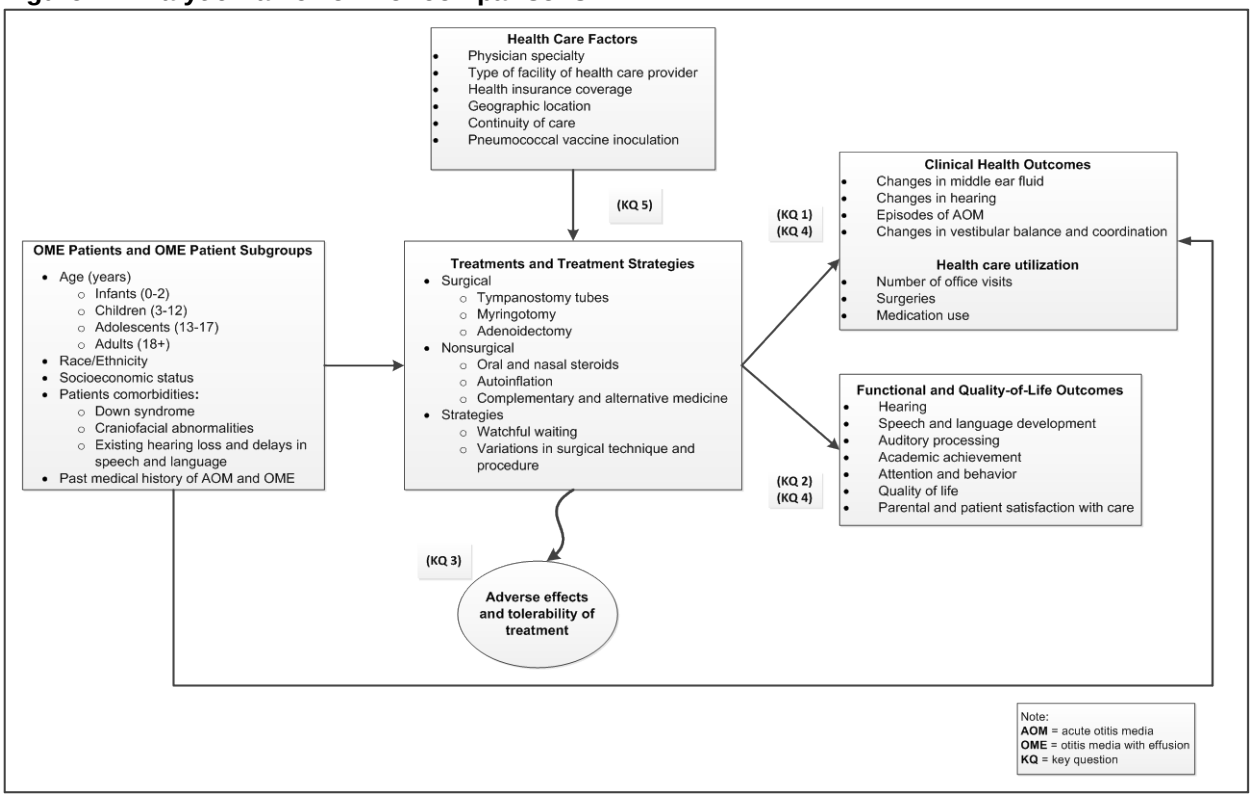
KQ4: What are the comparative benefits and harms of treatment options in subgroups of patients with OME?

KQ5: 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) 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 KQ1 and KQ2 on benefits, and also KQ4 on important subgroups) appear on the far right. KQ3 concerns harms (various types of adverse events). Finally, KQ5 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



Methods

Literature Search Strategy

Search Strategy

Five recently published systematic reviews on comparisons of interest were identified during the topic refinement stage of the review. As discussed in our review protocol, The Cochrane Collaboration conducted four of them, and the Swedish Council of Technology in Health Care commissioned the fifth. The reviews covered the following treatment options for OME: tympanostomy tubes, adenoidectomy, steroids, and autoinflation. To avoid duplicating the work of these teams, we used these reviews as a starting point. We limited our review and analysis for each of our KQs to evidence that these systematic reviews provided plus added evidence that these recent reviews did not consider (i.e., 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 Technical Expert Panel (TEP) and incorporated their input into our search strategy. We limited the electronic searches to English language materials, based on limited resources. We completed the initial search on 1/8/2012, and we will complete an update during peer review.

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 framework. The review only included English language studies of individuals with OME. We included the five systematic reviews identified during topic refinement and eligible studies not included in those reviews included randomized controlled trials (RCTs), nonrandomized controlled trials (NRCTS) and cohort studies. There were no other restrictions, which permitted studies that included individuals of any age, racial/ethnic background, or co-morbidity.

The treatments of interest were tympanostomy tubes, myringotomy, adenoidectomy, oral or intranasal steroids, autoinflation of the Eustachian tube, 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 Collaboration systematic review inclusion criteria.

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; health care utilization; functional and quality of life outcomes such as speech and language development, behavior, and parental satisfaction with care; and harms.

We were primarily interested in treatment outcomes of 3 months or longer but 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

Two people independently reviewed article abstracts using the inclusion/exclusion criteria. If both reviewers agreed that the study did not meet eligibility criteria, we excluded it; otherwise, two reviewers again independently reviewed the full-text article. 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 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. We abstracted the following information as presented in the systematic reviews and from the additional studies: characteristics of study populations, interventions, comparators, settings, study designs, methods, and results. We only reviewed individual studies included in the systematic reviews to determine the availability of subgroup analyses not included in the reviews. We did not reabstract the articles included in the systematic reviews. One trained reviewer initially abstracted the relevant data from each included article and a second member of the team reviewed each data abstraction against the original article for completeness and accuracy. All data abstraction was performed using Microsoft Excel® software.

Risk of Bias Assessment

For each included study, we assessed the potential for selection bias, performance bias, attrition bias, detection bias, and outcome reporting bias using an instrument designed to evaluate risk of bias in a trial or observational study and a second designed to evaluate the risk of bias of a systematic review that have been successfully used previously at our EPC. We did not reevaluate the risk of bias of the studies included in the systematic reviews but all had been determined to be low or medium risk of bias by the original review study authors. 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 are 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. They also did not lend themselves to updating the meta-analyses from the five earlier systematic reviews. Because we determined that quantitative analyses were not 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 included from our own searches.

Strength of the Body of Evidence

We graded the strength of evidence (SOE) 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.[18] 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 SOE indicates that we have high confidence that the evidence reflects the true effect. Moderate SOE implies that we have moderate confidence that the evidence reflects

the true effect. Low SOE suggests that we have low confidence that the evidence reflects the true effect. Insufficient SOE signifies either that evidence is completely unavailable or that it does not permit estimation of an effect.

Two reviewers assessed each domain independently and also assigned an overall grade 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. KQ4 includes a detailed analysis of intervention efficacy in population subgroups.

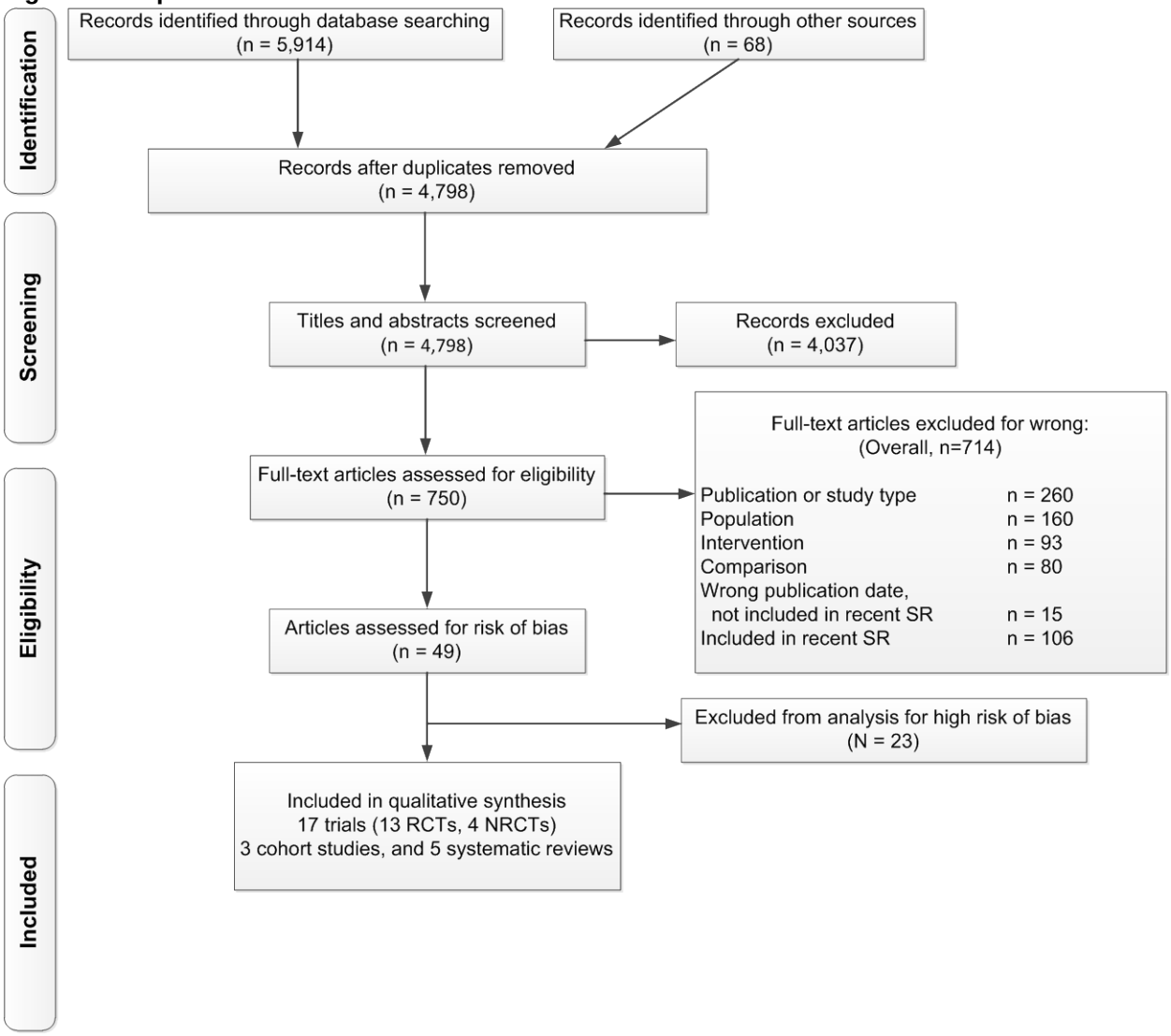
Results

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. Summary tables can be found in the full report. Evidence tables of included studies may be found in Appendix C, and the strength of evidence ratings for the main outcomes of each KQ are detailed in Appendix F.

Literature Searches

We identified a total of 4798 unduplicated citations and determined that 750 met criteria for full-text review (Figure B). We excluded 701 full-text articles based on our inclusion criteria and before risk of bias assessment. We further eliminated 23 articles because of high risk of bias. Overall, we included 21 full-text articles, detailing 20 studies (13 RCTs, four nonrandomized controlled trials, and three observational studies) and five systematic reviews. 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). Of these, six were RCTs, seven were non-randomized trials and the remainder were cohort studies. 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



Abbreviations: NRCT = non-randomized controlled trial; RCT = randomized controlled trial; SR = systematic review

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

Eight of the 20 studies and four of the five systematic reviews reported differences in one or more indices of OME signs and symptoms as a function of treatment. Two of the individual studies and three of the systematic reviews reported differences in hearing as a function of treatment. No studies reported health utilization or balance outcomes. Evidence for decrease in subsequent AOM was insufficient as only one study examined this outcome.

Tympanostomy Tube Comparisons

Seven individual studies[20-26] and seven studies from one systematic[10] review addressed tympanostomy tube comparisons. The seven individual studies included four RCTs,[20-22, 25] one nonrandomized controlled trial[26] and two observational studies.[23, 24] The Hellstrom et al. review[10]

contained seven studies, five of which were RCTs and two of which were nonrandomized controlled trials. These single studies compared different types of tubes (e.g., materials, size), approaches to insertion, or topical prophylaxis therapies. All comparisons were made between ears of the same individual. Primarily because of the diversity of comparisons, the evidence is insufficient for middle ear status or hearing.

Tympanostomy Tubes Versus Watchful Waiting/Myringotomy

Two of the individual studies that met our inclusion criteria[27, 28] and two systematic reviews[10, 12] addressed comparisons between trials of tympanostomy tubes with either myringotomy or watchful waiting. Browning et al.[12] reviewed 10 studies, eight of which were in comparison to watchful waiting or delayed treatment and two were in comparison to myringotomy in the control ear. Hellstrom et al.[10] included six of the studies that were in the Browning review. Both of the individual studies we reviewed and all of the studies included in the systematic reviews were RCTs.

Tympanostomy tube placement decreased time with middle ear effusion through 2 years post surgery (high [1 year] to moderate [2 year] SOE); evidence was insufficient for longer followup. Thereafter, OME decreased in watchful waiting and myringotomy groups as well. In contrast, tympanostomy tubes only improved hearing through 9 months post surgery (high [4 to 6 months] to moderate [6 to 9 months] SOE). Thereafter the differences in hearing became attenuated and were not significant at 7 to 12 months (low SOE) and 12 to 18 months post surgery (moderate SOE).

Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy or Adenoidectomy Alone

We identified eight studies examining outcomes in relation to tympanostomy tubes plus adenoidectomy as compared to myringotomy plus adenoidectomy or adenoidectomy alone.[29-36] Three of the studies compared tympanostomy tubes in one ear to a control ear in children who all had adenoidectomies. One of the studies was an RCT,[29] and the other two were nonrandomized controlled studies.[30, 31] The other five studies compared tympanostomy tubes to myringotomy, among children who all had adenoidectomies; four were RCTs,[32-35] and one was a nonrandomized control study.[36]

The evidence was insufficient for examining OME signs and symptoms, with only two single studies examining middle ear effusion and recurrence of OME. We found no differences in hearing at any endpoint in five studies between tympanostomy tubes and myringotomy among children who also received adenoidectomies (low SOE). We found mixed results for tubes compared with watchful waiting in children who also received adenoidectomies (insufficient SOE).

Myringotomy Comparisons

Only one RCT compared two different procedures for myringotomy on both middle ear and hearing outcomes.[37] 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.[38] 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

One Cochrane Collaboration systematic review by van den Aadweg et al.[13] provided all the evidence for adenoidectomy in comparison to tympanostomy tubes, myringotomy, or no surgery. The review included seven RCTs that were limited to OME patients. The trials examined adenoidectomy with and without myringotomy versus non-surgical treatment or myringotomy only; adenoidectomy with unilateral tympanostomy tubes versus a unilateral tympanostomy tube only (comparison by ears); and adenoidectomy with bilateral tympanostomy tubes versus bilateral tympanostomy tubes only.

Adenoidectomy was superior to no treatment for resolution of OME at both 6 months (risk difference of 0.27 measured through otoscopy and 0.22 as measured through tympanometry; high SOE) and 12 months post surgery (risk difference of 0.29 through tympanometry; high SOE). One single study found that adenoidectomy and myringotomy were superior to myringotomy alone for reducing time with effusion and improving hearing at 24 months (low SOE). There was insufficient evidence to determine the effectiveness of adenoidectomy as compared with no treatment, myringotomy, or tympanostomy tubes for AOM.

Oral or Topical Nasal Steroids

We included one RCT[39, 40] that examined topical intranasal steroids and one recent systematic review conducted by Cochrane Collaboration[15] that examined oral steroids and topical intranasal steroids. Simpson et al.[15] summarized the evidence from nine RCTs of oral steroids and two RCTs of topical intranasal steroids. Both the systematic review and the study we reviewed examined signs and symptoms of OME and hearing. Meta-analyses[15] comparing oral steroids with controls with and without antibiotics did not show differences in middle ear effusion at either 1-2 months post treatment (moderate SOE). There was insufficient evidence comparing oral steroids with controls for hearing at any time point. The RCT[39, 40] comparing intranasal steroids with controls did not find differences in OME cure rate or in hearing at one or more months post treatment (low SOE). There was insufficient evidence for comparing either oral or topical intranasal steroids with controls for any other clinical outcome.

Autoinflation

One Cochrane Collaboration systematic review conducted by Pera et al.[14] 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 and one study with adults, 16-75 years of age. All studies were in comparison to 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 SOE). 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 tympanostomy tubes versus watchful waiting, tympanostomy tubes plus adenoidectomy versus myringotomy plus adenoidectomy, and steroids versus control. In general, there were no differences between the treatments. The studies that are included are described under KQ1.

Tympanostomy Tubes Versus Watchful Waiting/Myringotomy

Meta-analysis reported by Browning et al.[12] did not find any differences in language development at 6 and 9 months post treatment between tubes and watchful waiting (low SOE). Individual studies included in the systematic review reported mixed findings for behavior outcomes (insufficient SOE). Evidence was insufficient for determining differences between tubes and watchful waiting for quality of life outcomes. No studies comparing tubes with myringotomy reported on functional or quality of life outcomes (insufficient SOE).

Tympanostomy Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy

One study comparing tubes plus adenoidectomy with myringotomy plus adenoidectomy reported quality of life outcomes.[35] The two groups did not differ at any time point (insufficient SOE). 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

One small study included in the systematic review[15] and the one clinical trial that met our inclusion criteria [39, 40] examined functional outcomes. Patients receiving intranasal steroids plus oral antibiotics did not differ in parents' assessment of their children's symptoms from patients receiving placebo plus antibiotics (low SOE); nor did patients receiving intranasal steroids differ from controls in parent reported hearing outcomes (low SOE). No studies comparing topical or oral steroids to control examined any other functional outcomes (insufficient SOE).

Key Question 3. Harms or Tolerability

Five of the treatment comparisons included in the review reported on harms. These include tube versus tube studies, tubes versus watchful waiting/myringotomy, tubes plus adenoidectomy versus myringotomy plus adenoidectomy/adenoidectomy alone, steroids, and autoinflation. Only a limited range of harms were included for any comparison. Few significant differences in harms were reported.

Tympanostomy Tube Comparisons

We reviewed five studies that reported on otorrhea[20] and one systematic review Hellstrom et al.[10] reported on three other studies that examined otorrhea. We found insufficient evidence for one type of tube or tube routine because the results were mixed. The other harms that were

reported in one or more studies include repeat tube placement, cholesteatoma, occlusion, tympanosclerosis, and the presence of granulation tissue. The results were reported in only one study, were non significant or were conflicting (insufficient SOE).

Tympanostomy Tubes Versus Watchful Waiting/Myringotomy

The two studies we reviewed[27, 28] and both systematic reviews[10, 12] that compared tympanostomy tubes to watchful waiting/myringotomy examined harms. These included otorrhea, acute AOM, atrophy, tympanosclerosis, perforation, cholesteatoma, and the presence of granulation tissue. In comparison to either ears with no surgery or myringotomy, ears with tympanostomy tubes were more likely to experience tympanosclerosis (low SOE) or otorrhea (low SOE). Evidence was insufficient for other harms due to either conflicting results or having been reported in only a single study.

Tubes Plus Adenoidectomy Versus Myringotomy Plus Adenoidectomy/Adenoidectomy Alone

We reviewed seven studies that examined harms.[29, 31-36] These included repeat tubes, otorrhea, perforation, and tympanosclerosis or myringosclerosis. Results were either mixed or were reported in single studies (insufficient SOE)

Oral or Topical Nasal Steroids

Both the study we reviewed[39, 40] and the systematic review[15] reported on harms. The trials[39, 40] 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 SOE). Evidence concerning serious harms was sparse for either nasal or oral steroids (insufficient SOE).

Autoinflation

The one systematic review that compared autoinflation to control[14] provided no quantitative information on rates of serious or mild harms, only verbal statements indicating that there were few harms noted (insufficient SOE).

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

Two treatment comparisons examined comparative effectiveness of interventions for subgroups of patients –tympanostomy tubes plus adenoidectomy versus myringotomy plus adenoidectomy/adenoidectomy alone and autoinflation.

Tubes plus Adenoidectomy Versus Myringotomy plus Adenoidectomy or Adenoidectomy Alone

One study that met our inclusion criteria[35] included children with sleep apnea and OME. The study did not report differences in hearing thresholds between children who received tubes plus adenoidectomy and children who received myringotomy plus adenoidectomy. Quality of life scores were inconsistent (insufficient SOE).

Autoinflation

One study included in the systematic review of autoinflation[14] 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 SOE).

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 SOE for comparative effectiveness of treatments on clinical outcomes. We are able to draw some conclusions regarding surgical treatments. We found high strength of evidence that in comparison to myringotomy or watchful waiting, tympanostomy tubes decreased the number of children with MEE at 1 year post surgery. Tubes continued to improve middle ear effusion at 2 years but the effect was observed less frequently. Tubes also improved hearing relative to watchful waiting but the effect was shorter in duration. We found only limited evidence for drawing conclusions about the relative benefits of tubes for other clinical outcomes such as OME recurrence or episodes of OME. We examined the evidence for whether tubes 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 there is low strength of evidence of no difference in hearing and insufficient evidence for any other clinical outcomes. We found high strength of evidence for concluding that adenoidectomy is superior to either tubes or no treatment for improving the likelihood of OME resolution at 6 and 12 months post surgery. We found low strength of evidence for adenoidectomy and myringotomy's superiority in relation to myringotomy alone at 2 years post surgery for improving OME resolution and hearing. Evidence was insufficient for other outcomes. All evidence concerning comparisons of tympanostomy tubes in relation to design or routes or techniques of insertion was evaluated as insufficient because there were only single studies that tested specific comparisons. Evidence was also insufficient for comparisons between different approaches to myringotomy with and without adenoidectomy due to the limited number of studies.

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
Tympanostomy tubes vs. watchful waiting or myringotomy	MA of 3 RCTs (N=574)	Tympanostomy tubes decreased persistent middle ear effusion at 1 year: 32% less time (95% CI, 17% to 48%)	High for benefit
	MA of 3 RCTs (N=426)	Tympanostomy tubes decreased persistent middle ear effusion at 2 years: 13% less time (95% CI, 8% to 17%)	Moderate for benefit
	MA of 3 RCTs (by ears) (N=230)	Tympanostomy tube groups had better measured hearing at 4-6 months: -10dB (95% CI, -19.12 to -1.05)	High for benefit
	MA of 3 RCTs (N=523)	Tympanostomy tube groups had better measured hearing at 6-9 months: -4.20dB (95% CI, -4.00 to -2.39)	Moderate for benefit
	MA of 3 RCTs (by ears) (N=234)	No difference between groups 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)	No difference between groups in measured hearing at 12 months: -0.41dB (95% CI, -2.37 to 1.54)	Moderate for no difference
	MA of 2 RCTs (N=283)	No difference in measured hearing between groups at 18 months: -0.02 dB (95% CI, -3.22 to 3.18)	Moderate for no difference
Tympanostomy tubes + adenoidectomy vs. myringotomy + adenoidectomy	5 studies: 2 RCTs by person (N=130), 2 RCTs (by ears) (N=85), 1 NRCT (by ears) (N=146)	No difference in measured hearing between groups at 6 and 12 months and greater than 3 years.	Low for no difference
Adenoidectomy vs. tympanostomy tubes or myringotomy/no surgery	MA of 2 RCTs (N=153); MA of 3 RCTs (N=297)	Adenoidectomy better OME resolution 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 (N=298)	Adenoidectomy better OME resolution at 12 months. The risk difference was 0.29 (95% CI, 0.19 to 0.39).	High for benefit
	1 study (N=237)	Adenoidectomy and myringotomy 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 study (N=237)	Adenoidectomy and myringotomy better hearing than with myringotomy alone at 24 months: -0.65 standard mean difference time with hearing level ≥ 20 worse ear (95% CI, -0.91 to -0.39)	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 vs. control	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. control	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

Abbreviations: 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; vs.= versus

We have reached some conclusions for nonsurgical interventions. We found low strength of evidence for concluding that oral steroids do not offer any improvements in OME at 1 to 2 months post treatment. Similarly, we found moderate evidence for concluding that oral steroids with antibiotics do not provide improvements in OME at 1 to 2 months. A recent low risk of bias study provided additional evidence that OME and hearing outcomes were not improved through

the use of topical intranasal steroids through 9 months post treatment. These findings support the current clinical practice guidelines against the use of oral and intranasal steroids in treating OME in children. Although we found low evidence that autoinflation improves middle ear effusion at less than 1 month post treatment, there was insufficient evidence for reaching conclusions for other outcomes because outcomes across studies testing autoinflation were not measured at consistent lengths of followup or through consistent measures.

KQ 2. Health-Related Quality Of Life and Functional Outcomes

Table B summarizes the SOE for health related quality of life and functional outcomes. We can provide limited evidence regarding these outcomes. We found that language comprehension and language expression outcomes at 6-9 months were not significantly better among children with OME who received tympanostomy tubes than among those who were limited to watchful waiting or myringotomy (strength of evidence low). Evidence was insufficient to reach conclusions related to differences in either behavioral or quality of life outcomes for this treatment comparison. Quality of life outcomes were measured in one small study comparing tympanostomy tubes and adenoidectomy versus myringotomy and adenoidectomy, but we considered the evidence to be insufficient to reach conclusions. We found that evidence was low for concluding that topical steroids do not improve parent reported hearing difficulties up to 9 months. However, evidence was insufficient to reach conclusions about other quality of 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
Tympanostomy tubes vs. watchful waiting or myringotomy	MA of 3 RCTs (N=394)	No difference in language comprehension at 6-9 months: Mean difference=0.09 (95% CI, -0.21 to 0.39)	Low for no difference
	MA of 3 RCTs (N=393)	No difference in language expression at 6-9 months: Mean difference=0.03 (95% CI, -0.41 to 0.49)	Low for no difference
Topical steroids vs. controls	1 study (N=144)	No difference in parent reported hearing difficulties at 3 and 9 months and median days with hearing loss at 3 months.	Low for no difference

Abbreviations: CI = confidence interval; MA = meta-analysis; N = number; vs. = versus; RCT = randomized control trial

KQ3. 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 for harms outcomes. Based on findings from five studies, we determined that we had low strength of evidence for concluding that tympanosclerosis was more common in children who had tympanostomy tubes than those who were actively monitored or who had myringotomy. In addition, we also had low evidence for concluding that otorrhea occurred more frequently in ears with tubes than those with myringotomy or no surgery. The results from the one study that met our inclusion criteria lead us to conclude that mild adverse events are not significantly higher through the use of topical nasal steroids than placebo with low strength of evidence for no difference. However, evidence was insufficient to reach conclusions related to oral steroids and serious adverse events from oral or topical steroids. We found no evidence concerning harms

from adenoidectomy, including no data on any risks from having a surgical procedure. Similarly, we found insufficient evidence concerning the surgical risks from the insertion of tympanostomy tubes or 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
Tympanostomy tubes vs. watchful waiting or myringotomy	5 studies (N=1129)	Tympanosclerosis occurred more frequently in ears that had tympanostomy tubes, based on examinations after the tubes had been extruded.	Low for harms
	4 studies (N=960)	Otorrhea occurred more frequently in ears with tympanostomy tubes.	Low for harms
Tympanostomy tubes plus adenoidectomy vs. adenoidectomy alone or with myringotomy	2 studies (N=237)	Tympanosclerosis occurred more frequently in ears with tympanostomy tubes.	Low for harms
Topical nasal steroids vs. control	1 study (N=170)	No difference in mild adverse events such as nasal stinging, dry throat, and cough	Low for no difference

Abbreviations: N = number; NR = not reported; SR = systematic review; vs. = versus;

KQ4. Outcomes for Important Patient Subgroups

Table D provides the limited evidence we found for patient subgroups. Although we had planned to examine treatment efficacy or harms for key subgroups characterized by clinical 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, tympanostomy tubes and myringotomy did not differ significantly in terms of any measured outcomes. The study of autoinflation that was included in the systematic review[14] 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 ($p<0.001$). 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
Tympanostomy tubes + adenoidectomy vs. myringotomy + adenoidectomy	1 RCT (N=52)	Children with sleep apnea and OME: no difference between tympanostomy tubes and myringotomy outcomes (all children had received adenoidectomies).	Insufficient (one study)
Autoinflation vs. control	1 RCT (N=198)	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)

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

KQ5: 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 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 non-infant, otherwise healthy children. However, the evidence base is quite limited for adults and for infant children or 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 tympanostomy tubes, myringotomy, adenoidectomy and watchful waiting as well as steroids upon the advice of our TEP. We provided evidence for autoinflation, an alternative non-invasive treatment strategy. We also sought to include CAM procedures, but no studies met our inclusion criteria. We did not limit the outcomes of interest. However, the bulk of the literature concerned reductions in OME, hearing, and a variety of harms that were not uniformly included in all studies. We did not limit the time frame for followup. Although most studies measured outcomes between 3 and 12 months post treatment, for any given comparison time frames were rarely uniform. Studies were conducted in clinical settings. They generally included populations from the United States and Western Europe, but there were a few from other countries including Japan, Egypt, and Iran.

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 there was no evidence. This includes infants and toddlers who are developmentally vulnerable for language acquisition and for whom a mild conductive loss over a shorter period of time can 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. Additionally, there is only limited research on treatment efficacy in adults as we were only able to identify one study that concerned treatments for adults.

The second area is to examine treatments that have heretofore not been subjected to rigorous procedures. For instance, despite the interest in CAM treatments, there is a lack of carefully designed investigations of these treatments. There are treatments being designed to counteract the ontological effects of gastroreflux disease; further research of promising treatments is welcome.

The third area in which we found a gap is methodological. There is a lack of uniformity in measures, lack of functional outcomes, time points for collecting outcomes, and inclusion of baseline measures. Few studies provide effect sizes and fail to report their statistical power. Missing data are often not addressed, and even if attrition is acknowledged, statistical procedures are rarely used to correct for this. Attention in this area would greatly improve the literature base.

Conclusions

Overall, we found uneven bodies of evidence across treatment comparisons and outcomes. Compared with watchful waiting or myringotomy alone, tympanostomy tubes decreased effusion

through at least 2 years of followup and improved hearing through at least 6 months. However, tube placement also increases the rate of multiple side effects such as otorrhea and tympanosclerosis. There was a low level of evidence that tube placement is not different than watchful waiting for functional outcomes, quality of life or long term outcomes. Adenoidectomy decreases the number of children with OME in the short term relative to watchful waiting. For children who are receiving adenoidectomy during an intervention, there is moderate evidence that the addition of tube placement does not improve outcomes compared with myringotomy alone. Additional research is needed to develop a comprehensive evidence base to support decision making among the various treatment options, particularly in subpopulations.

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Introduction

Background

Otitis media with effusion (OME) is defined as a collection of fluid in the middle ear without signs or symptoms of 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 occurs commonly during childhood, with as many as 90 percent of children (80% of individual ears) who will have at least one episode of OME by age 10.[2] Medical treatment of these effusions costs an estimated $4 billion annually.[2] Despite the high prevalence, indications for treatment with definitive, low-risk treatments and an understanding of the impact of prolonged OME on individual health outcomes have been elusive.

Anatomy and Cause of Otitis Media with Effusion

The cascade of physiologic changes that lead to OME are initiated with dysfunction of the Eustachian tube. Normally this tube aerates the middle ear by connecting it to the posterior pharynx. The function of the Eustachian tube becomes evident during atmospheric ascent or descent. The pressure sensation that is experienced when taking off in an airplane comes from middle ear barometric pressure changes. The "popping" of the ear after that represents opening of the orifice to the Eustachian tube in the posterior pharynx and equalization of pressure between atmospheric pressure and the barometric pressure in the middle ear.

Clinicians do not fully understand the pathophysiology of OME. 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.[3] However, various other potential explanations include ciliary dysfunction, proliferation of fluid producing goblet cells, allergy and residual bacterial antigens, and biofilm.[4] 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.

Several predisposing environmental factors are associated with an increased risk of developing OME.[5] These include being exposed to secondhand smoke, attending child care, and having environmentally induced allergies.

Populations With Otitis Media With Effusion

OME is typically considered an affliction of childhood. 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, 6, 7]

Some subpopulations of children are disproportionately affected by OME. Those with cleft palate, Down syndrome, and other craniofacial anomalies are at high risk for anatomic causes of OME and worse 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 existing hearing loss will be affected more dramatically 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 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.[10]

Symptoms of Otitis Media with Effusion

OME can be associated with discomfort and a feeling of fullness in the ear. Patients with OME are also prone to episodes of acute otitis media (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 about 10 decibels [dB]), but in some cases moderate or severe prolonged hearing loss can occur.[11]

Because hearing loss in young children may delay or permanently change their communication skills and may lead to behavioral and educational difficulties,[12] clinicians and others are concerned about the possible role of OME on these outcomes. Additionally, those with chronic Eustachian tube dysfunction and OME are at risk for structural damage of the tympanic membrane.[13]

Diagnosis of Otitis Media with Effusion

Diagnostically, the core feature of OME is middle ear effusion (MEE)—i.e., fluid behind the eardrum in the middle ear space. This condition can be difficult to identify visually; however, bubbles seen behind the tympanic membrane is an almost certain indicator (i.e., pathognomonic) of the presence of MEE.[12] Tympanocentesis (use of a needle to puncture the tympanic membrane to allow for fluid drainage) remains the gold standard for diagnosing MEE and OME.

Taking a careful history is important to identify risk factors for developing OME. For example, eliciting a history of recent upper respiratory infection, allergy, subjective hearing loss or imbalance, speech and language delay, and a history of cleft palate or Down syndrome is critical.

OME is distinguished from AOM by the lack of acute symptoms or signs of inflammation. Therefore, OME should *not* have purulent fluid or redness on examination of the ear. Another distinguishing feature between AOM and OME is the appearance of the tympanic membrane, which bulges with AOM and is typically retracted or neutral with OME. Although AOM also presents with fluid behind the tympanic membrane, it is defined as also including an acute onset and symptoms and signs of middle-ear inflammation.[12]

A variety of examination techniques are used to assist with identification of OME. The most studied diagnostic method is pneumatic otoscopy; in this step, clinicians blow air through the otoscope, causing movement of the tympanic membrane. The decreased movement when fluid is present behind the TM can be identified through comparison to normal membrane movement. This is an accurate way to diagnose MEE by trained examiners.[2]

Tympanometry is a diagnostic tool that indirectly measures middle ear pressure and tympanic membrane mobility. A “flat” tympanogram (Type B tympanogram) is consistent with OME.

OME often has a corresponding conductive hearing loss on 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 (which is the measure of loudness needed to respond to a sound).[14] In contrast, the average hearing levels for ears with OME often measure at 25 dB, with about 20 percent exceeding 35 dB.[1] Also, although usually not necessary to make a diagnosis, MEE can be demonstrated on imaging studies, such as a computed tomography (CT) scan of the temporal bone.

Treatments for Otitis Media With Effusion

Given the natural history of OME, particularly in relation to the high instance of spontaneous resolution, clinical decisions are complicated. Despite recent practice guidelines and systematic reviews,[8, 12, 15-21] the comparative benefits and harms of treatments and treatment strategies for OME are uncertain.

Surgical procedures, medications, and alternative treatments have all been used as treatments for OME. Table 1 lists the various surgical and nonsurgical interventions and overall strategies for treating OME. Treatments for OME generally try to improve Eustachian tube function (medical and physical treatments) or ventilate the middle ear while Eustachian tube function improves over time (surgical treatments).

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.
	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[22]
	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.
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 sound amplifier is placed into the external ear canal.	This 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.

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

Type Of Intervention	Treatment	Description	Presumed Mechanism of Action
Pharmacological interventions	Antibiotics and antimicrobials	Oral medications that kill or stop duplication of infectious agents such as bacteria are used.	Bacterial infections frequently precede or begin during OME episodes. Sterilization of middle ear fluid may decrease inflammation and allow more rapid resolution of Eustachian tube dysfunction.
	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.
Complementary and alternative therapies	Including, but not limited to dietary amendments and osteopathic manipulation	Varies by treatment.	Varies by treatment.
Other treatment strategies	Watchful waiting	Sometimes referred to as active observation, this involves delaying treatment while monitoring patient progress. This contrasts with immediately administering a treatment.	Not directly applicable.
	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.

Abbreviations: OME = otitis media with effusion.

During topic refinement, we looked at each treatment 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.

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

The interventions described below belong to one of the four main types of treatments noted in Table 1—i.e., 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.

Although the most recent guidelines for treating OME do not recommend the use of **myringotomy** alone,[12] more recent literature suggests that laser-assisted myringotomy may be a useful alternative to myringotomy plus tympanostomy tubes. These recent studies suggest that it may provide a treatment with fewer complications for selected subgroups of children and adults.[23-26] Because no systematic reviews have addressed the effectiveness of myringotomy alone, we searched for relevant randomized controlled trials (RCTs) and observational studies

examining myringotomy alone as a treatment strategy for OME in otherwise healthy children, special populations of children, and adults.

The harms and benefits of **tympanostomy tubes** for managing OME in children have been addressed by two recent systematic reviews identified during our topic refinement.[15, 17] They include a 2010 Cochrane review of 10 RCTs[17] of otherwise healthy children and a 2011 systematic review, commissioned by the Swedish Council on Technology Assessment in Health Care,[15] of 8 RCTs, not excluding special populations of children. For this review, we begin with these systematic reviews and searched for additional evidence.

A growing body of literature examines variations in tympanostomy tube-related surgical techniques and procedures for treating patients with OME. The 2011 Swedish systematic review[15] identified during our topic refinement considered various characteristics of tube design and surgical procedures. We searched for other relevant studies comparing tympanostomy tube materials, designs, and surgical procedures.

Adenoidectomy as a treatment for OME in children was also reviewed in a 2010 Cochrane Collaboration systematic review that we identified during our topic refinement.[18] The review included seven RCTs comparing adenoidectomy (with or without tympanostomy tubes) and nonsurgical management or tympanostomy tubes 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. Our search strategy assumed that this Cochrane 2010 review[18] identified all relevant RCT studies relating to both special populations and otherwise healthy children in the literature at the time of the review. We searched for additional evidence.

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 oropharyngeal pressure, transiently opening the Eustachian tube. A 2006 Cochrane Collaboration study identified during our topic refinement included six RCTs examining the use of autoinflation versus no treatment for hearing loss associated with OME.[19] Studies included children, adults, and special populations. 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 was the focus of a 2006 Cochrane Collaboration review identified during our topic refinement.[20] 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)[8] and the American Academy of Pediatrics (2004)[12] recommend against using oral or topical nasal steroids in treating children with OME. For the purposes of identifying the relevant literature for this review, we assume that the Cochrane Collaboration review identified all relevant RCTs as of the time of their review. We searched the published literature for new trials on treating OME with either oral or topical nasal steroids in children and observational studies from any time. In consultation with our Technical Expert Panel (TEP), we concluded that it would be useful to integrate newly identified studies with those previously identified through the Cochrane Collaboration review, because the newly integrated studies may result in conclusions different from those of the earlier review.[20] 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 addresses **complementary and alternative medicine (CAM) interventions** to treat patients with OME. The book *Evidence-Based Otitis Media*[27] lists

treatments and supportive studies for at least two CAM approaches: physical manipulation and restricted diets. Based on the recommendations of our TEP, in the current review we included only RCTs of CAM interventions.

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. We examine 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.[8, 12]

We considered whether to include 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. For ear-specific treatments or outcomes such as hearing thresholds or presence of fluid, ear-specific reports were included in this current review.

Treatments That Will Not Be 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,[8] 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. Hearing aids, therefore, will not be 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[21, 28] and clinical practice guidelines.[8, 12] A Cochrane review of OME for use in children identified 16 RCTs that included more than 1,800 subjects.[21] High-quality evidence on 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 increased 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 have, therefore, decided to exclude antihistamines and decongestants from the current review as a treatment that is definitively not effective and likely harmful.

Antimicrobials including antibiotics currently are not commonly used in the United States to treat OME and are not recommended in current U.S. guidelines.[12] Some conflicting evidence exists regarding the effectiveness and utility of antibiotics for treating patients with OME.[8, 12, 28] An upcoming Cochrane Collaboration review on the use of antibiotics for the treatment of OME in children was started in 2011 and is well under way.[29] We will not duplicate their efforts and have excluded antibiotics from the current comparative review.

Scope and Key Questions

Scope

The populations, interventions, comparators, outcomes, timeframes, and settings (PICOTS) for this review are summarized in Table 2. We have indicated above which treatments we will not cover because of clear evidence of no net benefits or irrelevance to the U.S. patient population.

Table 2. Core PICOTS for this review

Population	All individuals with OME. This includes younger and older children, adolescents, adults; individuals from different racial or 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 acute otitis media or OME.
Interventions	Surgical interventions: tympanostomy tubes (also referred to as PE tubes), myringotomy, and adenoidectomy, alone and in combination. Nonpharmacological and nonsurgical treatments or treatment strategies: autoinflation of the Eustachian tube. Complementary and alternative medicine interventions. Pharmacological treatments: oral or topical nasal steroids. Other treatment strategies: watchful waiting.
Comparators	Different combinations of the above interventions and strategies, including: head-to-head comparisons of one or more treatments, treatment strategies (e.g., watchful waiting vs. early treatment), or surgical procedures and techniques (e.g., one type of tympanostomy tube or procedure vs. another). Steroids only may be compared to placebo.
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, academic achievement, attention and behavior, quality of life, and parental satisfaction with care. Harms: all reported harms for each treatment option.
Timeframes	Short-term studies looking at outcomes from 0 to 3 months after intervention. Longer term studies looking at outcomes past 3 months and into adolescence or adulthood.
Settings	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.

Abbreviations: AOM = acute otitis media; OME = otitis media with effusion; PE = pressure equalization.

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 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 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:

a. Tympanostomy tubes,
b. Adenoidectomy with or without myringotomy,
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, difficulty in hearing), 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. Hearing,
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:

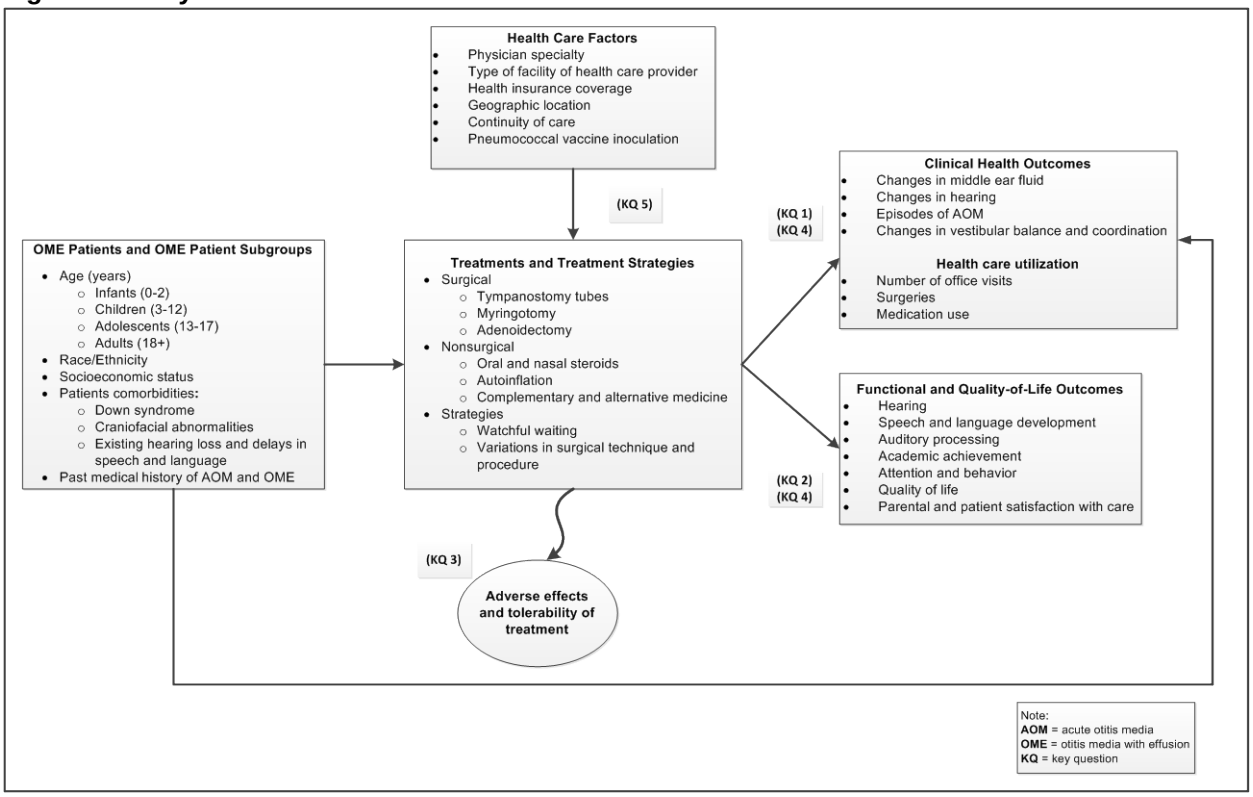
a. Patients of different age groups,
b. Patients of different racial or ethnic backgrounds,
c. Patients in different socioeconomic status groups,
d. Patients with comorbidities such as craniofacial abnormalities (e.g., cleft palate), Down syndrome, and existing speech, language and hearing problems, 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 1 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 1. Analytic framework for review of treatments of 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 key questions. 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 appendices, as follows: A, search strategies; B, list of studies excluded at full-text review with reasons for exclusion; C, evidence tables; D, abstract and full text forms; E, risk of bias tables; F, strength of evidence tables; G, glossary; and H is an 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.[30] Further, we used the PRISMA Statement as a guide to ensure transparent reporting.[31]

Topic Refinement and Protocol Review

The EPC developed this topic and key questions through a public process. The topic was nominated through an online public forum and subsequently developed and refined by a team at the EPC with input from Key Informants in the field. AHRQ posted key questions 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;[17-20] the Swedish Council on Technology Assessment in Health Care was commissioned the fifth.[15] These reviews covered the following OME-related treatment topics: autoinflation, nasal steroids, tympanostomy tubes, and adenoidectomy.

To avoid repeating or duplicating the work of these other systematic review teams, we limited our search, review, and analysis for each of our key questions (KQs) to evidence that these systematic reviews included plus evidence from other reports that these recent reviews would not have considered. These newer elements of our review include observational studies done at any time such as nonrandomized trials, newer trials 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 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 will conduct an update search 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.

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 (http://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 are pertinent but did not meet inclusion criteria for studies that we should consider for inclusion in this review.

Inclusion and Exclusion Criteria

Table 3 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 3. 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 paracenteisis), 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 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 Collaboration systematic 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, 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 post intervention. • 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.

Abbreviations: 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. We excluded studies that focused on the interventions of interest, such as tympanostomy tubes 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 all participants did not all have a diagnosis of OME.

Intervention

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 tympanostomy tubes. Interventions could also include adjunct therapy, such as topical substances to reduce the harms from tympanostomy tubes.

Comparators

All studies included in this review had to have at least two arms, and all participants had to have been diagnosed with OME. 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 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 arms.

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 speech, language, and cognitive development, behavior, quality-of-life, and satisfaction with care. Potential harms differ across interventions (i.e., surgical, pharmaceutical, device)

Timing

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

Setting

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

Study Designs

Table 4 describes the study design inclusion criteria developed for this report.

Table 4. 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, RCTs, and nonrandomized controlled trials, prospective and retrospective cohort studies and case-control studies not included in one of these 5 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 Collaboration or national government-commissioned systematic reviews, we searched only for new literature and observational studies 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. This included studies comparing different surgical techniques or different types of the same intervention (i.e., tympanostomy tubes, 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 covered in systematic reviews - Tympanostomy tubes vs. nonsurgical interventions In relation to otherwise healthy children, who would not be considered as members of subpopulations of interest because of comorbidities, we included evidence from two recent systematic reviews relevant to our KQs and searched all new RCT literature published one year prior to the last search, April 2006 forward. - Adenoidectomy with or without myringotomy In relation to otherwise healthy children, who would not be considered as members of subpopulations of interest because of comorbidities, we included evidence from two recent systematic reviews relevant to our KQs and searched all new RCT literature published one year prior to the last search, March 2008 forward. - Oral and topical nasal steroids In relation to otherwise healthy children, who would not be considered as members of subpopulations of interest because of comorbidities, we included evidence from two recent systematic reviews relevant to our KQs and searched all new RCT literature published one year prior to the last search, May 2005 forward. - Autoinflation In relation to otherwise healthy children, who would not be considered as members of subpopulations of interest because of comorbidities, we included evidence from two recent systematic reviews relevant to our KQs and searched all new RCT literature published one year prior to the last search, August 2005 forward.
Language of publication	Given the volume of literature on this topic, we limited our search to publications in the English language.

*Search to be updated when report is out for peer review.

Abbreviations: KQs = key questions; RCT = randomized controlled trial.

Study Selection

Two trained 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 trained 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. 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. We also reviewed the original studies included in the systematic reviews to determine if additional data concerning subgroup analyses were contained in any of the studies and not reported in the overall systematic review results. One trained reviewer initially abstracted the relevant data from each included article and a second 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 study, we assessed the potential for selection bias, performance bias, attrition bias, detection bias, and outcome reporting bias using instruments that have been successfully used previously by our EPC (Appendix tables E-1 through E-5). The risk of bias assessment was conducted using two tools, one appropriate for trials or observational studies (some questions concerning trial study design would be considered not applicable) and one appropriate for systematic reviews. Both tools were based on instruments that had been used successfully in earlier reviews conducted by our EPC. 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. 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 are summarized in 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, reports low attrition, and reports methods and outcomes clearly and precisely. 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 findings in the results chapter of this review. We list each study rated as high risk of bias and the main reason 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. 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 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, 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.[30] 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). When studies included in a body of evidence include both consistent and inconsistent findings, the presence of one or more consistent findings will result in a "consistent" grade for the outcome of interest.
- 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. When a body of evidence includes both indirect and direct measures, the presence of one or more direct measures will result in a "direct" grade.

- 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 5. 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.

Table 5. 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[30]

Two reviewers assessed each domain independently and also assigned an overall grade 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 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 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 efficacy 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, will be invited to provide external peer review of the draft comparative effectiveness review. AHRQ and an associate editor also provided comments. The draft report will be posted on the AHRQ Web site for 4 weeks to elicit public comment. We will respond to all reviewer comments and note any resulting revisions to the text in the "Disposition of Comments Report." This disposition report will be made available 3 months after the final CER is the posted on AHRQ Web site.

Results

Introduction

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

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

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

A description of all included studies, for each treatment comparison, is presented at the beginning of the results for KQ 1. Because KQ 1 includes all studies, a description of studies is not repeated for other KQs. We then present key points with grades for strength of evidence for major comparisons and outcomes; these are 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 in key points and do not repeat that point in detailed synthesis.

All results new to this systematic review are based on qualitative synthesis. Because of the heterogeneity of populations, interventions, or outcomes in the included studies, we could not do any new quantitative (pooling) analyses. We present results from meta-analyses that were conducted in the five earlier systematic reviews that are included as part of our evidence.

We included in these analyses only studies that we had rated as low or medium risk of bias. All studies are medium risk of bias unless otherwise specified as low. In summary tables that describe included studies, we specify not only study type (e.g., RCT, nonrandomized trial or observational study) but also whether, for RCTs, the randomization was done by ear or by participant. Studies rated high risk of bias are listed in Appendix E together with the principal reason(s) for that rating. Evidence tables for included studies can be found in Appendix C and include the risk of bias assessments for each of the included studies and systematic reviews. 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 may be found in Table 6.

Table 6. 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 Indicated by
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 grater hearing loss.	Reductions in ABGs
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: 15dB for young children, 20 dB for children through early adolescence; and 25 dB for older adolescents and adults.	Reduction in PTA HLs
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
Speech and Language: Receptive language Reynell Developmental Language Scales - Verbal Comprehension Scale - Expressive Language Scale	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, Reynell Developmental Language Scales	Expressive language measures how one produces oral 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

Results of Literature Searches

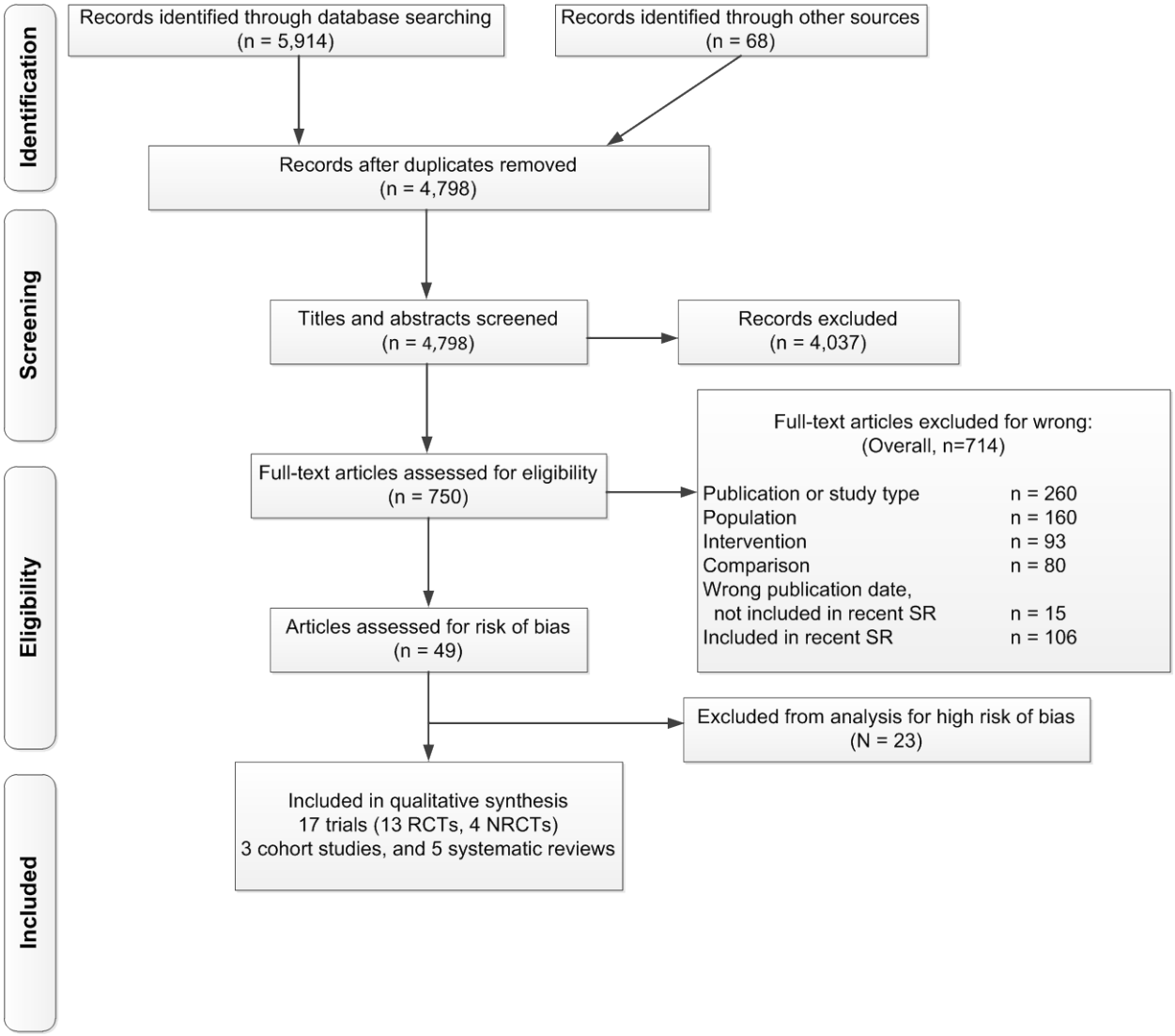
Figure 2 presents our literature search results. Literature searches through 2/28/2012 for the current report identified 4798 unduplicated citations. Appendix A provides a list of all search terms used and the results of each literature search.

After applying our eligibility and exclusion criteria to titles and abstracts of all identified citations, we selected 750 citations for full text review. We reapplied our inclusion criteria and excluded 701 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 49 publications included after full-text review (44 articles and 5 systematic reviews), we dropped 23 articles from further analysis because of their high risk of bias. Thus, we included

a total of 20 trials reported in 21 articles and 5 systematic reviews for qualitative synthesis. Evidence tables for these articles and systematic reviews are provided in Appendix C and risk of bias assessments can be found in Appendix D. Risk of bias assessments are also provided for the 23 high risk of bias studies in Appendix D.

Figure 2. Disposition of articles



Abbreviations: NRCT = non-randomized controlled trial; RCT = randomized controlled trial; SR = systematic review

Of the 20 studies (21 articles) included in this review, 13 were RCTs, four were non-randomized control trials, and three were retrospective cohort studies. We assessed 19 included studies as medium risk of bias and one as low 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).

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 tympanostomy tubes consisted of one recent systematic review[15] and seven additional studies[35-40] (Table 7). All studies compared groups by "ears." Of the seven additional studies we identified, four were RCTs,[35, 36, 39, 41] one was a nonrandomized controlled trial,[40] and two were observational studies.[37, 38] The Hellstrom et al.[15] systematic review included RCTs and nonrandomized control trials (i.e., systematically assigning one intervention to the left ear and the other for right ear). Tympanostomy tube comparisons included tube design (i.e., material, coatings, shape, and size) and routes or techniques for insertion. Broadly speaking, tympanostomy tubes are often categorized by expected length of time they can be expected to stay in place—chiefly, short- or long-term.

Table 7. Characteristics of studies: Tympanostomy tube comparisons

Study, Study Type, Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Follow-up	Age (Range)	Risk of Bias
Licameli et al., 2008[39] RCT by ear United States	G1: Phophoryl-choline-coated fluoroplastic Armstrong tube (N=70) G2: Uncoated fluoroplastic Armstrong tube (N=70)	NR	34 mos	Include: OME w/3-4 mos medical management	24 mos	Mean: 19 mos (8-51 mos)	Medium
McRae et al., 1989[41] RCT by ear England	G1: Shah Teflon tube + aspiration prior to placement (N=55) G2: Shah Teflon tube (no aspiration) (N=55)	Otoscopy and impedence audiometry	NR	Include: OME	24 mos	Mean: 5.7 years (2-10 years)	Medium
Oversen et al., 2000[35] RCT by person and by ear Demark	G1: TT + N-acetylcysteine instilled (N=37) G2: TT + placebo vehicle (N=38)	Otiomicrosco-pical examinations including tympanometry	3 mos	Include: OME, pressure <200mmHg Excluded: Recent antibiotics or AOM at time of surgery	39 mos	Mean: 38 mos (1-7 years)	Medium

Table 7. Characteristics studies: Tympanostomy tube comparisons (continued)

Study, Study Type, Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Follow-up	Age (Range)	Risk of Bias
Wielinga and Smyth, 1990[36] RCT by ear Ireland	G1: Goode Silicon tube (N=15) G2: Teflon Armstrong tube (N=15)	Otoscopy, PTA, tympanometry	6 mos	Include: 6 mos unsuccessful tx with standard decongestive meds; mucoid secretion aspiration, 1 patient adenoidectomy	7 years	Male mean: 7 years Female mean: 6 years	Medium
Abdullah et al., 1994[40] 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 MME Exclude: History of significant AOM	29 mos	Mean: 6 years	Medium
Iwaki et al., 1998[37] Observational by ear Japan	G1: Teflon Shepard tube (N=75) G2: Silicone Goode-T tube (N=39) G3: Silicone Paparella II tube (N=106)	Conductive hearing loss >25dB air-bone gap, Type B tympanogram	6 mos	Include: 25dB air-bone conductive hearing loss, Type B tympanogram, failed politerization and conservative management	24 mos	Mean yrs: G1: 6.2 G2: 6.2 G3: 5.8 (3-12)	Medium
Slack et al., 1987[38] Observational by ear England	G1: Shepard tube (N=214) G2: Shah tube (N=70) G3: Paparella tube (N=275) G4: Goode tube (N=4) G5: Reuter Bobbin TT (N=28) G6: Other type (N=63)	NR	NR	Include: OME, <16 years of age	30 mos	NR	Medium

Table 7. Characteristics of studies: Tympanostomy tube comparisons (continued)

Study, Study Type, Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Follow-up	Age (Range)	Risk of Bias
Hellstrom et al., 2011[15] Systematic Review International	Arms differ across comparisons: 2 trials (262 participants)	Swedish guidelines for diagnosis of OME as a painless inflammation with effusion in the middle ear with impaired hearing ≥ 3 mos; no other criteria specified	Minimum of 3 mos	Include: RCTs (individual or ear), NRCTs, and cohort studies published between 1966 and 2007 of efficacy of tubes on hearing, language development, and quality of life and of complications	Various	Children or adolescents	Medium

Abbreviations: AOM = acute otitis media; dB = decibels; G = group; NR = not reported; OME = otitis media with effusion; PTA = pure tone audiometry; RCT = Randomized controlled trial; tx = treatment; TT = tympanostomy tube.

Key Points

- Single small studies compared different types of tubes, approaches to insertion, or topical prophylaxis therapies for tube retention, OME recurrence, and hearing. Evidence was insufficient.
- No studies compared time with middle ear effusion, vestibular outcomes, or health care service use as a function of type of tympanostomy tube or routes or techniques in their insertion. The strength of evidence is considered insufficient because there are no studies.

Detailed Synthesis

Table 8 presents comparisons of tympanostomy tubes in relation to clinical and health care utilization outcomes. The Hellstrom et al.[15] systematic review identified two RCTs of children with OME who had different types of tubes placed and reported on outcomes including tube retention, OME recurrence, or other ear symptoms.[15] These included a study by Hampal et al. (1991) that compared the mini-Shah tube with a standard Shah tube; the standard Shah tube had a significantly lower rate of OME recurrence.[42] Heaton et al. (1991) compared Shepard tubes (considered shorter term tubes) and Sheehy tubes (considered longer term tubes). Sheehy tubes were retained significantly longer than Shepard tubes ($p<0.001$).[43]

Table 8. Clinical outcomes: Tympanostomy tube comparisons

Study	Arm (N)	Study Duration Until Outcome Measurement	Tube Retention (% Retained Unless Otherwise Noted)	OME Recurrence	Measured Hearing
Wielinga and Smyth, 1990[36]	G1: Goode Silicon tube (N=15) G2: Teflon Armstrong tube (N=15)	NR	Mean months (range) G1: 52.5 (5-88) G2:17.5 (1-56) (p=NR)	NR	Mean: 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 & 7	G1: 27 G2: 0 (p=NS)	NR	NR
Abdullah et al., 1994[40]	G1: Trimmed high grade silicone Shah permavent tube (N=25) G2: Polyethylene Shah tube (N=25)	Month 12	G1: 100 G2: 56 (p=NR)	NR	NR
		Month 29	G1: 71 G2: 18 (p=NR)	G1: 6% G2: 53% (p=NR)	NR
Licameli et al., 2008[39]	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[37]	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 post surgery 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
	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 8. Clinical outcomes: Tympanostomy tube comparisons (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Tube Retention (% Retained Unless Otherwise Noted)	OME Recurrence	Measured Hearing
Oversen et al., 2000[35]	G1: TT + N-acetylcysteine instilled (N=37) G2: TT + placebo vehicle (N=38)	Seen 1, 3, 6, 9, 12, 24, and 36 months post surgery	G1: mean 9 G2: mean 7 (p=0.14)	G1: 16% G2: 13% (p=NR)	NR
McRae et al., 1989[41]	G1: Shah Teflon tube + aspiration before placement (N=55) G2: Shah Teflon tube (no aspiration) (N=55)	3 months	G1: 90 G2: 92 (p=1.0)	NR	NR
		6 months	G1: 76 G2: 80 (p=0.71)	NR	NR
		12 months	G1: 47 G2: 41 (p=0.71)	NR	NR
		18 months	G1: 7.8 G2: 5.8 (p=1.0)	NR	NR
		24 months	G1: 2 G2: 0 (p=1.0)	NR	NR
Hellstrom et al., 2011[15] Systematic Review	1 study (N=116) G1: Shah tube G2: Mini-Shah	Year 1	G1: NR G2: NR P<0.001, favors G1	G1: NR G2: NR P<0.05, favors G1	
	1 study (N=146) G1: Shepard tube G2:Sheehy tube	Year 2	G1:NR G2:NR P< 0.0001, favors G2		

Abbreviations: dB = decibels; G = group; NR = not reported; NS = not statistically significant; OME = Otitis media with effusion; TT = tympanostomy tubes; vs. = versus.

Wielinga et al. demonstrated that after 1 year, silicone Goode-T tubes were more likely to be retained than Teflon Armstrong tubes.[36] Comparing two types of Shah tubes, Abdullah et al. 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.[40] Similarly, in an observational study, Iwaki et al. found that Goode-T tubes were retained on average 5 months longer than Shepard Teflon tubes, but that Paparella II tubes were retained the longest (10.7 vs. 5.9 vs. 15.1 months in place, respectively).[37]

Licameli et al. compared extrusion rates in Armstrong tubes (short-term tubes), with and without phosphorylcholine-coated fluoroplastic; the groups did not differ at 2 year followup (21% vs. 28%, respectively, p=0.84). Extrusion rates also were not found to differ based on whether N-acetylcysteine was infused at the time of insertion[35] or whether the ear was suctioned before tube placement.[41]

The included studies demonstrated a difference in tube retention time that is likely based on tube structure; Goode and Paparella II tympanostomy tubes were retained longer than Armstrong or Shepard tubes. This is consistent with the usual groupings of these types of tubes into shorter-

or longer-acting. Additionally, one study demonstrated that a silicone Shah tube was retained longer than polyethylene tube.[40]

Surgical Interventions: Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Description of Studies

The evidence consisted of two recent systematic reviews, one of which was a Cochrane Collaboration review by Browning et al. (2010)[17] and the second was by Hellstrom et al., (2011)[15] (Table 9). The Browning et al. review summarized 10 RCTs of tympanostomy tubes in treating children with OME; eight of which were in comparison to watchful waiting or delayed treatment and two were in comparison to myringotomy in the control ear. Hellstrom et al., (2011)[15] reviewed six trials comparing tympanostomy tubes to watchful waiting or myringotomy, all of which were also included in the Cochrane review by Browning et al. We identified two additional RCTs. The first compared tympanostomy tubes to myringotomy in children with conductive hearing loss and tympanostomy tubes to myringotomy or no surgery in children with normal hearing, at three year followup.[44] The second compared tympanostomy tubes to laser myringotomy at 6 month followup.[45] The Browning et al. systematic review was assessed as having a low risk of bias.

Table 9. Characteristics of studies: Tympanostomy tubes versus watchful waiting or myringotomy

Study, Study Type Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Study Followup	Age	Risk of Bias
Browning et al., 2010[17] Systematic Review International	Arms differ across comparisons: 10 trials (1728 participants)	Combination of otoscopy (including pneumatic and microscopic), tympanometry and audiometry.	NR	Include: RCTs of short-term tube; randomization could be by child or by ear Exclude: Observational studies or NRCTs; studies including adenoidectomy (unless the arms with adenoidectomy could be excluded)	Child:6-9 mos; 12 mos Ear: 4-6 mos; 7-12 mos	1-12 yrs	Low
Hellstrom et al., 2011[15] Systematic Review International	Arms differ across comparisons: 9 trials (1249 participants)	Swedish guidelines for diagnosis of OME as a painless inflammation with effusion in the middle ear with impaired hearing ≥ 3 mos; no other criteria specified	Minimum of 3 mos	Include: RCTs (individual or ear), NRCTs, and cohort studies published between 1966 and 2007 of efficacy of tubes on hearing, language development, and quality of life and of complications	Various	Children or adolescents	Medium

Table 9. Characteristics of studies: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study, Study Type Country	Arm (N)	Diagnosis Criteria	Wait Period Between Diagnosis and Study	Inclusion/ Exclusion Criteria	Length of Study Followup	Age	Risk of Bias
Koopman et al., 2004[45] RCT by ear Amsterdam	G1: TT + cold knife myringotomy (N=208) G2: Laser myringotomy (N=208)	Binocular otoscopy, tympanometry and audiometry	3 mos	Include: Bilateral OME; <11 yrs; 3 mos of hearing problem per parent report Exclude: Unilateral OME; uncooperative; clinically admitted patients, asymmetric perceptive hearing loss; previously operated ears with other than myringotomy or tube	6 mos	< 11 yrs	Medium
Mandel et al., 1989[44] RCT by cluster United States	Without "significant" hearing loss G1:Myringtomy (N=27) G2: Myringotomy + TT (N=30) G3: No surgery (N=39) With significant hearing loss G4: Myringotomy (N=12) G5: Myringotomy + TT (N=11)	Tympanometry and middle-ear muscle reflex testing	2 mos and medical tx	Include: MEE ≥ 2 mos duration persisting after at 1 14-day course of antimicrobial and pseudoephedrine Exclude: craniofacial malformations; systemic illnesses; hx of ear surgery	3 yrs	7 mos to 12 yrs	Medium

Abbreviations: Hx = history; meds = medications; MEE= middle ear effusion; Mos = months; NRCTs = nonrandomized controlled trials; OME = otitis media with effusion; RCT = randomized controlled trial; tube = tympanostomy tubes; tx = treatment; yrs = years.

Key Points

- Tympanostomy tube placement decreased time with persistent middle ear effusion at long term outcomes based on meta-analysis results; 32 percent over 1 year and 13 percent over 2 years. Strength of evidence was high at one year, based on large magnitude of effect, and moderate at two years (Table 10).
- Hearing outcomes were improved with tympanostomy tube placement for up to nine months. Strength of evidence was moderate. In contrast, at longer periods of followup, hearing differences become progressively smaller and were not significantly different at 7

to 12 month (low strength of evidence) and 12 to 18 month (moderate strength of evidence) follow-up periods. All findings were based on meta-analyses.

- We found one small RCT measuring AOM outcomes at 3 years that found no difference between groups. Strength of evidence is insufficient.
- We found no evidence concerning vestibular or health care use outcomes. Strength of evidence is insufficient for no evidence.

Table 10. Strength of evidence for KQ 1: Clinical outcomes and health care utilization

Comparison (G1 vs. G2)	OME Signs and Symptoms	Objective Hearing	AOM	Balance	Health Care Utilization
TT vs. watchful waiting or myringotomy	**High** 32% less time with TT at 1 year **Moderate** 13% less time with TT at 2 years **Insufficient** One study (N=119) time with OME at 3 years, no difference **Insufficient** OME recurrence (No studies)	**Moderate** Better hearing with TT at 4-6 months and 6-9 months **Low** No difference in hearing, by ear, at 7-12 months **Moderate** No difference in hearing, by child, at 12 and 18 months **Insufficient** One study by ear (N=72) at 24 months	**Insufficient** 1 Study	**Insufficient** (No studies)	**Insufficient** (No studies)

Abbreviations: MEE = middle ear effusion; OME = otitis media with effusion; TT = tympanostomy tubes.

Detailed Synthesis

Duration of Middle Ear Effusion

Browning demonstrated a lower likelihood of persistent middle ear effusion in children who received tympanostomy tubes instead of watchful waiting or myringotomy; at 1year post tubes, 32 percent less time (95% CI, 17% to 48%), based on a meta-analysis of three studies and 13 percent at 2 years (95% CI, 8% to 17%), based on a meta-analysis of three studies (Table 11).[17] Similarly, a recent RCT demonstrated less persistent middle ear effusion in subjects who had tympanostomy tubes versus laser myringotomy at monthly followup, at 1 through 6 months ($p<0.001$, at all time points).[45] An earlier RCT by Mandel et al. (1989) also found significantly lower rates of persistent effusion in children who had received tympanostomy tubes compared with myringotomy at 1year($p<0.001$), but results were no longer significant at 2 and 3 year followup.[44]

Table 11. Clinical outcomes: Tympanostomy tubes versus watchful waiting or myringotomy

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion	OME Recurrence/ Ventilation	AOM	Measured Hearing
Browning et al., 2010[17]	By child (1 study) (N=215)	3 months	NR	NR	NR	Bilateral tube vs. WW: Mean Diff: -11.9 (95% CI, -9.6, -14.2) (favors tube
	(MA:3 studies) (N=523)	6-9 months	NR	NR	NR	Bilateral tube vs. WW: Mean Diff: - 4.20 (95% CI, -6.00 to -2.39) (favors tube)
	(MA: 3 studies) (N=574)	12 months	Bilateral tube vs. myringotomy, delayed treatment or WW: Mean diff: -0.32 (95% CI, -0.48 to -0.17) (favors tube)	NR	NR	NR
	(MA: 2 studies) (N=328)	12 months	NR	NR	NR	Bilateral tubes vs. watchful waiting: Mean Diff - 0.41 (95% CI, -2.37, 1.54)
	MA: 2 studies (N=283)	18 months	NR	NR	NR	Bilateral tube vs. WW Mean Diff: -0.02 (95% CI, -3.22, 3.18)
	MA: 3 studies (N=426)	2 years	Bilateral tube vs. delayed treatment or WW: Mean diff: -0.13 (95% CI, -0.17, -0.08) (favors tube)	NR	NR	NR
	By ear MA: 3 studies (N=230 ears)	4 to 6 months	NR	NR	NR	Unilateral tube vs. WW (2 studies) or myringotomy (1 study): Mean Diff:-10.08 (95% CI, -19.12, -1.05) (favors tube
	MA: 3 studies (N=234 ears)	7 to 12 months	NR	NR	NR	Unilateral tube vs. WW (2 studies) or myringotomy (1 study): Mean Diff: -5.18 (95% CI, -10.43, 0.07) (favors tube)
	1 study (N=72 ears)	24 months	NR	NR	NR	Unilateral tube vs. myringotomy: Mean Diff: -2.1 (95% CI, 2.6, -6.8)

Table 11. Clinical outcomes: Tympanostomy tubes versus watchful waiting or myringotomy (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion	OME Recurrence/ Ventilation	AOM	Measured Hearing
Koopman et al., 2004[45]	G1: TT + cold knife myringotomy (N=208) G2: Laser myringotomy (N=208)	1 month	Absence of effusion G1:87.4% G2:46.6%	NR	NR	NR
		2 months	G1:81.9% G2:35.5%	NR	NR	NR
		3 months	G1:81.5% G2:38.6%	NR	NR	NR
		4 months	G1:75.5% G2:41.6%	NR	NR	NR
		5 months	G1:68.5% G2:39.1%	NR	NR	NR
		6 months	G1:70.7% G2:39.1% (all p<0.001[a])	NR	NR	NR
Mandel et al., 1989[44]	Without "significant" hearing loss: G1:Myringtomy G2: Myringotomy + TT G3: No surgery With "significant hearing" loss: G4: Myringotomy G5: Myringotomy + TT	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	NR	SRT in dB (2 months. post tx) Right ear G1: 18.5 G2: 16.2 G3: 6.2 G4: 22.0 G5: 5.5
	NR	2 years	G1:35.2% G2:20.4% G3:28.2% G4:39.9% G5:28.3% (p=NS)	NR	NR	NR
	NR	3 years	G1: 25.5% G2: 25.0% G3:19.2% G4: 14.4% G5: 30.3% (p=NS)	NR	Episodes/ person-year) G1: 0.58 G2: 0. 18 G3: 0.38 G4: 0.31 G5: 0.41	NR

[a]p values calculated by investigators

Abbreviations: AOM = acute otitis media; MA = meta-analysis; NR = not reported; NS = not significant; OME = otitis media with effusion; SRT = speech related threshold; TT = tympanostomy tube; WW = watchful waiting; vs.= versus.

Measured Hearing

Meta-analysis results of RCTs presented in the Browning et al. review (2010) showed a significant improvement in hearing in tympanostomy tube arms compared with watchful waiting or myringotomy in the short term but not after longer periods of followup.[17] More specifically, meta-analysis results of three studies randomized by ear, at 4 to 6 month followup, found mean differences in hearing to be -10.18 dB (95% CI, -19.12 to -1.05). (Negative results represent

hearing improvement in the tympanostomy tube group.) Meta-analysis results from three studies randomized by child also demonstrated significantly better hearing in the tympanostomy group at 6 to 9 month followup, -4.20 dB (95% CI, -6.00 to -2.39). However, hearing levels were no longer significantly different at 7 to 12 month followup based on meta-analysis results of three "by ear" studies, -5.18 dB (-10.43 to 0.07) and two meta-analyses of RCTs randomized by child, at 12 months and 18 months, both based on two studies (-0.41dB [95% CI, -2.37 to 1.54] and -0.02 dB [95% CI, -3.22 to 3.18], respectively).[17]

Recurrent AOM

After 3 years of observation, even though rates in all groups were low, children who had received tympanostomy tubes had the lowest relative rates of AOM after placement (significance not presented)[44].

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

Description of Studies

No systematic reviews were found that evaluated outcomes from tympanostomy tubes in addition to adenoidectomy. We identified eight studies that included adenoidectomy in both intervention groups and tympanostomy tubes in at least one of the intervention groups (Table 12).[46-53] Three of the studies compared tympanostomy tubes to controls by ear, among children who all had adenoidectomies.[46-48] The other five studies compared tympanostomy tubes to myringotomy, among children who all had adenoidectomies.[49-53] Length of study followup generally ranged from 2 days to 12 months. However, one study followed patients for 7 years.[53]

Table 12. 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	Risk of Bias
Brown, Richards, and Ambegaokar, 1978[46] RCT by ear Wales	G1: TT + adenoidectomy (N=55) G2: Adenoidectomy (N=55)	History, Otoscopy, Audiometry	Not specified	Not specified	48 hrs, 3 6, 9, 12 mos, 5 yrs	4-10 yrs	Medium

Table 12. 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 Follow-up	Age	Risk of Bias
Austin, 1994[47] NRCT by ear United States	G1: TT+ adenoidectomy (N=31) G2: Adenoidectomy (N=31)	Audiometry	Not specified	Include: Indication for adenotonsillectomy and OME, Resistant to ENT or pediatric management	3 mos	Not reported	Medium
Lindholdt, 1977[48] NRCT by ear Denmark	G1: TT+ adenoidectomy (N=91) G2: Adenoidectomy (N=91 ears	Tympanometry	Not specified	Include: Bilateral OME; minimal differences between ears in pressure and hearing Exclude: Previous ear surgery	Until extrusion ,18 mos	Mean: 4 yrs (range 1-10 yrs)	Medium
D'Eredita and Shah, 2006[49] RCT by person Italy	G1: CDLM + adenoidectomy (N=15) G2: TT + adenoidectomy (N=15)	Tympanometry	3 mos	Include: 3 mos of OME Exclude: Hx of prior surgery, craniofacial syndrome, MR or cognitive disorder	12 mos	4 yrs (range 2-6 yrs)	Medium
Popova et al., 2010[50] RCT by person Bulgaria	G1: TT + adenoidectomy (N=42) G2: Myringotomy + adenoidectomy (N=36)	Pneumatic otoscopy and tympanometry	3 mos	Include: OME for 3 mos; conductive hearing loss >20dB Excluded: Previous ear or throat surgery; craniofacial syndromes; destructive middle ear disease; conductive hearing loss attributed to destructive middle ear changes; sensorineural hearing loss	12 mos	G1: 60 mos G2: 61 mos	Medium
Shishegar and Hobhoghi, 2007[51] RCT by ear Iran	G1: TT + adenoidectomy (n=30 ears) G2: Myringotomy + adenoidectomy (N=30 ears)	Otoscopy, tympanometry, audiometry	NR	Include: Bilateral OME unresponsive to medical therapy Exclude: Prior ear surgery; prior adenoidectomy; no OME, cleft palate; perforated TM	6 mos	Range: 4-8 yrs	Medium

Table 12. 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	Risk of Bias
Vlastos et al., 2011[52] RCT by person Greece	G1: Adenoidectomy + TT (N=25) G2: Adenoidectomy + Myringotomy (N=27)	Otoscopy, tympanometry, and pure tone audiometry	NR	Include: Scheduled for adenoidectomy due to sleep apnea; bilateral OME; >3 yrs age Excluded: No OME; chronic OME; previous ear surgery; language delays; behavioral problems; anatomic changes	12 mos	G1: 4.6 yrs (range 3-7 yr) G2: 4.4 yrs (range 3-7 yr)	Medium
Tos and Stangerup, 1989[53] NRCT by ear Denmark	G1: TT + adenoidectomy (N=146) G2: Myringotomy + adenoidectomy (N=146)	NR	NR	Include: Bilateral OME	7 yrs	5 yrs	Medium

Abbreviations: dB = decibel; hrs = hours; Hx = history; mos = months; MR = mental retardation; NR = not reported; NRCT = nonrandomized controlled trial; OME = otitis media with effusion; RCT = randomized controlled trial; TM = tympanic membrane; TT = tympanostomy tubes; yrs = years; CDLM = Contact diode laser myringotomy

Key Points

- We found no differences in short-term and long-term hearing outcomes, when tympanostomy tubes or myringotomy were added as treatment in addition to adenoidectomy (Table 13). Strength of evidence was low.
- Evidence was insufficient in relation to differences in reoccurrence of OME.
- Evidence was insufficient for AOM, vestibular outcomes and health care service use because we found no studies.

Table 13. Strength of evidence for KQ 1: Clinical outcomes and health care utilization

Comparison (G1 vs. G2)	Middle ear effusion/ Time with effusion	OME Recurrence/ Ventilation	AOM	Measured Hearing
TT+adenoidectomy vs. Adenoidectomy alone	**Insufficient** Single study No difference	**Insufficient** (No studies)	**Insufficient** (No studies)	**Insufficient** No difference, single small study
TT+adenoidectomy vs. Myringotomy + adenoidectomy	**Insufficient** (No studies)	**Insufficient** Mixed results	**Insufficient** (No studies)	**Low** No difference (6 mos, 12 mos and >3 years)

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

Detailed Synthesis

Recurrence of Middle Ear Effusion

Two studies found conflicting results regarding middle ear ventilation or recurrence of OME. Results from one study indicated that the middle ear was likely to be ventilated longer after

tympanostomy tube placement than myringotomy when all individuals received adenoidectomy (6.3 months versus 3.5 months respectively, p<0.001) (Table 14).[49] A second study in which all participants received an adenoidectomy failed to find a difference in recurrence of OME between ears that received tubes and ears that received myringotomy.[50] Also, middle ear fluid reoccurrence was not significantly different among children with adenoidectomies who also received tympanostomy tubes in comparison to no additional surgery, at 5 year followup.[46]

Table 14. Clinical outcomes: Tympanostomy tubes plus adenoidectomy versus watchful waiting or myringotomy plus adenoidectomy or adenoidectomy alone

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion	OME Recurrence/ Ventilation	AOM	Measured Hearing
Brown et al., 1978[46]	G1: TT + adenoidectomy (N=55) G2: Adenoidectomy (N=55)	48 hrs 3 mos 5 yrs	NR	G1: 2% G2: 4% No "significant difference" in recurrence between groups	NR	PTA G1: 8.9 dB* G2: 24.7 dB G1: 11.4dB* G2: 16.6 dB G1: 17 dB G2: 14 dB *(significant but no p-value reported)
Austin, 1994[47]	G1: TT+ adenoidectomy (N=31 ears) G2: Adenoidectomy (N=31 ears)	1-3 mos	NR	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 Between tx: 1.9 dB
D'Eredita and Shah, 2006[49]	G1: CDLM + adenoidectomy (N=15)	NR	NR	Middle ear ventilation maintained G1: 3.5 mos G2: 6.3 mos p<0.001	NR	"Normal in both groups at 1 year followup"
	G2: TT + adenoidectomy (N=15)	3 mos	NR	Number ears ventilated (%) G1: 11 (36.6) G2: 30 (100) p=NR	NR	NR
Popova et al., 2010[50]	G1: TT + adenoidectomy (N=42) G2: Myringotomy + adenoidectomy (N=36)	1 mos 6 mos	NR	NR	NR	PTA G1: 13.9 dB G2: 14.1 dB p=0.83 G1: 7.6 dB G2: 8.0 dB p=0.68
	NR	12 mos	NR	OME recurrence G1: 14% G2: 10% p=0.547		G1: 5.5 dB G2: 6.3 p=0.24

Table 14. Clinical outcomes: Tympanostomy tubes plus adenoidectomy versus watchful waiting or myringotomy plus adenoidectomy or adenoidectomy alone (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion	OME Recurrence/ Ventilation	AOM	Measured Hearing
Shishegar and Hobhoghi, 2007[51]	G1: TT + adenoidectomy (n=30 ears) G2: Myringotomy + adenoidectomy (N=30 ears)	1 mos	NR	NR	NR	Air-bone gap improvement G1: 17.47 dB G2: 16.04 dB (p=ns) Mean SRT Hearing threshold G1: 18.3 G2: 17 dB (p=ns)
	NR	6 mos	NR	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)
Vlastos et al., 2011[52]	G1: TT + Adenoidectomy (N=25) G2: Myringotomy + Adenoidectomy (N=27)	6 mos	NR	NR	NR	Change in Hearing G1: -7.41 G2: -4.06 Mean HL Change 3.35 dB (95% CI, -6.64 to 10.35)
	NR	12 mos	NR	NR	NR	Change in Hearing G1: -8.06 dB G2: -7.40 dB Mean HL Change 0.66 dB(95% CI, -6.82 to 8.15)

Table 14. Clinical outcomes: Tympanostomy tubes plus adenoidectomy versus watchful waiting or myringotomy plus adenoidectomy or adenoidectomy alone (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion	OME Recurrence/ Ventilation	AOM	Measured Hearing
Tos and Stangerup, 1989[53]	G1: TT + adenoidectomy (N=146) G2: Myringotomy + adenoidectomy (N=146)	2-3 yrs	NR	NR	NR	PTA G1: 15.0 dB G2: 14.7 dB (p not reported) Gain after tx G1: 14.5 dB G2: 13.1 dB (p not reported)
		6-7 yrs	NR	NR	NR	PTA G1: 11.7 dB G2: 11.1 dB (p not reported) Gain after tx G1: 3.3 dB G2: 3.6 dB

Abbreviations: AOM = acute otitis media; dB = decibel; fU = followup; HL = hearing level; hrs = hours; mos = month; NR = not reported; OME = otitis media with effusion; PTA = pure tone audiometry; RCT = Randomized controlled trial; SRT = speech reception threshold; TT = tympanostomy tubes; tx = treatment; yrs = years.

Measured Hearing

Hearing outcomes were compared in two studies of tympanostomy tubes plus adenoidectomy versus adenoidectomy alone.[46, 47] Followup ranged from 2 days to 5 years. One of the studies found no difference in hearing at the post-operative assessment.[47] A second study[46] found hearing improvement during the first 3 months in the tympanostomy tube group, but by 5 years hearing levels were similar.[46]

In five studies that evaluated tympanostomy tubes versus myringotomy in children who had adenoidectomy, hearing was not significantly different at any time point, ranging from 1month to 6 year followup.[49-53]

Surgical Interventions: Myringotomy Comparisons

Description of Studies

The included evidence consisted of one RCT by Ragab[54] (Table 15). 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 15. 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	Risk of Bias
Ragab, 2005[54] RCT Egypt	G1: Radiofrequency myringotomy + Mitomycin C (N=30) G2: Radiofrequency myringotomy (no Mitomycin C) (N=30)	History, pneumatic otoscopy and tympanometry	NR	Include: Patients undergoing surgery for OME	3 mos	G1: 4.8 yr G2: 5.2 yr	Medium

Abbreviations: mos = months = OME = otitis media with effusion; RCT = randomized control trial; yr = years;

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 evidence is graded as insufficient.

Detailed Synthesis

OME Signs and Symptoms Outcomes

Ragab[54] examined resolution of middle ear effusion and reported a significant difference favoring radio frequency myringotomy with Mitomycin C ($p<0.01$) (Table 16). This study did not present data on either OME recurrence or AOM.

Table 16. Clinical outcomes: Myringotomy comparisons

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion/ Time With Effusion	Measured Hearing
Ragab, 2005[54]	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	Air Bone Gap Improvement: G1: 12 dB G2: 10 dB G1 vs. G2 p=NS

Abbreviations: AOM = acute otitis media; dB = decibel; OME = otitis media with effusion.

Hearing Outcomes

Both myringotomy with and without Mitomycin C groups demonstrated a significant air-bone gap improvement 3 months post surgery as compared with pre-surgery but there was no significant difference in improvement in air-bone gap improvement rates between the two groups.[54]

Surgical Interventions: Myringotomy with Adenoidectomy Comparisons

Description of Studies

One retrospective cohort study from the United States compared two different procedures for myringotomy—namely, laser myringotomy with cold knife myringotomy (Table 17).[55] 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 had a need for a second tube insertion.

Table 17. 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[55] Retrospective cohort USA	G1: Laser myringotomy with adenoidectomy (N=39) G2: Cold knife myringotomy with adenoidectomy (N=48)	Include: Children >4 yrs with refractory OME or with a need for a 2nd 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

Abbreviations: OME = otitis media with effusion; yrs = years.

Key Points

- A particular approach to myringotomy (laser versus cold knife) among patients who had also all received adenoidectomy displayed mixed findings in relation to clinical outcomes. The study did not find that laser myringotomy was superior to cold knife myringotomy in the percentage of patients with OME but did find a difference in the patency of ears (open hole based on myringotomy), post-operatively. Based on one small study, the evidence is graded as insufficient.
- This study 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 among children with middle ear effusion and patency of ears at the first post-surgery visit (Table 18). Laser myringotomy with adenoidectomy did not differ from cold knife myringotomy with adenoidectomy in the percentage of ears presenting with middle ear effusion at followup. However, the authors reported a significant difference in the percentage of ears that were patent at the first post-operative visit, favoring laser myringotomy with adenoidectomy ($p<0.01$).

Table 18. 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[55]	G1: Laser myringotomy with adenoidectomy (N=39) G2: Cold knife myringotomy with adenoidectomy (N=48)	Within 50 days	MEE G1: 10% G2: 15% p>0.1	Patency G1: 21% G2: 0% p<0.01

Abbreviations: MEE = middle ear effusion; OME = otitis media with effusion.

Surgical Interventions: Adenoidectomy Versus Other Interventions

Description of Studies

All of the evidence comparing the effectiveness of adenoidectomy to non-surgical interventions was obtained from a recent Cochrane Collaboration systematic review by van den Aadweg et al.[18] (Table 19). Included studies were limited to RCTs of non-infant children (2-14 years of age) with persistent OME who were followed for 6 months or more. The review included seven studies limited to OME patients (N=1,177). Treatment comparisons included: adenoidectomy with and without myringotomy versus non-surgical treatment or myringotomy only; adenoidectomy with unilateral tympanostomy tubes versus a unilateral tympanostomy tube only (comparison by ears); and adenoidectomy with bilateral tympanostomy tubes versus bilateral tympanostomy tubes only.

Table 19. 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[18] Systematic review International	Arms differ across comparisons: 7 trials (1,177 participants)	Various criteria including clinical judgment, otoscopy, tympanometry, pure tone thresholds	Various	Include: RCTs of adenoidectomy for otitis media compared with non-surgical tx or TT alone; children ≤18 yrs of age Exclude: Quasi randomized trials (e.g., allocation by DOB or record number)	At least 6 mos	2-14 yrs of age	Low

Abbreviations: DOB = date of birth; mos = months; RCT = Randomized controlled trial; tx = treatment; yrs = years.

Key Points

- Adenoidectomy was superior to both unilateral tympanostomy tube placement and watchful waiting to resolve OME at both 6 months and 12 months followup (Table 20).[18] 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 to myringotomy alone. Strength of evidence was low.
- OME resolution outcomes were mixed in studies examining whether the addition of tympanostomy tubes was superior to adenoidectomy alone. Strength of evidence was insufficient
- Evidence was insufficient to determine the comparative effectiveness of adenoidectomy versus no treatment or tympanostomy tubes in relation to hearing, vestibular, and health services related outcomes.

Table 20. Strength of evidence for KQ 1: Clinical outcomes and health care utilization

Comparison (G1 vs. G2)	OME Signs and Symptoms	Objective Hearing	AOM	Balance	Health Care Utilization
Adenoidectomy vs. no treatment or tympanostomy tubes	**High** OME resolution favors adenoidectomy vs. no treatment 2 MA at 6 mo, 1 MA at 12 mos	**Insufficient** Mixed results	**Insufficient** Mixed results	**Insufficient** No studies	**Insufficient** No studies
Adenoidectomy vs. myringotomy	**Low** Mean time with effusion favors adenoidectomy+ myringotomy over myringotomy alone at 24 mos, 1 RCT (N=237)	**Low** Hearing favors adenoidectomy+ myringotomy over myringotomy alone at 24 mos, 1 RCT (N=237)	**Insufficient** No studies	**Insufficient** No studies	**Insufficient** No studies

Abbreviations: OME = otitis media with effusion; AOM = acute otitis media; mos = months; MA = meta-analysis

Detailed Synthesis

OME Signs and Symptoms Outcomes

OME resolution was superior in the adenoidectomy group compared with no treatment in three meta-analyses that compared unoperated ears in patients with unilateral tympanostomy tubes, both at 6 months based on otoscopy (risk difference=0.27, based on 2 studies) and tympanometry (risk difference=0.22, based on 3 studies) and at 12 months based on tympanometry (risk difference=0.29, based on 3 studies) (Table 21).[18] We found that results were mixed across studies concerning whether the addition of tympanostomy tubes to adenoidectomy improved OME-related outcomes.

Table 21. 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[18]	1 study Adenoidectomy + unilateral TT vs. unilateral TT (N=72)	6 mos	NR	NR	NR	Mean hearing level (dB) Ad; 18.0 No tx: 21.1 SMD: -0.25 (95% CI, -0.71 to 0.22)
		12 mos	NR	Otoscopy Ad: 54% No tx: 37% Risk diff: 17% (95% CI, -6% to 40%)		Ad; 15.6 No tx: 18.4 SMD: -0.29 (95% CI, -0.76 to 0.17)
	1 study Adenoidectomy + unilateral TT vs. unilateral TT (N=81)	6 mos	NR	NR	NR	Mean hearing level (db) Ad: 20.4 No tx: 36.5 SMD: -1.37 (95% CI, -1.87 to -0.88)
		12 mos	NR	Otoscopy Ad: 69.4% No tx: 27.7% Risk diff: 42% (95% CI, 22% to 62%)	NR	Ad; 19.7 No tx: 27.4 SMD: -0.67 (95% CI, -1.12 to -0.22)
	1 study Adenoidectomy + Myringotomy vs. Myringotomy (N=88)	6 mos	NR	Normal ears (Type A tympanogram) Ad + M: 68% M: 52% Risk diff: 15% (95% CI, -5% to 46%)	NR	NR
	1 study Adenoidectomy + Myringotomy vs. Myringotomy (N=237)	24 mos	Mean time with effusion Ad + M: 0.302 M: 0.491 SMD: -0.76 (95% CI, -1.02 to -0.49)	NR	NR	Mean time HL $\geq$ 20 dB better ear Ad + M: 0.078 M: 0.186 SMD: -0.66 (95% CI, -0.93 to -0.40) Mean time HL $\geq$ 20 dB worse ear Ad + M: 0.220 M: 0.375 SMD: -0.65 (95% CI, -0.91 to -0.39)
	MA: 2 studies Adenoidectomy + unilateral TT vs. unilateral TT (N =153)	6 mos	NR	Otoscopy Ad + uni TT: 49% uni TT: 21% Risk diff: 0.27 (95% CI, 0.13 to 0.42)	NR	NR

Table 21. 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[18] (continued)	MA; 3 studies Adenoidectomy + unilateral TT vs. unilateral TT (N =297)	6 mos	NR	Tympanometry Ad + uni TT: 39% Uni TT: 17% Risk diff: 0.22 (95% CI, 0.12 to 0.32)	NR	NR
	MA; 3 studies Adenoidectomy + unilateral TT vs. unilateral TT (N =298)	12 mos	NR	Tympanometry Ad + uni TT: 47% uni TT: 20% Risk diff: 0.29 (95% CI, 0.19 to 0.39)	NR	NR
	1 study Adenoidectomy + bilateral TT vs. bilateral TT (N = 95)	12 mos	% with effusion Ad + bil TT: 18% bil TT: 23% Risk diff: -5% (95% CI, -8% to 17%)	NR	NR	NR
		24 mos	Ad + bil TT: 15% bil TT: 18% Risk diff: -3% (95% CI, -10% to 15%)	NR	NR	NR
	1 study Adenoidectomy + bilateral TT vs. bilateral TT (N=254)	24 mos	Mean time with effusion Ad + bil TT: 0.258 bil TT: 0.349 SMD: -0.40 (95% CI, -0.65 to -0.15	NR	NR	Mean time HL $\geq$ 20 dB better ear Ad + bil TT: 0.065 Bil TT: 0.101 SMD: -0.23 (95% CI, -0.48 to 0.02) Mean time HL $\geq$ 20 dB worse ear Ad + bil TT: 0.224 Bil TT: 0.304 SMD: -0.35 (95% CI, -0.60 to -0.11)
	1 study Adenoidectomy + bilateral myringotomy + unilateral TT vs. bilateral myringotomy + unilateral TT (N=149)	6 mos	NR	NR	NR	Change in mean dB Diff between Ad + bil M + uni TT vs.. bil M + uni TT: 4.3 (95% CI, 1.4 to 9.9)
	1 study Adenoidectomy + bilateral myringotomy + unilateral TT vs. bilateral myringotomy + unilateral TT (N=149)	12 mos	NR	NR	NR	Change in mean dB Diff between Ad + bil M + uni TT vs. bil M+ uni TT: 4.3 (95% CI, - 3.1 to 11.6)

Table 21. 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[18] (continued)	1 study Adenoidectomy + Myringotomy + bil TT vs. Myringotomy + bil TT (N=62)	18 mos	Mean time with effusion Ad + M + bil TT: 18% M + bil TT:12% Diff: 6% (95% CI, -12 to 24)	NR	NR	NR
	1 study Adenoidectomy + Myringotomy + bil TT vs. Myringotomy + bil TT (N=44)	18 mos	NR	NR	# episodes Ad + M + bil TT: 7 M + bil TT: 6 Risk diff: 5% (95% CI, -22 to 32)	NR
	1 study Adenoidectomy + Myringotomy + bil TT vs. Myringotomy + bil TT (N=62)	36 mos	Mean time with effusion Ad + M + bil TT: 21% M + bil TT:19% Diff: 2% (95% CI, -19 to 23)	NR	NR	NR
	1 study Adenoidectomy + Myringotomy + bil TT vs. Myringotomy + bil TT (N=39)	36 mos	NR	NR	# episodes Ad + M + bil TT: 17 M + bil TT: 21 Risk diff: -18% (95% CI, -37 to 1)	NR

Abbreviations: Ad = adenoidectomy; AOM = acute otitis media; bil = bilateral; dB = decibel; diff = difference; HL = hearing level; M = myringotomy; MA = meta-analysis; mos = months; MEE = middle ear effusion; OME = otitis media with effusion; SMD = standard mean difference; TT = tympanostomy tubes; tx = treatment; uni = unilateral.

Hearing Outcomes

Hearing measures and outcomes differed across studies in comparison to tympanostomy tubes and results were mixed. Adenoidectomy and myringotomy was found to be superior to myringotomy alone in one relatively large RCT (N=237) at 24 months in relation to hearing in both the better and worse ear.[18]

Other Outcomes

Episodes of AOM were measured in one study included in the systematic review and they did not differ at 18 or 36 months. No studies measured vestibular function.

Pharmaceutical Interventions: Oral or Topical Nasal Steroids

Description of Studies

The included evidence consisted of one recent Cochrane Collaboration systematic review[20] and one more recent trial, conducted by Williamson et al.[56, 57] (Table 22). The systematic review summarized evidence from nine RCTs of oral steroids and two RCTs of topical intranasal steroids, excluding studies limited to ears (rather than children). The Williamson et al. study with

topical intranasal steroids and was conducted by the UK Health Technology Assessment Programme, published as a report[57] and peer-reviewed manuscript.[56] All studies were in comparison with placebo controls. Neither included participants older than 12 years of age. The systematic review did not exclude children with comorbidities, whereas the Williamson et al. study excluded children with Down syndrome, cleft palate, and other comorbidities (Table 22). The Cochrane review included one to two and six month followup; the Williamson RCT included 1, 3, and 9 month followup. Both studies were assessed as low risk of bias.

Table 22. 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., 2010[20] Systematic review International	Arms differs across comparisons: 11 trials (862 participants)	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: otomicroscopy, 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	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.	1-2, and 6 months	0-12 years	Low

Table 22. 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
Williamson et al. 2009[56] Williamson et al. 2009[57] RCT UK	G1: Mometasone furoate nasal spray (N= 105) G2: Placebo spray (N=112)	Tympanometry	In year 1, after failing a second otoscopy screening after 3 mos of watchful waiting. Following protocol change at end of year 1, after failing a second otoscopic screening	Include: Hx of OME by medical record of ≥ 1 episodes in past year or a hx suggestive of OME. At time of study, dx of bil OME. Exclusion: Tympanometry screen passed (A or C1); large amounts of wax; uninterruptable tympanogram; co-morbidities including cleft palate; Down syndrome; primary ciliary dyskinesia; tubes or tympanic perforation, frequent or heavy epistaxis; hypersensitivity to mometasone; history of steroid use in previous 3 mos	1, 3, & 9 mos	4-11 yrs	Low

Abbreviations: db = decibel; bil = bilateral; dx = diagnosis; hx; history; Hz = Hertz; mos = months; NR = not reported; OME = otitis media with effusion; RCT = randomized control trial; yrs = years.

Key Points

- Meta-analyses comparing oral steroids and controls (N=106) did not show differences in middle ear effusion at 1 or 2 months followup (low strength of evidence) (Table 23).
- Meta-analyses comparing oral steroids and controls (N=243) (with oral antibiotic adjunctive therapy) did not show differences in middle ear effusion at 1 or 2 months 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 23. Strength of evidence: Clinical outcomes and health care utilization

Comparison	OME Signs And Symptoms	Measured Hearing
Oral steroids vs. control (1-2 mo)	**Low** Persisting OME: no difference MA, 3, 106	**Insufficient** Hearing gain: no diff 1, 49
Oral steroids + antibiotic vs. control + antibiotic (1-2 mo)	**Medium** 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 mo): 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

Detailed Synthesis

OME Signs and Symptoms Outcomes

The Cochrane systematic review[20] and one newer study from our search[56, 57] presented results on outcomes related to middle ear effusion through two measures: persisting OME and cure rates as measured by a flat tympanogram (Table 24). We found no differences in any treatment comparisons at any end points. At 1to 2 month followup, the systematic review found no difference between oral steroids versus controls in relation to persisting OME, OR=0.55 (95% CI, 0.21 to 1.48) based on a meta-analysis of three studies (N=106) or similarly for oral steroids versus controls, when both arms also received antibiotic treatment, OR=0.75 (95% CI, 0.45 to 1.27), based on a meta-analysis of three studies (N=243).[20]The Williamson et al. study also found no significant difference in cure rates in topical steroids versus controls at 1month, controlling for season, age, atrophy, and clinical severity, RR=0.97 (95% CI, 0.74 to 1.26) (N=194).

Table 24. 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., 2010[20]	MA: 3 studies (N=106)	1-2 months	Persisting OME Oral steroids vs. control Peto OR: 0.55 (95% CI, 0.21 to 1.48)	NR
	1 study (N=49)	NR	NR	Hearing gain by at least 10 dB Oral steroids vs. control OR: 1.47 (95% CI, 0.39 to 5.57) (baseline: NR)
	MA: 2 studies (N=243)	NR	Oral steroids + antibiotic vs. control + antibiotic Peto OR: 0.75 (95% CI, 0.45 to 1.27)	NR
	1 study (N=59)	3 mos	Topical intranasal steroid + oral antibiotic vs. placebo + antibiotic or antibiotic alone OR: 0.72 (95% CI, 0.21 to 2.44)	NR
	1 study (N=15)	6 mos	Oral steroids + antibiotic vs. control + antibiotic OR: 0.15 (95% CI, 0.00 to 7.80)	NR
Williamson et al. 2010[56] Williamson et al. 2009[57]	NR	NR	Topical steroids vs. control 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	NR
	G1: 96 G2: 98	1 mos	Diff in OR (adj): 0.934 (0.498 to 1.751) Diff in RR (adj): 0.97 (0.74 to 1.26)	NR
	G1: 86 G2: 86	3 mos	Diff in OR (adj): 1.451 (0.742 to 2.838) Diff in RR (adj): 1.23 (0.84 to 1.80)	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 (IQR) G1: 19.43 (14.64-1.21) G2: 21.15 (14.86-0.94) Baseline hearing G1: 30.97 (23.8-32.65) G2: 30.94(24.03-32.21)
	G1: 72 G2: 72	9 months	Diff in OR (adj): 0.822 (0.387 to 1.746) Diff in RR (adj): 0.90 (0.58 to 1.41)	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%) Hearing loss from tympanograms, median (IQR) G1:19.56(14.88-0.84) G2: 17.89 (14.11-3.55)

Abbreviations: adj = adjusted; CI = confidence interval; dB = decibel; diff = difference; IQR = interquartile range; MA = meta-analysis; mos = months; OME = otitis media with effusion; OR = Odds ratio; RR = relative risk.

At 3 month followup, we found no differences in middle ear effusion, as measured by persisting OME, related to intranasal steroid use with adjunctive antibiotic treatment in both

arms, based on evidence from one trial that was included in the systematic review (N=59).[20] We also found no differences in cure rates based on evidence from the Williamson et al., study (N=172).[56] Similarly, 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).[20] At 9 month followup, cure rates did not differ between topical steroids and control, based on the Williamson et al. study (N=144).[56]

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 26).[57] We did not find evidence related to hearing outcomes based on oral steroid treatment at 3 months or later.[20]

Other Outcomes

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

Nonpharmaceutical Interventions: Autoinflation

Description of Studies

The included evidence consisted of one recent Cochrane Collaboration review by Perera et al. (2009)[19] (Table 25) 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 and one study of adults, 16-75 years of age. 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 2 weeks post-treatment, one study 4 weeks post treatment and one study approximately 2 months post treatment. The other three trials recorded outcomes at the end of treatment, the length of which differed, with no further outcome measurement. The systematic review was assessed as medium risk of bias.

Table 25. 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[19] Systematic review International	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 tx had to be given to both arms; OME diagnosis needed to include tympanometry	3 trials: at end of tx 1 trial: 4 wks post tx 1 trial: 2 mos 1 trial: 3 mos	3-12 yrs 4-11 yrs 6-75 yrs 3-10 yrs	Medium

Abbreviations: mos = months; OME = otitis media with effusion; RCT = Randomized controlled trial; tx = treatment; wks =

weeks; yrs = years

Key Points

- Relative to control groups, groups receiving autoinflation improved middle ear status as measured by tympanometry a month or less from treatment initiation based on two meta-analyses of two studies in one systematic review (low evidence) but groups did not differ in improvement in tympanometry at more than one month from treatment (insufficient evidence) (Table 27).
- Groups receiving autoinflation did not differ significantly from controls in measured hearing (PTA) at either the end of treatment or 4 weeks after treatment (insufficient evidence).
- No included studies reported on AOM, balance, or use of health care services (insufficient evidence).

Table 26. 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 ≤ 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)

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

Detailed Synthesis

OME Signs and Symptoms Outcomes

The systematic review[19] presented results on improvement in middle ear status as measured with tympanometry (Table 27). 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.

Table 27. Clinical outcomes: Autoinflation

Study	Arm (N)	Study Duration Until Outcome Measurement	Middle Ear Effusion	Measured Hearing
Perera et al., 2009[19]	MA: 3 studies (N=225) MA: 2 studies (N=185) MA: 2 studies (N=185)	≤ 1 month	Tympanometry improvement B or C2 to C1 or A: RR: 1.65 (95% CI 0.49, 5.56) B to C1 or A RR: 2.71 (95% CI 1.43, 5.12) C2 to C1 or A RR: 3.84 (95% CI 1.94, 7.59)	
	MA: 2 studies (N=185)	> 1 month	B or C2 to C1 or A: RR 1.89 (95% CI 0.77, 4,67)	
	MA: 2 studies (N=125)	End of treatment (3 weeks in 1 study and 3 months in the other study)		Improvement in HL ≥ 10 dB (measured by PTA RR 0.80 (95% CI 0.22, 2.88)
	MA 2 studies (N=179)	End of treatment in 1 study and 4 weeks after treatment in the other study		Average HL measured by PTA Weighted Mean Diff 7.02 (95% CI, -6.92, 20.96)

Abbreviations: dB = decibel; HL = hearing level; MA = meta-analysis; mo = month; PTA = pure tone average; RR = relative risk;

In one meta-analysis of three studies, the authors 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, the review authors reported two additional meta-analysis sub-analyses 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 one month or less. However, in the meta-analysis of trials that examined ears at more than 1month from treatment initiation, they 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).

Hearing Outcomes

Two meta-analyses examined hearing outcomes. The autoinflation and control groups did not differ in hearing outcomes at the end of treatment of varying lengths or at 4 weeks after treatment, measured either by a change in hearing level as measured by pure tone audiometry as a discrete outcome or by the PTA hearing threshold.

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

- Speech and language development did not significantly differ between children receiving tympanostomy tubes and those receiving watchful waiting after 6 to 9 months and cognitive development after less than and more than a year (Table 28). Strength of evidence is low.
- Evidence is insufficient on differences in behavioral outcomes (mixed) and quality-of-life outcomes (one study) comparing tympanostomy tube and watchful waiting groups at less than one year. At one year or more, two studies found no difference in behavior (strength of evidence was low).
- No evidence was found comparing tympanostomy tubes and myringotomy in relation to other functional outcomes. Strength of evidence is insufficient.

Table 28. Strength of evidence for KQ 2: Tympanostomy tubes versus watchful waiting or myringotomy

Comparison (G1 vs. G2)	Speech/Language and Cognitive Development	Behavior	Quality of Life
TT vs. watchful waiting 6 to 9 months	**Low** No difference MA: 3, 394; Study: 1, 160	**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, 347	**Insufficient** No difference Study: 1 Study: 1, 176
TT vs. Myringotomy	**Insufficient** No studies	**Insufficient** No studies	**Insufficient** No studies

Abbreviations: TT = tympanostomy tubes

Detailed Synthesis

Speech/Language and Cognitive Outcomes

Two systematic reviews evaluated functional and quality of life outcomes in subjects who received tympanostomy tubes compared with watchful waiting or myringotomy (Table 29).[15, 17] Browning et al., (2010) performed meta-analysis of three studies measuring differences in language comprehension and language expression at six to nine months between tympanostomy tube 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], respectively). Browning et al. identified a single study that evaluated cognitive development at 9 month followup and found no significant difference.[17]

Table 29. Functional and health-related quality-of-life outcomes: Tympanostomy tubes versus other treatments

Study	Arm (N)	Study Duration Until Outcome Measurement	Speech/Language Cognitive Development	Behavior	Quality of Life
Browning et al., 2010[17]	MA=3 studies (N=394)	6-9 mos	Language Comprehension, Bil TT vs. WW: Mean Difference 0.09 (95% CI, -0.21, 0.39)	NR	NR
	MA=3 studies (N=393)	6-9 mos	Language Expression TT vs. WW: Mean Difference 0.03 (95% CI, -0.42, 0.49)	NR	NR
	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=ns)	NR	NR
	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)	Child Behavior Checklist Mean Total Problem Score TT vs. WW 50 vs. 49 (95% CI, -0.6 to 3.4)	NR
	1 study (N=176)	6 mos	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 29. Functional and health-related quality-of-life outcomes: Tympanostomy tubes versus other treatments (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Speech/ Language Cognitive Development	Behavior	Quality of Life
Browning et al., 2010[17] (continued)	(N=165)	12 mos	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
Hellstrom et al., 2011[15]	1 study (n=182)	9 mos	NR	Richman Behavioral Scale, % with Problems TT vs. WW 30% vs. 47% (95% CI, -33% to –2%) p=0.031 (favors tx)	.
		18 mos	NR	24% vs. 20% (95% CI, -10% to 19%) p=0.66	

Abbreviations: bil = bilateral; MA = meta-analysis; mos = months; TAIQOL = TNO-AZL Infant Quality of Life; TT = tympanostomy tubes; tx = treatment; WW = watchful waiting; yrs = years; vs.=versus

Behavior Outcomes

Both Browning et al. and Hellstrom et al. identified studies that examined differences in behavioral outcomes in studies of children with OME receiving treatment with tympanostomy tubes or watchful waiting.[15, 17] Results were mixed. Erickson Child mean scores did not significantly differ at 6 and 12 month followup[17], nor did Child Behavior Checklist Problem Scores at 3 year followup.[17] However, Richman Behavioral Scale scores were better in the tympanostomy tube group at 9, but not 18 month followup.[15]

Quality of Life

Browning et al. found no significant differences in a single study that evaluated quality of life using the TAIQOL (a generic quality-of-life measure for 1to 4 year olds) in children with OME who received tympanostomy tubes or watchful waiting at 6 and 12 month followup.[17]

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 tympanostomy tubes 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.

Detailed Synthesis

Only one small study (N=52) evaluated differences quality-of-life outcomes between children receiving tympanostomy tubes and adenoidectomy and those receiving myringotomy and adenoidectomy [52] (Table 30). While only one group improved from baseline, the difference between them was not significant.[52]

Table 30. 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[52]	G1: TT + adenoidectomy (N=25) G2: Myringotomy + adenoidectomy (N=27)	6 months		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		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)

Abbreviations: OM-6 = Otitis Media -6

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 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 (one study from the systematic review [N=39])[20] (Table 31). One other study did not find significant differences between groups in parent-reported hearing difficulties or days with hearing loss.[57]

Table 31. 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[20]	1 study (N=39)	3 mos	Symptom score Topical intranasal steroid + oral antibiotic vs. control + antibiotic or antibiotic alone Peto odds ratio: -4.50 (95% CI, -10.28 to 1.28)
Williamson et al., 2010[56] Williamson et al., 2009[57]	Baseline: (N=196)	Baseline: G1: 6.06 (2.83-8.57) G2: 5.88 (2.33-7.60)	Parent-reported hearing difficulties, median(IQR) Topical intranasal steroid vs. control
	G1: 86 G2: 86	3 mos	G1: 5.54 (0.90-8.43) G2: 3.92 (0.90-7.60) (p=NS)[a]
	G1: 72 G2: 72	9 mos	G1: 2.33 (0.21 to 7.60) G2: 2.33 (0.42-6.60) (p=NS)[a]
	G1: 86 G2: 86	3 mos	Days with hearing loss, median (IQR) G1: 4 (0 to 24.5) G2: 4 (0 to 18.5) p=0.45

[a]Calculated by authors

Abbreviations: CI = confidence interval; IQR = interquartile range; mos = months; N = number; NS = not sufficient.

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 tube type; Paparella tubes had the highest rates reported in two observational studies (insufficient 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 studies provided either conflicting results or no difference (insufficient evidence).

Detailed Synthesis

The systematic review by Hellstrom et al.[15] identified nine studies that compared type of tympanostomy tube or insertion technique and various side effects (Table 32).[15] All seven newly identified studies comparing the effectiveness of tubes examined various potential harms as well.[35-41]

Table 32. Treatment harms or tolerability: Tympanostomy tube comparison studies

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes	Otorrhea	Perforation	Cholesteatoma	Tympano-sclerosis	Occlusion	Granulation
Wielinga and Smyth, 1990[36]	G1: Silicon tube (N=15) G2: Teflon Armstrong tube (N=15)	NS	G1: 20% G2: 47%	G1: 13% G2: 20%	G1: 6% G2: 6%	G1: 0% G2: 0%	NR	NR	NR
Abdullah, Pringle and Shah, 1994[40]	G1: Trimmed high grade silicone Shah permavent tube (N=25) G2: Polyethylene Shah tube (N=25)	29 months	NR	NR	NR	NR	G1: 41% G2: 65% p=NR	NR	NR
Licameli et al., 2008[39]	G1: Phosphorylcholine -coated fluoroplastic Armstrong tube (N=70) G2: Uncoated fluoroplastic Armstrong tube (N=70)	24 months	NR	G1: 8.7% G2: 7.5% p=0.74	G1: 4.0% G2: 0% p=0.24	NR	NR	G1: 10.3% G2: 13.4 p=0.53	G1: 4.4% G2: 6.0% p=0.66
Iwaki et al., 1998[37]	G1: Teflon Shepard tube (N=75) G2: Silicone Goode-T tube (N=39) G3: Silicone Paparella II tube (N=106)	24 months	NR	G1: 12% G2: 36% G3: 38% p<0.01	G1: 0% G2: 7.7% G3: 10.4% p<0.05	G1: 1.3% G2: 0% G3: 0% p=NR	NR	NR	G1: 0% G2: 0% G3: 7.5% p<0.05

Table 32. Treatment harms or tolerability: Tympanostomy tube comparison studies (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes	Otorrhea	Perforation	Cholesteatoma	Tympano-sclerosis	Occlusion	Granulation
Slack, Gardner, and Chatfield, 1987[38]	G1: Shepard tube (N=214) G2: Shah tube (N=70) G3: Paparella tube (N=275) G4: Goode tube (N=4) G5: Reuter Bobbin (N=28) G6: Other types (N=63)	6 months		G1: 6.2% G2: - G3: 0%	NR	NR		NR	
		12 months		G1: 6.5% G2: 5.9% G3: 20% p>0.05					
		18 months		G1: 3.5% G2: 0% G3: 37.5% p<0.001					
		24 months		G1: 6.2% G2: 13.0% G3: 38.4% p<0.001					
		30 months		G1: - G2: 0% G3: 53.6% p<0.01					
Oversen et al., 2000[35] Demark	G1: TT + N-acetylcysteine instilled (N=37) G2: TT + placebo vehicle (N=38) G3: TT (N=75)	29 months		G1: 16% G2: 39% G3: 69% p<0.025	G1: 24% G2: 13% G3: 16% p>0.15				

Table 32. Treatment harms or tolerability: Tympanostomy tube comparison studies (continued)

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes	Otorrhea	Perforation	Cholesteatoma	Tympano-sclerosis	Occlusion	Granulation
McRae et al., 1989[41]	G1: Shah Teflon tube + aspiration prior to placement (N=55) G2: Shah Teflon tube (no aspiration) (N=55)						G1: 66% G2: 47% p<0.05		
Hellstrom et al., 2011[15]	24 Studies included 5475 subjects			3 Study: Touch vs. non-touch during surgery, no difference in otorrhea. 2 studies: Otic drops at insertion decreased otorrhea In both			1 Study: Shah worse than Mini-Shah after 2 years, p<0.001		

Otorrhea

Otorrhea rates were found to vary by type of tympanostomy tube inserted. Based on observational evidence, Paparella tympanostomy tubes had significantly higher otorrhea rates than Shepard and Shah tubes at 12, 24, and 30 months after placement in one study[38] and at 24 months in comparison to Teflon Shepard tubes in a second.[37]

Otorrhea rates were not significantly related to infusion of N-acetylcysteine at the time of insertion.[35] The systematic review included two studies that reported that topical antibiotics at the time of tympanostomy tube insertion decreased rates of otorrhea (data not provided).[15]

Repeat Tube Placement

In one trial, patients who received Teflon Armstrong tubes were more likely to undergo repeat tube placement than those receiving the silicone Goode-T tube (47% vs. 20%, respectively; no p value reported).[36] In one study, N-acetylcysteine infusion at the time of placement significantly reduced the need for repeat tube placement thereafter ($p<0.025$).[35]

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 either cholesteatoma formation by tube type,[36, 37] or occlusion rates.[39] One study in the systematic review examined tympanosclerosis as an undesired outcome.[58] Standard Shah tubes had higher tympanosclerosis rates than mini-Shah tubes, but the standard Shah tubes also had higher retention rates. Abdullah et al. found a possible increased rate of tympanosclerosis for polyethylene Shah tubes compared with silicone permavent Shah tube (65% vs. 41%, no p value reported). Aspiration prior to tube placement increased the tympanosclerosis rate ($p<0.05$).[41] Finally, Iwaki et al. demonstrated higher rates of granulation tissue at 24 months for silicone Paparella tube compared to either Goode-T silicone or Teflon Shepard tubes (7.5%, 0%, 0% respectively, $p<0.05$).[37]

Surgical Interventions: Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Key Points

- Otorrhea and tympanosclerosis were found to occur more frequently in ears that had tympanostomy tubes placed previously (Strength of evidence low).
- Evidence was insufficient for all other side effects or harms.

Detailed Synthesis

Otorrhea/AOM/Otalgia

Both identified studies[44, 45] and systematic reviews[15, 17] evaluated ear related side effects (Table 33). Otorrhea occurs with a perforated tympanic membrane or an in-place tympanostomy tube, so that outcome is unlikely to occur with watchful waiting.

Table 33. 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	Tympano-sclerosis Myringo-sclerosis	Perforation	Choleste-atoma	Granulation
Browning et al., 2010[17]	1 study by ear (N=78)	1 year	NR	NR	NR	TT vs. WW 38% vs. 1%	NR	NR	NR
	1 study by child (N=248)	24 months	NR	Otorrhea 2%	NR	TT vs. WW 27% vs. 0%	<1%	NR	NR
	1 study (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 study (N=236)	NR	NR	AOM TT vs. non-tubed 27% vs. 11%	NR	NR	NR	NR	NR

Table 33. 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	Tympano-sclerosis Myringo-sclerosis	Perforation	Cholesteatoma	Granulation
Hellstrom et al., 2011[15]	1 study (N=277)						TT vs. M 2.4% vs. 3%		
	1 study (N=111)						TT vs. M vs. no tx TT 5.6%	TT vs. M vs. no tx No surgery 5%	
	1 study (N=429)	5,6 years of age			TT vs. control TT worse RR 17.4	TT vs. control TT worse RR diff: 24.5			
	1 study (N=224)				TT vs. M No difference	TT vs. M TT worse, (p<.001)			
	1 study (N=150)				TT vs. control TT worse 13% vs. 1.3%	TT vs. control TT worse 33% vs. 6.7%			TT vs. control TT worse 4% vs. 0%
	1 study (N=222)	5 years 10 years			TT vs. control TT worse RR 80% RR 80%				
Koopman et al., 2004[45]	G1: TT + cold knife Myringotomy (N=208) G2: Laser Myringotomy (N=208)		NR	Otorrhea G1 more often than G2 p=0.0020 Otalgia without inflammation G1: 1 G2: 0	NR	NR	NR	NR	NR	NR

Table 33. 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	Tympano-sclerosis Myringo-sclerosis	Perforation	Cholesteatoma	Granulation
Mandel et al., 1989[44]	Without "significant" hearing loss" G1: Myringotomy G2: Myringotomy + TT G3: No surgery with significant hearing loss G4: Myringotomy G5: Myringotomy + TT		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 tubes	NR	NR	NR	G3: 1 ear	NR

Abbreviations: AOM = acute otitis media; M = myringotomy; RR = relative risk; TT = tympanostomy tubes; tx = treatment; WW = watchful waiting; yr = year;

Tympanosclerosis

The Hellstrom et al. and Browning et al. systematic reviews both considered rates of tympanosclerosis in tympanostomy tube versus watchful waiting or myringotomy groups.[15, 17] Tympanosclerosis rates were higher in the tympanostomy tube groups in five studies included in the two reviews in subsequent examinations after the tubes had been extruded.[15, 17]

Atrophy

Hellstrom identified four studies that evaluated atrophy subsequent to tympanostomy tubes versus myringotomy or watchful waiting.[15] Results were mixed. Tympanostomy tubes were associated with higher rates of atrophy in two studies and no different in the other two studies.

Other Harms

Hellstrom identified two studies[15] and Browning[17] identified one study that evaluated perforation following tympanostomy tube insertion in comparison with myringotomy or no treatment. In all studies, typanostomy tubes were associated with low rates of perforation, but no significance tests were reported. Similarly, cholesteatoma was reported in one study in Hellstrom; a low rate was only reported in the no treatment group, but no significance tests were reported. Hellstrom reported on granulation in one study comparing tympanostomy tubes with control. Tympanostomy tubes were associated with higher rates of granulation (4% to 0%), but no significance tests were reported.

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

Key Points

- The risk of tympanosclerosis were higher in the tympanostomy tube group than in groups either with no treatment in addition to adenoidectomy or myringotomy in addition to adenoidectomy (strength of evidence was low).
- Evidence for all other harms or side effects was insufficient because evidence was sparse or results were mixed (strength of evidence insufficient for all outcomes).

Detailed Synthesis

Tympanosclerosis

Two studies comparing tympanostomy tubes with myringotomy plus adenoidectomy or adenoidectomy alone found higher rates of tympanosclerosis in the tympanostomy tube group (Table 34).[46, 48, 53]

Otorrhea

Three studies that evaluated otorrhea after tympanostomy tube placement or myringotomy found mixed results.[49-51] One found no difference between interventions.[49] A second found higher rates with tympanostomy tubes.[50] A third found a lower rate in the tympanostomy tube group.[52]

Table 34. Harms or tolerability: Tympanostomy tubes plus adenoidectomy versus myringotomy plus adenoidectomy or adenoidectomy alone

Study	Arm (N)	Study Duration Until Outcome Measurement	Repeat Tubes/ Treat-ment Failure	Otorrhea	Perforation	Tympano-sclerosis Myringo-sclerosis
Brown et al., 1978[46]	G1: TT + AD (N=55) G2: AD (N=55)					G1: N=23 G2: N=0 p<0.05
Lindholdt, 1977[48]	G1: TT+ AD (N=91 ears) G2: AD (N=91 ears)		G1: 13 G2: 6			
D'Eredita and Shah, 2006[49]	G1: CDLM + AD (N=15) G2: TT + AD (N=15)	30 days		Otorrhea G2: 4 reports		
		2 months		G1: 2 reports		
		3 months		G2: 4 reports		
		1 year			G1: 0 G2: 1	
Popova et al., 2010[50]	G1: TT + AD (N=42) G2: M (N=36)			Otorrhea G1: 40% G2: 0%		
Shishegar and Hobhoghi, 2007[51]	G1: TT + AD (n=30 ears) G2: M + AD (N=30 ears)	>6 months		Otorrhea G1: 7% G2: 27% Over 6 mos. Percentage of TT occluded,: 17%		
Vlastos et al., 2011[52]	G1: TT + AD (N=25) G2: M + AD (N=27)		G2: 20% (tubes in non tube group)			
Tos and Stangerup, 1989[53]	G1: TT + AD (N=146) G2: M+ AD (N=146)					G1: 59% G2: 13% p<0.05

Abbreviations: AD = adenoidectomy; M = myringotomy; mos = months; TT = tympanostomy tubes, CDLM = Contact diode laser myringotomy

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

- We found no evidence examining harms or tolerability.

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 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).[20] 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.[56, 57]

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[20] 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.
Williamson et al. 2010[56] Williamson et al. 2009[57] RCT UK	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: 1.40 (95% CI, 0.56 to 3.49) Cough: 1.67 (95% CI, 0.85 to 3.29)

Abbreviations: RR = relative risk

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 there were no serious or lasing harms reported in the six studies of autoinflation but no data was provided (Table 36).[19] It reported that, in one trial, a patient stopped treatment because of pain.[19]

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[19]	NR	Variable	"None of the studies 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"

KQ 4: Comparative Effectiveness of Interventions for Subgroups of Patients

Surgical Interventions: Tympanostomy Tube Comparisons

Key Points

- No studies reported on patient subgroups. Evidence is insufficient.

Surgical Interventions: Tympanostomy Tubes Versus Watchful Waiting or Myringotomy

Key Points

- No studies reported on patient subgroups. Strength of evidence 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 was insufficient).

Detailed Synthesis

One study of children with sleep apnea and OME[52] did not find important differences in hearing thresholds after placement of tympanostomy tubes or myringotomy See Tables 14 and 30). 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 tube or myringotomy groups. At 6 months, results were mixed with some measures improving more quickly in the tympanostomy tube group, while on other measures tube and myringotomy were the same.[52] Twenty percent of the children who initially received a myringotomy, eventually also received tympanostomy tubes.[52] We were unable to compare this rate to 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[19] included adults (Table 37).[59] 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[19]	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)

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 and most commonly is a condition that 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 if it 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 (tympanostomy tubes, myringotomy, and adenoidectomy); nonpharmacological interventions (autoinflation); pharmacological (oral or nasal steroids); complementary and alternative medicine (CAM); and other treatment strategies (watchful waiting). The effectiveness of these interventions has been generally 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 who 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 13 randomized controlled trials (RCTs), four nonrandomized trials (e.g., studies comparing left and right ears), three observational studies, and five systematic reviews (four of which were limited to RCTs). By treatment comparison, the literature included:

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

We had no studies meeting inclusion criteria on any CAM interventions; all watchful waiting studies were combined with myringotomy so we have no independent body of information about other interventions.

Notably, 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 pure OME populations. We did not restrict concomitant conditions as long as the participants had OME. Although we had hoped to be able to provide evidence for different subpopulations, the review pertains mainly to typically developing children across a wide age range. We were unable to find studies on individuals with cleft palate or sensorineural hearing loss that met our inclusion criteria, and 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 and harms of treatment, only a handful included measures of speech, language, behavior, or quality of life. None of the studies 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 interventions, comparisons, and outcomes on which we had studies of at least low or medium risk of bias. 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.[30] We did not evaluate other strength of evidence domains (e.g., publication bias, 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 at all 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.

KQ 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.

Summary of Findings and Strength of Evidence

The evidence base consisted of 20 studies reported in 21 articles (13 RCTs, 3 NRCTs and 4 observational studies) and 5 systematic reviews that provided information on clinical outcomes for various surgical interventions, autoinflation, or steroids.

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
Tympanostomy tubes vs. watchful waiting or myringotomy	MA of 3 RCTs (N=574)	Tympanostomy tubes decreased persistent middle ear effusion at 1 year: 32% less time (95% CI, 17% to 48%)	High for benefit
	MA of 3 RCTs (N=426)	Tympanostomy tubes decreased persistent middle ear effusion at 2 years: 13% less time (95% CI, 8% to 17%)	Moderate for benefit
	MA of 3 RCTs (by ears) (N=230)	Tympanostomy tube groups had better measured hearing at 4-6 months: -10dB (95% CI, -19.12 to -1.05)	High for benefit
	MA of 3 RCTs (N=523)	Tympanostomy tube groups had better measured hearing at 6-9 months: -4.20dB (95% CI, -4.00 to -2.39)	Moderate for benefit
	MA of 3 RCTs (by ears) (N=234)	No difference between groups 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)	No difference between groups in measured hearing at 12 months: -0.41dB (95% CI, -2.37 to 1.54)	Moderate for no difference
	MA of 2 RCTs (N=283)	No difference in measured hearing between groups at 18 months: -0.02 dB (95% CI, -3.22 to 3.18)	Moderate for no difference
Tympanostomy tubes + adenoidectomy vs. myringotomy + adenoidectomy	5 studies: 2 RCTs by person (N=130), 2 RCTs (by ears) (N=85), 1 NRCT (by ears) (N=146)	No difference in measured hearing between groups at 6 and 12 months and greater than 3 years.	Low for no difference
Adenoidectomy vs. no treatment or tympanostomy tubes	MA of 2 RCTs (N=153); MA of 3 RCTs (N=297)	Adenoidectomy better OME resolution 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 (N=298)	Adenoidectomy better OME resolution at 12 months. The risk difference was 0.29 (95% CI, 0.19 to 0.39).	High for benefit
	1 study (N=237)	Adenoidectomy and myringotomy 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 study (N=237)	Adenoidectomy and myringotomy better hearing than with myringotomy alone at 24 months: -0.65 standard mean difference time with hearing level ≥ 20 worse ear (95% CI, -0.91 to -0.39)	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) or	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
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

Abbreviations: 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; vs. versus

Evidence concerning clinical outcome comparisons of tympanostomy tubes in relation to design (i.e., material, coatings, shape or size) or routes or techniques of insertion was considered insufficient because all single studies differed along one or more of these dimensions. Similarly, we found only one study examining different approaches to myringotomy without other interventions.

We found that tympanostomy tubes are more likely to decrease the time with persistent middle ear effusion over 1 year (high strength of evidence) and 2 years (moderate strength of evidence) compared to watchful waiting or myringotomy. Hearing, the more critical and patient-centered clinical outcome, was found to be superior with tympanostomy tubes as well, but for a shorter period of time, 4 to 6 months—measured by ears (high strength of evidence and 6 to 9 months—measured by child (moderate strength of evidence). Shorter time periods are likely to be more important for the youngest children (less 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 outcomes, hearing differences between groups became smaller and not significantly different, 7 to 12 months—measured by ears (low strength of evidence for no difference), 12 and 18 months—measured by child (moderate strength of evidence for no difference). We found limited evidence concerning this treatment comparison in relation to improving OME recurrence, ear ventilation, or episodes of AOM and are unable to comment on these outcomes. We were also unable to disentangle comparisons between tympanostomy tubes and watchful waiting (separately from myringotomy). Because of the limited number of available studies, these two approaches were combined in the systematic review from which we obtained this meta-analysis data.[17]

We examined whether tympanostomy tubes 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 and concluded that because of this consistent finding, strength of evidence was low for no difference.

Adenoidectomy was found to be superior to no treatment or tympanostomy tubes in relation to improving the probability of OME resolution at 6 month and 1 year followup (strength of evidence high). Evidence was insufficient to determine if adenoidectomy also was superior to tympanostomy tubes in relation to hearing outcomes. In addition, adenoidectomy and myringotomy was found to be superior to myringotomy alone in relation to time with effusion and hearing outcomes at 24 months (strength of evidence low). Based on these findings, our review suggests that middle ear ventilation through tympanostomy tubes could be reconsidered when adenoids are removed. Given the similarity of hearing outcomes when tympanostomy tubes or myringotomy are added to adenoidectomy, our findings also suggest that it is unclear whether additional benefit is obtained from the myringotomy procedure.

In relation to nonsurgical interventions, we found evidence of oral steroids providing no short-term improvements in OME (at 1 to 2 months) with the addition of antibiotics (moderate for no difference) and without (low for no difference). One new low risk of bias study provided additional evidence that OME and hearing outcomes are not improved through the use of topical intranasal steroids at up to 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.

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

KQ 2: Health-Related Quality Of Life and Functional Outcomes

As in KQ 1, we sought evidence of the effectiveness of the various interventions to improve quality of life and subjective hearing, speech and language, or behavior.

Summary of Findings and Strength of Evidence

Of the evidence meeting our inclusion criteria for the review overall, only a small number of studies included data on health-related quality of life and functional outcomes. Evidence was limited to the following intervention comparisons: tympanostomy tubes versus watchful waiting or myringotomy and tympanostomy tubes 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. Health-related quality of life and functional status

Intervention and Comparator	Number of Studies (Sample sizes)	Outcome and Results	Strength of Evidence
Tympanostomy tubes vs. watchful waiting or myringotomy	MA of 3 RCTs (N=394)	No difference in language comprehension at 6-9 months: Mean difference=0.09 (95% CI, -0.21 to 0.39)	Low for no difference
	MA of 3 RCTs (N=393)	No difference in language expression at 6-9 months: Mean difference=0.03 (95% CI, -0.41 to 0.49)	Low for no difference
Intranasal steroids vs. controls	1 study (N=144)	No difference in parent reported hearing difficulties at 3 and 9 months and median days with hearing loss at 3 months.	Low for no difference

Abbreviations: CI = confidence interval; MA = meta-analysis; N = number; vs. = versus

Language comprehension and language expression outcomes at 6-9 months were not significantly better among children with OME who received tympanostomy tubes than among those who were limited to watchful waiting or myringotomy (strength of evidence low). These findings correspond to clinical hearing outcomes also not being superior in the tympanostomy tube group after a similar period of followup. Evidence was insufficient to reach conclusions related to behavioral or quality of life outcomes differences for this treatment comparison.

Quality of life outcomes were measured in one small study comparing tympanostomy tubes and adenoidectomy versus myringotomy and adenoidectomy. Therefore, we considered the evidence to be insufficient to reach conclusions.

Parents' reports of their children's hearing difficulties were found in one low risk of bias study comparing intranasal steroids and controls (low SOE for no difference).

KQ 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 and tissue granulation. Specifically, in relation to tympanostomy tubes we considered otorrhea and perforation and such problems as diarrhea and nasal stinging in relation to steroid treatment. 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
Tympanostomy tubes vs. watchful waiting or myringotomy	5 studies (N=1129)	Tympanosclerosis occurred more frequently in ears that had tympanostomy tubes, based on examinations after the tubes had been extruded.	Low for harms
	4 studies (N=960)	Otorrhea occurred more frequently in ears with tympanostomy tubes.	Low for harms
Tympanostomy tubes plus adenoidectomy vs adenoidectomy alone or with myringotomy	2 studies (N=237)	Tympanosclerosis occurred more frequently in ears with tympanostomy tubes.	Low for harms
Topical nasal steroids vs. control	1 study (N=170)	No difference in mild adverse events such as nasal stinging, dry throat, and cough	Low for no difference

Abbreviations: N = number; NR = not reported; SR = systematic review; vs. = versus

We found consistent evidence that tympanosclerosis was more common in children who had tympanostomy tubes than those who were watched or who had myringotomy, both in comparison to adenoidectomy and watchful waiting or myringotomy (strength of evidence low). Otorrhea was also more common among ears with tympanostomy tubes (strength of evidence low).

The systematic review concerning nasal steroids[56] we included as evidence found few mild adverse events in the studies they reviewed. Similarly, one new study[57] found no differences between groups in relation to stinging nose, nose bleed, dry throat, or cough. We therefore conclude 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 concerning oral steroids and serious adverse events from oral or topical steroids.

We found no evidence concerning harms from adenoidectomy, including no data on any risks from having a surgical procedure. Similarly, we found insufficient evidence concerning the surgical risks from the insertion of tympanostomy tubes or myringotomy procedures.

KQ 4: Outcomes for Important Patient Subgroups

We aspired to differentiate treatment efficacy 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 are 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 (Table 41) Vlastos et al. performed a study specifically on 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.[52] A study of autoinflation that was included in the systematic review[19] included as evidence found differences in rates of recovery between those receiving autoinflation and those who were in the control group (strength of evidence low).

Table 41. Strength of evidence for subgroups

Intervention and Comparator	Number of Studies (Sample sizes)	Subgroup and Results	Strength of Evidence
Tympanostomy tubes + adenoidectomy vs. myringotomy + adenoidectomy	1 RCT (N=52)	Children with sleep apnea and OME: no difference between tympanostomy tubes and myringotomy outcomes (all children had received adenoidectomies)	Insufficient (one study)
Autoinflation vs. control	1 RCT (N=198)	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, 44% to 47%.	Low for benefit

Abbreviations: TT = tympanostomy tubes; OME = otitis media with effusion; tx = treatment

KQ 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 were conducted by the Cochrane Collaboration[18-20] and the fifth was sponsored by the Swedish government.[15] We sought to determine if 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, such as the comparative effectiveness of different types of tympanostomy tubes or different approaches to myringotomy as well as the use of CAM therapies in treating OME and the value of watchful waiting. Lastly, 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 due to preexisting comorbidities.

Overall, we found little new evidence that was not included in the earlier reviews. We found one new low risk of bias RCT concerning topical steroid treatment.[56, 57] However, new evidence from non-randomized trials and observational studies did not add appreciably to our understanding of these treatment comparisons. Nor were we able to uncover much evidence regarding special populations. Thus our conclusions are largely a compilation of those that have been made in the previous systematic reviews.

Implications for Clinical and Policy Decisionmaking

The evidence from this review largely reiterates that provided in past systematic reviews of treatments for OME. We did not find new evidence to refute the findings of Thomas et al.[20] concerning the lack of effectiveness of oral and intranasal steroids as treatment for OME and have provided additional evidence from a recent RCT of Williamson et al.[56, 57] that intranasal steroids were not found to be effective. This evidence supports the recommendations made by the American Academy of Pediatrics that neither oral nor topical nasal steroids be used in the treatment repertoire for OME.

We found some evidence that tympanostomy tubes are effective for reducing effusion and for improving hearing but their effect is limited, no doubt a consequence of the fact that effusion

resolves even if untreated. However, we do not have evidence regarding which types of tubes or tube routines for insertion are more beneficial for reducing fluid and mitigating harms and whether there are differences 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 sub-populations of children with cleft palate or Down syndrome need to follow a different treatment course as typically developing children.

Overall, there was evidence that children with tympanostomy tube placement for OME are more likely to have resolution of middle ear effusion for up to 2 years after the procedure. There was a similar difference noted 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 short and 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 negatively impact important outcomes, and how these may differ for individuals at different developmental stages and ages.

Many primary care providers refer patients with prolonged effusion and mild to moderate hearing loss to otolaryngologists for placement of tympanostomy tubes, after 3 months of effusion. However, our synthesis of the available evidence, did not find functional or quality of life differences between subjects who had tympanostomy tube placement versus watchful waiting for OME with only mild to moderate hearing loss.

Currently, many children with craniofacial syndromes or underlying hearing loss have tympanostomy tubes placed either prophylactically (e.g. 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 a more effective treatment for middle ear effusion relative to watchful waiting or tympanostomy tube placement. However, surgery for adenoidectomy is more invasive and raises concern that it may impose more short term complications than tympanostomy tubes but we did not find 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 expert opinions contained within clinical practice guidelines, clinician experience, 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.”[60]

Population

Findings about all interventions are likely to be applicable to non-infant, otherwise healthy children. However, the evidence base is limited for adults and for infant children or 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 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 co-morbidities, we were unable to find

sufficient, if any studies on these populations, and so do not know if the relative efficacy of treatment comparisons will be similar for them.

Intervention and Comparators

We present evidence on all of the commonly used treatments for OME, including tympanostomy tubes, myringotomy, adenoidectomy, and watchful waiting. We present evidence on oral and intranasal steroids because, while not currently recommended in major guidelines or approved by the Food and Drug Administration for treating children with OME, our TEP believed that it was still a commonly used intervention. We also include autoinflation, because, while not typically used in the U.S., offers an alternative non-invasive treatment strategy for older children and adults. We sought to determine the applicability of "watchful waiting" but because we were unable to isolate this approach from myringotomy, we were unable to determine the population and length of time that this approach may be most useful.

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, health care utilization as well as functional and quality of life outcomes. However, the bulk of the literature only examined whether the interventions reduced OME or improved hearing. A few studies included in the systematic reviews examined language development and behavior problems, and a few of the systematic reviews and two recent RCTs examined quality of life outcomes. No studies focused on parental and patient satisfaction with care or heath care utilization. Thus, there is little that we can say about these other important outcomes. We acknowledge the central role that continued effusion and hearing play in these other outcomes, yet the broad range of outcomes are important in their own right. Moreover, investigators chose different measures to index many of these outcomes (e.g., quality of life), so that 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 late effects of OME that failure to reach conclusions about effects of OME on long term speech and language are in part due to lack of uniformity in instrumentation. The most robust test of whether a particular treatment was efficacious is to examine treatment comparison pre-post differences; however, this was not uniformly done. There was a similar lack of uniformity in reporting harms and failure to provide information about patients in all arms of a study.

Time Frames

Studies varied in relation to their length of followup periods. Many included studies measured results between 3 months and 12 months following treatment. However, for some comparisons, such as differences between types of tympanostomy tubes and autoinflation and controls, followup was generally shorter. However, for any given comparison, time frames were rarely uniform, making cross-study integration difficult.

Settings

Studies were conducted in clinical setting and generally included populations from the United States and European countries. There were a few studies conducted in developing countries such as Bulgaria and non-Western countries, including Japan, Egypt, and Iran.

Limitations of the Review Process

As noted previously, we limited the synthesis to low and medium risk of bias. Given the limitations of the included studies and their applicability to other contexts, however, including high risk-of-bias studies would likely have increased the pool of evidence without resulting in more actionable evidence.

Limitations of the Evidence Base

The evidence base was limited by the decision to restrict studies to those that examined the treatments in individuals with OME. Much of the literature only indicated that the study participants had otitis media without providing information about the type 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.

The evidence base was further limited by a lack of low risk of bias studies. Overall, we rated only one of the 20 new studies included in our analysis as low risk of bias. Some of the major reasons we rated studies as medium risk of bias included lack of information regarding randomization, blindedness of providers, and high rates of attrition. Overall, the better studies were in the systematic reviews that we included in our review.

The evidence regarding management of OME is further confounded by a variety of methodological limitations. Studies employ a range of criteria for diagnostic inclusion as well as a wide variety in outcomes measures and scant description of how those measures are obtained. Even when measures are similar there are often variations in when they are collected, the qualifications of those conducting the measures, and the ways in which they are reported. Most studies include a wide range of children (2-14 years of age). It is likely that those children age 6 years or more who experience OME are at different risk than those who experience episodes of OME in their early years but who experience no episodes after age 4. Including all children in studies may mask the benefits of treatment of individuals at varying ages. Because of this heterogeneity, we were unable to perform any quantitative analysis.

Few studies provided a power analysis so making it difficult to interpret failure to find differences. However, we suspect that power was low given the relatively small, heterogeneous samples and extensive attrition in some trials.

Research Gaps

Given the severe limitations of the evidence base—both gaps 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 prior to surgical intervention with children Although children 3 years or older may be able to tolerate a mild-moderate hearing loss for a period of 3-6 months or longer without risk to language outcomes, the effect of the same hearing loss on children 24 months or younger is unknown. Children who are in the earliest stages of phonological and language development are likely to be much more vulnerable to the effects of OME induced hearing loss than children 3 years of age or older. A hearing loss of any degree creates a barrier to full access to the auditory signal. Infants and toddlers who are learning the rules that govern language comprehension and production are likely to be vulnerable to the hearing loss imposed by OME. Research in the area of infant speech perception and later outcomes has demonstrated that babies who were able to distinguish between two simple vowels /i/ (tea) and /u/ (two) at 6 months of age had larger vocabularies when they were 18 an 24 months old than those who could not. Early vocabulary development is important because it is one of the strongest predictors of academic achievement.[61]

In many instances children younger than 2 years of age are underrepresented in studies and when they are included the results are not portioned by age. We recommend that RCT's that include children at the most vulnerable ages examine effects of OME on morphosyntactical development (0-36 months) and report results partitioned by age groups reflecting developmental vulnerability.

Evidence regarding the impact of interventions for OME in at-risk sub-populations is virtually non-existent. Children with a variety of developmental or sensory delays are usually excluded from studies investigating treatment outcomes for OME, including those with Down syndrome, permanent sensorineural or conductive hearing loss, craniofacial anomalies affecting Eustachian tube function such as cleft palate, ciliary dyskinesia, and children on the autism disorder spectrum. All of these subgroups are at-risk for development of speech and language because of these comorbidities and the addition of a 15-20 dB hearing loss due to OME increases their vulnerability. Although RCTs may not be feasible because of ethical concerns, as well as the relatively low incidence of these conditions, carefully controlled observational studies are needed to guide management of OME in these subgroups.

Despite the high prevalence of OME in children with cleft palate,[62, 63] we found no evidence on treatment of OME in this population that met our inclusion criteria. Studies were mainly excluded because tympanostomy tube placement occurred prophylactically during other craniofacial surgery and was not limited to just to children with diagnoses of OME. A recent 2009 systematic review, conducted by Ponduri and colleagues,[64] assessed evidence on OME related symptoms and hearing, speech and language outcomes in children with cleft palate who received early placement of tympanostomy tubes. Only three of the studies included in the systematic report are limited to children who were diagnosed with OME at the time of initial assessment.[65-67] These studies were excluded for 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 University of Pittsburgh, are currently conducting an observational study of adults who have received tympanostomy tubes for the treatment of chronic OME and/or Eustachian tube function.[68] The described aims of the study are to explore the relationship

between the results of standard Eustachian tube function tests, and those for the anatomy and function of the Eustachian tube of adults with a disease condition that is likely to be caused by poor Eustachian tube function. The investigators plan to evaluate study participants for a number of disease conditions (examples: nasal allergy, acid reflux disease) that are related to poor Eustachian tube function. The investigators hypothesize that if the results of the standard Eustachian tube function tests can be explained by the physical anatomy of Eustachian tube and back of the nose, the functional anatomy (e.g. movements during swallowing) of the Eustachian tube, or the presence of allergy and/or acid reflux disease, these findings will encourage development and/or use of new medical and/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 mainly limited to resolution of OME and hearing. As important as these are because they can be easily measured, we do not know to what extent they are correlated with functional outcomes such as speech and language development and quality of life. Also, we found no information on how treatment choice during one OME episode affected later utilization of health care services. We believe that one area for future research is to establish whether treatments can impact these 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,[69] and speech recognition in noise.[61, 70] Presumably, these skills affect children's ability to attend to instruction in noisy classrooms. One small study by Hall et al.[71] found that tympanostomy tubes 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 only included a small number of children. However, replication with larger samples as part of a clinical trial would be extremely useful as there is relevance for daily life.

There were no studies that examined either health care utilization or parent satisfaction with care. Whether any of these treatments under question reduce time spent at the physician's office, along with costs associated with loss of productivity are not known. Anecdotally, we know that parents often request tympanostomy tubes because they hope that it will reduce time that their children are ill. The unexamined issue is whether receiving tubes or another treatment options affects these secondary outcomes.

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) or complications from adenoidectomy surgery.

Gaps in Interventions

This review provided little evidence regarding different types of tubes or routines for insertion. However, an ongoing Swedish trial plans to enroll 400 children between the ages of 1 and 10 in an RCT comparing complications from four types of tubes, two different materials, and two different shapes.[72] 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 tube from the tympanic membrane, and various harms including persistent tympanic membrane perforation, need for tube extraction (i.e., pain or infection), pain leading to health care contact, tube related ear infection, obstruction of tube and presence of myringosclerosis. The study will include both children with recurrent acute otitis media (RAOM) and OME, but presentation of the results (i.e., complications in OME and RAOM reported separately) could inform best practices in tympanostomy tube choice for children with OME.

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 CAMs, including dietary modifications, has been identified. We identified an ongoing, and potentially promising RCT that addresses the benefit of dietary modification in the treatment of OME.[73] The study, being conducted at the Department of Otolaryngology at the University Hospital 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, 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, bilateral myringotomy with tympanostomy tubes, in conjunction with food allergy testing and management; and bilateral myringotomy with tympanostomy tubes 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 tube expulsion, with a further year of followup evaluations at 3 month intervals. At the time of this report, this study is listed as recruiting.[73]

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 and some researchers believe gastroesophageal reflux disease (GERD) may be a cause of OME.[74] We identified two unpublished trials which evaluate the treatment of OME in children with Proton Pump Inhibitors, anti-reflux medication. One study of chronic OME is listed as completed,[72] with December 2009 reported as the final data collection date for the primary outcome measure(s), however we were unable to identify any related publications, 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. While the primary goal of this study is to collect data for the purposes of 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 lansoprazole. The larger clinical trial that is set to follow could provide a clearer picture of the role gastric reflux in OME, and inform treatment decisions although recent evidence of risks associated with proton-pump inhibitor use in children will need to be incorporated into treatment decisions.[75]

A prospective cohort study, ongoing since 2006, in children 3 to 6 years of age who underwent tympanostomy tube insertion for chronic OME aims to determine if Eustachian tube function tests and gas exchange tests can be used to successfully predict whether a child who has tympanostomy tubes surgically placed in their eardrum because of middle-ear disease will redevelop the disease again after the tube is nonfunctional and/or expelled.[76] The investigators

state that the results of this 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 tympanostomy tubes become nonfunctioning or extruded.

Deficiencies in Methods

Meta-analyses can be used to strengthen the power for finding effects in studies where there are a limited number of participants in individual studies. However, in many cases meta-analysis is hampered by methodological differences in studies. In particular, vastly different outcome measures and outcome assessment times limits the studies that can be included. If there was agreement among investigators about outcomes to be included in studies, more quantitative analyses could be performed. 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, we found uneven bodies of evidence across treatment comparisons. In particular, limited data was available on primary patient-centered outcomes: hearing loss, functional limitations, and quality of life. Additional research is needed to develop a sufficient evidence base to support treatment decisions, particular in subpopulations.

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