Evidence-based Practice Center Systematic Review Protocol

Project Title: Tympanostomy Tubes

I. Background and Objectives for the Systematic Review

Uncertainty in the comparative effectiveness of tympanostomy tubes for children with otitis media, indications for tympanostomy in children, prescription of antibiotics for children with tube otorrhea, and prophylactic water precaution devices prompted AHRQ to commission a review of the evidence to help inform recommendations concerning surgical indications and management strategies for tympanostomy tube placement.

The pathogenesis of otitis media often involves an antecedent viral upper respiratory tract infection that causes Eustachian tube obstruction, negative middle ear pressure, and accumulation of fluid in this normally air-filled space. Acute otitis media (AOM) is defined as the presence of fluid in the middle ear with signs and symptoms of an acute infection, such as fever and ear pain. Otitis media with effusion (OME) is defined as the presence of fluid in the middle ear behind an intact tympanic membrane without signs and symptoms of an acute infection; it is defined as chronic OME, if effusion persists for 3 months or longer.[1] The two clinical conditions, although distinctly defined, are, in fact, closely related and can overlap. Children with chronic OME are prone to recurrent AOM episodes, and after an AOM episode all children have OME for some time.[2] Myringotomy with tympanostomy tube placement is the most common ambulatory surgery performed on children in the United States, with almost 700,000 procedures performed yearly at an estimated annual cost of $1.8 billion.[3] The proceedings of the National Summit on Overuse, convened in 2012, reported that tympanostomy tube surgeries increased from just under 500,000 in 1996 to more than 650,000 in 2006, according to the National Center for Health Statistics. Based on a sample of continually enrolled children into a treatment pathways database and a Medicaid database, 2.5 percent of all U.S. children 2 years old and older had tympanostomy tubes inserted in 2010.[4] A 1994 study reported indications for tympanostomy tube placement in children: 30% were for persistent OME, 24% for recurrent AOM, and 46% of surgical candidates had both recurrent AOM and persistent OME.[5]

Chronic OME can result in hearing deficits, which may put a child at risk for speech and language delays, behavioral changes, and poor academic achievement. Recurrent AOM has been shown to impact quality of life for patients and their caregivers.[6] The comparative effectiveness of tympanostomy tubes for chronic OME and recurrent AOM is likely influenced by the many factors that affect the prognosis for middle ear disease in children, including current age, age at first diagnosis, frequency of respiratory tract infections and day care exposure.[7] Children with middle ear effusions that are bilateral and continuously present are likely at higher risk. Tube lifespan is likely to be an important mediator of comparative effectiveness.

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A risk-centered approach would ideally incorporate important known determinates of outcome in preference to a single threshold for duration or frequency of a diagnosis.[8]

Certain children, including those with Down syndrome and cleft palate, have a very high risk for middle ear disease. In a retrospective review of patients with Down syndrome, the authors found that the majority of patients required two or more sets of tubes during their childhood.[9] Due to the effects of palatal dysfunction on Eustachian tube function, children with cleft palate also have a high incidence of OME and associated hearing loss.[10] The American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) clinical practice guideline (CPG) identifies a subpopulation of children who may be at increased risk for speech, language, or learning problems from otitis media because of baseline sensory, physical, cognitive, or behavioral factors.[1] The inclination to treat OME more aggressively in these children is reflected in a study that found that approximately 1 in 6 children with autism spectrum disorder underwent tympanostomy tube placement.[11]

The AAO-HNS CPG concludes that the efficacy of tympanostomy tubes for preventing recurrent AOM is unclear, with systematic reviews reporting insufficient evidence, small short-term benefits, or moderate benefits of similar magnitude to antibiotic prophylaxis. They note the overall favorable natural history of otitis media.[12] The AAO-HNS CPG recommends that clinicians should offer tympanostomy tubes to children with recurrent AOM and middle ear effusions based on shared decisionmaking with the child's caregiver. They conclude that the effect is no longer significant if one considers RCTs limited to trials with AOM that clears between episodes (without chronic OME) and recommend that tubes not be placed in children with recurrent AOM who have a normal ear examination at the time of assessment for tube candidacy.[1] The American Academy of Pediatrics CPG discourages routine use of prophylactic antibiotics to prevent recurrent AOM.[13] The reluctance to use antibiotic prophylaxis because of concerns about antibiotic resistance may result in increased use of tympanostomy tubes in children with recurrent AOM. Attempts to promote the use of more rigorous criteria for the diagnosis of AOM may also result in improved comparative effectiveness of tympanostomy tubes.

A 2014 review by Tsao and Goode provides a narrative summary of their search for evidence regarding water precautions to prevent posttympanostomy tube otorrhea (Key Question [KQ] 4).[14] They discuss systematic reviews published in 1999 and 2002 and a randomized controlled a trial published in 2005, and conclude that water precautions should not be routinely advised.

Acute otorrhea is common after tympanostomy tube placement.[15] Postoperative otorrhea (up to 30 days after surgery) is common and reflects, in part, underlying (preoperative) middle ear glandular changes and inflammation. Some otorrhea is to be expected, since the role of the tube is to ventilate the middle ear. Episodes of otorrhea that reflect acute bacterial infection may be otherwise asymptomatic and less troublesome than episodes AOM in children with intact eardrums.[16] However, the otorrhea is sometimes chronic, associated with a foul odor, fever, or pain, and it may negatively affect quality of life. Treatment is aimed at eradicating bacterial infection, using antibiotic eardrops with or

ithout glucocorticoids (to reduce symptoms).[17] A number of subgroups of acute otorrhea exist, including: 1) otorrhea in the immediate postoperative period, 2) otorrhea caused by the same pathogens as AOM, including *Moraxella catarrhalis, Haemophilus influenzae*, and *Streptococcus pneumoniae*, and 3) otorrhea resulting from superinfection with *Staphylococcus aureus*, including methicillin resistant *Staphylococccus aureus* (MRSA) and *Pseudomonas* associated with biofilms.[18]

Recently, the Cochrane Ear, Nose and Throat Disorders Group published a protocol for a systematic review of pharmacological and conservative interventions for ear discharge associated with ventilation tubes outside the postoperative period.[19] When the Cochrane review is completed, it will overlap with KQ 5 of the current protocol.

We searched Devices@FDA.gov at www.accessdata.fda.gov/scripts/cdrh/devicesatfda/ for the classification product code "ETD" (tympanostomy tubes). This returned 109 records, all of which are deemed to be substantially equivalent to previous devices (indicating there are no new data that the FDA considered) or have original approvals that predate the electronic records and require either contacting the manufacturer for information or requesting it from the FDA.

The objectives for the systematic review are: 1) to evaluate the effectiveness of tympanostomy tubes in children with chronic otitis media with effusion and recurrent acute otitis media, 2) to evaluate the frequency of adverse effects and/or complications associated with tympanostomy tube placement, 3) to evaluate the necessity for water precautions in children with tympanostomy tubes, and 4) to evaluate the comparative effectiveness of available treatment for otorrhea in children with this complication.

II. The Key Questions

With input from clinical experts during Topic Refinement, we have developed the following KQs and study eligibility criteria to clarify the focus of the proposed systematic review. Based on public comments (solicited from June 22 to July 13, 2015), the previously posted KQs have been reorganized and revised to clarify the lists of outcomes, to clarify inclusion of the use of episodic or prophylactic antibiotic therapy as part of watchful waiting, and the definitions of chronic OME and recurrent AOM in the eligibility criteria have been clarified to enhance transparency.

The following are the KQs to be addressed by the review:

Question 1: For children with chronic otitis media with effusion, what is the effectiveness of tympanostomy tubes, compared to watchful waiting, on resolution of middle ear effusion, hearing and vestibular outcomes, quality of life and other patient-centered outcomes?

- **a.** What factors (such as age, age of onset, duration of effusion, comorbidities, and sociodemographic risk factors) predict which children are likely to benefit most from the intervention?

b. Does obtaining a hearing test help identify which children are more likely to benefit from the intervention?

Question 2: For children with recurrent acute otitis media, what is the effectiveness of tympanostomy tubes, compared to watchful waiting with episodic or prophylactic antibiotic therapy, on the frequency and severity of otitis media, quality of life, and other patient centered-outcomes? What factors (such as age, age of onset, number of recurrences, presence of persistent middle ear effusion, comorbidities, and sociodemographic risk factors, history of complications of acute otitis media, antibiotic allergy or intolerance) identify children who are most likely to benefit from the intervention?

Question 3: What adverse events, surgical complications, and sequelae are associated with inserting tympanostomy tubes in children with either chronic otitis media with effusion or recurrent acute otitis media?

Question 4: Do water precautions reduce the incidence of tympanostomy tube otorrhea, or affect quality of life?

Question 5: In children with tympanostomy tube otorrhea, what is the comparative effectiveness of topical antibiotic drops versus systemic antibiotics or watchful waiting on duration of otorrhea, quality of life, or need for tube removal?

Eligibility Criteria

For all KQs, the Eligibility Criteria will be:

Populations

All KQs: Ages: infant (28 days to 12 months), toddler (13 months to 2 years), early childhood (2 to 5 years), middle childhood (6 to 11 years), early adolescence (12 to 18 years).[21]

All KQs: Subpopulations:

- Down syndrome, cleft palate, other craniofacial anomalies, primary ciliary dyskinesia
- High-risk children: preexisting hearing loss, speech/language problems, or developmental disorders.
- Sociodemographic risk factors

KQ 1: Children with chronic OME (allow study-specific definitions of "chronic" but use as a standard definition effusion that persists for 3 months or longer[1]). Exclude children with chronic suppurative otitis media.

KQ 2: Children with recurrent AOM (allow study-specific definitions of "recurrent" but use as a standard definition three or more well-documented and separate AOM episodes in the past 6 months or at least four well-documented and separate AOM episodes in the past 12 months with at least one in the past 6 months[1])

- With middle ear effusion

- Without middle ear effusion

KQ 3, 4: Children with tympanostomy tubes placed for OME or AOM
KQ 5: Children with acute tympanostomy tube otorrhea beyond the immediate postoperative period (allow study-specific definitions of "postoperative period," but use as a standard definition otorrhea occurring more than 30 days after surgery).

- Symptomatic or asymptomatic

Interventions/Exposures

- KQ 1, 2, 3: Myringotomy with tympanostomy tube placement with or without adenoidectomy
  - Short-term tubes (generally last 10 to 18 months)
  - Long-term tubes (e.g. T-tubes, typically remain in place for several years)
- KQ 4: Water precautions
  - Avoidance of high-risk activities
  - Ear plugs, headbands, other canal occlusion methods
  - Ototopical antibiotic prophylaxis
- KQ 5: Ototopical preparations
  - Ototopical antibiotics
    - FDA approved (i.e., ofloxacin otic 0.3%)
    - Other, non-FDA approved (e.g. ciprofloxacin 0.3%)
  - Combination antibiotic and corticosteroid drops
    - FDA approved (i.e., ciprofloxacin 0.3% + dexamethasone 0.1%)
    - Other, non-FDA approved preparations (e.g. hydrocortisone + bacitracin + colistin)

Comparators

- KQ 1:
  - Watchful waiting
  - Adenoidectomy
- KQ 2:
  - Systemic antibiotics for recurrent episodes of AOM
  - Prophylactic antibiotics
  - Adenoidectomy
- KQ 3: No comparator
- KQ 4:
  - No water precautions
  - Ear plugs
  - Prophylactic ear drops after water exposure
  - Avoidance of higher risk activities
- KQ 5:
  - Watchful waiting
  - Oral (systemic) antibiotics

Outcomes

- KQ 1, 2: Comparative effectiveness of tympanostomy tubes
  - Hearing and vestibular outcomes
    1. Improved hearing levels (audibility)
    2. Tests of auditory perception and discrimination (clarity)
    3. Balance and coordination (vestibular function)
  - Quality of life and patient-centered outcomes
    1. Global and otitis-specific child and parental quality of life
    2. Speech and language outcomes
    3. Educational achievement
    4. Behavioral outcomes such as disobedience, enuresis, or tantrums
  - Intermediate outcomes
    1. Prevalence of middle ear effusion
    2. Antibiotic use
    3. Recurrent AOM/otorrhea (KQ 2)
    4. Need for replacement of tympanostomy tubes
- KQ 3: Adverse events, surgical complications, and sequelae
  - Intraoperative and immediate postoperative anesthetic and surgical adverse events
  - Medium-term
    1. Otorrhea
    2. Blockage of the tube lumen
    3. Granulation tissue
    4. Premature extrusion
    5. Tympanostomy tube displacement into the middle ear
    6. Persistent perforation of the tympanic membrane, possibly
    7. Other reported (plausibly related to TT)
  - Long-term
    1. Myringosclerosis
    2. Tympanic membrane atrophy, atelectasis and retraction pockets
    3. Worsened hearing thresholds
    4. Other reported (plausibly related to TT)

- KQ 4: Water precautions:
  - Final health or patient-centered outcomes
    1. Child and parental quality of life
  - Intermediate outcomes
    1. Otorrhea, incidence and duration
- KQ 5 Treatment of otorrhea:
  - Final health or patient-centered outcomes
    1. Global and otitis-specific child and parental quality of life
  - Intermediate outcomes
    1. Duration of otorrhea
    2. Need for removal of tympanostomy tube

Timing

- Any duration of followup

Setting

- Primary and specialty care

Study Design

- Randomized controlled trials (all KQ)
  - Per ear comparative trials will be excluded
- Nonrandomized comparative studies, prospective or retrospective (all KQ)
- Prospective surgical single group studies enrolling at least 50 subjects (KQ 3)
- Population based retrospective single group studies (registry studies) with ≥1000 subjects (KQ 3)

Comments About the Eligibility Criteria

The preliminary literature search identified a large number of observational studies of various types. There is interest in comparative effectiveness of tympanostomy tubes in high-risk and at-risk populations, and in defining harms. Children at high risk of chronic otitis media or recurrent acute otitis media have been excluded from randomized controlled trials. Many randomized trials are relatively small, limiting their ability to define risks of less common harms.

III. Analytic Framework

To guide the assessment of studies that examine the association between tympanostomy tube placement and intermediate and final health outcomes, and harms (KQs 1, 2 and 3; Figure 1), need for water precautions (KQ 4; Figure 2), and treatment of otorrhea (KQ 5; Figure 3), the analytic frameworks map the specific linkages associating the populations of interest, the exposures, modifying factors, and outcomes of interest.

The frameworks graphically present the key components of well-formulated study questions:

1) Who are the participants (i.e., what is the population and setting of interest, including the diseases or conditions of interest)?
2) What are the interventions?
3) What are the outcomes of interest (intermediate and health outcomes)?

These analytic frameworks depict the chains of logic that evidence must support to link the studied interventions studied.

Figure 1. Tympanostomy Tubes in Children with Chronic OME or Recurrent AOM (Key Questions 1, 2, and 3)

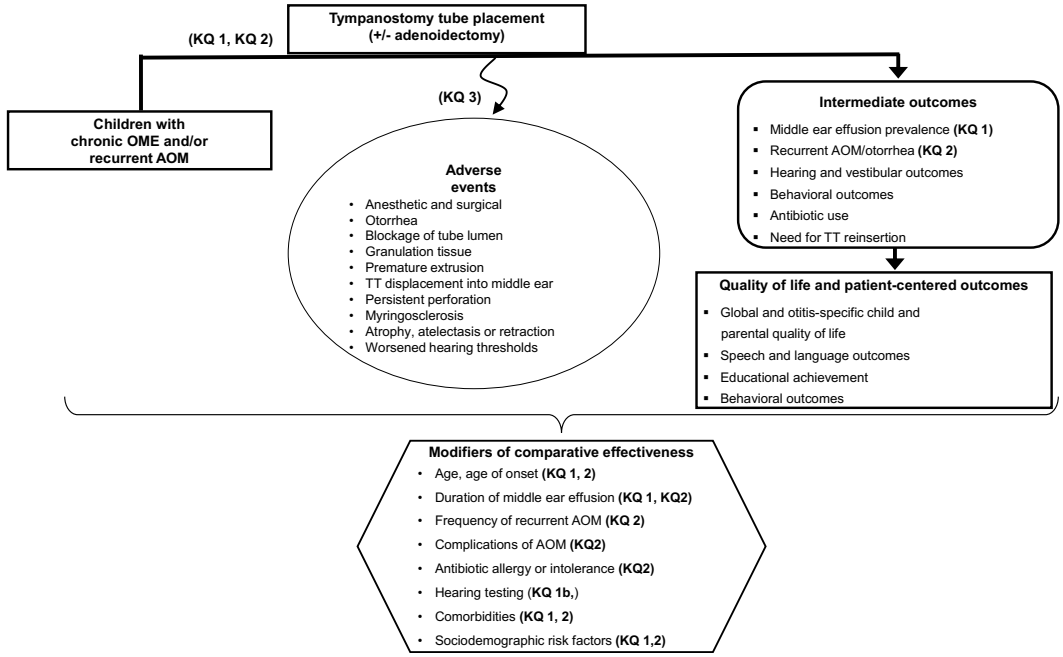


Figure 2. Need for Water Precautions in Children with Tympanostomy Tubes (Key Question 4)

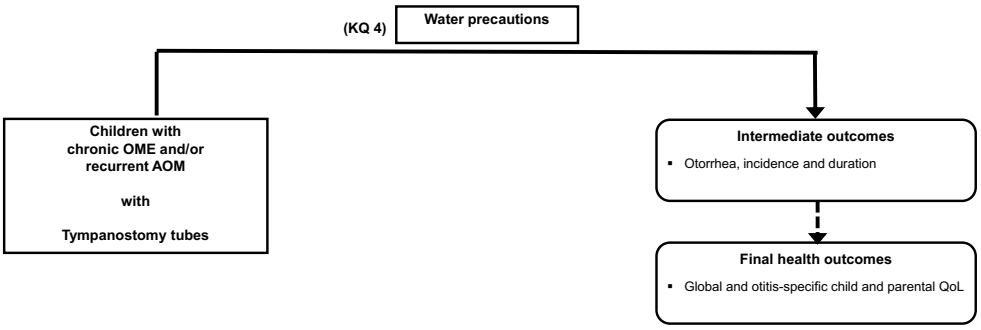
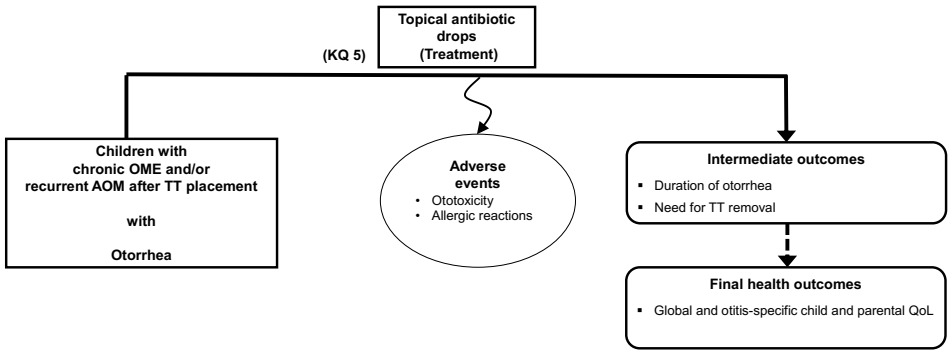


Figure 3. Treatment of Otorrhea in Children with Tympanostomy Tubes (Key Question 5)



IV. Methods

The Evidence-based Practice Center (EPC) will conduct the review based on a systematic review of the published scientific literature using established methodologies as outlined in the Agency for Healthcare Research and Quality's (AHRQ) Methods Guide for Comparative Effectiveness Reviews.[20]

Criteria for Inclusion/Exclusion of Studies in the Review – Please refer to Section II *The Key Questions*, where the Eligibility Criteria are listed after the KQs.

Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies to Answer the KQs – We will conduct literature searches of all studies in MEDLINE®, both the Cochrane Central Trials Registry and Cochrane Database of Systematic Reviews, EMBASE®, and CINAHL® databases (from inception) to identify primary research studies meeting our criteria. These databases should more than adequately cover the published literature on this topic. We anticipate using the search strategy in Appendix A, adapted as needed for each database. The search strategy will be peer reviewed by an independent, experienced information specialist/librarian. We will ask the TEP to provide citations of potentially relevant articles. Additionally, we will peruse the reference lists of published clinical practice guidelines, relevant narrative and systematic reviews, and Scientific Information Packages from manufacturers. We will use existing systematic reviews primarily as sources of studies; we will extract and incorporate all studies *de novo* and will not summarize or incorporate existing systematic reviews, per se. (We may compare and contrast our review conclusions with those from existing systematic reviews in the Discussion section.) Clinicaltrials.gov and the Food and

Drug Administration websites will be searched. All articles identified through these sources will be screened for eligibility using the same criteria as was used for articles identified through literature searches. Peer and public review will provide an additional opportunity for the TEP and other experts in the field to ensure that no key publications have been missed. The search will be updated upon submission of the draft report for peer and public review.

All citations found by literature searches, including from sources other than electronic databases (e.g., TEP, existing systematic reviews) will be independently screened by two researchers. At the start of citation screening, we will implement a training session, in which all researchers will screen the same articles and conflicts will be discussed. We will iteratively continue training until we have reached agreement regarding the nuances of the eligibility criteria for screening. During double-screening, we will resolve conflicts as a group. All screening will be done in the open-source, online software Abstrackr (http://abstrackr.cebm.brown.edu/).

Data Extraction and Data Management – Each study will be extracted by one methodologist. The extraction will be reviewed and confirmed by at least one other experienced methodologist. Any disagreements will be resolved by discussion among the team. Data will be extracted into customized forms in Systematic Review Data Repository (SRDR) online system (http://srdr.ahrq.gov), each designed to capture all elements relevant to the KQs. Upon completion of the review, the SRDR database will be made accessible to the general public (with capacity to read, download, and comment on data). The basic elements and design of these forms will be the similar to those we have used for other comparative effectiveness reviews and will include elements that address population characteristics; descriptions of the interventions, exposures, and comparators) analyzed; outcome definitions; effect modifiers; enrolled and analyzed sample sizes; study design features; funding source; results; and risk of bias questions.

Assessment of Methodological Risk of Bias of Individual Studies – We will assess the methodological quality of each study based on predefined criteria. For RCTs, we will use the Cochrane risk of bias tool [22], which asks about risk of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential biases. For observational studies, we will use relevant questions from the Newcastle Ottawa Scale.[23] Any quality issues pertinent to specific outcomes within a study will be noted and applied to those outcomes. Any quality issues pertinent to specific outcomes within a study will be noted and considered when determining the overall strength of evidence for conclusions related to those outcomes.

Data Synthesis – All included studies will be summarized in narrative form and in summary tables that tabulate the important features of the study populations, design, intervention, outcomes, and results. We plan to build off of and improve on the tables used in previous systematic reviews. These included descriptions of the study design, sample size intervention(s), followup duration, outcomes, and study quality.

We will analyze different study designs separately and, if appropriate, together. We will compare and contrast populations, exposures, and results across study designs. We will examine any differences in findings between observational and intervention studies. We will evaluate the risk of bias factors as possible explanations for any heterogeneity.

We expect to conduct random effects model meta-analyses of comparative studies, if they are sufficiently similar in population, interventions, and outcomes. Specific methods and metrics (summary measures) to be meta-analyzed will depend on available, reported study data, but we expect to summarize odds ratios of categorical outcomes and, if pertinent, net change of continuous outcomes (e.g., quality of life scores). Statistical heterogeneity will be explored qualitatively and, if appropriate data are available, we may also conduct metaregression analyses to evaluate study, patient, and intervention features, (as listed in the KQs) to evaluate dose-response. We will explore subgroup differences within (and possibly across) studies based on the list of comparisons described in the KQs. We will also explore the possibility of conducting a network meta-analysis of clinical outcomes to compare treatment alternatives across studies.

Grading the Strength of Evidence (SOE) for Major Comparisons and Outcomes – We will grade the strength of the body of evidence as per the AHRQ methods guide on assessing the strength of evidence.[24] We plan to assess the strength of evidence for each outcome. Following the standard AHRQ approach, for each intervention and comparison of intervention, and for each outcome, we will assess the number of studies, their study designs, the study limitations (i.e., risk of bias and overall methodological quality), the directness of the evidence to the KQs, the consistency of study results, the precision of any estimates of effect, the likelihood of reporting bias, and the overall findings across studies. Based on these assessments, we will assign a strength of evidence rating as being either high, moderate, or low, or there being insufficient evidence to estimate an effect. The data sources, basic study characteristics, and each strength-of-evidence dimensional rating will be summarized in a "Summary of Evidence Reviewed" table detailing our reasoning for arriving at the overall strength of evidence rating.

Assessing Applicability – We will assess the applicability within and across studies with reference to children in the populations of interest (chronic OME, recurrent AOM and children with tympanostomy tubes), and whether interventions and comparators are used in current practice.

V. References

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VI. Definition of Terms

Chronic OME – chronic otitis media with effusion (lasting 3 months or more)
Recurrent AOM – recurrent acute otitis media (Three or more well-documented and separate AOM episodes in the past 6 months or at least 4 well-documented and separate AOM episodes in the past 12 months with at least 1 in the past 6 months)

VII. Summary of Protocol Amendments

No protocol amendments to date.

VIII. Review of Key Questions

AHRQ posted the KQs on the Effective Health Care Website for public comment. The EPC refined and finalized the KQs after review of the public comments, and input from Key Informants. This input is intended to ensure that the KQs are specific and relevant.

IX. 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 healthcare 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 TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

X. Technical Experts

Technical Experts constitute a multidisciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes and identify particular studies or databases to search. They are selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicting opinions are common and perceived as health scientific discourse that results in a thoughtful, relevant systematic review. Therefore study questions, design, and 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 do they contribute to the writing of the report. They have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts

and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

XI. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. The EPC considers all peer review comments on the draft report in preparation of the final report. Peer reviewers do not participate in writing or editing of the final report or other products. The final report does not necessarily represent the views of individual reviewers. The EPC will complete a disposition of all peer review comments. The disposition of comments for systematic reviews and technical briefs will be published three months after the publication of the evidence report.

Potential Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than $10,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

XII. EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than $1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of interest that cumulatively total greater than $1,000 will usually disqualify EPC core team investigators.

XIII. Role of the Funder

This project was funded under Contract No. HHSA 290 2012 00012 I from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The Task Order Officer reviewed contract deliverables for adherence to contract requirements and quality. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Appendix A

Herewithin are the literature searches conducted to date in four databases, as noted.

MEDLINE (5/26/15 6553 citations)

((otitis) OR (“glue ear”) OR "Otitis Media with Effusion"[Mesh] OR "Otitis Media, Suppurative"[Mesh] OR "Ear, Middle/secretion"[Mesh] OR (middle and ear and (effusion* or infect* or inflame* or disease*)) OR ((OME OR SOM or AOM) AND (otitis OR ear)) OR ((mucoid* AND middle AND ear) OR (mucous AND middle AND ear) OR (seromuc* AND middle AND ear)))
AND
(tympanostomy OR grommet* OR ((ear or “pressure equalization” or PE or myringotomy or ventilating or ventilation) and (tube or tubes)) OR “Otitis Media with Effusion/surgery”[mesh] OR "Middle Ear Ventilation"[Mesh] OR ((middle AND (ear OR tympanic)) AND (tube or tubes)) OR "Otologic Surgical Procedures"[Mesh] OR T-tube or tabulation)

COCHRANE: (7/13/15 393 citations)

((otitis) OR (“glue ear”) OR [mh “Otitis Media with Effusion”] OR [mh “Otitis Media, Suppurative”] OR [mh “Ear, Middle/secretion”] OR (middle and ear and (effusion* or infect* or inflame* or disease*)) OR ((OME OR SOM or AOM) AND (otitis OR ear)) OR ((mucoid* AND middle AND ear) OR (mucous AND middle AND ear) OR (seromuc* AND middle AND ear)))
AND
(tympanostomy OR grommet* OR ((ear or “pressure equalization” or PE or myringotomy or ventilating or ventilation) and (tube or tubes)) OR [mh “Otitis Media with Effusion/surgery”] OR [mh "Middle Ear Ventilation"] OR ((middle AND (ear OR tympanic)) AND (tube or tubes)) OR [mh “Otologic Surgical Procedures"] OR T-tube or tabulation)

CINAHL (7/13/15 852 citations)

((MH "Otitis") OR (MH "Otitis Media with Effusion") OR (MH "Otitis Media") OR otitis OR (“glue ear”) OR (MH "Ear, Middle") OR (middle and ear and (effusion* or infect* or inflame* or disease*)) OR ((OME OR SOM or AOM) AND (otitis OR ear)) OR ((mucoid* AND middle AND ear) OR (mucous AND middle AND ear) OR (seromuc* AND middle AND ear)))
AND
(tympanostomy or myringotomy OR (MH "Middle Ear Ventilation") OR grommet* OR ((ear or “pressure equalization” or PE or myringotomy or ventilating or ventilation) and (tube or tubes)) OR ((middle AND (ear OR tympanic)) AND (tube or tubes)) OR (MH "Ear Surgery") OR T-tube or tabulation)

EMBASE (7/14/15 5556 citations)

(otitis OR 'otitis media'/exp OR glue ear OR (middle and ear and (effusion* or infect* or inflame* or disease*)) OR ((OME OR SOM or AOM) AND (otitis OR ear)) OR ((mucoid* AND middle AND ear) OR (mucous AND middle AND ear) OR (seromuc* AND middle AND ear)))

AND

(tympanostomy OR 'tympanostomy tube'/exp OR 'myringotomy'/exp OR 'middle ear ventilation'/exp OR grommet* OR ((ear or “pressure equalization” or PE or myringotomy or ventilating or ventilation) and (tube or tubes)) OR ((middle AND (ear OR tympanic)) AND (tube or tubes)) OR T-tube or tabulation)