Washington State Health Care Authority
Health Technology Assessment

Tympanostomy Tubes

Draft Evidence Report: Peer Review & Response

October 16, 2015

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Responses To Public Comments

Spectrum Research is an independent vendor contracted to produce evidence assessment reports for the Washington HTA program. For transparency, all comments received during the public comment periods are included in this response document. Comments related to program decisions, process, or other matters not pertaining to the evidence report are acknowledged through inclusion only.

This document responds to clinical and peer reviews from the following parties:

1. Carol MacArthur, MD (peer reviewer)
2. Jack Paradise, MD (peer reviewer)

No other comments (including public comments) were received.

Specific responses pertaining to each comment are included in Table 1.

Page (Section)	Comment	Response
Carol MacArthur, MD (peer reviewer)		
Introduction (general comments)	• Overview of topic is adequate? Yes • Topic of assessment is important to address? Very much so. • Public policy and clinical relevance are well defined? Yes.	Thank you for your feedback.
Page 1 (sixth paragraph)	You state: "Approximately 1 mm in diameter, functioning tubes equalize middle ear pressure with atmospheric pressure and allow fluid drainage, alleviating symptoms of otitis media". The internal diameter of the tympanostomy tube lumen is about 1 mm, but the outer diameter is around 2 mm. Not sure if this fine point matters or not. Maybe just say 1 mm *in internal* diameter.	Thank you for your comment; the suggested change has been made.
Page 5 (TT (Unilateral versus No treatment (contralateral) for OME))	Should there be a horizontal line in this table to tell the reader where the TT (unilat vs no treatment contralateral) for OME studies start in the table?	Thank you for your comment; we have verified that the horizontal is correctly placed.
Background (general comments)	• Content of literature review/background is sufficient? Yes	Thank you for your feedback.
Page 40 (section 2.1.1, second paragraph)	I recommend the following changes in wording: "OME is diagnosed *via ear examination and sometimes* pneumatic otoscopy, 105 which tests the movement of the ear drum; ears with middle ear effusion are often *stiff* ~~stretched taut~~ and have limited or lack of movement when air is blown into the ear during otoscopy."	Thank you for your comment; the suggested changes have been made.
Page 40 (section 2.1.1, third paragraph)	Regarding section 2.1.1 third paragraph – you use 20 dB as "normal hearing" but normal hearing ranges from 0-20 dB, so all changes reported really should be reported in a range to include normal hearing down to 0 dB, not just 20dB. Children who benefit from the improved hearing from tubes can receive benefit when they hear at 0 dB while previously hearing at around 20-25 dB even.	Thank you for your comment, this has been corrected.
Page 43 (section 2.2.3)	This statement is incorrect. "*Adverse events related to tympanostomy tubes can be either transient (e.g., otorrhea) or cosmetic (e.g., cholesteatoma).*" Cholesteatomas are NOT cosmetic; myringosclerosis can be considered "cosmetic", but not cholesteatomas. Cholesteatomas if left	Thank you for your comment, this has been corrected.

Page (Section)	Comment	Response
	untreated can wreak havoc with the middle ear, mastoid, ossicles and can in the long run, invade the cranial cavity if left untreated. I would change the word "cosmetic" to "chronic".	
Page 43 (cholesteatoma paragraph)	Change the following statement as indicated: "Cholesteatomas are abnormal skin growths in the middle ear that can grow in size, *causing hearing loss, dizziness, mastoiditis or even intracranial infections* ~~*muscle weakness*~~*.2 Surgical treatment is the only effective management. Managed early, cholesteatomas are treatable with middle ear surgical excision* ~~*antibiotics, ear drops, and cleaning of the ear*~~*; otherwise, tympanomastoid surgery is needed for larger cholesteatomas. Cholesteatoma incidence in tube-extruded ears occurs in approximately 0.7% of children with OM.71"*	Thank you for your comment; the suggested changes have been made.
Page 43 (blockage of tube lumen paragraph)	Change this sentence as follows: Blockage can *sometimes* be treated by inserting otopical drops for about a week, *however, often the tube will remain non functional and need to be replaced..137*	Thank you for your comment; the suggested changes have been made.
Page 43 (granulation tissue paragraph)	Change this sentence as follows: Granulation tissue, or granulomas, ~~are accumulated squamous debris~~ *is new connective tissue and capillaries that form around the tube and are estimated to develop in 8% of children"*.137	Thank you for your comment; the suggested changes have been made.
Page 45 (section 2.3.3)	Adenoidectomy IS guideline-driven: (Otolaryngol Head Neck Surg. 2004 May;130(5 Suppl):S95-118. Clinical practice guideline: Otitis media with effusion.Rosenfeld RM[1], Culpepper L, Doyle KJ, Grundfast KM, Hoberman A, Kenna MA, Lieberthal AS, Mahoney M, Wahl RA, Woods CR Jr, Yawn B; American Academy of Pediatrics Subcommittee on Otitis Media with Effusion; American Academy of Family Physicians; American Academy of Otolaryngology--Head and Neck Surgery.): ~~*Although*~~ *Adenoidectomy is* ~~*not*~~ *guideline-recommended for children presenting with OME age 4 and older or for children presenting for their second set of tubes* ~~*without adenoid disease,*~~*15 studies have found that* ~~*it*~~ *adenoidectomy is effective for treating OM in this population.49,113*	Thank you for your comment. The cited guideline states (see section 9 (surgery)): "When a child becomes a surgical candidate, tympanostomy tube insertion is the preferred initial procedure; adenoidectomy should not be performed unless a distinct indication exists (nasal obstruction, chronic adenoiditis)." The text in section 2.3.3 has been expanded as such and now states: "Further, adenoidectomy is not guideline-recommended as a first procedure in children presenting with OME unless additional conditions such as nasal obstruction or chronic adenoiditis exist."
Page 45 (antibiotics, end of second sentence)	Only in the instance of a patent PE tube or perforated eardrum. Otherwise, typical AOM is treated by observation or oral antibiotics. When treating with topical antibiotics, you are really	Thank you for your comment; corrections have been made to the text.

Page (Section)	Comment	Response
	talking about tympanostomy tube otorrhea which is preferentially treated by topical antibiotics.	
Page 45 (antibiotics, last sentence)	amoxicillin-clavulanate or or Ciprofloxicin-dexamethasone optic solution are NOT topical antibiotics drops. Please delete.	Thank you for your comment; the suggested change has been made.
Page 45 (other medications, re: mucolytics and antihistamines with oral decongestants)	and are not recommended in OME guidelines. HYPERLINK "http://www.ncbi.nlm.nih.gov/pubmed/15138413" \o "Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery." Otolaryngol Head Neck Surg. 2004 May;130(5 Suppl):S95-118.	Thank you for your comment; this has been clarified in the text.
Page 47 (American Acadamy of Otolaryngology… 2013)	along with hearing loss by audiogram	Thank you for your comment; the guideline referenced was double-checked and does not specify hearing loss as an indication for tubes in children with recurrent AOM.
Page 65 (CADTH report)	TULA definition? Maybe it is present in the report earlier, but I have missed it. Be sure to define.	Thank you for your comment; no definition was provided in the corresponding publication nor were we able to find one, thus “TULA” has been changed to “Tula”.
Page 87 (footnote for table 6)	and rarely, anaphylaxis or Stevens-Johnson syndrome	Thank you for your comment; this has been added to the footnote.
Report objectives and key questions (general comments)	• Aims/objectives clearly address relevant policy and clinical issue? Yes • Key questions clearly defined and adequate for achieving aims? Yes	Thank you for your feedback.
Methods (general comments)	• Method for identifying relevant studies is adequate? Yes • Criteria for the inclusion and exclusion of studies is appropriate? Yes • Method for Level of Evidence (LoE) rating is appropriate and clearly explained? Yes • Data abstraction and analysis/review are adequate? Yes	Thank you for your feedback.
Results (general	• Amount of detail presented in the results section appropriate? Yes	Thank you for your feedback.

Page (Section)	Comment	Response
comments)	• Key questions are answered? Yes • Figures, tables and appendices clear and easy to read? Yes • Implications of the major findings clearly stated? Yes	
Jack Paradise, MD (peer reviewer)		
Page 1 (Executive Summary Introduction)	I still think that the introduction does not make sufficiently clear the distinction between recurrent AOM and persistent OME. I sent the following in an earlier communication: "First of all, disease definition. I think it's important to make it clear at the onset that what is at issue here is the use of tubes for two distinctly different--although occasionally overlapping--conditions, namely (1) recurrent acute otitis media (AOM) and (2) persistent otitis media with effusion (OME). (Effusion, purulent in nature, is an integral feature of AOM, but custom dictates that in general terminology, OME refers to usually noninfectious inflammation accompanied by sterile effusion, whereas in AOM the effusion is by definition not sterile (although sometimes difficult to identify, resulting in false negatives)." I think it would be worthwhile to indicate in this initial paragraph that both recurrent AOM and persistent OME are problems that mainly affect children under the age of 3 yr. Note a few specific suggestions in the sticky note associated with the following paragraph.	Thank you for your comments. Modifications have been made to this section to clarify these points.
Page 1	References are listed alphabetically and some appear to bear no relation to numbers shown in text. This prevents me from checking the accuracy of many of the statements. See comment below re 2 Mandel trials. Also, there are 2 sets of references, beginning on pages 19 and 226, respectively. Why 2 sets? Which one will be used?	Thank you for your comment. In order for the Executive Summary to function as a standalone document, it has its own set of references.
Page 1	…particularly recurrent AOM and long-term, persistent OME, . . . and in the case of OME, may impede child development. AOM usually causes fever and earache (otalgia)…	Thank you for your comment. The suggested changes have been made.
Page 1 (3rd paragraph)	The conclusions of the studies are probably wrong. Suggest you change "indicate" to "have suggested." Section also redundant with following paragraph.	Thank you for your comment. The suggested change has been made.

Page (Section)	Comment	Response
Page 1 (4th paragraph)	There has been concern that chronic OME. (Delete "OME, especially." There never has been concern about short-lived episodes of OME).	Thank you for your comment. The suggested changes have been made.
Page 2 (1st paragraph)	TT has not been shown to improve QoL Some studies have suggested that TT may improve QoL …	Thank you for your comment. The suggested change has been made.
Page 2 (policy context)	Add "persistent." (Most episodes of OME are transitory and of no concern.)	Thank you for your comment. The suggested change has been made.
Page 2 (objectives)	Virtually no such thing as OM without effusion. Would change to "treating recurrent AOM or persistent OME."	Thank you for your comment. The suggested change has been made.
Page 3 (Key Questions)	I don't recall that there is later consideration of SES.	Thank you for your comment. No studies were identified that evaluated whether socioeconomic status modified the treatment effect of tubes versus any comparator of interest.
Page 5 (Summary strength of evidence table)	It doesn't seem to me that "Outcome" is the appropriate heading for the first column. I would suggest "Clinical Question."	Thank you for your comment. We have left this as “Outcome” in accordance with the “Outcomes” component of the PICO (population, intervention, comparator, outcomes) table (Table 1).
Page 5 (Summary strength of evidence table)	I think it would be helpful for the reader to add reference numbers to the various studies, once the numbering has been clarified.	Thank you for your comment. The references have been left out in order to simplify the table and instead the study names have been provided.
Introduction (general comments)	The overview of the topic is exhaustive and comprehensive, and reflects a great deal of effort. It addresses the key questions thoroughly. I have found a few major areas of concern and a large number of minor ones. To simplify the task of addressing the total of 133 comments, they are shown in individual “sticky notes” that the Adobe Reader program makes possible and that are sprinkled throughout the text adjoining the relevant sections. They can be read by simply rolling the cursor over the marginal icons or double-clicking the icons. In addition to these, there are a number of minor grammatical errors--particularly inclusion of inappropriate words such as “and” or “the,” and omission of others, perhaps because of typos. I have not marked these, but it would be a good idea for someone to inspect the document and correct them.	Thank you for your comment. The individual sticky note comments have been addressed.

Page (Section)	Comment	Response
Introduction (general comments)	The overview includes recommendations from the literature, but draws no conclusions about recommended practices and includes no recommendation of its own. Apart from specific issues, I find much of the document quite repetitive and somewhat tedious, but this may be a required format.	Thank you for your comment. The introduction is intended to provide background to the topic at hand rather than formulate specific recommendations or conclusions. The body of the report evaluates the evidence and from that conclusions for the critical outcomes of importance were drawn (see Section 5). The Washington State Health Technology Clinical Committee (HTCC) will use these conclusions to formulate policy recommendations at the November 2015 meeting.
Page 10 (TT versus antibiotics for AOM)	Should read "TT vs. prophylactic antibiotics for recurrent AOM"	Thank you for your comment. The suggested change has been made.
Page 10 (TT versus placebo or no treatment for AOM)	There was no "no treatment" group in this study--only TT, antibiotic, and placebo. Should add "recurrent" before AOM.	Thank you for your comment. The suggested changes have been made.
Page 10 (TT (Unilateral) Versus Myringotomy Or No Treatment For AOM or OME)	Add "recurrent" before AOM.	Thank you for your comment. The suggested change has been made.
Page 12 (TT versus no treatment for AOM)	Should read "recurrent" AOM. Same for next row.	Thank you for your comment. The suggested changes have been made.
Page 10, 13 (TT versus antibiotics for AOM)	Should read "TT vs. prophylactic antibiotics for recurrent AOM"	Thank you for your comment. The suggested changes have been made.
Page 13 (TT versus placebo or no treatment for AOM)	There was not a "no treatment" group in this study--only TT, antibiotic, and placebo	Thank you for your comment. The suggested change has been made.
Page 13 (TT (Unilateral) Versus Myringotomy Or No Treatment For	Add "recurrent" before AOM.	Thank you for your comment. The suggested change has been made.

Page (Section)	Comment	Response
AOM or OME)		
Page 15 (TT versus antibiotics for AOM)	Should read "TT vs. prophylactic antibiotics for recurrent AOM"	Thank you for your comment. The suggested changes have been made.
Page 15 (TT versus placebo or no treatment for AOM)	There was no "no treatment" group in this study--only TT, antibiotic, and placebo. Should add "recurrent" before AOM. Same for next row (Le).	Thank you for your comment. The suggested changes have been made.
Page 13 (TT vs. WW for OME)	The impact statement is incorrect. In both Mandel trials, perforation occurred only in the TT groups. The reports might have been written more clearly, but careful reading shows that perforation was mentioned only in connection with the TT groups. It is important to correct this, because perforation is an important potential sequela of tube insertion and one of the main reasons for conservatism in considering whether tubes are advisable. I think the quality of these studies could be considered moderate.	Thank you for your comment; this information has been updated. The quality of the studies has been formally graded as described in the methods and in the appendix.
Page 15 (Summary for chronic otorrhea)	Statement not correct. See next comment	Thank you for your comment. The statement has been double-checked for accuracy; please see response to next comment for details.
Page 15 (TT versus WW for OME; TT versus myringotomy for OME)	Statements are not correct. In Mandel 1989, persistent otorrhea developed only in 2 children who received tubes, one of whom had originally been in the no-surgery group but received a tube because of treatment failure. In Mandel 1992 the report described the occurrence of otorrhea (only in children who received tubes initially or eventually) but there was no mention of whether or not the otorrhea was chronic.	Thank you for your comment. The statements here have been double-checked for accuracy. In Mandel 1989, you are correct that there was one event in each treatment group; data are presented here according to randomization group in accordance with the intention-to-treat principle, thus there was one event reported for each treatment group. For Mandel 1992 the results presented here refer to those in the last sentence of the results section of the study: “two subjects developed chronic suppurative otitis media with tympanostomy tubes in place…”

Page (Section)	Comment	Response
Page 16 (TT+Ad versus myringotomy+Ad for OME)	Statement re Popova is not correct. From the abstract: "None of the patients with A+M had episodes with otorrhea which contrasted with the 40% occurrence rate in the A+T group."	Thank you for your comment. The results referred to on page 16 concern chronic otorrhea (which we defined as 3 or more episodes per year) rather than any otorrhea. In this study, 5% (2/42) of TT+Ad patients had this condition compared with 0% (0/36) of myringotomy + Ad patients, a difference which was not statistically significant. (These results are presented in Table 3 of the Popova study.)
Page 25 (Appraisal, 1st paragraph, sentence starting with “Further”)	Not true for most children. Would at least qualify the sentence by adding "inordinately prolonged" before hearing loss	Thank you for your comment. The suggested change has been made.
Page 28 (Outcomes assessed, hearing)	Not correct. Conventional classification is: 26-40 (mild); 41-70 (moderate); >71 (severe).	Thank you for your comment. The classification levels provided were obtained from the current American Academy of Otolaryngology guidelines (Rosenfeld 2013, as referenced) and were double-checked for accuracy.
Page 40 (Background)	Reference numbers different from those in identical paragraph in Executive Summary.	Thank you for your comment. In order for the Executive Summary to function as a standalone document, it has its own set of references, which are thus different than those in the full report.
Page 42 (background, last paragraph)	I don't think "span" is the right term. I would suggest "the tube is inserted through the tympanic membrane and held in place by flanges on the inner and outer surfaces of the membrane, respectively. The tube keeps the incision open . . ."	Thank you for your comment. The suggested change has been made.
Page 42 (background, last paragraph)	tube otorrhea is discharge originating from the middle-ear cavity only.	Thank you for your comment. The suggested change has been made.
Page 43 (background, consequences and adverse events)	Cholesteatoma is certainly not cosmetic!	Thank you for your comment. This sentence has been removed.
Page 43 (background, tympanosclerosis)	that form "in the tympanic membrane in response ..."	Thank you for your comment. The suggested change has been made.

Page (Section)	Comment	Response
Page 44 (background, atelectasis)	Atelectasis is a result of prior tube insertion, which is probably the main cause in children. Tube dysfunction alone is a possible cause.	Thank you for your comment. The sentence has been modified.
Page 44 (background, harms of anesthesia)	I think it would be advisable to mention the possible risk of any anesthesia affecting the developing brain in children <3 yrs. of age. See Rapaport, N Engl J Med 2011;364:1387. Advises forgoing elective surgical procedures in children less than age 3.	Thank you for your comment. Some additional text has been added on this topic based on the provided reference.
Page 44 (background, first paragraph in comparator treatments section)	This paragraph involves misconceptions. Details (except for adenoidectomy) apply to OME rather than recurrent AOM See attachment to my email to Robin Hashimoto as suggested replacement.	Thank you for your comment. The suggested change has been made.
Page 45 (background, comparator treatments, watchful waiting or delayed tube insertion section)	I would insert "or undue persistence" after "changes in symptomatology."	Thank you for your comment. The suggested change has been made.
Page 45 (background, comparator treatments, myringotomy section)	After "middle ear," I suggest you delete "fluid" and instead add "of exudate in individual cases of AOM, and to drain the middle ear of fluid in cases of persistent OME.	Thank you for your comment. The suggested change has been made.
Page 45 (background, comparator treatments, adenoidectomy section)	Our studies of adenoidectomy in showed appreciable benefit in children who had previously undergone tube insertion, but only limited, short-term efficacy in those who had not undergone tube insertion. See JAMA 1990; 263:2066-2073 and JAMA 1999;282:945-953.	Thank you for your comment. Some additional text has been added based on the provided reference.
Page 45 (background, comparator treatments, antibiotics section)	Topical treatment is used only for tube otorrhea, not for recurrent AOM. Insufficient distinction between recurrent AOM and persistent OME. Paragraph would benefit from being rewritten. See my email to Robin Hashimoto for suggested rewrite.	Thank you for your comment. The suggested changes have been made.
Page 45 (background, comparator treatments, other medications	Insufficient distinction between recurrent AOM and persistent OME. See email to Robin Hashimoto for rewrite:	Thank you for your comment. The suggested changes have been made.

Page (Section)	Comment	Response
section)		
Page 45 (background, comparator treatments, autoinflation of the Eustachian tube section)	Inner ear is not correct. See email attachment to Robin H for rewrite of paragraph.	Thank you for your comment. The suggested changes have been made.
Page 46 (background, first paragraph of Clinical Guidelines)	Insert recurrent before AOM	Thank you for your comment. The suggested change was not made as it would misrepresent the search terms used.
Page 51 (background, Table 2 (clinical guidelines), Darwin guideline (sentence before point 3)	Partial sentence	Thank you for your comment; this has been corrected.
Page 62 (background, Table 3 (previous HTAs), Berkman 2013 row)	Should this be less time with OM or OME? ("32% less time with TT at 1 year or more after surgery…")	Thank you for your comment; it should read "32% less time with persistent middle ear effusion"; this has been corrected.
Page 72 (background, Table 3 (previous HTAs), Simpson row)	Measures were not of hearing improvement, but rather of children's development.	Thank you for your comment; this has been corrected.
Page 73 (background, Table 3 (previous HTAs), Rovers row)	relationship rather than accumulation? (Under TT vs. WW: "Children with more than one risk factor—including status of day-care attendance, gender, and season— appeared to benefit slight more from treatment with ventilation tubes, but the accumulation was only weak, like most of the individual risk factors.")	Thank you for your comment. "Accumulation" has been changed to "association".
Page 76 (background, Table 3 (previous HTAs), Lous row)	Instead of "ears without treatment" should it not be "ears with myringotomy only"? (Under TT vs. Myringotomy: "Ears treated with tubes had 1.2 fewer attacks of AOM in the first six months after treatment (95% CI 0.2 – 2.2) compared with ears without treatment.")	Thank you for your comment; this has been corrected.

Page (Section)	Comment	Response
Page 99 (Otorrhea section)	Otorrhea, from Paradise trial, reported by Ah-Tye et al. Pediatrics 2001;107:1251-1258.	Thank you, the data have been added.
Page 100 (1st paragraph of attention and behavioral outcomes section)	Should be no differences	Thank you, the correction has been made.
Page 105 (first sentence of first paragraph)	No difference in what?	Thank you for your comment, this has been clarified in the text.
Page 105 (last sentence of first paragraph)	Who reported?	Thank you for your comment, this has been clarified in the text.
Page 112 (last sentence of page)	I think this should be "no difference."	Thank you, the correction has been made.
Page 139 (by-child analysis paragraph)	p=0.0626 is not significant	Thank you, the correction has been made.
Page 142 (re-insertion of TT paragraph)	In Leek study patients underwent bilateral myringotomy, not bilateral TT.	Thank you for your comment; this section pertains to insertion of TT following the initial procedure (of unilateral TT versus unilateral myringotomy); the text should have not specified “bilateral” and this has been deleted.
Page 154 (hearing paragraph)	No patients had TT+Ad. Instead had myringotomy+Ad	Thank you, the correction has been made.
Page 155 (surgery paragraph)	Don't understand "need for TT + Ad." The 2 groups being compared are TT vs. Ad + myringtomy.	Thank you for your comment; in this study (Casselbrant 2009), patients in the TT group who needed reinsertion of TT were also recommended to undergo adenoidectomy. This has been clarified in the text.
Page 156 (first three lines of text)	Sentence is unclear and should be rewritten particularly portion following first semicolon: “…; though TT patients required significantly more medical treatments per child than the TT+Ad group received significantly more medical retreatments for AOM than the myringotomy+Ad group (1.2 vs. 0.7 medical treatments per child, ME 0.6, 95% CI 0.2 to 0.9, p=0.0021).”	Thank you for your comment; this sentence has been rewritten for clarity.

Page (Section)	Comment	Response
Page 156 (first paragraph of study characteristics section)	Second sentence not clear. Should read "All patients were randomized to receive or not receive adenoidectomy, and each patient received unilateral TT with the ear randomly chosen." Adenoidectomy is not a unilateral procedure. Also the reference numbers for Maw and Bawden are incorrect.	Thank you for your comment; this sentence has been rewritten for clarity; the reference numbers have been corrected.
Page 157 & 158 (Table 19 & 20 titles)	It is not TT vs Ad. It is Ad + unilateral TT vs no Ad + unilateral TT. Suggest you revise title accordingly, and combine Tables 19 and 20 to a single table.	Thank you for your comment. The Table titles have been rewritten for clarity; however Tables 19 and 20 were not combined due to space limitations.
Page 157 (Table 19, Dempster row)	Not correct to say "no treatment." Suggest you revise according to previous comment re text.	Thank you for your comment. This has been changed to “no procedure”.
Page 159 (second paragraph of hearing section)	What about no-Ad patients? Between which groups? Paragraph needs revision.	Thank you for your comment; this issue has been clarified in the text.
Page 159 (Figure 26)	I am unable to understand this and the subsequent figures. Is it TT vs no TT irrespective of Ad vs no Ad, and Ad vs no Ad irrespective of TT vs no TT? The studies did not compare adenoidectomy alone vs TT alone because there were no such subjects.	Thank you for your comment. As stated at the beginning of the section, “the way both trials were designed (patients randomized to adenoidectomy or no adenoidectomy, ears randomized to no procedure or tubes) means that each group has results for one ear only.” Although you’re correct, the studies did not compare adenoidectomy alone vs. TT alone, we are able to draw comparisons for the TT ear in no adenoidectomy patients to the ear that did not undergo a procedure in adenoidectomy patients.
Page 160 (second paragraph of OME recurrence section)	What about no-adenoidectomy patients? Also applies to Figs. 28 and 29.	Thank you for your comment; this issue has been clarified in the text.
Page 164 (heading for section 4.1.10 on AOM patients)	In this and related headings would add "Recurrent" before AOM.	Thank you for your comment. The suggested changes have been made.
Page 173 (Table 26, Casselbrant row)	"6-12" should probably be followed by "months." Last portion of cell not comprehensible.	Thank you for your comment. The suggested correction was made, and the text was clarified to indicate the conditions in which tube re-insertion could be performed for this study.

Page (Section)	Comment	Response
Page 175 (studies included section)	For clarity, in paragraph heading, suggest inserting "recurrent" before AOM and "persistent" before OME. Also for clarity suggest that language of final paragraph of section 4.1.12 regarding randomization be moved up to replace description of randomization here. Mean age is stated again in next paragraph and could be deleted here.	Thank you for your comment. The suggested changes have been made except for deleting mean age, as we wanted to make that information consistently available in the first paragraph of all sections.
Page 177 (Table 28)	Would add "or no TT"	Thank you for your comment. Instead of substituting “no TT” for “no treatment”, we have substituted “no procedure” to indicate that neither TT or myringotomy were performed.
Page 180 (Harms)	The abstracts and some of the texts both in Mandel 1989 and in Mandel 1992 describe perforation only in reference to subjects who underwent myringotomy with tube insertion. No perforations developed in subjects who did not undergo TT. Johnston was first author in reference #70, although the data came from my trial. I have rewritten this entire paragraph as I think advisable. It is in the attachment to my email to Robin.	Thank you for your comment; that the perforations occurred only in patients who received TT insertion was added to the text.
Page 182 (first paragraph)	See earlier sticky note re the Mandel trials. Perforation only in ears that received TT.	Thank you for your comment; that the perforations occurred only in patients who received TT insertion was added to the text.
Page 183 (second half of first paragraph)	Dislocation rather than extrusion; the tube falls in, it's not pushed in.	Thank you, the correction has been made.
Page 184 (third paragraph)	See prev note re extrusion	Thank you, the correction has been made.
Page 184 (OME: Tubes vs. Adenoidectomy heading)	Paragraph heading incorrect. There were actually 4 groups--see next sticky note.	Thank you for your comment. The heading has been clarified.
Page 184 (fourth paragraph)	Not quite correct. Children were randomized to either adenoidectomy or no adenoidectomy. Within each of these groups, each child received unilateral TT, with the choice of which ear made randomly. Thus there were actually four treatment groups. For clarity, should add the Dempster reference to the Maw-Bawden references in the same set of parentheses; otherwise reader might assume from	Thank you for your comment. This has been clarified in the text to avoid future misunderstanding.

Page (Section)	Comment	Response
	preceding paragraph that it was Casselbrant was the other trial.	
Page 185 (second and fourth paragraph)	why mention 0%?	Thank you for your comment; that the authors evaluated and reported that the tube pushed into the middle ear in 0% of patients is useful information and thus has been included here.
Page 185 (fourth paragraph)	I don't find any mention of vaginitis or urticaria in Casselbant.	Thank you for your comment. These events are mentioned in Casselbrant 1992 on page 281 in the second to last sentence of the section “Ultimate treatment failures”.
Page 186 (second paragraph)	No suppurative complications in Casselbrant	Thank you, the correction has been made.
Page 186 (fourth full paragraph)	Tests for interaction were done routinely, altho not mentioned in the report. Would prefer "reported" to "performed."	Thank you, the suggested change has been made here (and for all studies where we stated that a test for interaction was not performed, as suggested in the email you sent Robin Hashimoto 9/5/2015).
Page 189 (Differential efficacy paragraph in section 4.3.6)	Statement re interaction contradicts preceding statement.	Thank you for your comment, however, no contradiction was identified in the referenced text: “One RCT formally tested for interaction: Gates 1987/1989[48,49] (mean age NR, age 4-8 years at enrollment, CoE II). **Differential efficacy** Gates[48,49] conducted a test for interaction to evaluate whether any prespecified baseline characteristics modified the outcomes of time with effusion as well as time to recurrence. No interaction was found between the group, outcomes, and any characteristic tested (age, sex, ethnic group, laterality of effusion, referral source), however no details or data were reported.”

Page (Section)	Comment	Response
Page 191 (re: Berman study)	OME, not AOM.	Thank you for your comment. Upon reassessing the study, we agree with your comment that the study evaluated persistent OME following an initial diagnosis of AOM and have made the change as suggested.
Page 192 (re: Gates study)	What does 0.05 refer to?	Thank you; it refers to 0.05 QALY, and this has been clarified in the text.
Page 195 (Cholesteatoma study references)	Instead of Paradise, should be Johnston (ref 70).	Thank you for your comment; for ease of referencing the results in the overall strength of evidence tables, we have referred to studies with more than one publication by the name of the study or the author's last name associated with the majority of papers for a given study. Thus, in this case we referenced the Paradise study as a whole. The specific references are available in the results section.
Page 195-196 (Perforation)	Perforations occurred only in TT subjects.	Thank you for your comment; that the perforations occurred only in patients who received TT insertion was added to the text.
Page 196 (chronic otorrhea, ≤36 months)	2/109 =1.8%	Thank you for your comment. The data referred to here have been double-checked for accuracy and a clarification has been made in the text: "Persistent otorrhea … occurred in 2.2% of all patients who ultimately received tubes (2/89) (including those randomized to TT, WW, and myringotomy) in another trial (Mandel 1992).
General comments regarding the quality of the report	The overall quality of the report is "good" (with options of "superior", "good", "fair", and "poor").	Thank you for your feedback.