Effectiveness of Tympanostomy Tubes for Otitis Media: A Meta-analysis

Dale W. Steele, MD, MS,[a,b,c,d] Gaelen P. Adam, MLIS,[a] Mengyang Di, MD, PhD,[a] Christopher H. Halladay, ScM,[a] Ethan M. Balk, MD, MPH,[a,b] Thomas A. Trikalinos, MD, PhD[a,b]

abstract

CONTEXT: Tympanostomy tube placement is the most common ambulatory surgery performed on children in the United States.

OBJECTIVES: The goal of this study was to synthesize evidence for the effectiveness of tympanostomy tubes in children with chronic otitis media with effusion and recurrent acute otitis media.

DATA SOURCES: Searches were conducted in Medline, the Cochrane Central Trials Registry and Cochrane Database of Systematic Reviews, Embase, and the Cumulative Index to Nursing and Allied Health Literature.

STUDY SELECTION: Abstracts and full-text articles were independently screened by 2 investigators.

DATA EXTRACTION: A total of 147 articles were included. When feasible, random effects network meta-analyses were performed.

RESULTS: Children with chronic otitis media with effusion treated with tympanostomy tubes compared with watchful waiting had a net decrease in mean hearing threshold of 9.1 dB (95% credible interval: −14.0 to −3.4) at 1 to 3 months and 0.0 (95% credible interval: −4.0 to 3.4) by 12 to 24 months. Children with recurrent acute otitis media may have fewer episodes after placement of tympanostomy tubes. Associated adverse events are poorly defined and reported.

LIMITATIONS: Sparse evidence is available, applicable only to otherwise healthy children.

CONCLUSIONS: Tympanostomy tubes improve hearing at 1 to 3 months compared with watchful waiting, with no evidence of benefit by 12 to 24 months. Children with recurrent acute otitis media may have fewer episodes after tympanostomy tube placement, but the evidence base is severely limited. The benefits of tympanostomy tubes must be weighed against a variety of associated adverse events.

[a]*Evidence-based Practice Center, Center for Evidence Synthesis in Health,* [b]*Department of Health Services, Policy and Practice, School of Public Health,* [c]*Department of Emergency Medicine, Section of Pediatrics–Hasbro Children's Hospital, and* [d]*Department of Pediatrics, Alpert Medical School, Brown University, Providence, Rhode Island*

Dr Steele conceptualized and designed the review, designed data collection instruments and supervised data collection, performed data analysis and interpretation of data, and drafted and revised the manuscript; Ms Adam performed the literature search, participated in data collection, performed analysis and interpretation of data, and critically reviewed the manuscript; Dr Di and Mr Halliday participated in data collection, analysis, and interpretation of data, and reviewed and revised the manuscript; Dr Balk assisted in conceptualization and design, reviewed data collection, collected data, and critically reviewed the manuscript; and Dr Trikalinos oversaw protocol conception and design and analysis and interpretation of data, performed supplemental analysis, and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted.

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 US Department of Health and Human Services.

To cite: Steele DW, Adam GP, Di M, et al. Effectiveness of Tympanostomy Tubes for Otitis Media: A Meta-analysis. *Pediatrics.* 2017;139(6):e20170125

Myringotomy with tympanostomy tube placement is the most common ambulatory surgery performed on children in the United States,[1] with 667 000 children aged <15 years undergoing tympanostomy tube placement in 2006.[2] The effectiveness of tympanostomy tubes for chronic otitis media with effusion (OME) and recurrent acute otitis media (AOM) is likely influenced by the many factors that affect the prognosis for middle ear disease in children. These factors include current age, age at first diagnosis, frequency of respiratory tract infections, and day care exposure.[3]

The American Academy of Otolaryngology–Head and Neck Surgery clinical practice guideline recommends that clinicians should offer bilateral tympanostomy tube insertion to children with bilateral OME for ≥3 months and who have documented hearing difficulties. They may offer tympanostomy tubes to children with unilateral or bilateral OME with symptoms that are likely attributable to OME which include, but are not limited to, vestibular problems, poor school performance, behavioral problems, ear discomfort, or reduced quality of life.[4]

The American Academy of Pediatrics' clinical practice guideline for diagnosis and management of AOM states that clinicians may offer tympanostomy tubes for recurrent AOM (3 episodes in 6 months or 4 episodes in 1 year with 1 episode in the preceding 6 months).[5] The American Academy of Otolaryngology–Head and Neck Surgery clinical practice guideline further recommends that clinicians not perform tympanostomy tube insertion when middle ear effusion is not present at the time of assessment for tube placement; they argue that the presence of effusion serves as both a marker for the accuracy of the diagnosis of AOM and an indicator of underlying Eustachian tube dysfunction with decreased ability to clear middle ear fluid after an episode of AOM.[4]

In the present systematic review, we synthesized the available evidence regarding the effectiveness of tympanostomy tubes (with or without adenoidectomy) compared with watchful waiting in children with chronic OME and children with recurrent AOM. We also summarized the frequency of adverse events associated with tympanostomy tubes.

This review is derived from an Agency for Healthcare Research and Quality–commissioned comparative effectiveness review (Tympanostomy Tubes in Children With Otitis Media) conducted by the Brown Evidence-based Practice Center. The full review and review protocol (PROSPERO registry number: CRD42015029623) are available at http://www.effectivehealthcare.ahrq.gov.

METHODS

The approaches outlined in the Agency for Healthcare Research and Quality's Methods Guide for Comparative Effectiveness Reviews were followed.[6]

Search Strategy and Study Selection

This study evaluated published, peer-reviewed studies in which at least 1 arm included children receiving tympanostomy tubes; conference abstracts were excluded. We included randomized controlled trials (RCTs) and nonrandomized comparative studies (NRCS), prospective and retrospective, in which treatment with tympanostomy tubes was assigned on a per-patient basis. Studies with per-ear assignment were excluded (eg, tympanostomy tubes placed by design in 1 ear only). For adverse events, prospective surgical studies enrolling at least 50 subjects (including arms of RCTs or NRCS with ≥50 patients) and population-based retrospective single-group studies (registry studies) with at least 1000 subjects were included.

Literature searches without language restrictions were conducted in Medline, the Cochrane Central Trials Registry and Cochrane Database of Systematic Reviews, Embase, and the Cumulative Index to Nursing and Allied Health Literature (from inception) to identify primary research studies meeting the study criteria. Citations found by literature searches were independently screened by 2 researchers, using the open-source, online software abstrackr (http://abstrackr.cebm.brown.edu/).[7] Conflicts were resolved by discussion until a group consensus was reached.

Data Extraction and Analysis

Each study was extracted by 1 methodologist; the extractions were reviewed and confirmed by at least 1 other methodologist. We conducted quantitative analysis for outcomes with at least 5 studies which report results that could be combined in a meta-analysis. Bayesian network meta-analysis was performed by using the R *gemtc* package.[8] Estimation was performed with Markov chain Monte Carlo methods via the JAGS software,[9] using initial values drawn randomly from the marginal distributions of the priors of respective parameters. We fit 4 Markov chain Monte Carlo chains. After a burn-in of 5000 iterations, we monitored the convergence of random effects means and variances automatically by checking every 10 000 iterations whether the Gelman-Rubin diagnostic was <1.05 with 95% probability for all monitored parameters. After convergence was reached, an additional 10 000 iterations were run. All models converged within 10 000 iterations. Model fit was assessed by comparing the posterior mean of the residual deviance versus the number of data points. The ratio of residual deviance to number of

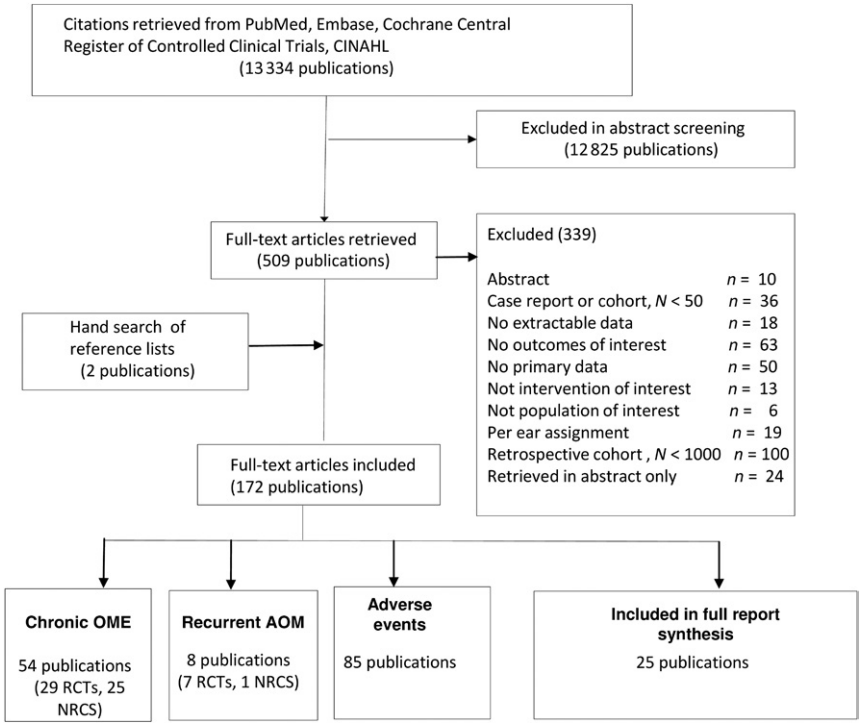

FIGURE 1
Literature flow diagram. CINAHL, Cumulative Index to Nursing and Allied Health Literature.

data points ranged from 0.97 to 1.06, suggesting an adequate model fit.

Network meta-analysis is an extension of pairwise meta-analyses that simultaneously combines direct (when interventions are compared head-to-head) and indirect (when interventions are compared through other reference interventions) evidence. Combining the direct and indirect evidence not only improves the precision of estimates but also provides estimates for all pairwise comparisons, including those missing from the direct evidence.[10] Statistical heterogeneity was explored qualitatively. Because of the relatively small number of studies, and the little variability in characteristics, meta-regression analyses were not performed.

Assessment of Study Risk of Bias and Strength of Evidence

The methodologic quality of each study was assessed on the basis of predefined criteria. For RCTs, the Cochrane risk of bias tool was used.[11] The strength of evidence was graded according to the Agency for Healthcare Research and Quality's methods guide on assessing the strength of evidence.[12]

RESULTS

Figure 1 displays the results of the literature search and selection process.

Effectiveness of Tympanostomy Tubes in Children With OME

A total of 54 publications were identified. Of these, 29 articles reported the results of 16 RCTs.[13–41] Twenty-four publications reported the results of 24 NRCS that assessed the effectiveness of tympanostomy tubes in pediatric patients with chronic middle ear effusion.[42–65] These studies evaluated multiple interventions (tympanostomy tubes, tympanostomy tubes with adenoidectomy, myringotomy with adenoidectomy, myringotomy alone, adenoidectomy alone, oral antibiotic prophylaxis, and watchful waiting).

Hearing thresholds were measured in 16 RCTs. In 10 of these RCTs, mean hearing thresholds were reported according to study arm at various time points. For the network meta-analysis of these RCTs, we classified hearing thresholds obtained at 1 to 3 months as "early"; hearing thresholds obtained between 12 and 24 months were classified as "late." Not all studies had interventions at both early and late time points. Thus, the network of comparators differs for early and late comparisons.

Figure 2 illustrates the effectiveness of various interventions at 1 to 3 months compared with watchful waiting. Mean hearing thresholds improved (ie, decreased) by an average of 9.1 dB after insertion of the tympanostomy tubes and by 10 dB after tympanostomy tube insertion with adenoidectomy. As shown in Table 1, the strategies with the highest probability of being among the 3 most effective interventions with respect to early improvements in hearing thresholds were tympanostomy tubes, tympanostomy tubes with adenoidectomy, and myringotomy with adenoidectomy.

Five RCTs reported hearing thresholds at 12 to 24 months. As shown in Fig 3, by 12 to 24 months, the mean difference in hearing thresholds for tympanostomy tubes alone, compared with watchful waiting, was 0 dB (95% credible interval: −4 to 3). As can be seen in Table 2, tympanostomy tube insertion with adenoidectomy and myringotomy with adenoidectomy were the 2 most effective strategies with respect to late hearing thresholds. Tympanostomy tubes alone, antibiotic prophylaxis, and watchful waiting were among the 3 least effective strategies.

Eight studies (5 RCTs, 3 NRCS, and 1 that combined both designs) in 12

articles reported on 119 quality of life and patient-centered outcomes (cognitive, language, and behavioral) in 1665 children over multiple time points and arms. In general, the results were not significant (only 14 of 119 had significant results), and they varied in magnitude and direction, even across subscales of the same test.

Effectiveness of Tympanostomy Tubes in Children With Recurrent AOM

We identified 8 publications, reporting results from 7 RCTs[66–72] and 2 NRCS[69,73] that reported outcomes for children with recurrent AOM.

Three RCTs compared tympanostomy tubes with placebo or no treatment. The first trial reported that 3 of 20 children in the placebo group had no further episodes of AOM, compared with 12 of 22 in the tympanostomy tube group ($P = .01$), with an attack rate of 2.0 infections per child in the placebo group, compared with 0.86 in the tympanostomy tube group ($P = .006$). The authors reported a post hoc subgroup comparison of treatment failure (≥2 episodes in 3 months) rates. Children without middle ear effusion at study entry had significantly fewer bouts of AOM ($P < .05$) and lower attack rates than children with middle ear effusion. However, in a logistic model of treatment failure, adjusted for presence of middle ear effusion, the treatment according to subgroup interaction term is nonsignificant ($P = .69$). This analysis relies on a small sample ($n = 42$) and is therefore underpowered, but it provides no evidence that the presence or absence of middle ear effusion at study entry influenced the efficacy of tympanostomy tubes.[66]

A second trial reported that the rate of new episodes per arm was 1.08 in the placebo group versus 1.02 in the tympanostomy tube group ($P = .25$).

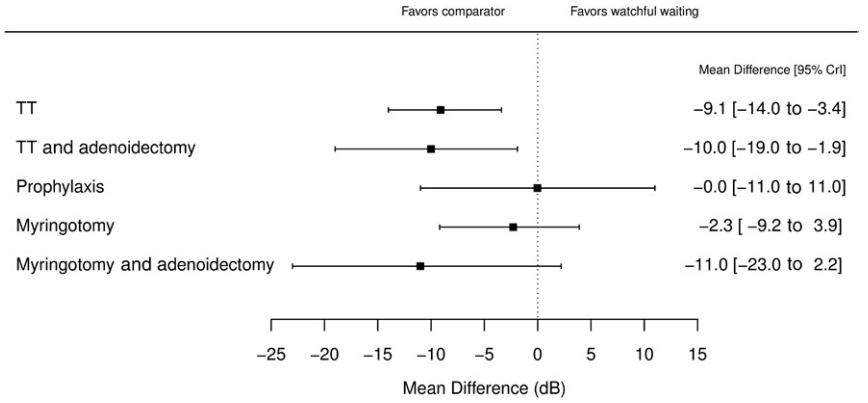

FIGURE 2
Early (1–3 months) decrease (improvement) in mean hearing thresholds compared with watchful waiting. CrI, credible interval; TT, tympanostomy tubes.

TABLE 1 Probabilities That an Intervention Is Among the 3 Most Effective With Respect to Early Hearing Thresholds

Intervention	Probability (%) of Being Among the 3 Most Effective Interventions	Probability (%) of Being Among the 3 Least Effective Interventions
TT	97	3
TT + adenoidectomy	96	4
Myringotomy	8	92
Myringotomy + adenoidectomy	91	9
Antibiotic prophylaxis	6	94
Watchful waiting	1	99

TT, tympanostomy tubes.

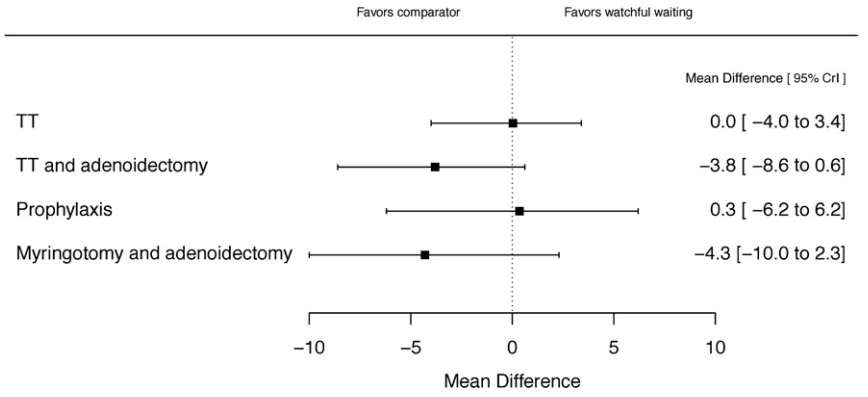

FIGURE 3
Late (12–24 months) decrease (improvement) in mean hearing thresholds compared with watchful waiting. CrI, credible interval; TT, tympanostomy tubes.

In the placebo group, 40% had no further episodes of AOM, compared with 35% in the tympanostomy tube group. However, tympanostomy tube placement significantly decreased the percentage of time with AOM (6.6%) compared with placebo (15.0%; $P < .001$).[67]

The third, most recent trial reported failure rates (defined as at least 2 episodes of AOM in 2 months, 3 in 6 months, or persistent effusion lasting at least 2 months), percentage of children with no recurrent AOM, cumulative number of AOM episodes, and 1-year incidence rates. There

was an absolute difference in the proportion of failures of −13% (95% confidence interval: −25 to −1) between the tympanostomy tube and control groups, favoring tympanostomy tubes. The 1-year incidence rate (infections per child per year) was 0.55 (95% confidence interval: 0.93 to 0.17) lower in the tympanostomy tube group compared with the control group.[71]

We were unable to provide pooled results due to the small number of studies, multiple interventions, and heterogeneity in reported outcomes. The limited available evidence suggests that tympanostomy tube placement decreases the risk of recurrent AOM. Aside from the first study,[66] we found no direct evidence to evaluate whether the presence of middle ear effusion at the time of surgical evaluation modifies the effectiveness of tympanostomy tube placement for recurrent AOM because the other 2 studies specifically excluded patients with current middle ear effusion.[67,71]

Three RCTs evaluated tympanostomy tubes alone versus adenoidectomy and tympanostomy tubes. Of these trials, none reported a difference in recurrent episodes of AOM.[69–71]

Risk of bias across outcomes ranged from moderate to high.

Adverse Events Associated With Tympanostomy Tubes

We extracted data on the occurrence of 11 adverse events from 85 cohorts and from the tympanostomy tube arms of included RCTs and NRCS. The number of publications reporting each event and the median (with 25th and 75th percentiles) percentage of patients and ears are summarized in Supplemental Table 4; references for these adverse events are also supplied.[13,19,21,30,39,52,67,71,74–158]

In general, the study-specific definitions of adverse events were poorly reported and/or highly variable between studies. Not all cohorts followed up all patients until extrusion of the tube, nor was follow-up complete in all studies. Several adverse event categories (eg, otorrhea, premature extrusion, myringosclerosis) have very wide interquartile ranges, likely due to highly variable definitions. Other adverse events, such as hearing loss and cholesteatoma, are likely confounded by the severity of preexisting and ongoing middle ear disease.

The main conclusions and interpretations, including strength of evidence assessments based on our meta-analysis, are summarized in Supplemental Table 3.

TABLE 2 Probabilities That an Intervention Is Among the 2 Most Effective With Respect to Late Hearing Thresholds

Intervention	Probability (%) of Being Among the 2 Most Effective Interventions	Probability (%) of Being Among the 3 Least Effective Interventions
TT	5	95
TT + adenoidectomy	92	8
Myringotomy + adenoidectomy	88	12
Antibiotic prophylaxis	10	90
Watchful waiting	4	96

TT, tympanostomy tubes.

DISCUSSION

Tympanostomy tube placement (compared with watchful waiting) in children with chronic middle ear effusion, results in improved average hearing thresholds at 1 to 3 months after surgery (a period when the majority of tubes are functioning). Mean hearing thresholds after tube placement with or without adenoidectomy improved by ∼10 dB when assessed at 1 to 3 months.

By 1 to 2 years after surgery, when most tubes have extruded, hearing thresholds are no longer different, likely reflecting the usually favorable natural history of spontaneous resolution of middle ear effusion in most children in both groups. There is limited evidence regarding quality of life outcomes, but neither of the 2 studies that evaluated parental stress and health-related quality of life found significant improvements in surgically treated children compared with watchful waiting.

Tympanostomy tubes did not consistently improve cognition, behavior, or quality of life, but low statistical power prevents any definitive conclusions, and the results apply to otherwise healthy children with no baseline disorders or delays in language, cognition, or behavior. With the exception of a few NRCS, comparative trials systematically exclude patients with cleft palate and Down syndrome, thus limiting the applicability of the evidence for these and other similar subgroups who experience a higher burden of middle ear disease. Similarly, patients at increased risk of developmental or behavioral sequelae from middle ear disease have not been included (or at least identified) in trials to date.

Given the sparse data and limitations inherent to the synthesis of aggregate data, we were unable to perform an analysis of factors which would predict those children more likely to benefit from tympanostomy tubes for chronic middle ear effusion. Additional insight was provided by an individual patient data meta-analysis that focused on interactions between treatment and baseline characteristics.[159] The meta-analysis found significant interactions between day care attendance in children aged ≤3 years, and in children >4 years of age with a hearing level of ≥25 dB

in both ears, and concluded that tympanostomy tubes might be most effective in young children attending day care, or in older children with persistent hearing impairments at least 12 weeks. However, average hearing level at baseline did not obviously modify effectiveness. Our meta-analysis of hearing levels used average pure tone hearing levels (typically reported as an average over frequencies of 500, 1000, 2000, and 4000 Hz). This single outcome measure is likely insufficient to fully elucidate the complex relationships between hearing, speech perception, and development in children.

Our network meta-analysis suggests a trend toward improved hearing thresholds in children undergoing adenoidectomy, but credible intervals are wide and include the null effect. An individual patient data meta-analysis of children with persistent OME concluded that adenoidectomy is most beneficial in children aged ≥4 years, with no significant benefit of adenoidectomy in children <4 years old.[160] This evidence is reflected in a recently updated clinical practice guideline for OME, which promotes tympanostomy tubes as the primary surgical intervention for younger children and reserves adenoidectomy for children ≥4 years or those with a distinct indication for the procedure other than OME.[161]

In children with recurrent AOM, the limited available evidence suggests that tympanostomy tubes decrease the number of additional episodes and the overall number of episodes of recurrent AOM. The degree to which the presence of middle ear fluid at the time of evaluation for surgery will affect the effectiveness of the tympanostomy tubes is unclear.

Three RCTs consistently found no difference in recurrent episodes of AOM in children who underwent tympanostomy tube placement with adenoidectomy compared with tympanostomy tube placement alone.[69–71]

Our systematic review of adverse events associated with tympanostomy tube placement provides a descriptive summary of the observed frequency in published cohorts. However, the study-specific definitions of adverse events are highly variable and poorly reported. Some adverse events, such as hearing loss and cholesteatoma, are likely confounded by the severity of preexisting and ongoing middle ear disease.

Limitations

The available evidence base is composed of studies that evaluate multiple interventions. Several of these (eg, myringotomy alone and oral antibiotic prophylaxis) are rarely used or not recommended[5] in current practice. We used indirect evidence from a network meta-analysis to augment the direct evidence relating to the comparisons of current interest. The key assumption of the network meta-analysis is that of consistency of direct and indirect effects. Consistency is likely to hold when the distribution of effect modifiers is similar across trials. If this assumption is violated, there may be inconsistency between the direct evidence and indirect evidence of treatment comparisons.

Reporting of possible sociodemographic risk factors is sparse and inconsistent, which limits our ability to draw conclusions about which of these factors might influence the relative effectiveness of tympanostomy tubes.

Current recommended indications for tympanostomy tube placement largely reflect the inclusion criteria used in existing clinical trials. Given the usually favorable natural history of middle ear effusion, well-validated prognostic models are urgently needed to stratify the risk of individual children in terms of their risk for persistence of middle ear effusion and/or recurrent AOM.

Assessing the effectiveness of tympanostomy tubes in children with recurrent AOM is particularly challenging because an episode of AOM in control children (with an intact tympanic membrane) results in otalgia and inflammatory changes, whereas children with a functioning tympanostomy tube may present with varying degrees of otorrhea. Outcomes that rely on simple counts or rates of otorrhea fail to account for the variable character of otorrhea with respect to duration, character, and patient impact. For example, otorrhea may be transient (of little to no concern), recurrent (of more concern but usually readily managed), or chronic (of considerable concern and difficult to manage).

Future Research Needs

Pragmatic trials are needed, particularly in children with recurrent AOM, but also in children with chronic OME or some combination of both. Because tympanostomy tubes are no longer effective after extrusion, future trials should record per-ear and per-patient outcomes conditional on whether the tympanostomy tube has been extruded. Future studies should also conduct appropriate analyses to estimate the causal effects of tympanostomy tubes among children who still have the tubes in place. Future trials would benefit from standardization of disease definitions and consistent definition of core outcomes and adverse events.

Exploring treatment effect heterogeneity (ie, differential effects of interventions in populations at different risk levels for outcomes of interest) should be a priority. There is particular need for randomized studies evaluating tympanostomy tubes in higher risk groups, such as patients with cleft palate, Down syndrome, and children with neurodevelopmental disorders.

CONCLUSIONS

Overall, the evidence suggests that tympanostomy tubes in children with persistent middle-ear effusion result in short-term improvements in hearing compared with watchful waiting. However, there is no evidence of a sustained benefit.

Our network meta-analysis of hearing thresholds suggests the possibility of a more sustained improvement in hearing thresholds in at least some children who undergo adenoidectomy and tympanostomy tube placement. A nuanced understanding of which children may benefit from adenoidectomy is limited by the small evidence base and our use of aggregate data.

The evidence suggests that treatment with tympanostomy tubes did not improve cognition, behavior, or quality of life. However, the evidence is sparse and prevents any definitive conclusions. The results apply to otherwise healthy children without baseline disorders or delays in language or cognition. They provide little guidance for the treatment of children who may be at increased risk for speech, language, or learning problems because of baseline sensory, physical, cognitive, or behavioral factors.

Children with recurrent AOM may have fewer episodes after tympanostomy tube placement, but the evidence base is severely limited. It is unclear whether quality of life outcomes are improved. The benefits of tympanostomy tubes must be weighed against a variety of adverse events associated with—although not necessarily caused by—this treatment.

ACKNOWLEDGMENTS

Special thanks to Joseph Lau for his advice and guidance; Ian Pan and Nathan Coopersmith for assistance with screening and extraction; and Jenni Quiroz and Jenna Legault and for their assistance throughout the systematic review process.

ABBREVIATIONS

AOM: acute otitis media
NRCS: nonrandomized comparative studies
OME: otitis media with effusion
RCT: randomized controlled trial

DOI: https://doi.org/10.1542/peds.2017-0125

Accepted for publication Mar 15, 2017

Address correspondence to Dale W. Steele, MD, MS, Center for Evidence Synthesis in Health, Box G-S121-8, Brown University, Providence, RI 02912. E-mail: dale_steele@brown.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: All authors received funding for this project under Contract HHSA290-2015-00002-I from the Agency for Healthcare Research and Quality, US Department of Health and Human Services.

FUNDING: Supported by the Agency for Healthcare Research and Quality (contract: HHSA290-2015-00002-I).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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Pediatrics; originally published online May 16, 2017;
DOI: 10.1542/peds.2017-0125

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