

What are the Long Term Effects and Stratifiers on Hearing from Having Tympanostomy Tube Insertion? A Systematic Review

Susan Amin ^{1*}, Rama Nakdali ¹, Rula Naqi ¹, Nada Alawi ¹

¹ Department of Craniofacial Development and Orthodontics, Kings College London, Guy's Hospital, London, United Kingdom

* **Corresponding Author:** Susan Amin, Department of Craniofacial Development and Orthodontics, Kings College London, Guy's Hospital, London, United Kingdom. E-mail: susan.amin.uk@gmail.com

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Abstract

Introduction: Middle ear disease is common in childhood and is often associated with hearing loss. Seventy-one percent of all children have at least an episode of Otitis Media with Effusion (OME) by the age of three. The high incidence of OME in patients with middle ear disease has led to the conclusion that treatment with Tympanostomy Tube Insertion (TTI) would solve the inevitable hearing loss associated with middle ear disease. Studies reporting an association between hearing loss and TTI are conflicting and warrant a systematic review of the evidence.

Methods: A dual review process was used to assess eligible studies drawn from PubMed, Medline via Ovid, and Science direct, reference lists from 2007 to 2018. Five studies were selected.

Results: Three studies did not specify a primary outcome measure in terms of the types of hearing loss i.e. did not specifically measure CHL and reported benefits in hearing with TTI. The other studies reported incidences of CHL with the use of the TTI. Shorter tubes tended to reduce long term complications. Tube stay-time was on average 6-12 months and required follow up as a result of an increase in complications. The number of insertions was positively correlated with children with symptomatic pathology. Tube location is important as medial displacement can occur as well as not checking tube function. Children aged from zero to six years old benefitted the most from TTI as their hearing loss tended to be the greatest at the baseline compared to older children.

Conclusion: An extensive systematic review identified five studies examining hearing loss and TTI in young children from 2007 to 2018. There are two main findings from this review. First, two studies reported hearing loss in two studies with TTI. Second, the association between hearing loss and TTI may be influenced by the type of hearing loss measure, technical aspects of TTI, and demographic and health characteristics. These findings are strengthened by evidence from a large (n = 3128) globally representative sample of young adults. A proportion of children may experience conductive hearing loss with TTI, and we recommend allied health professionals and general practitioners increase their awareness and understanding of the hearing loss experienced during TTI.

Keywords: Child, Preschool, Middle Ear, Hearing Loss, Conductive, Tympanostomy Tube Insertion, Myringostomy, Grommet Insertion, Otitis Media, Otitis Media with Effusion, Nonsuppurative Otitis Media, Technical Aspects, General Practitioners, Otorhinolaryngology

Introduction

Middle ear disease is common in childhood and is often associated with hearing loss. Seventy-one percent of all children have at least an episode of otitis media by age three years.^{1,2} There are two types of otitis media. Recurrent acute otitis media, which is defined as either three or more acute infections of the middle ear cleft in a six-month period and Otitis Media with Effusion (OME) which is when a collection of non-purulent fluid builds up in the middle ear space. This fluid may accumulate in the middle ear as a result of an upper respiratory infection, cold or a sore throat.

OME is usually self-limited, which means, the fluid usually resolves on its own within four to six weeks. However, in some instances the fluid may persist for a longer period of time and cause a temporary decrease in hearing or the fluid may become infected (acute otitis media).

When children require surgery for OME, insertion of tympanostomy tubes is the preferred initial procedure, with candidacy dependent primarily on hearing status, associated symptoms, and the child's developmental risk.³

The high incidence of OME in patients with middle ear disease led to the conclusion that treatment with Ventilation Tube Insertions (VTIs) or Tympanostomy Tube Insertions (TTIs) or grommets would solve the inevitable hearing loss associated with middle ear disease and prevent the sequence of OME including cholesteatoma formation, retraction pockets, ossicular fixation, and atelectasis.⁴ Studies have confirmed that early intervention with TTI provides an appreciable benefit with regards to short-term hearing, between six to 12 months.⁵⁻⁷ This regimen usually requires TTIs to be completed in the first year of life to reduce further complications. These complications include increased risk of otitis media because of their immature immune systems and poor Eustachian tube function. This is a tube-like connection between the middle ear and back of the nose that normally ventilates the middle ear space and equalizes pressure with the external environment.⁸

However, currently the use of prophylactic tympanostomy tubes is being heavily scrutinised due to associated complications such as; perforations, otorrhea, eardrum atrophy, granulation tissue, and tympanosclerosis (which can be as high as 80%). Prophylactic VTs are tubes placed in patients who have not yet met the threshold for tympanostomy tube placement dictated in clinical practice guidelines.⁴

Other studies have revealed that children who undergo multiple TTIs increase their risk of conductive hearing loss in long term.⁹

Children with OME less than three months and those without effusion at the time of evaluation should not receive tubes (in the absence of other developmental concerns).^{10,11}

A large number of reviews on the use of tympanostomy

for OME have been published. However, many of these were narrative,¹² others were systematic investigations that pertained mainly to otherwise healthy children with normal development³ or were in symptomatic patients with syndromes such as cleft palate.⁴ Despite all the mentioned complications of tympanostomy, there are no sufficient systematic reviews or meta-analysis that show the exact association, incidence, and prevalence of each complication. Having such studies provide guidance for practitioners in deciding the treatment option for each patient by balancing risks and benefits. Thus, this systematic review focuses on conductive hearing loss after tympanostomy in children.

The primary aim of this study was to synthesize the available evidence to assess if there is an association between conductive hearing loss and TTI. The secondary aim was to examine whether study (e.g., design, outcome measures), technical (e.g., tube type, tube stay-time, number of insertions, tube location, prior pathological status), age of participant (e.g., demographic, health) characteristics may influence the association between hearing loss and TTI.

Materials and Methods

Search Strategy and Selection Criteria

The intervention in our review was TTIs and the incidences of conductive hearing loss. A systematic review of the literature was conducted using CINAHL, PubMed/MEDLINE and science direct. Details of the electronic search strategy, including the search terms used, have been presented in Table 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in this systematic review.¹³

Table 1. Search Strategy

	Search details	Medline Citations	PubMed citations	Science direct	Total citations
1	Conductive hearing loss	5,597	1,322	1,428	8,347
2	Middle ear hearing loss	19,852	3,761	3,651	27,264
3	Tympanostomy	1,626	945	423	2,994
4	Ventilation tube insertion	1,486	1,445	6,012	8,943
5	Otitis media with effusion	345	1,453	7,349	9,147
6	#1 and #2	6	870	4,860	5,736
7	#1 or #2 and #3	418	72	75	565
8	#1 or #2 and #3 or #4 and #5	92	250	52	394

The used selection process is outlined in Figure 1. The titles and abstracts of the selected articles were

screened for the inclusion criteria and the full articles were retrieved. Overall, 394 abstracts were reviewed.

Three hundred and twenty citations were excluded for various reasons including 71 for duplication (Figure 1). This left a sample of 74 papers where the full text was obtained. Thirty of these papers only described a study protocol (did not report results) and were excluded. Twenty-six papers were excluded for the following reasons: Papers looking at transcription marker expression during the course of TTI, drugs that could be used in addition to TTI and that affect TTI, types of bacteria that could contaminate tubes and how to manage TTI other symptoms of acute otitis media, markers of middle ear pathology, spoke of incisions but no insertions and complications of ear structures. Thirteen papers were excluded for reasons pertaining to best clinical practice on TTIs and cost. Five papers were included in the final analysis.

Figure 1. Data not Shown

Data Extraction and Quality Assessment

Data extracted from articles included study design, sample size, sample characteristics, mean age at baseline of intervention, types of interventions, duration of intervention, and follow-up information. Two independent reviewers extracted data. The quality of each article was evaluated by three methods. First method, Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) checklist. The checklist consists of seven sections: Title, Abstract, Introduction (rationale and objectives), Methods (protocol and registration, eligibility criteria, information sources, search, study selection, data collection process, data items, risk of bias in individual studies, summary measures, synthesis of results, risk of bias across studies and additional analyses), Results (study selection, study characteristics, risk of bias within studies, results of individual studies, synthesis of results, risk of bias across studies and additional analysis), Discussion (summary of evidence, limitations and conclusion) and funding. The second method was the PRISMA flow chart (identification, screening, eligibility). The third and last method was the Newcastle Ottawa scale. It is a 'star system' where a study is judged on three broad perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control or cohort studies respectively. The best studies are given the highest

stars, which is nine stars.

Results

Our quality assessment found different designs in the studies. Four studies were on a case series and one was a randomised controlled trial. Information was also extracted from the papers in relation to stratifiers associated with TTI such as tube type, tube stay-time and number of insertions, tube location, prior pathological status, age and their contribution to hearing (Table 2). We therefore decided not to exclude any of the studies but described the methodological problems in each paper, and extracted as much information as possible from each paper. Authors are listed in alphabetical order.

Because of the different designs we were not able to perform any meta-analysis. As we were evaluating the effect of an intervention with a possible outcome randomised trials, in which interventions are assigned in an experimental fashion so that there are no important differences between those receiving and not receiving the intervention of interest would have been appropriate. Randomisation was included for both children and ear in one study for children (TTI versus no TTI), for ears (TTI one ear only).¹⁴ Three studies were randomised by children and one was randomised by ears, i.e. one ear had the tube and the other ear had no treatment. One study had four comparison groups¹⁵ and one had six.¹⁶ (Table 3).

Data and outcomes were extracted directly from the full text paper and has been presented in Table 4.

Study Characteristics

The five studies included 3128 individuals (Table 2) and two studies included the bulk of these participants.^{14,17} The first study was a systematic review that recruited the participants from the Cochrane ENT disorders register.¹⁴ The second study included participants recruited from a clinical database at Boston Children's hospital, USA.¹⁷ The mean age of study participants at baseline ranged from three months to 16 years (Table 4).

One study achieved seven stars using the Newcastle-Ottawa scale,¹⁸ while four studies scored six stars as there was no statement to indicate no history of disease and subjects were lost to equipment breakdown and dropping out.¹⁴⁻¹⁷ Overall, as the star ratings were fairly high, this points out that studies were of a mostly moderate quality.

Table 2. Design, Inclusion Criteria and Number of Patients

Study	Design and Follow up	Intervention	Inclusion criteria	Number recruited
14	Randomised controlled trial We included 10 trials (1728 participants). We searched the Cochrane ENT Disorders Group Trials Register, other electronic databases and additional sources for published and unpublished trials (most recent search: 22 March 2010)	TTI	Randomised by ears or children Level was 31 to 33 dB HL. Outcomes include age-specific child tests (e.g. of comprehension), or auditory performance tests (e.g. speech in noise) by clinician. Domains considered most relevant include speech and language, cognition and mental development, behaviour, impact on the family, physical health, reported hearing difficulty, and their overall effect on quality of life and functioning. OME bilaterally for 90 days or unilaterally 135 days.	1728
15	Case series- Cohort had their first TTI between January 2006 and December 2008. Design parameters Patient data on demographic profile, presenting complaints, indications, medical history, ear examination, hearing threshold and tympanometry evaluations, and complications of TTI were collected.	TTI	OME that persists longer than 3 months. A telephone survey of parents was performed with questions on whether the parents felt that the hearing loss associated with the OME had adversely impacted school performance prior to TTI, and if school performance in such cases have improved after TTI.	105
16	Case series- over three years Medical records of thirty-nine children who were referred for either conductive or mixed hearing loss post-tympanostomy tube placement were reviewed for clinical histories, physical examinations, audiological evaluations, diagnostic studies, consultations, and surgical findings.	TTI	Referral by health service provider to a tertiary paediatric hospital.	39
17	Case series and medical review for 12 months. The medical records were reviewed with information abstracted for sex, date of birth, date of TT I insertion, dates and results of preoperative and postoperative audiometric evaluations, tympanometry. Results, and medical histories of patients who were found to have hearing losses.	TTI	The i2b2 (Informatics for Integrating Biology and the Bedside). Database at Boston Children's Hospital, a centralized repository of clinical data, was queried for the Current Procedural Terminology(CPT) code for TT placement (69436) over the year period of June1,2010,through June1,2011	1175
18	Case series 6-66 months. The medical records of 162 ears of 87 children (52 male and 35 female) were reviewed retrospectively. The children were between 3 to 16 years old (mean age = 8.1 ± 3.1). The patients were followed up 6–66 months (mean 23.3 ± 14.9 months) after tympanostomy tube insertion. We reviewed age, sex, time to tube extrusion and complications.	TTI	OME for at least three months.	87

Hearing Characteristics

Three studies did not specify a primary outcome measure in terms of the types of hearing loss i.e. did not specifically measure CHL.^{14,15,18} Two studies reported incidences of CHL and sensorineural deafness with the use of the TTI.^{16,17} The other studies reported benefits in overall hearing with the TTI.^{14,15,18} A study follow up showed that TTIs were mainly beneficial in the first six months. At six to nine months of follow up, the mean hearing level in the children treated with TTI

measured by tympanometry (n = 271) was 4.2 dB better (95% CI 2.4 to 6.0 dB) than the mean hearing levels of those in the 'watchful waiting/active monitoring group (n = 252). At 12 months follow up, no differences in mean hearing levels were found primarily due to natural resolution (Table 4).¹⁴ In another study, the hearing thresholds were determined by age-appropriate hearing tests with pure tone audiogram, play audiometry or auditory brainstem evoked response. Hearing pre- and post-TTI insertion showed improvement in all

Table 3. Problems and Drop Outs

Study	Problem with study design/ medical issue	Comparison groups	Drop out after randomisation
14	Different studies yield different results and in some studies tests for wellbeing may not have been used as well as compared to others.	Children and ears randomised. One group also included a watchful waiting group with no intervention.	
15	14 needed a repeat TT and 12 further surgery.	Four comparison groups Below three years old. Three to six years old. Six to twelve years old Twelve to eighteen years old.	
16	Incidence not determined as many from outside institutions	Children randomised	
17	Inability to obtain ear specific data. Some tubes were non-functional. Data collected in a clinical setting Operative audiometric evaluations were variable. Performance of audiometry, timing of evaluation, and completeness of testing all varied.	Children randomised	Drop-outs 26(1.1%)
18	Displacement of tubes.	Six comparison groups Unilateral TTI Adenoidectomy with TTI Multiple TTI First tube only Second tube Third tube	No tube (1) (1.1%)

Table 4. Outcomes at the End of Follow up for Each Study

Study	Intervention group (number completed)	Age	Gender	Primary effect measure	Hearing after 6 months	Hearing after two years
14	1728 TT	5-7 years		12 dB benefit (95% CI 10-14 dB)	4dB benefit in hearing (95% CI 2-6dB)	No difference in hearing levels
15	105 TT	3 months to 15 years	60M 45 F	32% improvement on both sides 23.5 dB right side and 24.6 dB left side for all age groups	-	-
16	39 TT	5.92 years average	39 M	22(56%) had CHL and mixed hearing loss).	-	-
17	1466 (84.2%) functional TT	1.48-4.94 years	1364 M 910F	15 (0.66%) CHL	-	-
18	87 TT	3-16 years	52 M 35 F	No hearing loss	-	-

frequencies for all four age groups. The average pre-TTI hearing on the right was 34.4 dB +/- 0.9 and 36.1 dB +/- 4.3 on the left. The average post TTI hearing was 23.5 dB +/- 10 on the right and 24.6 dB +/- 6.8 on the left. The improvement was 32% on both sides which is statistically significant ($p < 0.05$) (Table 4).¹⁵ In another study, no hearing loss was found in the study participants although complications related to the tubes were seen that included myringosclerosis (34.6%), persistent perforation (5.6%), atrophy (23.5%), retraction (16.7%) and medial displacement of tubes (1.2%).¹⁸

Conductive hearing loss

Two studies in this review have reported conductive hearing loss as a result of TTI use for OME. One study mentions a 56% incidence of conductive hearing loss or mixed hearing loss. This study also mentions that the actual incidence could not be determined as many patients were from outside institutions and data regarding TTI were unobtainable (Table 3).¹⁶ In the other study, 15 patients (0.66%) were found to have conductive hearing loss in the absence of middle ear effusion.¹⁷ However in this article it does mention within

this case series of 2274, there are no patients with permanent postoperative hearing loss after a normal preoperative audiometric evaluation result with no comorbidities or complications (Upper 95% CI 0.13%). The patients who had CHL in this study had underlying syndromes such as cleft lip and palate¹⁷ (Table 4).

Length of Follow Up

The follow up periods used in the studies ranged up to 2010¹⁴ three years^{15,16} one year¹⁷ and 5 years.¹⁸ Of interest, the longest studies reported no CHL in their analysis and hearing improved in the patients overall^{14,15,18} (Table 2).

Placement of Tube and Age

One study compared hearing levels at different ages of TTI insertion and it was found that hearing pre and post TTI showed improvement in all frequencies for all four age groups and there was a significant (32%) improvement for both right and left sides of the ear after TTI¹⁵ (Table 3).

Effectiveness of Tympanostomy for Hearing Loss

Three studies reported TTI being effective in preventing hearing loss associated with OME.^{14,15,18} Yaman compared single tubes with multiple tubes and found no evident hearing loss. Browning found that the mean hearing level was 10dB better with TTI after insertion and was 6dB after two years (Table 4).

Age of Insertion

The worst hearing was seen in children between zero to three years old, which coincides with the time when hearing is crucial to speech and language acquisition. Nine percent of children between the ages of three and six were presented with behavioural issues. Most of the children needing TTI insertion for chronic OME were less than six years old and these were the ones who benefited the most compared to those children with a much smaller hearing loss at the baseline.¹⁵

Tube Stay-time

Yaman reports the follow up period to be the time from tube insertion to the control end time of six to 12 months.¹⁸ Anything longer than this is linked to issues.¹⁴

Location of Tube

Myringotomy with tympanostomy tube placement

refers to a surgical procedure in which a small incision is made in the tympanic membrane and a pressure equalization tube is placed. This allows air exchange through the tympanic membrane and aeration of the middle ear space. In a study, 2% of tubes were displaced medially. There was no report if this affected the final outcomes as these were reinserted.¹⁸

Discussion

The aim of this paper was to systematically review TTI interventions in children and the long term effects on hearing as a result of this treatment as well as stratifiers related to the TTI and how they relate to the side effects. The studies sourced were heterogeneous in terms of the design type and outcomes assessed.

Hearing Level and TTI

An abundance of literature refers to the benefits of hearing with the use of the TTI.^{14,15,18} This coincides with similar data that also report an improvement in hearing with the use of TTI.^{19,20,21} Rover compares the hearing levels of the patients after either having a TTI or just having a Watchful Waiting (WW) period. After six months of follow up in this group, there was a 5.6 dB benefit of hearing in the TTI group compared to the WW group. However, after 12 months this benefit disappears.²⁰ This contrasts however with two of our studies that have found CHL with the use of a TTI.^{16,17} This is similar to data from other studies that also report a decrease in hearing after TTI. For example, a study reports a 3.3-fold increase in the risk of mean hearing thresholds in the TTI group.²²⁻²⁴ However, a number of patients had underlying conditions such as cleft palate at the time of TTI and this could have been a contributor to the incidences of CHL.²⁵

In terms of conductive hearing loss, it was difficult to get an exact incidence. The incidence noted in Whittemore 2016 of 0.66 % was mostly with patients who were symptomatic for an underlying disorder such as cleft palate. There was also a greater proportion of boys in the two studies that were diagnosed with conductive and mixed hearing loss. In one study, they had a higher rate of the third window effect.¹⁷ This is where in the presence of a third window, incoming acoustic energy from the oval window is shunted away, decreasing transmission to the round window. This result reduces sound perception because less acoustic energy is available to the hair cells.²⁶ In the other

study, 56% had mixed and conductive hearing loss.¹⁶ The other studies did not report on a gender difference in the hearing levels after TTI. Further investigation with a longitudinal study with a larger patient population is needed to confirm these findings.

Measuring the Hearing Loss

In terms of diagnosing the hearing loss in the different studies, a mixture of Computed Tomography (CT) testing to investigate the temporal bone as it provides a superior evaluation of the bony sound conduction pathway was used to diagnose 16 out of 24 patients in a study. Vestibular-Evoked Myogenic Potential (VEMP) testing was used to investigate the presence of a third window for vestibular function to make a diagnosis in three out of four children in the same study.¹⁷ VEMP testing can be measured quickly and easily and is much more specific than CT.²⁷ New-born baby screening was not considered effective having missed out patients who had a congenital abnormality.¹⁶ Further investigations could take note of these methods when measuring conductive hearing loss.

Tube Stay Time

One study reported non-functional tubes that contributed to hearing loss.¹⁸ When results such as these are observed, serial audiological and otologic evaluations should be performed to ensure stability of the hearing loss while tubes are in place and functional. An audiological evaluation following TT extrusion or removal is imperative in these cases, to ensure a return to normal hearing. Tube stay-time was on average six to 12 months and required follow up as a result of an increase in complications when tube stay time was up to 36 months.²⁸ In the present study, we benefited from studies that had longer follow up times.^{14,15,18} Identification of hearing loss as early as possible is critical for children's social and cognitive development. The link between hearing loss and speech/language development and delay is well documented. In a study, it was reported to be higher among females even after controlling for a wide range of confounding factors.²⁹ Yaman reports the follow up period to be the time from tube insertion to the control end time of six to 12 months.¹⁸

Tube Placement and Size

In terms of placement of the tube Nurliza's study of 2011 coincides with a similar study in six-year-old

students where if the tube was placed earlier or later there were no difference in the hearing loss and this was unrelated to the presence or type of tympanic membrane abnormality.²¹ In another study it was noted that the type of tube could have an impact where results in one study were generalised to short tubes where there was reduced incidence of otorrhea compared to long tubes.³⁰ In another study it was noted that children with craniofacial abnormalities tended to have a significantly higher rate of TTI and tended to have more prolonged issues with Eustachian tube dysfunction and often require multiple sets of tympanostomy tubes compared to children with no underlying disorders.³¹

Location and No of Insertions

The number of insertions was positively correlated with children with symptomatic pathology.²¹ Tube location is important as medial displacement can occur as well as not checking tube function.¹⁸

Age

A prior pathological status (a status preceding a pathological condition) was associated with an increase in conductive hearing loss and children aged from zero to six years old benefitted the most from TTI as their hearing loss tended to be the greatest at the baseline compared to older children. Yet age was not such a big factor in terms of hearing loss as all aged children in one study achieved benefit on their hearing loss with TTI.¹⁵

Strengths

This review is strengthened due to a large population size with the correct age group. Also, the majority of the studies were also in good agreement with each other where use of TTI is beneficial to the hearing loss associated with OME in short term.

Limitations

A limitation of this review was that only papers written in English were included, possibly resulting in the omission of important studies. Additionally, only three databases were searched, which may have limited the findings of the review. Sample sizes could have been bigger to increase the validity and accuracy. Nonetheless, the findings help to elicit the current state of issue in general.

Children aged from zero to six years old benefitted

the most from TTI as their hearing loss tended to be the greatest at the baseline compared to older children. Yet, age was not such a big factor in terms of hearing loss as all aged children in one study achieved benefit on their hearing loss with TTI. More studies are needed to look at the effects of age and TTI.

Conclusion

An extensive systematic review identified five studies examining hearing loss and TTI in young children from 2008 to 2018. There are two main findings from this review. First, two studies reported hearing loss in two studies with TTI. Second, the association between hearing loss and TTI may be influenced by type of hearing loss measure, technical aspects of TTI, and demographic and health characteristics. These findings are strengthened by evidence from a large (n = 3128) globally representative sample of young adults. A proportion of children may experience conductive hearing loss with TTI, and we recommend allied health professionals and general practitioners to increase their awareness and understanding of the hearing loss experienced during TTI.

TTI is a viable treatment for the prevention of hearing loss associated with OME for any age. Short tubes, less insertions and no prior pathological status were important for long term benefit.

Authors' Contributions

Study concept and design: SA. Data extraction (abstracts and full articles): RN and NA. Independent review of full articles: RN and NA. Data analysis and interpretation: RN. Quality review RN and SA. Drafting of the manuscript SA. Editing and reviewing the final manuscript: RN, NA and SA. All authors read and approved the final manuscript.

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Conflict of Interest

The authors declare that they have no conflicts interest.

References

- Rosenfeld RM, Culpepper L, Yawn BP, Mahoney MC. Otitis media with effusion clinical practice guideline. *Am Fam Physician*. 2004;69(12):2776.
- Engel JA, Straetemans M, Zielhuis GA. Birth characteristics and recurrent otitis media with effusion in young children. *Int J Pediatr Otorhinolaryngology*. 2005;69(4):533-40. doi:10.1016/j.ijporl.2004.11.026
- Rosenfeld RM, Schwartz SR, Pynnonen MA, Tunkel DE, Hussey HM, Fichera JS, et al. Clinical practice guideline: tympanostomy tubes in children—executive summary. *Otolaryngol Head Neck Surg*. 2013;149(1):8-16. doi:10.1177/0194599813490141
- Vlastarakos PV, Nikolopoulos TP, Korres S, Tavoulari E, Tzagaroulakis A, Ferekidis E. Grommets in otitis media with effusion: the most frequent operation in children. But is it associated with significant complications?. *Eur J Pediatr*. 2007;166(5):385-91. doi:10.1007/s00431-006-0367-x
- Ponduri S, Bradley R, Ellis PE, Brookes ST, Sandy JR, Ness AR. The management of otitis media with early routine insertion of grommets in children with cleft palate—a systematic review. *Cleft Palate Craniofac J*. 2009;46(1):30-8. doi:10.1597/07-219.1
- Paradise JL, Bluestone CD. Early treatment of the universal otitis media of infants with cleft palate. *Pediatrics*. 1974;53(1):48-54. doi:10.1542/peds.53.1.48
- Moore IJ, Moore GF, Yonkers AJ. Otitis media in the cleft palate patient. *Ear Nose Throat J*. 1986;65(7):291-5.
- Bluestone CD, Swartz JD. Human evolutionary history: consequences for the pathogenesis of otitis media. *Otolaryngol Head Neck Surg*. 2010;143(6):739-44. doi:10.1016/j.otohns.2010.08.015
- Sheahan P, Blayney AW, Sheahan JN, Earley MJ. Sequelae of otitis media with effusion among children with cleft lip and/or cleft palate 1. *Clin Otolaryngol Allied Sci*. 2002;27(6):494-500. doi:10.1046/j.1365-2273.2002.00607.x
- Maw AR, Parker A. Surgery of the tonsils and adenoids in relation to secretory otitis media in children. *Acta Otolaryngol*. 1988;105(sup454):202-7. doi:10.3109/00016488809125027
- Zielhuis GA, Rach GH, van den Bosch A, van den Broek P. The prevalence of otitis media with effusion: a critical review of the literature. *Clin Otolaryngol Allied Sci*. 1990;15(3):283-8. doi:10.1111/j.1365-2273.1990.tb00787.x
- Yules RB. Current concepts of treatment of ear disease in cleft palate children and adults. *Cleft Palate J*. 1975;12(3):315-22.
- Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol*. 2009;62(10):e1-34. doi:10.1016/j.jclinepi.2009.06.006
- Browning GG, Rovers MM, Williamson I, Lous J, Burton MJ. Grommets (ventilation tubes) for hearing loss associated with otitis media with effusion in children. *Cochrane Database Syst Rev*. 2010(10):CD001801. doi:10.1002/14651858.CD001801.pub3
- Nurliza I, Lim L. Retrospective review of grommet insertions for otitis media with effusion in children in Singapore. *Med J Malaysia*. 2011;66(3):22.
- Whittemore Jr KR, Dornan BK, Lally T, Dargie JM. Persistent conductive or mixed hearing loss after the placement of tympanostomy tubes. *Int J Pediatr Otorhinolaryngol*. 2012;76(10):1465-70. doi:10.1016/j.ijporl.2012.06.022
- Whittemore KR, Dornan BK, Dargie JM, Zhou G. Perioperative hearing evaluations for patients undergoing tympanostomy tube placement. *JAMA Otolaryngol Head Neck Surg*. 2016;142(11):1070-4. doi:10.1001/jamaoto.2016.1980
- Yaman H, Yilmaz S, Alkan N, Subasi B, Guclu E, Ozturk O. Shepard grommet tympanostomy tube complications in children with chronic otitis media with effusion. *Eur Arch Otorhinolaryngol*. 2010;267(8):1221-4. doi:10.1007/s00405-010-1220-4
- Valtonen HJ, Qvarnberg YH, Nuutinen J. Otolological and audiological outcomes five years after tympanostomy in early childhood. *Laryngoscope*. 2002;112(4):669-75. doi:10.1097/00005537-200204000-00014
- Rovers MM, Straatman H, Ingels K, van der Wilt GJ, van den Broek P, Zielhuis GA. The effect of short-term ventilation tubes versus watchful waiting on hearing in young children with persistent otitis media with effusion: a randomized trial. *Ear Hear*. 2001;22(3):191-9.
- Johnston LC, Feldman HM, Paradise JL, Bernard BS, Colborn DK, Casselbrant ML, et al. Tympanic membrane abnormalities

- and hearing levels at the ages of 5 and 6 years in relation to persistent otitis media and tympanostomy tube insertion in the first 3 years of life: a prospective study incorporating a randomized clinical trial. *Pediatrics*. 2004;114(1):e58-67. doi:10.1542/peds.114.1.e58
22. Stenstrom R, Pless IB, Bernard P. Hearing thresholds and tympanic membrane sequelae in children managed medically or surgically for otitis media with effusion. *Arch Pediatr Adolesc Med*. 2005;159(12):1151-6. doi:10.1001/archpedi.159.12.1151
 23. Brown MK, Richards SH, Ambegaokar AG. Grommets and glue ear: a five-year follow up of a controlled trial. *J R Soc Med*. 1978;71(5):353-6.
 24. Pichichero ME, Berghash LR, Hengerer AS. Anatomic and audiologic sequelae after tympanostomy tube insertion or prolonged antibiotic therapy for otitis media. *Pediatr Infect Dis J*. 1989;8(11):780-7. doi:10.1097/00006454-198911000-00010
 25. Goudy S, Lott D, Canady J, Smith RJ. Conductive hearing loss and otopathology in cleft palate patients. *Otolaryngol Head Neck Surg*. 2006;134(6):946-8. doi:10.1016/j.otohns.2005.12.020
 26. Ho ML, Moonis G, Halpin CF, Curtin HD. Spectrum of third window abnormalities: semicircular canal dehiscence and beyond. *Am J Neuroradiol*. 2017;38(1):2-9. doi:10.3174/ajnr.A4922
 27. Zhou G, Gopen Q, Poe DS. Clinical and diagnostic characterization of canal dehiscence syndrome: a great otologic mimicker. *Otol Neurotol*. 2007;28(7):920-6. doi:10.1097/MAO.0b013e31814b25f2
 28. Di Francesco R, Paulucci B, Nery C, Bento RF. Craniofacial morphology and otitis media with effusion in children. *Int J Pediatr Otorhinolaryngol*. 2008;72(8):1151-8. doi:10.1016/j.ijporl.2008.03.027
 29. Niclasen J, Obel C, Homøe P, Kurvel-Hanquist A, Dammeyer J. Associations between otitis media and child behavioural and learning difficulties: Results from a Danish cohort. *Int J Pediatr Otorhinolaryngol*. 2016;84:12-20. doi:10.1016/j.ijporl.2016.02.017
 30. Kay DJ, Nelson M, Rosenfeld RM. Meta-analysis of tympanostomy tube sequelae. *Otolaryngol Head Neck Surg*. 2001;124(4):374-80. doi:10.1067/mhn.2001.113941
 31. Mohammed H, Martinez-Devesa P. Complications of long-term ventilation tubes. *J Laryngol Otol*. 2013;127(5):509-10. doi:10.1017/S0022215113000388