Evidence tables for review question: What intraoperative or postoperative interventions are effective at preventing otorrhoea (ear discharge) after surgery for OME-related hearing loss in children under 12 years?

Table 4: Evidence tables

Mair, 2016

Bibliographic Reference	Mair, Eric A; Moss, Jonathan R; Dohar, Joseph E; Antonelli, Patrick J; Bear, Moraye; LeBel, Carl; Randomized Clinical Trial of a Sustained-Exposure Ciprofloxacin for Intratympanic Injection During Tympanostomy Tube Surgery.; The Annals of otology, rhinology, and laryngology; 2016; vol. 125 (no. 2); 105-14

Study details

Country/ies where study was carried out	USA
Study type	Randomised controlled trial (RCT)
Study dates	January 2013 - June 2013
Inclusion criteria	Children aged 6 months to 12 years with confirmed bilateral middle ear effusion with indication of tympanostomy tube placement
Exclusion criteria	History of ear and mastoid surgery, requirement of concurrent surgery, sensorineural hearing loss, history of other chronic or recurrent bacterial infection, history of tympanic membrane perforation, known immunodeficiency, abnormal tympanic membrane or middle ear, use of topical nonsteroid otic medication within 1 day of randomisation, use of topical, inhale or nasal steroid during study, requirement/use of systemic or topical antimicrobial or antifungal medications, concurrent use of oral anti-inflammatory medication, history of allergic reaction to ciprofloxacin or any of the components of OTO-201, serious illness or medical condition, use of an investigational medication or device in the month prior to screening, history of exposure to OTO-201, and menarcheal or post-menarcheal female, and children aged 4 years or younger who did not complete in distortion product otoacoustic emission (DPOAE) test in both ears and visual reinforcement audiometry (VRA) test in 1 ear at 2 frequencies.

Patient characteristics	N=83 (Intraoperative intratympanic ciprofloxacin injection 4 mg: N=21; Intraoperative intratympanic ciprofloxacin injection 12 mg: N=19; Placebo: N=22; Sham: N=21) Mean age in years (SD): Intraoperative intratympanic ciprofloxacin injection 4 mg: 2.9 (2.6) Intraoperative intratympanic ciprofloxacin injection 12 mg: 2.8 (2.2) Placebo: 2.5 (1.9) Sham: 2.8 (2.3) Sex (male/female): Intraoperative intratympanic ciprofloxacin injection 4 mg: 15/6 Intraoperative intratympanic ciprofloxacin injection 12 mg: 10/9 Placebo: 12/10 Sham: 15/6
Intervention(s)/control	Intraoperative intratympanic ciprofloxacin injection (4 mg): intratympanic administration of ciprofloxacin otic suspension 4 mg into both ears following myringotomy Intraoperative intratympanic ciprofloxacin injection (12 mg): intratympanic administration of ciprofloxacin otic suspension 12 mg into both ears following myringotomy Placebo: vehicle administered following myringotomy Sham: air administered following myringotomy
Duration of follow-up	Children were assessed on days 4, 8, 15, and 29.
Sources of funding	Industry funded
Sample size	N=83
Other information	Otorrhoea was assessed by visual external ear examination.

DPOAE: distortion product otoacoustic emission test; RCT: randomised controlled trial; VRA: visual reinforcement audiometry test

Outcomes

Intraoperative intratympanic ciprofloxacin injection (4 mg) versus intraoperative intratympanic ciprofloxacin injection (12 mg) versus placebo versus sham: Otorrhoea and adverse effects of intervention

Outcome	Intraoperative intratympanic ciprofloxacin injection (4 mg), N = 21	Intraoperative intratympanic ciprofloxacin injection (12 mg), N = 19	Placebo, N = 22	Sham, N = 21
Otorrhoea (15 days after surgery) Custom value	2/21	2/19	8/22	5/20
Adverse effects of intervention (treatment-emergent adverse events such as otorrhoea, pyrexia, upper respiratory tract infection, ear infection and diarrhoea) Custom value	13/21	9/19	12/22	18/20

CIP: ciprofloxacin

Critical appraisal - Cochrane RoB2

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(No information on allocation sequence concealment. No significant differences between groups at baseline.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(People delivering the intervention were aware of the intervention; however, there is no reason to believe that deviations from the intended intervention arose due to trial context. Appropriate analysis was used.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(The data were available for 99% of participants for all outcomes.)*

Section	Question	Answer
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Methods of measuring the outcomes were appropriate, and no difference in measurement of the outcomes between intervention groups. Outcome assessors were blinded to intervention status.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(There is clear evidence that all eligible reported results for the outcome correspond to all intended outcome measurements and analyses.)*
Overall bias and Directness	Risk of bias judgement	Some concerns *(The study is judged to raise some concerns in at least one domain.)*
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	None

RoB: risk of bias

Park, 2016

Bibliographic Reference	Park, Albert H; White, David R; Moss, Jonathan R; Bear, Moraye; LeBel, Carl; Phase 3 Trials of Thermosensitive Ciprofloxacin Gel for Middle Ear Effusion in Children with Tubes.; Otolaryngology--head and neck surgery: official journal of American Academy of Otolaryngology-Head and Neck Surgery; 2016; vol. 155 (no. 2); 324-31

Study details

Country/ies where study was carried out	Canada and USA

Study type	Randomised controlled trial (RCT)
Study dates	November 2013 - June 2014
Inclusion criteria	Children aged 6 months to 17 years who are undergoing tympanostomy tube placement for otoscopically confirmed middle ear effusion on the day of surgery
Exclusion criteria	Requirement of any other surgery concurrently, previous history of mastoid surgery, recurrent or chronic bacterial infections, sensorineural hearing loss, tympanic membrane perforation, immunodeficiency disease, abnormal middle ear or tympanic membrane, use of topical nonsteroid otic medication within 1 day of randomisation, use of otic or topical steroid within 3 days of randomisation, systemic corticosteroid within 7 days of randomisation, use of systemic or topical antimicrobial or antifungal medications, concurrent use of oral anti-inflammatory medication, history of allergic reaction to ciprofloxacin or any of the components of OTO-201, and post-menarcheal or menarcheal female.
Patient characteristics	N=532 (Intraoperative intratympanic ciprofloxacin injection 6 mg: N=357; Sham: N=175) Mean age in years (SD): Intraoperative intratympanic ciprofloxacin injection 6 mg: 2.3 (1.9) Sham: 2.6 (2.3) Sex (male/female): Intraoperative intratympanic ciprofloxacin injection 6 mg: 200/157 Sham: 104/71 Positive microbiology culture (at least one ear): Intraoperative intratympanic ciprofloxacin injection 6 mg: N=70 Sham: N=49
Intervention(s)/control	Intraoperative intratympanic ciprofloxacin injection (6 mg): a single 0.1 ml (6 mg) intratympanic administration of a thermosensitive otic suspension of ciprofloxacin into each ear followed by tympanostomy tube placement Sham: the syringe was empty (tympanostomy tube placement alone)
Duration of follow-up	Children were assessed on days 4, 8, 15, and 29.

Sources of funding	Industry funded
Sample size	N=532
Other information	Otorrhoea was assessed by visual external ear examination

RCT: randomised controlled trial; SD: standard deviation

Outcomes

Intraoperative intratympanic ciprofloxacin injection (6 mg) versus sham: Otorrhoea, adverse effects of intervention, tube blockage and tube extrusion

Outcome	**Intraoperative intratympanic ciprofloxacin injection (6 mg), N = 357**	**Sham, N = 175**
Otorrhoea (29 days after surgery) Custom value	37/352	41/174
Adverse effects of intervention (Treatment-emergent adverse events such as pyrexia, pain, cough, nasopharyngitis, upper respiratory tract infection, irritability, vomiting, nasal congestion and rhinorrhoea; up to 29 days) Custom value	189/357	95/173
Tube blockage (29 days after surgery) Custom value	18/357	7/173
Tube extrusion (29 days after surgery) Custom value	3/357	1/173

Critical appraisal - Cochrane RoB2

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(No information on allocation sequence concealment. No significant differences between groups at baseline.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Other than people delivering the intervention, all persons in the trial such as staffs, carers and participants were blinded to the interventions. There is no reason to believe that deviations from the intended intervention arose due to trial context. Appropriate analysis was used.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(The data were available for nearly all participants (99%) for all outcomes.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Methods of measuring the outcomes were appropriate, and no difference in measurement of the outcomes between intervention groups. Outcome assessors were blinded to intervention status.)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(There is clear evidence that all eligible reported results for the outcome correspond to all intended outcome measurements and analyses.)*
Overall bias and Directness	Risk of bias judgement	Some concerns *(The study is judged to raise some concerns in at least one domain.)*
Overall bias and Directness	Overall Directness	Directly applicable (Although the inclusion criteria extended to children aged up to 17 years old, the mean age and standard deviation of the participants were well within our target age of up to 12 years)

Section	Question	Answer
Overall bias and Directness	Risk of bias variation across outcomes	None

RoB: risk of bias

Subtil, 2019

Bibliographic Reference	Subtil, Joao; Jardim, Ana; Araujo, Joao; Moreira, Carla; Eca, Tiago; McMillan, Merlin; Simoes Dias, Sara; Vera Cruz, Paulo; Voegels, Richard; Paco, Joao; Rosenfeld, Richard; Effect of Water Precautions on Otorrhea Incidence after Pediatric Tympanostomy Tube: Randomized Controlled Trial Evidence.; Otolaryngology--head and neck surgery: official journal of American Academy of Otolaryngology-Head and Neck Surgery; 2019; vol. 161 (no. 3); 514-521

Study details

Country/ies where study was carried out	Portugal
Study type	Randomised controlled trial (RCT)
Study dates	February 2015 - August 2017
Inclusion criteria	Children aged 2-10 years with chronic otitis media with effusion (OME) with indication for surgery and concurrent adenoidectomy (either for OME or for a concurrent diagnosis of recurrent acute otitis media, chronic nasal inflammatory symptoms, obstructive sleep apnea, recurrent adenoiditis or sinusitis) and primary caregivers willing to follow the recommendations in either group.
Exclusion criteria	Craniofacial anomalies, history of tympanic surgery and tympanostomy, unilateral surgery, unavailable for follow-up or unable to understand questionnaires in Portuguese, immunodeficiency, poor compliance with prescribed precautions, premature tube extrusion, more than three episodes of otorrhoea and any complication (e.g., acute mastoiditis) during the study.

Patient characteristics	N=291 (Water precautions: N=149; No precautions: N=142) Mean age in years (SD): 4.4 (1.7) *Not reported split by intervention group* Sex (male/female): Water precautions: 74/56 No precautions: 64/50 Children with swimming activities at least once a week: Water precautions: N=82 No precautions: N=64
Intervention(s)/control	Water precautions: wearing moldable silicone earplugs and headbands for swimming and earplugs for bathing and showering No precautions: showering or swimming with no protection
Duration of follow-up	Children were assessed every 2 months for up to 6 months
Sources of funding	None
Sample size	N=291
Other information	N=244 participants included in final analyses Otorrhoea was reported by parents and then confirmed with a specialist. Children underwent tympanostomy tube (ventilation tube) surgery, and the same surgical technique, canal disinfection, and type of tympanostomy tube (fluoroplastic Shepard tube) were used. Children did not receive any other topical treatment.

RCT: randomised controlled trial; SD: standard deviation

Outcomes

Water precautions versus no precautions: Otorrhoea and quality of life

Outcome	Water precautions, N = 149	No precautions, N = 142
Otorrhoea (from 2 weeks after surgery to 6 months) Custom value	41/130	25/114
Quality of life (improvement in quality of life; at 2 months) Custom value	113/130	99/114

Critical appraisal – Cochrane RoB2

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(No information on allocation sequence concealment. No significant differences between groups at baseline.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Blinding of participants and personnel may not be possible due to the nature of the intervention; however, there is no reason to believe that deviations from the intended intervention arose due to trial context. Appropriate analysis was used.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Some concerns *(Loss to follow up and discontinued intervention greater in no precautions group compared with water precautions for all outcomes (20% vs 13%); however, intention to treat analysis confirmed that the result was not biased by missing outcome data.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	High *(Methods of measuring the outcomes were appropriate, and no difference in measurement of the outcomes between intervention groups. No information if*

Section	Question	Answer
		outcome assessors were blinded to intervention status. Outcomes reported by patients or parents, such as otorrhoea and quality of life, are somewhat subjective and may be influenced by knowledge of assigned intervention.)
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(There is clear evidence that all eligible reported results for the outcome correspond to all intended outcome measurements and analyses.)*
Overall bias and Directness	Risk of bias judgement	High *(The study is judged to be at high risk of bias in at least one.)*
Overall bias and Directness	Overall Directness	Directly applicable *(Quality of life was assessed with the PedsQL tool, which is not OME specific)*
Overall bias and Directness	Risk of bias variation across outcomes	None

PedsQL: Pediatric Quality of Life Inventory; RoB: risk of bias

Wang, 2022

Bibliographic Reference	Wang, Luke Chenkan; Phyland, Debra Jean; Giddings, Charles Edward; A randomised clinical trial of single or extended dosing ciprofloxacin versus no intervention for prevention of ventilation tube otorrhoea and obstruction (PreVenTO2).; Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery; 2022; vol. 47 (no. 2); 287-294

Study details

Country/ies where study was carried out	Australia

Study type	Randomised controlled trial (RCT)
Study dates	May 2018 - June 2020
Inclusion criteria	Children aged 17 years or under who are undergoing bilateral VT surgery with or without concurrent upper airway surgery for recurrent acute otitis media or chronic otitis media with effusion
Exclusion criteria	History of allergic reaction to quinolone, purulent middle ear effusion, or significant middle ear condition that needs intervention and insertion of long-term VT
Patient characteristics	N=296 (Intraoperative ciprofloxacin drops: N=102; Intraoperative and postoperative ciprofloxacin drops: N=94; No topical ciprofloxacin: N=100) Median age in years (IQR): Intraoperative ciprofloxacin drops: 4.09 (2.81-6.06) Intraoperative and postoperative ciprofloxacin drops: 4.04 (2.46-6.55) No topical ciprofloxacin: 3.63 (2.25-5.91) Sex (male/female): Intraoperative ciprofloxacin drops: 58/29 Intraoperative and postoperative ciprofloxacin drops: 43/37 No topical ciprofloxacin: 52/37 Children with chronic otitis media with effusion: Intraoperative ciprofloxacin drops: N=56 Intraoperative and postoperative ciprofloxacin drops: N=55 No topical ciprofloxacin: N=58 Children without previous tonsillectomy or adenoidectomy: Intraoperative ciprofloxacin drops: N=78 Intraoperative and postoperative ciprofloxacin drops: N=70 No topical ciprofloxacin: N=78
Intervention(s)/control	Intraoperative ciprofloxacin drops: children received 5 drops of topical ciprofloxacin 0.3% (Ciloxan® ear drops, Novartis AU) into each ear after insertion of VT

	Intraoperative and postoperative ciprofloxacin drops: children received 5 drops of topical ciprofloxacin 0.3% (Ciloxan® ear drops, Novartis AU) into each ear during surgery as well as twice a day for 5 days postoperatively No topical ciprofloxacin: Children did not receive any topical ciprofloxacin
Duration of follow-up	Children were assessed at 6-weeks after surgery
Sources of funding	Not industry funded
Sample size	N=296
Other information	n=512 ears of N=256 participants included in final analyses Analysis was based on a by-ear basis, and each ear was considered as an individual data point. All children received the same type of tympanostomy tube (Reuter-Bobbins VT) using a standardised technique. Otorrhoea was assessed by otoscopy and parent-reported history. Tube blockage was assessed by pneumatic otoscopy and tympanometry.

IQR: interquartile range; RCT: randomised controlled trial

Outcomes

Intraoperative ciprofloxacin drops versus intraoperative and postoperative ciprofloxacin drops versus no topical ciprofloxacin: Otorrhoea and tube blockage

Outcome	Intraoperative ciprofloxacin drops, N = 102	Intraoperative and postoperative ciprofloxacin drops, N = 94	No topical ciprofloxacin, N = 100
Otorrhoea (6 weeks after surgery) Number of ears Custom value	8/174	14/160	24/178

Outcome	Intraoperative ciprofloxacin drops, N = 102	Intraoperative and postoperative ciprofloxacin drops, N = 94	No topical ciprofloxacin, N = 100
Tube blockage (6 weeks after surgery) Number of ears Custom value	11/174	8/160	21/178

Critical appraisal - Cochrane RoB2

Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Low *(Process of allocation controlled by an external unit, sealed opaque envelopes used for generation of randomisation sequence and allocation concealment. No significant differences between groups at baseline.)*
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(No information on blinding of personnel; however, there is no reason to believe that deviations from the intended intervention arose due to trial context. Appropriate analysis was used.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(The data were available for 95% of participants.)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Methods of measuring the outcomes were appropriate, and no difference in measurement of the outcomes between intervention groups. Outcome assessors and data analysts were blinded to intervention status.)*

Section	Question	Answer
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low *(There is clear evidence that all eligible reported results for the outcome correspond to all intended outcome measurements and analyses.)*
Overall bias and Directness	Risk of bias judgement	Low *(The study is judged to be at low risk of bias for all domains.)*
Overall bias and Directness	Overall Directness	Indirectly applicable *(Population is indirect because 34% had recurrent acute otitis media. Although the inclusion criteria extended to children aged up to 17 years old, the mean age and standard deviation of the participants were well within our target age of up to 12 years.)*
Overall bias and Directness	Risk of bias variation across outcomes	None

RoB: risk of bias