Otitis externa

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ABSTRACT

INTRODUCTION: Otitis externa is thought to affect 10% of people at some stage, and can present in acute, chronic, or necrotising forms. Otitis externa may be associated with eczema of the ear canal, and is more common in swimmers, humid environments, people with absence of ear wax or with narrow ear canals, hearing-aid users, and after mechanical trauma. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of empirical and prophylactic treatments for otitis externa? We searched: Medline, Embase, The Cochrane Library, and other important databases up to October 2007 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found nine systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: oral antibiotics, specialist aural toilet, topical acetic acid drops or spray, topical aluminium acetate drops, topical antibacterials, topical antifungals, topical anti-infective agents, topical corticosteroids, and water exclusion.

QUESTIONS

INTERVENTIONS

EMPIRICAL TREATMENTS FOR OTITIS EXTERNA

Likely to be beneficial

Unknown effectiveness

Unlikely to be beneficial

PROPHYLACTIC TREATMENTS FOR OTITIS EXTERNA

Unknown effectiveness

To be covered in future updates

Surgery for ear canal stenosis after otitis externa

Treatment for necrotising otitis externa

Footnote

*Categorisation based on consensus

Key points

- Otitis externa is thought to affect 10% of people at some stage, and can present as acute, chronic, or necrotising forms.

  Otitis externa may be associated with eczema of the ear canal, and is more common in swimmers, humid environments, people with absence of ear wax or narrow ear canals, hearing-aid users, and after mechanical trauma.

  The most common pathogens are *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

  Fungal overgrowth can occur, especially after prolonged antibiotic use.

- Topical antibacterial agents are likely to improve signs and symptoms of otitis externa.

  Combining topical antibacterial agents and corticosteroids (methylprednisolone–neomycin drops) is likely to be more effective than placebo in reducing signs and symptoms of otitis externa over 28 days.

  We don't know whether any one topical antibacterial regimen should be used in preference to another.

- Consensus suggests thattopical corticosteroids alone may reduce signs and symptoms of otitis externa, but few good-quality studies have been found assessing these agents alone in this population.

- We don't know whether topical antifungal agents or specialist aural toilet improve symptoms of otitis externa.

- Oral antibiotics have not been shown to be beneficial.

Consensus suggests that adding oral antibiotics to topical anti-infective agents will not improve symptoms compared with topical agents alone.

- Topical acetic acid is likely to increase cure of otitis media when used with topical anti-infective agents and corticosteroids, but is less effective when used alone.
- Prophylactic treatments to prevent otitis externa (topical acetic acid, topical corticosteroids, and water exclusion) have not been evaluated in clinical trials.

DEFINITION

Otitis externa is inflammation of the external ear canal, often with infection. This inflammation is usually generalised throughout the ear canal, so is often referred to as "diffuse otitis externa". This review excludes localised inflammations, such as furuncles. Otitis externa has acute (<6 weeks), chronic (>3 months), and necrotising (malignant) forms. Acute otitis externa may present as a single episode, or may recur. It causes pain with aural discharge and associated hearing loss. [1] If the ear canal is visible, it appears red and inflamed. *Pseudomonas aeruginosa* and *Staphylococcus aureus* are the most frequent bacterial pathogens in otitis externa. Fungal overgrowth (e.g., with *Aspergillus niger*) is also common, especially after prolonged antibiotic treatment. Chronic otitis externa may result in canal stenosis with associated hearing loss, for which it may be difficult to fit hearing aids. Necrotising otitis externa is defined by destruction of the temporal bone, usually in people with diabetes or in people who are immunocompromised, and can be life threatening. [2] In this review, we look at the empirical treatment of only acute and chronic otitis externa.

INCIDENCE/ PREVALENCE

Otitis externa is common worldwide. The exact incidence is unknown, but 10% of people are thought to have been affected at some time. [3] The condition does affect children, but is more common in adults. It accounts for a large proportion of the workload in otolaryngology departments, but milder cases are often managed in primary care. [3]

AETIOLOGY/ RISK FACTORS

Otitis externa may be associated with local or generalised eczema of the ear canal. It is more common in swimmers, humid environments, people with an absence of ear wax or narrow external ear canals, hearing-aid users, and after mechanical trauma. [4]

PROGNOSIS

We found few reliable data. Many cases of otitis externa resolve spontaneously over several weeks or months. Acute episodes tend to recur, although risk of recurrence is unknown. Experience suggests that chronic inflammation affects a small proportion of people after a single episode of acute otitis externa, and can, rarely, lead to canal stenosis. [1]

AIMS OF INTERVENTION

To improve or abolish symptoms; to prevent recurrence and complications, with minimal adverse effects.

OUTCOMES

Symptom improvement: severity and duration of signs and symptoms (pain, discharge, hearing loss, redness); **Cure rate:** defined as complete resolution of signs and symptoms; **Recurrence:** quality of life; adverse effects of treatment.

METHODS

Clinical Evidence search and appraisal October 2007. The following databases were used to identify studies for this review: Medline 1966 to October 2007, Embase 1980 to October 2007, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials 2007, Issue 3. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD) — for Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA), Turning Research into Practice (TRIP), and NICE. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the author for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews and RCTs in any language, at least single blinded, and containing more than 20 individuals of whom more than 80% were followed up. The minimum length of follow-up required to include studies was one month. We excluded all studies described as "open", "open label", or not blinded unless blinding was impossible. In addition, we use a regular surveillance protocol to capture harms alerts from organisations, such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the review as required. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 22). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of empirical treatments for otitis externa?

OPTION ALUMINIUM ACETATE (TOPICAL) FOR TREATING OTITIS EXTERNA

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- We found no direct information about whether topical aluminium acetate is more effective than no active treatment.
- Topical aluminium acetate may be as effective as a topical antibacterial–corticosteroid at improving cure rates in people with acute otitis externa.

Benefits and harms

Aluminium acetate drops versus placebo:

We found no systematic review or RCTs.

Aluminium acetate drops versus topical antibacterial–corticosteroid:

We found one RCT. [5]

Cure rate

Aluminium acetate drops compared with topical antibacterial–corticosteroid Aluminium acetate drops may be as effective at increasing cure rates or reducing time to clinical cure at 4 weeks in people with acute diffuse otitis externa (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Cure rate					
[5] RCT	126 people with any severity of acute diffuse otitis externa on otoscopy in a primary-care setting If present, people in both groups had discharge removed (no further details given on technique)	**Clinical cure rate , 4 weeks** 59/65 (91%) with aluminium acetate drops 49/61 (80%) with polymyxin–neomycin–hydrocortisone drops Each treatment given for 14 days	P >0.2 The RCT may be underpowered to identify a clinically important difference in efficacy between the two treatments used	⟷	Not significant
Mean time to clinical resolution					
[5] RCT	126 people with any severity of acute diffuse otitis externa on otoscopy in a primary-care setting If present, people in both groups had discharge removed (no further details given on technique)	**Mean time to clinical resolution** 9.4 days with aluminium acetate drops 11.1 days with polymyxin–neomycin–hydrocortisone drops Each treatment given for 14 days	P >0.2 The RCT may be underpowered to identify a clinically important difference in efficacy between the two treatments used	⟷	Not significant

Symptom improvement

No data from the following reference on this outcome. [5]

Recurrence

No data from the following reference on this outcome. [5]

Quality of life

No data from the following reference on this outcome. [5]

Adverse effects

No data from the following reference on this outcome. [5]

Aluminium acetate drops versus topical antibacterials alone, topical antifungals, topical corticosteroids alone, topical acetic acid, or oral antibiotics:

We found no systematic review or RCTs.

Further information on studies

Comment: **Clinical guide:**
Although we have not identified an RCT comparing topical aluminium acetate versus no active treatment, the cure rates reported in the included RCT suggest that topical aluminium acetate is likely to be beneficial. [5] Topical aluminium acetate is often used for the treatment of fungal otitis externa, or as a prophylactic treatment of recurrent otitis externa. However, there is little evidence to confirm these beneficial effects.

OPTION ANTIBACTERIALS (TOPICAL; WITH OR WITHOUT CORTICOSTEROIDS)

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- Topical antibacterial agents are likely to improve signs and symptoms of otitis externa.
- Combining topical antibacterial agents and corticosteroids (methylprednisolone–neomycin drops) is likely to be more effective than placebo in reducing signs and symptoms of otitis externa over 28 days.
- We don't know whether any one topical antibacterial regimen should be used in preference to another.
- We found no clinically important results about topical antibacterials compared with no active treatment in people with otitis externa.

Benefits and harms

Topical antibacterials alone versus placebo:

We found no systematic review or RCTs.

Topical antibacterials alone versus topical aluminium acetate, topical antifungals, topical corticosteroids, or oral antibiotics:

We found no systematic review or RCTs.

Adding oral antibiotics to topical antibacterials:

See option on oral antibiotics, p 16 .

Topical antibacterial–corticosteroids versus placebo:

We found one RCT. [6]

Cure rate

No data from the following reference on this outcome. [6]

Symptom improvement

Topical antibacterial–corticosteroid compared with placebo Topical antibacterial–corticosteroid (methylprednisolone–neomycin drops) is more effective at improving symptoms of otitis externa at 28 days (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom improvement					
[6] RCT	40 people in secondary care with mild, moderate, or severe acute/chronic diffuse otitis externa All people in the RCT had "cleansing" of their external ear canals (details not reported)	**Symptoms and signs ("good" response) , 28 days** 11/20 (55%) with methylprednisolone–neomycin drops 2/20 (10%) with placebo Treatment given for 10 days	P <0.001	○○○	methylprednisolone–neomycin

Recurrence

No data from the following reference on this outcome. [6]

Quality of life

No data from the following reference on this outcome. [6]

Adverse effects

No data from the following reference on this outcome. [6]

Topical antibacterials (with or without corticosteroids) versus each other:

We found one systematic review (search date 2005) on topical antimicrobial therapy for the treatment of acute otitis externa. [7] We found two additional RCTs comparing different regimens of topical antibacterials. [8] [9]

Cure rate

Topical antibacterials (with or without corticosteroid) compared with each other We don't know which antibiotic (with or without corticosteroid) is more effective at improving clinical cure rates (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Clinical cure rate					
[7] Systematic review	936 people with otitis externa 3 RCTs in this analysis All people in the RCT had "cleansing" of their external ear canals (details not reported)	**Clinical cure rate , 14 to 28 days** with topical quinolone antibiotics with topical non-quinolone antibiotics Absolute results not reported	Absolute rate difference 0.04 95% CI –0.01 to +0.08 P = 0.145 Only one RCT included in the meta-analysis compared topical quinolone alone versus topical non-quinolone alone, which may affect the generalisability of these results (see further information on studies for more details)	⟷	Not significant
[8] RCT	601 people with any severity of acute diffuse otitis externa on otoscopy in a primary-care setting	**Clinical cure rate , 1 month** 215/242 (89%) with ofloxacin 206/232 (89%) with neomycin–hydrocortisone–polymyxin B drops Each treatment given for 10 days	P = 0.86	⟷	Not significant
Microbiological cure rate					
[8] RCT	601 people with any severity of acute diffuse otitis externa on otoscopy in a primary-care setting	**Microbiological cure rate , 1 month** 85/93 (91%) with ofloxacin 97/103 (94%) with neomycin–hydrocortisone–polymyxin B drops Each treatment given for 10 days	P = 0.77	⟷	Not significant
Resolution					
[9] RCT	55 people with moderate–severe acute or chronic diffuse otitis externa on otoscopy, in a secondary-care setting All people received microsuction if discharge was present	**Resolution , 1 month or until resolution of all symptoms and signs** 27/34 (79%) with triamcinolone–neomycin 10/21 (48%) with hydrocortisone–neomycin–polymyxin B Each treatment given for 10 days	P <0.01	○○○	triamcinolone–neomycin

Symptom improvement

No data from the following reference on this outcome. [7] [8] [9]

Recurrence

No data from the following reference on this outcome. [7] [8] [9]

Quality of life

No data from the following reference on this outcome. [7] [10] [11]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[7] Systematic review	1330 people with otitis externa 3 RCTs in this analysis All people in the RCT had "cleansing" of their external ear canals (details not reported)	**Adverse effects** with topical quinolone antibiotics with topical non-quinolone antibiotics Absolute results not reported No further data reported on type of adverse effects	Absolute rate difference 0.002 95% CI –0.07 to +0.08 P = 0.963 Only one RCT included in the meta-analysis compared topical quinolone alone versus topical non-quinolone alone, which may affect the generalisability of these results (see further information on studies for more details)	⟷	Not significant
[8] RCT	601 people with any severity of acute diffuse otitis externa on otoscopy in a primary-care setting	**Local pruritus** 25/158 (16%) with ofloxacin 18/156 (12%) with neomycin–hydrocortisone–polymyxin B drops Each treatment given for 10 days	P = 0.33	⟷	Not significant
[8] RCT	601 people with any severity of acute diffuse otitis externa on otoscopy in a primary-care setting	**Dizziness and vertigo** 4/158 (2.5%) with ofloxacin 2/156 (1.3%) with neomycin–hydrocortisone–polymyxin B drops Each treatment given for 10 days	P value not reported		

No data from the following reference on this outcome. [9]

Topical antibacterial–corticosteroids versus topical aluminium acetate:
See option on topical aluminium acetate, p 3 .

Topical antibacterial–corticosteroid versus topical acetic acid:
See option on topical acetic acid, p 12 .

Topical antibacterial–corticosteroid–acetic acid versus topical antibacterial–corticosteroid alone:
We found one RCT. [12]

Cure rate

Topical antibacterial–corticosteroid–acetic acid compared with topical antibacterial–corticosteroid Neomycin–dexamethasone–acetic acid spray is more effective than framycetin–gramicidin–dexamethasone drops at improving signs and symptoms of severe acute or chronic diffuse otitis externa at 1 month (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Cure rate					
[12] RCT	60 people with any severity of acute or chronic diffuse otitis externa on otoscopy, in a primary-care setting	**Symptom free , 1 month** 26/32 (81%) with neomycin–dexamethasone–acetic acid spray 6/26 (23%) with framycetin–gramicidin–dexamethasone drops Treatments were given for 10 days	P <0.0001	○○○	neomycin–dexamethasone–acetic acid spray
[12] RCT	60 people with any severity of acute or chronic diffuse otitis externa on otoscopy, in a primary-care setting	**Free of clinical signs , 1 month** 17/32 (53%) with neomycin–dexamethasone–acetic acid spray 10/28 (36%) with framycetin–gramicidin–dexamethasone drops Treatments were given for 10 days	P <0.05	○○○	neomycin–dexamethasone–acetic acid spray

Symptom improvement

No data from the following reference on this outcome. [12]

Recurrence

No data from the following reference on this outcome. [12]

Quality of life

No data from the following reference on this outcome. [13]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[12] RCT	60 people with any severity of acute or chronic diffuse otitis externa on otoscopy, in a primary-care setting	**Local stinging or burning in first few days of treatment** 6/32 (19%) with neomycin–dexamethasone–acetic acid spray	Significance not assessed		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		3/26 (12%) with framycetin–gramicidin–dexamethasone drops			

Topical antibacterial–corticosteroid–acetic acid versus topical acetic acid alone:
We found one RCT. [14]

Cure rate

Topical antibacterial–corticosteroid–acetic acid compared with topical acetic acid alone Neomycin–dexamethasone–glacial acetic acid spray is more effective at increasing the proportion of people with inactive disease at 4 weeks (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Inactive disease					
[14] RCT	53 people in secondary care with acute otitis externa on otoscopy All people included in the study received aural toilet before randomisation to treatment Full population in RCT were people with acute otitis externa or an infected mastoid cavity (109 people; see further information on studies for more details)	**Inactive disease , 4 weeks** 18/21 (86%) with neomycin (3250 U/mL)–dexamethasone (0.1%)–glacial acetic acid (2%) 12/32 (38%) with glacial acetic acid (2%) spray alone	P <0.0005	○○○	neomycin–dexamethasone–glacial acetic acid

Symptom improvement

No data from the following reference on this outcome. [14]

Recurrence

No data from the following reference on this outcome. [14]

Quality of life

No data from the following reference on this outcome. [14]

Adverse effects

No data from the following reference on this outcome. [14]

Further information on studies

[7] One RCT compared topical quinolone alone versus topical quinolone plus corticosteroid versus topical non-quinolone plus corticosteroid, and one RCT compared topical quinolone plus corticosteroid versus topical non-quinolone plus corticosteroid. Ciprofloxacin was the quinolone antibiotic used in all studies included in the meta-analysis, either alone or in combination with hydrocortisone. The non-quinolone antibiotics investigated were tetramycin and neomycin–polymyxin combination. Pooling data from different groups may fail to demonstrate true significant differences, which would be identified if specific combinations were compared separately.

[14] At 2 weeks' follow-up, people with no sign of active disease were instructed to discontinue use of their spray. Those with active disease underwent additional aural toilet and continued with their assigned treatment for a further 2 weeks. The RCT carried out an ITT analysis (assigned explicit allocation of poor outcome to those not completing the protocol).

Comment: None.

OPTION ANTIFUNGALS (TOPICAL; WITH OR WITHOUT CORTICOSTEROIDS)

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- We don't know whether topical antifungal agents improve symptoms of otitis externa.
- We found no direct information about whether topical antifungals are more effective than no active treatment in people with otitis externa.
- We found no clinically important results about topical antifungals (alone or in combination with other anti-infective agents or corticosteroids) compared with oral antibiotics, topical corticosteroids, topical aluminium acetate drops, topical acetic acid, or other topical anti-infective agents in people with otitis externa.

Benefits and harms

Topical antifungals (with or without corticosteroids, or in combination with oral antibiotics) versus placebo:

We found no systematic review or RCTs assessing the effects of topical antifungals in people with otitis externa.

Topical antifungals (with or without corticosteroids, or in combination with oral antibiotics) versus topical aluminium acetate, topical antibacterials, topical corticosteroids, topical acetic acid, or oral antibiotics:

We found no systematic review or RCTs assessing the effects of topical antifungals in people with otitis externa.

Further information on studies

Comment: **Clinical guide:**
Clinical guide There is little evidence assessing the use of topical antifungal agents in acute otitis externa. Fungal otitis externa may be suspected by otoscopic examination findings of hyphae or spores (e.g., *Aspergillus niger*), or by swab cultures. People with fungal otitis externa have often had previous prolonged courses of a combination of corticosteroid plus antibiotic agents. In this group of people, it may be appropriate to use topical antifungal agents or other antiseptic agents, such as aluminium acetate or acetic acid. Antiseptic agents have the advantage that they are not

ototoxic or allergenic, meaning they are probably safer, particularly in the long term. However, anecdotal evidence suggests they may cause more discomfort, which may lead to poor compliance and resultant poor efficacy.

OPTION CORTICOSTEROIDS (TOPICAL) FOR TREATING OTITIS EXTERNA

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- Consensus suggests that topical corticosteroids alone may reduce signs and symptoms of otitis externa, but few good-quality studies have been found assessing these agents alone in this population.
- Likely to be beneficial categorisation based on consensus, as in all RCTs reported in this option corticosteroids have been given in combination with another agent. We found no direct information from RCTs about whether topical corticosteroids alone are better than placebo in the treatment of people with otitis externa.
- We found no clinically important results about topical corticosteroids alone compared with oral antibiotics, topical antifungals, topical aluminium acetate drops, topical acetic acid, or other topical anti-infective agents in people with otitis externa.

Benefits and harms

Topical corticosteroids alone versus placebo:

We found no systematic review or RCTs with sufficient follow up. We found one RCT with short follow-up assessing the effects of budesonide drops (please see comments section). [15]

Topical corticosteroids alone versus topical aluminium acetate, topical antibacterials, topical antifungals, topical corticosteroids, topical acetic acid, or oral antibiotics:

We found no systematic review or RCTs.

Low- versus high-potency corticosteroids:

We found no systematic review or RCTs.

Topical corticosteroid–acetic acid versus topical acetic acid:

See option on topical acetic acid, p 12 .

Topical corticosteroid–antibacterial versus topical acetic acid alone:

See option on topical acetic acid, p 12 .

Topical corticosteroid–antibacterial versus topical aluminium acetate:

See option on topical aluminium acetate, p 3 .

Topical corticosteroid–antibacterial–acetic acid versus topical corticosteroid–antibacterial:

See option on topical antibacterial agents (with or without corticosteroids), p 4 .

Further information on studies

Comment: One double-blind RCT with a short follow-up period compared budesonide drops versus placebo drops in a secondary-care setting for 7 days. [15] It found that budesonide drops significantly improved symptoms and signs compared with placebo after 10 days (change from baseline in a global clinical score ranging from 0 [no symptoms/signs] to 3 [severe symptoms/signs]: –2.29 with budesonide v +0.23 with placebo; P = 0.001). The RCT found that a similar proportion of people using budesonide and placebo had adverse effects, including external ear canal disorders (sticky ear canal, ear wax), headache, and dizziness (10/30 [33%] with budesonide *v* 9/30 [30%] with placebo; significance not reported). [15]

Clinical guide:
In current UK practice, most clinicians would use a combination of topical corticosteroid plus antibiotic agent as first-line treatment of acute otitis externa. Some argue that microbial swabs should be taken at first attendance to tailor antimicrobial treatment in persisting cases, but this is supported by only anecdotal evidence. If there are concerns of a possible underlying tympanic membrane perforation, then a topical quinolone may be used in preference to other potentially ototoxic antibiotic preparations. However, in an acute ear infection with discharge, it may be difficult to differentiate between an external- and middle-ear infection. We do not know if quinolones are as effective as aminoglycosides in treating middle-ear infections. In the UK, the consensus opinion is that aminoglycoside/corticosteroid combination therapy can be used if limited to a course of under two weeks. It may be that the lack of a corticosteroid/quinolone combined agent in the UK has discouraged the use of quinolones. Clinicians giving corticosteroids in combination with quinolones are required to write two separate prescriptions, which may also affect patient compliance.

OPTION ACETIC ACID (TOPICAL) FOR TREATING OTITIS EXTERNA

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- Topical acetic acid is likely to increase cure of otitis media when used with topical anti-infective agents and corticosteroids, but is less effective when used alone.
- We found no direct information about whether topical acetic acid is better than no active treatment.

Benefits and harms

Topical acetic acid versus placebo:

We found no systematic review or RCTs.

Topical acetic acid versus topical aluminium acetate, topical antibacterial alone, topical antifungals, topical corticosteroids, or oral antibiotics:

We found no systematic review or RCTs.

Topical acetic acid versus topical antibacterial–corticosteroid:

We found one RCT. [16]

Cure rate

Topical acetic acid compared with topical antibacterial–corticosteroid Topical acetic acid is less effective at increasing cure rates at 21 days and in people with diffuse acute otitis externa (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Cure rate					
[16] RCT **3-armed trial**	213 adults in primary care with any severity of diffuse acute otitis externa on otoscopy The third arm assessed triamcinolone–acetic acid drops All groups received aural toilet (suction or expandable sponge wick) as required	**Cure rate , 21 days** 40/65 (62%) with acetic acid 63/73 (86%) with dexamethasone–neomycin–polymyxin drops 138 people in this analysis	OR 3.9 95% CI 1.7 to 9.1 OR for antibiotic–corticosteroid versus acetic acid	●●○	dexamethasone-neomycin-polymyxin

Symptom improvement

Topical acetic acid compared with topical antibacterial–corticosteroid Topical acetic acid is less effective at reducing median time to recovery in people with diffuse acute otitis externa (moderate-quality evidence)

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Median time to recovery					
[16] RCT **3-armed trial**	213 adults in primary care with any severity of diffuse acute otitis externa on otoscopy The third arm assessed triamcinolone–acetic acid drops All groups received aural toilet (suction or expandable sponge wick) as required	**Median time to recovery** 8.0 days with acetic acid 6.0 days with dexamethasone–neomycin–polymyxin drops 138 people in this comparison	Reported as significant P value not reported	○○○	dexamethasone-neomycin-polymyxin

Recurrence

Topical acetic acid compared with topical antibacterial–corticosteroid Topical acetic acid is less effective at reducing the risk of recurrence at 21 to 48 days in people with diffuse acute otitis externa (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[16] RCT **3-armed trial**	213 adults in primary care with any severity of diffuse acute otitis externa on otoscopy The third arm assessed triamcinolone–acetic acid drops All groups received aural toilet (suction or expandable sponge wick) as required	**Recurrence , 21 to 48 days** 21/47 (45%) with acetic acid 14/68 (21%) with dexamethasone–neomycin–polymyxin drops 138 people in this analysis	OR 0.4 95% CI 0.2 to 1.0 OR for antibiotic–corticosteroid versus acetic acid	●●○	dexamethasone-neomycin-polymyxin

Quality of life

No data from the following reference on this outcome. [16]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[16] RCT **3-armed trial**	213 adults in primary care with any severity of diffuse acute otitis externa on otoscopy The third arm assessed triamcinolone–acetic acid drops All groups received aural toilet (suction or expandable sponge wick) as required	**Adverse effects** with acetic acid with dexamethasone–neomycin–polymyxin drops 74% of people reported at least one adverse effect Adverse effects included local burning, pain, and irritation	Difference among groups reported as not significant P value not reported	⟷	Not significant

Topical acetic acid versus topical acetic acid–corticosteroid:
We found one RCT. [16]

Cure rate

Topical acetic acid alone compared with topical acetic acid–corticosteroid Topical acetic acid is less effective at increasing cure rates at 21 days in people with diffuse acute otitis externa (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Cure rate					
[16] RCT **3-armed trial**	213 adults in primary care with any severity of diffuse acute otitis externa on otoscopy The third arm assessed dexamethasone-neomycin-polymyxin All groups received aural toilet (suction or expandable sponge wick) as required	**Cure rate , 21 days** 40/65 (62%) with acetic acid 54/61 (89%) with triamcinolone–acetic acid 126 people in this analysis	OR 4.8 95% CI 1.9 to 12.3 OR for corticosteroid–acetic acid versus acetic acid	●●○	triamcinolone–acetic acid

Symptom improvement

Topical acetic acid alone compared with topical acetic acid–corticosteroid Topical acetic acid seems less effective at reducing median time to recovery in people with diffuse acute otitis externa (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Median time to recovery					
[16] RCT **3-armed trial**	213 adults in primary care with any severity of diffuse acute otitis externa on otoscopy The third arm assessed dexamethasone–neomycin–polymyxin All groups received aural toilet (suction or expandable sponge wick) as required	**Median time to recovery** 8.0 days with acetic acid 7.0 days with triamcinolone–acetic acid 126 people in this analysis	Reported as significant P value not reported	○○○	triamcinolone–acetic acid

Recurrence

Topical acetic acid compared with topical acetic acid–corticosteroid Topical acetic acid is less effective at reducing the risk of recurrence in people with diffuse acute otitis externa (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[16] RCT **3-armed trial**	213 adults in primary care with any severity of diffuse acute otitis externa on otoscopy The third arm assessed dexamethasone–neomycin–polymyxin All groups received aural toilet (suction or expandable sponge wick) as required	**Recurrence , 21 to 48 days** 21/47 (45%) with acetic acid 15/57 (26%) with triamcinolone–acetic acid 126 people in this analysis	OR 0.3 95% CI 0.1 to 0.7 OR for corticosteroid–acetic acid versus acetic acid	●●○	triamcinolone–acetic acid

Quality of life

No data from the following reference on this outcome. [16]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[16] RCT **3-armed trial**	213 adults in primary care with any severity of diffuse acute otitis externa on otoscopy The third arm assessed dexamethasone–neomycin–polymyxin	**Adverse effects** with acetic acid with triamcinolone–acetic acid Absolute results not reported 74% of people reported at least one adverse effect	Difference among groups reported as not significant P value not reported	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	All groups received aural toilet (suction or expandable sponge wick) as required	Adverse effects included local burning, pain, and irritation			

Topical acetic acid versus topical antibacterial–corticosteroid–acetic acid:

See option on topical antibacterial agents (with or without corticosteroids), p 4 .

Topical acetic acid–antibacterial–corticosteroid versus topical antibacterial–corticosteroid:

See option on topical antibacterial agents (with or without corticosteroids), p 4 .

Further information on studies

Comment: None.

OPTION ANTIBIOTICS (ORAL)

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- Oral antibiotics have not been shown to be beneficial.
- We found no clinically important results from RCTs about whether oral antibiotics are better than no active treatment or topical anti-infective agents in people with otitis externa.

Benefits and harms

Oral antibiotics versus placebo:

We found no systematic review or RCTs.

Oral antibiotics versus topical aluminium acetate, topical antibacterials, topical antifungals, topical corticosteroids, or topical acetic acid:

We found no systematic review or RCTs.

Further information on studies

Comment: None.

OPTION ANTIBIOTICS (ORAL) PLUS ANTI-INFECTIVE AGENTS (TOPICAL)

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- Consensus suggests that adding oral antibiotics to topical anti-infective agents will not improve symptoms compared with topical agents alone.
- We found no clinically important results from RCTs about whether oral antibiotics in combination with a topical anti-infective agent are better than a topical anti-infective agent alone in people with otitis externa.

Benefits and harms

Oral antibiotics plus topical antibacterial versus topical antibacterial alone:

We found no systematic review or RCTs.

Oral antibiotics plus topical antifungal versus topical antifungal alone:

We found no systematic review or RCTs.

Further information on studies

Comment:

Oral antibiotics plus topical antifungal versus placebo:

One double-blind RCT with a short follow-up period compared 5 days of oral trimethoprim–sulfamethoxazole (co-trimoxazole) versus placebo in a primary-care setting. [17] Both groups also received repeated applications of ointment containing triamcinolone, neomycin, and gramicidin, and had suction of the external canal if discharge was present. The RCT found no significant difference between groups in symptom severity scores, duration of symptoms, or cure rate (improvement in mean symptom severity score on scale ranging from 1 [no symptoms] to 5 [severe symptoms]: 0.72 with added oral co-trimoxazole *v* 0.69 with added placebo, P >0.4; mean duration of symptoms: 3.1 days with added oral co-trimoxazole *v* 3.1 days with placebo, P >0.5; cure rates: 18/47 [38%] with added oral co-trimoxazole *v* 21/53 [40%] with placebo, P >0.8). The RCT gave no information on adverse effects.

Clinical guide:

There is consensus that adding oral antibiotics to topical anti-infective agents will not confer additional benefit in people with otitis externa.

OPTION SPECIALIST AURAL TOILET

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- We don't know whether specialist aural toilet improve symptoms of otitis externa.
- We found no direct information from RCTs about whether specialist aural toilet is more effective than no active treatment.

Benefits and harms

Specialist aural toilet versus no aural toilet:

We found no systematic review or RCTs.

Different types of specialist aural toilet versus each other:

We found one RCT. [18]

Cure rate

Different types of specialist aural toilet compared with each other We don't know whether ear wicks plus anti-infective drops are more effective than gauze impregnated with an anti-infective agent at increasing cure rates at 4 weeks in people with moderate to severe acute diffuse otitis externa (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Cure rate					
[18] RCT	94 people with moderate to severe acute diffuse otitis externa on oto-scopy in a sec-ondary-care setting	**Resolution rate , 4 weeks** 30/47 (64%) with ear wick 33/47 (70%) with ribbon gauze Resolution was defined as ab-sence of symptoms and signs See further information on studies for details of treatment regimens	P = 0.58	⟷	Not significant

Symptom improvement

No data from the following reference on this outcome. [18]

Recurrence

No data from the following reference on this outcome. [18]

Quality of life

No data from the following reference on this outcome. [18]

Adverse effects

No data from the following reference on this outcome. [18]

Further information on studies

[18] The RCT compared an ear wick plus anti-infective drops (framycetin–gramicidin–dexamethasone or flumetasone) removed after 3 days versus ribbon gauze impregnated with anti-infective ointment (framycetin–gramicidin or triamcinolone–gramicidin–neomycin–nystatin) removed after 3 days.

Comment: None.

QUESTION What are the effects of prophylactic treatments for otitis externa?

OPTION ACETIC ACID (TOPICAL) FOR PREVENTING OTITIS EXTERNA

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- We found no direct information from RCTs on the effects of prophylaxis with topical acetic acid for people with otitis externa.

Benefits and harms

Acetic acid (topical) versus no acetic acid, or versus other treatments:

We found no systematic review or RCTs of acetic acid drops or spray.

Further information on studies

Comment: None.

OPTION CORTICOSTEROIDS (TOPICAL) FOR PREVENTING OTITIS EXTERNA

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- We found no direct information from RCTs on the effects of prophylaxis with topical corticosteroids for people with otitis externa.

Benefits and harms

Corticosteroids (topical) versus no corticosteroid, or versus other treatments:

We found no systematic review or RCTs of corticosteroid drops or spray.

Further information on studies

Comment: None.

OPTION WATER EXCLUSION FOR PREVENTING OTITIS EXTERNA

- For GRADE evaluation of interventions for Otitis externa, see table, p 22 .
- We found no direct information from RCTs about water exclusion for prevention of otitis externa.

Benefits and harms

Water exclusion versus no water exclusion, or versus other treatments:

We found no systematic review or RCTs of water exclusion.

Further information on studies

Comment: **Clinical guide:**
Most clinicians recommend water exclusion precautions for prevention, as well as treatment, of otitis externa. There is currently only anecdotal evidence to support this as an intervention, and RCTs to assess the effectiveness of this intervention are warranted.

GLOSSARY

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Topical acetic acid One RCT comparing neomycin–dexamethasone–glacial acetic acid versus glacial acetic acid alone added; [14] benefits data enhanced; categorisation unchanged (Unknown effectiveness). The RCT found that a larger proportion of people had inactive disease after treatment with neomycin–dexamethasone–glacial acetic acid compared with glacial acetic acid alone at 4 weeks.

Topical antibacterials (with or without corticosteroids): One systematic review [7] and one additional RCT added; [14] benefits and harms data enhanced; categorisation unchanged (Likely to be beneficial). The review found no significant difference between topical quinolone antibiotics and topical non-quinolone antibiotics in clinical cure rate at 14 to 28 days. However, the analysis included some RCTs comparing quinolone antibiotics and non-quinolone antibiotics in combination with corticosteroids, which may affect the generalisability of the results. The additional RCT found that a larger proportion of people had inactive disease at 4 weeks after treatment with neomycin–dexamethasone–glacial acetic acid compared with glacial acetic acid alone.

Oral antibiotics plus topical anti-infective agents Reevaluation of the evidence led to a change in categorisation to Unlikely to be beneficial by consensus.

Topical corticosteroids Re-evaluation of the evidence led to a change in categorisation to Likely to be beneficial by consensus, as in all RCTs reported in this option corticosteroids have been given in combination with another agent.

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Disclaimer

GRADE **Evaluation of interventions for Otitis externa.**

Important outcomes			Cure rate, Quality of life, Recurrence, Symptom improvement						
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of empirical treatments for otitis externa?									
1 (126) [5]	Cure rate	Aluminium acetate drops versus topical antibacterial–corticosteroid	4	–2	0	0	0	Low	Quality points deducted for sparse data and lack of power to detect clinically important differences between groups
1 (40) [6]	Symptom improvement	Topical antibacterial–corticosteroids versus placebo	4	–1	0	0	0	Moderate	Quality point deducted for sparse data.
3 (1465) [7] [8] [9]	Cure rate	Topical antibacterials (with or without corticosteroids) versus each other	4	–1	–1	–1	0	Very low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results among studies. Directness point deducted for inconsistent comparators
1 (60) [12]	Cure rate	Topical antibacterial–corticosteroid–acetic acid versus topical antibacterial–corticosteroid alone	4	–1	0	0	0	Moderate	Quality point deducted for sparse data.
1 (53) [14]	Cure rate	Topical antibacterial–corticosteroid–acetic acid versus topical acetic acid alone	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (138) [16]	Cure rate	Topical acetic acid versus topical antibacterial–corticosteroid	4	–1	0	0	+1	High	Quality point deducyed for sparse data. Effect size point added for odds ratio of 2–5
1 (138) [16]	Symptom improvement	Topical acetic acid versus topical antibacterial–corticosteroid	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (138) [16]	Recurrence	Topical acetic acid versus topical antibacterial–corticosteroid	4	–1	0	0	+1	High	Quality point deducted for sparse data. Effect-size point added for odds ratio of 0.2–0.5
1 (126) [16]	Cure rate	Topical acetic acid versus topical acetic acid–corticosteroid	4	–1	0	0	+1	High	Quality point deducted for sparse data. Effect-size point added for odds ratio of 2 to 5
1 (126) [16]	Symptom improvement	Topical acetic acid versus topical acetic acid–corticosteroid	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (104) [16]	Recurrence	Topical acetic acid versus topical acetic acid–corticosteroid	4	-1	0	0	+1	High	Quality point deducted for sparse data. Effect-size point added for odds ratio of 0.2 to 0.5
1 (94) [18]	Cure rate	Different types of specialist aural toilet versus each other	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for disparity in active agents used

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.