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## Antibiotic prophylaxis in clean and clean-contaminated ear surgery (Review)

Verschuur HP, de Wever W, van Benthem PP

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[Intervention Review]

# Antibiotic prophylaxis in clean and clean-contaminated ear surgery

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## ABSTRACT

### Background

This is an update of a Cochrane Review first published in Issue 3, 2004 and previously updated in 2007.

Ear surgery may be performed in the treatment of chronic otitis media, ossicular chain disorders, tympanic membrane perforations and otitis media with effusion. Postoperative infection in ear surgery may result in wound infections, infection of the middle ear or mastoid resulting in discharge from the ear canal, failure of the tympanic membrane to close, or labyrinthitis due to infection in, or adjacent to, the inner ear. These complications may be associated with discomfort and inconvenience for the patient, an increase in morbidity and an increase in the costs of medical care.

### Objectives

To assess the effects of local and/or systemic antibiotics for preventing complications such as postoperative discharge, graft failure and labyrinthitis in patients undergoing clean or clean-contaminated ear surgery.

### Search methods

We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE, CINAHL, Web of Science, BIOSIS Previews, Cambridge Scientific Abstracts, mRCT and additional sources for published and unpublished trials. The date of the most recent search was 31 August 2009.

### Selection criteria

Randomised or quasi-randomised trials involving patients undergoing clean or clean-contaminated types of ear surgery. Skull base surgery was excluded. We included any regimen of local and/or systemic antibiotic prophylaxis administered at or around the time of surgery compared to placebo, no antibiotic or an alternative intervention group. Outcome measures were infection, discharge, graft failure, labyrinthitis and adverse effects of prophylaxis.

### Data collection and analysis

When possible, we contacted investigators for additional information on data and methodological issues. At least two authors independently extracted data and assessed trial quality.

### Main results

Eleven studies were included in the review. The methodological quality of the trials was fair to good. However, most studies presented insufficient methodological detail. Although definitions of outcome measures were heterogeneous, pooling of results was possible. There

were no significant differences between antibiotic prophylaxis groups and control groups in terms of reduction of postoperative infections, graft failures, draining outer ear canals and adverse drug effects.

**Authors' conclusions**

There is no strong evidence that the large-scale use of prophylactic antibiotics in clean and clean-contaminated ear surgery is helpful in reducing postoperative complications such as wound infection, discharge from the outer ear canal, labyrinthitis and graft failure.

**PLAIN LANGUAGE SUMMARY****Preventative antibiotics (prophylaxis) in clean and clean-contaminated ear surgery**

Ear surgery, as surgery in general, can be divided into several categories: clean, clean-contaminated, contaminated and dirty surgery. Postoperative complications can include wound infection, discharge from the outer ear canal, labyrinthitis and graft failure. This review aimed to demonstrate whether the use of antibiotic prophylaxis in ear surgery can be helpful in reducing postoperative complications in clean or clean-contaminated surgery. There is no current evidence from randomised controlled trials showing that there is any antibiotic substance, in any regime, which can contribute to reducing complications in any type of clean or clean-contaminated surgical procedure in the ear.

## BACKGROUND

This is an update of a Cochrane Review first published in Issue 3, 2004 and previously updated in 2007.

Ear surgery may be performed in the treatment of a number of disorders including chronic otitis media (with or without cholesteatoma), ossicular chain disorders, tympanic membrane perforations and otitis media with effusion. Postoperative infection following ear surgery may result in:

- wound infections;
- infection of the middle ear or mastoid, resulting in discharge from the ear canal;
- failure of the tympanic membrane to close; or
- labyrinthitis due to infection in, or adjacent to, the inner ear.

These complications may be associated with discomfort and inconvenience for the patient, an increase in morbidity and an increase in the costs of medical care.

Surgical procedures have conventionally been classified as clean, clean-contaminated, contaminated and dirty (Waddell 1994). A surgical operation is clean if there is no break in aseptic technique and the respiratory, gastrointestinal or genitourinary tracts are not entered. Procedures entering the oropharynx, sterile genitourinary or biliary tract, the gastrointestinal or respiratory tracts, or requiring a minor break in aseptic technique are considered to be clean-contaminated surgery. Contaminated surgery is defined as the presence of acute inflammation, infected bile or urine, or gross spillage from the gastrointestinal tract. When established infection exists, it is classified as dirty surgery.

The principles of prophylaxis against post-surgical infection were established in the laboratory in the early 1960s (Burke 1961). The administration of antibiotics prior to surgery is now widely used in certain types of operations (Kaiser 1986). Generally speaking, prophylaxis during clean operations without implantation of a foreign body is not recommended, due to the low incidence of postoperative infection (Garner 1988). Prophylaxis during clean-contaminated or infected surgery can be useful in reducing postoperative infection. It has been claimed that antibiotic prophylaxis during ear surgery reduces infection rates (Govaerts 1998). As the pathogenesis of post-surgical infection after ear surgery is similar to any other type of clean, clean-contaminated or infected surgery, subgroup analysis is important with respect to bacterial contamination. Ear surgery and mode of contamination should be divided into the following distinct categories.

A. Any type of clean surgery. This includes all types of reconstructive tympanoplasties, such as myringoplasty, stapedotomy and stapedectomy. It also includes all types of canal wall up procedures in which the preoperative middle ear is not infected (i.e. a preoperative dry ear). Facial nerve decompression also falls into this category.

B. Any procedure in which preoperative discharge is present, i.e. a clean-contaminated or infected ear. This includes any type of surgery for chronic otitis media (with or without cholesteatoma).

C. The insertion of ventilating tubes for otitis media with effusion (glue ear). This category can be subdivided into ears with no glue (clean), seromucous glue (clean/clean-contaminated) and purulent

glue (infected). The use of antibiotic prophylaxis in ventilation tube insertion will be considered in a separate review.

D. Any type of oto-neurosurgical procedure in which there is a large exposure or even a breach of the dura: vestibular nerve section, translabyrinthine acoustic neuroma removal, decompression of the endolymphatic sac, etc. These types of operations are not considered in this review.

The incidence of postoperative infections in these groups varies. Estimates have ranged from less than 5% in clean procedures to more than 10% in contaminated and dirty procedures (Govaerts 1998). This supports the idea that different types of surgery should be considered separately, with regard to the risk of bacterial contamination. Other authors, however, suggest that combining data from similar prophylactic regimens used during different otologic surgical procedures is appropriate (Jackson 1988). Furthermore, there might be a difference in effectiveness between different antibiotic regimens, e.g. systemic or local antibiotics. A number of randomised controlled trials have compared the use of systemic antibiotic to the use of a placebo or no antibiotic (Bagger-Sjoberg 1987; Eschelman 1971; Jackson 1988; John 1988; Lildholdt 1986; Pirodda 1994; Winerman 1981). Others have compared the use of systemic antibiotics together with local antibiotics to the use of a local antibiotic alone (Donaldson 1966; Govaerts 1998; Hester 1998). Another study has compared the use of a local antibiotic alone to no antibiotic (Tong 2002).

Antibiotics given during mastoidectomy for acute mastoiditis are not considered to be prophylactic but therapeutic. Any study addressing this issue was not included.

A number of descriptive reviews of antibiotic prophylaxis in ear surgery have been published, in which some attempt has been made to assess methodological quality and include this in the interpretation of results (Govaerts 1998; Jackson 1988). However, there is sufficient persisting uncertainty about the effectiveness and cost-effectiveness of antibiotic prophylaxis during the surgical treatment of ear diseases to justify a systematic review of the evidence from randomised trials.

## OBJECTIVES

To determine whether the prophylactic administration of antibiotics in patients undergoing clean or clean-contaminated otologic surgical procedures reduces the incidence of postoperative infection. This includes wound infections, any infection of the middle ear, mastoid or external ear itself, manifesting as postoperative discharge or inner ear infection (labyrinthitis).

The following hypotheses were tested:

1. the use of antibiotic prophylaxis leads to a reduction in the proportion of patients developing a postoperative infection, compared with those given a placebo, no prophylaxis, or an alternative antibiotic regime;
2. the use of antibiotic prophylaxis leads to a decrease in graft failure rates in patients undergoing any type of tympanic membrane or middle ear reconstruction.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

The predetermined inclusion criteria were broad so as to include any randomised controlled study testing a prophylactic antibiotic in ear surgery.

1. The study had to test some method of antibiotic prophylactic intervention aimed at reducing the wound infection rate in ear surgery and compare it with a placebo or alternative intervention group.
2. The study had to be a controlled study, randomised or quasi-randomised.
3. The study population had to be defined to enable identification of the operative intervention, ideally with relevant subgroups given if more than one.
4. Postoperative infection had to be one of the primary outcome measures.

#### Types of participants

Any patient undergoing clean or clean-contaminated types of ear surgery.

#### Types of interventions

Any regimen of systemic or local antibiotic prophylaxis administered at or around the time of surgery.

#### Types of outcome measures

We considered trials if the primary outcome of the study was postoperative infection, reported as one of the following:

- wound infection;
- discharge from the outer ear canal;
- labyrinthitis;
- graft failure;
- adverse reaction to antibiotic (gastrointestinal symptoms, skin reactions);
- length of hospital stay;
- re-operation due to infection.

### Search methods for identification of studies

We conducted systematic searches for randomised controlled trials. There were no language, publication year or publication status restrictions. The last search update was 31 August 2009, following a previous search update in June 2007.

#### Electronic searches

We searched the following databases from their inception: the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library* Issue 3, 2009); PubMed; EMBASE; CINAHL; LILACS; KoreaMed; IndMed; PakMediNet; CAB Abstracts; Web of Science; BIOSIS Previews; CNKI; mRCT (Current Controlled Trials); ClinicalTrials.gov; ICTRP (International Clinical Trials Registry Platform); and Google.

We modelled subject strategies for databases on the search strategy designed for CENTRAL. Where appropriate, we combined subject strategies with adaptations of the highly sensitive search strategy designed by the Cochrane Collaboration for identifying randomised controlled trials and controlled clinical trials (as described in *The Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.1, Box 6.4.b. ([Handbook 2008](#))). Search strategies for key databases including CENTRAL are shown in [Appendix 1](#).

#### Searching other resources

We scanned reference lists of identified studies for further trials. We searched PubMed, TRIPdatabase, NHS Evidence - ENT and Audiology and Google to retrieve existing systematic reviews possibly relevant to this systematic review, in order to search their reference lists for additional trials. We sought abstracts from conference proceedings via the Cochrane Ear, Nose and Throat Disorders Group Trials Register.

### Data collection and analysis

#### Selection of studies

Two authors independently used titles, keywords and (if available) abstracts of the identified citations to exclude trials which clearly did not meet the inclusion criteria of the review. Authors and journal names were blinded at this stage. If one of the authors concluded that the trial might possibly meet the criteria, the full paper was obtained for further study. We then assessed hard copies of the articles passing this initial screening to determine whether they met the inclusion criteria described previously for this review. From this stage on, blinding of authors and journal names was no longer feasible. We compared the results of the two independent selections. We resolved disagreements by discussion.

#### Data extraction and management

Two authors jointly extracted data. There was no blinding of journal and author names and affiliations. We resolved disagreements by discussion.

With regard to subgroup analysis, we extracted the following data if available:

- range of patients' age;
- basic hospital infection rate at time of study;
- indication for surgery (otitis media with effusion, tympanic membrane perforation, cholesteatoma, conductive hearing loss);
- surgical techniques (myringoplasty, ossiculoplasty, mastoidectomy, stapes surgery) performed in the study;
- intraoperative condition, such as normal, clear secretion, inflamed, purulent;
- onset of administration (preoperative, intraoperative, postoperative); and
- duration of administration (single shot, repeated  $\leq$  24 hours, > 24 hours).

#### Assessment of risk of bias in included studies

Two authors independently assessed concealment of treatment allocation using the standard Cochrane criteria: adequate (A), unclear (B), inadequate (C) or allocation concealment was not

used (D). There was no blinding of journal and author names and affiliations.

We resolved disagreement in the assessment by discussion. Two authors jointly extracted data according to methodological criteria which did not involve subjective interpretation:

- loss to follow up:  $\leq 10\%$ ,  $> 10\%$  and  $\leq 20\%$ , or  $> 20\%$ ;
- range of length of follow up:  $\geq 14$  days,  $\geq 7$  and  $< 14$  days, or  $< 7$  days;
- blinding of participants;
- blinding of medical staff;
- blinding of outcome assessors;
- blinding of those responsible for data analysis;
- study sponsored by pharmaceutical company;
- results specified respective to different surgeons.

We conducted a sensitivity analysis by comparing the effect of inclusion and exclusion of studies of different qualities. No quality scale was used.

### Data synthesis

We grouped antimicrobial agents used for therapy and/or prophylaxis by their molecular class. Each molecular class was divided into subgroups by main antimicrobial activity against intra-aural pathogens, thus every antibiotic substance occurred in exactly one subgroup. We classified regimes in terms of subgroups and combinations of subgroups.

We classified onset of administration as preoperative or perioperative (including intraoperative and postoperative). We classified dosage as prophylaxis within 24 hours and treatment for more than 24 hours, thus each arm of each controlled study referred to a specific regime/dosage pattern. We pooled all studies where the antibiotics under comparison were assigned to the same set of regime/dosage pattern.

We grouped the antimicrobial agents used for prophylaxis by their way of administration, e.g. systemic, local or a combination of local and systemic, thus creating subgroups for the method of administration of the drug. If possible, we formed different subgroups for the type of surgical procedure, e.g. clean or clean-contaminated. This resulted, where possible, in six different comparisons (clean or clean-contaminated surgery; systemic antibiotics versus no antibiotics; systemic and local antibiotics versus local antibiotics; local antibiotics versus no antibiotics).

Tables of comparison included the following outcomes.

1. Postoperative fever ( $> 37^\circ\text{C}$  ( $98^\circ\text{F}$ ) for  $\geq$  five days).
2. Postoperative wound infections (discharge of pus or necessity for additional interventions).
3. Postoperative change of antibiotic treatment (regime and/or dosage).
4. Adverse drug effects (minor symptoms such as laboratory findings, rash).
5. Adverse drug effects (major symptoms such as clinical/laboratory signs of organ dysfunction).
6. Graft failure rates.
7. Closure of the tympanic membrane.

8. Bacterial eradication (comparison of intra- and postoperative cultures).
9. Death from any cause.

We summarised outcomes 1) to 3) as "Postoperative infection (Yes/No)"; outcomes 4 and 5 as "Adverse effects (Yes/No)"; outcomes 6 and 7 as "Graft failure (Yes/No)"; and listed outcomes 8 and 9 separately.

We determined summary odds ratios (OR) with 95% confidence intervals (CI) using both a fixed-effect model (Mantel-Haenszel) and a random-effects model (Der Simonian and Laird).

We also determined the risk differences (RD) between different regime/dosage patterns (difference in the failure rate) and a 95% confidence interval. In the event of a statistically significant risk difference, we determined the number of patients needed to be treated in order to prevent one failure (NNT) for every comparison of regime/dosage pattern.

We reviewed a test of heterogeneity and an appraisal of individual study odds ratio within each comparison of regime/dosage pattern to determine if similar results were obtained from each study. Where significant heterogeneity existed, we examined the trials for specific potential clinical differences.

We assessed potential effects of publication bias on the results of the meta-analysis from a funnel graph of the sample size plotted against the odds ratio.

We planned to conduct subgroup analyses for:

- children and adults (adults  $\geq 16$  to 17);
- surgical techniques: intraoperative and/or histological diagnosis: normal, inflamed, purulent;
- preoperative, intraoperative and postoperative onset of administration;
- duration of administration (single shot, repeated  $\leq 24$  hours, repeated  $> 24$  hours); and
- mode of administration.

However, neither the original data nor additional data supplied by study authors allowed subgroup analysis for children and adults, surgical techniques, intra-operative and/or histological diagnosis, onset of administration or duration of administration of the drug.

## RESULTS

### Description of studies

The most recent update search (August 2009) identified no new studies. From previous searches (June 2007) thirteen publications regarding the use of any regimen of antibiotic prophylaxis in ear surgery appeared to meet the inclusion criteria. One study was presented as a randomised controlled trial, but appeared to be a case report (Leonard 1967). One study compared two different antibiotic regimens, and was therefore not suitable for this review (Liu 1983). Thus, we included 11 studies in the review.

We contacted authors, if possible. We asked questions about methodological issues and, when needed, we requested original data. Five authors responded. Details of the participants, interventions and outcomes in those studies are presented in



the table 'Characteristics of included studies'. As is presented in this table, the studies were very heterogeneous with regard to the chosen antibiotic and dosage, and onset and duration of administration. Therefore, pooling of results by different regime/dosage pattern was impossible. Assuming the choice for an antibiotic is a rational one, we decided to make no distinction between different regime/dosage patterns, and just refer to an antibiotic as being used or not.

Seven studies compared the use of systemic antibiotics to the use of a placebo or no antibiotic (Bagger-Sjoback 1987; Eschelman 1971; Jackson 1988; John 1988; Lildholdt 1986; Pirodda 1994; Winerman 1981). Three studies compared the use of systemic antibiotics together with local antibiotics to the use of a local antibiotic alone (Donaldson 1966; Govaerts 1998; Hester 1998). Finally, only one study compared the use of a local antibiotic alone to no antibiotic (Tong 2002).

Subgroup analysis was not possible for the type of surgical procedure, e.g. clean or clean-contaminated, because most studies did not present their results in sufficient detail. Unfortunately, although the study authors were contacted, they could not provide us with more detailed results.

Subgroup analysis was also not possible for children and adults, because age was not assessed in sufficient detail in any study.

Bagger-Sjoback 1987 focused on different clean and clean-contaminated procedures, such as myringoplasties, stapedectomies and radical mastoidectomies (91 patients). The antibiotic used was phenoxymethylpenicillin. Both the antibiotic and placebo group received hydrocortisone soaked gauze in the outer ear canal after surgery. The most important outcome measure was postoperative infection one week after surgery.

Donaldson 1966 focused on different types of myringoplasties (96 patients). The antibiotic used was sulfamethoxazole. After surgery, both antibiotic and placebo group received polymyxin/neomycin/hydrocortisone soaked sponges in the outer ear canal. The outcome measures were postoperative infection after ten days and after six weeks, closure of the tympanic membrane, and (mild) adverse effects.

Eschelman 1971 designed a three-arm trial. The authors used two different antibiotics, penicillin and ampicillin, compared to a placebo. Three different groups of patients were identified: 1) tympanomastoidectomies with cholesteatomas; 2) tympanoplasties and tympanomastoidectomies without cholesteatomas; and 3) stapedectomies and exploratory tympanotomies. The outcome measure was postoperative infection. A total of 107 patients were enrolled.

Govaerts 1998 presented a large study (750 patients were enrolled). Different procedures were carried out, such as tympanoplasties and radical mastoidectomies. The antibiotic used was cefuroxime. The most important outcome measure was postoperative infection within two weeks after surgery.

Hester 1998 used different antibiotics in a two-arm trial, depending on the specific need of the patients (ampicillin/sulbactam/amoxicillin/clavulanate, cefazolin/cefalexin, erythromycin or clindamycin). Both antibiotic and placebo group received neomycin/polymyxin/hydrocortisone otic drops during the

period following surgery. All procedures were tympanoplasties, tympanomastoidectomies or radical mastoidectomies. The outcome measures were graft failure within three weeks after surgery and after six months, and postoperative infection within three weeks after surgery. A total of 146 patients were enrolled in this study.

Jackson 1988 presented the largest study on this subject. He enrolled 3481 patients who underwent a broad variety of procedures, including some neurotological procedures. The antibiotics used were cephalotin and cefazolin. Unfortunately, he did not present subgroup analyses. Therefore, the only outcome measure suitable for this review was graft failure after three weeks of surgery. In 2136 of the 3481 patients a graft was used.

John 1988 investigated a total of 130 myringoplasties. The antibiotic used was a combination of ampicillin and flucloxacillin. The outcome measure was 'success', defined as closure of the tympanic membrane after eight weeks.

Lildholdt 1986 focused on patients undergoing surgery for chronic otitis media, who had positive pre-operative cultures for *Pseudomonas aeruginosa* (26 patients). The antibiotic used was ceftazidime. The outcome measures were dryness of the outer ear canal postoperatively and after two months, and graft failure after two months.

Pirodda 1994 enrolled 100 patients in the study, who underwent myringoplasties, tympanoplasties or tympanomastoidectomies. Ceftriaxone was the antibiotic used. After one week, one month and two months, the status of the following outcome measures were assessed: 1) retro-auricular incision; 2) outer ear canal; 3) tympanic membrane; and 4) mastoid cavity.

Tong 2002 was the only study which used only a local antibiotic (ofloxacin otic drops). In a three-arm trial, two different dosages of otic drops were compared with each other and with a third group which received no antibiotic treatment. All 101 patients underwent tympanoplasties. The outcome measure was 'success', defined as closing of the tympanic membrane after eight weeks.

Winerman 1981 investigated a study population of 72 patients who all underwent closed cavity procedures. In the antibiotic group, 30 patients received clindamycin and gentamycin. Six patients received only clindamycin because preoperative cultures showed no need for the use of gentamycin. The most important outcome measure was the occurrence of infectious complications within three months after surgery, which was not specifically defined.

### Risk of bias in included studies

The two authors initially agreed on about 90% of the assessments of methodological quality. All disagreements were dissolved by discussion. We designed a criteria list with validity items to score the methodological quality of the studies. We used a standard form for evaluating randomised controlled trials, made by the Evidence-Based Guideline Development (EBRO) for this purpose (Table 1). Table 2 presents the scores on these validity items of the criteria list. The methodological quality of the included studies was fair to good. Many studies reported on randomised treatment allocation, but (a) failed to describe the exact procedure or (b) whether concealed allocation had been performed. Information on blinding the outcome assessor (e) was often not provided. Also the information on blinding of patients (c) and physician (d), and about

loss to follow up (g) was often not provided. Although only two studies scored positive on all items of the criteria list, none of the studies were considered to contain 'fatal flaws'.

With regard to specific studies, we can mention the following.

[Bagger-Sjoback 1987](#) was a well-designed and performed study. However, the authors withdrew four patients and addressed them as being lost to follow up. These patients developed clinical signs of infection and were withdrawn for proper treatment. These patients should, in fact, have been taken along in further analyses. In our analysis, we followed a 'worst-case scenario'.

[Donaldson 1966](#) offered very little information on methodological procedures. Moreover, the authors reported some patients not to be seen on every visit during follow up. Unfortunately they did not report to which arm of the trial these patients belonged. In our analyses, we followed a 'worst case scenario', assuming these patients were in the control group.

[John 1988](#) used a questionable method of randomising patients: by flipping a coin. Moreover, the 110 patients were not equally divided (treatment:control rate was 55:75). After contacting them, the authors assured us that this was merely coincidence, and that the tossing of the coin had proven this to be an adequate method of randomisation.

## Effects of interventions

It appeared to be impossible to present subgroup analyses for children and adults, surgical techniques, intra-operative and/or histological diagnosis, onset of administration and duration of administration of the drug. The data in the studies were not presented in sufficient detail to make this possible. Subgroup analyses for different ways of administering the drug, e.g. systemic or local, was possible.

Pooling of data was possible. However, it should be taken into consideration that most studies did not present subgroup analyses for specific procedures, or for the distinction between clean and clean-contaminated procedures. Moreover, in some studies, outcome measures were not specified. Still, we believe that pooling of these data is appropriate.

### 1. Effect of antibiotic prophylaxis in clean and clean-contaminated ear surgery

#### 1.1. Effect of antibiotic prophylaxis on postoperative infection within three weeks after surgery

Six studies assessed the effect of antibiotic prophylaxis on the incidence of postoperative infection within three weeks from surgery ([Bagger-Sjoback 1987](#); [Donaldson 1966](#); [Eschelman 1971](#); [Govaerts 1998](#); [Hester 1998](#); [Pirodda 1994](#)). A total of 1291 patients was investigated. Infection occurred in 34 of the 671 patients who had received prophylaxis (5.1%), and in 38 of the 620 control patients (6.1%). The odds ratio (OR) (fixed-effect) was 0.73 (confidence interval (CI) 0.45 to 1.20), which is not significant.

#### 1.2. Effect of antibiotic prophylaxis on postoperative infection six weeks after surgery

Two studies assessed the effect of antibiotic prophylaxis on the incidence of postoperative infection after six weeks of surgery ([Donaldson 1966](#); [Pirodda 1994](#)). A total of 196 patients was

investigated. Infection occurred in eight of the 98 patients who had received prophylaxis (8.1%), and in 10 of the 98 control patients (10.2%). The odds ratio (fixed-effect) was 0.78 (95% CI 0.30 to 2.07), which is not significant.

#### 1.3. Effect of antibiotic prophylaxis on postoperative infection within three months after surgery

Two studies assessed the effect of antibiotic prophylaxis on the incidence of postoperative infection within three months from surgery ([Pirodda 1994](#); [Winerman 1981](#)). A total of 172 patients was investigated. Infection occurred in nine of the 86 patients who had received prophylaxis (10.5%), and in nine of the 86 control patients (10.5%). The odds ratio (fixed-effect) was 1.00 (95% CI 0.38 to 2.66), which is not significant.

#### 1.4. Effect of antibiotic prophylaxis on the postoperative status of the outer ear canal two months after surgery

Two studies assessed the effect of antibiotic prophylaxis on the postoperative status of the outer ear canal two months after surgery ([Lildholdt 1986](#); [Pirodda 1994](#)). A total of 126 patients was investigated. Two months after surgery three of the 64 (4.7%) patients receiving prophylaxis, suffered from a draining outer ear canal. In the control group this was eight of the 62 patients (12.9%). The odds ratio (fixed-effect) was 0.29 (95% CI 0.08 to 1.13), which is not significant.

#### 1.5. Effect of antibiotic prophylaxis on graft failure rate within three weeks after surgery

Two studies assessed the effect of antibiotic prophylaxis on graft failure rates within three weeks from surgery ([Hester 1998](#); [Jackson 1988](#)). A total of 2282 patients was investigated. Within three weeks after surgery, graft failure had occurred in 13 of the 1189 patients who had received prophylaxis (1.1%), and in 17 of the 1093 patients who were in the control group (1.6%). The odds ratio (fixed-effect) was 0.71 (95% CI 0.35 to 1.45), which is not significant.

#### 1.6. Effect of antibiotic prophylaxis on graft failure rate between six weeks and three months after surgery

Six studies assessed the effect of antibiotic prophylaxis on graft failure rates between six weeks and three months after surgery ([Donaldson 1966](#); [Hester 1998](#); [John 1988](#); [Lildholdt 1986](#); [Pirodda 1994](#); [Tong 2002](#)). A total of 599 patients was investigated. Graft failure occurred in 42 of the 304 patients who had received prophylaxis (13.8%), and in 44 of the 295 patients who were in the control group (14.9%). The odds ratio (fixed-effect) was 0.86 (95% CI 0.53 to 1.41), which is not significant.

#### 1.7. Effect of antibiotic prophylaxis on graft failure rate within three months after surgery

A total of seven studies assessed the effect of antibiotic prophylaxis on graft failure at one point or another within three months ([Donaldson 1966](#); [Hester 1998](#); [Jackson 1988](#); [John 1988](#); [Lildholdt 1986](#); [Pirodda 1994](#); [Tong 2002](#)). A total of 2739 patients was investigated. Graft failure occurred in 55 of the 1426 (3.9%) patients who had received prophylaxis, and in 59 of the 1313 (4.5%) patients in the control group. The odds ratio (fixed-effect) was 0.84 (95% CI 0.56 to 1.26), which is not significant.

### **1.8. Effect of antibiotic prophylaxis on adverse drug effects**

Two studies assessed the incidence of adverse drug effects (Donaldson 1966; Govaerts 1998). A total of 841 patients was investigated. Only four of the 428 patients (0.9%) who had received an antibiotic substance suffered from adverse drug effects. On the other hand, five of the 413 patients (1.2%) who had not received an antibiotic suffered from adverse (drug) effects. The odds ratio (fixed-effect) was 0.73 (95% CI 0.20 to 2.64), which is not significant.

### **1.9. Effect of antibiotic prophylaxis on bacterial eradication**

No study compared intra- and postoperative cultures.

### **1.10. Effect of antibiotic prophylaxis on death from any cause**

No study reported death from any cause.

Subgroup analyses were then made for different types of administration of the antibiotic prophylaxis:

## **2. Effect of systemic antibiotic prophylaxis versus no antibiotics in clean and clean-contaminated ear surgery**

### **2.1. Effect of systemic antibiotic prophylaxis versus no antibiotics on postoperative infection within three weeks after surgery**

Three studies assessed the effect of systemic antibiotic prophylaxis versus no antibiotics on the incidence of postoperative infection within three weeks from surgery (Bagger-Sjoback 1987; Eschelman 1971; Pirodda 1994). A total of 299 patients was investigated. Infection occurred in 20 of the 172 patients who had received prophylaxis (11.6%), and in 14 of the 127 control patients (11.0%). The odds ratio (fixed-effect) was 1.02 (confidence interval (CI) 0.49 to 2.15), which is not significant.

### **2.2. Effect of systemic antibiotic prophylaxis versus no antibiotics on postoperative infection six weeks after surgery**

One study assessed the effect of systemic antibiotic prophylaxis versus no antibiotics on the incidence of postoperative infection after six weeks of surgery (Pirodda 1994). A total of 100 patients was investigated. Infection occurred in five of the 50 patients who had received prophylaxis (10.0%), and in four of the 50 control patients (8.0%). The odds ratio (fixed-effect) was 1.28 (95% CI 0.32 to 5.07), which is not significant.

### **2.3. Effect of systemic antibiotic prophylaxis versus no antibiotics on postoperative infection within three months after surgery**

Two studies assessed the effect of systemic antibiotic prophylaxis versus no antibiotics on the incidence of postoperative infection within three months from surgery (Pirodda 1994; Winerman 1981). A total of 172 patients was investigated. Infection occurred in nine of the 86 patients who had received prophylaxis (10.5%), and in nine of the 86 control patients (10.5%). The odds ratio (fixed-effect) was 1.00 (95% CI 0.38 to 2.66), which is not significant.

### **2.4. Effect of systemic antibiotic prophylaxis versus no antibiotics on the postoperative status of the outer ear canal two months after surgery**

Two studies assessed the effect of systemic antibiotic prophylaxis versus no antibiotics on the postoperative status of the outer ear canal two months after surgery (Lildholdt 1986; Pirodda 1994). A

total of 126 patients was investigated. Two months after surgery three of the 64 (4.7%) patients receiving prophylaxis, suffered from a draining outer ear canal. In the control group this was eight of the 62 patients (12.9%). The odds ratio (fixed-effect) was 0.29 (95% CI 0.08 to 1.13), which is not significant.

### **2.5. Effect of systemic antibiotic prophylaxis versus no antibiotics on graft failure rate within three weeks after surgery**

One study assessed the effect of systemic antibiotic prophylaxis versus no antibiotics on graft failure rates within three weeks from surgery (Jackson 1988). A total of 2136 patients was investigated. Within three weeks after surgery, graft failure had occurred in 13 of the 1118 patients who had received prophylaxis (1.2%), and in 15 of the 1018 patients who were in the control group (1.5%). The odds ratio (fixed-effect) was 0.79 (95% CI 0.37 to 1.66), which is not significant.

### **2.6. Effect of systemic antibiotic prophylaxis versus no antibiotics on graft failure rate between six weeks and three months after surgery**

Three studies assessed the effect of systemic antibiotic prophylaxis versus no antibiotics on graft failure rates between six weeks and three months after surgery (John 1988; Lildholdt 1986; Pirodda 1994). A total of 256 patients was investigated. Graft failure occurred in 18 of the 119 patients who had received prophylaxis (15.1%), and in 18 of the 137 patients who were in the control group (13.1%). The odds ratio (fixed-effect) was 1.13 (95% CI 0.52 to 2.49), which is not significant.

### **2.7. Effect of systemic antibiotic prophylaxis versus no antibiotics on graft failure rate within three months after surgery**

A total of four studies assessed the effect of systemic antibiotic prophylaxis versus no antibiotics on graft failure at one point or another within three months (Jackson 1988; John 1988; Lildholdt 1986; Pirodda 1994). A total of 2392 patients was investigated. Graft failure occurred in 31 of the 1237 (2.5%) patients who had received prophylaxis, and in 33 of the 1155 (2.9%) patients in the control group. The odds ratio (fixed-effect) was 0.93 (95% CI 0.54 to 1.61), which is not significant.

### **2.8. Effect of systemic antibiotic prophylaxis versus no antibiotics on adverse drug effects**

No study assessed the effect of systemic antibiotic prophylaxis versus no antibiotics on the incidence of adverse drug effects.

### **2.9. Effect of systemic antibiotic prophylaxis versus no antibiotics on bacterial eradication**

No study compared intra- and postoperative cultures.

### **2.10. Effect of systemic antibiotic prophylaxis versus no antibiotics on death from any cause**

No study reported death from any cause.

### **3. Effect of systemic and local antibiotic prophylaxis versus local antibiotics in clean and clean-contaminated ear surgery**

#### **3.1. Effect of systemic and local antibiotic prophylaxis versus local antibiotics on postoperative infection within three weeks after surgery**

Three studies assessed the effect of systemic and local antibiotic prophylaxis versus local antibiotics on the incidence of postoperative infection within three weeks from surgery (Donaldson 1966; Govaerts 1998; Hester 1998). A total of 992 patients was investigated. Infection occurred in 14 of the 499 patients who had received systemic and local prophylaxis (2.8%), and in 24 of the 493 control patients (4.9%). The odds ratio (fixed-effect) was 0.56 (confidence interval (CI) 0.29 to 1.10), which is not significant.

#### **3.2. Effect of systemic and local antibiotic prophylaxis versus local antibiotics on postoperative infection six weeks after surgery**

One study assessed the effect of systemic and local antibiotic prophylaxis versus local antibiotics on the incidence of postoperative infection after six weeks of surgery (Donaldson 1966). A total of 96 patients was investigated. Infection occurred in three of the 48 patients who had received systemic and local prophylaxis (6.3%), and in six of the 48 control patients (12.5%). The odds ratio (fixed-effect) was 0.47 (95% CI 0.11 to 1.99), which is not significant.

#### **3.3. Effect of systemic and local antibiotic prophylaxis versus local antibiotics on postoperative infection within three months after surgery**

No study assessed the effect of systemic and local antibiotic prophylaxis versus local antibiotics on the incidence of postoperative infection within three months from surgery.

#### **3.4. Effect of systemic and local antibiotic prophylaxis versus local antibiotics on the postoperative status of the outer ear canal two months after surgery**

No study assessed the effect of systemic and local antibiotic prophylaxis versus local antibiotics on the postoperative status of the outer ear canal two months after surgery.

#### **3.5. Effect of systemic and local antibiotic prophylaxis versus local antibiotics on graft failure rate within three weeks after surgery**

One study assessed the effect of systemic and local antibiotic prophylaxis versus local antibiotics on graft failure rates within three weeks from surgery (Hester 1998). A total of 146 patients was investigated. Within three weeks after surgery, graft failure had occurred in none of the 71 patients who had received systemic and local prophylaxis (0%), and in two of the 75 patients who were in the control group (2.7%). This was, however, not significant. The odds ratio (fixed-effect) was 0.21 (95% CI 0.01 to 4.36).

#### **3.6. Effect of systemic and local antibiotic prophylaxis versus local antibiotics on graft failure rate between six weeks and three months after surgery**

Two studies assessed the effect of systemic and local antibiotic prophylaxis versus local antibiotics on graft failure rates between six weeks and three months after surgery (Donaldson 1966; Hester 1998). A total of 242 patients was investigated. Graft failure occurred

in 13 of the 119 patients who had received systemic and local prophylaxis (10.9%), and in 22 of the 123 patients who were in the control group (17.9%). The odds ratio (fixed-effect) was 0.54 (95% CI 0.25 to 1.15), which is not significant.

#### **3.7. Effect of systemic and local antibiotic prophylaxis versus local antibiotics on graft failure rate within three months after surgery**

These results are the same as 3.6.

#### **3.8. Effect of systemic and local antibiotic prophylaxis versus local antibiotics on adverse drug effects**

Two studies assessed the effect of systemic and local antibiotic prophylaxis versus local antibiotics on the incidence of adverse drug effects (Donaldson 1966; Govaerts 1998). A total of 841 patients was investigated. Only four of the 428 patients (0.9%) who had received systemic and local antibiotic prophylaxis suffered from adverse drug effects. On the other hand, five of the 413 patients (1.2%) who had received only a local antibiotic suffered from adverse (drug) effects. The odds ratio (fixed-effect) was 0.73 (95% CI 0.20 to 2.64), which is not significant.

#### **3.9. Effect of systemic and local antibiotic prophylaxis versus local antibiotics on bacterial eradication**

No study compared intra- and postoperative cultures.

#### **3.10. Effect of systemic and local antibiotic prophylaxis versus local antibiotics on death from any cause**

No study reported death from any cause.

### **4. Effect of local antibiotic prophylaxis versus no antibiotics in clean and clean-contaminated ear surgery**

Only one study compared the use of local antibiotic prophylaxis alone to no antibiotics (Tong 2002). This study only assessed the effect on graft failure rate within three months after surgery (comparisons 4.6 and 4.7). A total of 101 patients was investigated. Graft failure occurred in 11 of the 66 patients who had received prophylaxis (13.8%), and in four of the 35 patients who were in the control group (11.4%). The odds ratio (fixed-effect) was 1.55 (95% CI 0.45 to 5.28), which is not significant.

## **DISCUSSION**

This review included 11 randomised controlled trials comparing a certain antibiotic in a certain regime/dosage pattern with a control group. These patterns were investigated during different otologic surgical procedures (clean as well as contaminated types of surgery). Often no subgroup analysis was presented with regard to type of surgery, e.g. clean or clean-contaminated. This is also the reason why, unfortunately, we could not perform any sub-analysis with regard to type of surgery. This is specifically the case in Jackson 1988. This well-designed and performed study investigated 3481 patients and included some procedures which we did not investigate. The authors' most important conclusion, however, is that there is no need at all for the use of antibiotic prophylaxis in ear surgery in terms of reducing postoperative complications such as infection and graft failure. We have, however, been able to assess subgroup analyses with regard to the method of administration of the antibiotic, e.g. systemic and/or local.

The methodological quality of the included studies, scored by the use of a list of validity criteria, was fair to good. Often insufficient detail was given on methodological procedures. This could, of course, enhance bias. Nevertheless, it was the authors' opinion that none of the included studies contained fatal flaws.

Many studies differed in the definition of certain outcome measures, or did not define them at all. This made the pooling of results difficult. However, the authors believed that the character of the subject of this review allows more differences in defining these measures than other subjects, therefore allowing the pooling of results. One has to realise, however, that when we pooled results to evaluate an effect within three weeks, some studies had an evaluation after two weeks, while another study could have evaluated after two and a half weeks.

None of the trials in itself showed any significant difference in any of their outcome measures, independent of the quality of the study. Pooling of results did not change any of those views. Therefore, on the basis of the data available, there seems no significant contribution for antibiotic prophylaxis in ear surgery, in term of reduction of postoperative complications such as infection and graft failure.

## **AUTHORS' CONCLUSIONS**

### **Implications for practice**

There is no evidence that the use of prophylactic antibiotics in clean or clean-contaminated ear surgery, in any regimen, is helpful

in reducing postoperative complications such as wound infection, discharge from the outer ear canal, labyrinthitis and graft failure.

### **Implications for research**

More than ten different studies all concluded that there is no need for antibiotic prophylaxis in clean and clean-contaminated ear surgery. This review supports this conclusion. Therefore, there seems to be no need for an additional randomised controlled trial on this subject. However, there has never been a large study focusing on either clean or clean-contaminated procedures alone. Taking into account the fact that there might be a difference in *a priori* risk of postoperative infection between clean and clean-contaminated procedures, a large study focusing merely on clean or clean-contaminated ear surgery, could be beneficial. Furthermore, a study focusing on different populations of patients, e.g. the elderly or children, could be interesting. It should also be noted that when the low incidence of postoperative infections is taken into consideration, for a new randomised controlled trial to have enough statistical power it would have to include a very large number of patients.

## **ACKNOWLEDGEMENTS**

We would like to thank Rob Scholten and Jan Schoones for their help and Martin Offringa for his moral support. Furthermore, we would like to thank the doctors Bagger-Sjoberg, Govaerts, John, Lildholdt and Tong, for being so kind as to reply to requests for more details.

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#### **Donaldson 1966** {published data only}

Donaldson JA, Snyder IS. Prophylactic chemotherapy in myringoplasty surgery. *Laryngoscope* 1966;**76**:1201-14.

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#### **Hester 1998** {published data only}

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#### **Jackson 1988** {published data only}

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#### **John 1988** {published data only}

John DG, Carlin WV, Lesser HJ, Carrick DG, Fielder C. Tympanoplasty surgery and prophylactic antibiotics: surgical results. *Clinical Otolaryngology* 1988;**13**(3):205-7. [MEDLINE: 3402097]

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Lildholdt T, Felding JU, Juul A, Kristensen S, Schouenborg P. Efficacy of perioperative ceftazidime in the surgical treatment of chronic otitis media due to *Pseudomonas aeruginosa*. Preliminary report of a prospective, controlled study. *Archives of Oto-rhino-laryngology* 1986;**243**(3):167-9. [MEDLINE: 3530224]

#### **Pirodda 1994** {published data only}

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#### **Tong 2002** {published data only}

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#### **Winerman 1981** {published data only}

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#### **Liu 1983** {published data only}

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#### **Garner 1988**

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#### **Kaiser 1986**

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#### **Waddell 1994**

Waddell TK, Rotstein ODSO. Antimicrobial prophylaxis in surgery. Committee on Antimicrobial Agents, Canadian Infectious Diseases Society. *Canadian Medical Association Journal* 1994;**151**(7):925-31.

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies [ordered by study ID]

**Bagger-Sjoback 1987**

Methods	Randomised controlled trial
Participants	I: - myringoplasty - ossiculoplasty - combined approach tympanoplasty - radical mastoidectomy - revision surgery - stapedectomy - others
Interventions	(1) phenoxymethylpenicillin + hydrocortisone impregnated gauze (2) hydrocortisone impregnated gauze
Outcomes	- Postoperative infection after 6 to 8 days
Notes	—

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

**Donaldson 1966**

Methods	Randomised controlled trial
Participants	I: - myringoplasty (different types)
Interventions	(1) sulfamethoxazole + polymyxin B - neomycin - hydrocortisone impregnated sponge (2) polymyxin B - neomycin - hydrocortisone impregnated sponge
Outcomes	- Postoperative infection after 10 days - Postoperative infection after 6 weeks - Adverse effects of antibiotics - Closure of tympanic membrane
Notes	—

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

**Eschelman 1971**

Methods	Randomised controlled trial
Participants	I: - tympanomastoidectomy (with cholesteatoma)

**Antibiotic prophylaxis in clean and clean-contaminated ear surgery (Review)**

**Eschelman 1971** (Continued)

- II:  
 - tympanoplasty  
 - tympanomastoidectomy (without cholesteatoma)
- III:  
 - stapedectomy  
 - exploratory tympanotomy

Interventions	(1) penicillin (2) ampicillin (3) placebo
Outcomes	- Postoperative infection
Notes	—
<b>Risk of bias</b>	
<b>Bias</b>	<b>Authors' judgement</b> <b>Support for judgement</b>
Allocation concealment?	Low risk                      A - Adequate

**Govaerts 1998**

Methods	Randomised controlled trial
Participants	I: - surgery for otosclerosis - tympanoplasty (different types) - radical mastoidectomy - tympanotomy without reconstruction
Interventions	(1) cefuroxime + oxytetracycline - polymyxin B - postoperative packing (2) oxytetracycline - polymyxin B - postoperative packing
Outcomes	- Postoperative infection within 2 weeks after surgery - Adverse effects
Notes	—
<b>Risk of bias</b>	
<b>Bias</b>	<b>Authors' judgement</b> <b>Support for judgement</b>
Allocation concealment?	Low risk                      A - Adequate

**Hester 1998**

Methods	Randomised controlled trial
Participants	I: - tympanoplasty - tympanomastoidectomy - radical mastoidectomy

**Antibiotic prophylaxis in clean and clean-contaminated ear surgery (Review)**



**Hester 1998** (Continued)

Interventions	(1) ampicillin/sulbactam/Augmentin or cefazolin/cephalexin or erythromycin or clindamycin + bacitracin gauze + neomycin - polymyxin - hydrocortisone drops (2) bacitracin gauze + neomycin - polymyxin - hydrocortisone drops
Outcomes	- Postoperative infection within 3 weeks - Graft failure within 3 weeks - Graft failure after 3 months
Notes	—

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

**Jackson 1988**

Methods	Randomised controlled trial
Participants	I: - a wide variety of surgical procedures, including neurotological surgery
Interventions	(1) cephalothin or cefazolin or oxacillin or vancomycin (2) no antibiotic
Outcomes	- Graft failure after 3 weeks
Notes	—

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

**John 1988**

Methods	Randomised controlled trial
Participants	I: - tympanoplasty
Interventions	(1) ampicillin + flucloxacillin (2) no antibiotic
Outcomes	- Closure of tympanic membrane after 8 weeks
Notes	—

**Risk of bias**

**John 1988** (Continued)

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

**Lildholdt 1986**

Methods	Randomised controlled trial	
Participants	I: - surgery for chronic otitis media	
Interventions	(1) ceftazidim (2) no antibiotic	
Outcomes	- Postoperative discharge - Discharge after 2 months - Graft failure after 2 months	
Notes	All patients had positive pre-operative <i>Pseudomonas</i> swabs	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

**Pirodda 1994**

Methods	Randomised controlled trial	
Participants	I: - mastoidectomy (different types) II: - tympanoplasty (different types)	
Interventions	(1) ceftriaxone (2) no antibiotic	
Outcomes	- Discharge after 1 week, 1 month and 2 months - Perforation of the tympanic membrane after 1 week, 1 month and 2 months - Stable situation after 1 week, 1 month and 2 months	
Notes	—	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

**Tong 2002**

Methods	Randomised controlled trial
Participants	I: - tympanoplasty
Interventions	(1) pre-operative ofloxacin drops, 10 minutes a day, for two weeks (2) pre-operative ofloxacin drops, 3 minutes a day, for two weeks (3) no antibiotic
Outcomes	- Closure of tympanic membrane after 8 weeks
Notes	—

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

**Winerman 1981**

Methods	Randomised controlled trial
Participants	I: - tympanomastoid surgery (closed cavity procedure)
Interventions	(1) clindamycin + gentamycin (2) placebo
Outcomes	- Infectious complications within 3 months
Notes	6 of the 36 patients in the antibiotic group received only clindamycin

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

**Characteristics of excluded studies [ordered by study ID]**

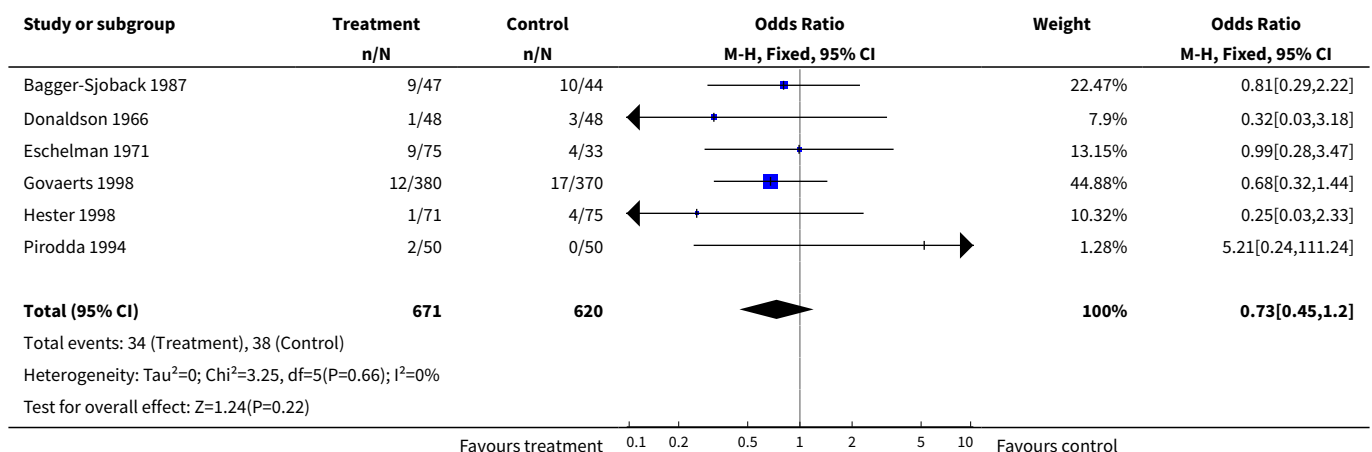
Study	Reason for exclusion
<a href="#">Leonard 1967</a>	This study was presented as a randomised controlled trial, but turned out to be a case report
<a href="#">Liu 1983</a>	This study compared two different antibiotic regime/dosage patterns (penicillin versus penicillin + gentamycin), and could therefore not be used

**DATA AND ANALYSES**

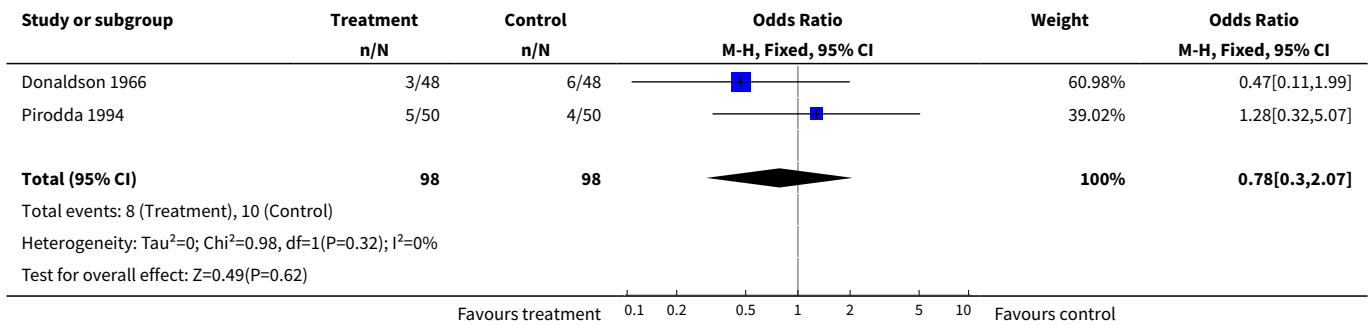
**Comparison 1. Antibiotics in clean and clean-contaminated ear surgery**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Effect of antibiotics on postoperative infection within three weeks after surgery	6	1291	Odds Ratio (M-H, Fixed, 95% CI)	0.73 [0.45, 1.20]
2 Effect of antibiotics on postoperative infection after six weeks	2	196	Odds Ratio (M-H, Fixed, 95% CI)	0.78 [0.30, 2.07]
3 Effect of antibiotics on postoperative infection within three months after surgery	2	172	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.38, 2.66]
4 Effect of antibiotics on the status of the outer ear canal two months after surgery	2	126	Odds Ratio (M-H, Fixed, 95% CI)	0.29 [0.08, 1.13]
5 Effect of antibiotics on graft failure rate within three weeks after surgery	2	2282	Odds Ratio (M-H, Fixed, 95% CI)	0.71 [0.35, 1.45]
6 Effect of antibiotics on graft failure rate between six weeks and three months after surgery	6	599	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.53, 1.41]
7 Effect of antibiotics on graft failure within three months after surgery	7	2735	Odds Ratio (M-H, Fixed, 95% CI)	0.84 [0.56, 1.26]
8 Effect of antibiotics on adverse drug effects	2	841	Odds Ratio (M-H, Fixed, 95% CI)	0.73 [0.20, 2.64]

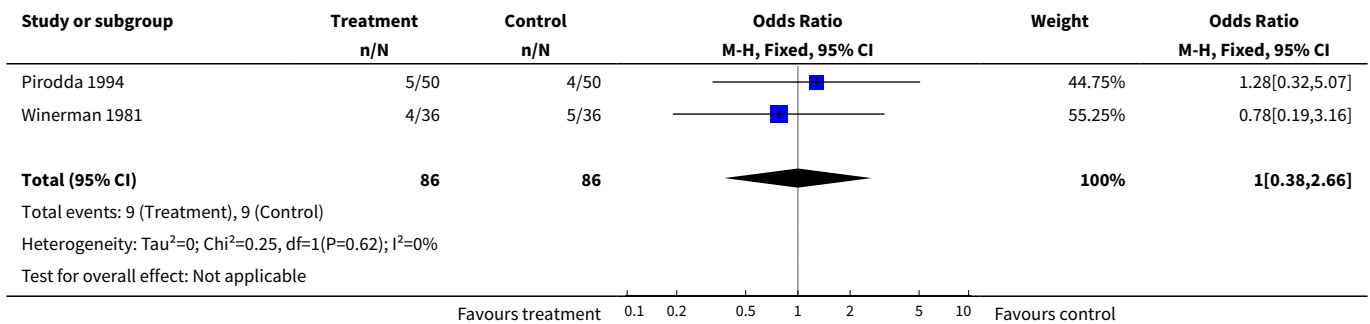
**Analysis 1.1. Comparison 1 Antibiotics in clean and clean-contaminated ear surgery, Outcome 1 Effect of antibiotics on postoperative infection within three weeks after surgery.**



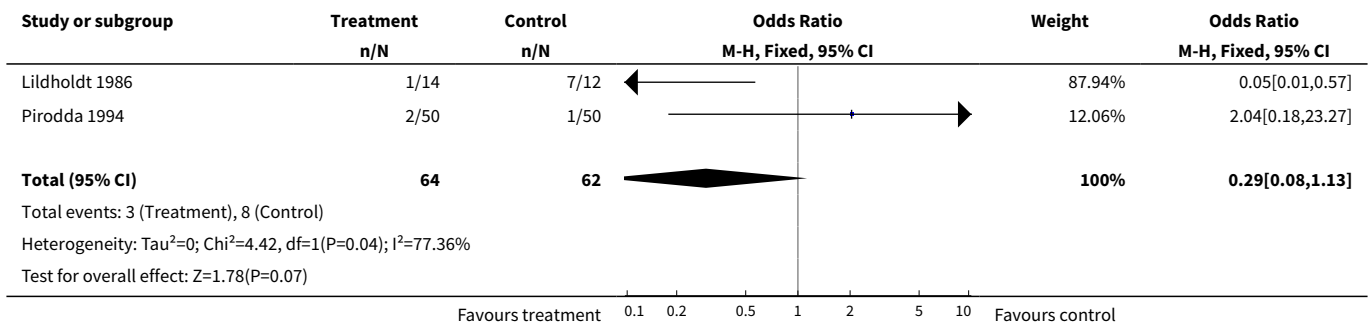
**Analysis 1.2. Comparison 1 Antibiotics in clean and clean-contaminated ear surgery, Outcome 2 Effect of antibiotics on postoperative infection after six weeks.**



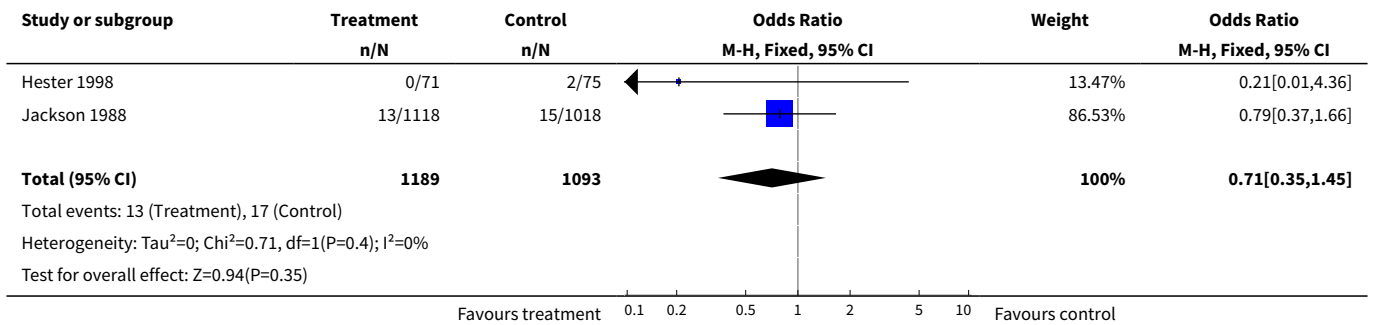
**Analysis 1.3. Comparison 1 Antibiotics in clean and clean-contaminated ear surgery, Outcome 3 Effect of antibiotics on postoperative infection within three months after surgery.**



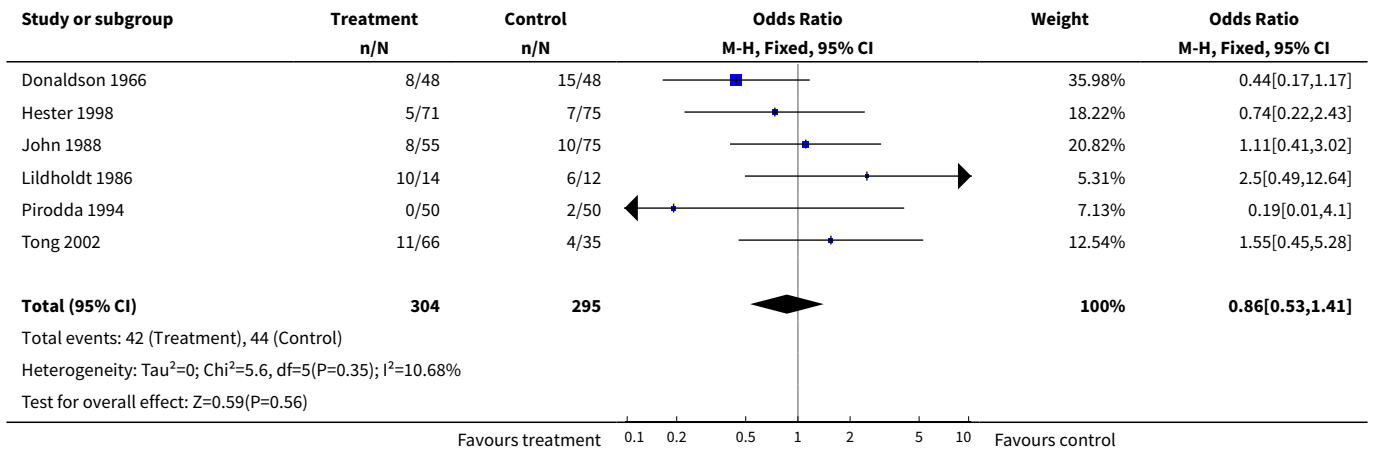
**Analysis 1.4. Comparison 1 Antibiotics in clean and clean-contaminated ear surgery, Outcome 4 Effect of antibiotics on the status of the outer ear canal two months after surgery.**



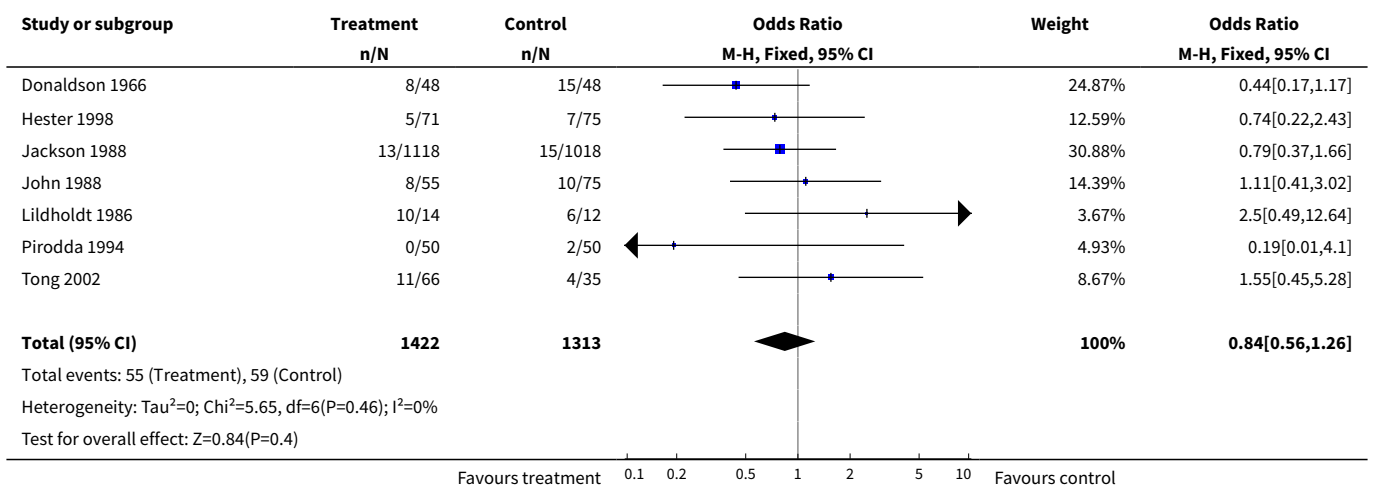
**Analysis 1.5. Comparison 1 Antibiotics in clean and clean-contaminated ear surgery, Outcome 5 Effect of antibiotics on graft failure rate within three weeks after surgery.**



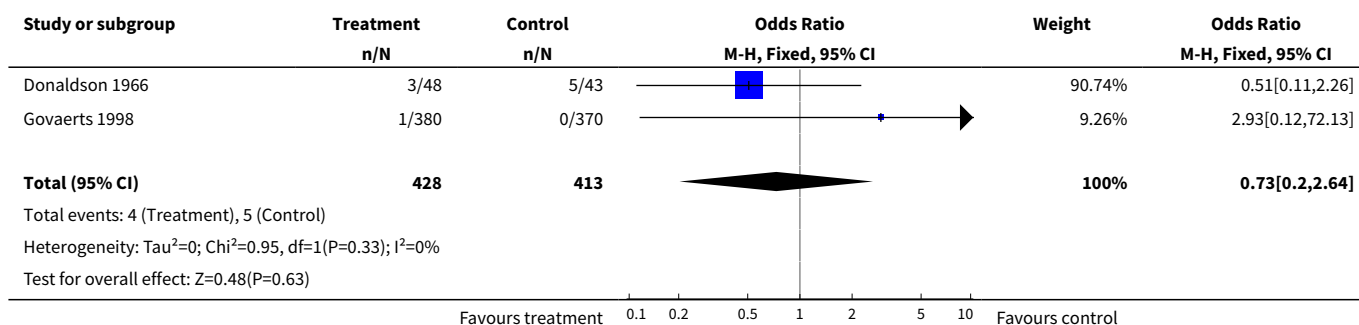
**Analysis 1.6. Comparison 1 Antibiotics in clean and clean-contaminated ear surgery, Outcome 6 Effect of antibiotics on graft failure rate between six weeks and three months after surgery.**



**Analysis 1.7. Comparison 1 Antibiotics in clean and clean-contaminated ear surgery, Outcome 7 Effect of antibiotics on graft failure within three months after surgery.**



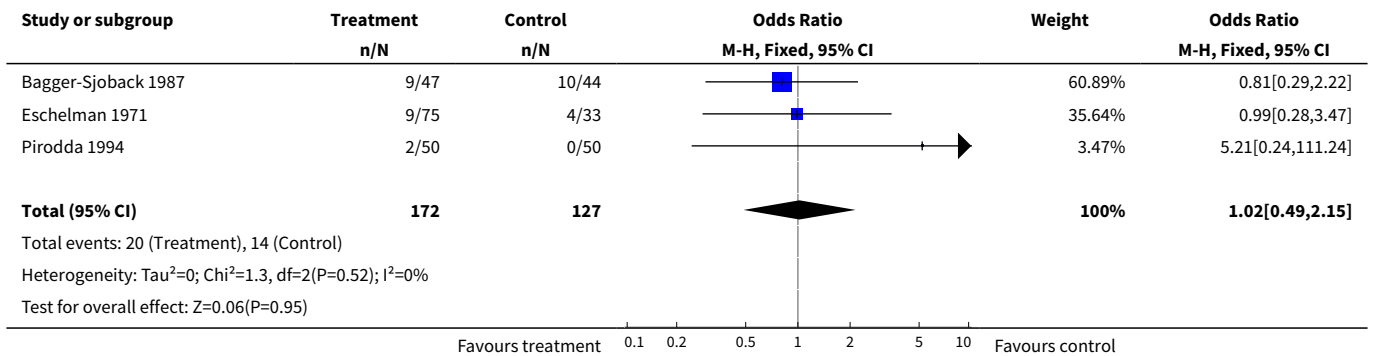
**Analysis 1.8. Comparison 1 Antibiotics in clean and clean-contaminated ear surgery, Outcome 8 Effect of antibiotics on adverse drug effects.**



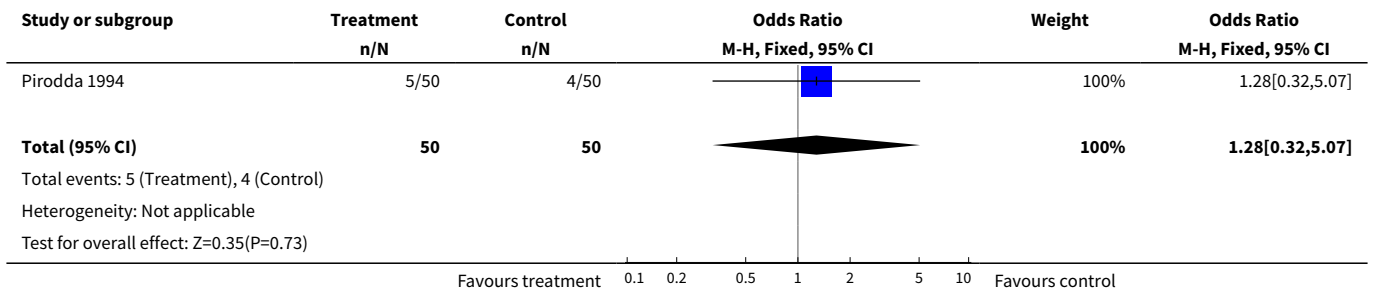
**Comparison 2. Systemic antibiotics versus no antibiotics in clean and clean-contaminated ear surgery**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Effect of systemic antibiotics on postoperative infection within three weeks after surgery	3	299	Odds Ratio (M-H, Fixed, 95% CI)	1.02 [0.49, 2.15]
2 Effect of systemic antibiotics on postoperative infection after six weeks	1	100	Odds Ratio (M-H, Fixed, 95% CI)	1.28 [0.32, 5.07]
3 Effect of systemic antibiotics on postoperative infection within three months after surgery	2	172	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.38, 2.66]
4 Effect of systemic antibiotics on the status of the outer ear canal two months after surgery	2	126	Odds Ratio (M-H, Fixed, 95% CI)	0.29 [0.08, 1.13]
5 Effect of systemic antibiotics on graft failure rate within three weeks after surgery	1	2136	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.37, 1.66]
6 Effect of systemic antibiotics on graft failure rate between six weeks and three months after surgery	3	256	Odds Ratio (M-H, Fixed, 95% CI)	1.13 [0.52, 2.49]
7 Effect of systemic antibiotics on graft failure within three months after surgery	4	2392	Odds Ratio (M-H, Fixed, 95% CI)	0.93 [0.54, 1.61]
8 Effect of systemic antibiotics on adverse drug effects	0	0	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

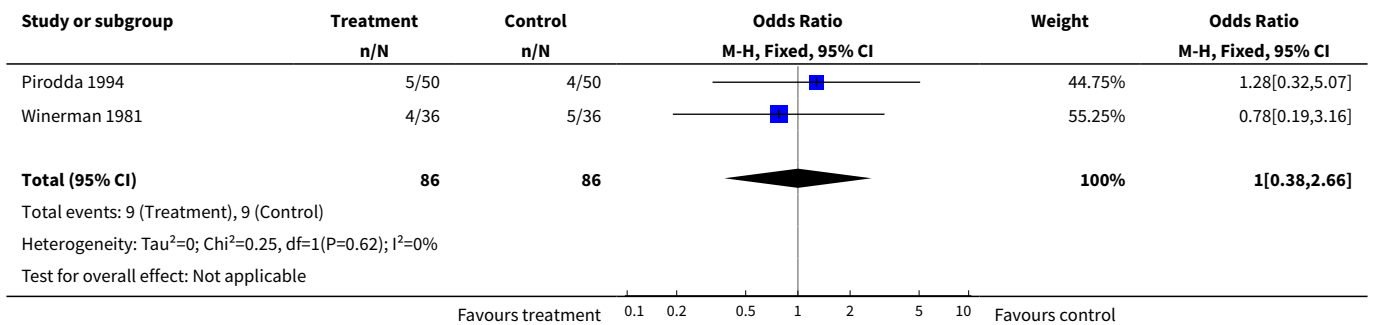
**Analysis 2.1. Comparison 2 Systemic antibiotics versus no antibiotics in clean and clean-contaminated ear surgery, Outcome 1 Effect of systemic antibiotics on postoperative infection within three weeks after surgery.**



**Analysis 2.2. Comparison 2 Systemic antibiotics versus no antibiotics in clean and clean-contaminated ear surgery, Outcome 2 Effect of systemic antibiotics on postoperative infection after six weeks.**

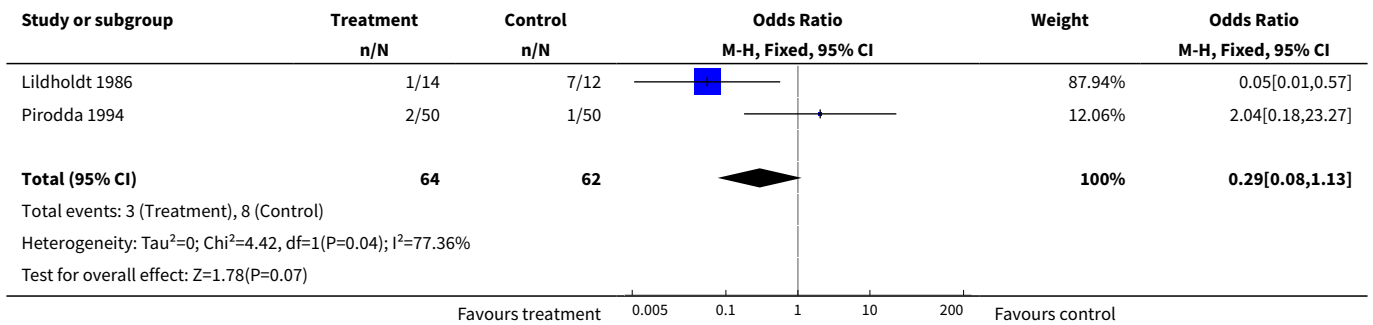


**Analysis 2.3. Comparison 2 Systemic antibiotics versus no antibiotics in clean and clean-contaminated ear surgery, Outcome 3 Effect of systemic antibiotics on postoperative infection within three months after surgery.**

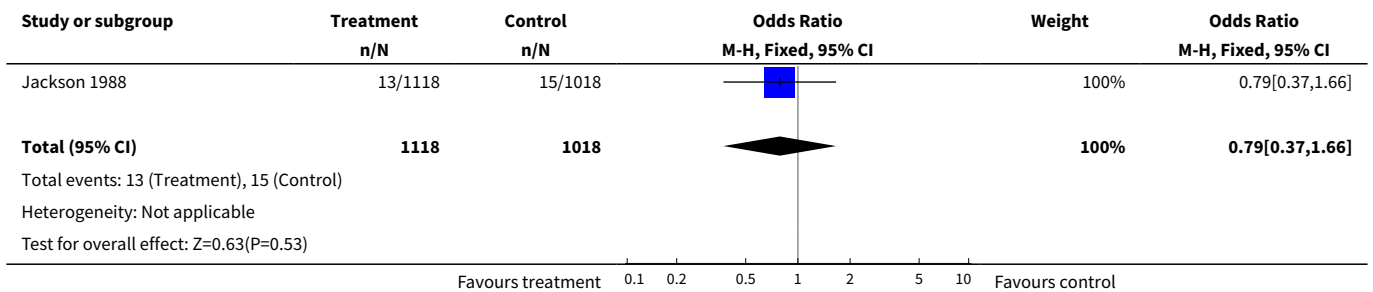




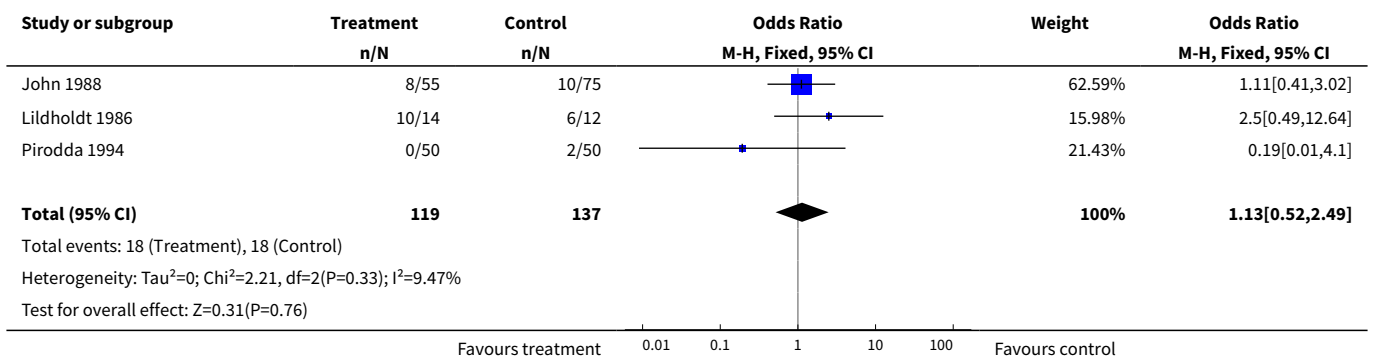
**Analysis 2.4. Comparison 2 Systemic antibiotics versus no antibiotics in clean and clean-contaminated ear surgery, Outcome 4 Effect of systemic antibiotics on the status of the outer ear canal two months after surgery.**



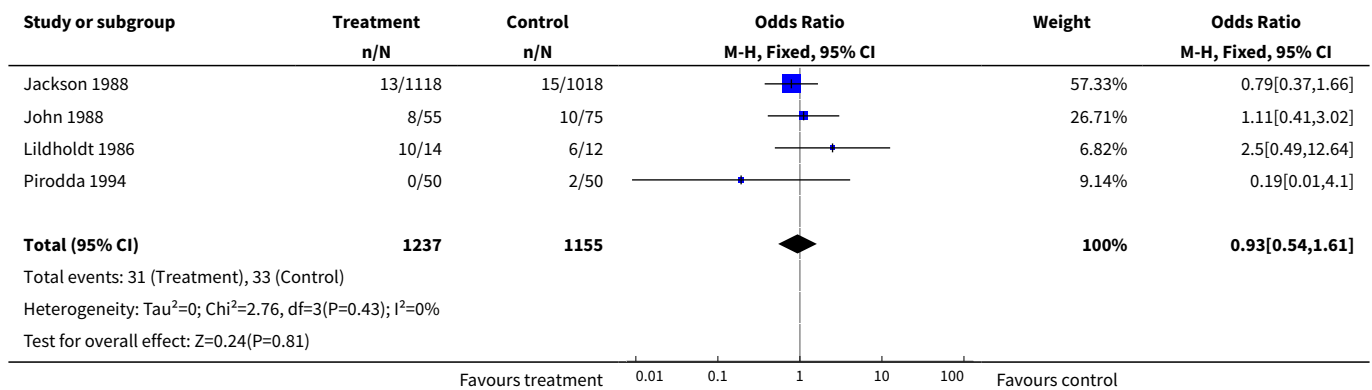
**Analysis 2.5. Comparison 2 Systemic antibiotics versus no antibiotics in clean and clean-contaminated ear surgery, Outcome 5 Effect of systemic antibiotics on graft failure rate within three weeks after surgery.**



**Analysis 2.6. Comparison 2 Systemic antibiotics versus no antibiotics in clean and clean-contaminated ear surgery, Outcome 6 Effect of systemic antibiotics on graft failure rate between six weeks and three months after surgery.**



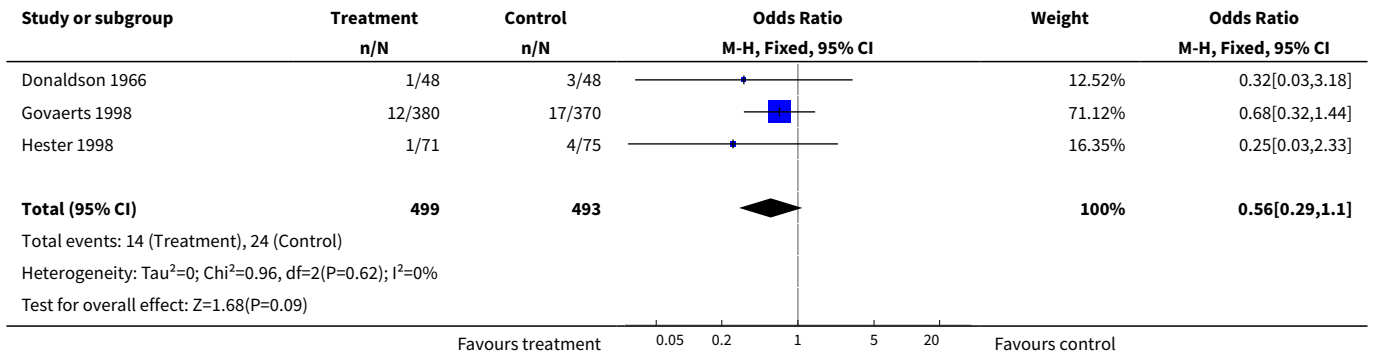
**Analysis 2.7. Comparison 2 Systemic antibiotics versus no antibiotics in clean and clean-contaminated ear surgery, Outcome 7 Effect of systemic antibiotics on graft failure within three months after surgery.**



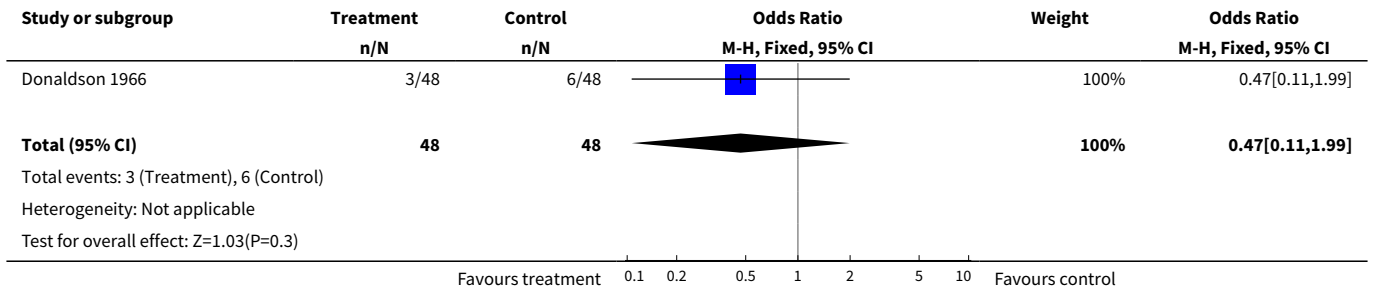
**Comparison 3. Systemic and local antibiotics versus local antibiotics in clean and clean-contaminated ear surgery**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Effect of systemic and local antibiotics on postoperative infection within three weeks after surgery	3	992	Odds Ratio (M-H, Fixed, 95% CI)	0.56 [0.29, 1.10]
2 Effect of systemic and local antibiotics on postoperative infection after six weeks	1	96	Odds Ratio (M-H, Fixed, 95% CI)	0.47 [0.11, 1.99]
3 Effect of systemic and local antibiotics on postoperative infection within three months after surgery	0	0	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Effect of systemic and local antibiotics on the status of the outer ear canal two months after surgery	0	0	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Effect of systemic and local antibiotics on graft failure rate within three weeks after surgery	1	146	Odds Ratio (M-H, Fixed, 95% CI)	0.21 [0.01, 4.36]
6 Effect of systemic and local antibiotics on graft failure rate between six weeks and three months after surgery	2	242	Odds Ratio (M-H, Fixed, 95% CI)	0.54 [0.25, 1.15]
7 Effect of systemic and local antibiotics on graft failure within three months after surgery	2	242	Odds Ratio (M-H, Fixed, 95% CI)	0.54 [0.25, 1.15]
8 Effect of systemic and local antibiotics on adverse drug effects	2	841	Odds Ratio (M-H, Fixed, 95% CI)	0.73 [0.20, 2.64]

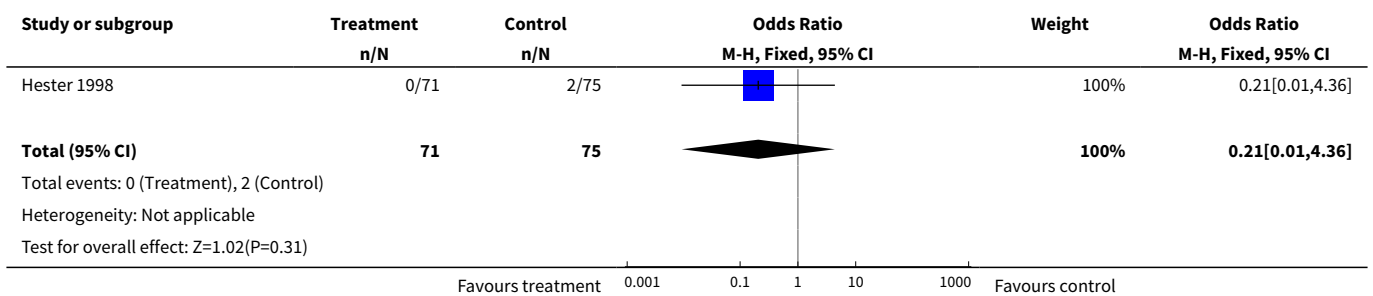
**Analysis 3.1. Comparison 3 Systemic and local antibiotics versus local antibiotics in clean and clean-contaminated ear surgery, Outcome 1 Effect of systemic and local antibiotics on postoperative infection within three weeks after surgery.**



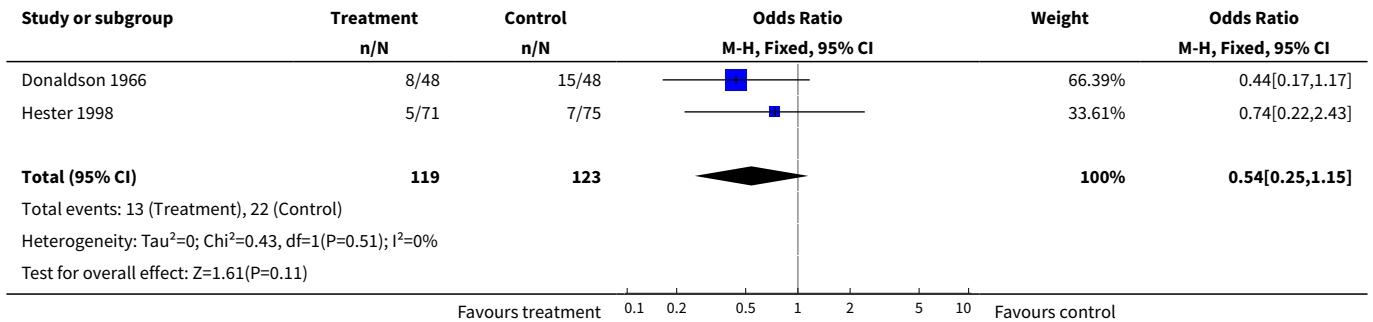
**Analysis 3.2. Comparison 3 Systemic and local antibiotics versus local antibiotics in clean and clean-contaminated ear surgery, Outcome 2 Effect of systemic and local antibiotics on postoperative infection after six weeks.**



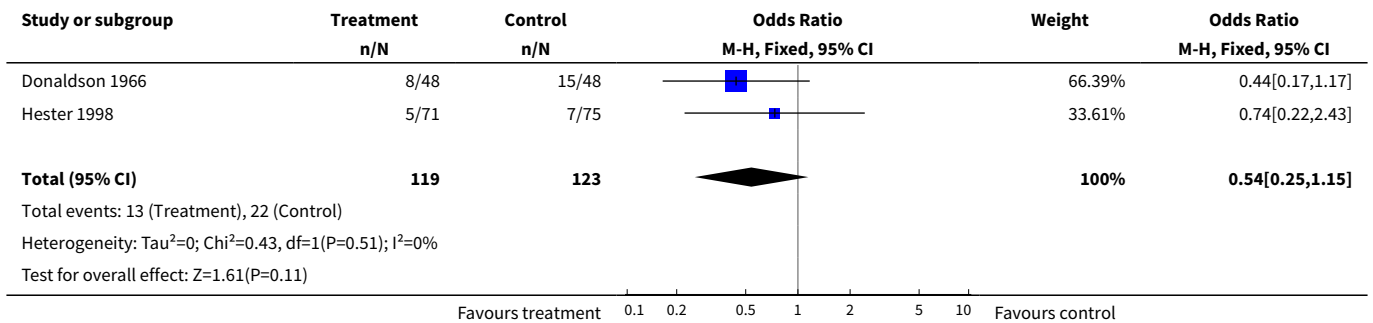
**Analysis 3.5. Comparison 3 Systemic and local antibiotics versus local antibiotics in clean and clean-contaminated ear surgery, Outcome 5 Effect of systemic and local antibiotics on graft failure rate within three weeks after surgery.**



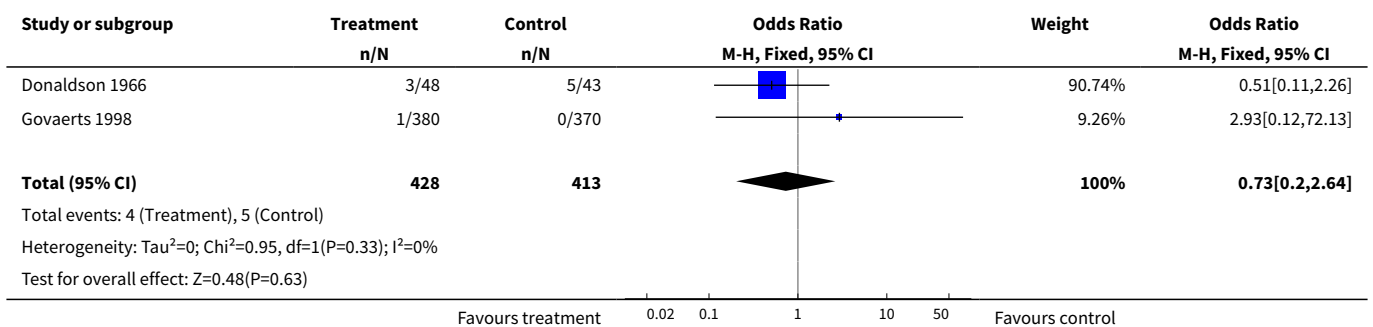
**Analysis 3.6. Comparison 3 Systemic and local antibiotics versus local antibiotics in clean and clean-contaminated ear surgery, Outcome 6 Effect of systemic and local antibiotics on graft failure rate between six weeks and three months after surgery.**



**Analysis 3.7. Comparison 3 Systemic and local antibiotics versus local antibiotics in clean and clean-contaminated ear surgery, Outcome 7 Effect of systemic and local antibiotics on graft failure within three months after surgery.**



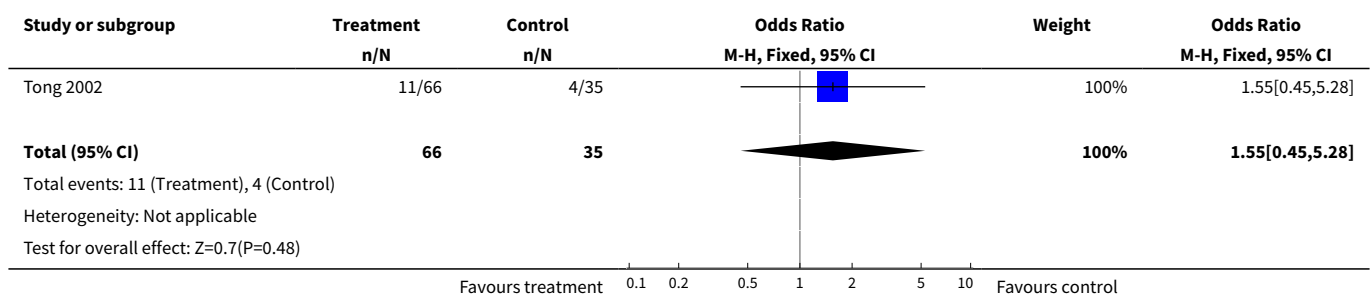
**Analysis 3.8. Comparison 3 Systemic and local antibiotics versus local antibiotics in clean and clean-contaminated ear surgery, Outcome 8 Effect of systemic and local antibiotics on adverse drug effects.**



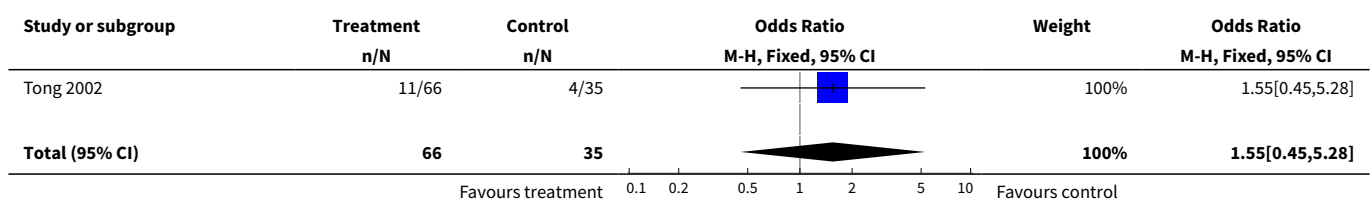
**Comparison 4. Local antibiotics versus no antibiotics in clean and clean-contaminated ear surgery**

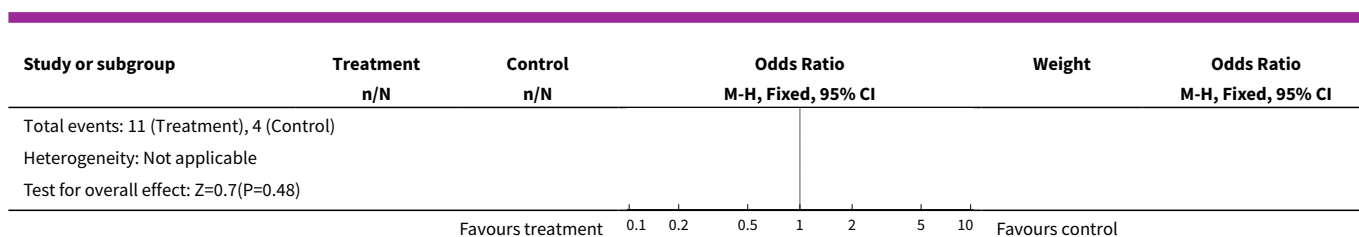
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Effect of local antibiotics on postoperative infection within three weeks after surgery	0	0	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Effect of local antibiotics on postoperative infection after six weeks	0	0	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Effect of local antibiotics on postoperative infection within three months after surgery	0	0	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Effect of local antibiotics on the status of the outer ear canal two months after surgery	0	0	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Effect of local antibiotics on graft failure rate within three weeks after surgery	0	0	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Effect of local antibiotics on graft failure rate between six weeks and three months after surgery	1	101	Odds Ratio (M-H, Fixed, 95% CI)	1.55 [0.45, 5.28]
7 Effect of local antibiotics on graft failure within three months after surgery	1	101	Odds Ratio (M-H, Fixed, 95% CI)	1.55 [0.45, 5.28]
8 Effect of local antibiotics on adverse drug effects	0	0	Odds Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

**Analysis 4.6. Comparison 4 Local antibiotics versus no antibiotics in clean and clean-contaminated ear surgery, Outcome 6 Effect of local antibiotics on graft failure rate between six weeks and three months after surgery.**



**Analysis 4.7. Comparison 4 Local antibiotics versus no antibiotics in clean and clean-contaminated ear surgery, Outcome 7 Effect of local antibiotics on graft failure within three months after surgery.**





## ADDITIONAL TABLES

**Table 1. Criteria list for the assessment of methodological quality of included studies**

Item ID	Description	Implementation
Patient selection		NOTE: all criteria were scored yes (+), no (-) or don't know (?)
a	Was an adequate method of randomisation applied?	A random (unpredictable) allocation sequence must have been applied. Methods of allocation using date of birth, date of admission, hospital numbers, or alternation are not considered to be appropriate.
b	Was the treatment allocation concealed?	Allocation should be performed by an independent person who is not responsible for determining eligibility for inclusion. This person has no information about the patients included in the trial and has no influence on the allocation sequence or the decision about eligibility for inclusion.
c	Were the patients blinded to the intervention?	Adequate information about blinding must be provided
d	Were the treating physicians blinded to the intervention?	Adequate information about blinding must be provided
e	Were the outcome assessors blinded to the intervention?	Adequate information about blinding must be provided
f	Were the groups similar at baseline with regard to the most important prognostic indicators?	Groups must be similar at baseline with regard to at least 3 of the 4 prognostic indicators of age, sex, duration of symptoms and value of main outcome measure(s)
g	Was the drop-out/loss to follow-up rate described and acceptable?	Included patients who did not complete the follow-up period, or were not included in the analysis, must have been described. If the percentage of drop-outs and loss to follow up is < 20% and the loss to follow up does not lead to substantial bias, a '+' is scored. (N.B. this percentage is arbitrary, and not supported by empirical evidence).
h	Did the analysis include an intention-to-treat analysis?	For all randomised patients, the most important moments of effect measurement should have been reported/analysed (minus missing values), irrespective of non-compliance and co-interventions
i	Were the index and control intervention(s) explicitly described?	Adequate description for index and control intervention(s), so that the treatment could be replicated

**Table 2. Validity scores (a-i)**

Reference	a	b	c	d	e	f	g	h	i
	Adequate randomisation	Adequate blinding concealment	Adequate patient blinding	Adequate treating physician blinding	Adequate assessor blinding	Groups similar at baseline	Drop-out rate described and acceptable	Intention-to-treat analysis	Index and control intervention explicit
Bagger-Sjback 1987	+	+	+	+	+	+	+	-	+
Donaldson 1966	?	?	?	?	?	+	+	+	+
Eschelman 1971	+	+	?	+	?	?	?	?	+
Govaerts 1998	+	+	+	+	+	+	+	+	+
Hester 1998	-	?	?	?	?	+	?	+	+
Jackson 1988	+	+	?	+	?	+	+	+	+
John 1988	+	+	?	?	?	?	?	+	+
Lildholdt 1986	+	-	-	-	-	+	?	+	+
Pirodda 1994	+	?	?	?	?	+	+	+	+
Tong 2002	+	+	-	+	+	+	?	+	+
Winerman 1981	+	?	?	?	?	+	?	+	+

**APPENDICES**
**Appendix 1. Search strategies**

PubMed	EMBASE (Ovid)	CINAHL (EBSCO)
#1 "Ear" [MeSH] OR EAR* [ti] OR TYMPANIC [ti] OR STAPES [ti] OR EUSTACHIAN [ti] OR OTOLOGIC* [ti] OR ENDOLYMPHATIC [ti] OR AURICULAR [ti] #2 DISEASE* [ti] OR DISORDER* [ti] #3 #1 AND #2 #4 "Ear Diseases" [Mesh] OR (OTITIS [tiab] OR OTOSCLEROSIS [tiab] OR CHOLESTEATOMA [tiab] OR (TYMPANIC [tiab] AND MEMBRANE [tiab] AND PERFORAT* [tiab]) OR (TYMPANIC [tiab] AND MEMBRANE [tiab] AND RUPTURE* [tiab]) OR (OSSICULAR [tiab] AND CHAIN [tiab] AND DISORDER [tiab]) OR (GLUE [tiab] AND EAR [tiab]) #5 "Surgical Procedures, Operative" [Mesh] OR SURG* [ti] OR OPERAT* [ti] #6 (POST [tiab] AND OPERAT* [tiab]) OR (POST [tiab] AND SURG* [tiab]) OR ((POSTSURG* [tiab] OR POSTOPERATIVE* [tiab]) AND INFECTION* [tiab]) #7 (#3 OR #4) AND (#5 OR #6) #8 "Otologic Surgical Procedures" [Mesh] #9 TYMPANOPLAST* [tiab] OR TYMPANOTOM* [tiab] OR TYMPANOMASTOIDECTOM* [tiab] OR "TYMPANOMASTOID SURGERY" [tiab] OR MASTOIDECTOM* [tiab] OR STAPEDECTOM* [tiab] OR STAPEDOTOM* [tiab] OR MYRINGOPLAST* [tiab] OR (MIDDLE [tiab] AND EAR [tiab] AND RECONSTRUCT* [tiab]) OR (MIDDLE [tiab] AND EAR [tiab] AND VENTILAT* [tiab]) OR (GROMMET* [tiab] AND INSERT* [tiab]) OR (TYMPANIC [tiab] AND MEMBRANE [tiab] AND SURG* [tiab]) OR (EAR [tiab] AND SURG* [tiab]) OR (AURICULAR [tiab] AND SURG* [tiab]) OR OSSICULOPLAST* [tiab] OR (FACIAL [tiab] AND NERVE [tiab] AND DECOMPRESSION* [tiab]) OR (STAPES [tiab] AND SURG* [tiab]) OR (OSSICULAR [tiab] AND REPLACE* [tiab]) OR (OSSICULAR [tiab] AND IMPLANT* [tiab]) OR (COCHLEAR [tiab] AND IMPLANT* [tiab]) OR (ENDOLYMPHATIC [tiab] AND SHUNT* [tiab]) OR (ENDOLYMPHATIC* [tiab] AND SURG* [tiab]) OR (LABYRINTH [tiab] AND SURG* [tiab]) OR (STAPES [tiab] AND SURG* [tiab]) #10 "Ear/surgery"[Mesh] #11 "Ear Diseases/surgery"[Mesh] #12 #7 OR #8 OR #9 OR #10 OR #11 #13 "ANTI BACTERIAL AGENTS" [Mesh] OR "ANTIBIOTIC PROPHYLAXIS" [Mesh] OR "Lac-	1 exp Ear/ or (EAR* or TYMPANIC or STAPES or EUSTACHIAN or OTOLOGIC* or ENDOLYMPHATIC or AURICULAR).ti. 2 (disease* or disorder*).ti. 3 exp ear disease/ or (OTITIS or OTOSCLEROSIS or CHOLESTEATOMA or (TYMPANIC and MEMBRANE and PERFORAT*) or (TYMPANIC and MEMBRANE and RUPTURE*) or (OSSICULAR and CHAIN and DISORDER) or (GLUE and EAR)).tw. 4 exp surgery/ or (surg* or operat* or (POST and OPERAT*) or (POST and SURG*) or ((POSTSURG* or POSTOPERATIVE* and INFECTION*))).tw. 5 1 and 2 6 3 or 5 7 6 and 4 8 exp ear surgery/ or (TYMPANOPLAST* or TYMPANOTOM* or TYMPANOMASTOIDECTOM* or "TYMPANOMASTOID SURGERY" or MASTOIDECTOM* or STAPEDECTOM* or MYRINGOPLAST* or (MIDDLE and EAR and RECONSTRUCT*) or (MIDDLE and EAR and VENTILAT*) or (GROMMET* and INSERT*) or (TYMPANIC and MEMBRANE and SURG*) or (EAR and SURG*) or (AURICULAR and SURG*) or OSSICULOPLAST* or (FACIAL and NERVE and DECOMPRESSION*) or (STAPES and SURG*) or (OSSICULAR and IMPLANT*) or (COCHLEAR and IMPLANT*) or (ENDOLYMPHATIC and SHUNT*) or (ENDOLYMPHATIC* and SURG*) or (LABYRINTH and SURG*) or (STAPES and SURG*)).tw. 9 exp ear disease/su [Surgery] 10 8 or 7 or 9 11 exp Antibiotic Agent/ or exp Antibiotic Prophylaxis/ or exp lactam/ or exp quinolone derivative/ 12 (ANTIBIOT* or (ANTI and BIOT*) or ANTIMICROBIAL* or (ANTI and MICROBIAL*) or BACTERIOCID* or ANTIBACTERIAL* or (ANTI and BACTERIAL*) or CHEMOTHERAPY or PENICILLIN or AMOXICILLIN or AMPICILLIN or "CLAVULANIC ACID" or	S1 (MH "Ear") S2 TI EAR* or TYMPANIC or STAPES or EUSTACHIAN or OTOLOGIC* or ENDOLYMPHATIC or AURICULAR S3 TI disease* OR disorder* S4 S1 or S2 S5 S3 and S4 S6 (MH "Ear Diseases+") S7 TX OTITIS or OTOSCLEROSIS or CHOLESTEATOMA S8 S5 or S6 or S7 S9 (MH "Surgery, Operative+") S10 TX surg* or operat* or POSTSURG* or POSTOPERATIVE* S11 S9 or S10 S12 S8 and S11 S13 (MH "Ear Surgery+") S14 S12 or S13 S15 (MH "Antibiotics+") or (MH "Antibiotic Prophylaxis") S16 TX ANTI BIOT* or ANTIMICROBIAL* or BACTERIOCID* or ANTIBACTERIAL* or CHEMOTHERAPY or PENICILLIN or AMOXICILLIN or AMPICILLIN or "CLAVULANIC ACID" or AMOXICLAV or AUGMENTIN or TICARCILLIN or TIMENTIN or FLUCLOXACILLIN or FLUAMPICIL or MAGNAPEN or PIPERACILLIN or TAZOCIN or CEPHALOSPORIN* or CEFACLOR or DISTACLOR or CEFADROXIL or BAXAN or CEFALOXIN or CEPOREX or KEFLEX or CEFAMANDOLE or KEFADOL or CEFAZOLIN* or KEFZOL or CEFIXIME or SUPRAX or CEFOTAXIME or CLAFORAN or CEFOXITIN or MEFOXIN or CEFPIROME or CEFROM or CEFPODOXIME or ORELOX or CEFPROZIL or CEFZIL or CEFRADINE or VELOSEL or CEFTAZIDIM or ORTUM or KEFADIM or CEFTRIAXONE or ROCEPHIN or CEFUROXIME or ZINACEF or ZINNAT or CEFONICID or AZTREONAM or AZACTAM or IMPENEM or ILASTATIN or PRIMAXIN or MEROPENEMTX ANTI BIOT* or ANTIMICROBIAL* or BACTERIOCID* or ANTIBACTERIAL* or CHEMOTHERAPY or PENICILLIN or AMOXICILLIN or AMPICILLIN or "CLAVULANIC ACID" or AMOXICLAV or AUGMENTIN or TICARCILLIN or TIMENTIN or FLUCLOXACILLIN or FLUAMPICIL or MAGNAPEN or PIPERACILLIN or TAZOCIN or CEPHALOSPORIN* or CEFACLOR or DISTACLOR or CEFADROXIL or BAXAN or CEFALOXIN or CEPOREX or KEFLEX



(Continued)

tams" [Mesh] OR "QUINOLONONES" [Mesh] OR "Macrolides" [Mesh]  
 #14 ANTIBIOT\* [tiab] OR (ANTI [tiab] AND BIOT\* [tiab]) OR ANTIMICROBIAL\* [tiab] OR (ANTI [tiab] AND MICROBIAL\* [tiab]) OR BACTERIOCID\* [tiab] OR ANTIBACTERIAL\* [tiab] OR (ANTI [tiab] AND BACTERIAL\* [tiab]) OR CHEMOTHERAPY [tiab] OR PENICILLIN [tiab] OR AMOXICILLIN [tiab] OR AMPICILLIN [tiab] OR "CLAVULANIC ACID" [tiab] OR AMOXICLAV [tiab] OR AUGMENTIN [tiab] OR TICARCILLIN [tiab] OR TIMENTIN [tiab] OR FLUCLOXACILLIN [tiab] OR FLUAMPICIL [tiab] OR MAGNAPEN [tiab] OR PIPERACILLIN [tiab] OR TAZOCIN [tiab] OR CEPHALOSPORIN\* [tiab] OR CEFACLOR [tiab] OR DISTACLOR [tiab] OR CEFADROXIL [tiab] OR BAXAN [tiab] OR CEFALEXIN [tiab] OR CEPOREX [tiab] OR KEFLEX [tiab] OR CEFAMANDOLE [tiab] OR KEFADOL [tiab] OR CEFAZOLIN\* [tiab] OR KEFZOL [tiab] OR CEFIXIME [tiab] OR SUPRAX [tiab] OR CEFOTAXIME [tiab] OR CLAFORAN [tiab] OR CEFOXITIN [tiab] OR MEFOXIN [tiab] OR CEFPIROME [tiab] OR CEFROM [tiab] OR CEFPODOXIME [tiab] OR ORELOX [tiab] OR CEFPROZIL [tiab] OR CEFZIL [tiab] OR CEFRADINE [tiab] OR VELOSEL [tiab] OR CEFTAZIDIM [tiab] OR ORTUM [tiab] OR KEFADIM [tiab] OR CEFTRIAXONE [tiab] OR ROCEPHIN [tiab] OR CEFUROXIME [tiab] OR ZINACEF [tiab] OR ZINNAT [tiab] OR CEFONICID [tiab] OR AZTREONAM [tiab] OR AZACTAM [tiab] OR IMIPENEM [tiab] OR ILASTATIN [tiab] OR PRIMAXIN [tiab] OR MEROPENEM [tiab]  
 #15 TETRACYCLINE\* [tiab] OR DETECLO [tiab] OR DEMECLEOCYCLIN [tiab] OR LEDERMYCIN [tiab] OR DOXYCYCLINE [tiab] OR VIBRAMYCIN [tiab] OR MINOCYCLINE [tiab] OR MINOCINE [tiab] OR OXYTETRACYCLINE [tiab] OR TERRAMYCIN [tiab] OR MACROLIDE\* [tiab] OR ERYTHROMYCIN [tiab] OR ERYMAX [tiab] OR ERYTHROCIN [tiab] OR ERYTHROPEL [tiab] OR AZITHROMYCIN [tiab] OR ZITHROMAX [tiab] OR CLARITHROMYCIN [tiab] OR KLARICID [tiab] OR TELITHROMYCIN [tiab] OR KETEK [tiab] OR TRIMOXAZOLE [tiab] OR SEPTIN [tiab] OR TRIMETHOPRIM [tiab] OR MONOTRIM [tiab] OR TRIMOPAN [tiab] OR METRONIDAZOLE [tiab] OR FLAGYL [tiab] OR METROLYL [tiab] OR PHENOXYMETHYLPENICILLIN [tiab] OR SULFAMETHOXAZOLE [tiab] OR OXACILLIN [tiab] OR CEPHALOTHIN [tiab] OR SULBACTAM [tiab] OR OFLOXACIN [tiab] OR CLINDAMYCIN [tiab] OR GENTAMYCIN [tiab] OR VANCOMYCIN [tiab]  
 #16 #13 OR #14 OR #15  
 #17 #12 AND #16

AMOXICLAV or AUGMENTIN or TICARCILLIN or TIMENTIN or FLUCLOXACILLIN or FLUAMPICIL or MAGNAPEN or PIPERACILLIN or TAZOCIN or CEPHALOSPORIN\* or CEFACLOR or DISTACLOR or CEFADROXIL or BAXAN or CEFALEXIN or CEPOREX or KEFLEX or CEFAMANDOLE or KEFADOL or CEFAZOLIN\* or KEFZOL or CEFIXIME or SUPRAX or CEFOTAXIME or CLAFORAN or CEFOXITIN or MEFOXIN or CEFPIROME or CEFROM or CEFPODOXIME or ORELOX or CEFPROZIL or CEFZIL or CEFRADINE or VELOSEL or CEFTAZIDIM or ORTUM or KEFADIM or CEFTRIAXONE or ROCEPHIN or CEFUROXIME or ZINACEF or ZINNAT or CEFONICID or AZTREONAM or AZACTAM or IMIPENEM or ILASTATIN or PRIMAXIN or MEROPENEM).tw.  
 13 (TETRACYCLINE\* or DETECLO or DEMECLEOCYCLIN or LEDERMYCIN or DOXYCYCLINE or VIBRAMYCIN or MINOCYCLINE or MINOCINE or OXYTETRACYCLINE or TERRAMYCIN or MACROLIDE\* or ERYTHROMYCIN or ERYMAX or ERYTHROCIN or ERYTHROPEL or AZITHROMYCIN or ZITHROMAX or CLARITHROMYCIN or KLARICID or TELITHROMYCIN or KETEK or TRIMOXAZOLE or SEPTIN or TRIMETHOPRIM or MONOTRIM or TRIMOPAN or METRONIDAZOLE or FLAGYL or METROLYL or PHENOXYMETHYLPENICILLIN or SULFAMETHOXAZOLE or OXACILLIN or CEPHALOTHIN or SULBACTAM or OFLOXACIN or CLINDAMYCIN or GENTAMYCIN or VANCOMYCIN).tw.  
 14 11 or 13 or 12  
 15 10 and 14

or CEFAMANDOLE or KEFADOL or CEFAZOLIN\* or KEFZOL or CEFIXIME or SUPRAX or CEFOTAXIME or CLAFORAN or CEFOXITIN or MEFOXIN or CEFPIROME or CEFROM or CEFPODOXIME or ORELOX or CEFPROZIL or CEFZIL or CEFRADINE or VELOSEL or CEFTAZIDIM or ORTUM or KEFADIM or CEFTRIAXONE or ROCEPHIN or CEFUROXIME or ZINACEF or ZINNAT or CEFONICID or AZTREONAM or AZACTAM or IMIPENEM or ILASTATIN or PRIMAXIN or MEROPENEM  
 S17 TX TETRACYCLINE\* or DETECLO or DEMECLEOCYCLIN or LEDERMYCIN or DOXYCYCLINE or VIBRAMYCIN or MINOCYCLINE or MINOCINE or OXYTETRACYCLINE or TERRAMYCIN or MACROLIDE\* or ERYTHROMYCIN or ERYMAX or ERYTHROCIN or ERYTHROPEL or AZITHROMYCIN or ZITHROMAX or CLARITHROMYCIN or KLARICID or TELITHROMYCIN or KETEK or TRIMOXAZOLE or SEPTIN or TRIMETHOPRIM or MONOTRIM or TRIMOPAN or METRONIDAZOLE or FLAGYL or METROLYL or PHENOXYMETHYLPENICILLIN or SULFAMETHOXAZOLE or OXACILLIN or CEPHALOTHIN or SULBACTAM or OFLOXACIN or CLINDAMYCIN or GENTAMYCIN or VANCOMYCINTX  
 TETRACYCLINE\* or DETECLO or DEMECLEOCYCLIN or LEDERMYCIN or DOXYCYCLINE or VIBRAMYCIN or MINOCYCLINE or MINOCINE or OXYTETRACYCLINE or TERRAMYCIN or MACROLIDE\* or ERYTHROMYCIN or ERYMAX or ERYTHROCIN or ERYTHROPEL or AZITHROMYCIN or ZITHROMAX or CLARITHROMYCIN or KLARICID or TELITHROMYCIN or KETEK or TRIMOXAZOLE or SEPTIN or TRIMETHOPRIM or MONOTRIM or TRIMOPAN or METRONIDAZOLE or FLAGYL or METROLYL or PHENOXYMETHYLPENICILLIN or SULFAMETHOXAZOLE or OXACILLIN or CEPHALOTHIN or SULBACTAM or OFLOXACIN or CLINDAMYCIN or GENTAMYCIN or VANCOMYCIN  
 S18 S15 or S16 or S17  
 S19 S14 and S18

(Continued)

**Web of Science**
**BIOSIS Previews/ CAB Abstracts  
(Ovid)**
**CENTRAL**

#1 TI=((EAR\* or TYMPANIC or STAPES or EUSTACHIAN or OTOLOGIC\* or ENDOLYMPHATIC or AURICULAR) AND (disease\* OR disorder\*))

#2 TS=(surg\* or operat\* or POSTSURG\* or POSTOPERATIVE\*)

#3 #2 AND #1

#4 TS=(TYMPANOPLAST\* or TYMPANOTOM\* or TYMPANOMASTOIDECTOM\* or "TYMPANOMASTOID SURGERY" or MASTOIDECTOM\* or STAPEDECTOM\* or STAPEDOTOM\* or MYRINGOPLAST\* or (MIDDLE and EAR and RECONSTRUCT\*) or (MIDDLE and EAR and VENTILAT\*) or (GROMMET\* and INSERT\*) or (TYMPANIC and MEMBRANE and SURG\*) or (EAR and SURG\*) or (AURICULAR and SURG\*) or OSSICULOPLAST\* or (FACIAL and NERVE and DECOMPRESSION\*) or (STAPES and SURG\*) or (OSSICULAR and REPLACE\*) or (OSSICULAR and IMPLANT\*) or (COCHLEAR and IMPLANT\*) or (ENDOLYMPHATIC and SHUNT\*) or (ENDOLYMPHATIC\* and SURG\*) or (LABYRINTH and SURG\*) or (STAPES and SURG\*))

#5 #4 OR #3

#6 TS=(ANTIBIOT\* or (ANTI and BIOT\*) or ANTIMICROBIAL\* or (ANTI and MICROBIAL\*) or BACTERIOCID\* or ANTIBACTERIAL\* or (ANTI and BACTERIAL\*) or CHEMOTHERAPY or PENICILLIN or AMOXICILLIN or AMPICILLIN or "CLAVULANIC ACID" or AMOXICLAV or AUGMENTIN or TICARCILLIN or TIMENTIN or FLUCLOXACILLIN or FLUAMPICILIN or MAGNAPEN or PIPERACILLIN or TAZOCIN or CEPHALOSPORIN\* or CEFACLOR or DISTACLOR or CEFADROXIL or BAXAN or CEFALEXIN or CEPOREX or KEFLEX or CEFAMANDOLE or KEFADOL or CEFAZOLIN\* or KEFZOL or CEFIXIME or SUPRAX or CEFOTAXIME or CLAFORAN or CEFOXITIN or MEFOXIN or CEFPIROME or CEFROM)

#7 TS=(CEFPODOXIME or ORELOX or CEFPROZIL or CEFZIL or CEFRADINE or VELOSEL or CEFTAZIDIM or ORTUM or KEFADIM or CEFTRIAXONE or ROCEPHIN or CEFUROXIME or ZINACEF or ZINNAT or CEFONICID or AZTREONAM or AZACTAM or IMPENEM or ILASTATIN or PRIMAXIN or MEROPENEM)

#8 TS=(TETRACYCLINE\* or DETECLOR or DEMECLEOCYCLIN or LEDERMYCIN or DOXYCYCLINE or VIBRAMYCIN or MINOCYCLINE or MINOCINE or OXYTETRACYCLINE or TERAMYCIN or MACROLIDE\* or ERYTHROMYCIN or ERYMAX or ERYTHROCIN or ERYTHROPED or AZITHROMYCIN or ZITHROMAX or CLARITHROMYCIN or KLARICID or TELITHROMYCIN or KETEK or TRIMOXA-

1 exp Ear/ or (EAR\* or TYMPANIC or STAPES or EUSTACHIAN or OTOLOGIC\* or ENDOLYMPHATIC or AURICULAR).ti.

2 (disease\* or disorder\*).ti.

3 exp ear disease/ or (OTITIS or OTOSCLEROSIS or CHOLESTEATOMA or (TYMPANIC and MEMBRANE and PERFORAT\*) or (TYMPANIC and MEMBRANE and RUPTURE\*) or (OSSICULAR and CHAIN and DISORDER) or (GLUE and EAR)).tw.

4 exp surgery/ or (surg\* or operat\* or (POST and OPERAT\*) or (POST and SURG\*) or ((POSTSURG\* or POSTOPERATIVE\*) and INFECTION\*)).tw.

5 1 and 2

6 3 or 5

7 6 and 4

8 exp ear surgery/ or (TYMPANOPLAST\* or TYMPANOTOM\* or TYMPANOMASTOIDECTOM\* or "TYMPANOMASTOID SURGERY" or MASTOIDECTOM\* or STAPEDECTOM\* or STAPEDOTOM\* or MYRINGOPLAST\* or (MIDDLE and EAR and RECONSTRUCT\*) or (MIDDLE and EAR and VENTILAT\*) or (GROMMET\* and INSERT\*) or (TYMPANIC and MEMBRANE and SURG\*) or (EAR and SURG\*) or (AURICULAR and SURG\*) or OSSICULOPLAST\* or (FACIAL and NERVE and DECOMPRESSION\*) or (STAPES and SURG\*) or (OSSICULAR and REPLACE\*) or (OSSICULAR and IMPLANT\*) or (COCHLEAR and IMPLANT\*) or (ENDOLYMPHATIC and SHUNT\*) or (ENDOLYMPHATIC\* and SURG\*) or (LABYRINTH and SURG\*) or (STAPES and SURG\*)).tw. (15601)

9 8 or 7

10 exp Antibiotic Agent/ or exp Antibiotic Prophylaxis/ or exp lactam/ or exp quinolone derivative/ (0)

11 (ANTIBIOT\* or (ANTI and BIOT\*) or ANTIMICROBIAL\* or (ANTI and MICROBIAL\*) or BACTERIOCID\* or ANTIBACTERIAL\* or (ANTI and BACTERIAL\*) or CHEMOTHERAPY or PENICILLIN or AMOXICILLIN or AMPICILLIN or "CLAVULANIC ACID" or AMOXICLAV or AUGMENTIN or TICARCILLIN or TIMENTIN or FLUCLOXACILLIN or FLUAMPICIL or MAGNAPEN or PIPERACILLIN or TAZOCIN or CEPHALOSPORIN\* or CEFACLOR or DISTACLOR or CEFADROXIL or BAX-

#1 EAR explode all trees (MeSH)

#2 (EAR\* OR TYMPANIC OR STAPES OR EUSTACHIAN OR OTOLOGIC\* OR ENDOLYMPHATIC OR AURICULAR).ti.

#3 #1 OR #2

#4 (DISEASE\* OR DISORDER\*).ti.

#5 #3 AND #4

#6 EAR DISEASES explode all trees (MeSH)

#7 OTITIS OR OTOSCLEROSIS OR CHOLESTEATOMA OR TYMPANIC NEXT MEMBRANE NEAR PERFORAT\* OR TYMPANIC NEXT MEMBRANE NEXT RUPTURE\* OR OSSICULAR NEXT CHAIN NEAR DISORDER OR GLUE NEXT EAR

#8 #5 OR #6 OR #7

#9 SURGICAL PROCEDURES OPERATIVE explode all trees (MeSH)

#10 (SURG\* OR OPERAT\*).ti.

#11 ((POST NEXT OPERAT\* OR POST NEXT SURG\* OR POSTSURG\* OR POSTOPERATIVE\*) NEXT INFECTION\*)

#12 #9 OR #10 OR #11

#13 #8 AND #12

#14 OTOLOGIC SURGICAL PROCEDURES explode all trees (MeSH)

#15 TYMPANOPLAST\* OR TYMPANOTOM\* OR TYMPANOMASTOIDECTOM\* OR TYMPANOMASTOID NEXT SURGERY OR MASTOIDECTOM\* OR STAPEDECTOM\* OR STAPEDOTOM\* OR MYRINGOPLAST\*

#16 MIDDLE NEXT EAR NEAR RECONSTRUCT\* OR MIDDLE NEXT EAR NEAR VENTILAT\* OR GROMMET\* NEAR INSERT\* OR TYMPANIC NEXT MEMBRANE NEAR SURG\* OR EAR NEAR SURG\* OR AURICULAR NEAR SURG\* OR OSSICULOPLAST\* OR FACIAL NEXT NERVE NEAR DECOMPRESSION\*

#17 STAPES NEXT SURG\* OR OSSICULAR NEAR REPLACE\* OR OSSICULAR NEAR IMPLANT\* OR COCHLEAR NEAR IMPLANT\* OR ENDOLYMPHATIC NEAR SHUNT\* OR ENDOLYMPHATIC NEAR SURG\* OR LABYRINTH NEAR SURG\* OR STAPES NEAR SURG\*

#18 EAR [su] explode all trees (MeSH)

#19 EAR DISEASES [su] explode all trees (MeSH)

#20 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19

#21 ANTI-BACTERIAL AGENTS explode all trees (MeSH)

#22 ANTIBIOTIC PROPHYLAXIS single term (MeSH)

#23 LACTAMS explode all trees (MeSH)

#24 QUINOLONES explode all trees (MeSH)

#25 MACROLIDES explode all trees (MeSH)

#26 ANTIBIOT\* OR ANTI NEXT BIOT\* OR ANTIMICROBIAL\* OR ANTI NEXT MICROBIAL\* OR

(Continued)

ZOLE or SEPTRIN or TRIMETHOPRIM or MONOTRIM or TRIMOPAN or METRONIDAZOLE or FLAGYL or METROLYL or PHENOXYMETHYLPENICILLIN or SULFAMETHOXAZOLE or OXACILLIN or CEPHALOTHIN or SULBACTAM or OFLOXACIN or CLINDAMYCIN or GENTAMYCIN or VANCOMYCIN)  
 #9 #8 OR #7 OR #6  
 #10 #9 AND #5

AN or CEFALEXIN or CEPOREX or KEFLEX or CEFAMANDOLE or KEFADOL or CEFAZOLIN\* or KEFZOL or CEFIXIME or SUPRAX or CEFOTAXIME or CLAFORAN or CEFOXITIN or MEFOXIN or CEFPIROME or CEFROM or CEFPODOXIME or ORELOX or CEFPROZIL or CEFZIL or CEFRADINE or VELOSEL or CEFTAZIDIM or ORTUM or KEFADIM or CEFTRIAXONE or ROCEPHIN or CEFUROXIME or ZINACEF or ZINNAT or CEFONICID or AZTREONAM or AZACTAM or IMPENEM or ILASTATIN or PRIMAXIN or MEROPENEM).tw.  
 (910130)  
 12 (TETRACYCLINE\* or DETECLO or DEMECLEOCYCLIN or LEDERMYCIN or DOXYCYCLINE or VIBRAMYCIN or MINOCYCLINE or MINOCINE or OXYTETRACYCLINE or TERRAMYCIN or MACROLIDE\* or ERYTHROMYCIN or ERYMAX or ERYTHROCIN or ERYTHROPEd or AZITHROMYCIN or ZITHROMAX or CLARITHROMYCIN or KLARICID or TELITHROMYCIN or KETEK or TRIMOXAZOLE or SEPTRIN or TRIMETHOPRIM or MONOTRIM or TRIMOPAN or METRONIDAZOLE or FLAGYL or METROLYL or PHENOXYMETHYLPENICILLIN or SULFAMETHOXAZOLE or OXACILLIN or CEPHALOTHIN or SULBACTAM or OFLOXACIN or CLINDAMYCIN or GENTAMYCIN or VANCOMYCIN).tw.  
 (116296)  
 13 10 or 11 or 12  
 14 9 and 13

BACTERIOCID\* OR ANTIBACTERIAL\* OR ANTINEXT BACTERIAL\*  
 #27 PENICILLIN\* OR AMOXICILLIN OR AMPICILLIN OR CLAVULANIC NEXT ACID OR AMOXICLAV OR AUGMENTIN OR TICARCILLIN OR TIMENTIN OR FLUCLOXACILLIN OR FLUAMPICIL OR MAGNAPEN OR PIPERACILLIN OR TAZOCIN  
 #28 CEPHALOSPORIN\* OR CEFACLOL OR DISTACLOR OR CEFADROXIL OR BAXAN OR CEFALEXIN OR CEPOREX OR KEFLEX OR CEFAMANDOLE OR KEFADOL OR CEFAZOLIN\* OR KEFZOL OR CEFIXIME OR SUPRAX OR CEFOTAXIME OR CLAFORAN OR CEFOXITIN OR MEFOXIN OR CEFPIROME OR CEFROM OR CEFPODOXIME OR ORELOX OR CEFPROZIL OR CEFZIL OR CEFRADINE OR VELOSEL OR CEFTAZIDIM OR FORTUM OR KEFADIM OR CEFTRIAXONE OR ROCEPHIN OR CEFUROXIME OR ZINACEF OR ZINNAT OR CEFONICID OR AZTREONAM OR AZACTAM OR IMPENEM OR CILASTATIN OR PRIMAXIN OR MEROPENEM  
 #29 TETRACYCLINE\* OR DETECLO OR DEMECLEOCYCLIN OR LEDERMYCIN OR DOXYCYCLINE OR VIBRAMYCIN OR MINOCYCLINE OR MINOCINE OR OXYTETRACYCLINE OR TERRAMYCIN  
 #30 MACROLIDE\* OR ERYTHROMYCIN OR ERYMAX OR ERYTHROCIN OR ERYTHROPEd OR AZITHROMYCIN OR ZITHROMAX OR CLARITHROMYCIN OR KLARICID OR TELITHROMYCIN OR KETEK OR TRIMOXAZOLE OR SEPTRIN OR TRIMETHOPRIM OR MONOTRIM OR TRIMOPAN OR METRONIDAZOLE OR FLAGYL OR METROLYL  
 #31 PHENOXYMETHYLPENICILLIN OR SULFAMETHOXAZOLE OR OXACILLIN OR CEPHALOTHIN OR SULBACTAM OR OFLOXACIN OR CLINDAMYCIN OR GENTAMYCIN OR VANCOMYCIN  
 #32 #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31  
 #33 #20 AND #32

## WHAT'S NEW

Date	Event	Description
31 August 2009	New search has been performed	Update searches conducted 31 August 2009 identified no new studies matching the inclusion criteria

## HISTORY

Protocol first published: Issue 1, 2003

**Antibiotic prophylaxis in clean and clean-contaminated ear surgery (Review)**

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Review first published: Issue 3, 2004

Date	Event	Description
28 August 2008	Amended	Converted to new review format
5 June 2007	New search has been performed	An extensive update of the literature search was performed in June 2007. No new studies were found in addition to the studies described in the original review. No textual changes have been made to the results, conclusions or recommendations.

## CONTRIBUTIONS OF AUTHORS

All authors contributed equally to searching for studies, initial screening and study selection, quality assessment, writing to study authors, data extraction and data analysis.

Hendrik Verschuur drafted protocol and review text.

## DECLARATIONS OF INTEREST

None known.

## INDEX TERMS

### Medical Subject Headings (MeSH)

\*Antibiotic Prophylaxis; Ear Diseases [\*surgery]; Graft Rejection [prevention & control]; Labyrinthitis [prevention & control]; Randomized Controlled Trials as Topic; Suppuration [prevention & control]; Surgical Wound Infection [\*prevention & control]

### MeSH check words

Adult; Child; Humans