WHO Surgical Site infection Prevention Guidelines

Web Appendix 25

Summary of a systematic review on surgical antibiotic prophylaxis prolongation

1. Introduction

The preventive effect of the routine use of preoperative surgical antibiotic prophylaxis (SAP) on the occurrence of surgical site infections (SSI) prior to non-clean and implant surgery has long been recognized. However, the benefit of continued SAP after completion of the procedure is unclear. Increasing evidence shows that a single preoperative dose of SAP (and possible additional intraoperative doses according to the duration of the operation) may be non-inferior to additional postoperative multiple doses for the prevention of SSI. Despite this, surgeons still have a tendency to routinely continue SAP up to several days after surgery [1,2].

The use and duration of postoperative prophylaxis has been specified in clinical practice guidelines issued by professional societies or national authorities. Several of these guidelines, such as those published by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) [3], and the American Society of Health Care Pharmacists (ASHP) [4] recommend discontinuing SAP within 24 hours after surgery. The United States (US) Institute of Healthcare Improvement recommends discontinuing SAP within 24 hours in general and within 48 hours in cardiac surgery [5]. Other guidelines published by the United Kingdom (UK) National Institute for Health and Care Excellence (NICE) [6], the Scottish Intercollegiate Guidelines Network (SIGN) [7], the Royal College of Physicians of Ireland [8] and the UK Department of Health [9], recommend a single dose of preoperative SAP and no postoperative continuation with or without exceptions for specific surgical procedures.

2. PICO question

Does continued postoperative SAP reduce the risk of SSI compared with preoperative and (if necessary) intraoperative prophylaxis only?

- **P**opulation: patients of any age undergoing surgical procedures who need to receive SAP
- **I**ntervention: continued postoperative antibiotic prophylaxis
  Comparator: single-dose antibiotic prophylaxis only (and possible additional intraoperative doses according to duration of the operation)
- **O**utcome: SSI, SSI-attributable mortality

3. Methods

The following databases were searched: Medline (PubMed); Cumulative Index to Nursing and Allied Health Literature (CINAHL); Cochrane Central Register of Controlled Trials (CENTRAL); and WHO regional medical databases. The time limit

for the review was between 1 January 1990 and 1 October 2015. Language was restricted to English, German and Spanish. A comprehensive list of search terms was used, including Medical Subject Headings (MeSH) (Appendix 1).

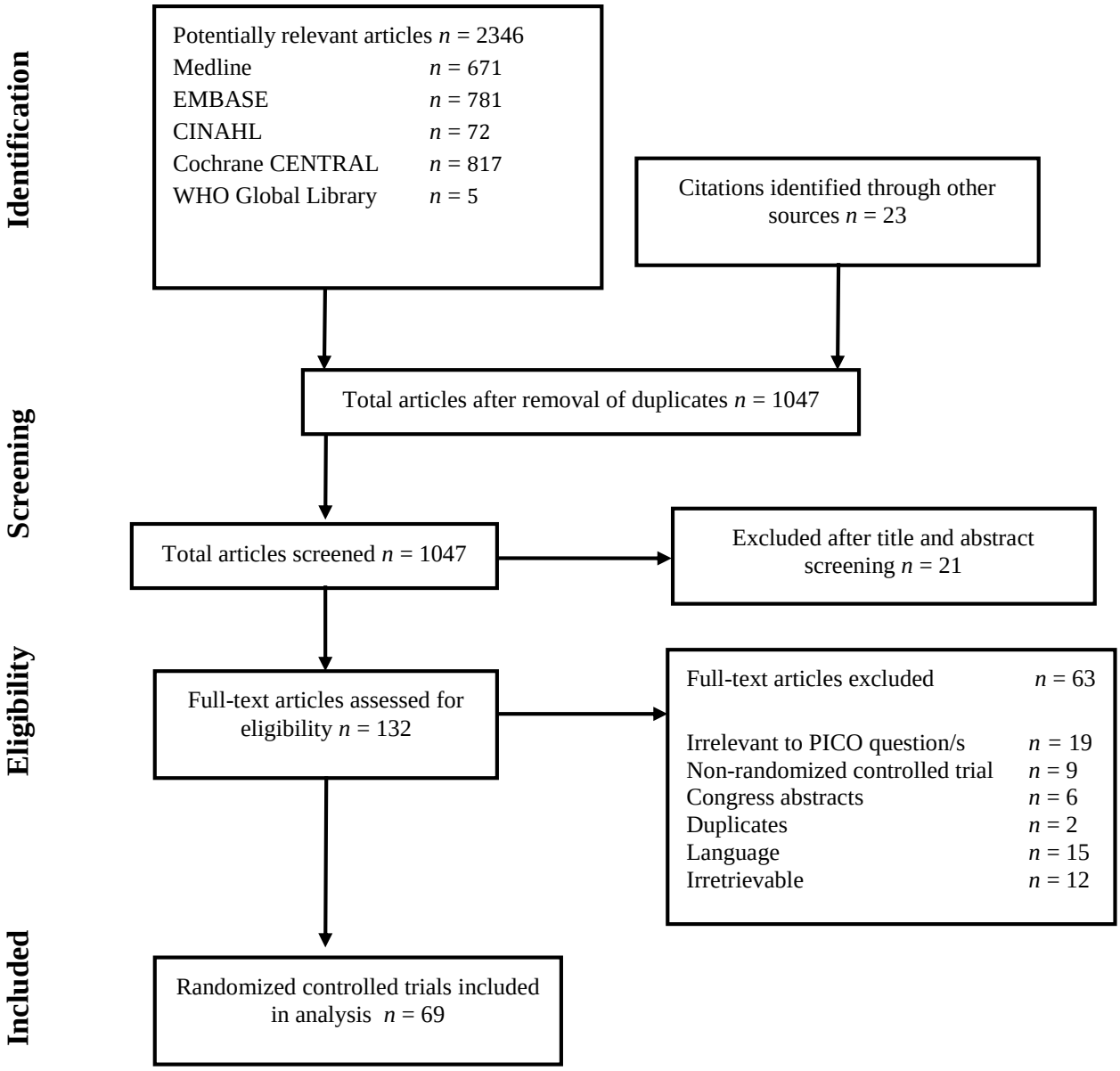
Two independent reviewers screened titles and abstracts of retrieved references for potentially relevant studies. The full text of all potentially eligible articles was obtained. Two authors independently reviewed the full text articles for eligibility based on inclusion criteria. Duplicate studies were excluded. Only studies comparing the same agent in the same dosage (per administration) were included. The first dose was always administered preoperatively.

Two authors extracted data in a predefined evidence table (Appendix 2) and critically appraised the retrieved studies using the Cochrane collaboration tool [10] for assessing risk of bias (Appendix 3). Any disagreements were resolved through discussion after consultation of the senior author, when necessary.

Meta-analyses of available comparisons of SAP were performed using Review Manager version 5.3 as appropriate [11] (Appendix 4). Odds ratios (OR) and the mean difference with 95% confidence intervals (CI) were extracted and pooled for each comparison with a random effects model. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology [12] (GRADE Pro software, http://gradepro.org/ [13]) was used to assess the quality of the retrieved evidence (Appendix 5).

4. Study selection

Flow chart of the study selection process



5. Summary of the findings

A total of 69 randomized controlled trials (RCTs) [14-82] investigating the optimal duration of antibiotic prophylaxis in a variety of surgical procedures with an SSI outcome were identified. A total of 21 243 patients were included, mostly adults. Only 2 studies [18,58] addressed specifically the paediatric population. Fifteen studies [16,17,28,30,32,33,51,54,56,69,73-75,83,84] reported that some paediatric patients were included, but most were adult patients. Fourteen [17,29,34-36,50,51,54,56,69,71,73,75,80] of the included studies were conducted in low- and middle-income countries.

Both the intervention and control group received the same preoperative regimen in all the included studies and only differed in the postoperative continuation of antibiotic prophylaxis. Only studies comparing the same antibiotic agent in the same dosage (per administration) were considered in order to prevent confounding by the type of antibiotic. The first dose of antibiotic prophylaxis was always administered preoperatively. In addition to the single dose, possible additional dose/s according to the duration of the operation were given, depending on the protocol used in the trial.

To investigate the optimal duration of antibiotic prophylaxis, the Guideline Development Group (GDG) agreed to not only assess trials comparing a continued postoperative antibiotic prophylaxis with a single dose antibiotic prophylaxis only (or repeated according to duration of the operation), but also to assess trials that compared different regimens of prolonged postoperative antibiotic prophylaxis.

Accordingly, the following **comparisons** were made:

1. Any prolonged regimen vs. no postoperative dose (44 RCTs)
2. A prolonged regimen less than 24 hours postoperative vs. a single postoperative dose (one RCT)
3. A prolonged regimen more than 24 hours postoperative vs. a prolonged regimen less than 24 hours postoperative (23 RCTs)
4. A prolonged regimen more than 48 hours postoperative vs. a prolonged regimen less than 48 hours postoperative (3 RCTs)
5. Type of procedure with a prolonged antibiotic regimen
    a. Cardiac surgery
    b. Vascular surgery
    c. Orthognathic surgery

The results of the meta-analyses based on these comparisons are shown in Appendix 4.

1. Forty-four RCTs [14-56,82] including 17 805 patients and comparing any prolonged regimen of antibiotic prophylaxis with no postoperative antibiotic prophylaxis were identified. These studies included a variety of surgical procedures: appendectomy [14-18]; colorectal surgery [19-21]; upper gastrointestinal tract surgery [22-25]; cholecystectomy [26]; hepatobiliary surgery [85]; mixed general surgery [28-33,82]; caesarean section [34-36]; gynaecological surgery [37,38]; orthopaedic and trauma surgery [39,40]; spine surgery [41]; cardiac surgery [42,43]; thoracic surgery [44]; vascular surgery [45]; transplantation surgery [46]; head and

neck surgery [47,86]; ear, nose and throat surgery [49]; maxillofacial surgery [50-53]; and orthognathic surgery [54-56].

Only 3 trials [20,43,45] showed a decreased risk of SSI when antibiotic prophylaxis was prolonged postoperatively. The remaining 40 trials showed no difference in risk. The analysis was further stratified according to the type of procedure. No significant difference in the risk of SSI was found with the exception of cardiac, vascular and orthognathic surgery for which prolonged antibiotic prophylaxis resulted in a decreased risk of SSI (Appendix 4, comparisons 5a-5c).

Meta-analysis of the 44 RCTs [14-56,82] (Appendix 4, comparison 1) demonstrated that prolonged postoperative antibiotic prophylaxis had no benefit when compared to a single dose of antibiotic prophylaxis in reducing SSI after surgery (OR: 0.89; 95% CI: 0.77-1.03).
The quality of the evidence for this comparison was moderate due to the risk of bias (Appendix 5).

2. One study [57] including 227 patients undergoing colorectal surgery compared the continuation of antibiotic prophylaxis up to 16 hours postoperatively with a single postoperative dose. The trial [57] (Appendix 4, comparison 2) demonstrated that the continuation of prolonged antibiotic prophylaxis up to a last dose at 16 hours postoperatively had no benefit in reducing SSI when compared to a single postoperative dose (OR: 0.82; 95% CI: 0.47-1.40).
The quality of evidence was very low due to risk of bias and imprecision (Appendix 5).

3. Twenty-three trials [16,17,58-78] including 3084 patients compared any prolonged regimen of more than 24 hours postoperatively with a postoperative regimen of less than 24 hours. These studies included a wide variety of surgical procedures: colorectal surgery [58-61,78]; cholecystectomy [62]; gynaecological surgery [77]; spine surgery [63]; cardiac surgery [64,65]; head and neck surgery [66-68]; ear, nose and throat surgery [69]; maxillofacial surgery [70]; orthognathic surgery[71-75]; and others [76].

   Only one trial [72] in orthognathic surgery showed a decreased risk of SSI when antibiotic prophylaxis was prolonged for more than 24 hours postoperatively. Twenty trials showed no difference in risk and 2 trials had no SSI events [73,78]. The analysis was further stratified by the type of surgical procedure, but no significant difference in the risk of SSI was observed according to the procedure. Meta-analysis of these 23 RCTs [16,17,58-78] (Appendix 4, comparison 3) demonstrated that a prolonged antibiotic prophylaxis regimen of more than 24 hours postoperatively had no benefit in reducing SSI when compared to a prolonged regimen of less than 24 hours (OR: 0.89; 95% CI: 0.69-1.16).
   The quality of evidence was moderate due to the risk of bias (Appendix 5).

4. Three studies [79-81] including 457 patients undergoing hepatobiliary [79], cardiac [80] and head and neck surgery [81] compared any prolonged postoperative regimen of more than 48 hours with a prolonged regimen of less than 48 hours. The individual trials showed no difference in the risk of SSI. The

analysis was further stratified by the type of surgical procedure, but no significant difference in the risk of SSI was observed according to the procedure. Meta-analysis of the trials [79-81] (Appendix 4, comparison 4) demonstrated that a prolonged antibiotic prophylaxis regimen of more than 48 hours had no benefit when compared to a prolonged regimen for up to 48 hours in reducing SSI (OR: 1.04; 95% CI: 0.50-2.16).
The quality of evidence was very low due to the risk of bias and imprecision (Appendix 5).

5. Types of procedure associated with a decreased risk of SSI with a prolonged antibiotic regimen.

   a) Cardiac surgery
   Five studies [42,43,64,65,80] compared different postoperative antibiotic regimens in cardiac surgery. Among these, 2 studies [42,43] compared any prolonged regimen with no postoperative antibiotic prophylaxis. Two other studies [64,65] compared continuation of antibiotic prophylaxis for more than 24 hours postoperatively with continuation for less than 24 hours. One study [80] compared continuation of postoperative antibiotic prophylaxis for longer than 48 hours with regimens continuing for less than 48 hours. Separate meta-analyses were performed for the three comparisons, when appropriate (Appendix 4, comparison 5a).
      i. Meta-analysis of the 2 RCTs [42,43] comparing any prolonged regimen with no postoperative antibiotic prophylaxis demonstrated that the former had a benefit in terms of reducing SSI (OR: 0.43; 95% CI: 0.25-0.76).
      The quality of evidence was low due to the risk of bias and imprecision (Appendix 5).

      ii. Meta-analysis of the 2 RCTs [64,65] comparing postoperative antibiotic prophylaxis for more than 24 hours with continuation for less than 24 hours demonstrated that the former had no benefit in terms of reducing the risk of SSI (OR: 0.74; 95% CI: 0.32-1.73).
      The quality of evidence was very low due to the risk of bias and imprecision (Appendix 5).

      iii. One RCT [80] comparing the continuation of postoperative antibiotic prophylaxis for longer than 48 hours with continuation for less than 48 hours demonstrated that the former had no benefit in terms of reducing the risk of SSI (OR: 0.53; 95% CI: 0.15-1.93).
      The quality of evidence was very low due to the risk of bias and imprecision (Appendix 5).

   b) Vascular surgery
   One RCT [45] in patients undergoing vascular surgery compared the continuation of antibiotic prophylaxis until all lines were removed with a single dose of antibiotic prophylaxis and demonstrated that the former had a significant benefit in terms of reducing the risk of SSI (Appendix 4, comparison 5b; OR: 0.50; 95% CI: 0.25-0.98).

The quality of evidence was low due to the risk of bias and imprecision (Appendix 5).

c) Orthognathic surgery
Eight studies [54-56,71-75] compared different postoperative antibiotic regimens in orthognathic surgery. Among these, 3 studies [54-56] compared any prolonged regimen with no postoperative prolongation of antibiotic prophylaxis. Five other studies [71-75] compared continuation of antibiotic prophylaxis for more than 24 hours postoperatively with continuation for less than 24 hours. Meta-analyses were performed for each of these comparisons (Appendix 4, comparison 5c).

i. Meta-analysis of the 3 RCTs [54-56] comparing any prolonged regimen with no postoperative antibiotic prophylaxis demonstrated that the former had a benefit in terms of reducing SSI (OR: 0.30; 95% CI: 0.10-0.88).
The quality of evidence was low due to the risk of bias and imprecision (Appendix 5).

ii. Meta-analysis of the 5 RCTs [71-75] comparing postoperative antibiotic prophylaxis for more than 24 hours with continuation for less than 24 hours demonstrated that the former had no benefit in terms of reducing the risk of SSI (OR: 0.34; 95% CI: 0.08-1.44).
The quality of evidence was very low due to the risk of bias and imprecision (Appendix 5).

In conclusion, the retrieved evidence can be summarized as follows:

- **Postoperative continuation of antibiotic prophylaxis vs. a single dose of antibiotic prophylaxis** (comparison 1):
Overall, a moderate quality of evidence shows that the postoperative continuation of antibiotic prophylaxis has neither benefit nor harm in reducing SSI rates when compared to a single dose of antibiotic prophylaxis.
    a. In cardiac surgery (comparison 5a), a low quality of evidence shows that the continuation of antibiotic prophylaxis for up to 24 hours postoperatively has a benefit in reducing the SSI rate when compared to a single dose of antibiotic prophylaxis. A very low quality of evidence showed that continuation beyond 24 hours postoperatively has no benefit.
    b. In vascular surgery (comparison 5b), a low quality of evidence shows that the continuation of antibiotic prophylaxis until all lines are removed has a benefit in reducing the SSI rate when compared to a single dose of prophylaxis.
    c. In orthognathic surgery (comparison 5c), a low quality of evidence shows that the continuation of antibiotic prophylaxis for up to 24 hours postoperatively had a benefit in reducing the SSI rate when compared to a single dose of antibiotic prophylaxis. A very low quality of evidence showed that continuation beyond 24 hours postoperatively had no benefit in reducing SSI.

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The included studies have some limitations. The quality of the included RCTs was moderate. Most studies had an unclear or high risk of bias in at least one or more domains. Differences and inconsistencies were noted in the SSI definitions, patient population and antibiotic regimen.

6. Other factors considered in the review

The systematic review team identified the following other factors to be considered.

Potential harms

Twenty-three studies [16,17,21,22,24-26, 31,33,37,47, 49,52,54,55,57,66-69,73,80,81] described the presence or absence of possible harms and adverse events related to SAP prolongation. Five studies reported more adverse effects in the intervention group. Among these, one study [16] reported a significantly higher number of cases of clostridial enterocolitis. Other studies reported a higher frequency of rash, erythema, phlebitis and hypotension [57], unspecified local side-effects [33] gastrointestinal disturbance [69], or nausea, diarrhoea, skin rash or pruritus [49]. The remaining 18 studies [17,21,22,24-26,31,37,47,52,54,55,66-68,73,81] reported that there were no adverse events attributable to the intervention in both groups. Although it is an important concern, the risk of antimicrobial resistance possibly due to the prolonged administration of antibiotics has not been assessed by any of the included studies.

Resource use

Studies addressing cost-effectiveness reported a cost reduction associated with shorter antibiotic prophylaxis regimens that varied from US$ 36,90 to US$ 1664 [15,38,46,49,77,87] depending also on the treatment of side-effects and duration of hospitalization. There is a need to raise awareness and provide education on the rational use of antibiotics and antibiotic stewardship among both health care workers (surgeons in particular, with reference to this recommendation) and patients.

7. Key uncertainties and future research priorities

The systematic review team identified the following key uncertainties and future research priorities.

There is a need for further well-designed RCTs in cardiac and vascular surgery as well as in low- and middle-income countries and in the paediatric population. More research is needed to demonstrate the linkage between the prolongation of SAP and the emergence of antibiotic resistance. Furthermore, future trials should investigate the effect of prolonged antibiotic prophylaxis on the microbiome.

APPENDICES

Appendix 1: Search terms

Medline (through PubMed)

1. surgical wound infection"[Mesh] OR surgical site infection*[tiab] OR SSI[tiab] OR SSIs[tiab] OR surgical wound infection*[tiab] OR surgical infection*[tiab] OR post-operative wound infection*[tiab] OR postoperative wound infection*[tiab]
2. antibiotic prophylaxis"[Mesh] OR antimicrobial[tiab] OR antibiotic*[tiab]
3. (prolong*[tiab] OR duration[tiab] OR short[tiab] OR long[tiab] OR single dose*[tiab] OR single dosage*[tiab] OR single dosis[tiab] OR singular dose*[tiab] OR singular dosage*[tiab] OR singular dosis[tiab] OR multi dose*[tiab] OR multi dosage*[tiab] OR multi dosis[tiab] OR multiple dose*[tiab] OR multiple dosage*[tiab] OR multiple dosis[tiab])
4. trial[ti]) OR randomly[tiab]) OR clinical trial as topic[mesh:noexp]) OR placebo[tiab]) OR randomized[tiab]) OR controlled clinical trial[pt]) OR randomized controlled trial[pt]
5. 1 AND 2 AND 3 AND 4

EMBASE

1. surgical infection/ or (SSI or SSIs).ti,ab,kw. or ((surg* or postoperat* or post-operat*) adj3 infect*).ti,ab,kw.
2. antibiotic prophylaxis/ or (antimicrobial or antibiotic*).ti,ab,kw.
3. exp drug dose/ or treatment duration/ or (prolong* or duration*).ti,ab,kw. or ((single or singular or multi*) adj3 (dose* or dosage* or dosis)).ti,ab,kw. or ((short* or long*) adj3 (duration* or course*)).ti,ab,kw.
4. controlled clinical trial/ or randomized controlled trial/ or exp "clinical trial (topic)"/ or (randomly or randomized or placebo).ti,ab,kw. or trial.ti.
5. 1 and 2 and 3 and 4

Cochrane Central Register (CENTRAL)

1. MeSH descriptor: [surgical wound infection] explode all trees
2. SSI or SSIs:ti,ab,kw (word variations have been searched)
3. (surg* or postoperat* or post-operat*) near/3 infect*:ti,ab,kw (word variations have been searched)
4. #1 or #2 or #3
5. MeSH descriptor: [antibiotic prophylaxis] explode all trees
6. antimicrobial or antibiotic*:ti,ab,kw (word variations have been searched)
7. #5 or #6
8. prolong* or duration*:ti,ab,kw (word variations have been searched)
9. (single or singular or multi*) near/3 (dose* or dosage* or dosis):ti,ab,kw (word variations have been searched)
10. (short* or long*) near/3 (duration* or course*):ti,ab,kw (word variations have been searched)
11. #8 or #9 or #10
12. #4 and #7 and #11 in Trials

CINAHL

1. (MH "surgical wound infection") OR (TI (surgical site infection* OR SSI OR SSIs OR surgical wound infection* OR surgical infection* OR post-operative wound infection* OR postoperative wound infection*) OR AB (surgical site infection* OR SSI OR SSIs OR surgical wound infection* OR surgical infection* OR post-operative wound infection* OR postoperative wound infection*))
2. (MH "antibiotic prophylaxis") OR TI (antimicrobial OR antibiotic*) OR AB (antimicrobial OR antibiotic*)
3. (MH "treatment duration") OR TI (prolong* OR duration OR short OR long OR single dose* OR single dosage* OR single doses OR singular dose* OR singular dosage* OR singular doses OR multi dose* OR multi dosage* OR multi doses OR multiple dose* OR multiple dosage* OR multiple doses) OR AB (prolong* OR duration OR short OR long OR single dose* OR single dosage* OR single doses OR singular dose* OR singular dosage* OR singular doses OR multi dose* OR multi dosage* OR multi doses OR multiple dose* OR multiple dosage* OR multiple doses)
4. (MH "randomized controlled trials") OR (MH "clinical trials+") OR TI trial OR (TI controll* AND trial*) OR AB (TI controll* AND trial*) OR (TI (randomly OR placebo OR randomi?ed) OR AB (randomly OR placebo OR randomi?ed))
5. S1 AND S2 AND S3 AND S4

WHO Global Health Library

1. (surgical site infection)
2. (wound infections)
3. (wound infection)
4. filter Subject [Mesh] antibiotic prophylaxis

ti: title; ab: abstract; kw: key word

Appendix 2: Evidence table

Author Year	Design, scope, participants (number)	Type of surgery	CDC wound classi-fication	Intervention	Control	Follow-up	Primary outcome	Results	Adverse events/ remarks	Comparison
Rajabi 2012[17]	RCT single centre 291	Appendectomy (open) Uncomplicated Included paediatric patients (age 15-70 years)	II-III	B) A+1 day ceftriaxone (1 g) IV every 12 hours, metronidazole 500 mg IV every 8 hours. C) A+ 3 days ceftriaxone (1 g) every 12 hours, metronidazole 500 mg every 8 hours.	A) Ceftriaxone 1 g IV + metronidazole 500 mg IV at induction.	10 days after discharge	Discharge of pus that required surgical drainage before discharge.	According to groups (intervention vs. control): A) 8/97 B) 6/97 C) 5/97	No AE	Single vs. prolonged <24 hours vs. >24 hours
Hussain 2012[14]	RCT single centre 377	Appendectomy (open) Uncomplicated	II-III	B) A+ single dose of cefuroxime and metronidazole 8 hours postoperatively.	A) Cefuroxime + metronidazole 1-2 hours before surgery.	30 days postoperatively	Pus discharge from the wound that necessitated wound	According to groups (intervention vs. control): A) 9/195 B) 8/182	NR	Single vs. prolonged

							opening and drainage.			
Mui 2005[16]	RCT single centre 269	Appendectomy (open) Uncomplicated Including paediatric patients (age 15-70 years)	II-III	B) A+2 more IV antibiotic doses (A). C) A+5-day course of antibiotics. IV (A) until orally was tolerated (cefuroxime 250 mg 2 times daily + metronidazole 400 mg 3 times daily).	A) Cefuroxime 1.5 g IV metronidazole 500 mg IV at introduction of general anaesthesia.	30 days postoperatively	Discharge of pus that required surgical drainage before discharge.	According to groups (intervention vs. control): A) 6/92 B) 6/94 C) 3/83	B) 1 *C. difficile* C) 4 *C. difficile*	Single *vs.* prolonged <24 hours vs. >24 hours
Liberman 1995[15]	RCT single centre 99	Appendectomy (open) Uncomplicated Including paediatric patients (children under 12 years excluded)	II-III	B) A + 3 additional doses every 6 hours.	A) 2 g cefoxitin 15 minutes preoperatively + postoperative placebo.	3 weeks postoperatively	If peri-incisional erythema and incisional drainage present, it was classified as a wound infection.	According to groups (intervention vs. control): A) 5/45 B) 1/54	NR	Single vs. prolonged
Tsang 1992[18]	RCT single centre 103	Appendectomy (open) Uncomplicated	II-III	B) A + 2 more postoperative doses (A) at 8 hour intervals.	A) 1.5 mg/kg gentamicin + 7.5 mg/kg metronidazole with the pre-	4 weeks	Evidence of purulent discharge from the wound with or	According to groups (intervention vs. control): A) 1/48	NR	Single vs. prolonged

		Paediatric patients			anaesthetic medication.		without a positive bacteriological culture.	A) 1/55		
Ishibashi 2014[60]	RCT single centre 297	Elective re-sectional surgery for rectal cancer	II-III	B) A + 4 postoperative doses of flomoxef 1g over 2 consecutive postoperative days (total of 5).	A) 1 dose of flomoxef IV + 1 dose of flomoxef 1 hour after completion of surgery.	30 days	CDC	According to groups (intervention vs. control): A) 7/139 B) 10/140	NR	<24 hours vs. >24 hours
Suzuki 2011[21]	RCT single centre 370	Elective laparotomy for colon cancer	II-III	B) A + 2 times a day 1g flomoxef (until postoperative day 3).	A) Single dose of flomoxef 1 g before surgery.	30 days	Macroscopic abscess or purulent discharge observed on the operative wound. Organ/space SSI was defined as infection in the organ subjected to surgery.	According to groups (intervention vs. control): A) 16/179 B) 15/181	No AE	Single vs. prolonged
Ishibashi 2009[59]	RCT single centre 275	Elective surgery for colon cancer	II-III	B) A+ 4 additional doses (A) for 2 consecutive days.	A) 1 g of cefotiam or cefmetazole after induction of anaesthesia + 1 additional dose 1 hour postoperatively.	30 days	CDC	According to groups (intervention vs. control): A) 7/136 B) 9/139	NR	<24 hours vs. >24 hours

Fujita 2007[20]	RCT multicentre 377	Elective colorectal surgery	II-III	B) Single dose of 1 g IV cefmetazole just before skin incision + postoperatively at 8 hours and 16 hours after the first dose.	A) Single dose of 1 g cefmetazole just before skin incision.	NR	NR	According to groups (intervention vs. control): A) 32/190 B) 17/187	NR No redosing Longer procedure duration in single dose group	Single vs. prolonged
McArdle 1995[61]	RCT single centre 169	Colorectal surgery	II-III	B1) A1 + 80 mg gentamicin + 500 mg metronidazole IV 3 x 3 times daily. B2) A2+750 mg ciprofloxacin 3 x 2 times daily postoperatively and 500 mg metronidazole IV 3 x3 times daily	500 mg metronidazole IV at induction of anaesthesia A1) + gentamicin 120 mg IV at induction of anaesthesia + at 8 and 16 hours (80 mg gentamicin + 500 mg metronidazole). A2) + ciprofloxacin 1000 mg orally 1 hour prior to surgery + 500 g metronidazole at 8 hours &16 hours postoperatively.	4 weeks after discharge	Pus either discharging spontaneously or requiring drainage. Major wound sepsis was defined as the discharge of pus with constitutional disturbance.. Minor wound infections include patients with cellulitis and a positive wound culture.	A1) 13/45 A2) 4/40 B1) 7/42 B2) 4/42	NR	<24 hours vs. >24 hours <24 hours vs. >24 hours

Karran 1993[57]	RCT single centre 227	Elective colorectal surgery	II-III	B) A + 500 mg imipenem IV 8 hours + 16 hours after surgery.	A) 1 g imipenem IV at induction + 1 g 3 hours after surgery.	6-8 weeks	Purulent discharge from the wound, positive bacteriological culture, deep abscess.	A) 44/113 B) 39/114	A) 2 phlebitis B) 1 rash, 1 erythema, 1 phlebitis, 2 hypotension	Single postoperative vs. multiple postoperative < 24 hours
Akgur 1992[58]	RCT single centre 30	Colostomy closure Paediatric patients	II-III	B) Both agents started orally 48 hours before the operation + A, continued until the end of postoperative day 5	A) cotrimoxazole 8 mg/kg IM 1 hour preoperatively + ornidazole 20 mg/kg IV at induction of anaesthesia + repeat at 12 hours after initial dose.	30 days	Drainage from the wound that yielded micro-organisms in at least one of the two cultures obtained.	A) 1/15 B) 1/15	NR	<24 hours vs. >24 hours
Cuthbertson 1991[19]	RCT multicentre 278	Elective abdominal surgery where the large bowel was opened	II-III	B) A + same dose (A) 2 hours after commencement of surgery	A) Timentin 3.1 g just before skin incision.	30 days	Purulent discharge from the suture line or if there was a non-purulent discharge that contained pathogenic bacteria.	A) 16/143 B) 17/128	NR	Single vs. prolonged
Becker 1991[78]	RCT single centre 40	Elective colorectal surgery	II-III	B) A+ cefoxitin 1 g IV 6 hourly for 5 days, beginning 6	A) Cefoxitin 2 g IV before operation and at 6 hours and 12	56 days	Purulent drainage, regardless of culture results,	A) 0/22 B) 0/18	NR	<24 hours vs. >24 hours

				hours after the fixed postoperative dose.	hours after the initial dose.		or if non-purulent material contained pathogenic bacteria.			
Fujita 2015[22]	RCT single centre 257	Thoracoscopic oesophagectomy or transthoracic oesophagectomy	II	B) A+ 2 times daily until postoperative day 2	A) 4 x 1g cefmetazole every 3 hours starting from induction of anaesthesia	30d	CDC	A) 31/129 B) 34/128	No AE	Single *vs.* prolonged
Imamura 2012[24]	RCT multicentre 355	Elective surgery for gastric cancer	II	B) A + 1 g of cefazolin on postoperative day 0 and every 12 hours until postoperative day 2	A) 1 g of cefazolin 30 minutes after anaesthesia and an additional dose every 3 hours during surgery	30 days	CDC	A) 8/176 B) 16/179	No AE	Single vs. prolonged

Haga 2012[23]	RCT single centre 325	Elective surgery for gastric cancer	II	B) A + 5 additional doses every 12 hours postoperatively	A) After induction of anaesthesia 1 g of cefazolin was administered IV + additional dose when surgery exceeded 3 hours	30 days	CDC	A) 15/164 B) 10/161	NR	Single vs. prolonged
Mohri 2007[25]	RCT multicentre 486	Elective gastric cancer surgery	II	B) A + 7 additional doses at 12-hour intervals.	A) 1 g cefazolin IV or 1.5 g ampicillin sulbactam IV 30 minutes preoperatively + repeat if duration >3 hours.	6 weeks	CDC	A) 23/243 B) 21/243	No AE	Single vs. prolonged
Regimbeau 2014[26]	RCT multicentre 414	Cholecystectomy for acute mild or moderate calculous cholecystitis Open or laparoscopic	II-III	B) A + the same regimen for 5 days IV or oral if tolerated.	A) 2 g amoxiclav 3 times daily before surgery and at injection of general anaesthesia.	30 days	CDC	A) 22/207 B) 21/207	No AE	Single vs. prolonged
Lau 1990[62]	RCT single centre 203	Early open cholecystectomy for acute cholecystitis	II-III	B) A+ continuation of 500 mg doses at 6- hour intervals for 7 days	A) Cefamandole 2 g IV just before surgery + 500 mg 6 hours and 12 hours later.	1 year	Purulent discharge, serous discharge + positive	A) 7/100 B) 6/103	NR	<24 hours vs. >24 hours

							bacteriological cultures, serous discharge after the patient had returned home. lntraperitoneal abscess was diagnosed by ultrasonic evidence of an abscess and by laparotomy.			
Meijer 1993[27]	RCT multicentre 1004	Biliary surgery	II	B) A + instead of placebo 0.75 g cefuroxime.	A) 1.5g cefuroxime IV at time of induction + placebo at 8 hours and 16 hours postoperatively.	4-6 weeks	0: No sign of infection. 1: Minor infection (erythema, stitch abscess or skin edge necrosis). 2: Major infection (purulent discharge or wound dehiscence). Pus could be detected within a few days of operation (in-hospital	A) 64/501 B) 64/503	NR	Single vs. prolonged

							wound infection) or its appearance could be delayed for as long as 3 weeks (delayed wound infection).			
Togo 2007[79]	RCT single centre 180	Hepatectomy without reconstruction of biliary/intestinal tract	II	B) A for 5 days.	A) 1 g of flomoxef 30 minutes before surgery + redose every 3 hours during surgery, 1 g 2 hours after the completion of surgery and then 2 g a day after the operation day (1 g every 12 hours) for 2 days.	30 days	CDC	A) 4/89 B) 4/91	NR	<48 hours vs. >48 hours
Abro 2014[29]	RCT single centre 208	Clean-contaminated elective surgery	I-III	B) A+ 1 g at 8 and 16 hours postoperatively.	A) 2 g ceftriaxone at induction of anaesthesia (gastrointestinal and urinary tract: + 250 mg gentamicin and	35 days	Pain at the operative site, persistent fever >38°C wound erythema, tenderness, wound discharge	A) 10/104 B) 7/104	NR	Single vs. prolonged

					500 mg metronidazole).		and dehiscence.			
Becker 2008[31]	RCT single centre 44	Elective repair of abdominal incisional hernia >6 cm with onlay polyprolene mesh	I	B) A + 3 times daily until drain tubes removed.	A) 1 g cefazoline IV 30 minutes prior to surgery.	30 days	CDC	A) 4/21 B) 7/21	No AE	Single vs. prolonged
Scher 1997[82]	RCT single centre 768	Elective clean-contaminated operations on the gastrointestinal or biliary tracts	II	B) A + 3 additional 1 g doses of cafazolin every 8 hours.	A) 1 g of cefazolin 15-30 minutes preoperatively + repeat if procedure duration > 3 hours.	NR	NR "Wound surveillance by infection control nurses."	A) 15/382 B) 14/386	NR	Single vs. prolonged
Kow 1995[32]	RCT single centre 1010	All types of surgery involving the viscera (elective and emergency) Including paediatric patients (age 16 years and over)	II-III	C) A + repeat at 6 hours and 12 hours. D) B + repeat of cefotaxime at 6 hours and 12 hours.	A) Cefoxitin 2 g on induction of anaesthesia. B) Cefotaxime 1 g + metronidazole 500 mg on induction of anaesthesia.	4-6 weeks	Presence of purulent discharge from the wound or a serous discharge with a positive culture of pathogenic organism(s).	A) 17/252 B) 14/264 C) 17/254 D) 10/240	NR	Single vs. prolonged

Turano 1992[33]	RCT single centre 3567	Abdominal, gynaecological and urology Including paediatric patients (age 2-97 years)	II-III	C) A + 2 1 g doses IV at 6- hour intervals after the first dose.	A) 1 g of cefotaxime IV 30 minutes prior to incision (repeat in 6 hours if procedure >3 hours).	7 days/discharge	Discharge of serous or seropurulent material from the wound within 7 days of operation	A) 28/1802 B) 39/1765	Unspecified systemic side-effects: A) 20 B) 20 Unspecified local side-effects: A) 10 B) 40	Single vs. prolonged
Bates 1992[30]	RCT multicentre 900	At-risk abdominal sssswwwithpots urgery with with surgery with potential opening of a viscus Including paediatric patients (age 16 years and over)	II-IV	B) A+ additional dose a at 8 hours and 16 hours at 8 at 8 and 16 hours.	A) 250 mg amoxicillin/ clavulanic acid 125 mg on clavulanic acid 125 mg on induction of anaesthesia (IV bolus 1.2 g).	30 days	A clear collection of pus which empties itself spontaneously or after incision.	A) 48/449 B) 49/451	NR	Single vs. prolonged
Aberg 1991[28]	RCT single centre 428	Elective abdominal surgery Including paediatric patients (16 years and over)	II-III	B) Triple dose (A).	A) Single dose of cefuroxime with addition of metronidazole if needed.	30 days	Discharge of pus.	A) 8/207 B) 15/221	NR	Single vs. prolonged
Westen 2015[36]	RCT multicentre	Elective and emergency	II	B) A + 500 mg amoxicillin and 500 mg	A) 1 g ampicillin	30 days	All clinical signs of infection	A) 6/89 B) 9/87	NR	Single vs. prolonged

	176	caesarean section		metronidazole IV at 8 and 16 hours followed by 500 mg moxicillin and 400 mg metronidazole postoperatively 3 times daily on days 3-5.	and 500 mg metronidazole IV 20 minutes before caesarean section.		starting from presence of erythema (not exclusively serous discharge or gaping).			
Shaheen 2014[35]	RCT single centre 100	Elective caesarean section	II	B) A + 2 doses of 1 g cefotaxime IV every 12 hours followed by cefuroxime 400 mg postoperatively for 5 days.	A) 1 g of cefotaxime IV 30 minutes before the operation.	6 weeks	Superficial or deep infection, pus discharge, abscess formation, wound dehiscence, and haematoma formation.	A) 5/50 B) 6/50	NR	Single vs. prolonged
Lyimo 2013[34]	RCT single centre 500	Emergency caesarean section	II	B) A+ metronidazole 500 mg every 8 hours for 24 hours postoperatively.	A) Gentamicin (3 mg/kg) plus metronidazole (500 mg) IV 30 to 60 minutes before the operation.	30 days	CDC	A) 12/250 B) 16/250	NR	Single vs. prolonged
Su 2005[38]	RCT single centre 532	Gynaecological surgery Hysterectomy, abdominal laparoscopic and vaginal,	II	B) A + another 3 doses (A) every 6 hours postoperatively.	A) Cefazolin 1 g at induction of anaesthesia + redose if duration >4 hours.	90 days	1) Abdominal wound infection or trocar wound infection (including	A) 1/267 B) 1//264	NR	Single vs. prolonged

		ovarian cystectomy					wound discharge or abscess). 2) Pelvic abscess or tubo-ovarian abscess. 3) Vaginal cuff abscess. 4) Post-operative septicemia.			
Chang 2005[77]	RCT single centre 156	Laparo-scopically-assisted vaginal hysterectomy	II	B) A up to 30-60 hours.	A) 2 g cephalothin (+1 g every 6 hours) and 80 mg gentamicin (+60-80 mg every 8 hours) for <24 hours	7 days after discharge	Pelvic cellulitis, vaginal cuff abscess, pelvic abscess, wound infection	A) 2/74 B) 3/82	NR	<24 hours vs. >24 hours
Cartaña 1994[37]	RCT single centre 58	Wertheim megs	II	B) A + repeat 6 hours and 12 hours postoperatively.	A) 4 g piperacillin 30 minutes before surgery.	4 days	Surgical wound exudate cultures, if present, or culture of the liquid obtained by puncturing the wound's edges to isolate aerobic and anaerobic organisms.	A) 5/28 B) 1/30	No AE	Single vs. prolonged

Buckley 1990[39]	RCT single centre 204	Hip pinning or Austin Moore hemiarthroplasty. Intertrochanteric /subcapital hip fracture	I	B) A+ 1 g every 6 hours IV for 3 doses (total 4).	A) Cefazolin 2 g IV at induction of anaesthesia.	6 weeks	Clinical criteria/purulent discharge with or without + culture.	A) 2/83 B) 2/121	NR	Single vs. prolonged
Garotta 1991[40]	RCT multicentre 614	All fractures	I	B) A + 2 g at 12 hours postoperatively.	A) Ceftizoxime 2 g preoperatively.	1year	Wound infection (purulent exudation with positive microbiologic culture).	A) 2/301 B) 3/313	NR	Single vs. prolonged
Takemoto 2015[63]	RCT single centre 314	Thoracic/lumbar spine surgery + drain for degenerative/ idiopathic spine deformity	I	B) A for drain duration (average of 3.2 days). Dose and regimen not specified beyond duration.	A) 24 hours of cefazolin (methicillin-resistant *Staphylococcus aureus*, allergy, or recent surgery: vancomycin or clindamycin). Dose and regimen not specified beyond duration.	1 year	CDC	A) 21/170 B) 19/144	NR	<24 hours vs. >24 hours

Hellbusch 2008[41]	RCT multicentre 233	Clean instrumented lumbar spinal fusion for degenerative disease	I	B) A + 1 g of cefazolin IV every 8 hours for 3 days followed by 7 days of oral cephalexin 500 mg every 6 hours.	A) Cefazolin IV 30 minutes before incision (1 g <100 kg <2 g) + redose if procedure duration exceeded 3 hours.	21 days at least	If the wound appeared red or oedematous or if there was drainage.	A) 5/117 B) 2/116	NR	Single vs. prolonged
Gupta 2010[80]	RCT single centre 227	CABG/ valve replacement under cardiopulmonary bypass	I	B) A + 2 4 hours (without placebo) (73 hours).	A) IV ceftazidime pentahydrate + amikacin at anaesthesia induction and a second dose if surgery exceeded 5 hours. Antibiotics were continued for (48 hours) + 24 hours placebo.	Definition 30 days	CDC	A) 5/119 B) 8/108	NR	48 hours vs. >48 hours
Lin 2011[64]	RCT single centre 231	Non-emergency CABG surgery	I	B) A+ 2 days (72 hours)	A) 1 g cefazolin within 1 hour prior to incision + additional dose when surgery was prolonged (every 3-4 hours) + 3 doses every 8 hours after	30 days	CDC	A) 13/120 B) 9/111	NR	<24 hours vs. >24 hours

					surgery (24 hours)					
Niederhauser 1997[65]	RCT single centre 53	Patients with severe heart failure who could not be weaned from cardiopulmonary bypass without IABP(IABP)	I	B) A+ thereafter: ticarcillin/ clavulanate 5.2 g every 8 hours for 2 days + vancomycin 500 mg every 12 hours until removal of IABP. (NB: Different postoperative agent.)	A)1 g of cefazolin at induction of anaesthesia, 1 g after 8 hours, 1 g after 16 hours.	3-540 days	CDC	A) 1/25 B) 1/28	NR	<24 hours vs. >24 hours
Nooyen 1994[42]	RCT single centre 844	CABG	I	B) A+ 750 mg cefuroxime 3 times daily for 3 consecutive days.	A) 20 mg/kg cefuroxime IV at induction of anaesthesia.	NR	Redness, purulent discharge and a positive culture.	A) 12/419 B) 6/425	NR	Single vs. prolonged
Tamayo 2007[43]	RCT single centre 838	CABG, valve or both	I	B) A + 2 x 1g every 8 hours (24 hours).	A) 2 g cefazolin IV 20-30 minutes after induction of anaesthesia + redose when procedure exceeded >3 hours	12 months	CDC	A) 35/419 B) 15/419	NR	Single vs. prolonged
Olak 1991[44]	RCT single centre	Thoracotomy/ lung resection	II	B) A+ 5 doses of cefazolin 1 g every 8 hours	A) 1 dose of 2 g cefazolin IV at induction of	6 weeks	Any wound that discharged,	A) 0/99 B) 2/100	NR	Single vs. prolonged

	199			(without placebo)	anaesthesia + 5 x placebo every 8 hours.		spontaneously or otherwise, purulent material with or without culture of a pathogen.			
Hall 1998[45]	RCT single centre 302	Vascular surgery (open arterial)	I	B) A + 6-hourly interval repeat until lines were removed <5 days.	A) Ticarcillin 3.0 g clavulanate 0.1 g IV immediately after induction of anaesthesia.	42 days after surgery	Discharge of pus or a serous discharge containing pathogenic organisms.	A) 28/153 B) 15/149	NR	Single vs. prolonged
Orlando 2015[46]	RCT multicentre 205	Renal transplant surgery	I	B) A+ cefazolin 1 g or cefotaxim 1 g every 12 hours until removal of Foley catheter (postoperative days 3-5).	A) 1 Shot of broad-spectrum antibiotic (cephalosporin cefazolin 2 g, cefotaxim 1 g).	30 days	CDC	A) 2/103 B) 1/102	NR	Single vs. prolonged
Liu 2008[67]	RCT single centre 53	Head and neck surgery that would enter the upper aero digestive tract (including free flap)	II	B) A extended to 72 hours.	A) Clindamycin 300 mg IV 1 hour before incision and then at 6-hour intervals over a period of 24 hours.	30 days	CDC	A) 8/26 B) 5/27	No AE	<24 hours vs. >24 hours
Carroll 2003[66]	RCT single centre 74	Surgical ablation of head and neck malignancies with free flap	II	B) A extended to 15 doses (5 days).	A) Clindamycin 900 mg IV initiated immediately preoperatively	7 days/discharge	Clinical signs of infection in wound colour and drainage.	A) 4/35 B) 4/39	No AE	<24 hours vs. >24 hours

		reconstruction involving the upper aero digestive tract			and repeated every 8 hours for a total of 3 doses. 24 hours					
Righi 1996[68]	RCT single centre 162	Oncologic surgery in the head and neck involving the upper aero digestive tract (excluding free flap)	II	B) A, extended to 9 doses and 3 doses respectively. 72 hours	A) Clindamycin 600 mg IV at induction followed by 3 doses one every 8 hours + cefonicid 1 g IV at induction. followed by 1g after 12 hours. 24 hours	20 days	Purulent drainage (either spontaneously or by incision) or muco-cutaneous fistula interpreted as wound infection.	A) 2/81 B) 3/81	No AE	<24 hours vs. >24 hours
Sawyer 1990[81]	RCT multicentre 50	Major head and neck procedures involving the upper aerodigestive tract	II	B) Preoperative dose plus at least 7 days of antibiotics. Metronidazole 500 mg every 6 hours, cefazolin 1 g every 8 hours IV	A) Preoperative dose plus 2 days of antibiotics. Metronidazole 500 mg every 6 hours, cefazolin 1 g every 8 hours IV	NR	Major wound infection was defined as wound breakdown and undermining of tissues sufficient to allow packing of the wound. Lesser complications, such as cellulitis or a	A) 8/25 B) 5/25	No AE	<48 hours *vs.* >48 hours

							tiny fistula, allowing only entry of a cotton-tipped applicator were considered as minor.			
Maier 1992[47]	RCT single centre 106	Parotidectomy, sinus surgery, neck dissection with no transcutaneous exploration of the aerodigestive tract	I-II	B) A + 8 hours and 16 hours postoperatively. Three shot 24-hour regimen of 1.5 g cefuroxime.	A) 1.5 g cefuroxime directly preoperative	NR	Wound infection	A) 0/53 B) 0/53	No AR	Single *vs.* prolonged
Mann 1990[48]	RCT single centre 113	Procedures for benign and malignant processes in the head and neck region	II	B) A + repeat at night and the next morning (24 hours).	A) Preoperative 2 g cefotiam + 500 mg metronidazole + redose cefotiam when duration >3 hours.	NR	Purulent discharge.	A) 8/55 B) 10/58	NR	Single vs. prolonged
Bidkar 2014[69]	RCT single centre 78	Tympanoplasty with cortical mastoidectomy for active and inactive mild chronic otitis media	I-III	B) A+ oral cefixime 200 mg 12-hourly for 8 days or more.	A) IV cefuroxime 1.5 g 30 minutes before incision, followed by 750 mg 12-hourly until 24 hours postoperatively.	3 weeks	Wound infection.	A) 1/39 B) 2/39	A) 19 B) 1 (gastro-intestinal disturbance)	<24 hours vs. >24 hours

		Included paediatric patients (12-60 years)								
Rajan 2005[49]	RCT single centre 200	Septorhinoplasty	II	B) A + postoperative oral course of amoxicillin-clavunate 1000 mg 2 times daily.	A) Preoperative IV amoxicillin-clavulanate 2.2 g 30 minutes before incision.	30 days	Wound infection.	A) 0/100 B) 3/100	B) 29 A) 2 (nausea, diarrhoea, skin rash, pruritus)	Single vs. prolonged
Campos 2015[50]	RCT single centre 74	Surgery for facial fracture reduction and fixation Intra and extra oral. When required, titanium plates and screws were used.	I-II	B) A+ 4 x 1 g cefazolin in 24 hours.	A) 2 g cefazolin IV preoperative Redose when duration >4 hours.	6 weeks	a) Pus drainage at the fracture site or in the vicinity of the surgical intervention site; b) increased swelling 7 days after the operation; c) presence of a fistula in the area of the surgical intervention or at the site of the fracture, with active drainage; d) other clinical features observed by the evaluator,	A) 6/42 B) 1/32	NR	Single vs. prolonged

							including typical signs of infection such as fever, oedema and localized redness.			
Lindeboom 2005[52]	RCT single centre 124	Intraoral bone grafting for endosseous implantation	II	B) A + 300 mg clindamycin instead of placebo.	A) 600 mg clindamycin orally 60 minutes preoperatively + 4 x placebo every 6 hours.	8 weeks postoperatively	CDC	A) 6/62 B) 5/62	NR	Single vs. prolonged
Lindeboom 2003[53]	RCT single centre 70	Bilateral sagittal ramus osteotomy of the mandi	II	B) A+ clindamycin IV instead of placebo.	A) 400 mg clindamycin IV 15 minutes before incision + placebo every 6 hours for 24 hours.	3 months	Presence of purulent drainage (either spontaneously or by incision), accompanied by pain or tenderness, localized swelling, redness, and heat or fever (>38.5° C) or an increase in localized swelling after an initial postoperative	A) 2/35 B) 1/35	No AE	Single vs. prolonged

							decrease of oedema, together with pain, discomfort, induration, and an increase in body temperature (>38.5° C).			
Cioaca 2002[51]	RCT single centre 140	Aseptic oral and maxillofacial surgery that does not involve the implantation of foreign material Included paediatric patients (17-70 years)	II	C) A + 5-day redose every 8 hours instead of placebo. D) B + 5-day redose every 8 hours instead of placebo.	A) 2.4 mg amoxicillin-clavulanate IV at induction + 5-day placebo. B) 2 g cefazolin at induction + 5-day placebo.	14 days	Purulent discharge.	A) 1/35 B) 2/34 D) 2/35 C) 0/33 A+B 3/69 C+D 2/68	NR	Single vs. prolonged Single vs. prolonged
Abubaker 2001[70]	RCT single centre 30	Uncomplicated fractures of the mandible. requiring closed reduction and mandibulo-maxillar fixation or with open reduction and internal fixation	II	B) A + 500 mg penicillin postoperatively every 6 hours for 5 days.	A) 2 million units aqueous penicillin IV every 4 hours from admission through to the preoperative and intraoperative phase and for 12 hours postoperatively	6 weeks	1. Purulent drainage from the surgical or fracture site. 2. Increased facial swelling beyond postoperative day 7.	A) 2/16 B) 2/14	NR	<24 hours vs. >24 hours

					+ oral placebo every 6 hours for 5 days.		3. Fistula formation at the surgical or fracture site, with evidence of drainage. 4. Fever associated with local evidence of infection (swelling, erythema, or tenderness).			
Eshghpour 2014[73]	RCT single centre 50	Bi-maxillary orthognathic surgery Included paediatric patients (17-35 years)	II	B) A + 500 mg amoxicillin syrup postoperatively every 8 hours for a total of 1 week.	A) 1 g cefazolin 30 minutes prior to surgery + same dose 4 hours after 1st injection + placebo.	6 weeks	Facial swelling, purulent discharge from the incision site, drainage, wound dehiscence, pain, or erythema.	A) 0/25 B) 0/25	No AE	<24 hours vs. >24 hours
Wahab 2013[56]	RCT single centre 60	Bilateral sagittal split osteotomy Orthognathic surgery Included paediatric patients (age 17-37 years)	II	B) A + 2 doses of 500 mg amoxicillin IV every 4 hours	A) 1 g amoxicillin at induction + 2 saline solution doses IV every 4 hours	2 months	CDC	A) 6/30 B) 1/30	NR	Single vs. prolonged

Danda 2010[54]	RCT single centre 150	Orthognathic surgery Included paediatric patients (15-37 years)	II	B) A + 500 g ampicillin IV instead of placebo.	A) 1 g ampicillin IV at induction + placebo saline every 6 hours for 24 hours.	4 weeks	1. Purulent discharge from an incision. 2. Sero-sanguineous drainage and a wound culture positive for a known pathogen. 3. Clinician diagnosis of infection.	A) 7/75 B) 2/75	No AE	Single vs. prolonged
Kang 2009[55]	RCT single centre 56	Orthognathic surgery	II	B) A + 1g cefpiramide two times daily until 3 days after surgery.	A) 1 g of a third-generation cephalosporin (cefpiramide) IV 30 minutes before surgery.	2 weeks	CDC	A) 3 /28 B) 2 /28	No AE	Single **vs.** prolonged
Jansisyanont 2008[75]	RCT multicentre 122	Orthognathic surgery Included paediatric patients (17-47 years)	II	C) A (without postoperative dose) + 625 mg amoxicillin/ clavulanic acid postoperatively every 8 hours for 5 days. D) B (without postoperative dose) + 500 mg amoxicillin postoperatively	A) 1.2 g amoxicillin/ clavulanic acid 30 minutes preoperatively + every 8 hours during the procedure + 1 single dose 8 hours postoperatively. B) 2 million units of aqueous penicillin IV 30	6 weeks	CDC	A) 1/33 C) 0/28 B) 0/29 D) 1/32 A+B 1/62 C+D 1/60	NR	<24 hours vs. >24 hours

				every 8 hours for 5 days.	minutes preoperatively + every 4 hours during the procedure + 1 single dose 4 hours postoperatively.					
Baqain 2004[71]	RCT single centre 34	Orthognathic surgery	II	B) A+ 500 g amoxicillin postoperatively every 8 hours for 5 days instead of placebo	A) 1 g amoxicillin IV at induction of anaesthesia + 500 mg IV 3 hours postoperatively + placebo every 8 hours for 5 days.	6 weeks	A score system based on facial swelling and/or pain; presence or absence of extraoral erythema; wound exudate; isolation of pathogens; pyrexia; and wound dehiscence.	A) 4/17 B) 2/17	NR	<24 hours vs. >24 hours
Bentley 1999[72]	RCT single centre 30	Orthognathic surgical procedures	II	B) A + penicillin G, one million units IV every 6 hours for 8 doses, followed by penicillin V suspension 300 mg postoperatively every 6 hours	A) Penicillin G, two million units IV immediately preoperatively, and one million units IV every 3 hours intraoperatively and once postoperatively	30 days	CDC	A) 9/15 B) 1/15	NR	<24 hours vs. >24 hours

				for 8 doses instead of placebo.	3 hours after the last intraoperative dose. + Placebo					
Fridrich 1994[74]	RCT single centre 30	Orthognathic surgical procedures Including paediatric patients (15-55 years)	II	B) Penicillin G 2 million units IV preoperatively + every 4 hours until the IV was discontinued on postoperative day 1. 500 mg penicillin VK was continued 4 times daily for 1 week. (NB: intra-operative redose differs in frequency.)	A) Penicillin G 2 million units IV, preoperatively and + every 2 hours until participants reached the recovery room where the final dose was given	8 weeks	Infection.	A) 1/16 B) 1/14	NR	<24 hours vs. >24 hours
Bozorgzadeh 1999[76]	RCT single centre 300	Surgery for penetrating abdominal trauma Included paediatric patients (12-69 years)	II-III	B) 5 days of IV cefoxitin, with the first 1 g dose given in the emergency department immediately after the determination of	A) 24 hours of IV cefoxitin with the first 1 g dose given in the emergency department immediately after the	30 days	CDC	A) 24 /148 B) 26 /152	NR	<24 hours vs. >24 hours

				the requirement for laparotomy followed by administration every 6 hours for a total of 20 doses.	determination of a requirement for laparotomy, followed by administration every 6 hours for a total of 4 doses.					

RCT: randomized controlled trial; CDC: Centers for Disease Control and Prevention; IV: intravenous; AE: adverse event/s; AB: antibiotic; NR: not recorded; SSI: surgical site infection; IM: intramuscular; CABG: coronary artery bypass grafting; IABP: intra-aortic balloon pumping.

Appendix 3. Risk of bias assessment of the included studies (Cochrane Collaboration tool)

RCT, author, year, reference	Sequence generation	Allocation concealment	Participants and caregivers blinded	Outcome assessors blinded	Incomplete outcome data	Selective outcome reporting
Appendectomy						
Rajabi-Masshadi 2012[17]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Hussain 2012[14]	Low	Unclear	Unclear	Unclear	Low	Low
Mui 2005[16]	Low	Unclear	Unclear	Unclear	Low	Low
Liberman 1995[15]	Low	Unclear	Unclear	Unclear	Low	Low
Tsang 1992[18]	Low	High	High	Unclear	Low	Low
Colorectal						
Ishibashi 2014[60]	Low	Unclear	Unclear	Unclear	Low	Low
Suzuki 2011[21]	Low	Unclear	Unclear	Unclear	Low	Low
Ishibashi 2009[59]	Low	Unclear	Unclear	Unclear	Low	Low
Fujita 2007[20]	Low	High	Unclear	Unclear	High	High
McArdle 1995[61]	Unclear	Unclear	Unclear	Unclear	Low	Low
Karran 1993[57]	Unclear	Unclear	Unclear	Unclear	Low	Low
Akgur 1992[58]	Unclear	Unclear	Unclear	Unclear	Low	Low
Cuthbertson 1991[19]	Low	Low	Unclear	Low	Low	High
Becker 1991[78]	Unclear	Unclear	Unclear	Low	Low	Low
Upper gastrointestinal tract						
Fujita 2015[22]	Unclear	Unclear	Unclear	Unclear	Low	Low
Imamura 2012[24]	Low	High	High	High	Low	Low
Haga 2012[23]	Low	Unclear	Unclear	Unclear	Low	Low
Mohri 2007[25]	Low	Low	High	Low	Low	Low
Cholecystectomy						
Regimbeau 2014[26]	Low	High	High	Unclear	Low	Low

Lau 1990[62]	Unclear	Unclear	Unclear	Low	Low	Low
Hepatobiliary						
Meijer 1993[27]	Low	Unclear	Unclear	Unclear	Low	Low
Togo 2007[79]	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Mixed general						
Abro 2014[29]	Unclear	Unclear	Unclear	Unclear	Low	Low
Becker 2008[31]	Unclear	Unclear	Unclear	Unclear	Low	Low
Scher 1997[82]	Low	Low	Low	Low	Low	Low
Kow 1995[32]	Low	Low	Unclear	Unclear	Low	Low
Turano 1992[33]	Unclear	Unclear	High	High	Low	Low
Bates 1992[30]	Low	High	Unclear	Low	Low	Low
Aberg 1991[28]	Unclear	Unclear	High	High	Low	Low
Caesarean section						
Westen 2015[36]	Low	Low	Unclear	Unclear	Low	Low
Shaheen 2014[35]	Low	Unclear	Unclear	Unclear	Low	Low
Lyimo 2013[34]	Low	Unclear	High	High	Low	Low
Gynaecological						
Su 2005[38]	Low	High	Unclear	Unclear	Low	Low
Cartaña 1994[37]	Low	High	Unclear	Unclear	Low	Low
Chang 2005[77]	Low	Unclear	High	Unclear	Low	Low
Orthopaedic/trauma						
Buckley 1990 [39]	Unclear	Unclear	Unclear	Unclear	Low	High
Garotta 1991[40]	Low	High	Unclear	Unclear	Low	Low
Takemoto 2015[63]	Low	Unclear	Unclear	Unclear	Low	High
Hellbusch 2008[41]	Unclear	Unclear	Unclear	Unclear	Low	Low
Cardiac						
Gupta 2010[80]	Low	Low	Low	Low	Low	High

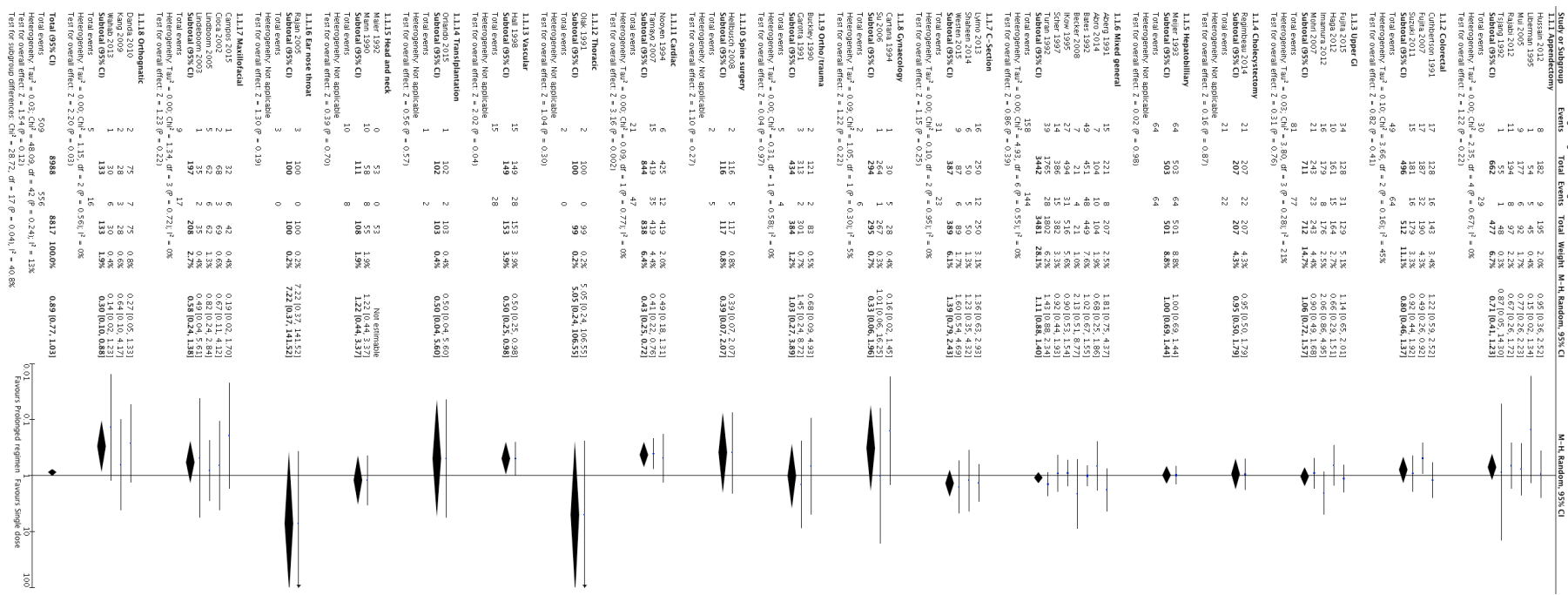
Lin 2011[64]	Low	Unclear	Unclear	Unclear	Low	Low
Niederhauser 1997[65]	Low	High	High	High	Low	Low
Nooyen 1994[42]	Low	Low	Unclear	Low	Low	Low
Tamayo 2007[43]	Low	Unclear	Unclear	Unclear	Low	High
Vascular						
Hall 1998[45]	Low	Low	Unclear	Unclear	Low	Low
Thoracic						
Olak 1991[44]	Low	Unclear	Low	Unclear	Low	Unclear
Kidney transplant						
Orlando 2015[46]	Low	Low	Unclear	Unclear	Low	Low
Head and neck						
Liu 2008[67]	Low	High	Unclear	Unclear	Low	Low
Carroll 2003[66]	Unclear	Unclear	Unclear	Low	Low	High
Righi 1996[68]	Unclear	Unclear	Unclear	Unclear	Low	Low
Sawyer 1990[81]	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Maier 1992[47]	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Mann 1990[48]	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Ear, nose and throat						
Bidkar 2014[69]	Low	Unclear	Unclear	Unclear	Low	Low
Rajan 2005[49]	Low	Low	Unclear	Unclear	Low	Low
Maxillofacial						
Campos 2015[50]	Unclear	Unclear	Unclear	Unclear	High	High
Lindeboom 2005[52]	Low	Unclear	Unclear	Low	Low	Low
Lindeboom 2003[53]	Low	High	Unclear	Low	Low	Low
Cioaca 2002[51]	Unclear	Unclear	Unclear	Low	Low	Low
Abubaker 2001[70]	Unclear	Low	Low	Low	Low	Low
Orthognathic						
Eshghpour 2014[73]	Unclear	Unclear	Unclear	Unclear	Low	Low

Wahab 2013[56]	Unclear	Unclear	Unclear	Unclear	Low	Low
Danda 2010[54]	Unclear	Unclear	Unclear	Unclear	Low	Low
Kang 2009[55]	Low	Unclear	Unclear	Unclear	Low	Low
Jansisyanont 2008[75]	Unclear	Unclear	Low	Unclear	High	Low
Baqain 2004[71]	Low	Low	Low	Low	Low	Unclear
Bentley 1999[72]	Unclear	Unclear	Low	Low	Low	High
Fridrich 1994[74]	Unclear	Unclear	Unclear	Unclear	Low	Low
Other						
Bozorgzadeh 1999[76]	Unclear	Unclear	Unclear	Unclear	Low	Low

RCT: randomized controlled trial

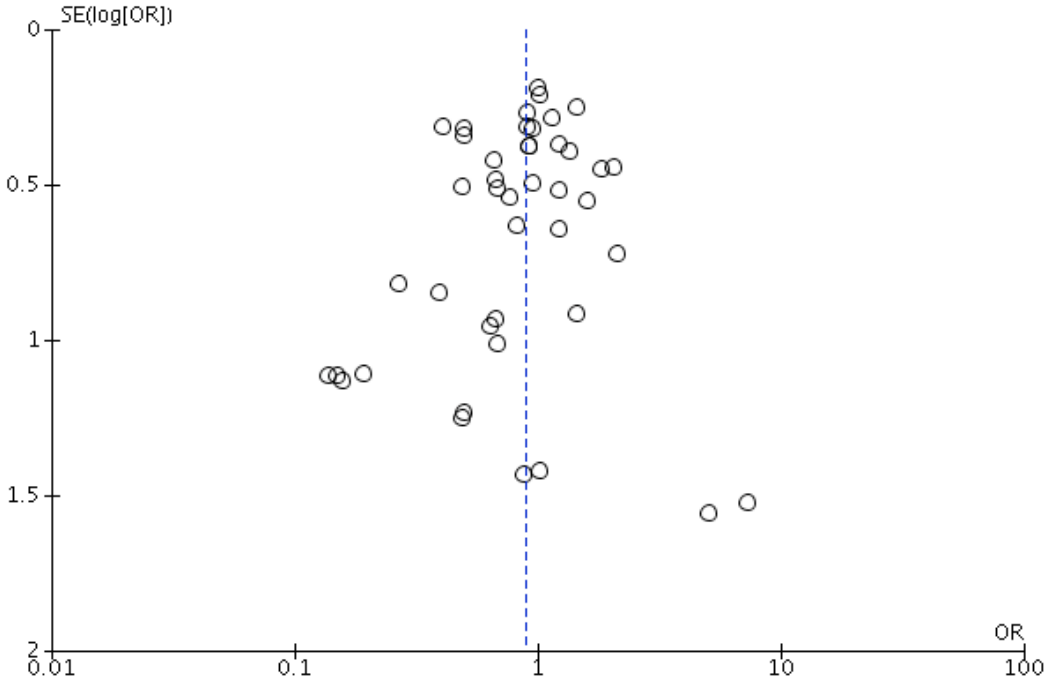
Appendix 4: Comparisons

Comparison 1: Postoperative continuation vs. single dose of antibiotic prophylaxis, outcome SSI



SSI: surgical site infection; GI: gastrointestinal; CI: confidence interval

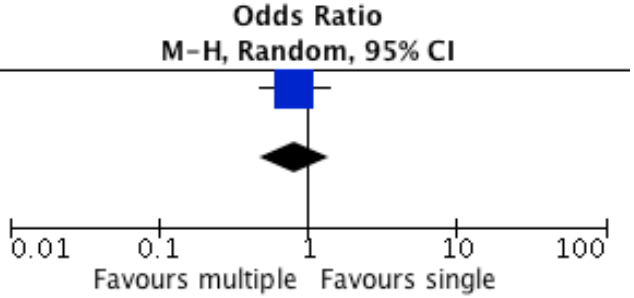
Funnel plot 1. Postoperative continuation vs. single dose of antibiotic prophylaxis, outcome SSI



Comparison 2: Postoperative continuation of antibiotic prophylaxis for up to 24 hours vs. a single postoperative dose, outcome SSI

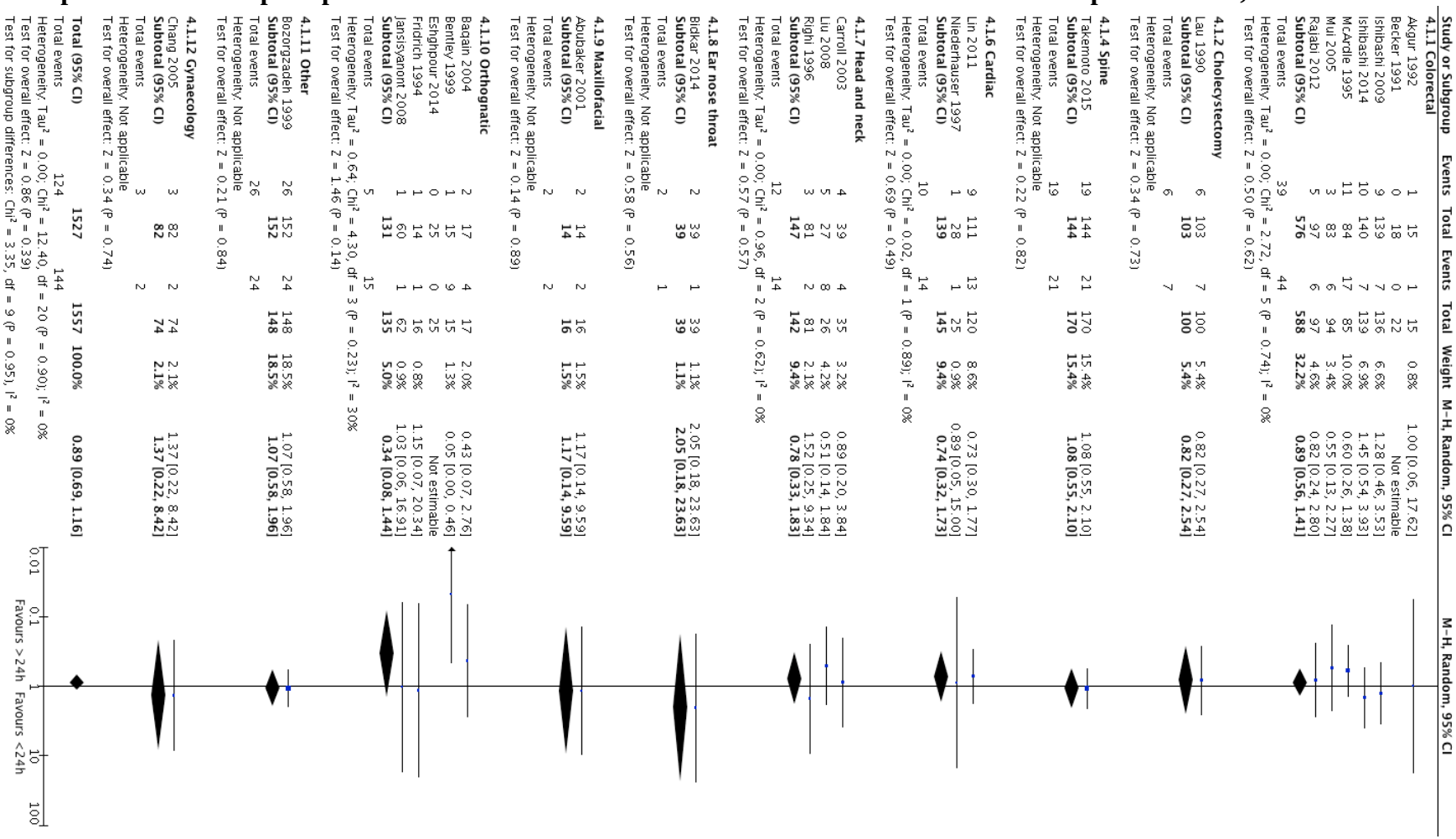
Study or Subgroup	Multiple postop Events	Total	Single postop Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Karran 1993	39	114	44	113	100.0%	0.82 [0.47, 1.40]
Total (95% CI)		**114**		**113**	**100.0%**	**0.82 [0.47, 1.40]**
Total events	39		44			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.74 (P = 0.46)



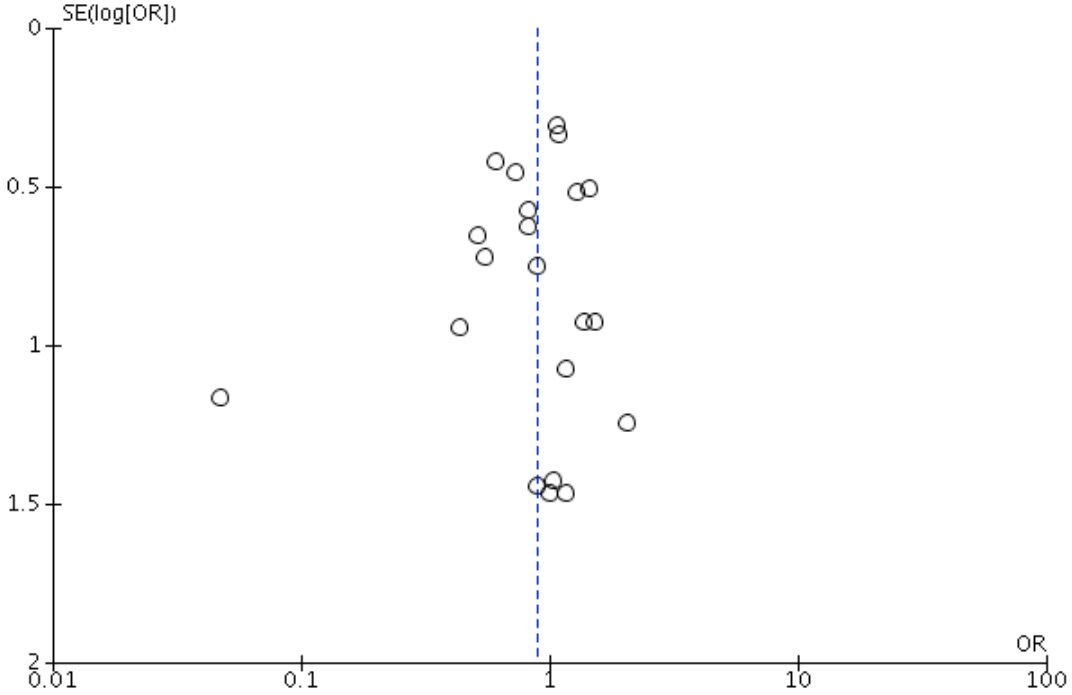
SSI: surgical site infection; M-H: Mantel-Haenszel (test); CI: confidence interval

Comparison 3: SAP – postoperative continuation for more than 24 hours vs. continuation for up to 24 hours, outcome SSI

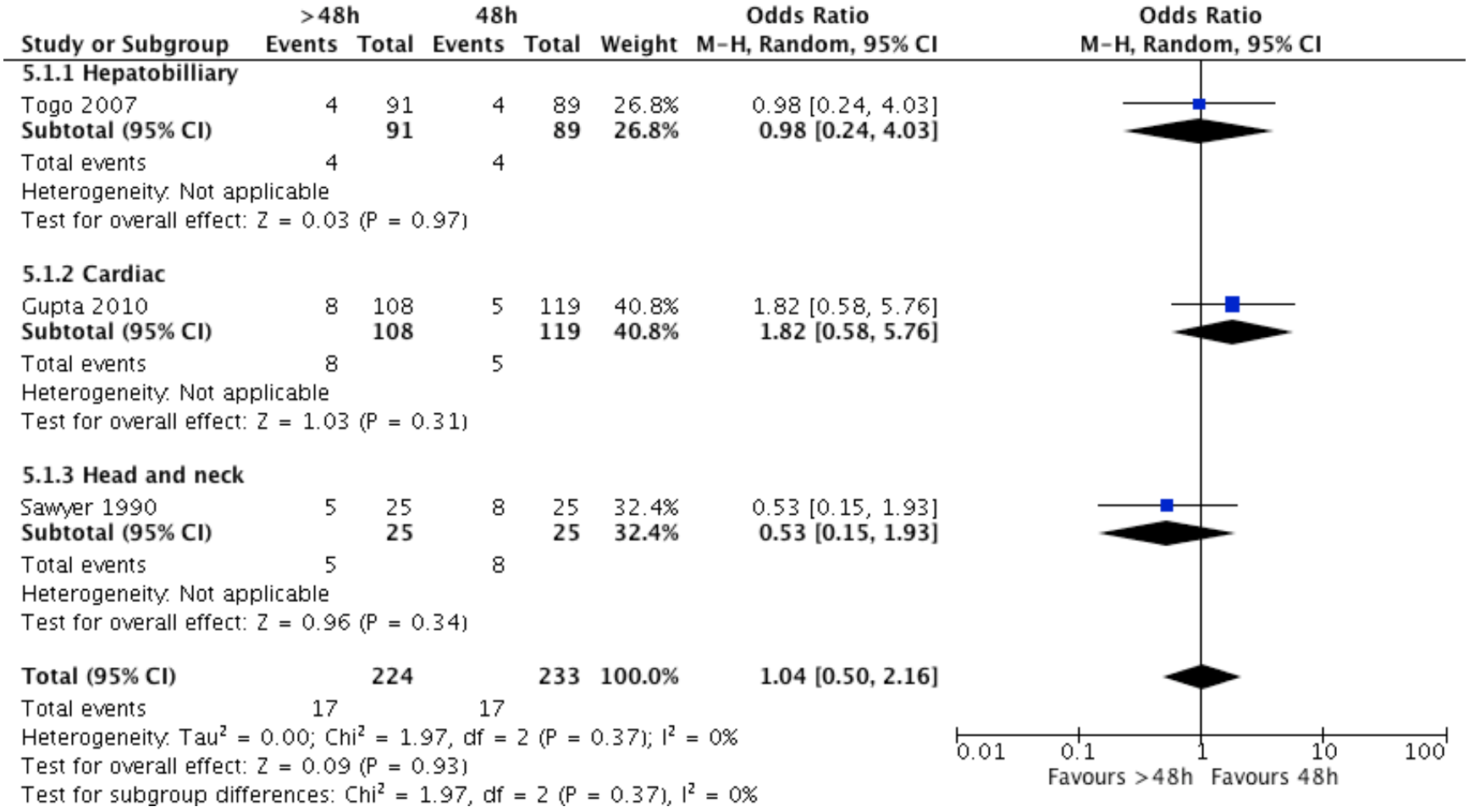


SAP: surgical antibiotic prophylaxis; SSI: surgical site infection; M-H: Mantel-Haenszel (test); CI: confidence interval

Funnel plot 3. SAP – postoperative continuation for more than 24 hours vs. continuation for up to 24 hours, outcome SSI

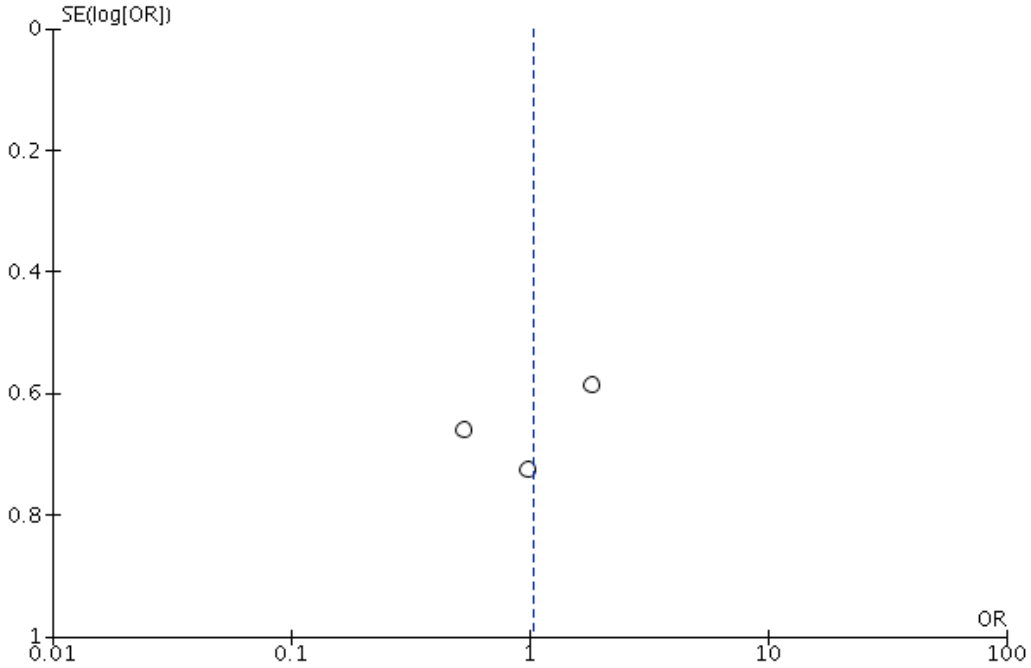


Comparison 4: SAP – postoperative continuation for more than 48 hours vs. continuation for up to 48 hours, outcome SSI



SAP: surgical antibiotic prophylaxis; SSI: surgical site infection; M-H: Mantel-Haenszel (test); CI: confidence interval

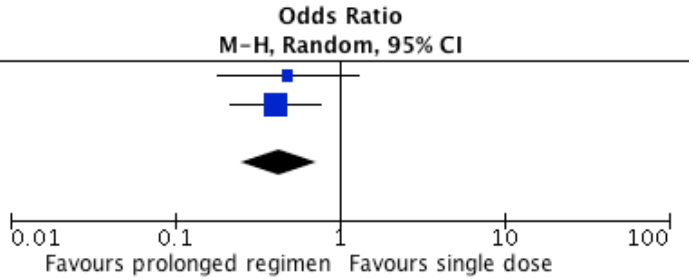
Funnel plot 4. SAP – postoperative continuation for more than 48 hours vs. continuation for up to 48 hours, outcome SSI



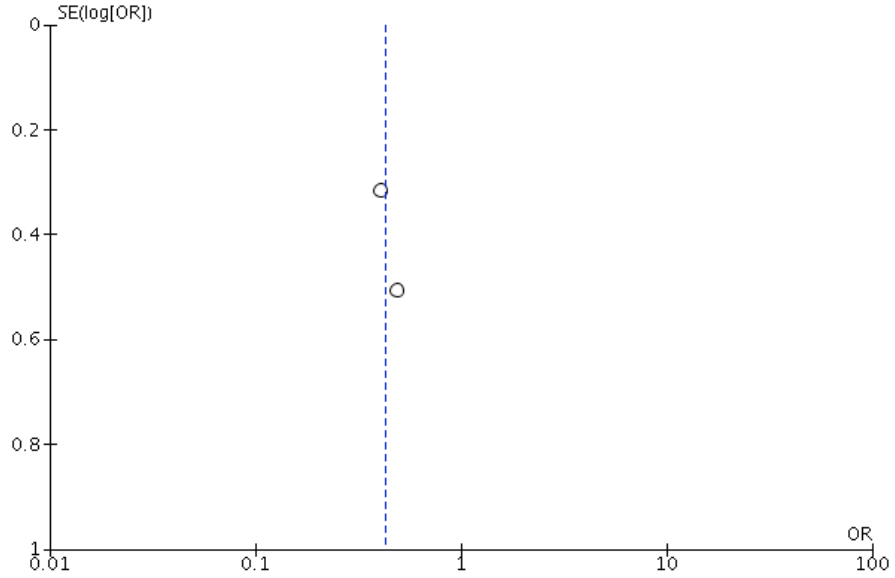
Comparison 5a: Types of procedure with a decreased risk of SSI with a prolonged antibiotic regimen: cardiac surgery
(i) Prolonged regimen vs. a single dose

Study or Subgroup	Prolonged regimen Events	Total	Single dose Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Nooyen 1994	6	425	12	419	28.2%	0.49 [0.18, 1.31]
Tamayo 2007	15	419	35	419	71.8%	0.41 [0.22, 0.76]
Total (95% CI)		**844**		**838**	**100.0%**	**0.43 [0.25, 0.72]**
Total events	21		47			

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.77); I² = 0%
Test for overall effect: Z = 3.16 (P = 0.002)



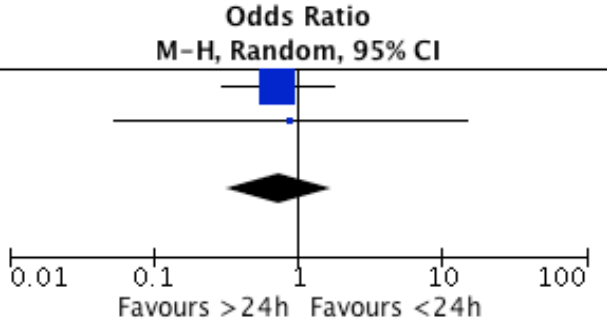
Funnel plot 5a. Types of procedure with a decreased risk of SSI with a prolonged antibiotic regimen: cardiac surgery
(i) Prolonged regimen *vs.* a single dose



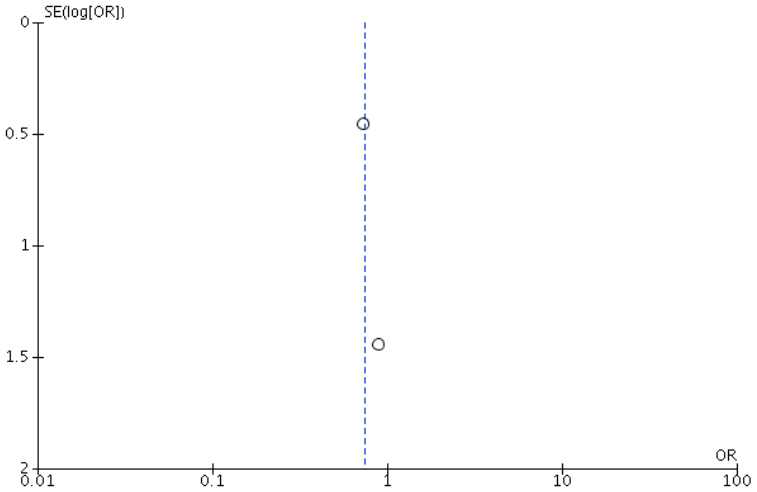
Comparison 5a: Types of procedure with a decreased risk of SSI with a prolonged antibiotic regimen: cardiac surgery
(ii) >24 hours vs. <24 hours

Study or Subgroup	>24h Events	>24h Total	<24h Events	<24h Total	Weight	Odds Ratio M-H, Random, 95% CI
Lin 2011	9	111	13	120	90.9%	0.73 [0.30, 1.77]
Niederhauser 1997	1	28	1	25	9.1%	0.89 [0.05, 15.00]
Total (95% CI)		**139**		**145**	**100.0%**	**0.74 [0.32, 1.73]**
Total events	10		14			

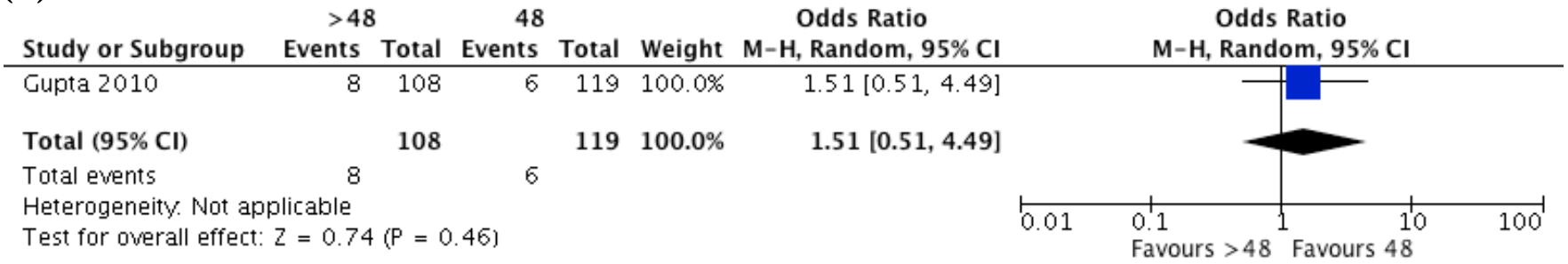
Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.89); I² = 0%
Test for overall effect: Z = 0.69 (P = 0.49)



Funnel plot 5a. Types of procedure with a decreased risk of SSI with a prolonged antibiotic regimen: cardiac surgery
(ii) >24 hours vs. <24 hours

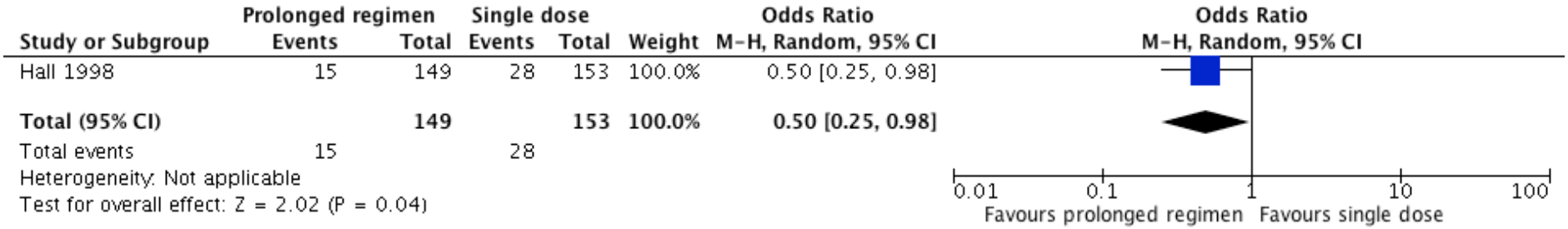


Comparison 5a: Types of procedure with a decreased risk of SSI with a prolonged antibiotic regimen: cardiac surgery
(iii) >48 hours vs. 48 hours



SSI: surgical site infection; M-H: Mantel-Haenszel (test); CI: confidence interval

Comparison 5b: Types of procedure with decreased risk of SSI with a prolonged antibiotic regimen: vascular surgery
(i) Prolonged regimen vs. a single dose

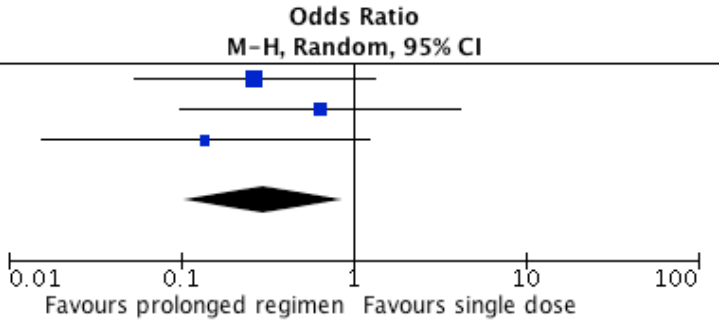


SSI: surgical site infection; M-H: Mantel-Haenszel (test); CI: confidence interval

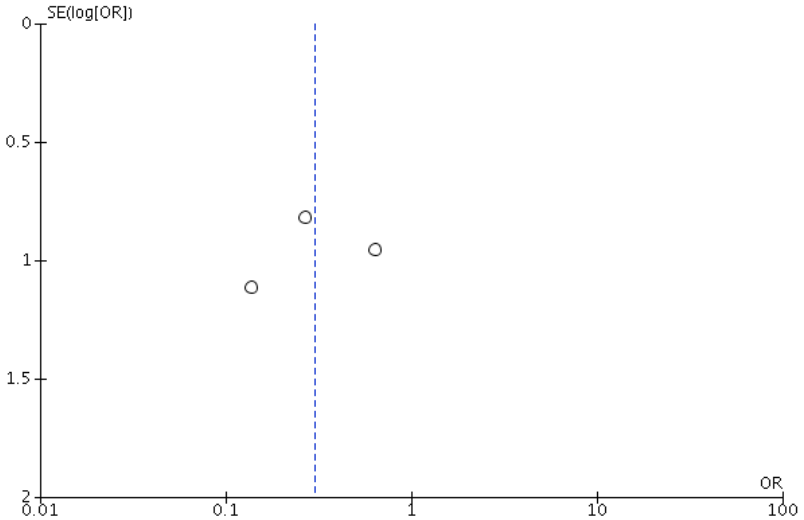
Comparison 5c: Types of procedure with decreased risk of SSI with a prolonged antibiotic regimen: orthognathic surgery
(i) Prolonged regimen vs. a single dose

Study or Subgroup	Prolonged regimen Events	Total	Single dose Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Danda 2010	2	75	7	75	43.9%	0.27 [0.05, 1.33]
Kang 2009	2	28	3	28	32.3%	0.64 [0.10, 4.17]
Wahab 2013	1	30	6	30	23.7%	0.14 [0.02, 1.23]
Total (95% CI)		**133**		**133**	**100.0%**	**0.30 [0.10, 0.88]**
Total events	5		16			

Heterogeneity: Tau² = 0.00; Chi² = 1.15, df = 2 (P = 0.56); I² = 0%
Test for overall effect: Z = 2.20 (P = 0.03)



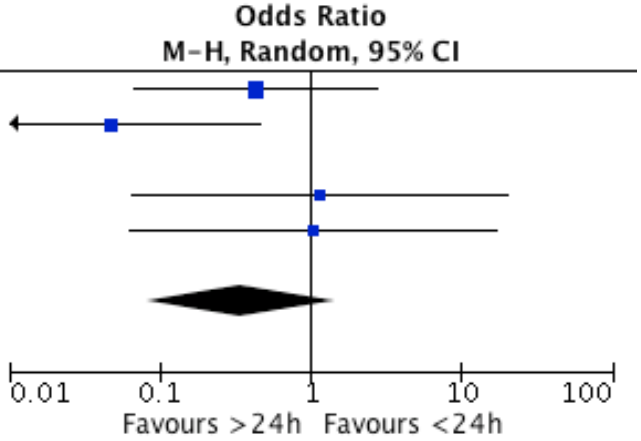
Funnel plot 5c. Types of procedure with decreased risk of SSI with a prolonged antibiotic regimen: orthognathic surgery
(i) Prolonged regimen vs. a single dose



Comparison 5c: Types of procedure with decreased risk of SSI with a prolonged antibiotic regimen: orthognathic surgery
(ii) >24 hours vs. <24 hours

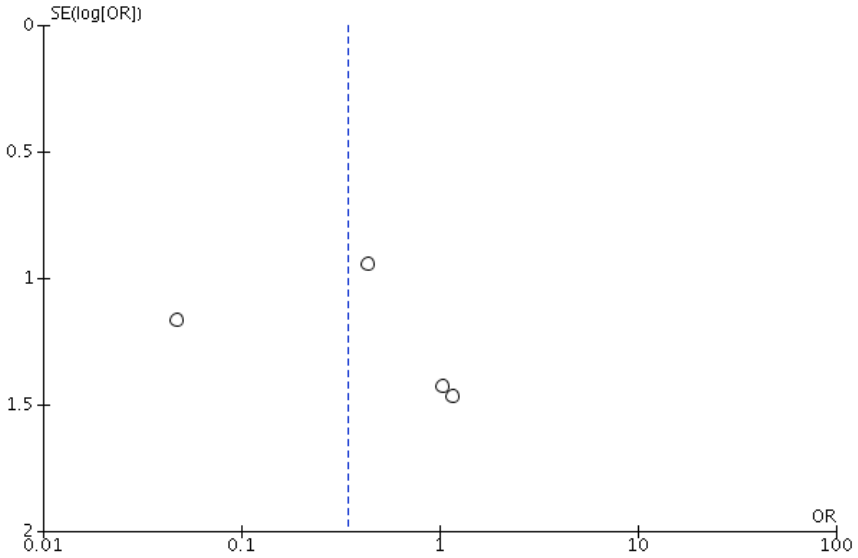
Study or Subgroup	>24h Events	>24h Total	<24h Events	<24h Total	Weight	Odds Ratio M-H, Random, 95% CI
Baqain 2004	2	17	4	17	34.5%	0.43 [0.07, 2.76]
Bentley 1999	1	15	9	15	26.6%	0.05 [0.00, 0.46]
Eshghpour 2014	0	25	0	25		Not estimable
Fridrich 1994	1	14	1	16	19.0%	1.15 [0.07, 20.34]
Jansisyanont 2008	1	60	1	62	19.8%	1.03 [0.06, 16.91]
Total (95% CI)		**131**		**135**	**100.0%**	**0.34 [0.08, 1.44]**
Total events	5		15			

Heterogeneity: $Tau^2 = 0.64$; $Chi^2 = 4.30$, df = 3 (P = 0.23); $I^2 = 30\%$
Test for overall effect: Z = 1.46 (P = 0.14)



SSI: surgical site infection; M-H: Mantel-Haenszel (test); CI: confidence interval

Funnel plot 5c. Types of procedure with decreased risk of SSI with a prolonged antibiotic regimen: orthognathic surgery (ii) >24 hours vs. <24 hours



Appendix 5: GRADE tables

Comparison 1: Continuation of antibiotic prophylaxis vs. a single dose

Quality assessment							№ of patients		Effect		Quality
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Prolonged antibiotic prophylaxis**	**Single dose of prophylaxis**	**Relative (95% CI)**	**Absolute (95% CI)**	
Surgical site infection overall											
44	RCT	serious [1]	not serious	not serious	not serious	none	509/8988 (5.7%)	556/8817 (6.3%)	**OR: 0.89** (0.77 to 1.03)	**7 fewer per 1000** (from 2 more to 15 fewer)	⊕⊕⊕◯ MODERATE

1. Risk of selection bias, performance bias, detection bias, attrition bias and reporting bias

RCT: randomized controlled trial; CI: confidence interval; OR: odds ratio

Comparison 2: Continuation of antibiotic prophylaxis for up to 24 hours vs. a single dose

Quality assessment							№ of patients		Effect		Quality
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Multiple postoperative doses**	**Single postoperative dose**	**Relative (95% CI)**	**Absolute (95% CI)**	
Surgical site infection											
1	RCT	serious [1,]	not serious	not serious	very serious [2]	none	39/114 (34.2%)	44/113 (38.9%)	**OR: 0.82** (0.47 to 1.40)	**46 fewer per 1000** (from 82 more to 159 fewer)	⨁◯◯◯ VERY LOW

1. Risk of selection and performance bias
2. Optimal information size not met and CI fails to exclude both appreciable benefit and harm (RR and RRR of 25%)

RCT: randomized controlled trial; CI: confidence interval; OR: odds ratio; RR: relative risk; RRR: relative risk reduction

Comparison 3: Continuation of antibiotic prophylaxis >24 hours postoperatively compared to continuation for up to 24 hours

Quality assessment							№ of patients		Effect		Quality
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Antibiotic prophylaxis continued >24 hours**	**Up to 24 hours**	**Relative (95% CI)**	**Absolute (95% CI)**	
Surgical site infection											
23	RCT	serious [1]	not serious	not serious	not serious	none	124/1527 (8.1%)	144/1557 (9.2%)	**OR: 0.89** (0.69 to 1.16)	**9 fewer per 1000** (from 13 more to 27 fewer)	⨁⨁⨁◯ MODERATE

1. Risk of selection bias, performance bias, detection bias, attrition bias and reporting bias

RCT: randomized controlled trial; CI: confidence interval; OR: odds ratio

Comparison 4: Continuation of antibiotic prophylaxis >48 hours compared to continuation for up to 48 hours

Quality assessment							№ of patients		Effect		Quality
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Antibiotic prophylaxis continued >48 hours**	**Up to 48 hours**	**Relative (95% CI)**	**Absolute (95% CI)**	
Surgical site infection											
3	RCT	serious [1]	not serious	not serious	very serious [2,3]	none	17/224 (7.6%)	17/233 (7.3%)	**OR: 1.04** (0.50 to 2.16)	**3 more per 1000** (from 35 fewer to 72 more)	⨁◯◯◯ VERY LOW

1. Risk of selection bias, performance bias, detection bias, attrition bias and reporting bias
2. Optimal information size not met and CI fails to exclude both appreciable benefit and harm (RR and RRR of 25%)

RCT: randomized controlled trial; CI: confidence interval; OR: odds ratio; RR: relative risk; RRR: relative risk reduction

Comparison 5a: How long should antibiotic prophylaxis be continued after cardiac surgery?

Quality assessment							№ of patients		Effect		Quality
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Prolonged antibiotic prophylaxis**	**Shorter**	**Relative (95% CI)**	**Absolute (95% CI)**	
Surgical site infection (Any prolonged regimen vs. a single dose)											
2	RCT	serious [1]	not serious	not serious	serious [2]	none	19/844 (2.3%)	42/838 (5.0%)	**OR: 0.43** (0.25 to 0.76)	**28 fewer per 1000** (from 12 fewer to 37 fewer)	⊕⊕◯◯ LOW
Surgical site infection (>24 hours vs. <24 hours)											
2	RCT	serious [1]	not serious	not serious	very serious [3]	none	10/139 (7.2%)	14/145 (9.7%)	**OR: 0.74** (0.32 to 1.73)	**23 fewer per 1000** (from 59 more to 63 fewer)	⊕◯◯◯ VERY LOW
Surgical site infection (>48 hours vs. 48 hours)											
1	RCT	serious [1]	not serious	not serious	very serious [3]	none	8/108 (7.4%)	5/119 (4.2%)	**OR: 1.82** (0.58 to 5.76)	**32 more per 1000** (from 17 fewer to 160 more)	⊕◯◯◯ VERY LOW

1. Risk of selection bias, performance bias, detection bias and reporting bias
2. Optimal information size not met
3. Optimal information size not met and CI fails to exclude both appreciable benefit and harm (RR and RRR of 25%)

RCT: randomized controlled trial; SSI: surgical site infection; CI: confidence interval; OR: odds ratio; RR: relative risk; RRR: relative risk reduction

Comparison 5b: How long should antibiotic prophylaxis be continued after vascular surgery?

Quality assessment							№ of patients		Effect		Quality
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Prolonged antibiotic prophylaxis**	**Single dose**	**Relative (95% CI)**	**Absolute (95% CI)**	
Surgical site infection											
1	RCT	serious [1]	not serious	not serious	serious [2]	none	15/149 (10.1%)	28/153 (18.3%)	**OR: 0.50** (0.25 to 0.98)	**82 fewer per 1000** (from 3 fewer to 130 fewer)	⨁⨁◯◯ LOW

1. Risk of detection and performance bias
2. Optimal information size not met

RCT: randomized controlled trial; CI: confidence interval; OR: odds ratio

Comparison 5c: How long should antibiotic prophylaxis be continued after orthognathic surgery?

Quality assessment							№ of patients		Effect		Quality
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Prolonged antibiotic prophylaxis**	**Single dose**	**Relative (95% CI)**	**Absolute (95% CI)**	
Surgical site infection (Any prolonged regimen *vs.* single dose)											
3	RCT	serious [1]	not serious	not serious	serious [2]	none	5/133 (3.8%)	16/133 (12.0%)	**OR: 0.30** (0.10 to 0.88)	**81 fewer per 1000** (from 13 fewer to 107 fewer)	⊕⊕◯◯ LOW
Surgical site infection (> 24 hours *vs.* <24 hours)											
5	RCT	serious [1]	not serious	not serious	very serious [3]	none	13/131 (9.9%)	7/135 (5.2%)	**OR 0.34** (0.08 to 1.44)	**34 fewer per 1000** (from 21 more to 47 fewer)	⊕◯◯◯ VERY LOW

1. Risk of selection bias, performance bias, detection bias and reporting bias
2. Optimal information size not met
3. Optimal information size not met and CI fails to exclude both appreciable benefit and harm (RR and RRR of 25%)

RCT: randomized controlled trial; CI: confidence interval; OR: odds ratio; RR: relative risk; RRR: relative risk reduction

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