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Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section (Review)

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[Intervention Review]

Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section

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ABSTRACT

Background

The single most important risk factor for postpartum maternal infection is cesarean section. Although guidelines endorse the use of prophylactic antibiotics for women undergoing cesarean section, there is not uniform implementation of this recommendation. This is an update of a Cochrane review first published in 1995 and last updated in 2010.

Objectives

To assess the effects of prophylactic antibiotics compared with no prophylactic antibiotics on infectious complications in women undergoing cesarean section.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 July 2014) and reference lists of retrieved papers.

Selection criteria

Randomized controlled trials (RCTs) and quasi-RCTs comparing the effects of prophylactic antibiotics versus no treatment in women undergoing cesarean section.

Data collection and analysis

Two review authors independently assessed the studies for inclusion, assessed risk of bias and carried out data extraction. The clinically important primary outcomes were wound infection, endometritis, serious maternal infectious complications and adverse effects on the infant. We presented dichotomous data as risk ratios (RR), with 95% confidence intervals (CIs) and combined trials in meta-analyses. We assessed the quality of evidence using the GRADE approach.

Main results

We identified 95 studies enrolling over 15,000 women. Compared with placebo or no treatment, the use of prophylactic antibiotics in women undergoing cesarean section reduced the incidence of wound infection (RR 0.40, 95% CI 0.35 to 0.46, 82 studies, 14,407 women), endometritis (RR 0.38, 95% CI 0.34 to 0.42, 83 studies, 13,548 women) and maternal serious infectious complications (RR 0.31, 95% CI 0.20 to 0.49, 32 studies, 6159 women). When only studies that included women undergoing an elective cesarean section were analyzed, there was also a reduction in the incidence of wound infections (RR 0.62, 95% CI 0.47 to 0.82, 17 studies, 3537 women) and endometritis (RR 0.38, 95% CI 0.24 to 0.61, 15 studies, 2502 women) with prophylactic antibiotics. Similar estimates of effect were seen whether the antibiotics

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were administered before the cord was clamped or after. The effect of different antibiotic regimens was studied and similar reductions in the incidence of infections were seen for most of the antibiotics and combinations.

There were no data on which to estimate the effect of maternal administration of antibiotics on infant outcomes. No studies systematically collected and reported on adverse infant outcomes nor the effect of antibiotics on the developing infant immune system. No studies reported on the incidence of oral candidiasis (thrush) in babies. Maternal adverse effects were also rarely described.

We judged the evidence for antibiotic treatment compared with no treatment to be of moderate quality; most studies lacked an adequate description of methods and were assessed as being at unclear risk of bias.

Authors' conclusions

The conclusions of this review support the recommendation that prophylactic antibiotics should be routinely administered to all women undergoing cesarean section to prevent infection. Compared with placebo or no treatment, the use of prophylactic antibiotics in women undergoing cesarean section reduced the incidence of wound infection, endometritis and serious infectious complications by 60% to 70%. There were few data on adverse effects and no information on the effect of antibiotics on the baby, making the assessment of overall benefits and harms difficult. Prophylactic antibiotics given to all women undergoing elective or non-elective cesarean section is beneficial for women but there is uncertainty about the consequences for the baby.

PLAIN LANGUAGE SUMMARY

Routine antibiotics at cesarean section to reduce infection

Women undergoing cesarean section have a five to 20-fold greater chance of getting an infection compared with women who give birth vaginally. These infections can be in the organs within the pelvis, around the surgical incision and sometimes the urine. The infections can be serious, and very occasionally can lead to the mother’s death. The potential benefits of reducing infection for the mother need to be balanced against any adverse effects such as nausea, vomiting, skin rash and rarely allergic reactions in the mother, and any effect of antibiotics on the baby, including thrush. This review looked at whether antibiotics are effective in preventing infection in women having a cesarean section. It also studied the effect of giving the antibiotics before or after the cord is clamped and different kinds of antibiotics. The review found 95 studies involving over 15,000 women. Routine use of antibiotics at cesarean section reduced the risk of wound and womb infections in mothers as well as the risk of serious complications of infections for the mothers by 60% to 70%. This was so whether the cesarean section was planned (elective) or not, and whether the antibiotics were given before or after clamping of the umbilical cord. The evidence to support antibiotic treatment was of moderate quality but often the way the study was done was not described well enough. None of the studies looked properly at possible adverse effects on the baby and so, although there are benefits for the mother, there is some uncertainty about whether there are any important effects on the baby.

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Summary of findings for the main comparison. Antibiotics versus no antibiotics for preventing infection after cesarean section

Antibiotics versus no antibiotics for preventing infection after cesarean section

Population: Women undergoing cesarean section.
Settings: Both high- and low-income countries.
Intervention: Antibiotic prophylaxis[1]

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Antibiotic prophylaxis				
Maternal wound infection	**Low (elective)[2]**		**RR 0.40** (0.35 to 0.46)	14407 (82 studies)	⊕⊕⊕⊖ **moderate** [3]	
	68 per 1000	**27 per 1000** (24 to 31)				
	Median[2]					
	89 per 1000	**36 per 1000** (31 to 41)				
	Other (includes emergency)[2]					
	97 per 1000	**39 per 1000** (34 to 45)				
Maternal endometritis	**Low (elective)[2]**		**RR 0.38** (0.34 to 0.42)	13548 (83 studies)	⊕⊕⊕⊖ **moderate** [3]	
	39 per 1000	**15 per 1000** (13 to 16)				
	Median[2]					
	160 per 1000	**61 per 1000** (54 to 67)				
	Other (includes emergency)[2]					

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	184 per 1000	**70 per 1000** (63 to 77)				
Maternal serious infectious complications	**25 per 1000** [4]	**8 per 1000** (5 to 12)	**RR 0.31** (0.2 to 0.49)	6159 (32 studies)	⊕⊕⊕⊖ **moderate** [5]	
Adverse effects on infant	See comment	See comment	Not estimable	0 (0)	See comment	Infant outcomes were not systematically collected nor reported. [6]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] All classes of antibiotics, dosing regimens (both before and after clamping of the cord) and routes of administration were included.
[2] The low risk baseline value is the mean of the control groups of studies reporting outcomes for elective cesarean sections; the other risk estimate is derived from the remaining studies in the review and includes emergency cesarean sections and studies which did not meet our criteria for elective.The median value from all studies is also reported.
[3] In most studies the assessment of bias was judged as unclear. In a third of studies the control group did not receive a placebo and lack of blinding could have influenced the assessment of outcomes. In less than 20% of studies was there an adequate description of sequence generation.
[4] The study population baseline risk is the mean value in the control groups from all studies that reported this outcome.
[5] There was no consistent approach to the definition of serious infectious complications; in only 32 studies was this outcome reported.
[6] No study reported effects of antibiotics on the infant immune system or outcome of oral thrush.

Summary of findings 2. Antibiotics versus no antibiotics for preventing infection after elective cesarean section

Antibiotics versus no antibiotics for preventing infection after elective cesarean section

Population: Women undergoing elective cesarean section
Settings: Both high- and low-income countries
Intervention: Antibiotic prophylaxis

Outcomes	Illustrative comparative risks* (95% CI)	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments

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	Assumed risk	Corresponding risk				
	Control	Antibiotic prophylaxis				
Maternal wound infection	**68 per 1000** [1]	**42 per 1000** (32 to 56)	**RR 0.62** (0.47 to 0.82)	3537 (17 studies)	⊕⊕⊕⊖ **moderate** [2]	
Maternal endometritis	**39 per 1000** [1]	**15 per 1000** (9 to 24)	**RR 0.38** (0.24 to 0.61)	2502 (15 studies)	⊕⊕⊕⊖ **moderate** [2]	
Maternal serious infectious complications	**0 per 1000**	**0 per 1000** (0 to 0)	**RR 1.01** (0.04 to 24.21)	545 (4 studies)	⊕⊕⊖⊖ **low** [3]	There was only one adverse event reported.
Adverse effects on infant	See comment	See comment	Not estimable	0 (0)	See comment	Infant outcomes were very infrequently reported

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] The study population baseline risk is the mean value in the control groups from all studies that included women undergoing elective cesarean section.
[2] In most studies the assessment of bias was judged as unclear.
[3] There was only one serious infectious complication reported.

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BACKGROUND

The single most important risk factor for postpartum maternal infection is cesarean section (Declercq 2007; Gibbs 1980). Women undergoing cesarean section have a five to 20-fold greater risk for infection and infectious morbidity compared with a vaginal birth. In Western countries the percentage of live births by cesarean section is around 27% (range 14.7% to 49%) (OECD 2013); in developing countries the overall rate is around 12% but varies widely by region (0.40% to 40%) (Thomas 2006). Infectious complications that occur after cesarean births are an important and substantial cause of maternal morbidity and are associated with a significant increase in hospital stay (Henderson 1995). Infections can affect the pelvic organs, the surgical wound, and the urinary tract.

Description of the condition

Infectious complications following cesarean birth include fever (febrile morbidity), wound infection, endometritis (inflammation of the lining of the uterus), and urinary tract infection. There can also occasionally be serious infectious complications including pelvic abscess (collection of pus in the pelvis), bacteremia (bacterial infection in the blood), septic shock (reduced blood volume due to infection), necrotizing fasciitis (tissue destruction in the uterine wall) and septic pelvic vein thrombophlebitis (inflammation and infection of the veins in the pelvis); sometimes these can lead to maternal mortality (Boggess 1996; Enkin 1989; Gibbs 1980; Leigh 1990).

Fever can occur after any operative procedure, and a low grade fever following a cesarean birth may not necessarily be a marker of infection (MacLean 1990). Without prophylaxis, the incidence of endometritis is about 20% and rates of wound infection and serious infectious complications as high as 25% have been reported (Enkin 1989). There has been no consistent application of a standard definition for endometritis nor wound infection, and surveillance strategies to confirm infection, especially following hospital discharge, vary widely (Baker 1995; Hulton 1992). Differences in ethnicity and socioeconomic status of the population studied will explain some of the variability in incidence, as will the use of different criteria to diagnose infection (Herbert 1999). Using the Centers for Disease Control (CDC) definitions for infection, the pooled mean rate of surgical site infections after cesarean section for US hospitals participating in the CDC and Prevention's National Nosocomial Infections Surveillance System (NNIS) from January 1992 through June 2004 was 3.15%, ranging from 2.71% for low-risk patients to 7.53% for high-risk patients (NNIS 2004). These rates, when compared with infection rates following other surgical procedures that are collected as part of the NNIS system, are high. Given the number of cesarean sections performed, these rates translate into very large numbers of women with an infectious complication following birth, and significant costs and morbidity.

Factors that have been associated with an increased risk of infection and infectious morbidity among women who have a cesarean include emergency cesarean section, labor and its duration, ruptured membranes and the duration of rupture, the socioeconomic status of the woman, number of prenatal visits, vaginal examinations during labor, internal fetal monitoring, urinary tract infection, anemia, blood loss, obesity, diabetes, general anesthesia, development of subcutaneous hematoma, the skill of the operator and the operative technique (Beattie 1994; Desjardins 1996; Enkin 1989; Gibbs 1980; Killian 2001; Magann 1995; Olsen 2008; Webster 1988). The association of bacterial vaginosis with an increased incidence of endometritis following cesarean birth has also been reported (Watts 1990).

The most important source of micro-organisms responsible for post-cesarean section infection is the genital tract, particularly if the membranes are ruptured. Even in the presence of intact membranes, microbial invasion of the intrauterine cavity is common, especially with preterm labor (Watts 1992). Infections are commonly polymicrobial (caused by many organisms). Pathogens isolated from infected wounds and the endometrium include *Escherichia coli* and other aerobic gram negative rods, group B streptococcus and other streptococcus species, *Enterococcus faecalis*, *Staphylococcus aureus* and coagulase negative staphylococci, anaerobes (including *Peptostreptococcus* species and *Bacteroides* species), *Gardnerella vaginalis* and genital mycoplasmas (Martens 1995; Roberts 1993; Watts 1991). Although *Ureaplasma urealyticum* is very commonly isolated from the upper genital tract and infected wounds, it is unclear whether it is a pathogen in this setting (Roberts 1993). Wound infections caused by *Staphylococcus aureus* and coagulase negative staphylococci arise from contamination of the wound with the endogenous flora of the skin at the time of surgery (Emmons 1988).

Description of the intervention

Guidelines recommend the use of antibiotics for prophylaxis for cesarean section, with the choice of antibiotic based on factors such as cost, half life, safety, antimicrobial resistance and spectrum of activity (ACOG 2011; Bratzler 2004; NICE 2011; SOGC 2010). There are over 20 antibiotic regimens that have been compared for cesarean section prophylaxis. Some of these drugs have activity against a narrow range of potential pathogens (e.g. metronidazole, gentamicin), others specifically have additional anaerobic activity (e.g. cefoxitin and cefotetan), others have activity against *Staphylococcus aureus* (e.g. cefazolin) and yet others have an extended spectrum of coverage (e.g. meropenem). Details of the different antibiotic regimens for prophylaxis at cesarean section that have been compared and their effectiveness are included in another Cochrane review (Alfirevic 2010)

There are differences in the route of administration of prophylactic antibiotics; for cesarean section the antibiotic is generally given intravenously. Usually a single dose is administered at the time of the procedure or multiple doses administered over a short period of time.

For cesarean section, prophylactic antibiotics are administered either before or after the cord is clamped (Classen 1992; Cunningham 1983; Wax 1997), although general guidelines for the prevention of surgical site infections now recommend the antimicrobial dose is administered before the incision to achieve low infection rates (Bratzler 2004). Recent meta-analyses on the timing of perioperative antibiotics for cesarean delivery have concluded that there was strong evidence that antibiotic prophylaxis that is given before skin incision decreases maternal infectious complications compared with intraoperative administration (Baaqeel 2013; Costantine 2008). However, it is argued that the timing of antibiotic administration may mask septic complications in the infant (Cunningham 1983). Additionally, if the antibiotic is given before cord clamping, the baby will be exposed to the antibiotic via the placenta, and there may be exposure through breast milk if the antibiotic is given either before or after

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cord clamping, though the passage of antibiotic through the breast milk is thought to minimal (Enkin 1989). Because of the potential for adverse outcomes for the baby and the effect on maternal infectious complications, this review investigated the timing of antibiotic administration (*see* Types of interventions).

How the intervention might work

General principles for the prevention of any surgical infection include sound surgical technique, skin antisepsis and antimicrobial prophylaxis (Owen 1994). Antibiotics administered prophylactically reduce the bacterial inoculum at the time of surgery and decrease the rate of bacterial contamination of the surgical site. An adequate antibiotic level in the tissue can augment natural immune defence mechanisms and help kill bacteria that are invariably inoculated into the wound at the time of surgery (Talbot 2005).

Potential adverse effects of antibiotic prophylaxis

There are commonly identified adverse effects of antibiotic therapy, which include gastrointestinal symptoms (nausea, vomiting or diarrhea), skin rashes, thrush (candidiasis, which can affect both mother and baby) and joint pain (Dancer 2004). There can also occasionally be blood problems, kidney or liver damage (Dancer 2004; Westphal 1994) and anaphylaxis (a hypersensitivity reaction to a foreign substance leading to shock and collapse, which can be fatal).

Because there are some data that antibiotics reaching the baby during labor, or in the very early postnatal period, can affect the pattern of bacterial flora in the infant gut, with the potential to affect the baby's developing immune system (Bedford Russell 2006; Weng 2013), it is important to assess the impact of antibiotics given to the mother on the baby's health.

Antibiotic prophylaxis may lead to increased drug resistant strains of bacteria which may be associated with infection. Resistant organisms may spread within the hospital and be associated with hospital-acquired drug resistant infections (Dancer 2004). These adverse effects cannot be assessed readily in randomized controlled trials, and additional research needs to be undertaken to assess the impact of prophylactic antibiotic use on the level of resistant bacteria, e.g. MRSA and *C. difficile* in hospitals.

Why it is important to do this review

Surveys suggest that there is inconsistent and variable application of the use of prophylactic antibiotics at cesarean sections (Huskins 2001; Morisaki 2014; Olsen 2008; Pedersen 1996). Prophylactic antibiotics have been shown, in previous versions of this review, to be effective in reducing febrile morbidity, endometritis, wound infection and urinary tract infection (Smaill 1995a; Smaill 1995b; Smaill 2002; Smaill 2010). In addition, both ampicillin and first generation cephalosporins appeared to have similar efficacy in reducing post-operative endometritis, and while there did not appear to be any added benefit in utilizing a more broad spectrum agent or a multiple dose regimen (Alfirevic 2010), other authors have questioned whether an extended spectrum agent should be recommended (Tita 2009). It is important to update this evidence with more recent studies, to update the review methodology, to perform a subgroup analysis based on class of antibiotic and also to address the question of whether increasing antimicrobial resistance has had an impact on the benefit of antibiotic prophylaxis.

The adverse effects of antibiotics for the woman and her infant and the potential for increased use of antimicrobial prophylaxis to contribute to the development of antimicrobial resistance are important considerations (Racinet 1990; Shlaes 1997), as are the cost-effectiveness of different strategies (Mugford 1989). As well, it is important to assess any possible impact of maternal antibiotic treatment on the baby, as there is evidence that antibiotics given near or shortly after birth can affect the infant's gut bacterial flora, with the potential to impact mucosal and systemic immune function (Bedford Russell 2006; Weng 2013).

Particularly controversial is whether antibiotic treatment should be given to all mothers or only to those at greatest risk of infection (Ehrenkranz 1990; Gilstrap 1988; Howey 1990; Suonio 1989). Women undergoing cesarean section can be divided into low- and high-risk groups for infection, with women undergoing an elective (planned or primary) procedure at lowest risk (ACOG 2011). Women at high risk include those undergoing cesarean section after rupture of the membranes or onset of labor (ACOG 2011). It has been suggested that institutions with a low levels of baseline infections may see no impact of routine use of antibiotics, while institutions with high baseline infection rates may see a benefit. We were interested to see if there was a difference in effectiveness depending on whether the women were at low or high risk of infection and performed a subgroup analysis based on whether the cesarean section was a planned procedure (elective) or whether there was active labor or ruptured membranes (non-elective).

This review will focus on whether antibiotics do more good than harm overall. Additional ways for trying to reduce post-cesarean infections include: skin preparation at cesarean section (Hadiati 2012); surgical technique (Dodd 2014), double gloving or changing gloves (or both) before closure; peritoneal lavage; and vaginal antiseptic solution preparation (Haas 2013).

OBJECTIVES

To determine, from the best evidence available, the effectiveness of prophylactic antibiotics compared with placebo, or no treatment, given to women when undergoing a cesarean section for reducing the incidence of febrile morbidity, wound infection, endometritis, urinary tract infection or any serious infectious complication, and to assess potential maternal adverse effects and any impact on the infant, either short term or long term.

METHODS

Criteria for considering studies for this review

Types of studies

All randomized controlled trials (RCTs) to evaluate the effects of prophylactic antibiotics in women undergoing cesarean section were included. Quasi-RCTs were also included. We planned to include cluster-RCTs should any be identified but cross-over trials are inappropriate for this question.

Types of participants

Women undergoing cesarean section, both elective (planned) and non-elective/emergency.

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Types of interventions

Trials were considered if they compared any prophylactic antibiotic regimen administered for cesarean section with placebo or no treatment.

Types of outcome measures

Primary outcomes

Maternal

1. Febrile morbidity (fever)
2. Wound infection (infection of the surgical incision)
3. Endometritis (inflammation of the lining of the womb)
4. Serious infectious complication (such as bacteremia, septic shock, septic thrombophlebitis, necrotizing fasciitis, or death attributed to infection)

Infant

1. Immediate adverse effects of antibiotics on the infant (unsettled, diarrhea, rashes)
2. Oral thrush (candidiasis)

Secondary outcomes

Maternal

1. Urinary tract infection
2. Adverse effects of treatment on the woman (e.g. allergic reactions, nausea, vomiting, diarrhea, skin rashes, yeast infections)
3. Length of stay in hospital

Infant

1. Length of stay in hospital
2. Long-term adverse effects (e.g. general health; frequency of visits to hospital)
3. Immune system development (using a validated scoring assessment)

Additional outcomes

1. Development of bacterial resistance
2. Cost

Search methods for identification of studies

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Electronic searches

We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (31 July 2014).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of Embase;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and Embase, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

Searching other resources

We searched the reference lists at the end of papers for further studies.

We did not apply any language restrictions.

Data collection and analysis

For methods used in the previous update, please see Smaill 2010.

For this update (2014), the following methods, based on a standard template used by the Cochrane Pregnancy and Childbirth Group, were used.

Selection of studies

Two review authors independently assessed for inclusion all the potential studies identified as a result of the search strategy. We resolved any disagreement through discussion.

Data extraction and management

We designed a form to extract data. For eligible studies, two review authors extracted the data using the agreed form. We resolved discrepancies through discussion. Data were entered into Review Manager software (RevMan 2014) and checked for accuracy. Where participants were randomized to more than two treatment groups either the intervention groups were combined to create a single pair-wise comparison or the no treatment group was divided approximately evenly into two or more groups and independent comparisons made between intervention and no treatment groups (see details in Characteristics of included studies).

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Any disagreement was resolved by discussion.

(1) Random sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

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We have assessed the method as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We have assessed the methods as:

- low risk of bias (e.g. telephone or central randomization; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes, but an overall estimate of performance bias was reported.

We have assessed the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes but an overall estimate of detection bias was reported.

We have assessed methods used to blind outcome assessment as:

- low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total randomized participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we re-included missing data in the analyses which we undertook.

We have assessed methods as:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as-treated' analysis done with substantial departure of intervention received from that assigned at randomization);
- unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

We assessed the methods as:

- low risk of bias (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of bias (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

We planned to describe for each included study any important concerns we had about other possible sources of bias.

For this update the quality of the evidence was assessed using the GRADE approach (Schunemann 2009) in order to assess the quality of the body of evidence relating to the following key outcomes for the main comparison of all cesarean sections and the subgroup of elective cesarean sections:

1. Wound infection
2. Endometritis
3. Serious infectious complications
4. Infant outcomes

GRADE profiler (GRADE 2008) was used to import data from Review Manager 5.3 (RevMan 2014) in order to create 'Summary of findings' tables. A summary of the intervention effect and a measure of quality for each of the above outcomes was produced using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high quality' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

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Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.

Continuous data

We used the mean difference if outcomes were measured in the same way between trials. We planned to use the standardized mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomized trials

We did not identify any cluster-randomized trials, but we would include cluster-randomized trials along with individually-randomized trials in the analysis if we identify any in future updates to this review. We would adjust their sample size using the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we used ICCs from other sources, we would report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If, in future updates, we identify cluster-randomized trials, we plan to synthesize the relevant information. We would consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomization unit is considered to be unlikely. We would also acknowledge heterogeneity in the randomization unit and perform a sensitivity analysis to investigate the effects of the randomization unit.

Cross-over trials

Cross-over trials are inappropriate for this question.

Dealing with missing data

For included studies, levels of attrition were noted. In a subsequent update of this review, we will include a sensitivity analysis, with poor quality studies with high levels of missing data excluded from the analysis.

For all outcomes, analyses were carried out, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomized to each group in the analyses. The denominator for each outcome in each trial was the number randomized minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the I^2 and Tau^2 or Chi^2 statistics. We regarded heterogeneity as substantial if an I^2 was greater than 30% and either the Tau^2 was greater than zero, or there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

We investigated reporting biases (such as publication bias) using funnel plots for the main analyses of the primary outcomes. In future updates, if asymmetry is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2014). We used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect, i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar.

We planned that if there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, we would use random-effects meta-analysis to produce an overall summary if an average treatment effect across trials was considered clinically meaningful. The random-effects summary would be treated as the average range of possible treatment effects and the clinical implications of treatment effects differing between trials would be discussed. If the average treatment effect was not clinically meaningful, we would not combine trials. Where we used random-effects analyses, the results were presented as the average treatment effect with 95% confidence intervals, and the estimates of Tau^2 and I^2.

Subgroup analysis and investigation of heterogeneity

We carried out the following subgroup analyses to address specific questions about particular patient groups and types of interventions.

1. By antibiotic regimen (see Table 1 for classification based on class of antibiotic, spectrum of activity and drug combinations).
2. By type of surgery: (a) elective cesarean section; (b) non-elective cesarean section; and (c) mixed or not defined. (Rupture of membranes for more than six hours or the presence of labor was used to differentiate a non-elective cesarean section from an elective procedure.)
3. By time of administration: (a) before cord clamping; (b) after cord clamping; (c) not defined.

The following outcomes were used in subgroup analysis.

Maternal

1. Febrile morbidity (fever)
2. Wound infection (infection of the surgical incision)
3. Endometritis (inflammation of the lining of the womb)
4. Serious infectious complication (such as bacteremia, septic shock, septic thrombophlebitis, necrotizing fasciitis, or death attributed to infection)
5. Urinary tract infection

Infant

1. Immediate adverse effects of antibiotics on the infant (unsettled, diarrhea, rashes)
2. Oral thrush (candidiasis)

If we had identified substantial heterogeneity, we would have investigated it using the subgroup analyses. We would have considered whether an overall summary was meaningful, and if it was, used random-effects analysis to produce it. We did assess

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subgroup differences by interaction tests available within RevMan (RevMan 2014). The results of subgroup analyses quoting the Chi^2 statistic and P value, and the interaction test I^2 value have been calculated.

Sensitivity analysis

We performed a sensitivity analysis to explore the effect of trial quality assessed by concealment of allocation (quasi-randomized trials), with these poor quality studies being excluded from the analyses, in order to assess whether this made any difference to the overall result. We plan to explore in a subsequent update to this review the effect of other sources of bias on the estimate of outcomes by performing additional sensitivity analyses, e.g. examine the effects of only including studies where there was a low risk of allocation bias and selection bias (i.e. effective blinding of participants and personnel).

RESULTS

Description of studies

Results of the search

The search of the Cochrane Pregnancy and Childbirth Group's Trials Register identified 134 reports of 120 studies. Ninety-five studies were included (Characteristics of included studies), 25 were excluded (Characteristics of excluded studies). We found no additional studies through searching reference lists.

Included studies

The 95 studies that met the inclusion criteria for this review enrolled over 15,000 women. For detailed information on the studies, *see* table of Characteristics of included studies. No study reported on baseline risk of infection before the intervention. Most studies adequately described the characteristics of the women who were enrolled, including details of the indication for cesarean section, mean duration of labor and membrane rupture and number of repeat sections. Several studies included a majority of women who were identified as from a low socioeconomic group, but other studies enrolled women who were not perceived to be at an increased risk of infection because of socioeconomic status. One study included information on the number of women who were HIV positive (Bagratee 2001). In no study were details on the incidence of bacterial vaginosis provided. One more recent study reported that there were no methicillin-resistant *Staphylococcus aureus* infections in the study population (Witt 2011).

Setting

While the majority of the studies included in the review were conducted in developed countries (e.g. US, Western Europe, Scandinavia, Canada and New Zealand), studies were reported from developing countries including Sudan, Nigeria, Tunisia, Kenya, Zimbabwe, and South Africa as well as Mexico, Greece, Turkey, Israel, the Middle East, China and Malaysia.

Type of cesarean section

One objective of this review was to study the effect of prophylaxis in both elective and non-elective cesarean sections, and strict definitions of an elective and non-elective cesarean section were used by the authors of this review to categorize women and studies. In 17 studies (N = 3500), data on women undergoing an elective cesarean section were available (Adam 2005; Bagratee 2001; Dashow 1986; Duff 1982; Huam 1997; Jaffe 1984; Jakobi 1994; Kolben 2001; Lemus 2005; Mahomed 1988; Rizk 1998; Rothbard 1975; Rouzi 2000; Shah 1998; Sziller 1994; Ujah 1992; Wu 1991). In 22 studies (N = 2500), there were data on non-elective procedures (Conover 1984; D'Angelo 1980; Elliott 1986; Freeman 1982; Fugere 1983; Gibbs 1981; Harger 1981; Hawrylyshyn 1983; Heilmann 1984; Jaffe 1984; Leonetti 1989; Moodley 1981; Ross 1984; Rothbard 1975; Ruiz-Moreno 1991; Scarpignato 1982; Schedvins 1986; Tzingounis 1982; Weissberg 1971; Wong 1978; Work 1977; Young 1983). Two studies included both women having elective cesareans and non-elective cesareans (Jaffe 1984; Rothbard 1975). The remaining, and the majority of studies did not differentiate between an elective or non-elective procedure, or the definitions used were not consistent with those used in this review; these have been grouped as 'both' or 'undefined'. Often a repeat section had been classified as elective by the study authors, but it was not always evident that all of these women were indeed not in labor and often the duration of membrane rupture was unclear. Fifty-nine studies (N = 8500) included women whose procedures were classified as undefined type of cesarean section (Adeleye 1981; Allen 1972; Apuzzio 1982; Battarino 1988; Bibi 1994; Bilgin 1998; Bourgeois 1985; Carl 2000; Chan 1989; Cormier 1989; Dashow 1986; De Boer 1989; Dillon 1981; Duff 1980; Engel 1984; Escobedo 1991; Gall 1979; Ganesh 1986; Garcia 1992; Gerstner 1980; Gibbs 1972; Gibbs 1973; Gordon 1979; Gummerus 1984; Hager 1983; Hagglund 1989; Ismail 1990; Jaffe 1985; Karhunen 1985; Kellum 1985; Kreutner 1978; Kristensen 1990; Lapas 1988; Levin 1983; Lewis 1990; McCowan 1980; Miller 1968; Moro 1974; Morrison 1973; Ng 1992; Oestreicher 1987; Padilla 1983; Phelan 1979; Polk 1982; Racinet 1990; Reckel 1985; Rehu 1980; Roex 1986; Rouzi 2000; Rudd 1981; Saltzman 1985; Sokolowski 1989; Stage 1982; Stiver 1983; Tully 1983; Turner 1990; Walss Rodriguez 1990; Witt 2011; Yip 1997). Two studies reported both elective and in labor/high risk (Dashow 1986) or emergency cesarean sections (Rouzi 2000); the in labor/high risk and emergency sections, however, did not meet our definition of non-elective and these have been classified as "undefined" .

Timing of antibiotic administration

Antibiotics for prophylaxis were administered intravenously either at the start of the operative procedure ("before cord") or at or after clamping of the cord. In 40 studies (N = 5600), data on outcomes were available when the antibiotic had been administered before clamping of the cord (Adam 2005; Adeleye 1981; Allen 1972; Bibi 1994; Chan 1989; De Boer 1989; Duff 1980; Duff 1982; Freeman 1982; Gall 1979; Gerstner 1980; Gibbs 1972; Gibbs 1973;Gordon 1979; Hagglund 1989; Heilmann 1984; Huam 1997; Jaffe 1984; Jaffe 1985; Kreutner 1978; Lapas 1988; Magro 1983; Mahomed 1988; McCowan 1980: Miller 1968; Moodley 1981; Moro 1974; Morrison 1973; Ng 1992; Phelan 1979; Reckel 1985; Rehu 1980; Ross 1984; Rothbard 1975; Stage 1982; Turner 1990; Tzingounis 1982; Witt 2011; Work 1977; Yip 1997). This was variably described as "pre-operatively", "with induction of anaesthesia" or "before clamping of the cord". In 51 studies (N = 8400), the antibiotic was administered at or after cord clamping (Apuzzio 1982; Bagratee 2001; Battarino 1988; Bourgeois 1985; Bilgin 1998; Carl 2000; Conover 1984; Cormier 1989; D'Angelo 1980; Dashow 1986; Dillon 1981; Elliott 1986; Engel 1984; Escobedo 1991; Fugere 1983; Ganesh 1986; Garcia 1992; Gibbs 1981; Gordon 1979; Gummerus 1984; Hager 1983; Harger 1981; Hawrylyshyn 1983; Ismail 1990; Jakobi 1994; Karhunen 1985; Kellum 1985; Kristensen 1990; Lemus 2005; Leonetti 1989; Levin 1983; Lewis 1990; Oestreicher 1987; Polk 1982; Racinet 1990;

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Rizk 1998; Roex 1986; Rouzi 2000; Rudd 1981; Ruiz-Moreno 1991; Saltzman 1985; Shah 1998; Sokolowski 1989; Stiver 1983; Sziller 1994; Tully 1983; Walss Rodriguez 1990; Witt 2011; Wong 1978; Wu 1991; Young 1983). Included in this group were studies where irrigation of the peritoneal or uterine cavity with an antibiotic containing solution was compared with either saline irrigation or no irrigation (Bourgeois 1985; Carl 2000; Conover 1984; Dashow 1986; Elliott 1986; Kellum 1985; Levin 1983; Lewis 1990; Rudd 1981; Wu 1991). There were six studies where there was insufficient information to know when the antibiotic had been administered, e.g. "operatively" or the results had been combined and these have been grouped together as "timing not defined" (Kolben 2001; Padilla 1983; Scarpignato 1982; Schedvins 1986; Ujah 1992; Weissberg 1971). In two studies, results were available for antibiotic administration both before and after clamping of the cord (Gordon 1979; Witt 2011).

Classes of antibiotics

The antimicrobial agents most often used in the trials included ampicillin, a first generation cephalosporin (usually cefazolin), a second generation cephalosporin (cefamandole or cefuroxime) or a cefamycin (cefoxitin, cefotetan), metronidazole, penicillins with an extended spectrum of activity (e.g. ticarcillin, mezlocillin or pipericillin), a beta-lactam/beta-lactamase inhibitor combination and an aminoglycoside-containing combination; *see* Characteristics of included studies for a classification of the antimicrobial agent used by antibiotic class. The penicillins have been divided into natural penicillin, penicillinase-resistant penicillins, aminopenicilins (ampicillin), extended spectrum penicillins which include carboxypenicillins (carbenicillin, ticarcillin) and ureidopenicillins (mezlocillin, pipericillin) and beta-lactam-beta-lactamase inhibitor combinations. The second generation cephalosporins include the cefamycins (cefoxitin and cefotetan) that have extended anaerobic coverage. In one study antimicrobial prophylaxis was administered by rectal suppository (De Boer 1989) and in four studies follow-up doses were administered by rectal suppository (Gerstner 1980; McCowan 1980; Ross 1984) or vaginal tablet (Sokolowski 1989). The duration of the post-operative treatment course varied from a single intravenous dose to as long as a week. While most studies were published in the 1980s, new studies have continued to be performed in the 1990s and the last study was published as recently as 2011.

Assessing outcomes

The clinical criteria listed to define endometritis were consistent across trials. Febrile morbidity is a standard obstetrical outcome and was generally consistently reported although there was some variation in the exact criteria used for height of fever, interval between febrile episodes and interval from the operative procedure. Urinary tract infection generally meant a positive urine culture; symptoms related to the urinary tract were rarely required to be present. Wound infection usually was a clinical diagnosis and generally included induration, erythema, cellulitis or various degrees of drainage. A positive microbiological diagnosis was rarely required for the diagnosis of either wound infection or endometritis. There was no consistent approach to the definition of serious infectious morbidity. For this review, all episodes of bacteremia have been classified as serious as have other complications such as pelvic abscess, pelvic thrombophlebitis and peritonitis. Some studies included other outcomes, e.g. need for additional antibiotic use and other infections, e.g. pneumonia. Some provided a measure of the fever as a 'fever index' which incorporated both the height of the fever and its duration. Where the duration of maternal hospital stay with its standard deviation was reported, this has been included.

Side effects

Very few studies appeared to have consistently sought maternal side effects or neonatal/infant side effects and similarly it was a minority of studies that collected data on infectious complications after discharge.

Costs

Three studies compared the cost of antibiotics between groups (Bibi 1994; Kristensen 1990; Racinet 1990). See Characteristics of included studies for details.

Excluded studies

Of those studies excluded from the analysis, some were because clinical outcomes for the women undergoing cesarean section were not reported separately or all women had received some form of antibiotic treatment and then were randomized to another intervention. For some studies, although the trial was initially randomized, part-way through the study the placebo arm was dropped. Due to the results on the initially randomized part of the study not being available, these studies were not included (*See* table of Characteristics of excluded studies for further details).

Risk of bias in included studies

The methodological quality of the trials was mostly unclear, explained in large part because the studies were undertaken a number of years ago, before the recent understanding of sources of bias in randomized controlled trials (Figure 1; Figure 2).

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Figure 1. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

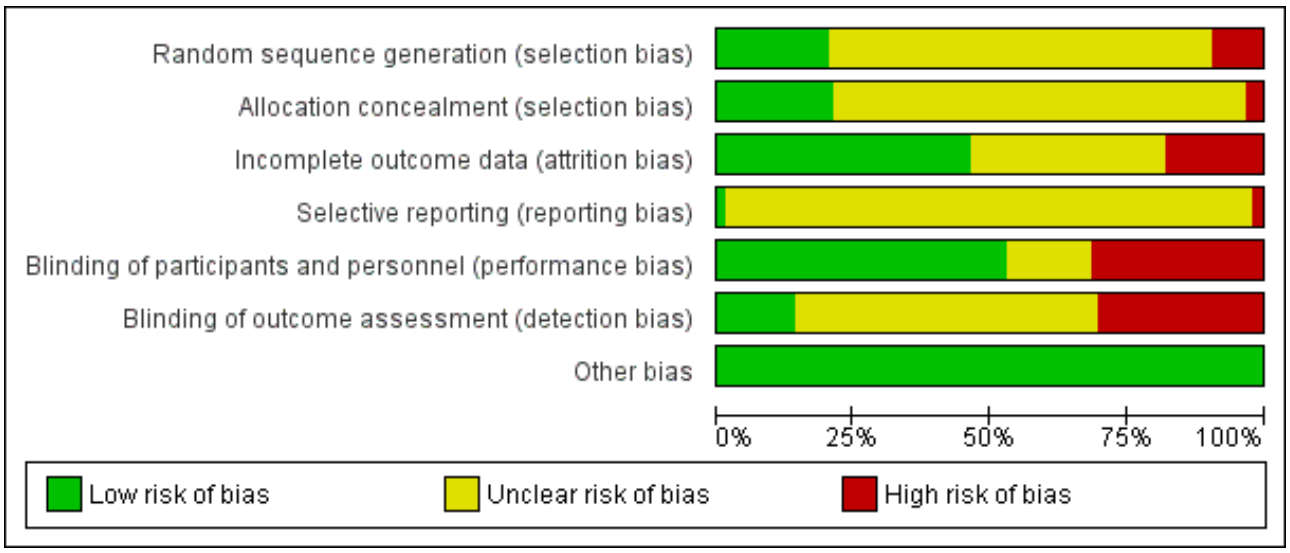

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Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

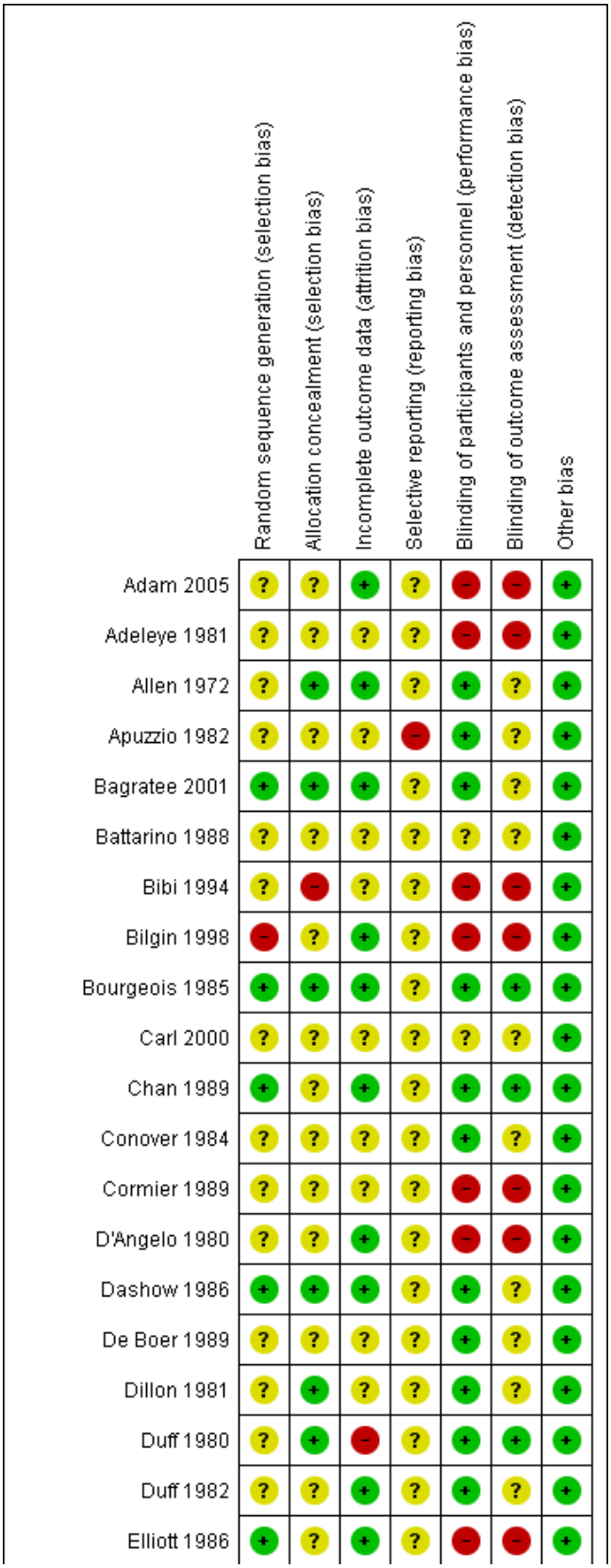

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Figure 2. (Continued)

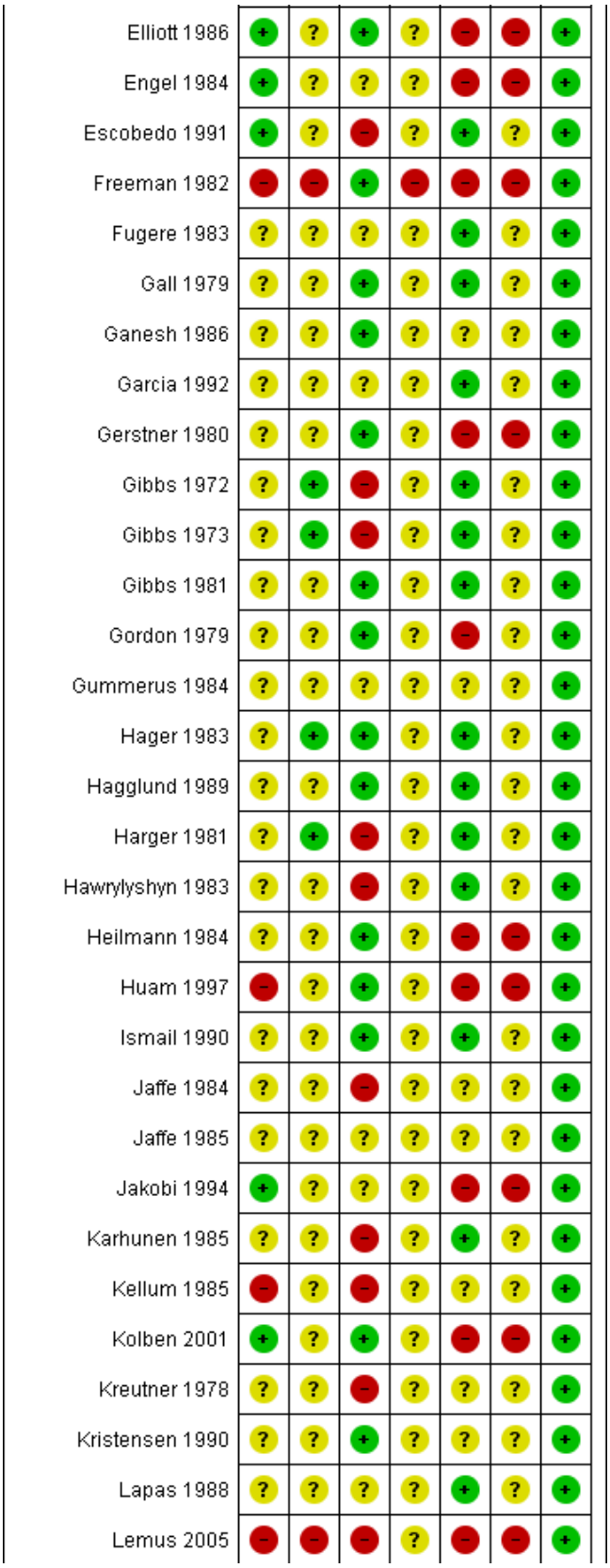

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Figure 2. (Continued)

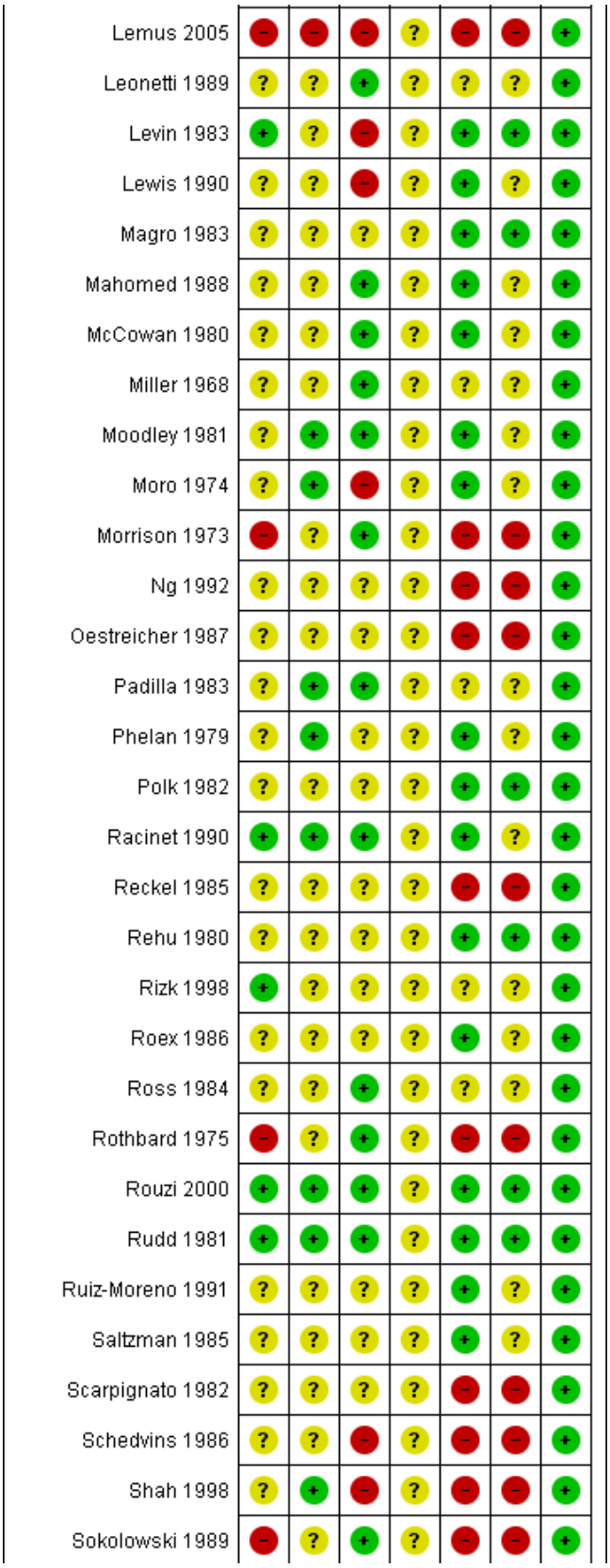

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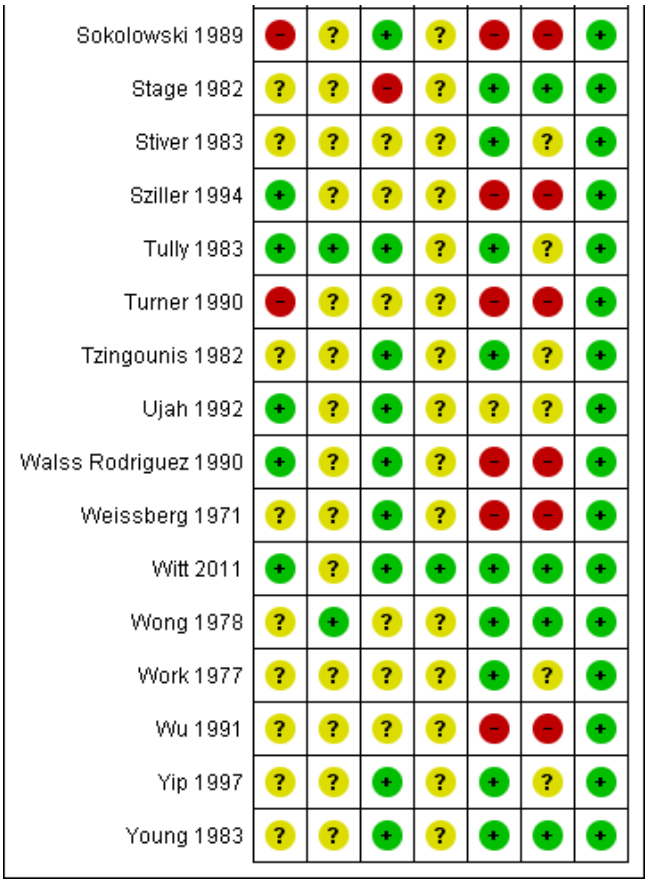
Figure 2. (Continued)



Allocation

In less than 20% of studies, we judged there was a low risk of selection bias based on an adequate generation of a randomized sequence, such as referring to a random number table or "drawing lots". Most studies, however, did not describe the sequence generation process and were assessed as "unclear". Several studies where participants were allocated to treatment group by date of birth or hospital number were classified as quasi-RCTs and judged at high risk of selection bias.

Blinding

In almost a third of studies there was no blinding and the control group received no treatment. Performance bias and detection bias were judged as low when there was an adequate description of the steps taken to ensure blinding. However, although many studies were described as "double-blind, placebo-controlled", there was often insufficient information provided to be confident all members of the study team were blinded to allocation, that the outcome assessment was performed without knowledge of the treatment group, nor certainty that the blind could not be broken. The outcomes of wound infection and endometritis, which require clinical judgement, could be influenced by lack of blinding.

Incomplete outcome data

In most studies, all women who were initially randomized were included in the outcomes and an intention-to-treat analysis was performed. Where dropouts were reported, insufficient data were usually provided for them to be included in an intention-to-treat analysis. Where the group allocation of dropouts was not provided, there was the possibility that there may have been selective withdrawals from one or other of the groups. There were some studies where a discrepancy in the numbers allocated to the randomized groups, unlikely to have occurred by chance, was not accounted for. In most cases the numbers in the placebo group were smaller than those in the treatment group, raising the possibility of selective withdrawals not mentioned in the published report.

Selective reporting

We judged this as unclear for all studies as there were no study protocols available. However, it does appear for most of the studies that all the expected outcomes were included.

Other potential sources of bias

We judged this as low for all studies as no other important sources of bias were identified.

Effects of interventions

See: **Summary of findings for the main comparison** Antibiotics versus no antibiotics for preventing infection after cesarean section; **Summary of findings 2** Antibiotics versus no antibiotics for preventing infection after elective cesarean section

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1. Antibiotic prophylaxis versus no prophylaxis (Analyses 1.1 to 1.7)

The overall findings were as follows:

Primary outcomes

There were reductions in all the maternal primary outcomes: febrile morbidity (average risk ratio (RR) 0.45; 95% confidence interval (CI) 0.40 to 0.51, 56 studies, 9046 women (Tau^2 = 0.07; Chi^2 = 89.58, df = 55 (P = 0.002); I^2 = 39% (Analysis 1.1); wound infection (RR 0.40; 95% CI 0.35 to 0.46, 82 studies, 14,407 women (Chi^2 = 102.56, df = 79 (P = 0.04); I^2 = 23% (Analysis 1.2); endometritis (RR 0.38; 95% CI 0.34 to 0.42), 83 studies, 13,548 women (Chi^2 = 90.59, df = 79 (P = 0.19); I^2 = 12% (Analysis 1.3); and serious infectious morbidity (RR 0.31; 95% CI 0.20 to 0.49, 32 studies, 6159 women (Chi^2 = 14.26, df = 27 (P = 0.98); I^2 = 0% (Analysis 1.4).

There was no evidence of substantial heterogeneity amongst the studies contributing to each of the outcomes reported except for what we judged a moderate degree of heterogeneity amongst those studies reporting febrile morbidity. This could be explained by different criteria used in the studies to define fever/ febrile morbidity. See Characteristics of included studies.

There were no data in any of the studies on the two infant primary outcomes of immediate adverse effects and infant thrush.

Secondary outcomes

There were reductions in maternal urinary tract infection (RR 0.56; 95% CI 0.49 to 0.65, 66 studies, 10,928 women (Analysis 1.5) . Only 13 studies collected data on maternal adverse effects; more adverse events were observed in the treatment group (RR 2.43; 95% CI 1.00 to 5.90), 2131 women (Analysis 1.6). The most common side effect was rash, followed by phlebitis at the site of the intravenous infusion. There were no serious drug-related adverse events reported. The difference in maternal length of stay in hospital (average mean difference (MD) -0.46, 95% CI -0.65 to -0.28), 3168 women (Analysis 1.7), reported in 19 studies was judged not clinically important.

There were no data in any of the studies on the other secondary outcomes.

Reporting bias

There was a potential for publication bias in the assessment of febrile morbidity, as judged by visual inspection of the funnel plot (Figure 3); however, we estimated that any reporting bias was unlikely to influence the results because of the large number of participants in the symmetrical part of the plot. There was no funnel plot asymmetry for the other primary outcomes (Figure 4; Figure 5; Figure 6).

Figure 3. Funnel plot of comparison: 1 Antibiotic versus no antibiotics, outcome: 1.1 Maternal febrile morbidity/ fever.

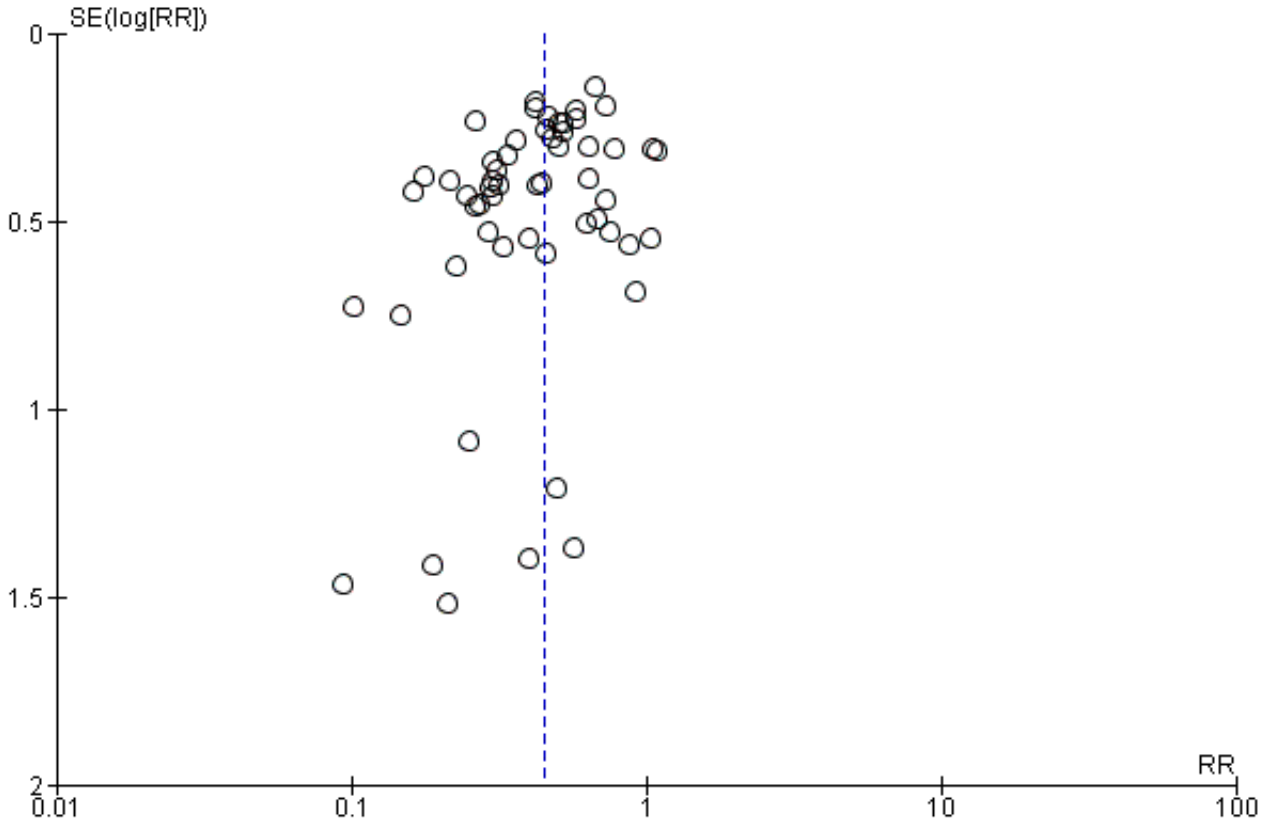

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Figure 4. Funnel plot of comparison: 1 Antibiotic versus no antibiotics, outcome: 1.2 Maternal wound infection.

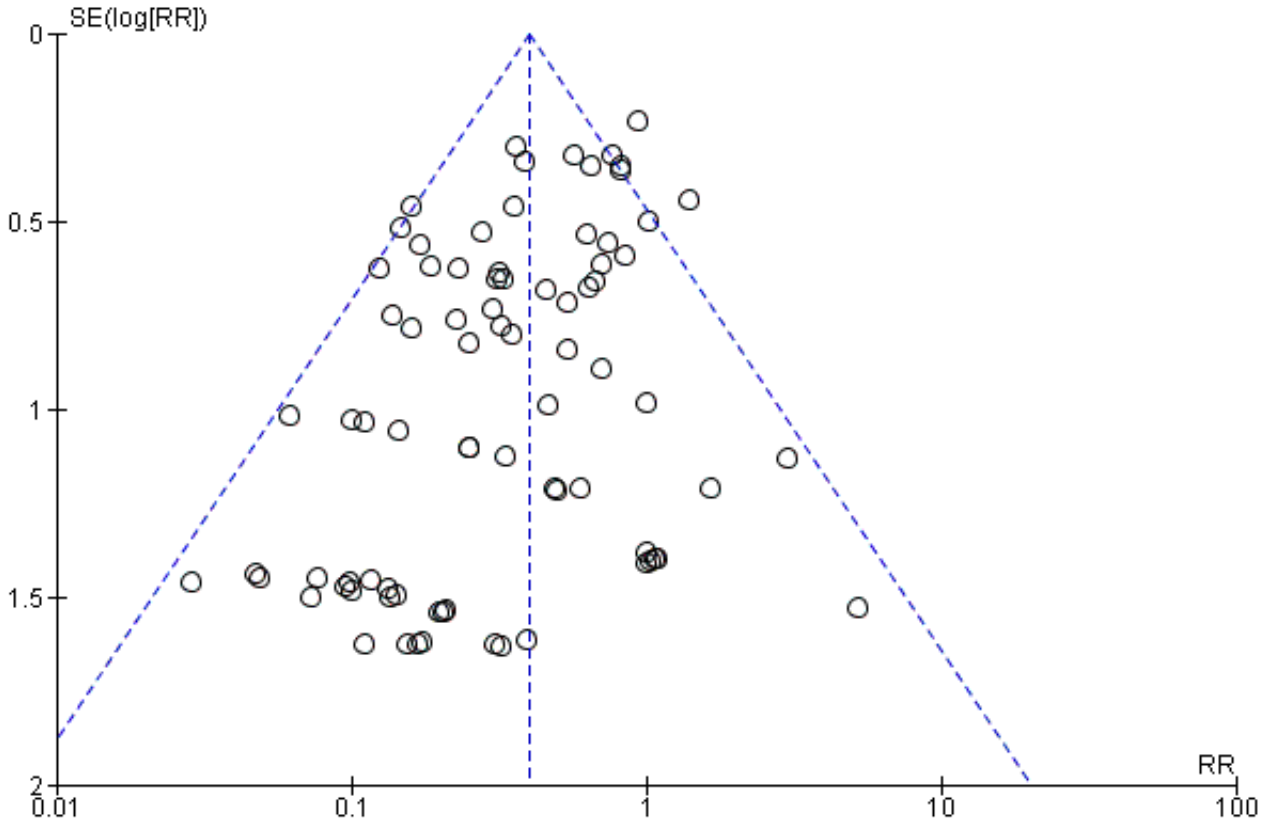

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Figure 5. Funnel plot of comparison: 1 Antibiotic versus no antibiotics, outcome: 1.3 Maternal endometritis.

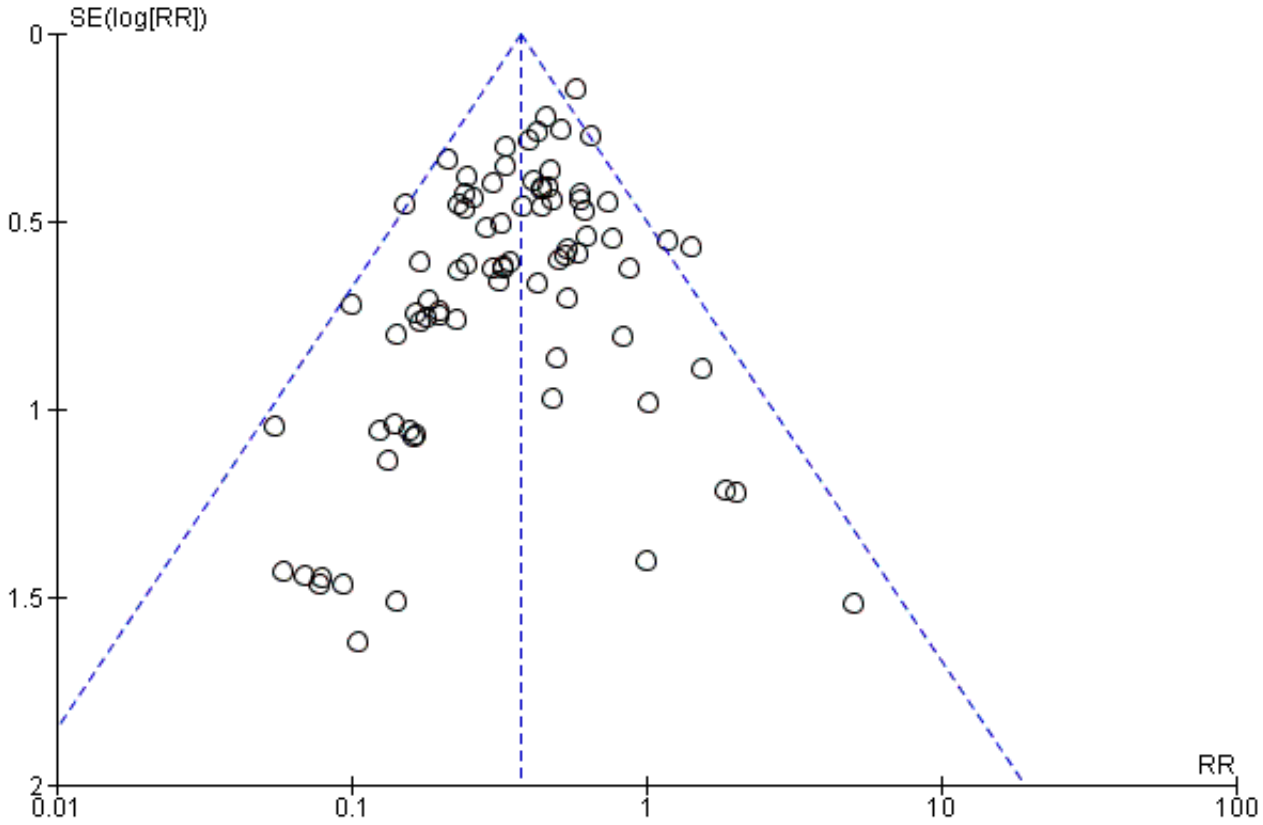

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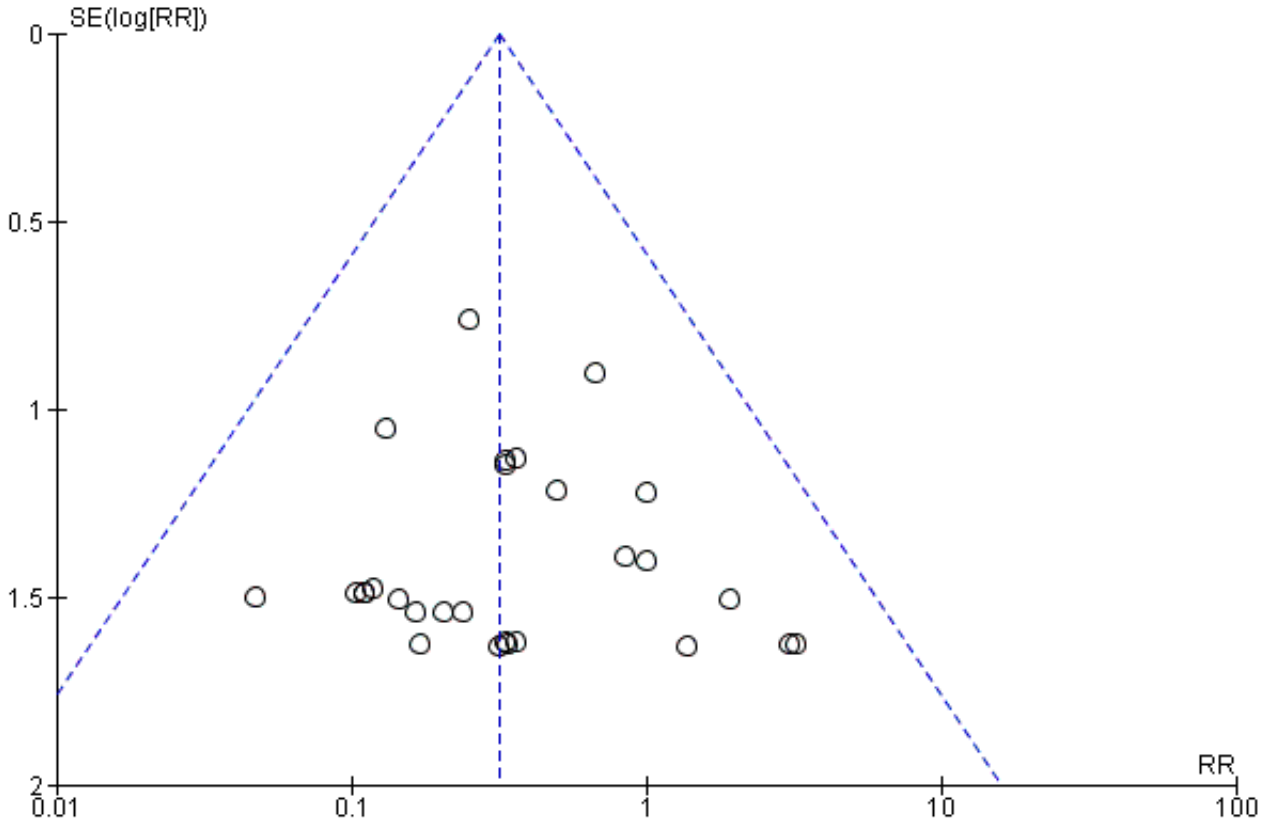
Figure 6. Funnel plot of comparison: 1 Antibiotic versus no antibiotics, outcome: 1.4 Maternal serious infectious complications.



Study quality

We undertook a sensitivity analysis on the primary outcomes by study quality, omitting the nine quasi-RCTs (Bilgin 1998; Freeman 1982; Huam 1997; Kellum 1985; Lemus 2005; Morrison 1973; Rothbard 1975; Sokolowski 1989; Turner 1990). The overall findings remained very similar with reductions for all the primary outcomes: febrile morbidity (average RR 0.47; 95% CI 0.41 to 0.53, 50 studies, 7852 women; wound infection (average RR 0.40; 95% CI 0.35 to 0.46, 76 studies, 12,669 women; endometritis (RR 0.39; 95% CI 0.35 to 0.43, 77 studies, 12,680 women). Serious infectious morbidity remained the same as the analysis contained no quasi-RCTs.

2. Antibiotic prophylaxis versus no prophylaxis, subgroups by antibiotic regimen (Analyses 2.1 to 2.7)

There were no studies that reported on treatment with monotherapy with a penicillinase-resistant penicillin, fourth generation cephalosporin, carbapenem, tetracycline, macrolide, and aminoglycosides. Approximately two thirds of studies evaluated treatment with a first or second generation cephalosporin, including cefamycins, or ampicillin.

For all subgroups based on antibiotic regimen there were reductions in the maternal primary outcomes and maternal urinary tract infections. By inspection of the graphs visually there was no evidence of a clinically important difference by drug class. The interaction test did not suggest a difference between subgroups for the primary outcomes of wound infection (Chi^2 = 17.77; P = 0.17; I^2 = 26.8%), serious infectious outcomes (Chi^2 = 3.07; P = 0.93; I^2 = 0%) and urinary tract infection (Chi^2 = 16.3; P = 0.13; I^2 = 32.5%), however the interaction test did show a difference among subgroups for the primary outcomes of febrile morbidity (Chi^2 = 45.8; P < 0.00001; I^2 = 73.8%) and endometritis (Chi^2 = 21.16; P = 0.07; I^2 = 38.6%). There was no evidence that a regimen with a broader spectrum of activity was any better than a drug with a narrow spectrum of activity or that any particular antibiotic regimen was ineffective. The largest risk reductions for wound infection were seen with the extended spectrum penicillin group (RR 0.18, 95% CI 0.09 to 0.39) and aminoglycoside containing regimens (RR 0.17 95% CI 0.08 to 0.34) (Analysis 2.2). For the first generation cephalosporins, the current recommended antibiotic for prophylaxis, the risk ratio for wound infection was 0.38 (95% CI 0.28 to 0.53) (Analysis 2.2). There was only one study that reported on lincomycin and no studies reported on clindamycin or a macrolide, which however are often given as an alternatives for prophylaxis in women who are allergic to penicillin. The reduction in the incidence of endometritis was similar amongst the different drug regimens (Analysis 2.3). The smallest reduction in endometritis was seen for beta lactamase inhibitor combinations (RR 0.67, 95% CI 0.27 to 1.66); for the first generation cephalosporins the relative risk was 0.42 (95% CI 0.33 to 0.54). Any comparison between regimens has, however, to be interpreted with caution given that the results are observational and not based on randomized comparisons. Please refer to the meta-analysis of studies that compared different regimens (Alfirevic 2010).

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3. Antibiotic prophylaxis versus no prophylaxis, subgroups by type of cesarean section (Analyses 3.1 to 3.7)

In both elective and emergency cesarean sections as well as the "both or not defined" subgroup there was a reduction in febrile morbidity, wound infection, endometritis and urinary tract infection although there were insufficient data to assess any differential effect on serious infectious complications. For elective cesarean sections, the risk ratio for wound infections was 0.62, 95% CI 0.47 to 0.82 (Analysis 3.2) and for endometritis the RR was 0.38, 95% CI 0.24 to 0.61 (Analysis 3.3). We inspected the graphs visually and saw no difference in maternal febrile morbidity, wound infection or endometritis, among the three groups and as well the confidence intervals for the summary estimates overlapped, however, the interaction test did show a difference among subgroups for the outcome of wound infection (Chi^2 = 13.53; P = 0.001; I^2 = 85.2%) and maternal urinary tract infection ((Chi^2 = 6.42; P = 0.04; I^2 = 68.8%), but no difference for the outcomes of febrile morbidity (Chi^2 = 0.47; P = 0.79; I^2 = 0%), endometritis (Chi^2 = 0.36; P = 0.84; I^2 = 0%), or serious infectious outcome (Chi^2 = 0.62; P = 0.73; I^2 = 0%).

4. Antibiotic prophylaxis versus no prophylaxis, subgroups by timing of administration (Analyses 4.1 to 4.7)

We inspected the graphs visually and found no difference in wound infection, endometritis or maternal urinary tract infection among the three groups and the confidence intervals for the summary estimates overlapped. As well, the interaction test did not suggest there was any real difference for the outcomes of wound infection (Chi^2 = 0.43; P = 0.81; I^2 = 0%), endometritis (Chi^2 = 3.74; P = 0.15; I^2 = 46.6%) and maternal urinary tract infection (Chi^2 = 2.07; P = 0.36; I^2 = 3.4%). However, the interaction test did suggest there was a difference among subgroups for the outcome of febrile morbidity (Chi^2 = 8.40; P = 0.01; I^2 = 76.2%). There was no difference among groups based on the interaction test for the outcome of serious maternal infectious complications (Chi^2 = 0.13; P = 0.94; I^2 = 0%), although there were insufficient data to conclude this with certainty. From these analyses there was no evidence that administering antibiotics before surgery was associated with a better outcome, but this conclusion needs to be interpreted with caution given that the results are observational and not based on randomized comparisons.

Other considerations

Infant

Infant outcomes were infrequently reported. No study reported on any long-term adverse effects on the infant or effect of antibiotics on the infant immune system. In addition, no studies reported on the incidence of oral candidiasis (thrush) in babies, which we had categorized as an adverse outcome.

Where Apgar scores were reported, there were no differences between the treatment and control groups (Adam 2005; Gordon 1979; Ng 1992; Rouzi 2000). One study collected information on birthweight, number of days in hospital, admission to neonatal intensive care, early neonatal death, respiratory distress syndrome and neonatal sepsis and there was no difference between the treatment and control groups (Rouzi 2000) and another study reported that neonatal outcomes (respiratory distress syndrome, intracranial hemorrhage, necrotizing enterocolitis, sepsis and neonatal death) were not different among treatment groups (Witt 2011). Some authors stated there were no complications in the babies due to drug administration, without further details (Gordon 1979; Moodley 1981) and that the administration of antibiotics did not interfere with routine pediatric cultures (Gall 1979) or the evaluation of newborn sepsis (Duff 1980).

There were few neonatal deaths and where they were reported, no relationship to the administration of antibiotic was reported (Adam 2005; De Boer 1989).

Only one study reported on infant outcomes at four weeks and in that study the three infants who had complications were all in the control group (Gordon 1979).

Costs

Three studies reported post-operative antibiotic costs. Drug costs were lower in the group receiving prophylaxis compared with the control group in one study (Kristensen 1990) but higher in the other two (Bibi 1994; Racinet 1990). *See* Characteristics of included studies table for details of costs.

Resistance

Changes in bacterial flora and the development of antibiotic resistant bacteria with the administration of antibiotics was not systematically collected in the studies included in this review, but several studies included detailed microbiological investigations, comparing the results of aerobic and anaerobic culture of the genital tract before and after the surgery and reporting on antimicrobial resistance in organisms associated with infection (Engel 1984; Fugere 1983; Gibbs 1981; Harger 1981; Ismail 1990; Karhunen 1985; Kreutner 1978; Miller 1968; Moro 1974; Rothbard 1975; Roex 1986; Stiver 1983).

There is a shift in the bacterial flora following the surgical procedure itself and return to the non-pregnant state and even in the control groups more gram positive aerobic organisms (including staphylococcal species and enterococci) were observed post-operatively (Engel 1984). Antibiotic prophylaxis was associated with increases in enterococci and gram-negative aerobic organisms (Engel 1984; Fugere 1983; Gibbs 1981; Kreutner 1978); cefazolin was associated with more anaerobic isolates (Engel 1984; Fugere 1983; Kreutner 1978) and cefoxitin and cefamandole with a decrease in anaerobic isolates (Engel 1984; Gibbs 1981).

Given that most regimens included a cephalosporin which has no activity against enterococci, it is not surprising that most studies reported significant increases in enterococcal colonization (Gibbs 1981; Ismail 1990; Stiver 1983). Harger reported that the isolates from infected sites in cefoxitin infected women showed a relative predominance of enterococci (Harger 1981). Ismail reported that enterococcal sepsis occurred in one patient and three others had significant enterococcal bacteriuria or urinary tract infection (Ismail 1990).

There were very few reports of resistant organisms developing following prophylaxis. No cefoxitin resistant strains of Enterobacteriaceae were isolated from stool samples after prophylaxis (Ismail 1990). In one study, there were more ampicillin resistant urinary tract infections when ampicillin was used for prophylaxis compared with control (9/17 versus 8/26) (Miller 1968). Rothbard reported one infection with an organism resistant to cephalothin and kanamycin used for prophylaxis (Rothbard 1975)

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and Duff reported an endometrial culture that grew *Klebsiella pneumoniae* resistant to ampicillin (Duff 1980). Engel reported urinary tract infections with mezlocillin resistant organisms (5/9) after mezlocillin prophylaxis and observed colonization with mezlocillin resistant strains of *E. coli* in cultures from the cervix (Engel 1984). In one study of cephalothin, all the organisms causing infection in the antibiotic group were described as sensitive to cephalothin *in vitro* (Moro 1974). In a study of cefoxitin prophylaxis, it was observed that the changes in endogenous flora were not associated with overgrowth of resistant pathogens, such as *Pseudomonas*, enterococci or *Enterobacter* (Roex 1986) and Karhunen reported no superinfections with resistant anaerobic organisms when tinidazole was used for prophylaxis (Karhunen 1985). Stiver confirmed that there was no increase in nosocomial infection (Stiver 1983).

DISCUSSION

Summary of main results

This review included 95 studies that evaluated the effect of antibiotics for preventing infection after cesarean section in over 15,000 women. Compared with placebo or no treatment, the use of prophylactic antibiotics in women undergoing cesarean section reduced the incidence of wound infection and endometritis by around 60% and serious maternal infectious complications were reduced by 70%. See Summary of findings for the main comparison. When only studies that included women undergoing an elective cesarean section were analyzed, wound infections were reduced by 40% and endometritis by 60%. See Summary of findings 2. Similar estimates of effect were seen whether the antibiotics were administered before the cord was clamped or after.

There were no data on which to estimate the effect of maternal administration of antibiotics on infant outcomes. No studies systematically collected and reported on adverse infant outcomes nor the effect of antibiotics on the developing infant immune system. No studies reported on the incidence of oral candidiasis (thrush) in babies. Maternal adverse effects were also rarely described.

The effect of different antibiotic regimens was studied and similar reductions in the incidence of infections seen for most of the antibiotics and combinations studied.

Febrile morbidity is common after cesarean section and, although not judged a clinically important outcome, it was reduced with the use of prophylactic antibiotics. Few of these women will have positive bacterial cultures or a specific indication for antimicrobial treatment, but these women often have specimens collected and empiric antibiotic therapy started. There was a similar reduction in the incidence of urinary tract infections.

Overall completeness and applicability of evidence

These studies enrolled over 15,000 women extending over a period of more than 40 years, but only seven studies were reported since 2000. The studies varied in setting (both low-income and high-income countries), antibiotic regimen, risk of infection and definitions of outcomes, but we did not find evidence of statistically important heterogeneity in the measurement of effect among the studies. The reductions in infection seen are clinically important. The results of these studies have been generalized to the whole population of women undergoing cesarean section and based on the steady accumulation of evidence have been incorporated into all recent guidelines (ACOG 2011; NICE 2011; SOGC 2010).

Inconsistent adherence to policies for administering antibiotic prophylaxis are reported (Huskins 2001; Mah 2001; Pedersen 1996) but simple quality improvement methods have been demonstrated to improve adherence with overall and timely administration of prophylaxis and reduce the infection rate (Weinberg 2001). It was also shown, in this study (Weinberg 2001) that a program that introduced a policy of universal prophylaxis for all women undergoing a cesarean section was more effective than one that required the obstetrician to decide whether a woman was high risk and mandated prophylaxis only for the high-risk women.

A statistically significant reduction in all the primary outcomes (febrile morbidity, wound infection, endometritis, serious maternal outcomes) was seen whether the antibiotic was administered before the clamping of the cord or after clamping of the cord. There was no significant difference in the estimates for these outcomes by the timing of administration and the confidence intervals were overlapping. It has, however, been shown that the lowest risk of surgical wound infection is associated with antibiotics administered in the pre-operative period as compared with the perioperative or post-operative period (Classen 1992). Although studies have not show an increase in infectious outcomes when the antibiotic was administered after the cord was clamped (Cunningham 1983; Gordon 1979; Wax 1997), meta-analyses of randomized controlled trials concluded that there was strong evidence that antibiotic prophylaxis given before skin incision decreased the incidence of postpartum endometritis and total infectious morbidities compared with after the cord was clamped (Baaqeel 2013; Costantine 2008). Pre-operative administration of antibiotics did not significantly affect proven neonatal sepsis, suspected sepsis or neonatal intensive care unit admissions. In a retrospective study on the effect of a change in policy to administer prophylactic antibiotics before skin incision, the overall rate of surgical site infections fell from 6.2% to 2.5% (Kaimal 2008).

Adverse effects

Maternal side effects were not consistently collected nor reported. Generally the side effects of a single antibiotic dose are mild, but rarely serious allergic reactions can occur. Although the risk of side effects reported in these studies was low, these data were incompletely collected, making it difficult to know accurately the incidence of the adverse effects of treatment and truly judge the benefits and harms of the intervention.

Infant outcomes were rarely systematically collected but when they were reported there was no evidence of any adverse effects associated with the administration of antibiotic. There is evidence that antibiotics given near or shortly after birth can affect the infant gut flora, with the potential to impact mucosal and systemic immune function (Bedford Russell 2006) but no study has prospectively examined the effect of any changes in flora on these or other outcomes. Oral yeast infection (thrush) was not an outcome reported in any of the included studies.

There are also unknown and unquantified effects of antibiotic use that include changing the normal maternal flora, effects on the presentation of infection in the infant, and the development of antimicrobial resistance. There are changes in bacterial flora with the administration of antibiotics, with an increase in enterococcal

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colonization and evidence of the development of antibiotic resistant bacteria but few incidences where this was associated with infectious complications (Galask 1987). In women who developed endometritis, prophylaxis with ampicillin or cefazolin alters the genital tract microflora, but this had no effect on cure rates (Newton 1998)

While increased use of antimicrobial prophylaxis may be one factor in increasing antimicrobial resistance (Shlaes 1997), there are no data supporting the contention that appropriate use of short course antimicrobial prophylaxis will cause significant bacterial resistance nor evidence that a policy of antibiotic prophylaxis for cesarean section has harmful effects that outweigh its benefits, even in those women perceived to be at low risk. Optimizing the choice and the duration of prophylactic antibiotic therapy is recommended as one strategy to prevent antimicrobial resistance (Shlaes 1997). Trends in antibiotic resistance should be monitored, reported and used to establish practice guidelines and monitor institutional policies. Susceptibility testing of significant bacterial isolates should guide antimicrobial therapy of individual women who develop infection despite prophylaxis.

Quality of the evidence

We used the GRADE approach to assess the quality for the evidence. We judged the evidence for antibiotic treatment compared with no treatment to be of moderate quality, meaning that further research would likely change our confidence in the result and the size of the estimate of the effect. Many of the included trials were more than 15 years old and lacked an adequate description of methods to allow a judgement on the risk of bias and for several studies there was clearly a high risk of bias.

Potential biases in the review process

We followed a well-characterized search strategy to identify relevant trials, including non-English language papers, but recognize that some trials may not have been available on-line, especially older studies performed before the availability of electronic databases. We were unable to contact most of the authors where we needed clarification of information because there were no up-to-date contact details and for foreign-language studies we relied on a translated copy, which was sometimes incomplete.

Agreements and disagreements with other studies or reviews

This review included in its definition of an elective cesarean section those women not in labor but with ruptured membranes for less than six hours, included studies that did not have a placebo arm and included studies that used antibiotic irrigation as well as systemic agents. A meta-analysis (Chelmow 2001) that used an expanded search strategy to identify additional relevant studies, and included only placebo-controlled studies of systemic antibiotics in women undergoing elective cesarean section who were non-laboring with intact membranes, showed a reduction in infections in this low-risk population and supports the conclusion of this review. In a prospective cohort study from a high-risk obstetrical unit in New York state, absence of antibiotic prophylaxis was identified by multiple logistic regression analysis as being independently associated with surgical site infection after cesarean section for both high-risk women and low-risk women and was identified as one of the modifiable factors (Killian 2001).

AUTHORS' CONCLUSIONS

Implications for practice

The conclusions of this review support the recommendations in guidelines that prophylactic antibiotics should be routinely administered to all women undergoing cesarean section to prevent infection. No conclusions can be drawn from this review about the relative benefit and harms of administering antibiotics before or after clamping of the cord nor which antimicrobial regimen should be selected, although a first generation cephalosporin was shown to be effective. Obstetric units should collect data on infection rates following cesarean section and adherence to guidelines for appropriate prophylactic antibiotic administration as important quality indicators.

Implications for research

Further placebo-controlled trials of the effectiveness of antibiotics with cesarean section are not ethically justified, but studies are needed to ascertain infant outcomes. Any future studies should use the list of outcomes identified here as a minimum data set and, in particular, include possible adverse effects on the infant and what role antimicrobial prophylaxis has on the development of antibiotic resistance. There should be research on methods to implement effective policies of prophylaxis for women undergoing cesarean section. Rates of infection following cesarean section are higher than for many other surgical procedures, even with a policy of uniform prophylaxis. Future research should look at interventions to reduce further the incidence of infection from that achieved with our current approach to antibiotic prophylaxis, e.g. the topical vaginal administration of metronidazole (Pitt 2001), the timing of antibiotic administration, whether there are advantages to an extended spectrum regimen (Tita 2009) and determine the role of surgical technique, pre- and intra-operative preparation and infection control policies on infection rates. Research into the perceptions of the advantages and disadvantages of the intervention from the perspective of the woman and the healthcare provider will help define educational and research needs.

Without any data on adverse events, the benefits versus harms of the intervention cannot be assessed, nor a group of women identified in whom prophylactic antibiotics need not be administered because of a very low risk of infection. There is a theoretical opportunity for a cost-effective analysis to be performed in a unit where routine prophylactic antibiotics are not administered to women undergoing an elective cesarean section and where the risk of infection is very low, in an attempt to identify women at increased risk of infection in whom prophylaxis may be cost-effective. However, there is currently no evidence to support such a strategy. Because of local variation in practice and women, the results of such research will likely only be applicable to an individual unit and not generalizable.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Adam 2005

Methods	RCT, 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: Sept 2003 to April 2004. Setting: New Halfa Teaching Hospital, Eastern Sudan. Inclusion criteria: planned elective CS (categorized as elective). N = 100. Exclusion criteria: antibiotics within 2 weeks; any visible infection; elevated temperature; allergic to antimicrobials; did not wish to participate.
Interventions	Intervention: 3rd generation cephalosporin: • ceftriaxone 1 g IV at anesthetic induction; • N = 50. Comparison: no treatment:

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Adam 2005 *(Continued)*

	• no treatment; • N = 50.
Outcomes	Post-operative febrile morbidity (oral temperature ≥ 38 °C twice at least 4 hrs apart after 1st 24 hrs. Post-operative infections (endometritis, wound infection, pelvic abscess, peritonitis, other febrile morbidity (UTI, chest infection, malaria). 2 perinatal deaths: 1 in each group due to respiratory distress and septicemia due to imperforate anus.
Notes	Low-income country. Class of antimicrobial: 3rd generation cephalosporin Subgroups: • elective CS; • before cord clamping. The 2 groups were well matched at enrolment and there were no statistical differences in the admission variables.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded after randomization; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Adeleye 1981

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported.

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Adeleye 1981 *(Continued)*

	Setting: University College Hospital, Ibadan, Nigeria. Majority of patients from low socioeconomic class. Inclusion criteria: both elective and non-elective cesarean deliveries. N = 106. Exclusion criteria: fever or obvious infection before operation.
Interventions	Intervention: • ampicillin 500 mg before operation and 250 mg 6 hrly for at least 7 days (IM until able to take orally); • N = 58. Comparison: no treatment: • no antibiotics unless temperature 38 degrees C after the 3rd post-operative day; • N = 48. Both groups received curative doses of chloroquine. Prophylaxis continued for 7 days.
Outcomes	Wound infection; UTI (not defined further); 'genital sepsis' (not defined further: study group 5/58; control group 15/48).
Notes	Low-income country. Class of antibiotic: aminopenicillin (ampicillin) Subgroups: • both elective and non-elective CS - data could not be separated by type CS; • before cord clamping. The 2 groups were comparable regarding age, parity and indications for CS.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Divided randomly into 2 groups". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss to follow-up reported; no participants excluded; imbalance in group size not accounted for (58 vs 48); ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.

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Adeleye 1981 *(Continued)*

Other bias	Low risk	Comment: no other sources of bias identified.

Allen 1972

Methods	Randomized, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: August 1970 to January 1971. Setting: Johns Hopkins University, Baltimore, US. Inclusion criteria: women undergoing CS (criteria not specified). N = 12. Exclusion criteria: evidence of clinical infection, history of penicillin allergy.
Interventions	Intervention: 1st generation cephalosporin: • cephalothin 1 g IV on call to operating room, further 2 g IV intra-operatively and every 6 hrs for 48 hrs, then 500 mg IM for additional 72 hrs; • N = 5. Comparison: placebo: • placebo; • N = 7.
Outcomes	Morbidity (temperature > 100.9^{0}F twice, 6 hrs apart after 1st 48 hrs or other clinical signs of infection); not separated. For this review, the authors' definition of morbidity has been classified as fever.
Notes	Part of a larger randomized trial of prophylactic antibiotics in gynecologic surgery; most patients (87%) were undergoing hysterectomy; only 12/300 patients enrolled underwent CS. Class of antibiotic: 1st generation cephalosporin. Subgroups: • type of CS unclear; • before cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Comment: randomized list of placebo or drug, kept in hospital pharmacy; code not broken until after patient classified as 'morbid' or 'non-morbid'.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up; no participants excluded; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.

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Allen 1972 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind". Comment: placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Apuzzio 1982

Methods	RCT: 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: October 1977 to June 1980. Setting: College Hospital, New Jersey, October. Women 'predominantly black (90%) and socio-economically disadvantaged'. Inclusion criteria: both elective and non-elective cesarean deliveries. N = 259. Exclusion criteria: antibiotics within 2 weeks; pyrexia; any visible infection; penicillin allergy; known medical illness that might cause pyrexia; internal fetal scalp or uterine monitoring.
Interventions	Intervention: carboxypenicillin: • ticarcillin 6 g IV within 15 minutes of cord clamping; • N = 139. Comparison: placebo: • saline placebo; • N = 120. Subset of 22 in each group received ticarcillin 3 g/saline 6-8 hrs post-operatively or saline placebo (results similar so authors combined results with single-dose group). No post-operative antibiotics unless pyrexial > 38 degrees C after day 1.
Outcomes	Endomyometritis (pyrexia, uterine tenderness and no evidence of other infection).
Notes	Authors' definition of low and high risk not comparable to definitions for elective/non-elective used in this review. Results for adolescent group (aged 15-18) reported in J Adolescent Health Care 1984;5:163-166. In that study, incidence of endomyometritis in elective section: 0% for treatment vs 43% for placebo (numbers not given). Class of antibiotic: extended spectrum penicillin (carboxypenicillin). Subgroups: • type of CS unclear; • after cord clamping.

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Apuzzio 1982 *(Continued)*

"The prophylaxis and placebo groups were essentially similar in regard to important demographic and obstetric parameters. There were no significant differences between the groups for any of the variables studied."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly divided into 2 groups". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss of participants to follow-up and no participant excluded after analysis, however discrepancy in group numbers (139 vs 120) not accounted for; ITT analysis.
Selective reporting (reporting bias)	High risk	Comment: a subset of 22 in each group received ticarcillin 3 g/saline 6-8 hrs post-operatively or saline placebo; the results were similar so authors combined results with single-dose group.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind". Comment: placebo-controlled (saline solution).
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Bagratee 2001

Methods	Randomized double-blind, placebo-controlled; 2 parallel groups.
Participants	Dates of data collection: not reported. Setting: Durban, South Africa. Inclusion criteria: women undergoing elective cesarean delivery. N = 475. Exclusion: prior antibiotics within 2 weeks, allergy to penicillin or cephalosporin, rupture of membranes.
Interventions	Intervention: cefamycin: • cefoxitin (2 g IV after cord clamping); • N = 237. Comparison: placebo: • matching placebo; • N = 238.

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Bagratee 2001 *(Continued)*

Outcomes	Febrile morbidity (oral temperature > 38ºC twice 6 hrs apart after 1st 24 hrs); wound infection (wound cellulitis, erythema, discharge with or without fever); endometritis (fever, uterine tenderness, malodorous lochia); UTI (fever and positive urine culture); pneumonia; duration of hospital stay.
Notes	11% were HIV positive; *Staphylococcus aureus* most common pathogen (43%) isolated. Class of antibiotic: cefamycin (2nd generation cephalosporin). Subgroups: • elective CS; • after cord clamping. The 2 groups were comparable regarding age, parity, gestational age, weight and pre-operative hemoglobin.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...randomized...a computer-based allocation...".
Allocation concealment (selection bias)	Low risk	Quote: "...consecutively numbered sealed envelopes...".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported; it appeared to be an ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind; placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Battarino 1988

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not stated. Detting: Cerignola, Italy. Inclusion criteria: women in labor and/or with ruptured membranes (mean duration of ruptured membranes 10 hrs), classified as both elective and non-elective in this review.

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Battarino 1988 *(Continued)*

	Exclusion criteria: not stated.
Interventions	Intervention 1: • ceftriaxone 1 g IV after cutting the cord and 1 g after 24 hrs; • N = 62. Intervention 2: • cefotaxime 1 g IV at the time of cutting the cord and every 12 hrs for a total of 4 doses; • N = 60. Intervention 3: • placebo (not further described); • N = 55. As both treatments are classified as 3rd generation cephalosporins, the 2 treatment groups have been combined in the analysis.
Outcomes	Febrile morbidity (2 or more readings ≥ 38°C at least 6 hrs apart after the 1st 24 hrs after surgery; endometritis (pain accompanied by fever, with or without purulent discharge from the vagina); wound infection (redness, induration, pain on palpation and purulent discharge); UTI (dysuria, pyuria and urine culture > 10^6 bacteria/mL); septic shock (classified as serious maternal infection); maternal stay (7.3 days for ceftriaxone group vs 7.4 days for cefotaxime vs 8.7 days for control group; variance not provided); additional antibiotics (11.3% vs 10% vs 27.2% for the 3 groups respectively).
Notes	Translated from Italian. The authors' definition of non-elective does not match those used in this review (included patients whose indication for CS was prior cesarean and fetal-pelvic disproportion). Class of antibiotic: 3rd generation cephalosporin. Subgroups: • both; • After cord clamping. There were no significant differences among the groups for age, parity, gestation, indication for cesarean section, duration of membrane rupture, duration of labor or number of vaginal examinations.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "At random". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss to follow-up reported (no explanation for small differences in numbers in each study group); no participants excluded; ITT analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.

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Battarino 1988 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "placebo-controlled". Comment: no additional details provided to judge.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Bibi 1994

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: February to July 1991. Setting: Sousse Hospital, Tunisia. Inclusion criteria: women undergoing elective CS or labor < 12 hrs (categorized as "both" for this review"). N = 269. Exclusion criteria: diagnosed amniotic infection; pyrexia ≥ 38ºC; cases of failed vaginal instrumental deliveries; antibiotics within 3 days; allergy to beta lactam antibiotics; cardiac disease; diabetes.
Interventions	Intervention: • cephapirine 1 g IV with induction of anesthesia and 6 hrs after operation, gentamycin 80 mg IM with induction, metronidazole 500 mg IV with induction; • N = 133. Comparison: no treatment: • no treatment; • N = 136.
Outcomes	Endometritis; wound infection; pyrexia only (≥ 38ºC 48 hrs after surgery): antibiotic 4/133 vs control 9/136; septicemia (0/133 vs 3/136, included as serious morbidity); duration of hospital stay (antibiotic 5.36 days vs control 6.21, P = 0.03, variance not given); cost of antibiotics given for treatment (440FF for treatment group vs 4294FF for control group).
Notes	Translated from French. Class of antibiotic: aminoglycoside-containing combination (1st generation cephalosporin, aminoglycoside and nitroimidazole (metronidazole). Subgroups: • both elective and non-elective CS - not able to separate the data by type of CS; • before cord clamping. Follow-up at 30 days (86%). The groups were similar for age, parity, duration of labor and other risk factors.

Risk of bias

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Bibi 1994 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "by chance". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	High risk	Comment: using random number table, patients allocated to treatment if the number is even, no treatment if the number is odd.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no losses or exclusions reported; it appears to be ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Bilgin 1998

Methods	Quasi-RCT; 5 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Bursa, Turkey. Inclusion criteria: women undergoing CS due to acute fetal distress. N = 119.
Interventions	Intervention 1: • ceftriaxone 1 g; • N = 25. Intervention 2: • mezlocillin 2 g; • N = 23. Intervention 3: • clindamycin 600 mg and amikacin 500 mg; • N = 18. Intervention 4: • sulbactam ampicillin 1 g (ampicillin + sulbactam); • N = 25.

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Bilgin 1998 *(Continued)*

	Comparison: • no treatment; • N = 28. IV after clamping of the cord. No treatment comparison was divided: 7 for each of the 4 groups (28/4).
Outcomes	Wound infection (redness, tenderness, pain and purulent discharge); UTI (renal angle tenderness, fever, dysuria and pyuria); endometritis (vaginal spotting, purulent discharge with fever and pain) plus positive cultures.
Notes	All wound infections were positive for coagulase negative staphylococcus. Class of antibiotic: 3rd generation cephalosporin vs extended spectrum penicillin (ureidopenicillin) vs aminoglycoside containing combination (lincosamide (clindamycin) and aminoglycoside) vs beta-lactamase inhibitor combination. Subgroups: • type of CS unclear; • after cord clamping. The 5 groups were comparable regarding maternal age, ruptured membranes, pelvic examinations, hemoglobin levels.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "...according to the last digital of the patient's file number...". Comment: Quasi-RCT.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported; it appeared to be an ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

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Bourgeois 1985

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: initiated March 1981. Setting: Charlottesville, Virginia, USA, almost all were indigent women. Inclusion criteria: both 'low risk' (labor < 6 hrs) and 'high risk' (> 6 hrs) women undergoing CS. N = 148 for this comparison. Exclusion criteria: allergy to penicillin or cephalosporin; antibiotic use within 7 days; antibiotics required for other reasons; pyrexia > 38ºC; foul amniotic fluid.
Interventions	Intervention: • cefamandole, 2 g in 1000 mL normal saline; • irrigation of the uterus and peritoneal cavity; • N = 73. Comparison 1: placebo: • saline placebo; • N = 75. Comparison 2: no treatment: • no irrigation group; • N = 44. As the objective of this review is to compare antibiotic with no antibiotic, rather than the effect of irrigation, only the 1st 2 groups are compared (double-blind comparison).
Outcomes	Metritis (pyrexia > 38ºC twice 8 hrs apart, after 24 hrs plus abnormal uterine tenderness, without another apparent source); duration of maternal stay (treatment 5.29 days vs placebo 6.32 days, variance could not be calculated).
Notes	Authors' definition of low and high risk do not correspond to those used for elective/non-elective in this review. No treated patients developed evidence of drug reaction. There were no serious infections (pelvic abscess or phlebitis) in either group. Class of antibiotic: 2nd generation cephalosporin. Subgroup: • both elective and non elective; • after cord clamping. The groups were comparable regarding gravidity, parity, maternal weight, hematocrit, etc.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A computer generated table of random numbers".
Allocation concealment (selection bias)	Low risk	Quote: "Assigned under the direction of the hospital pharmacy".

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Bourgeois 1985 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up reported; no participants excluded; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: partially double-blind placebo-controlled (3 groups: antibiotic irrigation, saline placebo irrigation, no irrigation). Physicians were unaware of the type of irrigation used.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: probably outcome assessment was blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Carl 2000

Methods	Randomly allocated (abstract only; no further details).
Participants	Setting: Texas, USA. Inclusion: women undergoing high-risk CS (definition not provided; classified as not-defined). N = 40.
Interventions	Intervention: • cefazolin 2 g in 1000 mL irrigation; • N = 20. Comparison: placebo: • normal saline 1000 mL irrigation; • N = 20.
Outcomes	Wound infection, endometritis, UTI.
Notes	Abstract only available. Class of antibiotic: 1st generation cephalosporin. Subgroups: • type of CS not defined; • after cord clamping. Follow-up 4-6 weeks post-operatively.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomly allocated..". Comment: no description of sequence generation process.

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Carl 2000 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no information provided.
Selective reporting (reporting bias)	Unclear risk	Comment: no information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: normal saline irrigation used in control group; no additional details provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information provided.
Other bias	Low risk	Comment: no other sources of bias identified.

Chan 1989

Methods	Randomized, placebo-controlled trial; 4 parallel groups (3 treatment, 1 placebo). Unit of randomization: individual.
Participants	Dates of data collection: October 1986 to February 1987. Setting: Prince of Wales Hospital, Hong Kong; mostly suburban or rural Chinese women of lower or middle class. Inclusion criteria: all women undergoing CS. N = 400. Exclusion criteria: receiving antibiotics; pyrexia > 37.4ºC; diagnosed infection; increased risk of infection, e.g. diabetes; known sensitivity to the antibiotics.
Interventions	Intervention 1: • ampicillin 1 g, IV at time of induction of anesthesia; • N = 96. Intervention 2: • ampicillin 1 g and metronidazole 500 mg; • N = 104. Intervention 3: • ampicillin 1 g and sulbactam 500 mg; • N = 99. Comparison: placebo: • placebo (normal saline); • N = 101. Placebo data were divided: 33 for each comparison (101/3).

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Chan 1989 *(Continued)*

Outcomes	Febrile morbidity (oral temperature of more than 38ºC at least twice after day 1); wound infection (induration, serosanguinous discharge or dehiscence with purulent discharge); UTI (positive culture); genital tract infection (pain and uterine tenderness, purulent uterine discharge with microbiological confirmation); any infection anywhere (antibiotic 75/299 vs placebo 28/101); post-operative antibiotic use (22/299 vs 9/101).
Notes	Only moderate or prolonged febrile morbidity (as defined) included. Class of antibiotic: aminopenicillin (ampicillin), other combination (ampicillin and metronidazole), beta-lactamase inhibitor combination. Subgroups: • type of CS unclear; • before cord clamping. The groups were comparable regarding age, parity, primary CS, indication for CS, urinary catheterization and vaginal examination before operation.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "list of random numbers consulted by nurse".
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up; no participants excluded; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind (the anesthetist was not blind); placebo (normal saline).
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All doctors and nurses looking after the patients were ignorant of the drug given until the end of the study". Comment: probably outcome assessment was blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Conover 1984

Methods	RCT; 4 parallel groups Unit of randomization: individual.
Participants	Dates of data collection: March to November 1982. Setting: Naval Hospital, San Diego, California.

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Conover 1984 *(Continued)*

	Inclusion criteria: women at increased risk of post-CS endometritis (in labor or with ruptured membranes). Classified as non-elective for this review. N = 124. Exclusion criteria: allergy to penicillin or cephalosporins; antibiotic use within 48 hrs; separate indication for use of antibiotics; temperature > 38 degrees C; chorioamnionitis; pyuria.
Interventions	Intervention 1: • cefoxitin, 2 g in 500 mL saline administered by irrigation of uterus and peritoneal cavity; • N = 37. Intervention 2: • cefoxitin, 2 g IV after clamping of the umbilical cord; • N = 31. Comparison 1: placebo for irrigation: • 500 mL normal saline by irrigation; • N = 23. Comparison 2: placebo for IV: • saline IV; • N = 33. We combined the cephalosporin groups and the 2 placebo groups for this review.
Outcomes	Endometritis (febrile morbidity and uterine tenderness); total infection-related morbidity (cefoxitin 10/68 vs saline 14/56); fever index; duration of IV antibiotics; additional antibiotics; days in hospital (no difference, variance not given).
Notes	1 woman developed an allergic reaction to cefoxitin (acute pruritic rash). There were 2 episodes of bacteremia (both in placebo groups); there were no episodes of septic pelvic thrombophlebitis nor drainage of pelvic abscess in either group. Class of antibiotic: cefamycin (2nd generation cephalosporin). Subgroups: • non-elective CS; • after cord clamping. The 4 groups were comparable regarding age, gravidity, parity, duration of pregnancy, socioeconomic status, maternal weight, hrs in labor, length of ruptured membranes, and other potential risk factors.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Each patient was designated to receive either normal saline or cefoxitin based on a computer generated table of random numbers". Comment: allocation to irrigation or IV prophylaxis based on last digit of social security number.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was provided.

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Conover 1984 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no losses and no exclusions were reported. Imbalance in randomized groups not accounted for (irrigation: cefoxitin 37 vs saline 23; overall 68 vs 56). ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Both antibiotic and normal saline were packaged identically to ensure that the administration was blinded". Comment: double-blind, placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Cormier 1989

Methods	Randomized trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Hopital Pellegrin, Bordeaux, France. Inclusion criteria: women undergoing CS; both elective and non-elective deliveries. N = 110. Exclusion criteria: allergy to beta-lactam antibiotics; pyrexia; indication for antibiotics.
Interventions	Intervention: • cefotetan, 2 g after clamping of umbilical cord; • N = 55. Comparison: no treatment: • no antibiotic; • N = 55.
Outcomes	Endometritis; urinary infection; local complications (classified as wound infection); fever only (cefotetan 0/55 vs control 6/55); antibiotic therapy (10/55 vs 25/55); mean days in hospital (10.0 vs 10.2, no variance given).
Notes	Translated from French. Class of antibiotic: cefamycin (2nd generation cephalosporin). Subgroups: • both elective and non-elective CS - data could not be separate by type CS; • after cord clamping. There were no significant differences between the groups for risk factors for infection.

Risk of bias

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Cormier 1989 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: allocated by sealed envelopes.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no losses or exclusions reported: analysis appears to be ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: no information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: not blinded, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

D'Angelo 1980

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not stated. Setting: Cleveland, Ohio, USA. Inclusion criteria: women in labor with ruptured membranes requiring internal monitoring (non-elective delivery). N = 80. Exclusion criteria: evidence of infection; penicillin or cephalosporin allergy.
Interventions	Intervention 1: cephalosporin: • cefazolin, 1 g IV short course - 6 hrly for 24 hrs; • N = 24. Intervention 2: cephalosporin: • cefazolin, 1 g IV long course - for 8 or more doses and cephalexin 500 mg orally 6 hrly for 5 days; • N = 25. Comparison: no treatment: • no prophylactic antibiotics; • N = 31. Short and long courses of cephalosporins combined for this review.

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D'Angelo 1980 *(Continued)*

	Administered after umbilical cord clamping.
Outcomes	Endometritis and/or wound infection (antibiotic 12/49 vs control 20/31).
Notes	It was possible to deduce the rate of endometritis alone, but not wound infection, for this review. 1 late infectious complication (wound dehiscence) in control group. Drug class: 1st generation cephalosporin. Subgroups: • non-elective CS; • after cord clamping. There were no statistical differences among the 3 groups for potential risk factors.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote:"Randomly assigned". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participants excluded after analysis. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding of participant or clinician; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Dashow 1986

Methods	Randomized, placebo-controlled trial; 5 parallel groups (4 treatment, 1 control). Unit of randomization: individual.
Participants	Dates of data collection: December 1982 to May 1984. Setting: Madigan Army Medical Centre, Tacoma, Washington, USA. Inclusion criteria: all women undergoing CS. N = 360. Exclusion criteria: penicillin or cephalosporin allergy; antibiotic therapy; known infectious process.

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Dashow 1986 *(Continued)*

Interventions	Intervention 1: cephalosporin: • cephapirin sodium, 2 g, irrigation during CS; • N = 79. Intervention 2: cephalosporin: • cefamandole nafate, 2 g, irrigation during CS; • N = 70. Intervention 3: • moxalactam disodium, 2 g, irrigation during CS; • N = 64. Intervention 4: penicillin (A4): • ampicillin sodium, 2 g, irrigation during CS; • N = 70. Comparison: placebo: • saline; • N = 77. A vitamin was added to each solution for disguise. Placebo data were divided: 19 for each of the 4 comparisons (77/4).
Outcomes	Fever (> 38^0C twice 6 hrs apart, excluding the 1st 24 hrs); endomyometritis (pyrexia > 37.8^0C, uterine tenderness and pelvic peritoneal irritation without other localizing signs of irritation; UTI (positive culture); wound infection; fever index; all infection-related morbidity; therapeutic antibiotics; mean postoperative days (variance not given).
Notes	3 episodes of pelvic thrombophlebitis (all in treated groups). Results were given for all women and women in labor, both high risk (corresponding to the category of non-elective deliveries) and all labor. The data for elective deliveries were deduced from these. Class of antibiotic: 1st generation cephalosporin vs 2nd generation cephalosporin vs monobactam vs aminopenicillin (ampicillin). Subgroups: • both elective and both/not defined CS - data separated by elective and both/not defined. The mean level of gravidity of the placebo group was higher than that of the cephapirin group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Computer-generated numbers using the mixed congruential method".
Allocation concealment (selection bias)	Low risk	Quote: "The pharmacy to assign each patient to 1 of 5 groups".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up; no participant excluded; ITT analysis.

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Dashow 1986 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind placebo-controlled trial. A vitamin was added to each solution for disguise.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

De Boer 1989

Methods	Randomized, double-blind, placebo-controlled; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: December 1983 to June 1985. Setting: Chogoria Hospital, Kenya. Inclusion criteria: all patients undergoing CS. N = 182. Exclusion criteria: clinical infection.
Interventions	Intervention: • metronidazole 1 g rectal suppository 10-45 minutes before and 8 hrs after procedure; • N = 91. Comparison: placebo: • placebo suppository; • N = 91.
Outcomes	Fever (> 37.9 ºC on at least 1 occasion); wound infection; mean febrile days (0.56 for treatment vs 1.23 for control), hospital days, any antibiotic use (18/91 vs 23/91).
Notes	Elective CS not defined. No adverse events on mother or babies noted. There was 1 grade 3 wound (defined as deep pelvic abscess or evidence of local or generalized peritonitis) in the treatment group as compared with 3 in the placebo group (classified as serious infectious morbidity). Class of antibiotic: nitroimidazole (metronidazole). Subgroups: • type of CS unclear; • before cord clamping. The 2 groups were comparable regarding age, parity, duration of labor, duration ruptured membranes, number of vaginal examinations, etc.

Risk of bias

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De Boer 1989 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized...". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: 7/189 patients initially randomized were not included in analysis because suppositories were incorrectly administered; as treated analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind; placebo suppository.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Dillon 1981

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: September 1979 and April 1980. Setting: Children's Hospital of Buffalo, USA. Inclusion criteria: all women undergoing CS (1 3rd elective). N = 101. Exclusion: evidence of active infection, penicillin or cephalosporin allergy; recent antibiotic treatment.
Interventions	Intervention: • cefoxitin 2 g IV; • N = 46. Comparison: placebo: • saline placebo; • N = 55. After clamping the umbilical cord and at 4 and 10 hrs post-operatively.
Outcomes	Febrile morbidity (temperature > 38 ºC twice 6 hrs apart after 1st 24 hrs); endometritis (fever, uterine tenderness, leukocytosis); wound infection (fever, cellulitis, exudate); maternal length of stay.
Notes	No serious life-threatening infection in either group; no drug-related adverse-effects.

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Dillon 1981 *(Continued)*

	Class of antibiotic: cefamycin (2nd generation cephalosporin). Subgroups: • both elective and non-elective CS - could not separate data by type CS; • after cord clamping. The 2 groups were comparable regarding age, status, race, obesity, obstetric factors and indication for surgery.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Numbered packages..." "...The random code was broken at the end of the study". Comment: no description of sequence generation process or further information provided.
Allocation concealment (selection bias)	Low risk	Comment: randomized by pharmacy.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss to follow-up reported; no participants excluded; ITT analysis. 9/110 'packages' not included (either damaged or patients failed to meet inclusion criteria). Imbalance in group size (46-placebo vs 55-cefoxitin) not explained.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, placebo-controlled (saline placebo).
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Duff 1980

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: October 1976 and March 1977. Setting: Walter Reed Army Medical Center, Washington DC. Inclusion criteria: all women undergoing either primary or repeat CS (44% elective). N = 57. Exclusion criteria: penicillin allergy; chorioamnionitis prior to surgery.

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Duff 1980 *(Continued)*

Interventions	Intervention: • ampicillin 1 g IV prior to surgery and 6 and 12 hrs post-operatively; • N = 26. Comparison: placebo: • placebo; • N = 31.
Outcomes	Febrile morbidity (> 100.3 ºF twice 6 hrs apart after 1st 24 hrs); endomyometritis (fever, uterine and abdominal tenderness, purulent lochia); UTI (positive culture); wound infection (induration, erythema and warmth with purulent drainage); need for antibiotics (treatment 3/26 vs placebo 13/31); maternal hospital stay (6.03 vs 6.9; no variance given).
Notes	Class of antibiotic: aminopenicillin (ampicillin). Subgroups: • both elective and non-elective CS; • before cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "In a ... randomized manner"...."There is a notable difference in the division of repeat sections between groups". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Comment: prepared by the hospital pharmacy.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: no losses to follow-up were reported. 23/80 excluded because of errors in dispensation of medication. Analysis was not ITT; data from excluded patients could not be re-included.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, placebo-controlled. The pharmacist was the only individual with access to the treatment protocol.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: probably outcome assessment was blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Duff 1982

Methods	Randomized placebo-controlled trial; 2 parallel groups.

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Duff 1982 *(Continued)*

	Unit of randomization: individual.
Participants	Dates of data collection: January 1970 to June 1980. Setting: Washington, DC. US. Inclusion criteria: women undergoing CS who were not in labor and did not have ruptured membranes (elective). N = 82.
Interventions	Intervention: • ampicillin 1 g 30 min prior to surgery and at 4 and 8 hrs post-operatively; • N = 42. Comparison: placebo: • placebo solution; • N = 40.
Outcomes	Febrile morbidity (> 100.4 ºF twice 6 hrs apart after the 1st 24 hrs); endomyometritis (fever, uterine and adnexal tenderness, purulent lochia); UTI; wound infection (induration, erythema and warmth with purulent drainage); need for antibiotics (treatment 1/42 vs placebo 6/40); maternal hospital stay (4.3 vs 4.6; no variance given).
Notes	No life-threatening infection related complications nor bacteremic episodes in either group. Class of antibiotic: aminopenicillin (ampicillin). Subgroups: • elective CS; • before cord clamping. The 2 groups were comparable regarding age, race, gravidity, parity and socioeconomic status.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: randomized; no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up; no participant excluded; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind" .... "placebo solution".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.

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Duff 1982 *(Continued)*

Other bias	Low risk	Comment: no other sources of bias identified.

Elliott 1986

Methods	RCT; 4 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Letterman Army Medical Center, California; Womack Army Community Hospital, North Carolina. Inclusion criteria: women in active labor or ruptured membranes and at least 1 digital vaginal examination (categorized as non-elective in this review although duration of membrane rupture not stated). N = 158. Exclusion criteria: allergy to penicillin or cephalosporin, fever > 37.7 ºC with suspicion of chorioamnionitis; antibiotic use within 2 weeks.
Interventions	Intervention 1: • cefoxitin, 2 g IV after clamping the cord, repeated every 6 hrs for 48 hrs = total 14 g; • N = 39. Intervention 2: • cefoxitin, 2 g uterine and peritoneal lavage, after delivery of the placenta; • N = 42. Intervention 3: • cefoxitin, 2 g irrigation plus 2 g IV repeated every 6 hrs for 48 hrs = total 14 g IV; • N = 38. Comparison: no treatment: • no therapy; • N = 39. The 3 treatment groups have been combined in this review.
Outcomes	Febrile morbidity (> 37.9 ºC twice 6 hrs apart after 1st 24 hrs); endometritis (fever and uterine tenderness); UTI (positive culture); wound infection (including fever, cellulitis and exudate); hospital stay (treatment 4.86 vs control 5.2; variance could not be calculated).
Notes	3 episodes of septicemia reported in control group vs none in treatment groups. No antibiotic reactions reported. Class of antibiotic: cefamycin (2nd generation cephalosporin). Subgroups: • non-elective CS; • after cord clamping. The 4 groups were comparable regarding age, parity, gestational age, rupture of membrane, labor, vaginal examination.

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Elliott 1986 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomized... using a table of random numbers...".
Allocation concealment (selection bias)	Unclear risk	Comment: insufficient information to judge.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded from the analysis; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Engel 1984

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: August 1980 to August 1981. Setting: Nordwest Hospital, Frankfurt, West Germany. Inclusion criteria: women undergoing CS. N = 100. Exclusion criteria: severe penicillin allergy, renal insufficiency, antibiotic use, amniotic infection.
Interventions	Intervention: • mezlocillin 4 g and oxacillin 2 g every 8 hrs after clamping of the cord for 3 doses; • N = 50. Comparison: no treatment: • no treatment; • N = 50.
Outcomes	Endometritis, UTIs, wound infections.
Notes	Detailed pre- and post-antibiotic microbiological cultures were performed; there were fewer gram positive cocci and more gram negative rods in cervical cultures of the treated group; more break-through infections in the treated group were with mezlocillin-resistant organisms.

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Engel 1984 *(Continued)*

Class of antibiotic: other combination (penicillinase-resistant penicillin (oxacillin) and ureidopenicillin (mezlocillin)).

Subgroups:

- type of CS unclear;
- after cord clamping.

"Both groups were statistically homogenous."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...a computerised list of randomization...".
Allocation concealment (selection bias)	Unclear risk	Comment: insufficient information to judge.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: although there is no report of losses or exclusions and analysis appears to be ITT, there is insufficient information to judge.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: not placebo-controlled. Single-blinded; women did not know their allocation but clinicians did.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: clinicians were aware of allocation.
Other bias	Low risk	Comment: no other sources of bias identified.

Escobedo 1991

Methods	Double-blind RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Date of data collection: March 1985 to August 1986. Setting: Mexico. Inclusion criteria: women undergoing CS (labor < 12 hrs, membrane rupture < 12 hrs, < 7 vaginal exams). N = 91. Exclusion: any antibiotic within 2 weeks, fever, clinical evidence of infection.
Interventions	Intervention: • ampicillin 1 g IV every 6 hrs x 3 then 1 g every 6 hrs x 7 days; • N = 23.

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Escobedo 1991 *(Continued)*

	Intervention: • ampicillin 1 g every 6 hrs x 3 doses then placebo; • N = 37. Comparison: placebo: • placebo; • N = 31. Antibiotics administered after surgery, within 2 hrs of the procedure. 2 treatment groups combined.
Outcomes	Fever > 38 ºC x 2 at least 6 hrs apart after 1st 24 hrs; endometritis (temperature > 38 ºC, purulent lochia, pain on internal examination); wound infection (increased warmth, size or color of wound, or purulent secretions); urine infection (dysuria and positive culture).
Notes	Paper was not written in English. Class of antibiotic: aminopenicillin (ampicillin). Subgroups: • type of CS unclear; • after cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...by computerized tables...".
Allocation concealment (selection bias)	Unclear risk	Comment: assignment to treatment group was performed using the computer card which is attached to the file; no additional information was provided.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 3 were lost to follow-up; 3 patients excluded for inadequate follow-up (group allocation not provided).and no exclusions were reported. No explanation provided for unequal size groups. The analysis was as treated with the available data.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, matching placebo doses.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

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Freeman 1982

Methods	Quasi-RCT, 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: Jan 1979 to May 1980. Setting: Riverside Osteopathic Hospital, Michigan, USA. Inclusion criteria: women at high risk (defined as presence of labor) undergoing CS. N = 118. Exclusion criteria: oral temperature > 38° C any time prior to surgery; antibiotic use within 2 weeks prior to admission; refusal to participate; repeat elective CS; compelling indication for antibiotics in the judgement of the physician.
Interventions	Intervention: • carbenicillin, 2 g IV within 1 hr prior to surgery then 6 and 12 hrs after operation for a total of 3 doses; • N = 34. Intervention: • cefazolin, 1 g IV within 1 hr prior to surgery, then 5 and 12 hrs after operation for total of 3 doses; • N = 28. Comparison: no treatment: • no treatment; • N = 56. Authors pooled data because they identified no difference in outcomes. Data are not presented individually, only pooled. We have therefore analyzed as "Other regimen".
Outcomes	Febrile morbidity (oral temperature > 38 °C twice at least 6 hrs apart after the 1st 24 hrs); wound infection (fever, cellulitis, and/or exudate); endometritis (fever, uterine tenderness and foul discharge, or fever and a positive culture with uterine tenderness and no other apparent cause); UTI (fever, urinary tract symptoms and/or positive culture > 100,000 organisms/mL if pre-operative culture negative); pulmonary infection (fever with abnormal chest x-ray and/or physical signs of consolidation); undetermined (persistent fever with no discernible signs of infection).
Notes	Results of 2 antibiotic groups reported together. Class of antimicrobial: other regimen (1st generation cephalosporin vs extended spectrum penicillin (carboxypenicillin (carbenicillin)). Subgroups: • non-elective CS; • before cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "By random distribution of the last digit of their hospital number" .... "Lack of any significant differences between the two groups confirmed adequate randomization". Comment: quasi-RCT.
Allocation concealment (selection bias)	High risk	Comment: no information provided.

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Freeman 1982 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded after randomization; ITT analysis.
Selective reporting (reporting bias)	High risk	Comment: authors chose to pool data from the 2 treatment groups because they identified no difference in outcomes. Data were not presented individually, only pooled.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Fugere 1983

Methods	Randomized, placebo-controlled trial; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: September 1980 to November 1981. Setting: Hopital Saint-Luc, Montreal, Canada. Inclusion criteria: women undergoing non-elective CS. N = 89. Exclusion criteria: not in labor with intact membranes, allergy to cephalosporins, antibiotic use within 48 hrs, fever, ruptured membranes for > 36 hrs.
Interventions	Intervention: • cefoxitin 2 g IV; • N = 30. Intervention: • cefazolin 1 g IV; • N = 30. Comparison: placebo: • placebo; • N = 29. At clamping of the cord and at 6 and 12 hrs later. Placebo group was divided 1/2 and for comparison with the 2 treatment groups.
Outcomes	Endometritis, wound infection, UTI (symptoms or 2 successive positive cultures) septicemia, pelvic abscess, pelvic thrombophlebitis. Follow-up at 6 weeks. No side effects observed.
Notes	There were no serious infections in any of the groups.

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Fugere 1983 *(Continued)*

In the placebo and cefazolin groups there was no increase in aerobic bacterial colonization of the cervix after 4 days but there was an increase in colonization by anaerobes; the opposite occurred in the group receiving cefoxitin.

Class of antibiotic: 1st generation cephalosporin vs cefamycin (2nd generation cephalosporin).

Subgroups:

- non-elective CS;
- after cord clamping.

The groups were comparable regarding demographic characters.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Quote: "A number (1 to 90) identified the boxes. The number was allocated randomly to a box". Comment: an envelope containing the randomization code was available in case of adverse reactions.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss to follow-up; 1 patient in the control group was excluded from analysis as no cultures were performed; as-treated analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double blind"..... "vitamin solution with a similar colour as the other preparations". Comment: placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Gall 1979

Methods	RCT, 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not stated. Setting: Duke Universtiy Medical Center, North Carolina, USA. Inclusion criteria: all women undergoing either a repeat CS or in labor. N = 95.

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Gall 1979 *(Continued)*

	Exclusion: clinical infection, ruptured membranes for > 12 hrs, prior antibiotics within 48 hrs, renal or hepatic disease.
Interventions	Intervention: • cefazolin 1 g IM pre-operatively (on call to the operating room) and cephalothin 2 g IV at 6, 12, and 24 hrs after 1st dose; • N = 46. Comparison: placebo: • placebo; • N = 49.
Outcomes	Wound infection (cellulitis, purulent exudate, intraperitoneal abscess or peritonitis); endometritis; UTI; maternal hospital stay.
Notes	No minor side effects (rash or pruritus) or major reactions (anaphylaxis) observed. 4 women (all in control group) had septicemia (counted as serious morbidity). Class of antimicrobial: 1st generation cephalosporin. Subgroups: • both elective and non-elective; • before cord clamping. The 2 groups were comparable regarding age, racial distribution, parity, number of catheterizations or length of time of indwelling catheter.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded after randomization; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind". Comment: placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

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Ganesh 1986

Methods	Randomized, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Date of data collection: November 1983 and December 1984. Setting: University Hospital, New Jersey; lower socioeconomic class (90% black). Inclusion criteria: women < 21 years old undergoing CS. N = 57. Exclusion: antibiotic use within 2 weeks; active infection or fever at delivery; penicillin or sulfa allergy; internal fetal monitoring.
Interventions	Intervention: • trimethoprim 240 mg and sulfamethoxazole 1200 mg IV after clamping of cord; • N = 29. Comparison: placebo: • placebo; • N = 28.
Outcomes	Endomyometritis (fever [> 100.3ºF twice within 24 hrs after 1st day], uterine tenderness, absence of another focus); UTI (fever and positive culture); wound infection (fever, abnormal appearing wound with cellulitis or a wound draining purulent material).
Notes	Authors' definition of high risk not comparable with that used in this review. The incidence of UTI and wound infection was similar between the groups (numbers not given). Class of antibiotic: trimethoprim/sulfamethoxazole. Subgroups: • type of CS unclear; • after cord clamping. The 2 groups were comparable regarding age, gravidity, vaginal examinations, duration of labor and duration of rupture of membranes, elective repeat CS.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly divided". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up reported; no participants excluded; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.

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Ganesh 1986 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: placebo-controlled; no further information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Garcia 1992

Methods	Randomized trial; 2 parallel groups. Unit of randomization: individual.
Participants	Date of data collection: not reported. Setting: Salamanca, Spain. Inclusion criteria: women undergoing CS (both emergency and elective). Definitions of emergency (in labor) and elective (planned) not consistent with definitions used in this review; classified as "both". Exclusion criteria: fever ≥ 37.5°C before or during childbirth; premature rupture of membranes > 12 hrs; allergic to penicillin or its derivatives; prior antibiotic therapy; signs of renal and hepatic dysfunction.
Interventions	Intervention 1: • cefonocid 2 g IV over 3-5 minutes after clamping of the cord; • N = 100. Intervention 2: • placebo (not described further); • N = 70.
Outcomes	Endometritis (fever, uterine tenderness and fetid discharge or fever and pathogenic organisms cultured from the lochia); wound infection (fever, induration and exudation and/or cultures of purulent exudate form the wound with or without fever); UTI (fever and urinary symptoms and/or positive urine culture with or without fever); pelvic septic thrombophlebitis (none in either group).
Notes	Translated from Spanish. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • type of CS both; • after cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly assigned". Comment: no description of sequence generation process.

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Garcia 1992 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss to follow-up or exclusion of participants reported; no explanation for uneven number of participants between groups.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind"; control group administered "a placebo".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Gerstner 1980

Methods	Randomized trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: August 1979 and April 1980. Setting: Universitats-Frauenklinik Wien, Austria. Inclusion criteria: women undergoing CS. N = 103.
Interventions	Intervention: • metronidazole 500 mg IV before induction of anesthesia and 12 and 24 hrs post-operatively, then rectal suppository x 4 days; • N = 53. Comparison: no treatment: • no treatment; • N = 50.
Outcomes	Fever (> 38ºC on 2 subsequent days); wound infection; endometritis; additional use of antibiotics (treatment 13/53 vs control 22/50); maternal hospital days.
Notes	Full translation pending. Class of antibiotic: nitroimidazole (metronidazole). Subgroups: • type of CS unclear; • before cord clamping.

Risk of bias

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Gerstner 1980 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized...". Comment: no description of sequence generation process and no further details provided in translation.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported; appears to be an ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Gibbs 1972

Methods	Random allocation is presumed although method not described.
Participants	Dates of data collection: November 1971 and April 1972. Setting: University of Pennsylvania. Inclusion criteria: women undergoing primary CS or repeat section. N = 61. Exclusion criteria: penicillin allergy, fever in labor.
Interventions	Intervention: • ampicillin 1 g, methicillin 1 g and kanamycin 0.5 g IM 15-30 minutes before, and at 2 and 8 hrs after delivery; • N = 33. Comparison: placebo: • placebo; • N = 28.
Outcomes	Endometritis (fever and uterine tenderness or fever and pathogenic organism without other cause); UTI; wound infection (fever, cellulitis and exudate); morbidity [fever > 100ºF in 2 separate 24 hr periods after 1st postpartum day or positive post-operative urine culture of > 100,000 colonies/mL] (treatment 9/33 vs placebo 17/28); UTI (fever and urinary tract symptoms or a single significant culture with or without fever); maternal hospital stay (6.5 vs 6.9 days; no variance given).

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Gibbs 1972 *(Continued)*

Notes	2 serious infections: 1 pelvic abscess in treatment group, 1 septicemia in placebo group. Authors' definitions of repeat and primary section not consistent with those used for elective/non-elective in this review. Class of antibiotic: aminoglycoside-containing combination (aminopenicillin (ampicillin), penicillinase-resistant penicillin (methicillin), aminoglycoside). Subgroups: • type of CS unclear; • before cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...the patient randomization" ... "The patient randomization is statistically acceptable". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Quote: "The materials were prepared by the pharmacy service in coded identical vials, containing identically appearing solutions".
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: 17 patients (28%) "were eliminated from the study, 6 for errors in giving the study medications, 5 for penicillin allergies, 3 for fever in labor, 2 for being started on ampicillin prophylaxis, and 1 for cesarean hysterectomy". Comment: no loss of participants to follow-up. Analysis done on included patients; no data available to incorporate data on patients eliminated.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: placebo-controlled; study described as double-blind.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Gibbs 1973

Methods	Random allocation is presumed although method not described.
Participants	Dates of data collection: August 1972 to February 1973. Setting: University of Pennsylvania. Inclusion criteria: women undergoing CS. N = 68. Exclusion criteria: penicillin allergy, fever in labor.
Interventions	Intervention:

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Gibbs 1973 *(Continued)*

	• ampicillin 1 g and kanamycin 0.5 g IM 15 to 30 minutes before, and at 2 and 8 hrs after delivery; • N = 34. Comparison: placebo: • placebo; • N = 34.
Outcomes	Endometritis (fever and uterine tenderness or fever and pathogenic organism without other cause); UTI; wound infection (fever, cellulitis and exudate; any grade); morbidity [fever > 100ºF in 2 separate 24 hr periods after 1st postpartum day or positive post-operative urine culture of > 100,000 colonies/mL] (treatment 8/34 vs placebo 22/34).
Notes	1 pelvic abscess in placebo group. Authors' definitions of repeat and primary section not comparable to those used for elective/non-elective in this review, categorized as 'both'. Class of antibiotic: aminoglycoside-containing combination. Subgroups: • type of CS unclear; • before cord clamping. The groups were comparable regarding age, rupture of membranes, indication for CS and anemia.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomization of patients is acceptable". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Quote: "The materials were prepared by the pharmacy service in coded identical vials, containing identically appearing solutions".
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "25 patients were eliminated because of penicillin allergy, fever in labor, errors in giving the medication, etc. None was used as a control". Comment: an ITT analysis was not performed and the data cannot be re-included.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: placebo-controlled; described as double-blind.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

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Gibbs 1981

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: October 1978 and July 1979. Setting: Robert B Green Memorial Hospital, Texas, US; patients indigent and predominantly Mexican-American. Inclusion criteria: women in labor with rupture of membranes (non-elective). Exclusion criteria: infection, antibiotics within prior 3 days, allergy to penicillin or cephalosporin; no consent.
Interventions	Intervention: • cefamandole 2 g IV after cord clamping, and at 4 and 8 hrs post-operatively; • N = 50. Comparison: placebo: • identical appearing placebo; • N = 50.
Outcomes	Endomyo(para)metritis; wound infection; maternal hospital stay; records reviewed 6 weeks to 6 months after discharge. 4 episodes of bacteremia (1 in treatment group, 3 in placebo) have been categorized as serious outcomes.
Notes	No incidence of pelvic abscess or septic thrombophlebitis in either group. Increase in Enterobacteriacae and enterococci and decrease in gram positive anaerobes and non-pathogens in prophylactic group. No adverse clinical or laboratory results attributable to treatment. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • non-elective CS; • after cord clamping. The 2 groups were comparable regarding age, parity, race, gestational age, weight, indications for CS, anesthesia, etc.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses to follow-up; no participants excluded; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.

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Gibbs 1981 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, identical-appearing placebo.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Gordon 1979

Methods	RCT, 3 parallel groups. Unit of randomization: individual.
Participants	Dates of collection: enrolment started November 1976. Setting: San Bernadino county and University of California at Los Angeles Medical Centers; primarily indigent cases. Inclusion criteria: women undergoing CS. N = 114. Exclusion: emergency section, penicillin allergy, fever > 38 degrees C, on antibiotics; declined to participate.
Interventions	Intervention: • ampicillin 1 g IV 15-30 minutes before surgery and at 2 and 8 hrs post-operatively; • N = 38. Intervention: • ampicillin 1 g IV immediately after cord clamping and at 2 and 8 hrs post-operatively (N = 40). Comparison: no treatment: • no antibiotic; • N = 36. Outcomes of both treatment groups combined.
Outcomes	Endometritis; wound infection; UTI; maternal hospital stay (5.1 and 4.7 for pre- and post-administration of antibiotics respectively vs 6.0 for no treatment, variance not given).
Notes	Although emergency CSs were excluded, the women enrolled did not conform to our definition of an elective section. Information on neonatal morbidity collected; there were 2 infants with definite infections in mothers who received no antibiotics and 1 infection in an infant where antibiotics were given after cord clamping. Class of antibiotic: aminopenicillin (ampicillin). Subgroups: • both elective and non-elective CS; • before cord clamping (N = 38) and after cord clamping (N = 40).

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Gordon 1979 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "at random". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded after randomization; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "...because of the different modes of administering the antibiotics, a double-blind study was not possible". Comment: no blinding; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The investigator was not intimately involved with the post-operative care ... and the pediatricians did not know into which group the mothers had been placed".
Other bias	Low risk	Comment: no other sources of bias identified.

Gummerus 1984

Methods	'Randomly divided' (no details provided); placebo-controlled.
Participants	Dates of data collection: December 1981 to August 1982. Setting: School of Midwifery, Helsinki, Finland. Inclusion criteria: women undergoing CS (average duration of labor 8 hrs 45 min; average duration of membrane rupture 6 hrs 48 min) N = 219. Exclusion: women undergoing elective CS (not defined further); antibiotics prior to procedure.
Interventions	Intervention: • metronidazole 500 mg IV after cutting of cord; • N = 109. Comparison: placebo: • placebo; • N = 110.
Outcomes	Fever (temperature ≥ 38ºC); wound infection, endometritis, sepsis (temperature > 38.5ºC and bacteremia); abscess of pouch of Douglas (1 in each group).
Notes	Translated from German.

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Gummerus 1984 *(Continued)*

Class of antibiotic: nitroimidazole (metronidazole).

Subgroups:

- type of CS unclear;
- after cord clamping.

The groups were comparable in respect of social status, age, parity, duration of pregnancy, primary section/repeat section, axillary temperature before the procedure, localization of skin incision, number of amnioscopes.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly" divided into 2 groups. Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no losses or exclusions reported; it appears the analysis was ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: placebo-controlled; no additional information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Hager 1983

Methods	Randomized, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Central Baptist Hospital, Lexington, Kentucky, US. Inclusion criteria: women undergoing primary, non-elective CS (while it appears most women were in labor and/or had ruptured membranes it is unclear whether all patients fulfilled our criteria for non-elective). N = 90. Exclusion: antibiotic use within 7 days, penicillin or cephalosporin allergy.
Interventions	Intervention:

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Hager 1983 *(Continued)*

	• cefamandole 500 mg IV immediately after the cord was clamped, again in the recovery room and 2 more doses 6 hrs apart; • N = 43. Comparison: placebo: • identical-appearing placebo; • N = 47.
Outcomes	Infectious morbidity (fever > 100.3ºF twice 6 hrs apart after 1st 24 hrs); endomyometritis (fever, uterine tenderness, and positive culture from endometrium); wound infection, UTI; maternal duration of stay (treatment 5.1 days vs placebo 5.4; not significant, no variance given).
Notes	There was 1 episode of bacteremia in the control group. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • type CS unclear; • after cord clamping. The 2 groups were comparable regarding age, race, parity, weight, type of anesthesia, operating time or pre-operative hematocrit.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Quote: "according to pre-numbered envelopes maintained in the central pharmacy".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up; no participant excluded; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind".... "identical appearing, equal volume solution".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Hagglund 1989

Methods	Randomized, placebo-controlled trial; 2 parallel groups.

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Hagglund 1989 *(Continued)*

	Unit of randomization: individual.
Participants	Dates of data collections: July 1983 and December 1986. Setting: University Hospital, Lund, Sweden. Inclusion criteria: women undergoing emergency CS (during labor and/or after rupture of membranes [duration not specified]); categorized as "both" for this review. N = 160. Exclusion criteria: fever > 38ºC, given antibiotics, chemotherapy or immunosuppressive therapy in prior 3 weeks, allergy to cephalosporins, alcohol or drug abuse, chronic disease of cardiovascular, renal, hepatic or gastrointestinal system, severe anemia.
Interventions	Intervention: • cefuroxime 1.5 g IV at the start of the operation and 12 hrs later; • N = 80. Comparison: placebo: • saline placebo; • N = 80.
Outcomes	Endometritis (fever > 38ºC twice at least 1 hr apart, after the 1st post-operative day, and increased tenderness of the uterus); wound infection (redness, tenderness, increased heat and edema of wound); UTI.
Notes	There were no cases of septicemia or abscess formation observed in either group. Only 55% of women had ruptured membranes (number > 6 hs not stated) and 77% were in labor; these definitions do not meet our criteria for non-elective section, categorized as 'both'. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • both elective and non-elective CS; • before cord clamping. The 2 groups were comparable regarding age, parity, previous CS, complications during pregnancy and gestational age at the operation.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...a pre-set randomized series in a double-blind manner...". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported. It appears to be an ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge.

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Hagglund 1989 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind". Comment: placebo-controlled (saline).
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Harger 1981

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not stated. Setting: Pittsburgh, Pennsylvania, US. Inclusion criteria: women undergoing CS after labor or rupture of membranes (method section unclear as to duration of ruptured membranes; it has been assumed that all women were in labor). N = 386. Exclusion criteria: elective CS without labor; already receiving antibiotics; fever or other evidence of infection; allergy to penicillin or cephalosporins; requiring endocarditis prophylaxis.
Interventions	Intervention: cephalosporin (B2a): • cefoxitin 2 g IV after cord clamping, and at 6 and 12 hrs after initial dose; • N = 196. Comparison: placebo: • matching mannitol and riboflavin placebo; • N = 190.
Outcomes	Febrile morbidity (fever > 37.9ºC twice at least 4 hrs apart after 1st post-operative day); endomyometritis (fever > 38ºC with uterine tenderness, maternal white blood cell count > 15000/cu mm, malodorous lochia and no apparent cause for fever); UTI; incision infection (purulent drainage with induration and tenderness); additional antibiotic therapy (treatment 26/196 vs placebo 68/190).
Notes	Increase in enterococci and decrease in *Staphylococcus aureus*, various streptococci, *E. coli* and a variety of anaerobes from infected sites in prophylactic group compared with placebo. Class of antibiotic: cefamycin (2nd generation cephalosporin). Subgroups: • non-elective CS; • after cord clamping. The 2 groups were comparable regarding demographic and obstetric variables and indications for CS.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

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Harger 1981 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Quote: "The hospital pharmacy prepared coded vials".
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: no loss to follow-up reported. 14/400 women initially randomized not included in final analysis (errors in protocol, 2 allergic to penicillin after 1st dose given and 2, who received cefoxitin, for infusion-related reactions); insufficient data provided to perform ITT analysis.
Selective reporting (reporting bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, identical appearing placebo.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Hawrylyshyn 1983

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: July 1980 to June 1981. Setting: Mount Sinai Hospital, Toronto, Canada. Inclusion criteria: women undergoing CS (at 'high' risk because of ruptured membranes in active labor); classified as 'non-elective'. N = 182. Exclusion criteria: febrile, antibiotic use in prior 24 hrs; allergy to penicillin or cephalosporin; significant hepatic or renal disease. Predominantly private, middle-class and in their late 20s.
Interventions	Intervention: cephalosporin (B2a): • cefoxitin 2 g IV at time of cord clamping; • N = 64. Intervention: cephalosporin (B2a): • cefoxitin 2 g at time of cord clamping and at 4 and 8 hrs post-operatively; • N = 60. Comparison: placebo: • identical-appearing placebo;

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Hawrylyshyn 1983 *(Continued)*

	• N = 58. Both treatment groups combined in this analysis.
Outcomes	Febrile morbidity (> 38ºC twice at least 8 hrs apart, after 1st post-operative day); endometritis (fever, foul, excessive lochia or uterine tenderness); UTI (fever and positive culture); wound infection (fever, cellulitis or exudate with positive cultures).
Notes	No adverse drug reactions in cefoxitin groups, no septicemia in any group; 4 patients in placebo group were considered seriously ill (although do not fit the criteria for serious morbidity in this review) compared to none in treatment groups. Antibiotic class: cefamycin (2nd generation cephalosporin). Subgroups: • non-elective CS; • after cord clamping. The 3 groups were comparable regarding age, parity, gestational age, duration of labor, duration of ruptured membranes, number of vaginal examinations, use of internal fetal monitoring or post-operative hemoglobin.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Quote: "...randomly packaged in identical vials coded from 1 to 200". Comment: insufficient information provided to judge.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: no loss of participants to follow-up; 7 patients were excluded after having entered the study. 1 patient was excluded because of an error in mixing and administering the IV injections; 6 patients were excluded because they became febrile within 8 hrs of operation and required immediate antibiotic therapy. As-treated analysis; data from excluded patients could not be re-included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "...double-blinded, placebo-controlled" ... "The medication and an identical appearing placebo were prepared prior to the study and ... packaged in identical vials....The attending physician was unaware of what regimen his patient received and the code numbers were revealed only after the study was completed".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The attending physician was unaware of what regimen his patient received". Comment: probably outcome assessment was blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

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Heilmann 1984

Methods	Randomized trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not stated. Setting: Essen, Germany. Inclusion criteria: women undergoing CS in labor (classified as non-elective). Exclusion criteria: none reported.
Interventions	Intervention 1: • cefoxitin 2 g within 3 minutes of anesthetic induction; • N = 30. Intervention 2: • no treatment; • N = 30.
Outcomes	Febrile morbidity (oral temperature > 30°C for at least 2 days); wound infection (reported as "healing difficulties" in translation of table); UTI (10^5 bacteria/mL after removal of the catheter); length of post-operative stay.
Notes	Translated from German. Class of antibiotic: cefamycin (2nd generation cephalosporin). Subgroups: • non-elective CS; • before cord clamping. The groups were comparable for age, weight, duration of operation, birthweight, duration of urinary catheter use, premature rupture of membranes > 12 hrs; intrauterine fetal monitoring; birthweight.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "open randomization". Comment: no additional information provided; no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up; analysis was ITT.
Selective reporting (reporting bias)	Unclear risk	Insufficient information provided.
Blinding of participants and personnel (performance bias)	High risk	Comment: no blinding; not placebo-controlled.

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Heilmann 1984 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Huam 1997

Methods	Quasi-RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: September 1994 to April 1995. Setting: University Hospital, Kuala Lumpur, Malaysia. Inclusion criteria: elective CS. Exclusion criteria: allergic to penicillin, evidence of infection, premature rupture of membranes, receiving antibiotics prior to CS.
Interventions	Intervention: • augmentin (amoxicillin-clavulanic acid)1.2 g IV either at the time general anesthesia was induced or after epidural block; • N = 100. Comparison: no treatment: • no treatment; • N = 100.
Outcomes	Febrile morbidity (fever > 38°C twice at least 4 hrs apart after the 1st 24 hrs); wound sepsis (defined and graded as a) erythema and/or induration, b) serous oozing, c) presence of pus, d) wound dehiscence); UTI (routine midstream urine on 3rd post-operative day > 100,000 organisms/mL); endometritis (fever, uterine tenderness and foul smelling lochia); pneumonia (cough, fever and/or radiographic evidence of pulmonary consolidation).
Notes	Class of antibiotic: beta-lactamase inhibitor combination. Subgroups: • elective CS; • before cord clamping. "Both the study groups and control group were comparable in terms of patient characteristics and operative variables."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Alternately allocated to either antibiotic group or control group". Comment: quasi-RCT.

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Huam 1997 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded after analysis; ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Ismail 1990

Methods	Double-blind, randomized, placebo-controlled; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: University of Illinois College of Medicine, Chicago, US (large, inner city hospital); majority of participants black (40%) or Hispanic (60%). Inclusion criteria: undergoing CS. N = 152. Exclusion: pre-operative fever, antibiotics within 1 week, membranes ruptured > 36 hrs, evidence of chorioamnionitis, penicillin or cephalosporin allergy.
Interventions	Intervention: cephalosporin (B2a): • cefoxitin 2 g after cord clamped and at 4 and 8 hrs; • N = 74. Comparison: placebo: • placebo; • N = 78.
Outcomes	Endometritis (fever and uterine tenderness or fever and pathologic organism without other focus); wound infection (fever, cellulitis and exudate); UTI (fever and symptoms or positive culture).
Notes	In the placebo group there were 8 episodes of serious morbidity (6 cases of sepsis; 1 pelvic abscess; 1 episode of pelvic thrombophlebitis) compared with 1 in the treated group (1 episode of sepsis). Routine post-operative cultures were performed: enterococci were isolated from 30/68 cases who received cefoxitin vs 15/74 who received placebo; there was no change in the rate of cefoxitin resistance in *Enterobacteriaceae* from the stool after prophylaxis. Class of antibiotic: cefamycin (2nd generation cephalosporin).

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Ismail 1990 *(Continued)*

	Subgroups: • type of CS unclear; • after cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized...". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported. The analysis appeared to be ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge
Other bias	Low risk	Comment: no other sources of bias identified.

Jaffe 1984

Methods	RCT, 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: March to October 1982. Setting: A Meir General Hospitla, Kfar Sava, Israel. Inclusion criteria: patients undergoing CS, classified as “no-labor” if cesarean was performed before onset of labor and “labor” if occurred after onset of labor. N = 113. Exclusion criteria: evidence of infection, known allergy to penicillin, antibiotic therapy during the previous 2 weeks.
Interventions	Intervention: extended spectrum penicillin: • mezlocillin 2 g IV 30 minutes before surgery, then 4 and 9 hrs after surgery; • N = 58. Comparison: placebo: • placebo IV 30 minutes before surgery, then 4 and 9 hrs after surgery;

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Jaffe 1984 *(Continued)*

	• N = 55.
Outcomes	Febrile morbidity (2 oral temperatures > 38°C at least 4 hrs apart after the 1st 24 hrs); endometritis (fever and uterine tenderness with or without a positive lochial culture and no other apparent cause of fever); UTI (> 10^5colonies/mL after a negative pre-operative culture); wound infection (fever, cellulitis, exudate and tenderness).
Notes	Class of antibiotic: extended spectrum penicillin (ureidopenicillin (mezlocillin)). Subgroups: • both elective and non-elective CS - data separated by elective and non-elective; • before cord clamping. "The groups did not differ significantly in obstetrical variables...indications for CS were similar in both groups."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 7 patients were excluded for errors in following the protocol; excluded patients not included in analysis; data cannot be imputed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Placebo-controlled". Comment: insufficient information to judge.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Jaffe 1985

Methods	Randomized placebo-controlled trial: 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not stated. Setting: Kfar-Sava, Israel. Inclusion criteria: women undergoing CS. N = 78.

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Jaffe 1985 *(Continued)*

	Exclusion: women with active infection, allergy to penicillin and antibiotic treatment within 2 weeks.
Interventions	Intervention: • mezlocillin 5 g IV during 30 minutes prior to surgery; • N = 38. Comparison: placebo: • placebo; • N = 40.
Outcomes	Febrile morbidity (> 38ºC twice at least 4 hrs apart after 1st 24 hrs post-operative); endometritis (fever and uterine tenderness); UTI (single culture of > 100,000 bacteria/mL); wound infection (redness, cellulitis, tenderness and exudate from incision).
Notes	Authors' definition of emergency not consistent with definitions used in this review (classified as 'both/undefined'). Class of antibiotic: extended spectrum penicillin (ureidopenicillin (mezlocillin)). Subgroups: • type of CS unclear; • before cord clamping. The 2 groups were comparable regarding age, parity, rupture of membranes, duration of ruptured membranes, number of vaginal examinations, duration of anesthesia, and indications for CS.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomly assigned..". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: it is unclear whether all patients randomized were included in the analysis but no losses or exclusions were reported. It appeared to be an ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Placebo-controlled". Comment: insufficient information to judge.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

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Jakobi 1994

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection; not reported. Setting: Rambam Medical Center, Haifa, Israel. Inclusion criteria: low-risk women requiring cesarean delivery (elective procedure, duration of membrane rupture < 3 hrs, no more than 2 vaginal examinations). N = 307. Exclusion: required a drug other than cefazolin for prophylaxis, fever, membrane rupture > 24 hrs.
Interventions	Intervention: • cefazolin 1 g after clamping of the cord; • N = 167. Comparison: no treatment: • no treatment; • N = 140.
Outcomes	Febrile morbidity (fever > 37.7ºC twice at least 4 hrs apart after 1st 24 hrs); endometritis (fever, uterine tenderness and abnormal lochia); UTI (fever and positive culture); wound infection (fever, cellulitis or exudate with positive culture); therapeutic antibiotic use (treatment group 6.5% vs 20% in control group, P < 0.001).
Notes	Although some women were in labor at the time of the procedure (mean duration of labor 53 and 44 minutes in the 2 groups), the study population so closely resembles the criteria for elective CS used in this review that the results have been included in the 'elective' category. Class of antibiotic: 1st generation cephalosporin. Subgroups: • elective CS; • after cord clamping. The groups were comparable regarding socioeconomic level, weight, gestational age, post-operative hemoglobin and operation time.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: Randomized "by computer program to 1 of 2 groups" at time of their first antenatal visit.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no losses to follow-up; no participant excluded. Imbalance in group size not accounted for (likely because randomization occurred at 1st antenatal visit and not all patients randomized were enrolled). ITT analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.

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Jakobi 1994 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Karhunen 1985

Methods	Randomized, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: May 1982 to August 1983. Setting: South Saimaa Central Hospital, Lappeenranta, Finland. Inclusion criteria: initially all women undergoing CS (N = 80); thereafter women undergoing non-elective (ruptured membranes) section.
Interventions	Intervention: nitroimidazole: • tinidazole 500 mg IV at cord clamping; • N = 75. Comparison: placebo: • identical placebo; • N = 77.
Outcomes	Febrile morbidity (> 38ºC on 2 post-operative days, excluding the 1st); endometritis (fever, foul lochia or uterine tenderness); wound infection (fever, cellulitis or exudate); UTI (fever and positive culture).
Notes	Authors' definition of non-elective (ruptured membranes) and elective (unruptured membranes) not consistent with the definitions used in this review; classified in this review as 'both'. Newborn infants observed for effects of tinidazole (although data not given). Class of antibiotic: nitroimidazole (tinidazole). Subgroups: • both elective and non-elective CS; • after cord clamping. The 2 groups were comparable regarding age, weight, gestational age, etc.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized according to a code". Comment: no description of sequence generation process.

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Karhunen 1985 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Quote: "Identical vials ... coded from 1 to 160". Comment: insufficient information to judge.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: no loss to follow-up reported; 8 women excluded: 4 because they were febrile before the operation, 4 because of mistakes in administration; data not provided to perform ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Placebo-controlled, double blind" ... "The code was first opened when the study was completed".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Kellum 1985

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: September 1982 to September 1983. Setting: University of Mississippi Medical Center. Inclusion criteria: women undergoing non-elective CS (including prolonged ruptured membranes and prolonged labor, as well as general risk factors such as poor nutrition and poverty). Exclusion: current antibiotics, known infectious process, allergy to cephalosporins.
Interventions	Intervention: 2nd generation cephalosporin: • cefamandole 2 g in 800 mL saline irrigation during the procedure; • N = 84. Intervention: placebo: • saline irrigation; • N = 86. Comparison: no treatment: • no treatment; • N = 92. As the objective of this review is to compare antibiotic with no antibiotic, rather than the effect of irrigation, the 2 irrigation groups are compared.
Outcomes	Febrile morbidity (> 100.6ºF twice 6 hrs apart after 1st post-operative day); serious morbidity (fever and endomyometritis or abscess requiring IV antibiotics for resolution).

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Kellum 1985 *(Continued)*

Notes	Authors' definition of high risk does not correspond to that used for non-elective in this review, classified as 'both'. The outcome of serious morbidity included endomyometritis and is classified as endometritis in this review. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • type CS unclear; • after cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Randomized by last digit of hospital admission number". Comment: quasi-randomized trial.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: no loss to follow-up or exclusion of participants reported, but follow up given for only 77/84 of treatment and 53/86 of placebo group for outcome of serious infection, without explanation; no evidence ITT analysis was performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: placebo-controlled (normal saline irrigation). No further information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Kolben 2001

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: January 1996 to December 1997. Setting:Technical University of Munich. Munich, Germany. Inclusion criteria: elective CS. N = 146. Exclusion criteria: evidence of pre-existing infections, labor, rupture of membranes, oral temperature > 37.5°C, antibiotic therapy within 72 hrs or surgery, immune deficiency, known allergic reaction to cephalosporins, age < 18 years.

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Kolben 2001 *(Continued)*

Interventions	Intervention: 2nd generation cephalosporin: • cefotiam, 2 g IV intraoperative; • N = 76. Comparison: placebo: • no treatment; • N = 70.
Outcomes	Febrile morbidity (oral temperature of > 38°C twice on at lease 2 occasions 24 hrs apart or > 38.5°C on 1 occasion after the 1st 24 hrs); wound infection (purulent material at site of incision), endometritis (fever, uterine tenderness and offensive lochia), UTI (> 100,000 bacteria/mL of midstream urine in patients with symptoms (urgency, dysuria, frequency).
Notes	Unable to confirm whether drug given after clamping of cord. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • elective CS; • timing of administration not specified. "No significant difference was detected between the 2 groups for age, gestational age, health insurance status, body mass index, kind of anesthesia, duration of surgery, or additional pregnancy risk factors."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "according to a computer generated random assignment".
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded after randomization. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded
Other bias	Low risk	Comment: no other sources of bias identified.

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Kreutner 1978

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: November 1975 to June 1976. Setting: Medical University Hospital of South Carolina. Inclusion criteria: all women undergoing CS (51/97 not in labor; 61/97 without ruptured membranes). N = 97. Exclusion criteria: signs of infection, allergy to penicillin or cephalosporin, antibiotics within 2 weeks; lack of consent.
Interventions	Intervention: 1st generation cephalosporin: • cefazolin 1 g IV pre-operatively and at 2 and 8 hrs post-operatively; • N = 48. Comparison: placebo: • similar volume of placebo; • N = 49.
Outcomes	Febrile morbidity (> 100.3ºF twice on any of 1st 10 postpartum days after the 1st); endometritis (fever and uterine tenderness, or fever and pathogen from endometrium without other cause); UTI (fever or positive culture and symptoms); wound infection (fever, cellulitis and/or exudate).
Notes	Aerobic isolates unchanged, fewer anaerobes in patients given placebo; most pathogens isolated were resistant to cefazolin whether treatment or placebo given. There were 2 episodes of septicemia (both in placebo group). Class of antibiotic: 1st generation cephalosporin. Subgroups: • both elective and non-elective CS; • before cord clamping. The 2 groups were comparable regarding race, age and type of CS.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Random allocation". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: no loss to follow-up reported. 6 women initially randomized not included in analysis (non-adherence or non-infectious complications). As-treated analysis performed; could not re-include data.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.

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Kreutner 1978 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "A similar volume of placebo" was administered to the control group. Comment: insufficient information to judge.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Kristensen 1990

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: February 1987 to March 1988. Setting: Odense University Hospital, Denmark. Inclusion criteria: women undergoing non-elective CS (58/201 without labor; 65/201 without ruptured membranes). N = 201. Exclusion: fever, antibiotics within 7 days, penicillin or cephalosporin allergy.
Interventions	Intervention: 2nd generation cephalosporin: • cefuroxime 750 mg IV after cord clamping; • N = 102. Comparison: no treatment: • no treatment; • N = 99.
Outcomes	Febrile morbidity (> 37.9ºC twice at least 6 hrs apart after 1st post-operative day); endometritis (fever, uterine tenderness and abnormal lochia); wound infection (fever, cellulitis and/or purulent discharge); UTI; cost of post-operative antibiotics (treatment $US0.69 vs control $US7.47); maternal hospital stay (treatment 8.1 vs control 8.0, no variance given).
Notes	No woman had a severe infection such as pelvic abscess or septic pelvic thrombophlebitis. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • type of CS unclear; • after cord clamping. The 2 groups were comparable regarding epidemiologic and obstetric data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomly..".

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Kristensen 1990 *(Continued)*

		Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Quote: "envelopes containing empty vial or vial containing treatment". Comment: insufficient information to judge.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported. The analysis appears to be by ITT.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Patients, attending physicians, and study coordinators were blind with regard to group assignments". Comment: not placebo-controlled; insufficient information to judge.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Lapas 1988

Methods	Double blind, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Athens, Greece. Inclusion criteria: women undergoing elective or non-elective CS. Age range 17-40 years. N = 100. Exclusion criteria: allergy to metronidazole, amnionitis, and pyrexia.
Interventions	Intervention: Nitroimidazole: • metronidazole 500 mg IV 2 hrs or immediately pre-operatively, 500 mg intraoperatively, 1000 mg 8 hrs post-operatively; • N = 50. Comparison: placebo: • placebo; • N = 50.
Outcomes	Wound infection; endometritis; inadequate wound healing (metronidazole 1/50 vs placebo 8/50); mean temperature (36.8ºC SD 1.02 vs 37.6, 1.03); duration of hospital stay.
Notes	Although the authors are not identical and the presentation of the data makes direct comparisons difficult, the description of the 2 studies cited is so similar that it is presumed the 2 citations refer to the same patient population. Translated from Bulgarian. Class of antibiotic: nitroimidazole (metronidazole).

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Lapas 1988 *(Continued)*

Subgroups:

- both elective and non-elective CS;
- before cord clamping.

There was no significant difference in parity and age between the groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Women were divided into 2 groups". Comment: insufficient information to judge.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no information available.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind; placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Lemus 2005

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Date of data collection: not reported. Setting: Hospital de Ginecologia y Obstetrcia num. 3 del Centro Medico La Raza, Mexico City, Mexico Inclusion criteria: women who had undergone CS with: no risk factors for wound infection at the time of the operation; no UTI or cervicovaginitis; intact membranes; less than 6 vaginal examination before the operation; no allergy to beta-lactam antibiotics; clean surgical procedure without prolonged stage of labor (less than 33 minutes); primary closure of the incision; no use of drains. Exclusion criteria: women with medical factors that would lead to inadequate wound healing (diabetes, obesity, malnutrition); post-surgical factors (asthma, pulmonary complications, coughing and vomiting after surgery); ascites; anemia; history of radiotherapy; anesthetic complications requiring intensive care admission; corticosteroid use; incomplete follow-up.
Interventions	Intervention 1:

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Lemus 2005 *(Continued)*

- cefotaxime 1 g every 8 hrs x 24 hrs;
- N = 500.

Intervention 2:

- no treatment;
- N = 500.

Outcomes	Wound infection (follow-up until day 30); definition of wound infection unclear.
Notes	Translated from Spanish Class of antibiotic: 3rd generation cephalosporin. Subgroups: • elective CS (based on inclusion criteria stating labor of less than 33 minutes); • after cord clamping (women had undergone CS).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: Women were allocated "at random and sequentially, but non-random" as it depended on the obstetrician to start the prophylaxis perioperatively.
Allocation concealment (selection bias)	High risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: women with incomplete follow-up were excluded.
Selective reporting (reporting bias)	Unclear risk	Comment: no information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding; not placebo-controlled; obstetrician started prophylaxis.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Leonetti 1989

Methods	Randomized placebo-controlled trial; 3 parallel groups. Unit of randomization: individual.
Participants	Date of data collection: not reported. Setting: Jersey City Medical Center, New Jersey; predominantly lower socioeconomic indigent women.

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Leonetti 1989 *(Continued)*

	Inclusion criteria: women undergoing primary CS after onset of labor (corresponds to the definition of non-elective). N = 150. Exclusion: febrile or infected, allergy to pipericillin.
Interventions	Intervention 1: ureidopenicillin: • pipericillin 4 g peri-operatively; • N = 50. Intervention 2: ureidopenicillin: • pipericillin 4 g peri-operatively and at 4 and 8 hrs post-operatively; • N = 50. Comparison: placebo: • placebo; • N = 50. Both treatment groups combined in analysis.
Outcomes	Febrile morbidity (> 38.0ºC twice at least 6 hrs apart after 1st post-operative day); endometritis (fever, tender uterus and purulent lochia); hospital stay (no significant difference, variance not given).
Notes	Use of saline or antibiotic lavage not allowed. No adverse reactions reported with treatment. Class of antibiotic: extended spectrum penicillin (ureidopenicillin (pipericillin)). Subgroups: • non-elective CS; • after cord clamping. The 3 groups were comparable regarding number of vaginal exams, hemoglobin levels and other risk factors.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomly divided..". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported. The analysis appears to be by ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "blinded". Comment: placebo-controlled; insufficient information to judge.

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Leonetti 1989 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Levin 1983

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: February to June 1982. Setting: Kaiser-Permanente Medical Center-Santa Clara, California. Inclusion criteria: all women undergoing CS (39/128 repeat section). N = 128. Exclusion: fever or infection, allergy to antibiotics.
Interventions	Intervention: 1st generation cephalosporin: • cephapirin 2 g in 1 L saline irrigation; • N = 44. Intervention: cefamycin: • cefoxitin 2 g in 1 L saline irrigation; • N = 41. Comparison: placebo: • identical appearing placebo saline irrigation; • N = 43. Placebo group divided 1/2 for comparison with 2 treatment groups.
Outcomes	UTI (positive culture); wound infection (purulent wound discharge with or without wound separation); endometritis (fever > 100.4ºF after 1st post-operative day, uterine tenderness, foul smelling lochia without other source).
Notes	Follow-up for 8 weeks. 1 patient in placebo group developed septic pelvic thrombophlebitis and septic pulmonary emboli, classified as a serious complication. Class of antibiotic: 1st generation cephalosporin vs cefamycin (2nd generation cephalosporin). Subgroups: • type of CS unclear; • after cord clamping. There were no statistically significant differences in mean gestational age, mean number of vaginal examination or mean duration of ruptured membranes between groups.

Risk of bias

Bias	Authors' judgement	Support for judgement

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Levin 1983 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "Sequenced randomly by lottery method".
Allocation concealment (selection bias)	Unclear risk	Comment: insufficient information to judge.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 4 patients were eliminated from the statistical analysis because of deviations from the protocol of irrigation technique. As-treated analysis. Data could not be re-included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "1 milliliter of multivitamin infusion was added to create an identical appearance of all solutions .... and bags sequenced randomly ... used in numerical order" ..". Patients, physicians, operative room personnel and data collectors were... blinded to the group assignment". Comment: double-blind; identical appearing placebo.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Patients, physicians, operative room personnel and data collectors were... blinded to the group assignment".
Other bias	Low risk	Comment: no other sources of bias identified.

Lewis 1990

Methods	Random, double-blind, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: July 1985 to January 1986. Setting: Louisiana State University Hospital; 90% indigent population. Inclusion criteria: women undergoing elective and non-elective CS (definitions of elective and emergency CS not provided; results combined in the analysis). Exclusion: antibiotic use within 2 weeks, allergy to penicillin.
Interventions	Intervention: carboxypenicillin: • ticarcillin 5 g in 1200 mL saline irrigation; • N = 112. Comparison: placebo: • saline irrigation; • N = 100. Results of the 2nd part of the study (cefoxitin vs ticarcillin) not included.
Outcomes	Febrile morbidity (> 100.3ºF twice at least 4 hrs apart after 1st post-operative day); endomyometritis, wound infection, UTI, septicemia, maternal hospital stay (treatment 4.5 vs placebo 5.4, no variance given).
Notes	Definition of elective and non-elective CS not provided.

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Lewis 1990 *(Continued)*

There were 3 episodes of septicemia in those women undergoing emergency section (2 in the control group and 1 in the placebo group).

Class of antibiotic: extended spectrum penicillin (carboxypenicillin (ticarcillin)).

Subgroups:

- both elective and non-elective CS;
- after cord clamping.

The duration of labor was significantly longer in the ticarcillin group than in the saline group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "... in a random double-blind manner". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 8 women were lost to follow-up; 7 women were excluded. As-treated analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Magro 1983

Methods	Randomized, placebo-controlled; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: November 1981 to May 1982. Setting: Milan, Italy. Inclusion criteria: women undergoing CS (both elective and non-elective); part of lager study (n = 100) of prophylaxis for obstetric and gynecological procedures. Exclusion criteria: infection, antibiotic therapy, hypersensitivity to penicillin or cephalosporin, abnormal liver or kidney function.
Interventions	Intervention 1:

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Magro 1983 *(Continued)*

	• cefuroxime 1 g IM 30 minutes before surgery and IV 3 and 10 hrs after surgery; • N = 23. Intervention 2: • physiological solution IM 30 minutes before surgery and IV 3 and 10 hrs after surgery; • N = 13.
Outcomes	Febrile morbidity (fever of > 37.5°C for 2 or more days following the operation). In addition patients were classified as having a satisfactory outcome (treatment n = 1; placebo n = 1), an average outcome (treatment n = 8; placebo n = 8), or a good outcome (treatment n = 14; placebo n = 4) based on fever, laboratory tests and clinical course.
Notes	Translated from Italian. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • both elective and non-elective CS; • before cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "by randomization". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: insufficient information to judge.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss to follow-up; difference in numbers between the 2 groups undergoing CS not explained. ITT analysis performed on available data.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blinded" .... "the patients and the doctors were unable to see which type of treatment the patients were receiving". Comment: placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: probably outcome assessment was blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Mahomed 1988

Methods	Double-blind, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: November 1986 and March 1987.

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Mahomed 1988 *(Continued)*

	Setting: University of Zimbabwe; patients enrolled between Inclusion criteria: all women undergoing elective CS (before onset of labor or rupture of membranes; corresponds to our definition of elective). N = 232.
Interventions	Intervention: drug combination [penicillin+ chloramphenicol]: • crystalline penicillin 2 MU and chloramphenicol 500 mg pre-operatively "before going to theatre"; • N = 115. Comparison: placebo: • matching placebo; • N = 117.
Outcomes	Fever (> 37.9ºC twice at least 4 hrs apart after 1st post-operative day); wound sepsis (graded as abnormal erythema and/or induration, oozing wound without frank pus or pus formation); endomyometritis (fever, uterine tenderness and foul-smelling lochia), pelvic abscess formation, bacteremia; maternal hospital stay (treatment 5.43 vs placebo 6.18, variance not given).
Notes	No woman developed pelvic abscess nor required a laparotomy. Class of antibiotic: other combination (crystalline penicillin and chloramphenicol). Subgroups: • elective CS; • before cord clamping. The groups were comparable regarding age, pre-operative weight, parity, previous CS, gestational age, and pre-operative hemoglobin.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized list..". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: insufficient information to judge.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported. Analysis appears to be ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Double-blind". Comment: matching placebo.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

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McCowan 1980

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: June to September 1979. Setting: National Women's Hospital, Auckland, New Zealand. Inclusion criteria: all women undergoing CS (8/73 were repeat). N = 73. Exclusion: already on antibiotics.
Interventions	Intervention: Nitroimidazole: • metronidazole, 500 mg IV prior to incision and metronidazole 2 g suppository at end of surgery; • N = 35. Comparison: placebo: • matching placebo infusion and suppository; • N = 38.
Outcomes	Fever (> 37.9ºC within 14 days of delivery); wound infection, endometritis, UTI, major complication (return to theatre or hospitalized > 10 days because of post-operative morbidity); need for antibiotic therapy (treatment 13 vs placebo 10); fever index (257 degree hrs vs 165 hrs).
Notes	1 major complication (not infectious) in each group (bleeding from lower segment in 1, major deep vein thrombosis extending into iliac veins in another). Drug class: nitroimidazole (metronidazole). Subgroups: • type of CS unclear; • before cord clamping. The groups were comparable regarding age and weight.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses to follow-up reported; no participants excluded. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias)	Low risk	Comment: double-blind, placebo-controlled.

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McCowan 1980 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Miller 1968

Methods	RCT: 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not specified. Setting: Durban, South Africa. Inclusion criteria: all patients undergoing CS. N = 300. Exclusion criteria: women with pre-existing UTI.
Interventions	Intervention: • ampicillin 500 mg IM pre-operatively and 8 hrly for 48 hrs followed by 500 mg orally 8 hrly for 4 days; • N = 150. Comparison: placebo: • no treatment for 1st 48 hrs then oral placebo 8 hrly for 4 days; • N = 150.
Outcomes	UTI (culture positive), intrauterine infection not defined further, classified as endometritis), wound infection.
Notes	Fewer postpartum urinary isolates in treated group were sensitive to ampicillin (8/17 vs 18/26). In the control group, 3 women developed pelvic abscesses (included as serious morbidity) and 1 patient required hysterectomy for secondary postpartum hemorrhage following severe *E. coli* intrauterine infection (included as serious morbidity). Class of antibiotic: aminopenicillin (ampicillin). Subgroups: • type of CS unclear; • before cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "on a random basis". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: insufficient information to judge.

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Miller 1968 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded after randomization. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "an oral placebo was given after 48 hours". Comment: partly placebo controlled. Insufficient information to judge whether there was blinding of study personnel.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Moodley 1981

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: University of Natal, Durban, South Africa. Inclusion criteria: women undergoing emergency CS (ruptured membranes for > 6 hrs and < 20 hrs; corresponds to our definition of non-elective). N = 60. Exclusion criteria: prior antibiotic therapy, fever > 37.2ºC, fetal tachycardia of > 160/minute.
Interventions	Intervention: lincosamides: • lincomycin 600 mg; • N = 20. Intervention: nitroimidazole: • metronidazole 500 mg; • N = 20. Comparison: • placebo; • N = 20. IV 2 hrs pre-operatively and 8 hrly for 48 hrs. Placebo data were divided: 1/2 for comparison with the lincosamide and 1/2 for comparisons with the nitroimidazole.
Outcomes	Wound discharge/abscess formation, puerperal sepsis (> 37.9ºC twice in 1st 48 hrs or > 37.5ºC from 2nd post-operative day), septicemia, UTI.
Notes	Authors' definition of puerperal sepsis has been classified as fever. No complications of drug administration reported in mothers or babies; no rash, diarrhea or nausea.

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Moodley 1981 *(Continued)*

Class of antibiotic: lincosamide (lincomycin) vs nitroimidazole (metronidazole).

Subgroups:

- non-elective CS;
- before cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Quote: "...using unmarked code-numbered separate boxes".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses to follow-up; no participants excluded. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind"; drug to be given was "in unmarked boxes in the original packing". Comment: placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Moro 1974

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Norfold General Hospital, Virginia; both private (N = 70) and clinic (N = 78) women included. Inclusion criteria: all women undergoing CS (49/148 were repeat procedure; 57/148 were not in labor). N = 148. Exclusion: membranes ruptured > 24 hrs.
Interventions	Intervention: 1st generation cephalosporin: • cephalothin 2 g IV 15-30 minutes prior to surgery and 1 g every 6 hrs for 36 hrs, then cephalexin 500 mg orally every 6 hrs until 5th post-operative day; • N = 74. Comparison: placebo:

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Moro 1974 *(Continued)*

	• identical appearing placebo; • N = 74.
Outcomes	Fever (> 100.3ºF twice after 48 hrs); endometritis (fever, uterine tenderness, foul-smelling or abnormal lochia and positive cultures); UTI, wound infection; maternal hospital stay (treatment 6.2 vs placebo 7.5, no variance given).
Notes	All bacterial isolates in treatment group were sensitive to cephalothin. Class of antibiotic: 1st generation cephalosporin. Subgroups: • type of CS unclear; • before cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Assigned in a random manner". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Comment: all preparations supplied by the pharmacy had a code number known only by the pharmacy.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 52/200 excluded for various reasons, including 14 because of protocol violations. As-treated analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, identical appearing placebo.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Morrison 1973

Methods	Quasi-RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: City of Memphis Hospitals, Tennessee; indigent women, many obstetric and metabolic complications. Inclusion criteria: all women undergoing CS. N = 330.

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Morrison 1973 *(Continued)*

	Exclusion criteria: febrile or infected.
Interventions	Intervention: drug combination [penicillin + aminoglycoside]: • aqueous penicillin 10 MU every 8 hrs and kanamycin 500 mg IM every 12 hrs pre-operatively and for 3 days post-operatively; • N = 115. Comparison: no treatment: • no treatment; • N = 115.
Outcomes	Fever (> 100.9ºF after 2nd post-operative day), severe pelvic infection (treatment 27% vs control 7%); 'free of infectious morbidity' (3.6 vs 6.8 days); maternal hospital stay (5.4 vs 8.8 days, no variance given).
Notes	No adverse drug reactions reported; no evidence of development of resistance reported. Unable to ascertain from description of study incidence of endometritis or wound infection; inadequate description of nature of severe pelvic infections (not included as outcome in analysis). 2 groups of women were studied retrospectively (N = 75); methods nor results do not specifically describe results of this group and it is unclear whether they have been included in the overall results. Class of antibiotic: aminoglycoside-containing combination (natural penicillin and aminoglycoside. Subgroups: • type of CS unclear; • before cord clamping. The 2 groups were comparable regarding gravidity, parity, age and operative indicators.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "...every other patient". Comment: quasi-RCT. Alternate allocation to treatment or no treatment.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up; no participants excluded. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

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Ng 1992

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: March to August 1991. Setting: Ipoh, Malaysia. Inclusion criteria: women undergoing CS. N = 222. Exclusions: hypersensitivity to 1 of antibiotics; presence of infection or fever; on antibiotics; multiple pregnancy.
Interventions	Intervention: 3rd generation cephalosporin: • cefoperazone 1 g every 12 hrs x 3; • N = 71. Intervention: • ampicillin 500 mg every 6 hrs x 4; • N = 74. Comparison: no treatment: • no treatment; • N = 77. At induction of anesthesia. Control data split to 6/35 and 5/35 for comparison with penicillin and cephalosporin respectively.
Outcomes	Wound infection (inflammation over wound with serous or purulent discharge); any antibiotics post-operatively (cefoperazone vs ampicillin vs no treatment: 6.6% vs 16.2% vs 25.7%). Hospital stay: ampicillin vs no treatment 5.57 days (SD 1.43) vs 6.5 days (SD 3.67).
Notes	Author's definition of emergency not consistent with criteria used in this review; classified as both/undefined. Class of antibiotic: 3rd generation cephalosporin or aminopenicillin (ampicillin). Subgroups: • type of CS unclear; • before cord clamping. The 3 groups were comparable regarding age, race, parity, gestational age, etc. The number of patients allocated to the control and cefoperazone group are different between the text and the table; the numbers in the text have been used.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized..". Comment: no description of sequence generation process.

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Ng 1992 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	2 patients excluded (1 from cefoperazone group, 1 from no treatment group); as-treated analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Oestreicher 1987

Methods	Randomized trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: June 1984 to October 1985. Setting: Berlin, Germany. Inclusion criteria: women undergoing primary CS with no complications (no additional details available); classified as "both or undefined". Exclusion criteria: women with diabetes or penicillin allergy.
Interventions	Intervention 1: • mezlocillin 4 g IV after delivery of the child; • N = 30. Intervention 2: • no treatment; • N = 30.
Outcomes	Fever (temperature of ≥ 38°C for 3 hrs), slowness of wound healing (4/30 vs 17/30 for treatment and control groups respectively); endometritis; UTI; stay > 10 days (12/30 vs 19/30); need for post-operative antibiotics (3/30 vs 6/30).
Notes	Translated from German. Class of antibiotic: extended spectrum penicillin. Subgroups: • both or undefined CS;

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Oestreicher 1987 *(Continued)*

- after cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no dropouts reported; no other details provided.
Selective reporting (reporting bias)	Unclear risk	Comment: no information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Padilla 1983

Methods	Randomized, double-blind, placebo-controlled trial; 2 parallel arms. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Johns Hopkins Hospital, Baltimore, US. Inclusion criteria: all women undergoing CS (35/71 were a repeat section). N = 71. Exclusion: fever, membrane rupture > 24 hrs, penicillin allergy, lack of consent.
Interventions	Intervention: • ampicillin 2 g pre-operatively; • N = 34. Comparison: placebo: • similar-appearing placebo; • N = 37.
Outcomes	Fever (> 37.0°C twice at least 6 hrs apart after 1st post-operative day); endometritis, UTI, wound infection, bacteremia, pelvic abscess, maternal hospital stay.

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Padilla 1983 *(Continued)*

Notes	The authors definition of primary and repeat are different from those used in this review and have not been analyzed separately; most women for repeat section were in early labor at the time the operation was performed. Study medications were administered pre-operatively when possible, however transit time delays resulted in patients receiving medication after the surgical procedure had started. There was 1 pelvic abscess in the placebo group; there were 3 episodes of bacteremia (1 *Klebsiella* spp. in treatment group, 2 group B streptococcal infections in placebo); combined for outcome of serious morbidity. Class of antibiotic: aminopenicillin (ampicillin). Subgroups: • type of CS unclear; • timing of administration not specified. "There were no statistically significant differences in (the epidemiologic and obstetric variables in the two groups) when the study and placebo groups were compared."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly assigned". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Quote: "The medication code was kept in the pharmacy".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded after randomization. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "... or a similar appearing placebo... all solutions were prepared (in the pharmacy)". Comment: insufficient information to judge.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Phelan 1979

Methods	Randomized, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: July to December 1976.

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Phelan 1979 *(Continued)*

	Setting: Naval Regional Medical Center, Portmouth, Virginia, US. Inclusion criteria: all women undergoing CS (46/122 were a repeat section). The authors' definition of primary and repeat do not correspond to definitions of elective and non-elective used in this review (repeat sections included women in labor with ruptured membranes). The results for these 2 categories have been combined in this review. Exclusion criteria: allergy to penicillin or cephalosporin, infection or receiving antibiotics.
Interventions	Intervention: 1st generation cephalosporin: • cefazolin 500 mg IV 30 minutes before and 500 mg at 2 and 1 g at 8 hrs after delivery; • N = 61. Comparison: placebo: • matching placebo; • N = 61.
Outcomes	Endometritis (fever and uterine tenderness or fever and pathogenic organism); UTI (fever and symptoms, or positive culture); wound infection (fever, cellulitis and exudate); maternal hospital stay (treatment 5.5 days vs placebo 5.7 days, no variance given).
Notes	2 women developed serious complications as stated by the authors: 1 in treatment group developed septic pelvic thrombophlebitis; 1 given placebo developed pneumonia and endoparametritis (both included in outcome of serious morbidity). Class of antibiotic: 1st generation cephalosporin. Subgroups: • both elective and non-elective CS; • before cord clamping. The 2 groups were comparable regarding age, height, weight, etc.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Quote: "All preparations supplied had a code number known only by the pharmacy".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: 8 women excluded for mistakes in protocol (no further details) could not be included in ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "All materials appeared similar in solution". Comment: described as double-blind, matching placebo.
Blinding of outcome assessment (detection bias)	Unclear risk	Comment: insufficient information to judge.

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Phelan 1979 *(Continued)*
All outcomes

Other bias	Low risk	Comment: no other sources of bias identified.

Polk 1982

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: July 1978 to October 1980. Setting: Brigham and Women's Hospital, Boston, Massachusetts, US. Inclusion criteria: all women undergoing CS (other than repeat section); criteria do not correspond with our definition of non-elective. N = 278. Exclusion: active infection, fever, membranes ruptured > 36 hrs, antibiotic therapy within 2 weeks, renal disease, allergy to penicillin or cephalosporin.
Interventions	Intervention: 1st generation cephalosporin: • cefazolin 2 g after cord clamped and at 4 and 8 hrs after 1st dose; • N = 146. Comparison: placebo: • matching placebo; • N = 132.
Outcomes	Fever (oral temperature > 100.3^{oF} on any of 2 of 1st 10 post-operative days); UTI, wound infection (only pus-draining included in outcome of wound infection); endometritis (fever, tenderness on pelvic examination, abnormal discharge); pelvic abscess; septic pelvic thrombophlebitis, bacteremia; subsequent antibiotic use (23% for placebo vs 12% for treatment).
Notes	Outcome of fever and minor wound infection combined (11/146 for treatment vs 13/132 for placebo). 4 episodes of bacteremia, all in placebo group. 1 episode of rash and 1 episode of phlebitis reported in treatment group vs none in control. Data collected at 6 weeks on 259/266 patients; 35% of infections diagnosed after discharge. Class of antibiotic: 1st generation cephalosporin. Subgroups: • type CS undefined; • after cord clamping. The 2 groups were comparable regarding age, BMI, proportion on private service, etc.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly allocated". Comment: no description of sequence generation process.

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Polk 1982 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: 12 participants withdrawn (8 treatment, 4 placebo) and started on therapeutic antibiotics by the surgeon because the operation had been prolonged or was complicated or the pre-operative specimen of urine disclosed significant bacteriuria; results on participants excluded could not be re-included in ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Participants, their physicians and all investigators were unaware of the assignment throughout the study". Comment: double-blind, matching placebo.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: probably outcome assessment was blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Racinet 1990

Methods	Randomized, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: July 1986 to December 1987. Setting: Grenoble, France. Inclusion criteria: 'low-risk' women, undergoing CS (27% in labor). N = 266. Exclusion: allergy to beta-lactam antibiotics, receipt of antibiotics within 3 days; ruptured membranes > 12 hrs; fever, amniotic infection, failure of instrumental manipulation.
Interventions	Intervention: • cefotetan 1 g IV at the time of cord clamping; • N = 136. Comparison: placebo: • placebo injection; • N = 130.
Outcomes	Endometritis, wound infection (includes superficial wound infection and deep abscess), isolated fever, UTI, bacteremia and septicemia; additional antibiotic use (10/136 in treatment group vs 19/130 in placebo); total antibiotic costs (76 francs in treatment group vs 52 francs in placebo); maternal hospital stay. Outcomes were evaluated daily during hospitalization and at 30 days.
Notes	There was 1 episode of septicemia in the placebo group. Class of antibiotic: cefamycin (2nd generation cephalosporin). Subgroups:

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Racinet 1990 *(Continued)*

- type of CS unclear;
- after cord clamping.

The 2 groups reported as comparable regarding demographic values.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...randomized by drawing of lots".
Allocation concealment (selection bias)	Low risk	Comment: allocation of treatment was in a closed envelope to be opened at the last moment by the anesthetist who only knew the nature of the administered treatment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported. Analysis appears to be ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, placebo-controlled. Placebo was 10 mL of physiologic "serum".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Reckel 1985

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Hanover, Germany. Inclusion criteria: women undergoing CS. N = 140.
Interventions	Intervention: ureidopenicillin: • mezlocillin 2 g IV half hr pre-operatively then every 8 hrs x 4; • N = 70. Comparison: no treatment: • no treatment; • N = 70.

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Reckel 1985 *(Continued)*

Outcomes	Wound infection (inflammation with or without exudation); endometritis (fever and tenderness of the uterus or fever with pathogens from the cervical canal); UTI (> 100,000 bacteria/mL).
Notes	1 episode of allergic skin reaction occurred with the injection of mezlocillin. Class of antibiotic: extended spectrum penicillin (ureidopenicillin (mezlocillin)). Subgroups: • type of CS unclear; • before cord clamping. The 2 groups were comparable regarding age, height, weight, and risk of wound infection. But risk of endometritis was not in balance in the 2 groups.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized..". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: 1 dropout (no treatment) reported. Analysis appears to be ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Rehu 1980

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: September 1977-January 1978. Setting: State Maternity Hospital, Helsinki, Finland. Inclusion criteria: all women undergoing CS. N = 128. Exclusion criteria: allergic to penicillin, clindamycin or gentamicin; emergency section.

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Rehu 1980 *(Continued)*

Interventions	Intervention: penicillin: • benzyl penicillin,10 MU IV; • N = 46. Intervention: combination (lincosamides plus aminoglycoside): • clindamycin, 500 mg IV plus gentamicin, 80 mg IM; • N = 42. Comparison: placebo: • vs glucose solution placebo, IV by infusion starting 30 minutes before operation and stopping 4 hrs after; • N = 40. Placebo data spilt for comparison with the 2 antibiotic groups.
Outcomes	Endometritis (fever, uterine tenderness and foul-smelling vaginal discharge); wound infection (all grades combined); hospital stay (treatment 7.7 vs 7.7 placebo; no variance given).
Notes	Data from a 4th group that consisted of patients allergic to 1 of the drugs or undergoing an emergency section have not been included. Drug class: natural penicillin or aminoglycoside-containing combination (lincosamide (clindamycin) and aminoglycoside). Subgroups: • type of CS unclear; • before cord clamping. The 1st 3 groups were comparable regarding number of amnioscopic examinations, number of vaginal examination, duration of labor and duration of intrauterine monitoring.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Assigned at random". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Quote: " ... in bottles containing code numbers". Comment: insufficient information to judge.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss to follow-up reported; 2 women excluded after initial randomization. ITT analysis with available data.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "the code was kept secret for persons performing the operations and observing the patients in the post-operative period".. Comment: placebo-controlled (glucose solution)

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Rehu 1980 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "the code was kept secret for persons .... observing the patients in the post-operative period".
Other bias	Low risk	Comment: no other sources of bias identified.

Rizk 1998

Methods	RCT: 2 parallel groups. Unit of randomization: individual.
Participants	Inclusion: women undergoing elective CS (absence of labor and before rupture of membranes). N = 120. Exclusion: allergy to penicillin or cephalosporin, prior antibiotic therapy within 7 days. Setting: United Arab Emirates.
Interventions	Intervention: 2nd generation cephalosporin: • cefuroxime 1.5 g after clamping of the cord; • N = 59. Comparison: no treatment: • no treatment; • N = 61.
Outcomes	Febrile morbidity (temperature of > 38ºC after 1st 48 hrs); endometritis (uterine tenderness and offensive lochia with fever and no other source); wound infection (erythema, induration or purulent discharge); UTI (> 100,000 bacteria/mL).
Notes	Majority of patients were indigent; follow-up at 6 weeks. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • elective CS; • after cord clamping. The 2 groups were comparable regarding age, parity, weight, gestational age and indication for cesarean.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...a computer generated number scheme..".
Allocation concealment (selection bias)	Unclear risk	Quote: "...randomization code and the mode of intervention was only known to the anesthesiology staff..".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no losses or exclusions were reported. Analysis appears to be ITT.

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Rizk 1998 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "patient and study co-ordinators unaware of group allocation". Comment: not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Roex 1986

Methods	Randomized, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: April 1983 to October 1984. Setting: Academisch Ziekenhuis der Vrije Universiteit, Amsterdam, The Netherlands. Inclusion criteria: all women undergoing CS (77/129 were elective sections). N = 129. Exclusion: active infection, antibiotics within 7 days, allergy to penicillin or cephalosporin, impaired liver or renal function.
Interventions	Intervention: cefamycin: • cefoxitin 2 g; • N = 64. Comparison: placebo: • matching placebo; • N = 65. IV bolus immediately following clamping of the cord and at 6 and 12 hrs later.
Outcomes	Febrile morbidity (> 38ºC for at least 24 hrs after 1st 24 hrs); endometritis (fever, fetid lochia and/or uterine tenderness on pelvic examination); wound infection (palpable induration, wound dehiscence and/or pus drained); UTI (positive culture), bacteremia.
Notes	1 episode of *Staphylococcus aureus* bacteremia (in cefoxitin group) not considered life-threatening (included in outcome of serious morbidity). No serious antibiotic side effects reported in cefoxitin-treated group; 1 patient in cefoxitin group developed diarrhea. Class of antibiotic: cefamycin (2nd generation cephalosporin). Subgroups: • both elective and non-elective CS; • after cord clamping. The 2 groups were comparable regarding demographic, obstetric and operative factors.

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Roex 1986 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly allocated". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Commentt: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: 21 women were excluded: 2 had fever prior to surgery, 2 because of a known allergy to penicillins; 8 women excluded because of protocol failures and 9 women for intraoperative complications (not defined further); as-treated analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Ross 1984

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Addenbrooke's Hospital, Cambridge, UK. Inclusion criteria: women undergoing emergency CS (in active labor with membrane rupture). N = 115. Exclusion criteria: pyrexia; antibiotic use within 2 weeks.
Interventions	Intervention: nitroimidazole: • metronidazole 500 mg; • N = 57. Comparison: placebo: • placebo; • N = 58. IV infusion at start of procedure; post-operatively metronidazole or placebo suppository twice daily for 5 days.

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Ross 1984 *(Continued)*

Outcomes	Pyrexia (> 38ºC twice 4 hrs apart after 1st 24 hrs); wound infection; endometritis (heavy, offensive lochia and pyrexia); UTI; antibiotic use (15/57 in treatment group vs 20/58 in control group).
Notes	1 woman in the control group developed a pelvic abscess. Length of admission not significantly different between the 2 groups (mean 7.4, SD 2.3 days). No adverse reactions occurred. Class of antibiotic: nitroimidazole (metronidazole). Subgroups: • non-elective CS; • before cord clamping. Comparison of the 2 groups showed similar risk factors.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized, sequential basis". Comment: insufficient description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Quote: "Antibiotic ... was provided without access to the 'trial code". Comment: insufficient information to judge.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up; no participant excluded. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: double-blind, placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Rothbard 1975

Methods	Quasi-RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: New York Medical College, New York, US. Inclusion criteria: all women undergoing CS divided into "no labor" and "labor" groups which correspond to the definitions of elective/non-elective used in this review. N = 100.

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Rothbard 1975 *(Continued)*

	Exclusion criteria: fever, antibiotic use within 2 weeks, ruptured membranes > 2 hrs, major penicillin allergy.
Interventions	Intervention: combination (cephalosporin + aminoglycoside): • cephalothin 2 g IV and kanamycin 1 g IM at induction of anesthesia, then cephalothin 2 g IV q6hrs x 8 doses and kanamycin 500 mg IM q12 hr x 4 doses; • N = 47. Comparison: no treatment: • no treatment; • N = 53.
Outcomes	Febrile morbidity (temperature greater that 100.4ºF orally on 2 consecutive days, excluding the 1st post-operative day); endometritis (fever, uterine tenderness and positive culture or fever and pathogenic organism); UTI, wound infection (fever and cellulitis or exudate). Data available on elective (defined as no labor) and non-elective (defined as presence of labor).
Notes	No difference in average duration of hospital stay between groups (data not shown). 1 woman (treatment group) developed endometritis with organism resistant to cephalothin and kanamycin. Class of antibiotic: aminoglycoside-containing combination (1st generation cephalosporin and kanamycin). Subgroups: • both elective and non-elective CS - data separated by elective and non-elective; • before cord clamping. The 2 groups were comparable regarding age, parity, ethnic background or type of anesthesia.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: Randomized "...using the last digit of their hospital chart number". Comment: quasi-RCT.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up; no participants excluded. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.

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Rothbard 1975 *(Continued)*

Other bias	Low risk	Comment: no other sources of bias identified.

Rouzi 2000

Methods	Randomized placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Jeddah, Saudi Arabia. Inclusion criteria: women undergoing CS (both elective and emergency). N = 441. Exclusions: use of antibiotics, fever or signs of infection; allergy to penicillin or cephalosporin.
Interventions	Intervention: cephalosporin: • cefazolin 1 g after clamping of the cord; • N = 221. Comparison: placebo: • matching placebo; • N = 220.
Outcomes	Febrile morbidity (> 38ºC twice 4 hrs apart after 1st 24 hrs); endometritis (fever, uterine tenderness and abnormal lochia); wound infection (fever, cellulitis or exudate with positive culture); UTI (fever and positive urine culture); pneumonia, bacteremia, pelvic abscess, unexplained fever, therapeutic antibiotics, length of post-operative stay. All outcomes are reported by emergency and elective CS separately, so when reporting overall outcomes, dichotomous data can be used but not continuous. Length of hospital stay therefore cannot be reported for the overall comparison.
Notes	Definition of emergency section (unscheduled) did not correspond to the definition of non-elective section used in this review; these patients have been analyzed in the "both or not-defined" group. Women undergoing elective section included women with scheduled section and with intact membranes and have been analyzed in the "elective" group. There were no significant differences in the fetal outcomes reported (definitions not consistent with those for this review; no serious side effects with cefazolin. Class of antibiotic: 1st generation cephalosporin. Subgroups: • both elective and both/not defined CS - data separated by elective and both/not defined; • after cord clamping. The 2 groups were comparable regarding maternal characteristics and emergency and elective CS.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "...computer-generated randomization..".

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Rouzi 2000 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "...each indistinguishable minibag was given a code number in the department of pharmaceutical care". Comment: there was, however, no information on how the codes were used and whether there was sequential opening.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported. Analysis appeared to be by ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "triple blind" ... "both the experimental drug and placebo were indistinguishable".
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: probably outcome assessment was blinded ("triple blind").
Other bias	Low risk	Comment: no other sources of bias identified.

Rudd 1981

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: Tripler Army Medical Center, Honolulu, Hawaii, US. Inclusion criteria: all women undergoing CS (19/60 women had ruptured membranes > 6 hrs; 40/60 were in active labor). N = 60 for this review. Exclusion: known infection, currently on antibiotics, allergic to penicillin or cephalosporin.
Interventions	Intervention: cephalosporin: • cefamandole 2 g in 800 mL normal saline irrigation; • N = 30. Comparison 1: placebo: • irrigation with 800 mL normal saline; • N = 30. Comparison 2: not included in analysis: • non-irrigation control group; • N = 30. Only comparison 1 was used for placebo.
Outcomes	Endomyometritis (fever, unusual uterine and parametrial tenderness without evidence of other source of infection); maternal length of stay.

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Rudd 1981 *(Continued)*

Notes	Length of hospital stay for the control group included results from both the no irrigation group and the placebo irrigation group (5.37 days vs 4.53 for treatment group). Class of antibiotic: 2nd generation cephalosporin. Subgroups: • both elective and non-elective CS, data cannot be separated; • after cord clamping. The 3 groups were comparable regarding age, parity, weight and socioeconomic background.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: randomly allocated using table of random numbers.
Allocation concealment (selection bias)	Low risk	Comment: randomly allocated by hospital pharmacy.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses were reported; no participants excluded. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, placebo-controlled. Vitamin solution added to make placebo visually identical; physicians and patients blinded to treatment.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: probably outcome assessment was blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Ruiz-Moreno 1991

Methods	Randomized, placebo-controlled; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting:Hospital Central Militar, Mexico city, Mexico. Women predominantly (78%) of low socioeconomic level. Inclusion criteria: women in active labor undergoing CS. N = 100. Exclusion: elective CS, evidence of infection, antibiotic use within 8 days, metronidazole intolerance, lack of consent.
Interventions	Intervention: nitroimidazole:

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Ruiz-Moreno 1991 *(Continued)*

	• metronidazole 1 g IV; • N = 50. Comparison: placebo: • identical appearing placebo; • N = 50. Immediately after cord clamping.
Outcomes	Endometritis (purulent and/or foul odor lochia); wound infection (wound edges tender, red and swollen, or frank pus or sanguino-purulent material exuded); UTI (bacteria seen in sediment); maternal hospital stay.
Notes	Class of antibiotic: nitroimidazole (metronidazole). Subgroups: • non-elective CS; • after cord clamping. The 2 groups reported as comparable regarding age and parity, etc.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized..". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no losses or exclusions were reported. Appears to be ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind; identical appearing placebo.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Saltzman 1985

Methods	RCT; 2 parallel groups.
Participants	Dates of data collection: not specified.

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Saltzman 1985 *(Continued)*

	Setting: Fairfax Hospital, Virginia, US. Women predominantly private. Inclusion: criteria: high-risk women undergoing CS (in active labor and/or ruptured membranes > 4 hrs); not consistent with the criteria for non-elective in this review: classified as "both/undefined" in this review. Exclusion: active infection, fever, antibiotic use within 3 days, allergy to penicillin or cephalosporins.
Interventions	Intervention: 3rd generation cephalosporin: • ceftizoxime 2 g; • N = 50. Comparison: placebo: • placebo; • N = 49. IV at time of cord clamping.
Outcomes	Febrile morbidity (oral temperature > 37.9ºC twice at least 8 hrs apart, after 1st 24 hr); endometritis (fever and foul lochia or uterine tenderness); UTI (fever and positive culture); wound infection (fever, abnormal-looking wound, surrounded by cellulitis and/or draining purulent material).
Notes	There was 1 drug reaction (maculopapular rash) in the treatment group. Women followed up at 6 weeks. Class of antibiotic: 3rd generation cephalosporin. Subgroups: • type of CS unclear; • after cord clamping. "The groups were comparable. No significant differences were observed between the 2 groups with respect to maternal age, parity, gestational age, duration of labor, duration of ruptured membranes or use of internal fetal monitoring. There were no significant differences regarding indication for CS".

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomized". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: 1 patient was removed from the study when she became febrile in the delivery room, not included in ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, placebo-controlled.

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Saltzman 1985 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Scarpignato 1982

Methods	RCT; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: November 1981 to March 1982. Setting: University of Parma, Parma, Italy. Inclusion criteria: women undergoing emergency CS (58/60 women in spontaneous labor; classified as non-elective). N = 60. Exclusion criteria: allergy to penicillin or cephalosporins; severe renal disease, history of pelvic infections.
Interventions	Intervention: 2nd generation cephalosporin: • cefuroxime 750 mg IM 30-60 minutes before surgery and 8 and 16 hrs after (short term); • N = 20. Intervention: cephalosporin (B2): • cefuroxime 750 mg 3 times a day for 5 days (1st dose being given post-operatively after the woman had returned to the ward) (long term); • N = 20. Comparison: no treatment: • no treatment; • N = 20. The results of both treatment groups have been combined.
Outcomes	Fever (> 100.3ºF twice 6 hrs apart); endometritis (fever and uterine tenderness); maternal stay (treatment 7.1 vs control 7.9 days, no variance given).
Notes	Note: the group given long-term prophylaxis received the 1st dose after return to the ward. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • non-elective CS; • timing of administration not specified. The 3 groups were comparable.

Risk of bias

Bias	Authors' judgement	Support for judgement

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Scarpignato 1982 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly assigned". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no losses to follow-up reported. 1 woman was excluded because of an allergic reaction to cefuroxime. Could not be re-included in ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Schedvins 1986

Methods	Randomized trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: November 1983 to October 1984. Setting: Sodersjukhuset, Stockholm, Sweden. Inclusion criteria: women with rupture of membranes for > 6 hrs (equivalent to non-elective group). N = 53. Exclusion criteria: fever or foul smell of amniotic fluid.
Interventions	Intervention: cephalosporins: • cefuroxime 1.5 g IV q8 hr for 24 hrs, starting immediately before or during the operation, followed by oral cefadroxil 500 mg twice daily for 6 days; • N = 26. Comparison: no treatment: • no treatment; • N = 27.
Outcomes	Endometritis (marked uterine tenderness with or without a foul discharge with fever at least twice); wound infection (redness, tenderness, induration and pus in the wound); UTI (positive culture).
Notes	Data provided (but not included) for a 2nd control group eligible for inclusion but not randomized. Numbers not provided to calculate mean maternal length of stay for the 2 randomized groups. Class of antibiotic: other regimen (2nd generation cephalosporin, then 1st generation cephalosporin).

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Schedvins 1986 *(Continued)*

	Subgroups: • non-elective CS; • timing of administration not specified. The 2 groups were comparable regarding age, parity, previous CS, duration of labor and membrane rupture.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly referred". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 11 patients "should have been given prophylactic treatment according to the study design but received no antibiotics and ... formed a second control group". As-treated analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Shah 1998

Methods	RCT; 4 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not reported. Setting: United Arab Emirates. Inclusion criteria: women undergoing elective CS (definition not provided). N = 198. Exclusion: hypersensitivity to penicillin or cephalosporin; prior antibiotic therapy within 3 days; hepatorenal insufficiency; positive cultures or definite evidence of infection.
Interventions	Intervention: penicillin (A3): • pipericillin 4 g IV after the cord was clamped; • N = 48. Intervention: penicillin (A3):

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Shah 1998 *(Continued)*

	• piperacillin 2 g IV after clamping of the cord and 2 g every 8 hrs x 2; • N = 52. Intervention: drug combination [cephalosporin (B1) plus nitroimidazole (I)]: • cephradine 500 mg plus metronidazole 500 mg both IV after the cord was clamped and every 8 hrs x 2; • N = 47. Comparison: no treatment: • no treatment; • N = 51. Results of the 2 penicillin treatment groups were combined for this review. Placebo data were divided: 2/3 for comparison with penicillin (A) and 1/3 for comparisons with the cephalosporin.
Outcomes	Febrile morbidity (fever > 38ºC twice 4 hrs apart after 1st day); endometritis (uterine and parametrial tenderness, foul smelling vaginal discharge); wound infection (local induration and tenderness with wound exudate).
Notes	3 women who developed drug reactions were excluded from study (1 from each of the treatment groups). Late morbidity evaluated at 4-6 weeks. Class of antibiotic: extended spectrum penicillin (ureidopenicillin (pipericillin)) vs other combination (1st generation cephalosporin plus nitroimidazole (metronidazole). Subgroups: • elective CS; • after cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized..". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Quote: "...consecutively numbered sealed envelopes..".
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 14 women were excluded (8/147 from treatment groups, 6/51 from control group). As-treated analysis with available outcome data.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.

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Shah 1998 *(Continued)*

Other bias	Low risk	Comment: no other sources of bias identified.

Sokolowski 1989

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Date of data collection: not stated. Setting: Magdeburg, Germany. Inclusion criteria: women undergoing CS (both elective and non-elective). Exclusion criteria: none reported.
Interventions	Intervention 1: • metronidazole 1 g post-operative days 1 and 2, then 500 mg from days 3 - 8 (vaginal tablet); • N = 172. Intervention 2: • no treatment; • N = 204.
Outcomes	Fever (> 37.5°C for at least 3 days post-operatively). Data also given for outcome of high fever (> 38.5°C) (7/172 vs 29/204 for treatment and control groups respectively); puerperal infection and wound infection were combined as "other diseases" (8/172 vs 11/204).
Notes	Translated from German. Class of antibiotic: nitroimidazoles. Subgroups: • both elective and non-elective CS; • after cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: Described as "by random selection"; women with surnames A-K received treatment, women with surnames L-Z did not. Comment: quasi-RCT.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up reported; no participant excluded.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.

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Sokolowski 1989 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Stage 1982

Methods	Randomized, placebo-controlled trial; 2 parallel groups (2:1 active:placebo randomization). Unit of randomization: individual. Part of a larger study looking at prophylaxis also in gynecologic surgery.
Participants	Dates of data collection: July 1976 to June 1978. Setting: 14 US centers. Inclusion criteria: all women undergoing CS (46% in labor). N = 199. Exclusion criteria: infection, allergy to penicillin or cephalosporins.
Interventions	Intervention: 1st generation cephalosporin: • cephradine 1 g IV; • N = 133. Comparison: placebo: • placebo; • N = 66. Within 1 hr prior to surgery, repeated at 4 hrs.
Outcomes	Febrile morbidity (oral temperature > 37.7ºC twice 4 hrs apart, after 1st 48 hrs); endometritis (uterine tenderness, fever and purulent discharge), wound infection (increased local tenderness, redness or swelling); UTI (positive culture); maternal length of stay (treatment 5.8 days vs placebo 7.57 days; P < 0.05, variance not given).
Notes	Class of antibiotic: 1st generation cephalosporin. Subgroups: • type of CS undefined; • before cord clamping. The 2 groups were comparable regarding age and other risk factors.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly allocated".

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Stage 1982 *(Continued)*

		Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: investigator provided with Individually. randomized block of patient numbers.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: dropouts in CS women not stated (overall: 11/319 from treated group, 8/172 from placebo group. As-treated analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: placebo-controlled; patients and investigators blind to allocation throughout the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: probably outcome assessment was blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Stiver 1983

Methods	Randomized, placebo-controlled trial; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collectin: no reported. Setting: 5 centers in Canada. Inclusion criteria: all women in labor or with ruptured membranes (duration of ruptured membranes not stated; mean duration 9.97 hrs; included in both category). N = 361.
Interventions	Intervention 1: 1st generation cephalosporin: • cefazolin 1 g; • N = 120. Intervention 2: cefamycin: • cefoxitin 2 g; • N = 124. Comparison: placebo: • placebo; • N = 117. Infused IV immediately after cord clamped and 6 and 12 hrs later. Results of both treatment groups combined.
Outcomes	Febrile morbidity (oral temperature > 37.9ºC twice at least 6 hrs apart after 1st 24 hrs); wound infection (redness, induration, tenderness and/or purulent discharge from the incision line); endometritis/parametritis (uterine and/or adnexal tenderness with fever) UTI (dysuria or pyuria and positive culture);

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Stiver 1983 *(Continued)*

	need for antibiotic therapy (11% for treatment groups vs 27% for placebo); maternal length of stay (7.3 and 7.4 days for treatment groups vs 7.9 for placebo).
Notes	Side effects documented: 2 infusion-related hypotensive episodes (1 with cefazolin, 1 with placebo that necessitated withdrawal from study); 6 episodes of phlebitis (5 in treated, 1 in placebo group); 1 episode of angioedema (placebo patient). Data provided on antibiotic resistance in wound isolates and screening cervical cultures. 1 episode of bacteremia (in placebo group); 1 episode of septic shock (in cefazolin-treated group); both outcomes included as serious morbidity. Follow up at 6 weeks. Class of antibiotic: 1st generation cephalosporin or cefamycin (2nd generation cephalosporin). Subgroups: • both elective and non-elective CS; • after cord clamping. The 3 groups were comparable regarding age, parity, gravidity, etc.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly assigned". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: 7 women (1 in treatment, 6 in placebo group) initially randomized but results not included, 6 because they failed to receive all 3 doses, 1 because of hypotensive episode with 1st dose. As-treated analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind, placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Sziller 1994

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: September 1990 to April 1991. Setting: Budapest, Hungary.

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Sziller 1994 *(Continued)*

	Inclusion criteria: women who had opted for elective CS before onset of labor (definition not provided; indications included chronic fetal distress, breech position, placenta previa/placental abruption, prior uterine surgery; classified as elective for this review). Exclusion criteria: symptoms of infection prior to surgery; any illness that increased risk of infection (e.g. diabetes); penicillin allergy.
Interventions	Intervention 1: • unasyn (1000 mg ampicillin/500 mg sulbactam) IV after clamping of the cord, and 6 and 12 hrs later; • N = 60. Intervention 2: • no treatment; • N = 44.
Outcomes	Fever (categorized as mild [up to 37.5°C after the 1st 24 hrs lasting for at least 2 days (treatment n = 4 vs no treatment n = 5)]; moderate [> 38°C for at least 2 days (n = 0 vs n = 2)]; severe [> 38°C lasting > 3 days (n = 0 vs n = 2)];wound infection (induration of the abdominal incision, serosanguinous or purulent discharge, dehiscence of the wound); endometritis (fever plus lower abdominal pain, uterine tenderness, odorous discharge from the uterine cavity); UTI (pathogenic bacteria from mid-stream urine); additional antibiotic treatment (treatment group n = 6 vs no treatment n = 13).
Notes	Translated from Hungarian. Class of antibiotic: beta-lactam/beta-lactamase inhibitor combination. Subgroups: • elective CS; • after cord clamping. No significant differences between groups for age, indications for CS, gestational age, birthweight and previous CS.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Random table".
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss to follow-up reported; no explanation for difference in numbers between groups (60 vs 44).
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information provided to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias)	High risk	Comment: probably outcome assessment was not blinded.

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Sziller 1994 *(Continued)*
All outcomes

Other bias	Low risk	Comment: no other sources of bias identified.

Tully 1983

Methods	Randomized, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual placebo-controlled; double-blind.
Participants	Dates of data collection: September 1978 to June 1980. Setting: Beth Israel Hospital, Boston, Massachusetts, US. Inclusion criteria: women undergoing primary CS (inclusion criteria not consistent with the definition of non-elective CS used in this review). N = 113. Exclusion criteria: < 18 years of age, membranes ruptured > 35 hrs, allergy to penicillin or cephalosporin, fever, infection or antibiotic use, significant underlying cardiac, renal or hepatic disease, unable to provide consent.
Interventions	Intervention: cefamycin: • cefoxitin 2 g IV immediately after the cord was clamped and at 4 and 8 hrs; • N = 52. Comparison: placebo: • matched placebo (mannitol with riboflavin); • N = 61.
Outcomes	Febrile morbidity (oral temperature > 37.9ºC twice at least 6 hrs apart after 1st 24 hrs); UTI (positive culture); wound infection (purulence, cellulitis or dehiscence); endometritis (fever, uterine tenderness, abnormal lochia); septicemia (positive blood culture in a clinically septic patient); additional antibiotic use (8 in treatment group vs 12 in placebo).
Notes	Both episodes of septicemia occurred in the placebo group. Class of antibiotic: cefamycin (2nd generation cephalosporin). Subgroups: • type of CS unclear; • after cord clamping. The 2 groups were comparable regarding age, BMI, gravidity, frequency of fetal monitoring, number of vaginal examinations, duration of labor, duration of ruptured membranes, duration of surgery and indications for CS.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Comment: randomized as determined by table of random numbers.
Allocation concealment (selection bias)	Low risk	Comment: sequential study numbers.

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Tully 1983 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up reported; 14 women (7 in each group) initially randomized were later excluded (all doses not administered, antibiotic therapy prior to surgery, antibiotic following surgery, incorrect dose schedule, infection prior to surgery, drug code broken for possible allergy. As-treated analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: randomization was blind to both patients and investigators. Placebo-controlled (mannitol with riboflavin).
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Turner 1990

Methods	Quasi-RCT, 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection; not reported. Setting: Hammersmith Hospital (N = 102) and Northwick Park Hospital (N = 99), London, England. Inclusion criteria: women undergoing CS (both elective and emergency). N = 201. Exclusion: on antibiotics, adverse reaction to penicillin or cephalosporin, pyrexia > 37.5 degrees C in labor, known vaginal pathogen, or suspected intrauterine infection.
Interventions	Intervention: 1st generation cephalosporin: • cephradine 2 g IV after induction of anesthesia and 1 g 6 and 12 hrs after the operation; • N = 101. Comparison: no treatment: • no treatment; • N = 100.
Outcomes	Puerperal infection (temperature > 37.5ºC after 24 hrs); endometritis (pyrexia with uterine or adnexal tenderness); wound infection (purulent discharge or erythema, induration and serous discharge with positive culture); UTI (> 100,000 colony forming units in urine culture); length of hospital stay (7.63 for treatment group, 7.18 for control group [SD not provided]).
Notes	Definitions of elective and emergency procedure, nor separate outcomes for each group, provided. Follow up completed 1987. Class of antibiotic: 1st generation cephalosporin. Subgroups: • both elective and non-elective CS;

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Turner 1990 *(Continued)*

- before cord clamping.

The 2 groups were comparable with respect to age, social class, single mother, weight, previous CS, the mode of onset of labor, the use of electronic fetal monitoring, the type of CS, gestational age, birthweight or the perinatal outcome.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "...alternate patients..". Comment: quasi-RCT.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no losses or exclusions were reported. Analysis appears to be ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding; not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Tzingounis 1982

Methods	Randomized, placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Date of data collection: not reported. Setting: Alexandra Maternity Hospital, Athens, Greece. Inclusion criteria: women in labor (non-elective). N = 96. Exclusion criteria: acute bleeding due to abruptio placentae, established infection.
Interventions	Intervention: 2nd generation cephalosporin: • cefuroxime 750 mg IV 1 hr or less before surgery and every 8 hrs for 72 hrs; • N = 46. Comparison: placebo: • matching placebo (comparable in appearance and viscosity); • N = 50.

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Tzingounis 1982 *(Continued)*

Outcomes	Febrile morbidity (oral temperature of > 100.3ºF twice 6 hrs apart) and infection of endometrium, urinary tract and wound (not defined); results of duration of maternal stay only provided for febrile patients.
Notes	No patients had any major complications from the use of cefuroxime. Class of antibiotic: 2nd generation cephalosporin. Subgroups: • non-elective CS; • before cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Selected in a random manner". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up; no participants excluded. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "double-blind".... "the placebo was comparable to cefuroxime in both appearance and viscosity of solution".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Ujah 1992

Methods	RCT, 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: August 1989 to July 1990. Setting: Jos Universtiy Teaching Hospitla, Jos, Nigeria. Inclusion criteria: healthy women scheduled for elective CS. N = 35. Exclusion criteria: labor, premature rupture of membranes, uncontrolled diabetes mellitus, sickle cell disease.
Interventions	Intervention: beta-lactam inhibitor combination:

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Ujah 1992 *(Continued)*

	• augmentin (amoxicillin-clavulanic acid) 1.2 g IV intraoperatively by the anesthetist; • N = 17. Comparison: placebo: • placebo (10 cc normal saline); • N = 18..
Outcomes	Febrile morbidity, wound erythema or induration, seropurulent discharge, pneumonia.
Notes	Developing country. Class of antibiotic: beta-lactamase inhibitor combination. Subgroups: • elective CS; • timing of administration not specified. "They were well matched for the (patient characteristics) considered .. and equally well matched for (preoperative, intraoperative and post-operative) variables."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Using a random list of numbers".
Allocation concealment (selection bias)	Unclear risk	Quote: "Randomization was performed by the nurse in charge of the antenatal ward using a random number list".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded after randomization. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: placebo-controlled; insufficient information to judge whether there was blinding of study personnel.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Walss Rodriguez 1990

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: July 1 to September 1988.

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Walss Rodriguez 1990 *(Continued)*

	Setting: Coah, Mexico. Inclusion criteria: women undergoing urgent CS. N = 120. Exclusion: fever, chorioamnionitis, penicillin allergy, antibiotic treatment in prior 2 weeks.
Interventions	Intervention: • ampicillin 2 g IV every 4 hrs x 3 after clamping of cord; • N = 59. Comparison: no treatment: • no treatment; • N = 61.
Outcomes	Febrile syndrome; wound infection; abdominal wall abscess; endometritis, length of hospital stay.
Notes	No definitions of outcomes provided. "Absceso de pared" has been translated as abdominal wall abscess. Abdominal wall abscess, infection of surgical scar and spontaneous reopening of the wound + infection have been classified as "wound infection". Class of antibiotic: aminopenicillin (ampicillin). Subgroups: • type of CS unclear; • after cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: Allocated "in random form" using a random table.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no losses or exclusions were reported. Analysis appears to be ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

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Weissberg 1971

Methods	RCT: 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: not specified. Setting: Miami, Florida, US. Mostly low-income or indigent Negro women from ghetto areas of large metropolitan area. Inclusion criteria: women undergoing primary CS after the onset of labor. N = 80. Exclusion criteria: none specified.
Interventions	Intervention: combination [penicillin + aminoglycoside]: • penicillin G 2 MU IV every 4 hrs and kanamycin 500 mg IM every 12 hrs as soon as it was decided to perform a CS, at the time of operation or immediately post-operatively and continued for a minimum of 3 days post-operatively; • N = 40. Comparison: no treatment: • no treatment; • N = 40.
Outcomes	Febrile morbidity (temperature of > 100.3ºF on any 2 days after 1st 24 hrs); UTI, endometritis and wound infection (not defined); maternal length of stay (treatment 5.8 days vs 8.7 days for control group, no variance given).
Notes	1 patient receiving penicillin had a drug rash on the 3rd day. Class of antibiotic: aminoglycoside-containing combination. Subgroups: • non-elective CS; • timing of administration not specified. "The clinical material in both groups was identical."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "selected at random". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Insufficient information to judge.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss of participants to follow-up; no participant excluded after randomization. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.

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Weissberg 1971 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Witt 2011

Methods	Randomized, double-blind, placebo-controlled; 3 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: March 2004 to January 2010. Setting: Medical University of Vienna, Vienna, Austria. Inclusion criteria: women undergoing cesarean delivery at term with gestational age ≥37 weeks and reassuring fetal heart traces. Rupture of membranes and labor contractions were allowed (not consistent with the criteria of elective CS used in this review; classified as "both or not defined"). Exclusion criteria: fever > 38°C, cephalosporin allergy, age < 18 years, exposure to any antibiotic within 1 week before delivery.
Interventions	Intervention 1: • cefazolin 2 g administered 20 - 30 minutes before skin incision; • N = 370. Intervention 2: • cefazolin 2 g administered immediately after clamping of the cord; • N = 371. Intervention 3: • placebo administered 20 - 30 minutes before skin incision; • N = 371. For the subgroups of class of antibiotic and type of CS, the 2 treatment groups have been combined (n = 741); for the timing of administration, the control group has been divided in 2 (n = 186).
Outcomes	Wound infection (purulent discharge or erythema (> 1 cm in diameter) and induration of the incision site; endometritis (fever, defined as axillary temperature of ≥ 38°C for at least 28 hrs, uterine tenderness and malodorous lochia); UTI (clinical symptoms, i.e. polyuria and dysuria, and positive dipstick nitrites); serious maternal infectious morbidity (pelvic abscess, sepsis). Neonatal outcomes (respiratory distress syndrome, intracranial hemorrhage, necrotizing enterocolitis, sepsis, neonatal death): no statistically significant difference (data not shown). Patients followed during hospital stay with a telephone call at 30 days and clinic visit for women with signs and symptoms of endometritis, wound infection or UTI.
Notes	Methicillin resistant *Staphylococcus aureus* was not noted in the study population. No difference in patient characteristics nor infection rates between early (March 2004 to June 2007) and late (July 2007 to January 2010) time periods.

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Witt 2011 *(Continued)*

Class of antibiotic: 1st generation cephalosporin.

Sugroups:

- both elective and non-elective CS;
- before and after clamping of cord.

The groups were balanced with regard to age, BMI, prevalence of gestational diabetes, history of allergy, immunosuppressive and anticoagulation therapy during pregnancy.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Computer generated randomization list".
Allocation concealment (selection bias)	Unclear risk	Comment: A study nurse checked the randomization list and handed the appropriate infusion bag to the anesthesiologist.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: 32 participants were lost to follow-up, protocol violations or withdrawal from the study (group 1 = 12; group 2 = 7; control = 13); included in ITT analysis.
Selective reporting (reporting bias)	Low risk	Comment: primary outcomes are reported.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: control group received 100 mL of identical appearing saline solution. Study nurse but not the patient, the surgeon or the anesthetist was aware of the allocation; patients and surgeons were masked to the administration schedule.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: evaluation of the infectious morbidity was performed by 2 residents masked to the group assignment. Neonatal outcomes were collected by neonatal staff unaware of the maternal group assignment.
Other bias	Low risk	Comment: no other sources of bias identified.

Wong 1978

Methods	Randomized placebo-controlled trial; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection: January 1975 to January 1977. Setting: Los Angeles County-University of Southern California Medical Center, Los Angeles, California, US, 87% Hispanic or Black. Inclusion criteria: women in labor with ruptured membranes who underwent internal fetal monitoring (classified as non-elective). N = 93. Exclusion: fever, other antibiotic use, penicillin allergy.
Interventions	Intervention: 1st generation cephalosporin: • cefazolin 1 g IV after the cord was clamped and at 4-6 hrs and 10-12 hrs post-operatively; • N = 48.

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Wong 1978 *(Continued)*

	Comparison: placebo: • placebo; • N = 45.
Outcomes	Standard temperature morbidity, endomyometritis, abdominal wound infection, urinary infections (no definitions provided for any outcomes).
Notes	2 women were said to develop a serious infection: 1 (cefazolin group) developed septic thrombophlebitis and is included as a serious outcome; the other (placebo group) was treated with antibiotics for prolonged fever (judged not to be a serious outcome for this review). Class of antibiotic: 1st generation cephalosporin. Subgroups: • non-elective CS; • after cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized to numbered packages". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Low risk	Quote: "... the agents having been randomized to numbered packages by the pharmacy department".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss to follow-up reported. 7 women initially randomized not included in final analysis because they did not meet all the criteria (allocated group unknown). As-treated analysis performed.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information provided
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: double-blind study, placebo-controlled; similar quantity of placebo given. The physician caring for the patient did not know which agent his patient received.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: probably outcome assessment was blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Work 1977

Methods	RCT; 2 parallel groups. Unit of randomization: individual.
Participants	Dates of data collection; not reported. Setting: University of Michigan Medical Center, Ann Arbour, Michigan, US.

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Work 1977 *(Continued)*

	Inclusion criteria: women in labor. N = 80. Exclusion criteria: acute bleeding due to abruptio placentae, infection on treatment; abnormal renal function, penicillin allergy.
Interventions	Intervention: 1st generation cephalosporin: • cephalothin 2 g IV within 1 hr of operation and at 4 and 8 hrs after; • N = 40. Comparison: placebo: • comparable appearing placebo; • N = 40.
Outcomes	Febrile morbidity (oral temperature > 100.3ºF twice 6 hrs apart); infection of endometrium, urinary tract and wound (definitions not provided); fever index (40 degree hrs for treatment group vs 83 for placebo group).
Notes	Class of antibiotic: 1st generation cephalosporin. Subgroups: • non-elective CS; • before cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Selected in random ... manner". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no loss to follow-up or exclusion of participants after randomization described, but results of only 80/85 participants reported; insufficient detail to know if the analysis was ITT.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The placebo was comparable to the cephalothin in both appearance and viscosity of solution". Comment: double blind, placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information provided.
Other bias	Low risk	Comment: no other sources of bias identified.

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Wu 1991

Methods	Randomized into 3 groups (irrigation vs systemic treatment vs no treatment).
Participants	Dates of data collection: May 1988 to August 1989. Setting: Beijing, China. Inclusion criteria: women undergoing both elective (N = 112) and non-elective (N = 105) CS. Only women undergoing an elective CS were randomized to treatment or no treatment and have been included in analysis. N = 112.
Interventions	Intervention: • ampicillin 6 g after delivery of the placenta, local irrigation; • N = 39. Intervention: combination [penicillin + aminoglycoside]: • penicillin 5.6 MU and gentamicin 240,000 U IV immediately after surgery and penicillin 1.6 MU and gentamicin 160,000 U per day IM x 3 days; • N = 41. Comparison: no treatment: • no treatment; • N = 32. Placebo data were divided: 1/2 for comparison with penicillin (A) and 1/2 for comparisons with the combined drug regimen.
Outcomes	Endometritis (presence of any 2 of following: temperature above 37.5ºC, uterine tenderness, foul vaginal discharge); abdominal wound infection (cellulitis with small amount of exudate within 2 months of operation); uterine incision infection (associated with late postpartum hemorrhage); fever index.
Notes	Women undergoing non-elective sections randomized to either treatment group (not included in this review). Class of antibiotic: amminoglycoside-containing combination (natural penicillin and gentamicin) or aminopenicillin (ampicillin). Subgroups: • elective CS; • after cord clamping.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "...randomized..". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no losses or exclusions were reported. Analysis appears to be ITT.

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Wu 1991 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Comment: no blinding, not placebo-controlled.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Comment: probably outcome assessment was not blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

Yip 1997

Methods	Randomized, placebo-controlled; 2 parallel groups.
Participants	Date of data collection: not reported. Setting: Prince of Wales Hospital, Hong Kong. Inclusion criteria: women undergoing CS. N = 320. Exclusion criteria: penicillin allergy, current antibiotic use, fever, receipt of steroid injection.
Interventions	Intervention: beta-lactam inhibitor: • augmentin 1.2 g (amoxycillin sodium 1000 mg and clavulanate potassium 200 mg) in 10 mL saline; • N = 160. Comparison: placebo: • saline placebo; • N = 160.
Outcomes	Febrile morbidity (2 oral temperatures > 37.9ºC at least 6 hrs apart after 1st 24 hrs); bacteriuria at day 3 (classified in this review as UTI); wound infection (purulent discharge, cellulitis, tenderness and wound abscess requiring incision and drainage); endometritis (fever, pelvic pain, uterine tenderness, purulent vaginal discharge without signs of infection in the lower genital tract); duration of hospital stay.
Notes	Sub-rectus Redivac drain routinely inserted. Class of antibiotic: beta-lactamase inhibitor combination. Subgroups: • type of CS unclear; • before cord clamping. The 2 groups were comparable regarding age, weight, parity, duration of labor, birthweight, etc.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomized".

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Yip 1997 *(Continued)*

		Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: assigned by the anesthetist.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up reported; no patients excluded from analysis. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: " double-blind" placebo-controlled (10 mL normal saline).
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: insufficient information to judge.
Other bias	Low risk	Comment: no other sources of bias identified.

Young 1983

Methods	Randomized, placebo-controlled trial; 2 parallel groups. Unit of randomization; individual.
Participants	Dates of data collection: May 1978 to July 1979. Setting: Los Angeles County-University of Southern California Medical Center, Los Angeles, California, US. Predominantly (91%) Hispanic or Black. Inclusion criteria: women in labor with an intrauterine pressure catheter and fetal scalp electrode (non-elective). N = 100. Exclusion criteria: fever, significant systemic disease.
Interventions	Intervention: cefamycin: • cefoxitin 1 g IV at time of cord clamping and at 4 and 8 hrs; • N = 50. Comparison: placebo: • matching placebo; • N = 50.
Outcomes	Endomyometritis, abdominal wound infection, serious complications; duration of maternal hospital stay (treatment 5.1 days vs control 5.9 days, not statistically significant, no variance given).
Notes	1 case of septic pelvic thrombophlebitis occurred in the treatment group; there were 8 episodes of bacteremia in the control group vs 1 in the treatment group; both outcomes combined under serious morbidity. Class of antibiotic: cefamycin (2nd generation cephalosporin).

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Young 1983 *(Continued)*

Subgroups:

- non-elective CS;
- after cord clamping.

The 2 groups were comparable regarding age and race.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomly assigned". Comment: no description of sequence generation process.
Allocation concealment (selection bias)	Unclear risk	Comment: no information was provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: no loss to follow-up reported; no participants excluded. ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Comment: insufficient information to judge.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: placebo-controlled; "similarly appearing placebo". "the physician team did not know which medication the patient was to receive."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: probably outcome assessment was blinded.
Other bias	Low risk	Comment: no other sources of bias identified.

BMI: body mass index
C: centigrade
CS: cesarean section
F: fahrenheit
hr: hour/hours
IM: intramuscularly
ITT: intention to treat
IV: intravenously
MU: million units
q 6 hrs: every 6 hours
RCT: randomized controlled trial
SD/sd: standard deviation
UTI: urinary tract infection
vs: versus

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

Study	Reason for exclusion
Ahued 1994	Study included women undergoing gynecological surgery; allocation of participants (N = 71) undergoing cesarean section to treatment or control group not provided.

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Study	Reason for exclusion
Andrews 2003	All participants received prophylaxis with cefotetan after cord clamping and were then randomized to receive doxycycline plus azithromycin vs placebo.
Cormier 1988	Did not include women undergoing cesarean section.
Creatsas 1980	Not relevant to this review. Ampicillin or gentamycin given prior to cesarean section in women with intrauterine infection, to measure transplacental transfer. No control group, and no clinical outcomes given.
De Palma 1980	Women at high risk (membranes ruptured for more than 6 hours) initially were randomized to early treatment (i.e. prophylactic therapy continued for 4 days) vs standard treatment (i.e. treatment only started when infection apparent). When the results were compared midway through the study, standard therapy was abandoned. The results for the 2 groups prior to abandoning the no treatment group could not be obtained from the paper.
Elliott 1982	Only the 1st 42 women were randomized to placebo or active treatment; after that a significant difference was observed between the placebo and treated groups and the placebo arms were discontinued. Further women were randomized to 2 different active treatments. The data for the 1st part of the study (with only the 1st 42 women) are not available from the published paper.
Harrigill 2003	Women were randomized to normal saline intra-abdominal irrigation vs no irrigation. All patients received cefazolin at the time of cord clamping.
Itskovitz 1979	Not all women were randomly allocated to treatment or no treatment. 150 women were assigned at random to each of the 2 wings of the department according to the day of their admission, each wing receiving women on alternate days. In both wings, of the last 50 women every 2nd woman served as a control. 50 women in 1 wing received IV cephalothin or oral cephalexin, 50 women in the other wing received IV or oral ampicillin. The 1st 50 women enrolled were all treated; separate results for the last 100 women (who were alternately allocated therapy or no treatment) are not available.
Kosus 2010	All women received ceftriaxone 1 g after clamping of the cord; women were randomized to irrigation of the subcutaneous tissue with rifamycin SV or no irrigation before closure of the subcutaneous tissue.
Krasnodebski 1997	Translated from Polish. No information is provided as to how participants were allocated to treatment or no treatment group.
Kreutner 1979	After approximately 70% of the planned study population had been randomized to placebo or 1 of 2 active treatment groups, an unacceptably high morbidity rate in the placebo group was confirmed and the placebo arm was discontinued. Further women were randomized to 2 different active treatments. The data for the 1st part of the study when women were randomized to treatment or placebo are not available from the published paper.
Louie 1982	Eligible women were in active labor with ruptured membranes. While this study initially included a placebo control group, this group was dropped after 30 women had been enrolled on the basis of ethical considerations about assigning women to a non-treatment group in which the likelihood of morbidity was high. Only 7 women (out of a total of 195 women entered) were randomized to placebo, separate results on the initial part of the study not available. The placebo (7) and treatment groups (188) were very imbalanced making a meaningful comparison between groups impossible.
Pawelec 1994	Abstract only; unable to confirm random allocation and method of allocation to no treatment group; data for separate outcomes of endometritis and wound infection not provided.
Petersen 1985	Included women undergoing obstetrical and gynecological procedures; outcomes for both groups combined and not provided separately for women undergoing cesarean section. Reported that

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Study	Reason for exclusion
	there was a only significant effect of cefotaxime in women with prolonged labor or "remote" rupture of the membranes (data not shown).
Pitt 2001	Women were randomized to receive intravaginal metronidazole or placebo gel during labor; most, but not all patients also received 1 prophylactic dose of cefazolin after cord clamping.
Roex 1987	This study compared one dose versus three doses of cefoxitin and only reported on antibiotic levels in breast milk.
Sanchez-Ramos 1999	Patients were randomized to metronidazole gel intravaginally or matching placebo, but most patients also received prophylactic antibiotics after cord clamping.
Sengupta 1976	In this study, in which women were alternately allocated to antibiotic prophylaxis or no treatment, the women enrolled were undergoing both gynecological and obstetrical surgery. Rates of infectious complications are given for all abdominal surgery (cesarean section, abdominal hysterectomy and laparotomy). Data specifically on the women who underwent cesarean section are, however, not available from the published study.
Skryten 1988	Abstract only. Rates for all post-operative infection morbidity and clinically significant genital tract-related infections (wound infections, endometritis) and abscess formation (septicemia) combined; rates for individual outcomes not provided.
Spreafico 1987	Results combined from 3 time periods. In only 1 period did it appear women were randomized to antibiotic therapy or no treatment; results just for this period not available in published report.
Voto 1986	All women received antibiotics (randomized to cefoxitin after cord clamping and then every 4 hours x 2 or oral ampicillin 2 g daily x 7 days); no clinical outcomes reported.
Wallace 1984	This was not a randomized trial of antibiotic prophylaxis. 3 distinct groups of women were studied: 1 group was part of randomized trial that compared extracorporeal cesarean section with prophylactic antibiotic; the 2nd group received extracorporeal cesarean section and no antibiotics; the 3rd group received extracorporeal cesarean section with antibiotics (the decision to administer antibiotics in the latter 2 groups was at the discretion of the physician).
Wells 1994	Absolute numbers cannot be calculated from data provided in abstract; no published version of this study identified.
Yamagishi 2009	Following normal delivery, women were randomized to no oral antibiotics, or 3 or 5 days of an oral antibiotic; did not include women undergoing cesarean section.
Yildirim 2009	Women undergoing elective cesarean section were randomized to cefazolin before skin incision or after umbilical cord clamping. There was no "no treatment" group.

IV: intravenous
vs: versus

DATA AND ANALYSES

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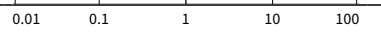
Comparison 1. Antibiotic versus no antibiotics

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maternal febrile morbidity/fever	56	9046	Risk Ratio (M-H, Random, 95% CI)	0.45 [0.40, 0.51]
2 Maternal wound infection	82	14407	Risk Ratio (M-H, Fixed, 95% CI)	0.40 [0.35, 0.46]
3 Maternal endometritis	83	13548	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.34, 0.42]
4 Maternal serious infectious complications	32	6159	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.20, 0.49]
5 Maternal urinary tract infection	66	10928	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.49, 0.65]
6 Maternal adverse effects	13	2131	Risk Ratio (M-H, Fixed, 95% CI)	2.43 [1.00, 5.90]
7 Maternal days in hospital	19	3168	Mean Difference (IV, Random, 95% CI)	-0.46 [-0.65, -0.28]

Analysis 1.1. Comparison 1 Antibiotic versus no antibiotics, Outcome 1 Maternal febrile morbidity/fever.

Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Adam 2005	1/50	2/50		0.26%	0.5[0.05,5.34]
Allen 1972	0/5	3/7		0.19%	0.19[0.01,3.03]
Bagratee 2001	20/240	19/240		2.38%	1.05[0.58,1.92]
Bibi 1994	4/133	9/136		0.95%	0.45[0.14,1.44]
Chan 1989	15/299	7/101		1.47%	0.72[0.3,1.72]
Dashow 1986	53/283	25/77		3.46%	0.58[0.39,0.86]
De Boer 1989	29/91	40/91		3.62%	0.73[0.5,1.06]
Dillon 1981	5/46	22/55		1.43%	0.27[0.11,0.66]
Duff 1980	7/26	13/31		1.79%	0.64[0.3,1.37]
Duff 1982	4/42	13/40		1.13%	0.29[0.1,0.82]
Elliott 1986	7/119	14/39		1.57%	0.16[0.07,0.38]
Engel 1984	5/50	19/50		1.39%	0.26[0.11,0.65]
Freeman 1982	3/62	12/56		0.87%	0.23[0.07,0.76]
Gerstner 1980	16/53	30/50		3.07%	0.5[0.32,0.8]
Hager 1983	4/43	11/47		1.07%	0.4[0.14,1.16]
Harger 1981	53/196	76/190		4.23%	0.68[0.51,0.9]
Hawrylyshyn 1983	13/124	18/58		2.21%	0.34[0.18,0.64]
Heilmann 1984	1/30	4/30		0.31%	0.25[0.03,2.11]
Huam 1997	8/100	18/100		1.7%	0.44[0.2,0.97]
Jaffe 1984	7/58	22/55		1.76%	0.3[0.14,0.65]
Jaffe 1985	6/38	20/40		1.67%	0.32[0.14,0.7]
Jakobi 1994	15/167	25/140		2.39%	0.5[0.28,0.92]
Kellum 1985	16/84	62/86		3.12%	0.26[0.17,0.42]
Kolben 2001	4/76	4/70		0.73%	0.92[0.24,3.54]
Kreutner 1978	13/48	17/49		2.38%	0.78[0.43,1.43]
Kristensen 1990	2/102	19/99		0.65%	0.1[0.02,0.43]
Leonetti 1989	10/100	16/50		1.93%	0.31[0.15,0.64]



Favours antibiotics — Favours control

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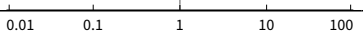
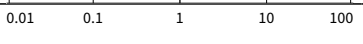
Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Lewis 1990	22/112	42/100		3.24%	0.47[0.3,0.73]
Magro 1983	1/23	1/13		0.2%	0.57[0.04,8.3]
Mahomed 1988	7/115	33/117		1.74%	0.22[0.1,0.47]
McCowan 1980	13/35	13/38		2.32%	1.09[0.59,2.01]
Moodley 1981	7/40	4/20		1.01%	0.88[0.29,2.64]
Moro 1974	6/74	20/74		1.51%	0.3[0.13,0.7]
Morrison 1973	25/115	59/115		3.55%	0.42[0.29,0.63]
Oestreicher 1987	5/30	8/30		1.2%	0.63[0.23,1.69]
Padilla 1983	5/34	22/37		1.52%	0.25[0.11,0.58]
Rizk 1998	6/59	6/61		1.06%	1.03[0.35,3.02]
Roex 1986	15/64	29/65		2.79%	0.53[0.31,0.88]
Ross 1984	6/57	9/58		1.26%	0.68[0.26,1.78]
Rothbard 1975	6/47	23/53		1.63%	0.29[0.13,0.66]
Rouzi 2000	15/221	41/220		2.57%	0.36[0.21,0.64]
Saltzman 1985	7/50	16/49		1.67%	0.43[0.19,0.95]
Scarpignato 1982	2/39	7/20		0.62%	0.15[0.03,0.64]
Shah 1998	13/139	14/45		2.07%	0.3[0.15,0.59]
Sokolowski 1989	30/172	85/204		3.72%	0.42[0.29,0.6]
Stage 1982	29/133	25/66		3.2%	0.58[0.37,0.9]
Stiver 1983	25/243	25/111		2.85%	0.46[0.28,0.76]
Sziller 1994	4/60	9/44		1%	0.33[0.11,0.99]
Tzingounis 1982	12/46	27/50		2.63%	0.48[0.28,0.84]
Ujah 1992	0/17	2/18		0.17%	0.21[0.01,4.1]
Walss Rodriguez 1990	0/59	5/61		0.18%	0.09[0.01,1.66]
Weissberg 1971	6/40	34/40		1.81%	0.18[0.08,0.37]
Wong 1978	12/48	20/51		2.4%	0.64[0.35,1.16]
Work 1977	14/40	27/40		3.04%	0.52[0.32,0.83]
Wu 1991	1/80	1/32		0.19%	0.4[0.03,6.2]
Yip 1997	6/160	8/160		1.13%	0.75[0.27,2.11]
Total (95% CI)	**5017**	**4029**		**100%**	**0.45[0.4,0.51]**
Total events: 621 (Antibiotics), 1155 (Control)					
Heterogeneity: Tau^2=0.07; Chi^2=89.58, df=55(P=0); I^2=38.6%					
Test for overall effect: Z=12.76(P<0.0001)					



Favours antibiotics — Favours control

Analysis 1.2. Comparison 1 Antibiotic versus no antibiotics, Outcome 2 Maternal wound infection.

Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Adam 2005	0/50	0/50			Not estimable
Adeleye 1981	11/58	14/48		2.44%	0.65[0.33,1.3]
Bagratee 2001	30/240	32/240		5.09%	0.94[0.59,1.49]
Bibi 1994	4/133	28/136		4.41%	0.15[0.05,0.41]
Bilgin 1998	0/91	5/28		1.33%	0.03[0,0.5]
Carl 2000	1/20	1/20		0.16%	1[0.07,14.9]
Chan 1989	27/299	12/101		2.86%	0.76[0.4,1.44]
Conover 1984	2/68	1/56		0.17%	1.65[0.15,17.69]
Cormier 1989	5/55	8/55		1.27%	0.63[0.22,1.79]



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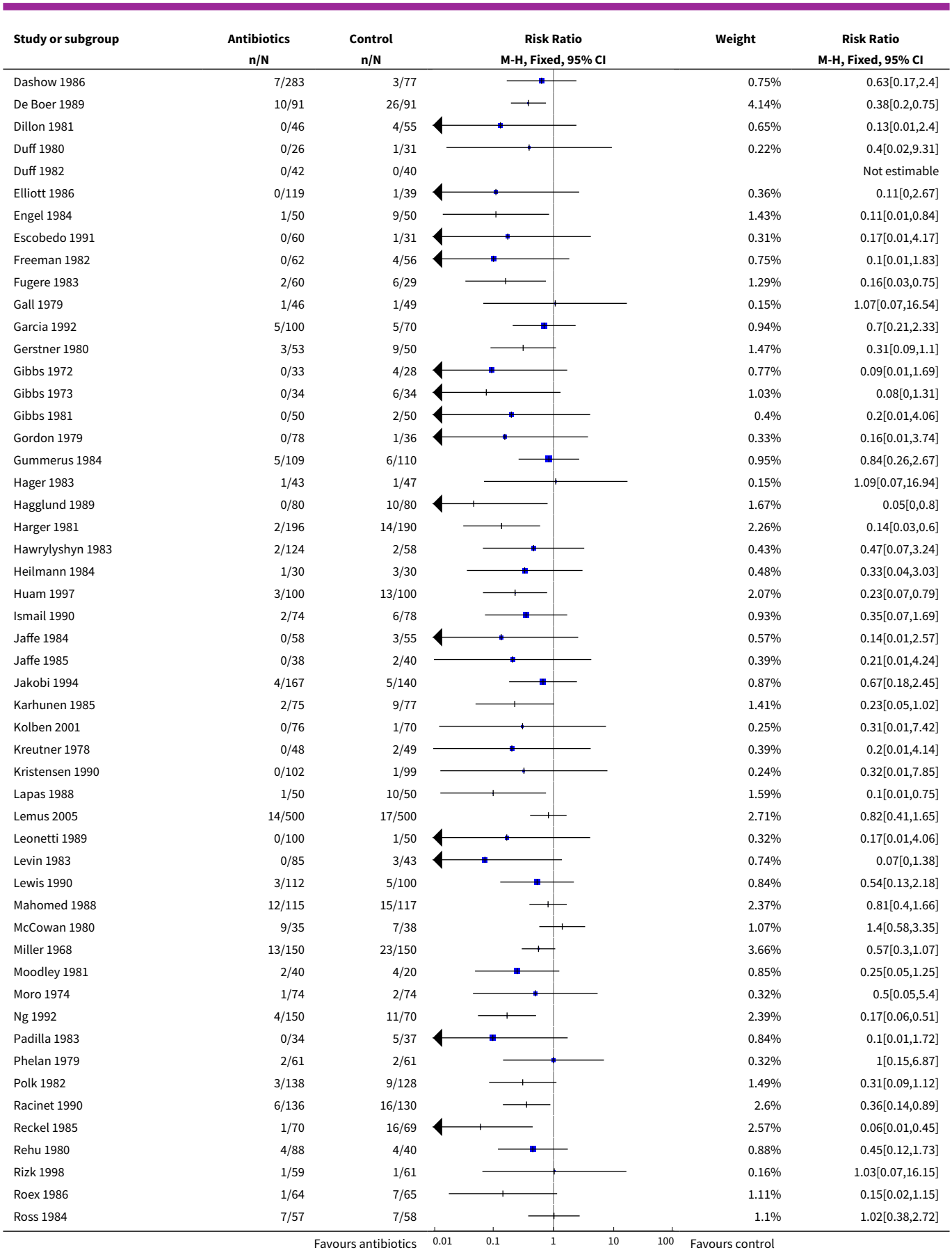

Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Dashow 1986	7/283	3/77		0.75%	0.63[0.17,2.4]
De Boer 1989	10/91	26/91		4.14%	0.38[0.2,0.75]
Dillon 1981	0/46	4/55		0.65%	0.13[0.01,2.4]
Duff 1980	0/26	1/31		0.22%	0.4[0.02,9.31]
Duff 1982	0/42	0/40			Not estimable
Elliott 1986	0/119	1/39		0.36%	0.11[0,2.67]
Engel 1984	1/50	9/50		1.43%	0.11[0.01,0.84]
Escobedo 1991	0/60	1/31		0.31%	0.17[0.01,4.17]
Freeman 1982	0/62	4/56		0.75%	0.1[0.01,1.83]
Fugere 1983	2/60	6/29		1.29%	0.16[0.03,0.75]
Gall 1979	1/46	1/49		0.15%	1.07[0.07,16.54]
Garcia 1992	5/100	5/70		0.94%	0.7[0.21,2.33]
Gerstner 1980	3/53	9/50		1.47%	0.31[0.09,1.1]
Gibbs 1972	0/33	4/28		0.77%	0.09[0.01,1.69]
Gibbs 1973	0/34	6/34		1.03%	0.08[0,1.31]
Gibbs 1981	0/50	2/50		0.4%	0.2[0.01,4.06]
Gordon 1979	0/78	1/36		0.33%	0.16[0.01,3.74]
Gummerus 1984	5/109	6/110		0.95%	0.84[0.26,2.67]
Hager 1983	1/43	1/47		0.15%	1.09[0.07,16.94]
Hagglund 1989	0/80	10/80		1.67%	0.05[0,0.8]
Harger 1981	2/196	14/190		2.26%	0.14[0.03,0.6]
Hawrylyshyn 1983	2/124	2/58		0.43%	0.47[0.07,3.24]
Heilmann 1984	1/30	3/30		0.48%	0.33[0.04,3.03]
Huam 1997	3/100	13/100		2.07%	0.23[0.07,0.79]
Ismail 1990	2/74	6/78		0.93%	0.35[0.07,1.69]
Jaffe 1984	0/58	3/55		0.57%	0.14[0.01,2.57]
Jaffe 1985	0/38	2/40		0.39%	0.21[0.01,4.24]
Jakobi 1994	4/167	5/140		0.87%	0.67[0.18,2.45]
Karhunen 1985	2/75	9/77		1.41%	0.23[0.05,1.02]
Kolben 2001	0/76	1/70		0.25%	0.31[0.01,7.42]
Kreutner 1978	0/48	2/49		0.39%	0.2[0.01,4.14]
Kristensen 1990	0/102	1/99		0.24%	0.32[0.01,7.85]
Lapas 1988	1/50	10/50		1.59%	0.1[0.01,0.75]
Lemus 2005	14/500	17/500		2.71%	0.82[0.41,1.65]
Leonetti 1989	0/100	1/50		0.32%	0.17[0.01,4.06]
Levin 1983	0/85	3/43		0.74%	0.07[0,1.38]
Lewis 1990	3/112	5/100		0.84%	0.54[0.13,2.18]
Mahomed 1988	12/115	15/117		2.37%	0.81[0.4,1.66]
McCowan 1980	9/35	7/38		1.07%	1.4[0.58,3.35]
Miller 1968	13/150	23/150		3.66%	0.57[0.3,1.07]
Moodley 1981	2/40	4/20		0.85%	0.25[0.05,1.25]
Moro 1974	1/74	2/74		0.32%	0.5[0.05,5.4]
Ng 1992	4/150	11/70		2.39%	0.17[0.06,0.51]
Padilla 1983	0/34	5/37		0.84%	0.1[0.01,1.72]
Phelan 1979	2/61	2/61		0.32%	1[0.15,6.87]
Polk 1982	3/138	9/128		1.49%	0.31[0.09,1.12]
Racinet 1990	6/136	16/130		2.6%	0.36[0.14,0.89]
Reckel 1985	1/70	16/69		2.57%	0.06[0.01,0.45]
Rehu 1980	4/88	4/40		0.88%	0.45[0.12,1.73]
Rizk 1998	1/59	1/61		0.16%	1.03[0.07,16.15]
Roex 1986	1/64	7/65		1.11%	0.15[0.02,1.15]
Ross 1984	7/57	7/58		1.1%	1.02[0.38,2.72]

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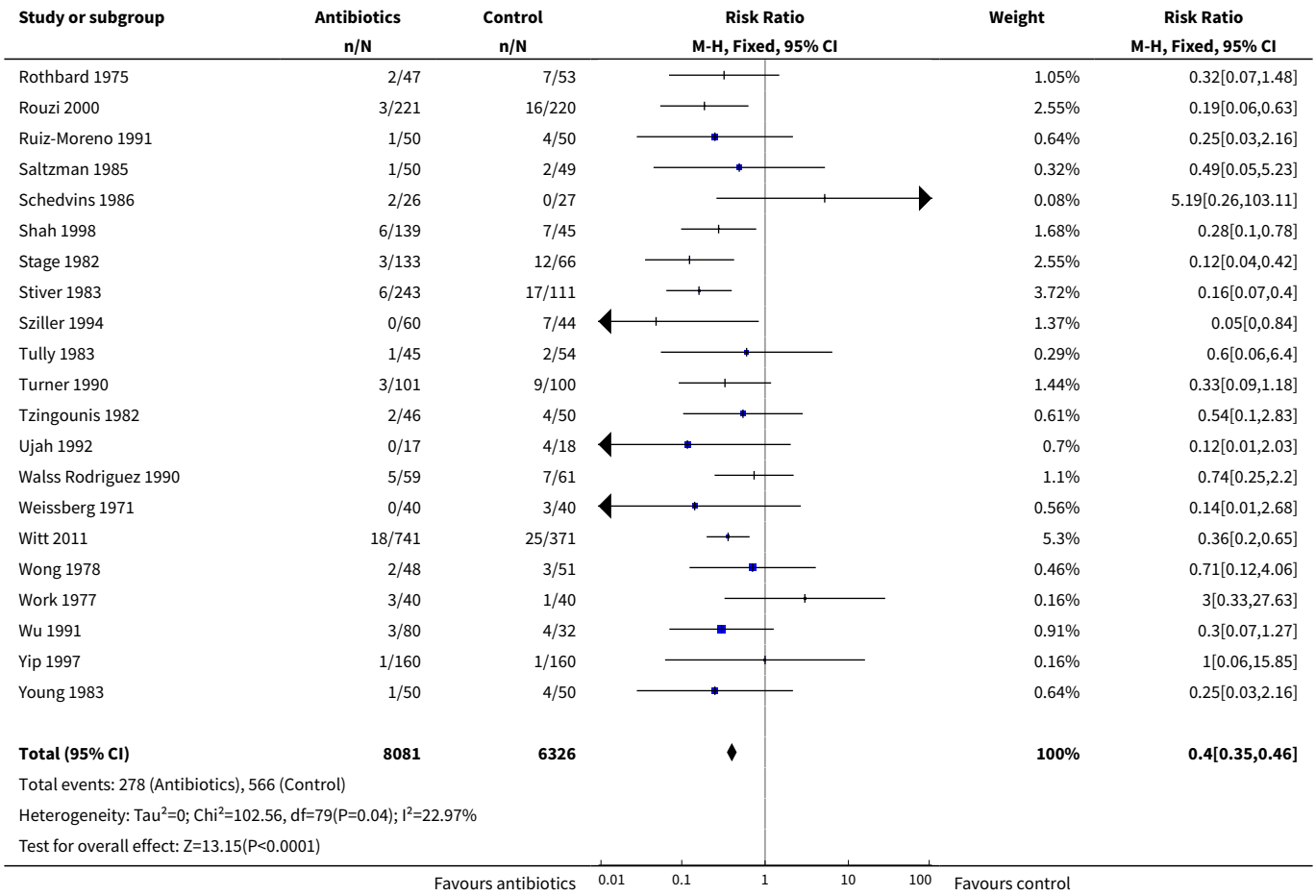
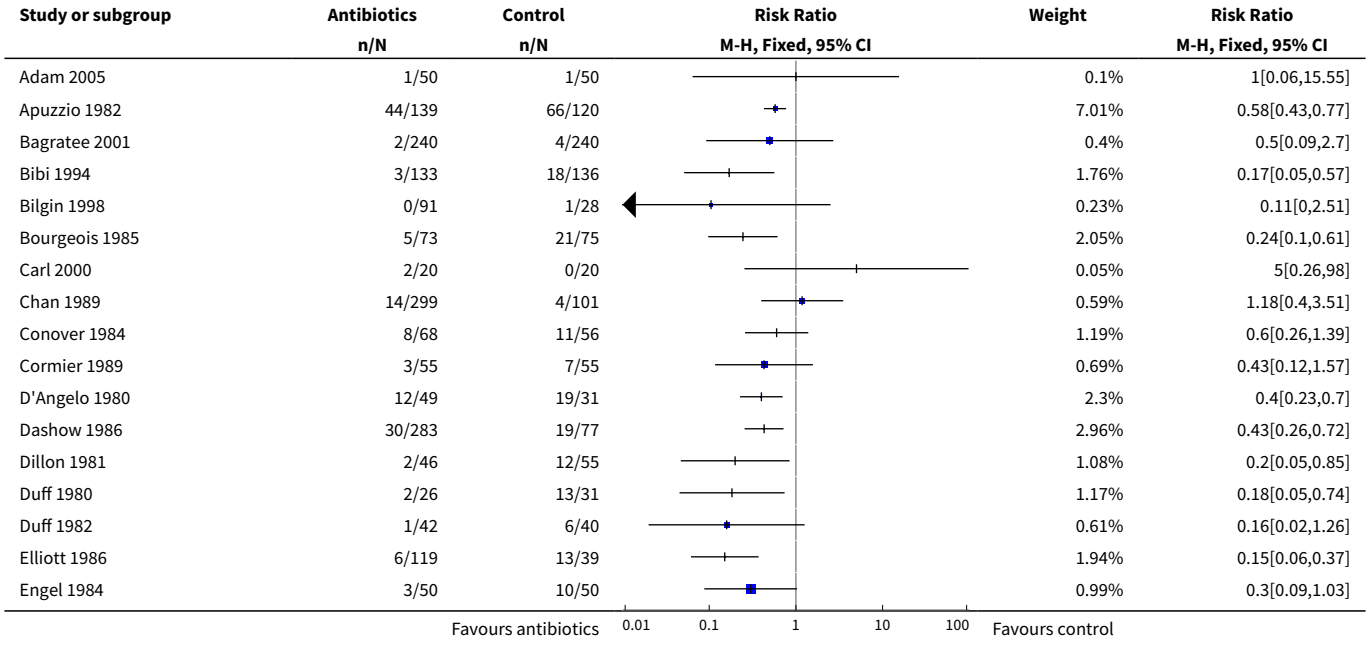


Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rothbard 1975	2/47	7/53		1.05%	0.32[0.07,1.48]
Rouzi 2000	3/221	16/220		2.55%	0.19[0.06,0.63]
Ruiz-Moreno 1991	1/50	4/50		0.64%	0.25[0.03,2.16]
Saltzman 1985	1/50	2/49		0.32%	0.49[0.05,5.23]
Schedvins 1986	2/26	0/27		0.08%	5.19[0.26,103.11]
Shah 1998	6/139	7/45		1.68%	0.28[0.1,0.78]
Stage 1982	3/133	12/66		2.55%	0.12[0.04,0.42]
Stiver 1983	6/243	17/111		3.72%	0.16[0.07,0.4]
Sziller 1994	0/60	7/44		1.37%	0.05[0,0.84]
Tully 1983	1/45	2/54		0.29%	0.6[0.06,6.4]
Turner 1990	3/101	9/100		1.44%	0.33[0.09,1.18]
Tzingounis 1982	2/46	4/50		0.61%	0.54[0.1,2.83]
Ujah 1992	0/17	4/18		0.7%	0.12[0.01,2.03]
Walss Rodriguez 1990	5/59	7/61		1.1%	0.74[0.25,2.2]
Weissberg 1971	0/40	3/40		0.56%	0.14[0.01,2.68]
Witt 2011	18/741	25/371		5.3%	0.36[0.2,0.65]
Wong 1978	2/48	3/51		0.46%	0.71[0.12,4.06]
Work 1977	3/40	1/40		0.16%	3[0.33,27.63]
Wu 1991	3/80	4/32		0.91%	0.3[0.07,1.27]
Yip 1997	1/160	1/160		0.16%	1[0.06,15.85]
Young 1983	1/50	4/50		0.64%	0.25[0.03,2.16]
Total (95% CI)	**8081**	**6326**		**100%**	**0.4[0.35,0.46]**
Total events: 278 (Antibiotics), 566 (Control)					
Heterogeneity: Tau^2=0; Chi^2=102.56, df=79(P=0.04); I^2=22.97%					
Test for overall effect: Z=13.15(P<0.0001)					

Analysis 1.3. Comparison 1 Antibiotic versus no antibiotics, Outcome 3 Maternal endometritis.



Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Adam 2005	1/50	1/50		0.1%	1[0.06,15.55]
Apuzzio 1982	44/139	66/120		7.01%	0.58[0.43,0.77]
Bagratee 2001	2/240	4/240		0.4%	0.5[0.09,2.7]
Bibi 1994	3/133	18/136		1.76%	0.17[0.05,0.57]
Bilgin 1998	0/91	1/28		0.23%	0.11[0,2.51]
Bourgeois 1985	5/73	21/75		2.05%	0.24[0.1,0.61]
Carl 2000	2/20	0/20		0.05%	5[0.26,98]
Chan 1989	14/299	4/101		0.59%	1.18[0.4,3.51]
Conover 1984	8/68	11/56		1.19%	0.6[0.26,1.39]
Cormier 1989	3/55	7/55		0.69%	0.43[0.12,1.57]
D'Angelo 1980	12/49	19/31		2.3%	0.4[0.23,0.7]
Dashow 1986	30/283	19/77		2.96%	0.43[0.26,0.72]
Dillon 1981	2/46	12/55		1.08%	0.2[0.05,0.85]
Duff 1980	2/26	13/31		1.17%	0.18[0.05,0.74]
Duff 1982	1/42	6/40		0.61%	0.16[0.02,1.26]
Elliott 1986	6/119	13/39		1.94%	0.15[0.06,0.37]
Engel 1984	3/50	10/50		0.99%	0.3[0.09,1.03]

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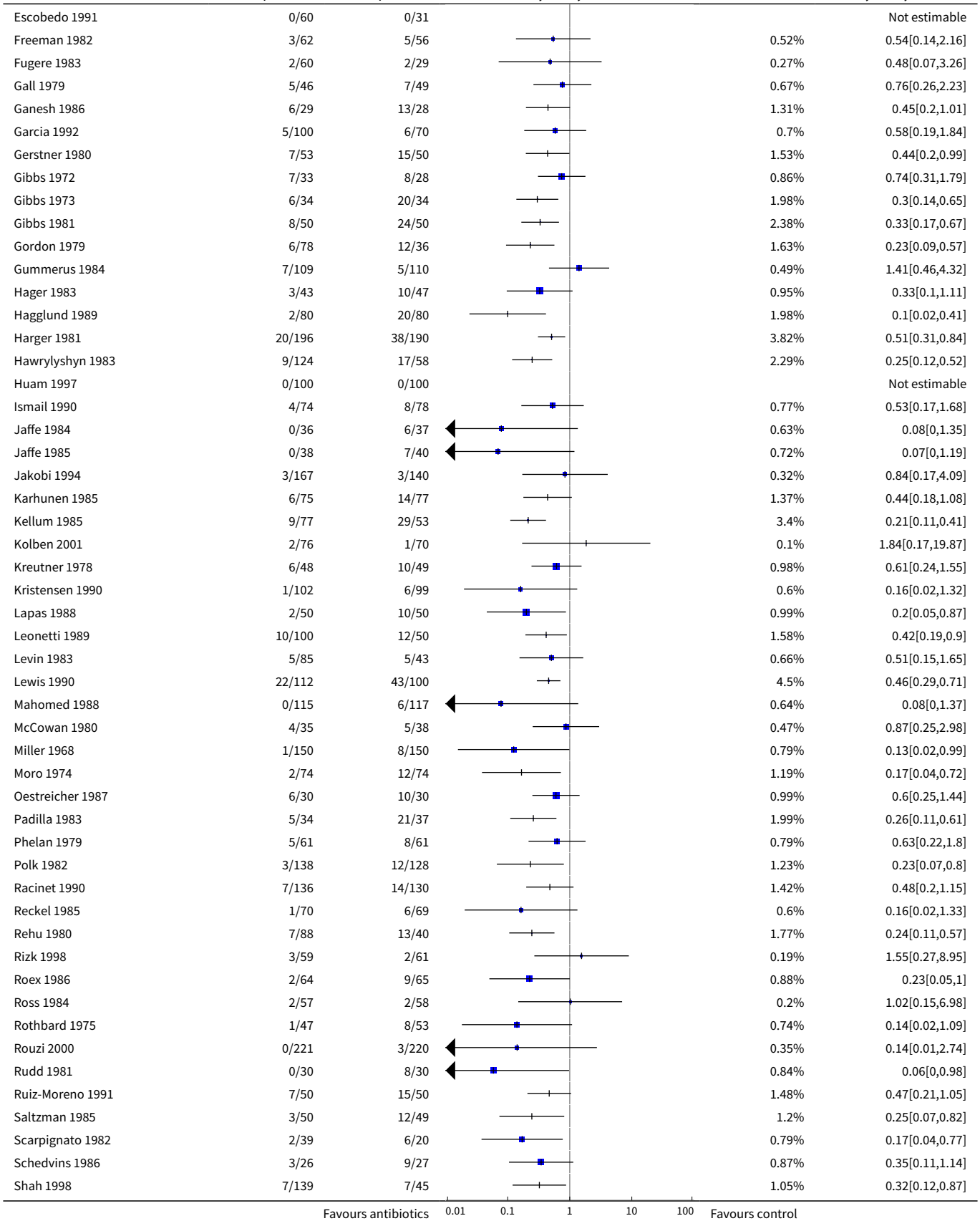

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Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Stage 1982	1/133	9/66		1.19%	0.06[0.01,0.43]
Stiver 1983	8/234	10/111		1.34%	0.38[0.15,0.94]
Sziller 1994	3/60	7/44		0.8%	0.31[0.09,1.15]
Tully 1983	3/45	11/54		0.99%	0.33[0.1,1.1]
Turner 1990	2/101	11/100		1.09%	0.18[0.04,0.79]
Tzingounis 1982	4/46	8/50		0.76%	0.54[0.18,1.68]
Walss Rodriguez 1990	0/59	5/61		0.54%	0.09[0.01,1.66]
Weissberg 1971	4/40	14/40		1.39%	0.29[0.1,0.79]
Witt 2011	2/741	7/371		0.92%	0.14[0.03,0.69]
Wong 1978	14/48	23/51		2.21%	0.65[0.38,1.1]
Work 1977	8/40	17/40		1.68%	0.47[0.23,0.96]
Wu 1991	1/80	3/32		0.42%	0.13[0.01,1.23]
Yip 1997	2/160	1/160		0.1%	2[0.18,21.84]
Young 1983	10/50	30/50		2.97%	0.33[0.18,0.61]
Total (95% CI)	**7630**	**5918**		**100%**	**0.38[0.34,0.42]**
Total events: 437 (Antibiotics), 933 (Control)					
Heterogeneity: Tau^2=0; Chi^2=90.94, df=80(P=0.19); I^2=12.03%					
Test for overall effect: Z=18.3(P<0.0001)					

Favours antibiotics 0.01 0.1 1 10 100 Favours control

Analysis 1.4. Comparison 1 Antibiotic versus no antibiotics, Outcome 4 Maternal serious infectious complications.

Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Adam 2005	0/50	0/50			Not estimable
Bibi 1994	0/133	3/136		4.45%	0.15[0.01,2.8]
Bourgeois 1985	0/73	0/75			Not estimable
Conover 1984	0/68	2/56		3.52%	0.17[0.01,3.37]
Dashow 1986	3/283	0/77		1.01%	1.92[0.1,36.83]
De Boer 1989	1/91	3/91		3.86%	0.33[0.04,3.15]
Dillon 1981	0/46	0/55			Not estimable
Duff 1982	0/42	0/40			Not estimable
Elliott 1986	0/119	3/39		6.76%	0.05[0,0.9]
Gall 1979	0/46	4/49		5.61%	0.12[0.01,2.14]
Gibbs 1972	1/33	1/28		1.39%	0.85[0.06,12.95]
Gibbs 1973	0/34	1/34		1.93%	0.33[0.01,7.91]
Gibbs 1981	1/50	3/50		3.86%	0.33[0.04,3.1]
Gummerus 1984	2/109	3/110		3.84%	0.67[0.11,3.95]
Hager 1983	0/43	1/47		1.85%	0.36[0.02,8.7]
Ismail 1990	1/74	8/78		10.02%	0.13[0.02,1.03]
Kreutner 1978	0/48	2/49		3.18%	0.2[0.01,4.14]
Levin 1983	0/85	1/43		2.55%	0.17[0.01,4.1]
Lewis 1990	1/76	2/75		2.59%	0.49[0.05,5.33]
Miller 1968	0/150	4/150		5.79%	0.11[0.01,2.05]
Padilla 1983	1/34	3/37		3.7%	0.36[0.04,3.32]
Phelan 1979	1/61	1/61		1.29%	1[0.06,15.63]
Polk 1982	0/138	4/128		6.01%	0.1[0.01,1.9]
Racinet 1990	0/136	1/130		1.97%	0.32[0.01,7.75]

Favours antibiotics 0.01 0.1 1 10 100 Favours control

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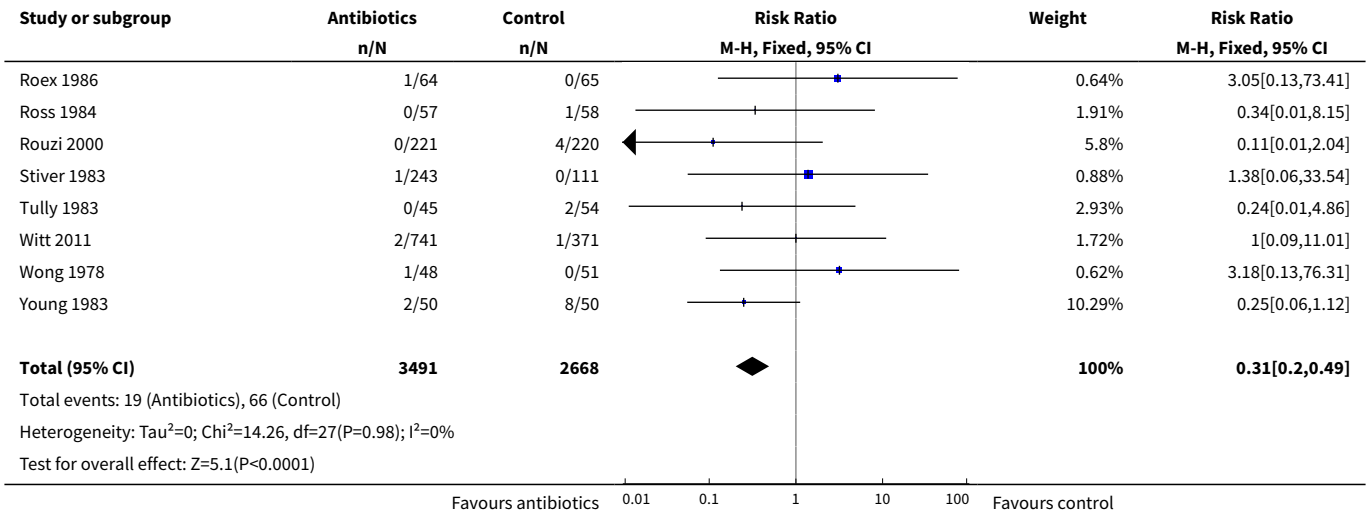
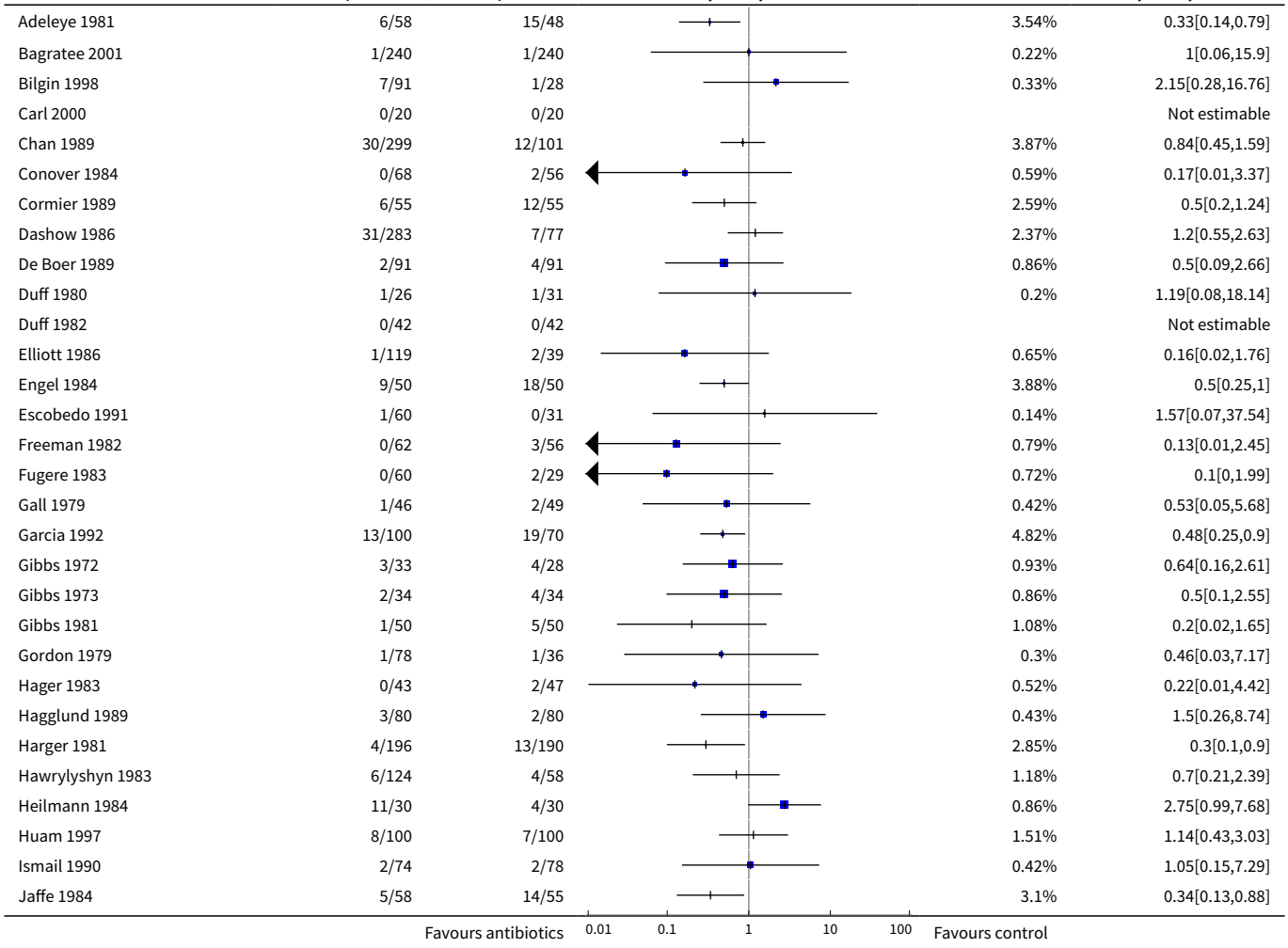


Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Roex 1986	1/64	0/65		0.64%	3.05[0.13,73.41]
Ross 1984	0/57	1/58		1.91%	0.34[0.01,8.15]
Rouzi 2000	0/221	4/220		5.8%	0.11[0.01,2.04]
Stiver 1983	1/243	0/111		0.88%	1.38[0.06,33.54]
Tully 1983	0/45	2/54		2.93%	0.24[0.01,4.86]
Witt 2011	2/741	1/371		1.72%	1[0.09,11.01]
Wong 1978	1/48	0/51		0.62%	3.18[0.13,76.31]
Young 1983	2/50	8/50		10.29%	0.25[0.06,1.12]
Total (95% CI)	**3491**	**2668**		**100%**	**0.31[0.2,0.49]**
Total events: 19 (Antibiotics), 66 (Control)					
Heterogeneity: Tau²=0; Chi²=14.26, df=27(P=0.98); I²=0%					
Test for overall effect: Z=5.1(P<0.0001)					

Analysis 1.5. Comparison 1 Antibiotic versus no antibiotics, Outcome 5 Maternal urinary tract infection.



Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Adeleye 1981	6/58	15/48		3.54%	0.33[0.14,0.79]
Bagratee 2001	1/240	1/240		0.22%	1[0.06,15.9]
Bilgin 1998	7/91	1/28		0.33%	2.15[0.28,16.76]
Carl 2000	0/20	0/20			Not estimable
Chan 1989	30/299	12/101		3.87%	0.84[0.45,1.59]
Conover 1984	0/68	2/56		0.59%	0.17[0.01,3.37]
Cormier 1989	6/55	12/55		2.59%	0.5[0.2,1.24]
Dashow 1986	31/283	7/77		2.37%	1.2[0.55,2.63]
De Boer 1989	2/91	4/91		0.86%	0.5[0.09,2.66]
Duff 1980	1/26	1/31		0.2%	1.19[0.08,18.14]
Duff 1982	0/42	0/42			Not estimable
Elliott 1986	1/119	2/39		0.65%	0.16[0.02,1.76]
Engel 1984	9/50	18/50		3.88%	0.5[0.25,1]
Escobedo 1991	1/60	0/31		0.14%	1.57[0.07,37.54]
Freeman 1982	0/62	3/56		0.79%	0.13[0.01,2.45]
Fugere 1983	0/60	2/29		0.72%	0.1[0,1.99]
Gall 1979	1/46	2/49		0.42%	0.53[0.05,5.68]
Garcia 1992	13/100	19/70		4.82%	0.48[0.25,0.9]
Gibbs 1972	3/33	4/28		0.93%	0.64[0.16,2.61]
Gibbs 1973	2/34	4/34		0.86%	0.5[0.1,2.55]
Gibbs 1981	1/50	5/50		1.08%	0.2[0.02,1.65]
Gordon 1979	1/78	1/36		0.3%	0.46[0.03,7.17]
Hager 1983	0/43	2/47		0.52%	0.22[0.01,4.42]
Hagglund 1989	3/80	2/80		0.43%	1.5[0.26,8.74]
Harger 1981	4/196	13/190		2.85%	0.3[0.1,0.9]
Hawrylyshyn 1983	6/124	4/58		1.18%	0.7[0.21,2.39]
Heilmann 1984	11/30	4/30		0.86%	2.75[0.99,7.68]
Huam 1997	8/100	7/100		1.51%	1.14[0.43,3.03]
Ismail 1990	2/74	2/78		0.42%	1.05[0.15,7.29]
Jaffe 1984	5/58	14/55		3.1%	0.34[0.13,0.88]

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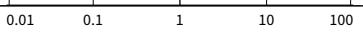
Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Jaffe 1985	2/38	15/40		3.15%	0.14[0.03,0.57]
Jakobi 1994	2/167	7/140		1.64%	0.24[0.05,1.13]
Karhunen 1985	3/75	2/77		0.43%	1.54[0.26,8.96]
Kolben 2001	6/76	2/70		0.45%	2.76[0.58,13.24]
Kreutner 1978	4/48	3/49		0.64%	1.36[0.32,5.76]
Kristensen 1990	0/102	2/99		0.55%	0.19[0.01,3.99]
Levin 1983	3/85	4/43		1.15%	0.38[0.09,1.62]
Lewis 1990	2/76	4/75		0.87%	0.49[0.09,2.61]
McCowan 1980	5/35	4/38		0.83%	1.36[0.4,4.65]
Miller 1968	17/150	26/150		5.61%	0.65[0.37,1.15]
Moro 1974	2/74	2/74		0.43%	1[0.14,6.91]
Oestreicher 1987	1/30	0/30		0.11%	3[0.13,70.83]
Padilla 1983	1/34	1/37		0.21%	1.09[0.07,16.73]
Phelan 1979	5/61	7/61		1.51%	0.71[0.24,2.13]
Polk 1982	6/138	11/128		2.46%	0.51[0.19,1.33]
Reckel 1985	4/70	13/69		2.82%	0.3[0.1,0.88]
Rizk 1998	3/59	3/61		0.64%	1.03[0.22,4.92]
Roex 1986	0/64	10/65		2.25%	0.05[0,0.81]
Ross 1984	2/57	2/58		0.43%	1.02[0.15,6.98]
Rothbard 1975	0/31	6/37		1.28%	0.09[0.01,1.56]
Rouzi 2000	15/221	41/220		8.87%	0.36[0.21,0.64]
Rudd 1981	0/30	0/30			Not estimable
Ruiz-Moreno 1991	4/50	4/50		0.86%	1[0.26,3.78]
Saltzman 1985	0/50	2/49		0.54%	0.2[0.01,3.98]
Schedvins 1986	0/26	2/27		0.53%	0.21[0.01,4.12]
Stage 1982	15/133	6/66		1.73%	1.24[0.5,3.05]
Stiver 1983	1/234	3/111		0.88%	0.16[0.02,1.5]
Sziller 1994	2/60	1/44		0.25%	1.47[0.14,15.67]
Tully 1983	5/45	0/54		0.1%	13.15[0.75,231.61]
Turner 1990	3/101	1/100		0.22%	2.97[0.31,28.08]
Tzingounis 1982	3/46	7/50		1.45%	0.47[0.13,1.7]
Weissberg 1971	4/40	20/40		4.31%	0.2[0.08,0.53]
Witt 2011	12/741	13/371		3.74%	0.46[0.21,1]
Wong 1978	4/48	4/51		0.84%	1.06[0.28,4.01]
Work 1977	3/40	7/40		1.51%	0.43[0.12,1.54]
Yip 1997	14/160	31/160		6.69%	0.45[0.25,0.82]
Total (95% CI)	**6165**	**4763**		**100%**	**0.56[0.49,0.65]**
Total events: 308 (Antibiotics), 429 (Control)					
Heterogeneity: Tau^2=0; Chi^2=75.08, df=62(P=0.12); I^2=17.42%					
Test for overall effect: Z=7.89(P<0.0001)					



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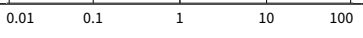
Analysis 1.6. Comparison 1 Antibiotic versus no antibiotics, Outcome 6 Maternal adverse effects.

Study or subgroup	Antibiotics n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Conover 1984	1/68	0/56		7.84%	2.48[0.1,59.67]
Dillon 1981	0/46	0/55			Not estimable



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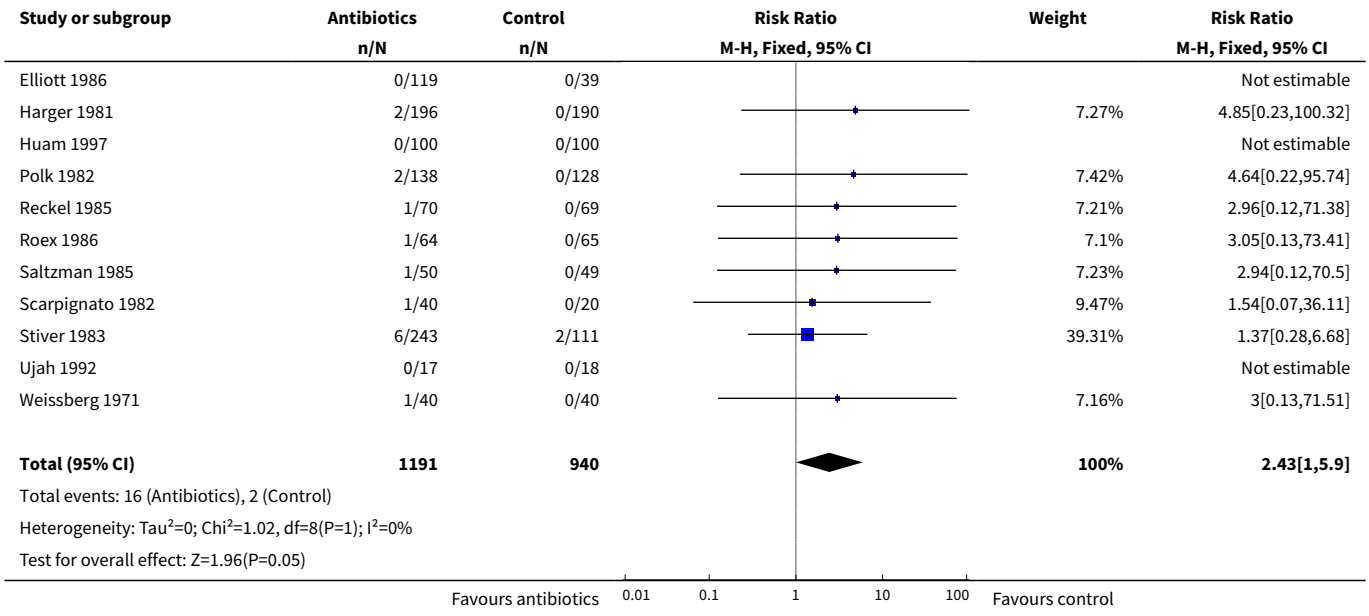
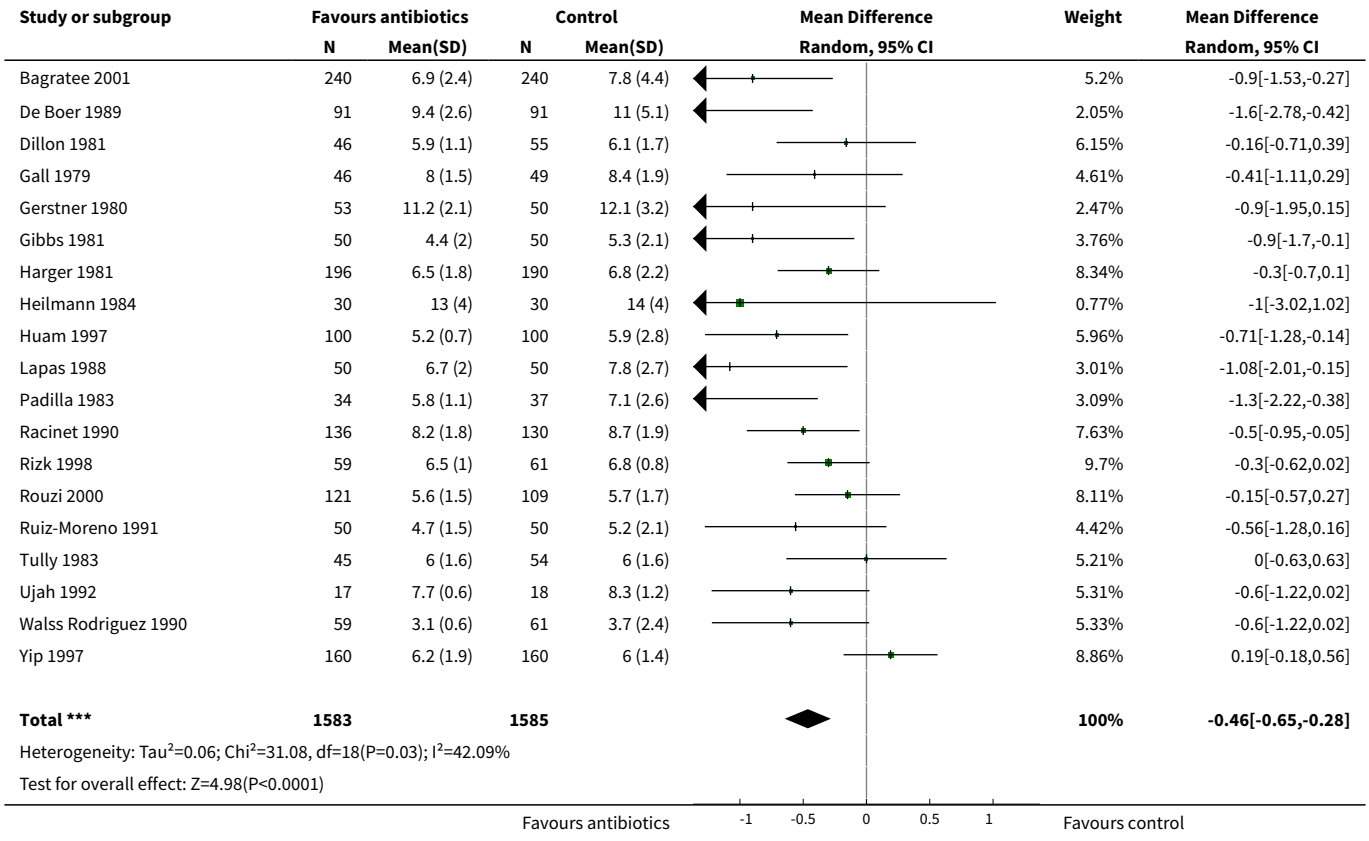


Analysis 1.7. Comparison 1 Antibiotic versus no antibiotics, Outcome 7 Maternal days in hospital.



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Comparison 2. Antibiotic versus no antibiotic - subgroup by class of antibiotic

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maternal febrile morbidity/fever	59		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Natural penicillins	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Aminopenicillins	7	603	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.26, 0.58]
1.3 Extended spectrum penicillins	6	736	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.28, 0.49]
1.4 Beta-lactamase inhibitor combinations	5	791	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.29, 0.79]
1.5 First generation cephalosporins	10	1436	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.44, 0.66]
1.6 Second generation cephalosporins	9	1001	Risk Ratio (M-H, Fixed, 95% CI)	0.35 [0.27, 0.46]
1.7 Cefamycins	9	1894	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.61, 0.88]
1.8 Third generation cephalosporins	3	376	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.27, 0.74]
1.9 Monobactams	1	98	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.29, 1.42]
1.10 Lincosamides	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.08, 3.05]
1.11 Nitroimidazoles	7	1098	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.48, 0.71]
1.12 Fluoroquinolones	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.13 Trimethoprim-sulfamethoxazole	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.14 Aminoglycoside-containing combination	5	668	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.24, 0.46]
1.15 Other antibiotic combination	4	530	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.17, 0.44]
1.16 Other regimen	1	118	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.07, 0.76]
2 Maternal wound infection	83		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Natural penicillins	1	66	Risk Ratio (M-H, Fixed, 95% CI)	0.43 [0.07, 2.87]
2.2 Aminopenicillins (ampicillin)	12	1323	Risk Ratio (M-H, Fixed, 95% CI)	0.50 [0.35, 0.72]
2.3 Extended spectrum penicillins	7	845	Risk Ratio (M-H, Fixed, 95% CI)	0.18 [0.09, 0.39]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.4 Beta-lactamase inhibitor combination	6	823	Risk Ratio (M-H, Fixed, 95% CI)	0.26 [0.13, 0.51]
2.5 First generation cephalosporin	17	3371	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.28, 0.53]
2.6 Second generation cephalosporin	9	1166	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.19, 0.75]
2.7 Cefamycins	16	2635	Risk Ratio (M-H, Fixed, 95% CI)	0.45 [0.33, 0.60]
2.8 Third generation cephalosporin	6	1519	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.26, 0.73]
2.9 Monobactams	1	98	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.05, 5.03]
2.10 Lincosamides	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.03, 2.44]
2.11 Nitroimidazoles	9	1074	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.34, 0.69]
2.12 Fluoroquinolones	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.13 Trimethoprim-sulfamethoxazole	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.14 Aminoglycoside-containing combination	8	654	Risk Ratio (M-H, Fixed, 95% CI)	0.17 [0.08, 0.34]
2.15 Other antibiotic combination	4	530	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.36, 1.02]
2.16 Other regimen	2	171	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.15, 2.30]
3 Maternal endometritis	84		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Natural penicillins	1	66	Risk Ratio (M-H, Fixed, 95% CI)	0.19 [0.05, 0.65]
3.2 Aminopenicillins (ampicillin)	10	1108	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.16, 0.38]
3.3 Extended-spectrum penicillins	9	1164	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.37, 0.58]
3.4 Beta-lactamase inhibitor combinations	5	788	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.27, 1.66]
3.5 First generation cephalosporin	18	3451	Risk Ratio (M-H, Fixed, 95% CI)	0.42 [0.33, 0.54]
3.6 Second generation cephalosporin	13	1563	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.20, 0.37]
3.7 Cefamycins	15	2535	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.28, 0.47]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.8 Third generation cephalosporin	4	408	Risk Ratio (M-H, Fixed, 95% CI)	0.28 [0.11, 0.69]
3.9 Monobactams	1	98	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.25, 1.54]
3.10 Lincosamides	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.11 Nitroimidazoles	8	919	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.37, 0.73]
3.12 Fluoroquinolones	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.13 Trimethoprim-sulfamethoxazole	1	57	Risk Ratio (M-H, Fixed, 95% CI)	0.45 [0.20, 1.01]
3.14 Aminoglycoside-containing combination	8	722	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.19, 0.45]
3.15 Other antibiotic combination	4	530	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.14, 0.75]
3.16 Other regimen	2	171	Risk Ratio (M-H, Fixed, 95% CI)	0.42 [0.17, 1.03]
4 Maternal serious infectious complications	34		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Natural penicillins	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Aminopenicillins (ampicillin)	4	542	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.06, 1.18]
4.3 Extended-spectrum penicillins	1	151	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.05, 5.33]
4.4 Beta-lactamase inhibitor combinations	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.5 First generation cephalosporin	10	2351	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.16, 0.95]
4.6 Second generation cephalosporin	5	522	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.06, 2.13]
4.7 Cefamycins	10	1372	Risk Ratio (M-H, Fixed, 95% CI)	0.22 [0.10, 0.49]
4.8 Third generation cephalosporin	3	376	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.12, 4.03]
4.9 Monobactams	1	98	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.06, 25.02]
4.10 Lincosamides	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.11 Nitroimidazoles	3	516	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.13, 1.65]
4.12 Fluoroquinolones	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.13 Trimethoprim-sulfamethoxazole	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.14 Aminoglycoside-containing regimens	3	398	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.06, 1.59]
4.15 Other antibiotic combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.16 Other regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal urinary tract infection	67		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Natural penicillins	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 Aminopenicillins (ampicillin)	9	1039	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.41, 0.90]
5.3 Extended-spectrum penicillin	6	571	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.20, 0.58]
5.4 Beta-lactamse inhibitor combination	5	788	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.41, 0.99]
5.5 First generation cephalosporin	17	3371	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.49, 0.93]
5.6 Second generation cephalosporin	9	1166	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.38, 0.89]
5.7 Cefamycins	14	2434	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.54, 1.00]
5.8 Third generation cephalosporin	3	308	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.04, 2.16]
5.9 Monobactams	1	98	Risk Ratio (M-H, Fixed, 95% CI)	1.44 [0.35, 5.91]
5.10 Lincosamides	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.11 Nitroimidazoles	5	622	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.53, 2.01]
5.12 Fluoroquinolones	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.13 Trimethoprim-sulfamethoxazole	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.14 Aminoglycoside-containing combination	5	266	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.15, 0.60]
5.15 Other antibiotic combination	2	237	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.32, 1.03]
5.16 Other regimen	2	171	Risk Ratio (M-H, Fixed, 95% CI)	0.16 [0.02, 1.29]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Maternal adverse effects	12		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Natural penicillins	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Aminopenisillins (ampicillin)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 Extended-spectrum penicillins	1	139	Risk Ratio (M-H, Fixed, 95% CI)	2.96 [0.12, 71.38]
6.4 Beta-lactamase inhibitor combination	2	235	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.5 First generation cephalosporin	3	507	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.15, 0.90]
6.6 Second generation cephalosporin	1	60	Risk Ratio (M-H, Fixed, 95% CI)	1.54 [0.07, 36.11]
6.7 Cefamycins	5	654	Risk Ratio (M-H, Fixed, 95% CI)	1.96 [0.41, 9.34]
6.8 Third generation cephalosporin	1	99	Risk Ratio (M-H, Fixed, 95% CI)	2.94 [0.12, 70.50]
6.9 Monobactams	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.10 Lincosamides	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.11 Nitroimidazoles	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.12 Fluoroquinolones	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.13 Trimethoprim-sulfamethoxazole	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.14 Amimnoglycoside-containing combination	1	80	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 71.51]
6.15 Other antibiotic combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.16 Other regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Maternal days in hospital	19		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Natural penicillins	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Aminopenicillins (ampicillin)	2	191	Mean Difference (IV, Fixed, 95% CI)	-0.82 [-1.33, -0.31]
7.3 Extended-spectrum penicillins	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.4 Beta-lactamase inhibitor combinations	3	555	Mean Difference (IV, Fixed, 95% CI)	-0.18 [-0.46, 0.09]

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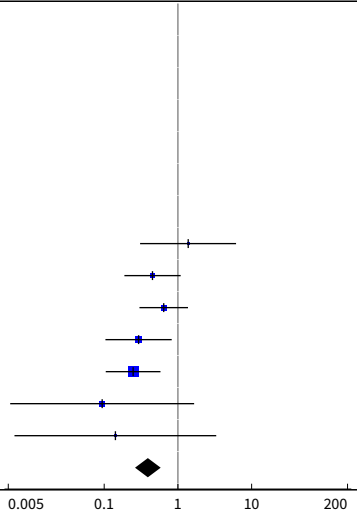
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.5 First generation cephalosporins	2	325	Mean Difference (IV, Fixed, 95% CI)	-0.22 [-0.58, 0.14]
7.6 Second generation cephalosporin	2	220	Mean Difference (IV, Fixed, 95% CI)	-0.38 [-0.69, -0.08]
7.7 Cefamycins	6	1392	Mean Difference (IV, Fixed, 95% CI)	-0.37 [-0.60, -0.15]
7.8 Third generation cephalosporin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.9 Monobactams	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.10 Lincosamides	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.11 Nitroimidazoles	4	485	Mean Difference (IV, Fixed, 95% CI)	-0.91 [-1.37, -0.45]
7.12 Fluoroquinolones	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.13 Aminoglycoside-containing combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.14 Other antibiotic combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.15 Trimethoprim-sulfamethoxazole	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.16 Other regimen	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 2.1. Comparison 2 Antibiotic versus no antibiotic - subgroup by class of antibiotic, Outcome 1 Maternal febrile morbidity/fever.

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.1.1 Natural penicillins					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.1.2 Aminopenicillins					
Chan 1989	8/96	2/33		4.5%	1.38[0.31,6.15]
Dashow 1986	10/70	6/19		14.26%	0.45[0.19,1.09]
Duff 1980	7/26	13/31		17.92%	0.64[0.3,1.37]
Duff 1982	4/42	13/40		20.12%	0.29[0.1,0.82]
Padilla 1983	5/34	22/37		31.84%	0.25[0.11,0.58]
Walss Rodriguez 1990	0/59	5/61		8.17%	0.09[0.01,1.66]
Wu 1991	0/39	1/16		3.18%	0.14[0.01,3.31]
Subtotal (95% CI)	**366**	**237**		**100%**	**0.39[0.26,0.58]**



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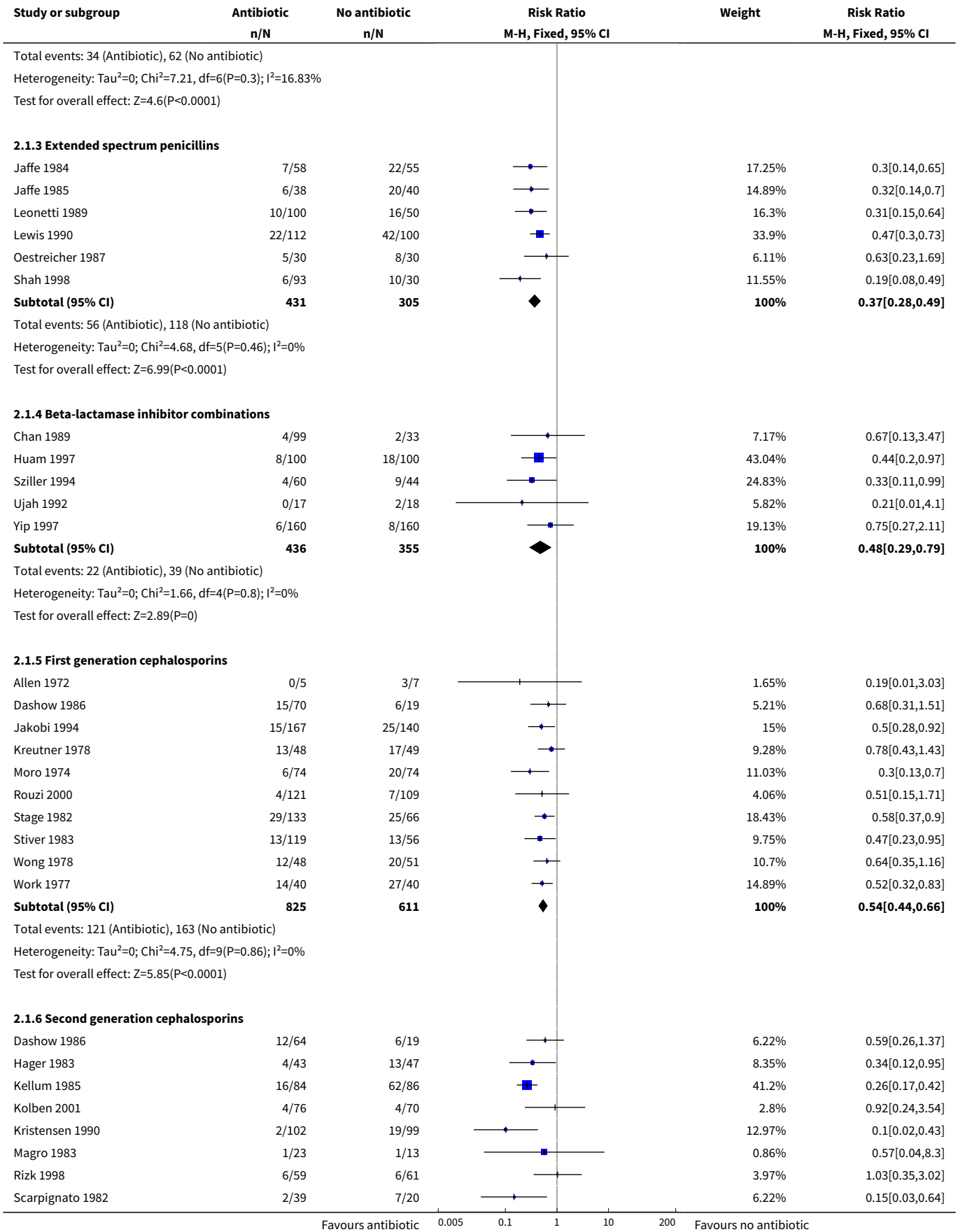

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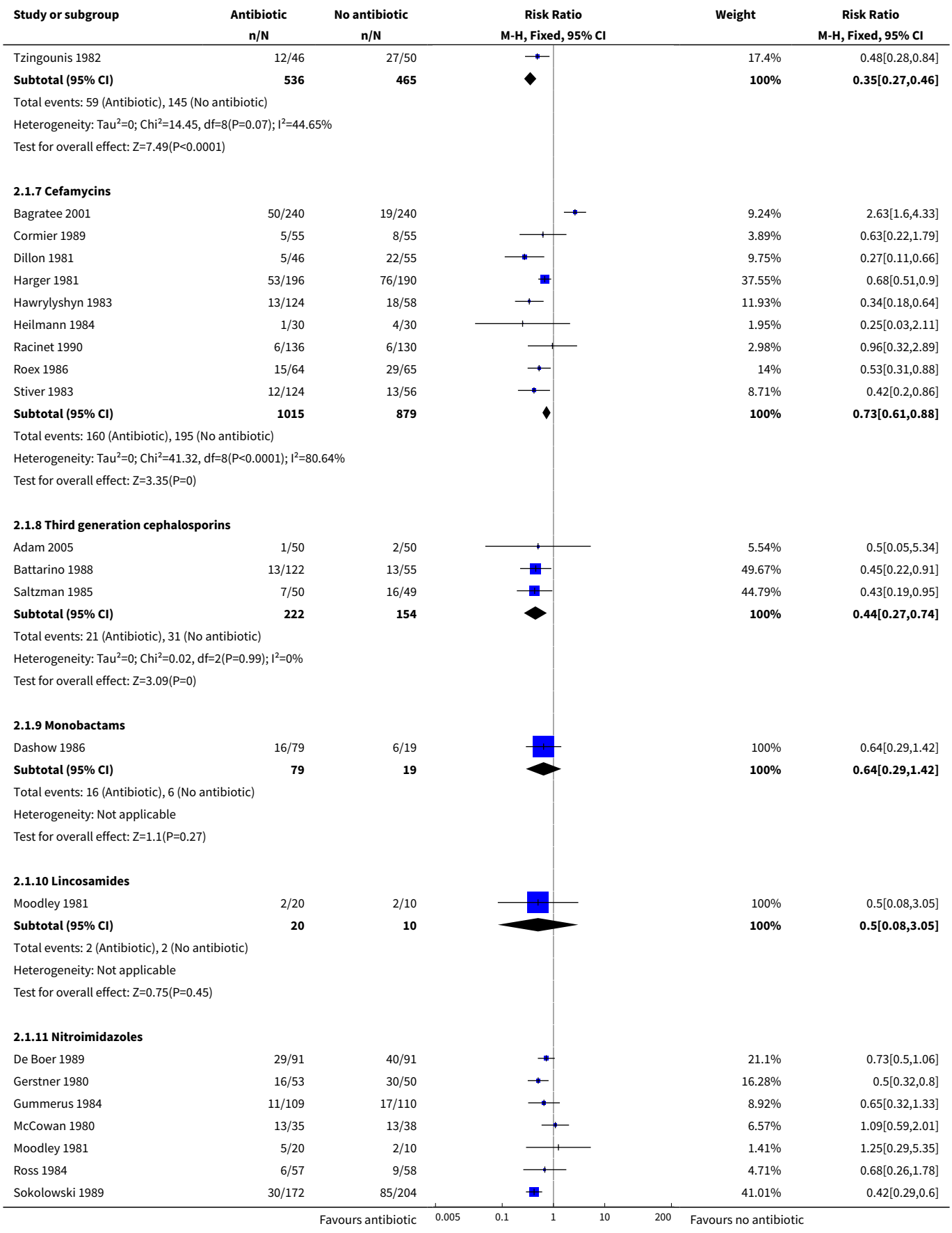

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Tzingounis 1982	12/46	27/50		17.4%	0.48[0.28,0.84]
Subtotal (95% CI)	**536**	**465**		**100%**	**0.35[0.27,0.46]**
Total events: 59 (Antibiotic), 145 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=14.45, df=8(P=0.07); I²=44.65%					
Test for overall effect: Z=7.49(P<0.0001)					
2.1.7 Cefamycins					
Bagratee 2001	50/240	19/240		9.24%	2.63[1.6,4.33]
Cormier 1989	5/55	8/55		3.89%	0.63[0.22,1.79]
Dillon 1981	5/46	22/55		9.75%	0.27[0.11,0.66]
Harger 1981	53/196	76/190		37.55%	0.68[0.51,0.9]
Hawrylyshyn 1983	13/124	18/58		11.93%	0.34[0.18,0.64]
Heilmann 1984	1/30	4/30		1.95%	0.25[0.03,2.11]
Racinet 1990	6/136	6/130		2.98%	0.96[0.32,2.89]
Roex 1986	15/64	29/65		14%	0.53[0.31,0.88]
Stiver 1983	12/124	13/56		8.71%	0.42[0.2,0.86]
Subtotal (95% CI)	**1015**	**879**		**100%**	**0.73[0.61,0.88]**
Total events: 160 (Antibiotic), 195 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=41.32, df=8(P<0.0001); I²=80.64%					
Test for overall effect: Z=3.35(P=0)					
2.1.8 Third generation cephalosporins					
Adam 2005	1/50	2/50		5.54%	0.5[0.05,5.34]
Battarino 1988	13/122	13/55		49.67%	0.45[0.22,0.91]
Saltzman 1985	7/50	16/49		44.79%	0.43[0.19,0.95]
Subtotal (95% CI)	**222**	**154**		**100%**	**0.44[0.27,0.74]**
Total events: 21 (Antibiotic), 31 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=0.02, df=2(P=0.99); I²=0%					
Test for overall effect: Z=3.09(P=0)					
2.1.9 Monobactams					
Dashow 1986	16/79	6/19		100%	0.64[0.29,1.42]
Subtotal (95% CI)	**79**	**19**		**100%**	**0.64[0.29,1.42]**
Total events: 16 (Antibiotic), 6 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.1(P=0.27)					
2.1.10 Lincosamides					
Moodley 1981	2/20	2/10		100%	0.5[0.08,3.05]
Subtotal (95% CI)	**20**	**10**		**100%**	**0.5[0.08,3.05]**
Total events: 2 (Antibiotic), 2 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.75(P=0.45)					
2.1.11 Nitroimidazoles					
De Boer 1989	29/91	40/91		21.1%	0.73[0.5,1.06]
Gerstner 1980	16/53	30/50		16.28%	0.5[0.32,0.8]
Gummerus 1984	11/109	17/110		8.92%	0.65[0.32,1.33]
McCowan 1980	13/35	13/38		6.57%	1.09[0.59,2.01]
Moodley 1981	5/20	2/10		1.41%	1.25[0.29,5.35]
Ross 1984	6/57	9/58		4.71%	0.68[0.26,1.78]
Sokolowski 1989	30/172	85/204		41.01%	0.42[0.29,0.6]

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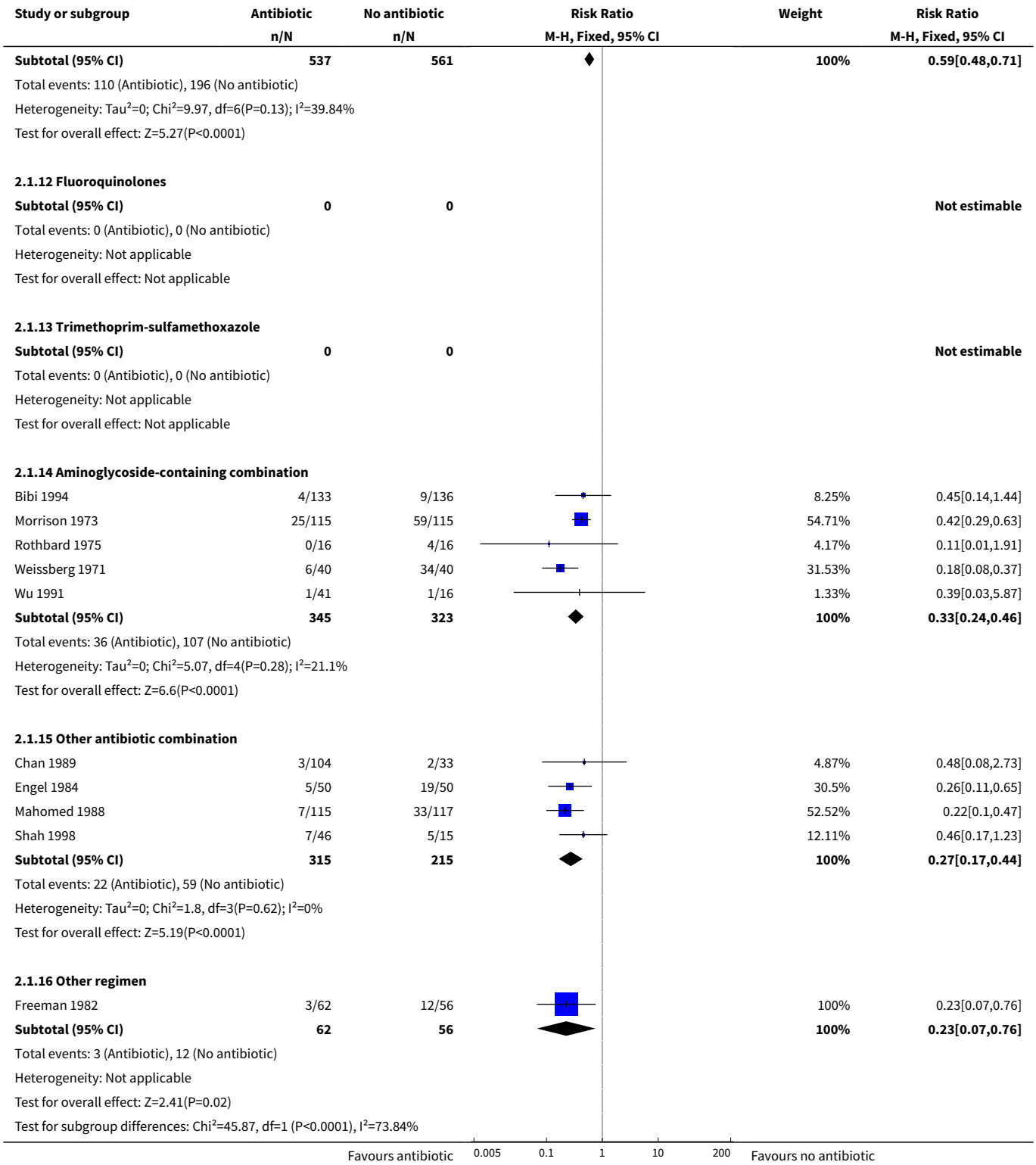

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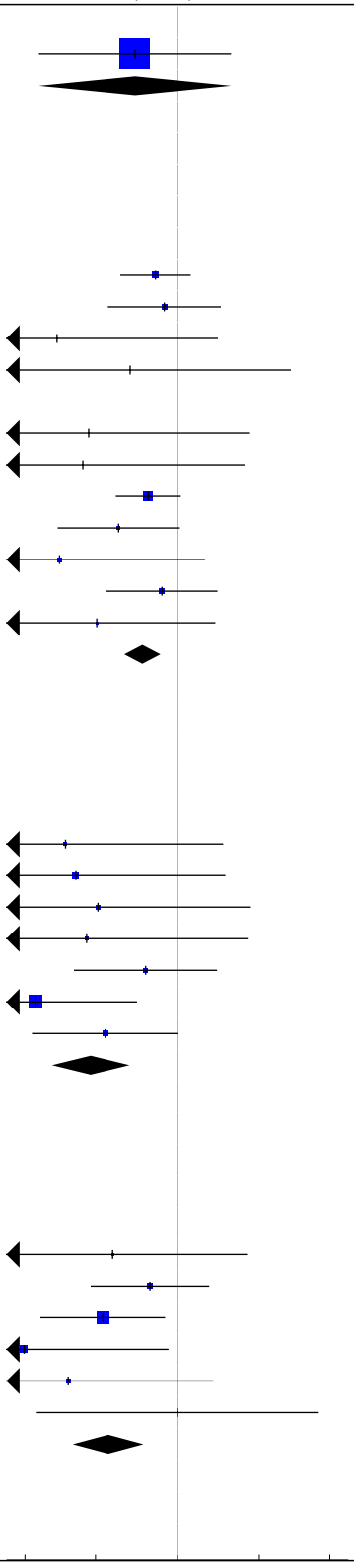
Analysis 2.2. Comparison 2 Antibiotic versus no antibiotic - subgroup by class of antibiotic, Outcome 2 Maternal wound infection.

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 Natural penicillins					
Rehu 1980	2/46	2/20		100%	0.43[0.07,2.87]
Subtotal (95% CI)	**46**	**20**		**100%**	**0.43[0.07,2.87]**
Total events: 2 (Antibiotic), 2 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.86(P=0.39)					
2.2.2 Aminopenicillins (ampicillin)					
Adeleye 1981	11/58	14/48		20.39%	0.65[0.33,1.3]
Chan 1989	9/96	4/33		7.92%	0.77[0.26,2.35]
Dashow 1986	0/70	1/19		3.12%	0.09[0,2.22]
Duff 1980	0/26	1/31		1.83%	0.4[0.02,9.31]
Duff 1982	0/42	0/40			Not estimable
Escobedo 1991	0/60	1/31		2.62%	0.17[0.01,4.17]
Gordon 1979	0/78	1/36		2.72%	0.16[0.01,3.74]
Miller 1968	13/150	23/150		30.61%	0.57[0.3,1.07]
Ng 1992	4/74	6/35		10.84%	0.32[0.1,1.05]
Padilla 1983	0/34	5/37		7.02%	0.1[0.01,1.72]
Walss Rodriguez 1990	5/59	7/61		9.16%	0.74[0.25,2.2]
Wu 1991	1/39	2/16		3.77%	0.21[0.02,2.11]
Subtotal (95% CI)	**786**	**537**		**100%**	**0.5[0.35,0.72]**
Total events: 43 (Antibiotic), 65 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=6.17, df=10(P=0.8); I^2=0%					
Test for overall effect: Z=3.79(P=0)					
2.2.3 Extended spectrum penicillins					
Bilgin 1998	0/23	1/7		5.97%	0.11[0.01,2.46]
Jaffe 1984	0/58	3/55		9.52%	0.14[0.01,2.57]
Jaffe 1985	0/38	2/40		6.46%	0.21[0.01,4.24]
Leonetti 1989	0/100	1/50		5.28%	0.17[0.01,4.06]
Lewis 1990	3/112	5/100		14.01%	0.54[0.13,2.18]
Reckel 1985	1/70	16/69		42.72%	0.06[0.01,0.45]
Shah 1998	3/93	4/30		16.04%	0.24[0.06,1.02]
Subtotal (95% CI)	**494**	**351**		**100%**	**0.18[0.09,0.39]**
Total events: 7 (Antibiotic), 32 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=3.7, df=6(P=0.72); I^2=0%					
Test for overall effect: Z=4.39(P<0.0001)					
2.2.4 Beta-lactamase inhibitor combination					
Bilgin 1998	1/25	1/7		4.52%	0.28[0.02,3.93]
Chan 1989	7/99	4/33		17.35%	0.58[0.18,1.87]
Huam 1997	3/100	13/100		37.6%	0.23[0.07,0.79]
Sziller 1994	0/60	7/44		24.97%	0.05[0,0.84]
Ujah 1992	0/17	4/18		12.66%	0.12[0.01,2.03]
Yip 1997	1/160	1/160		2.89%	1[0.06,15.85]
Subtotal (95% CI)	**461**	**362**		**100%**	**0.26[0.13,0.51]**
Total events: 12 (Antibiotic), 30 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=4.47, df=5(P=0.48); I^2=0%					
Test for overall effect: Z=3.85(P=0)					



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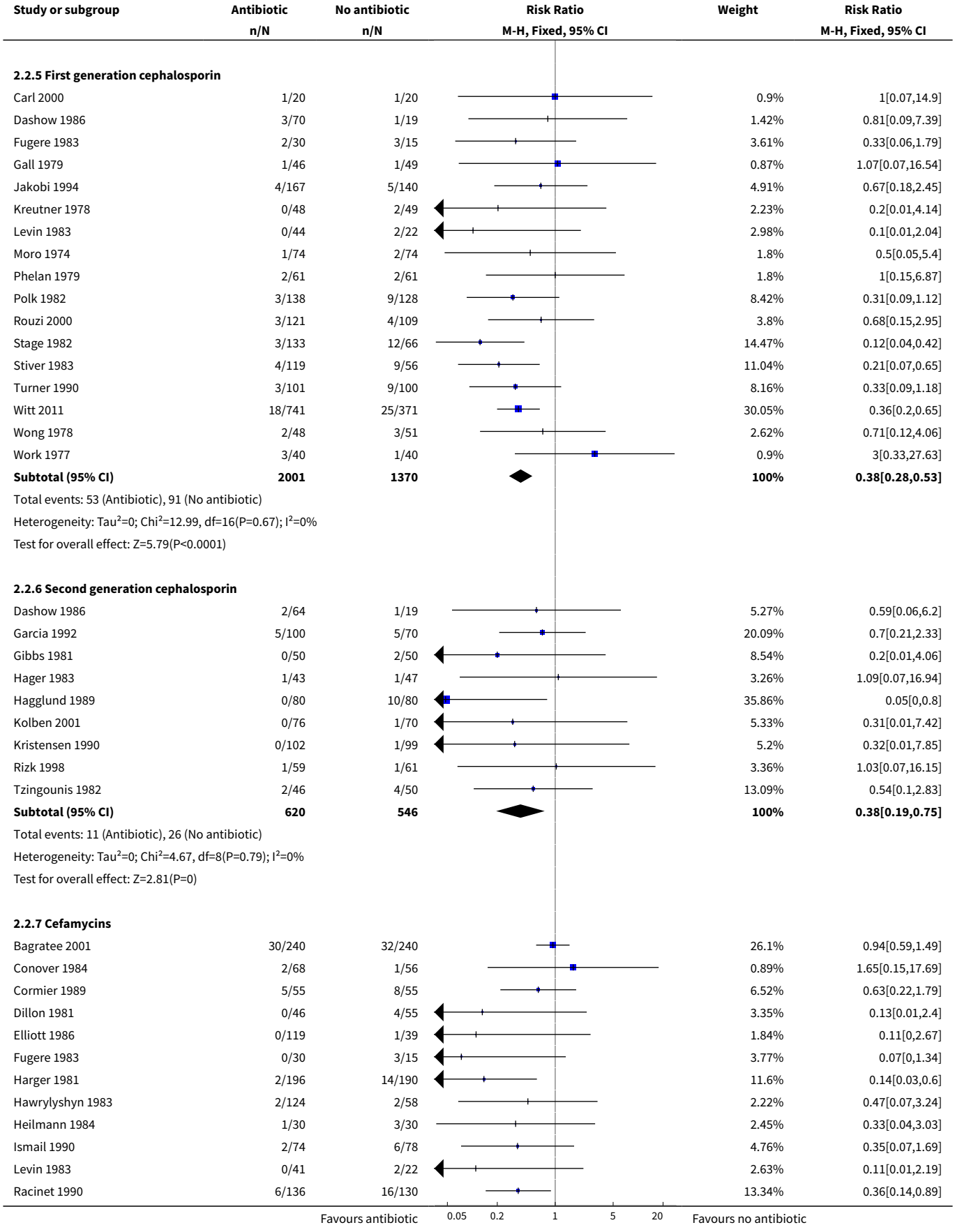

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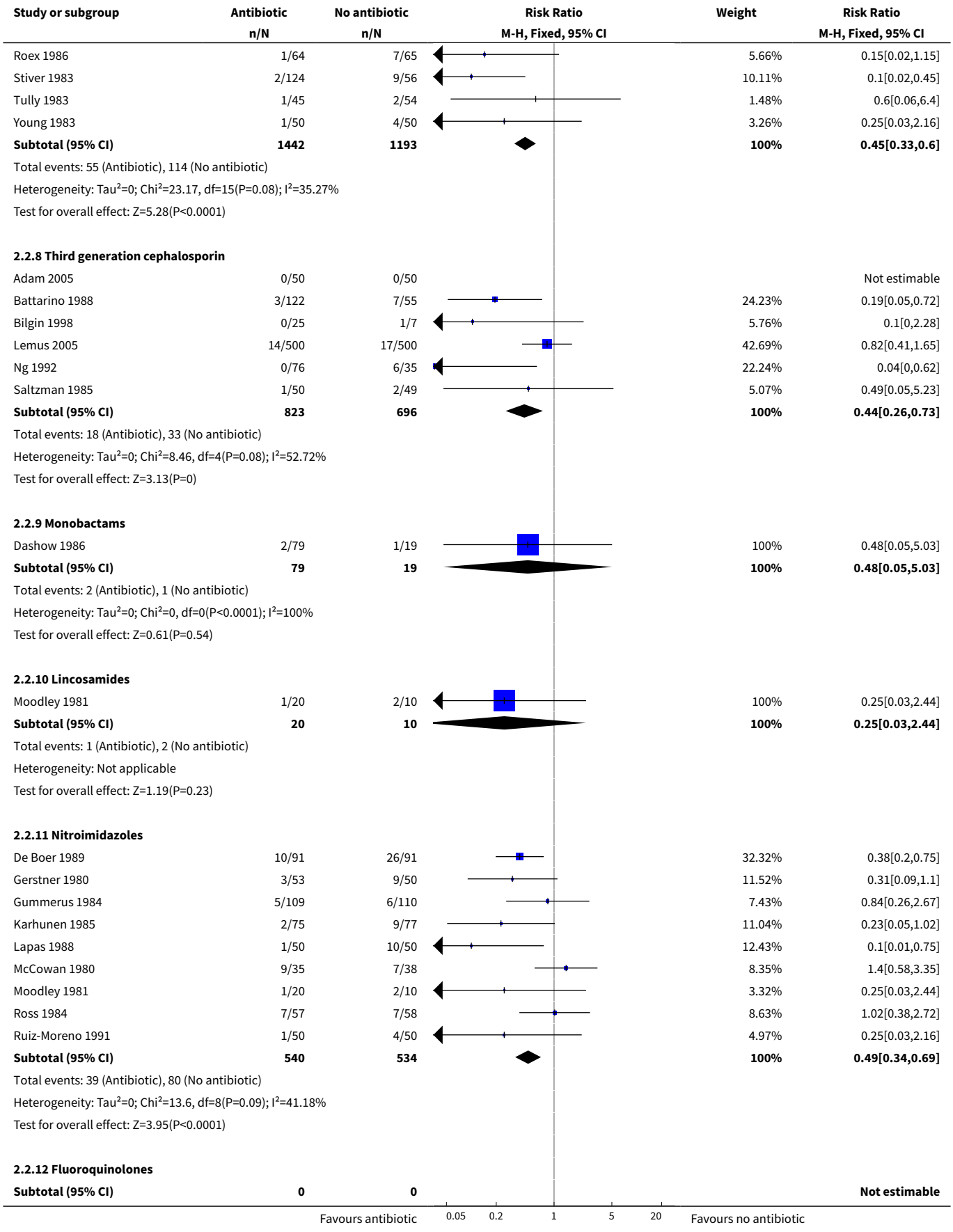

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Roex 1986	1/64	7/65		5.66%	0.15[0.02,1.15]
Stiver 1983	2/124	9/56		10.11%	0.1[0.02,0.45]
Tully 1983	1/45	2/54		1.48%	0.6[0.06,6.4]
Young 1983	1/50	4/50		3.26%	0.25[0.03,2.16]
Subtotal (95% CI)	**1442**	**1193**		**100%**	**0.45[0.33,0.6]**
Total events: 55 (Antibiotic), 114 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=23.17, df=15(P=0.08); I^2=35.27%					
Test for overall effect: Z=5.28(P<0.0001)					
2.2.8 Third generation cephalosporin					
Adam 2005	0/50	0/50			Not estimable
Battarino 1988	3/122	7/55		24.23%	0.19[0.05,0.72]
Bilgin 1998	0/25	1/7		5.76%	0.1[0,2.28]
Lemus 2005	14/500	17/500		42.69%	0.82[0.41,1.65]
Ng 1992	0/76	6/35		22.24%	0.04[0,0.62]
Saltzman 1985	1/50	2/49		5.07%	0.49[0.05,5.23]
Subtotal (95% CI)	**823**	**696**		**100%**	**0.44[0.26,0.73]**
Total events: 18 (Antibiotic), 33 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=8.46, df=4(P=0.08); I^2=52.72%					
Test for overall effect: Z=3.13(P=0)					
2.2.9 Monobactams					
Dashow 1986	2/79	1/19		100%	0.48[0.05,5.03]
Subtotal (95% CI)	**79**	**19**		**100%**	**0.48[0.05,5.03]**
Total events: 2 (Antibiotic), 1 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%					
Test for overall effect: Z=0.61(P=0.54)					
2.2.10 Lincosamides					
Moodley 1981	1/20	2/10		100%	0.25[0.03,2.44]
Subtotal (95% CI)	**20**	**10**		**100%**	**0.25[0.03,2.44]**
Total events: 1 (Antibiotic), 2 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.19(P=0.23)					
2.2.11 Nitroimidazoles					
De Boer 1989	10/91	26/91		32.32%	0.38[0.2,0.75]
Gerstner 1980	3/53	9/50		11.52%	0.31[0.09,1.1]
Gummerus 1984	5/109	6/110		7.43%	0.84[0.26,2.67]
Karhunen 1985	2/75	9/77		11.04%	0.23[0.05,1.02]
Lapas 1988	1/50	10/50		12.43%	0.1[0.01,0.75]
McCowan 1980	9/35	7/38		8.35%	1.4[0.58,3.35]
Moodley 1981	1/20	2/10		3.32%	0.25[0.03,2.44]
Ross 1984	7/57	7/58		8.63%	1.02[0.38,2.72]
Ruiz-Moreno 1991	1/50	4/50		4.97%	0.25[0.03,2.16]
Subtotal (95% CI)	**540**	**534**		**100%**	**0.49[0.34,0.69]**
Total events: 39 (Antibiotic), 80 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=13.6, df=8(P=0.09); I^2=41.18%					
Test for overall effect: Z=3.95(P<0.0001)					
2.2.12 Fluoroquinolones					
Subtotal (95% CI)	**0**	**0**			**Not estimable**

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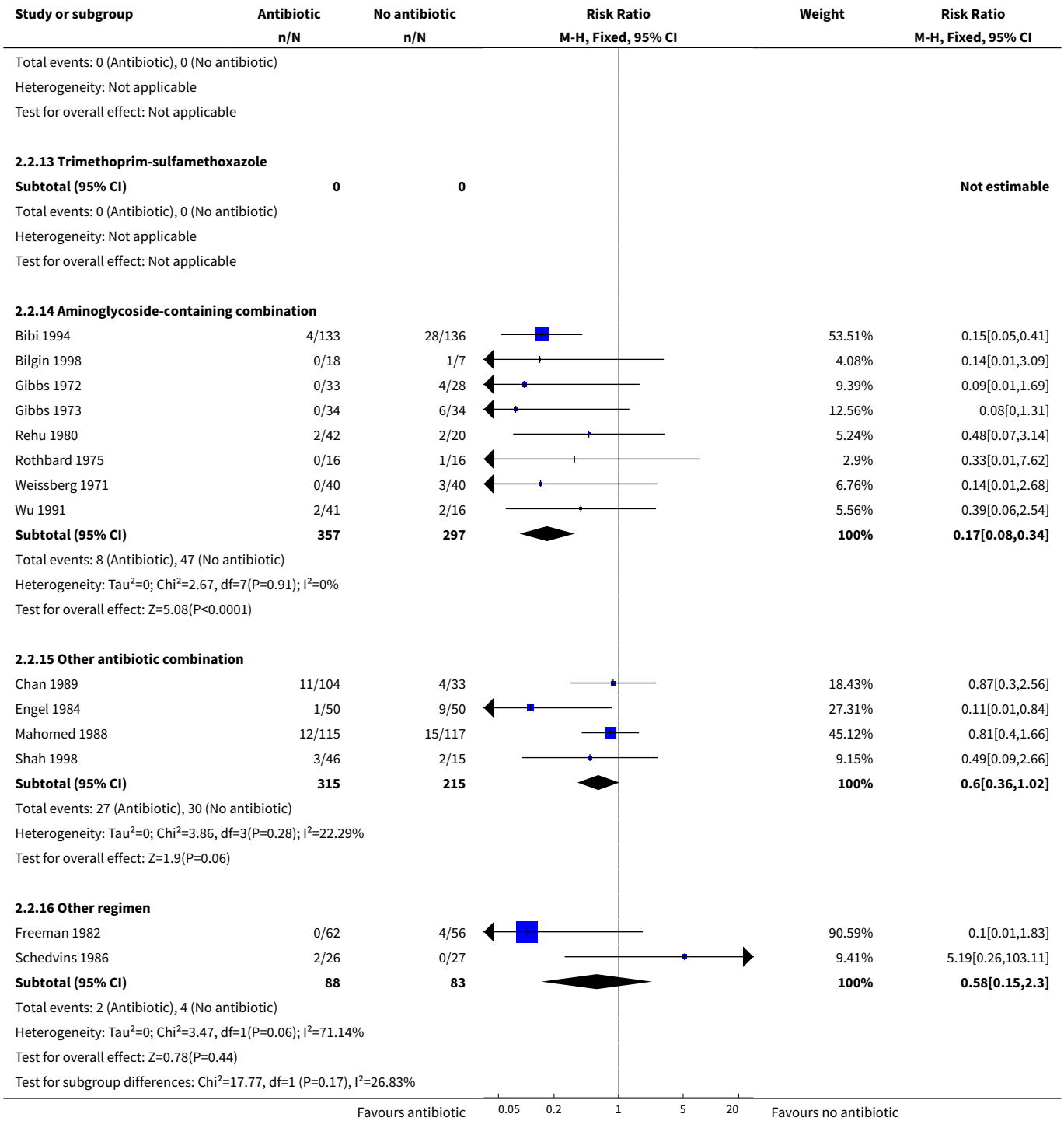

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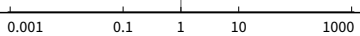
Analysis 2.3. Comparison 2 Antibiotic versus no antibiotic - subgroup by class of antibiotic, Outcome 3 Maternal endometritis.

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.3.1 Natural penicillins					
Rehu 1980	3/46	7/20		100%	0.19[0.05,0.65]
Subtotal (95% CI)	**46**	**20**		**100%**	**0.19[0.05,0.65]**
Total events: 3 (Antibiotic), 7 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.64(P=0.01)					
2.3.2 Aminopenicillins (ampicillin)					
Chan 1989	6/96	1/33		1.84%	2.06[0.26,16.5]
Dashow 1986	6/70	5/19		9.73%	0.33[0.11,0.95]
Duff 1980	2/26	13/31		14.68%	0.18[0.05,0.74]
Duff 1982	1/42	6/40		7.61%	0.16[0.02,1.26]
Escobedo 1991	0/60	0/31			Not estimable
Gordon 1979	6/78	12/36		20.32%	0.23[0.09,0.57]
Miller 1968	1/150	8/150		9.9%	0.13[0.02,0.99]
Padilla 1983	5/34	21/37		24.89%	0.26[0.11,0.61]
Walss Rodriguez 1990	0/59	5/61		6.69%	0.09[0.01,1.66]
Wu 1991	0/39	2/16		4.34%	0.09[0,1.68]
Subtotal (95% CI)	**654**	**454**		**100%**	**0.24[0.16,0.38]**
Total events: 27 (Antibiotic), 73 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=6, df=8(P=0.65); I^2=0%					
Test for overall effect: Z=6.26(P<0.0001)					
2.3.3 Extended-spectrum penicillins					
Apuzzio 1982	44/139	66/120		42.08%	0.58[0.43,0.77]
Bilgin 1998	0/23	0/7			Not estimable
Jaffe 1984	0/58	6/55		3.96%	0.07[0,1.27]
Jaffe 1985	0/38	7/40		4.34%	0.07[0,1.19]
Leonetti 1989	10/100	12/50		9.5%	0.42[0.19,0.9]
Lewis 1990	22/112	43/100		26.99%	0.46[0.29,0.71]
Oestreicher 1987	6/30	10/30		5.94%	0.6[0.25,1.44]
Reckel 1985	1/70	6/69		3.59%	0.16[0.02,1.33]
Shah 1998	3/93	4/30		3.59%	0.24[0.06,1.02]
Subtotal (95% CI)	**663**	**501**		**100%**	**0.46[0.37,0.58]**
Total events: 86 (Antibiotic), 154 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=7.62, df=7(P=0.37); I^2=8.19%					
Test for overall effect: Z=6.86(P<0.0001)					
2.3.4 Beta-lactamase inhibitor combinations					
Bilgin 1998	0/25	0/7			Not estimable
Chan 1989	5/99	1/33		14.18%	1.67[0.2,13.76]
Huam 1997	0/100	0/100			Not estimable
Sziller 1994	3/60	7/44		76.36%	0.31[0.09,1.15]
Yip 1997	2/160	1/160		9.45%	2[0.18,21.84]
Subtotal (95% CI)	**444**	**344**		**100%**	**0.67[0.27,1.66]**
Total events: 10 (Antibiotic), 9 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=2.83, df=2(P=0.24); I^2=29.31%					
Test for overall effect: Z=0.87(P=0.38)					



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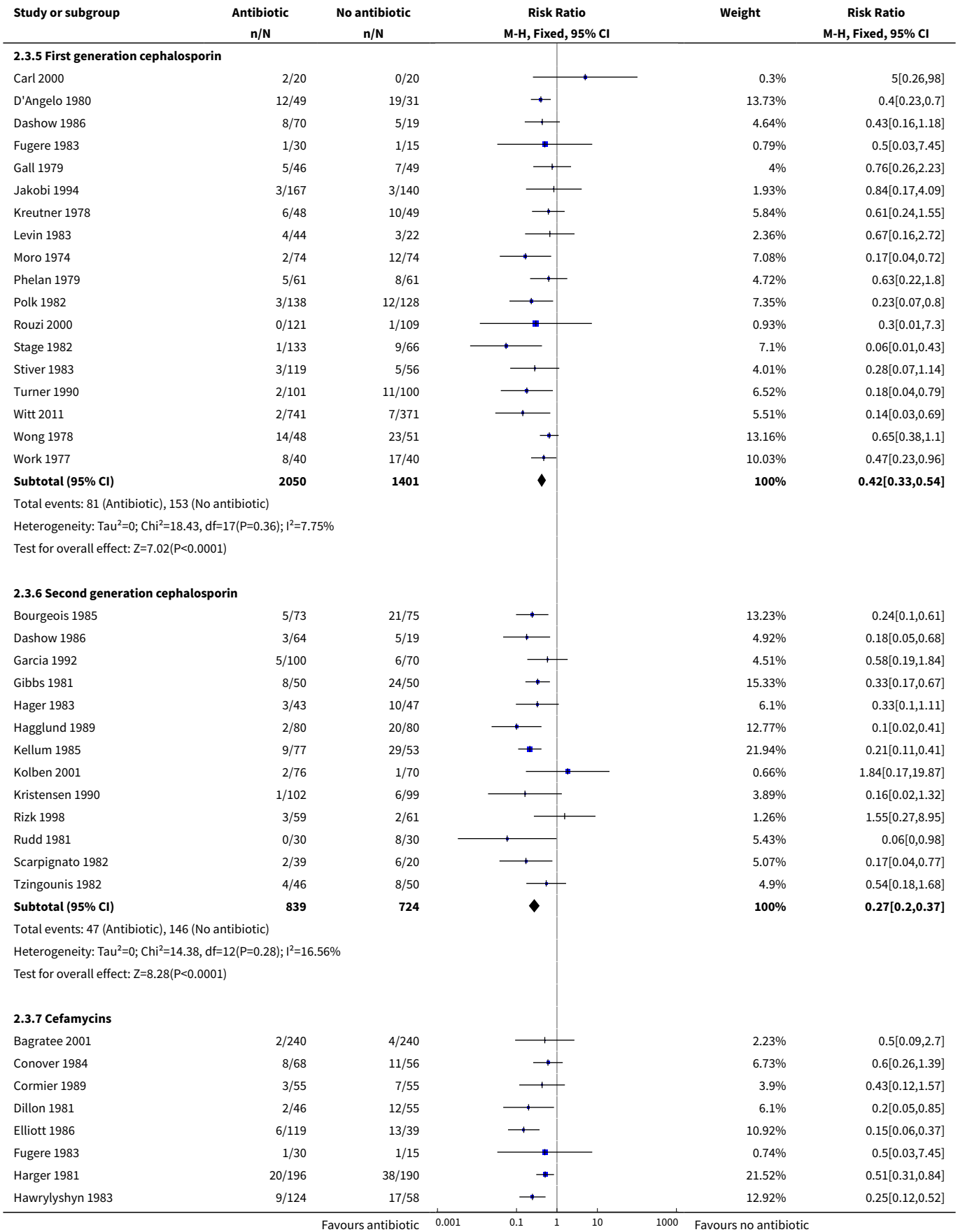

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.3.5 First generation cephalosporin					
Carl 2000	2/20	0/20		0.3%	5[0.26,98]
D'Angelo 1980	12/49	19/31		13.73%	0.4[0.23,0.7]
Dashow 1986	8/70	5/19		4.64%	0.43[0.16,1.18]
Fugere 1983	1/30	1/15		0.79%	0.5[0.03,7.45]
Gall 1979	5/46	7/49		4%	0.76[0.26,2.23]
Jakobi 1994	3/167	3/140		1.93%	0.84[0.17,4.09]
Kreutner 1978	6/48	10/49		5.84%	0.61[0.24,1.55]
Levin 1983	4/44	3/22		2.36%	0.67[0.16,2.72]
Moro 1974	2/74	12/74		7.08%	0.17[0.04,0.72]
Phelan 1979	5/61	8/61		4.72%	0.63[0.22,1.8]
Polk 1982	3/138	12/128		7.35%	0.23[0.07,0.8]
Rouzi 2000	0/121	1/109		0.93%	0.3[0.01,7.3]
Stage 1982	1/133	9/66		7.1%	0.06[0.01,0.43]
Stiver 1983	3/119	5/56		4.01%	0.28[0.07,1.14]
Turner 1990	2/101	11/100		6.52%	0.18[0.04,0.79]
Witt 2011	2/741	7/371		5.51%	0.14[0.03,0.69]
Wong 1978	14/48	23/51		13.16%	0.65[0.38,1.1]
Work 1977	8/40	17/40		10.03%	0.47[0.23,0.96]
Subtotal (95% CI)	**2050**	**1401**		**100%**	**0.42[0.33,0.54]**
Total events: 81 (Antibiotic), 153 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=18.43, df=17(P=0.36); I^2=7.75%					
Test for overall effect: Z=7.02(P<0.0001)					
2.3.6 Second generation cephalosporin					
Bourgeois 1985	5/73	21/75		13.23%	0.24[0.1,0.61]
Dashow 1986	3/64	5/19		4.92%	0.18[0.05,0.68]
Garcia 1992	5/100	6/70		4.51%	0.58[0.19,1.84]
Gibbs 1981	8/50	24/50		15.33%	0.33[0.17,0.67]
Hager 1983	3/43	10/47		6.1%	0.33[0.1,1.11]
Hagglund 1989	2/80	20/80		12.77%	0.1[0.02,0.41]
Kellum 1985	9/77	29/53		21.94%	0.21[0.11,0.41]
Kolben 2001	2/76	1/70		0.66%	1.84[0.17,19.87]
Kristensen 1990	1/102	6/99		3.89%	0.16[0.02,1.32]
Rizk 1998	3/59	2/61		1.26%	1.55[0.27,8.95]
Rudd 1981	0/30	8/30		5.43%	0.06[0,0.98]
Scarpignato 1982	2/39	6/20		5.07%	0.17[0.04,0.77]
Tzingounis 1982	4/46	8/50		4.9%	0.54[0.18,1.68]
Subtotal (95% CI)	**839**	**724**		**100%**	**0.27[0.2,0.37]**
Total events: 47 (Antibiotic), 146 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=14.38, df=12(P=0.28); I^2=16.56%					
Test for overall effect: Z=8.28(P<0.0001)					
2.3.7 Cefamycins					
Bagratee 2001	2/240	4/240		2.23%	0.5[0.09,2.7]
Conover 1984	8/68	11/56		6.73%	0.6[0.26,1.39]
Cormier 1989	3/55	7/55		3.9%	0.43[0.12,1.57]
Dillon 1981	2/46	12/55		6.1%	0.2[0.05,0.85]
Elliott 1986	6/119	13/39		10.92%	0.15[0.06,0.37]
Fugere 1983	1/30	1/15		0.74%	0.5[0.03,7.45]
Harger 1981	20/196	38/190		21.52%	0.51[0.31,0.84]
Hawrylyshyn 1983	9/124	17/58		12.92%	0.25[0.12,0.52]

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Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Ismail 1990	4/74	8/78		4.34%	0.53[0.17,1.68]
Levin 1983	1/41	3/22		2.18%	0.18[0.02,1.62]
Racinet 1990	7/136	14/130		7.98%	0.48[0.2,1.15]
Roex 1986	2/64	9/65		4.98%	0.23[0.05,1]
Stiver 1983	5/124	5/56		3.84%	0.45[0.14,1.5]
Tully 1983	3/45	11/54		5.58%	0.33[0.1,1.1]
Young 1983	0/10	30/50		6.04%	0.08[0.01,1.15]
Subtotal (95% CI)	**1372**	**1163**		**100%**	**0.36[0.28,0.47]**
Total events: 73 (Antibiotic), 183 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=11.75, df=14(P=0.63); I^2=0%					
Test for overall effect: Z=7.61(P<0.0001)					
2.3.8 Third generation cephalosporin					
Adam 2005	1/50	1/50		5.37%	1[0.06,15.55]
Battarino 1988	2/122	4/55		29.59%	0.23[0.04,1.19]
Bilgin 1998	0/25	0/7			Not estimable
Saltzman 1985	3/50	12/49		65.04%	0.25[0.07,0.82]
Subtotal (95% CI)	**247**	**161**		**100%**	**0.28[0.11,0.69]**
Total events: 6 (Antibiotic), 17 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=0.94, df=2(P=0.63); I^2=0%					
Test for overall effect: Z=2.78(P=0.01)					
2.3.9 Monobactams					
Dashow 1986	13/79	5/19		100%	0.63[0.25,1.54]
Subtotal (95% CI)	**79**	**19**		**100%**	**0.63[0.25,1.54]**
Total events: 13 (Antibiotic), 5 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.02(P=0.31)					
2.3.10 Lincosamides					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.3.11 Nitroimidazoles					
Ganesh 1986	6/29	13/28		16.69%	0.45[0.2,1.01]
Gerstner 1980	7/53	15/50		19.48%	0.44[0.2,0.99]
Gummerus 1984	7/109	5/110		6.28%	1.41[0.46,4.32]
Karhunen 1985	6/75	14/77		17.44%	0.44[0.18,1.08]
Lapas 1988	2/50	10/50		12.62%	0.2[0.05,0.87]
McCowan 1980	4/35	5/38		6.05%	0.87[0.25,2.98]
Ross 1984	2/57	2/58		2.5%	1.02[0.15,6.98]
Ruiz-Moreno 1991	7/50	15/50		18.93%	0.47[0.21,1.05]
Subtotal (95% CI)	**458**	**461**		**100%**	**0.52[0.37,0.73]**
Total events: 41 (Antibiotic), 79 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=6.34, df=7(P=0.5); I^2=0%					
Test for overall effect: Z=3.73(P=0)					
2.3.12 Fluoroquinolones					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Antibiotic), 0 (No antibiotic)					

Favours antibiotic Favours no antibiotic

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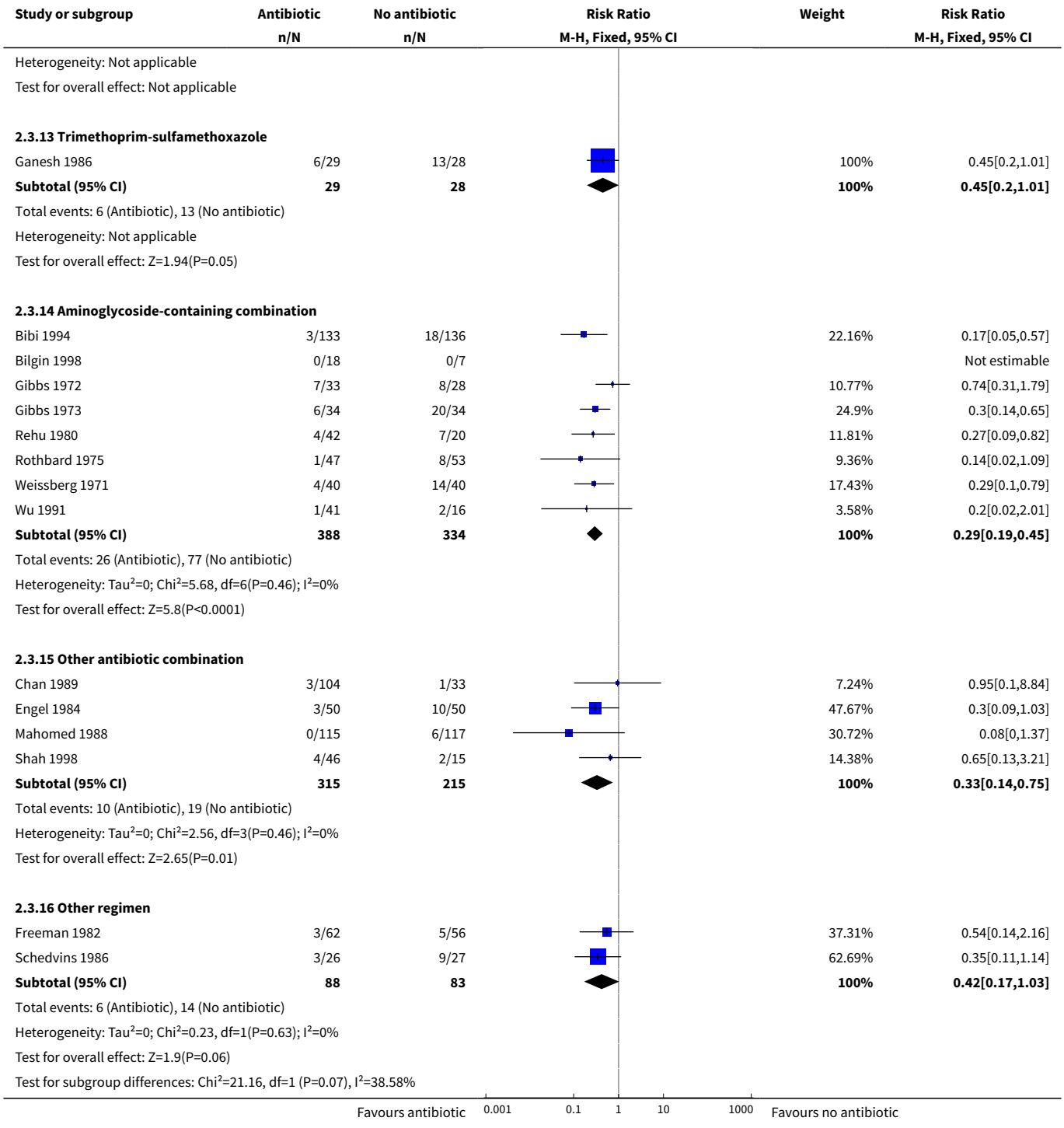

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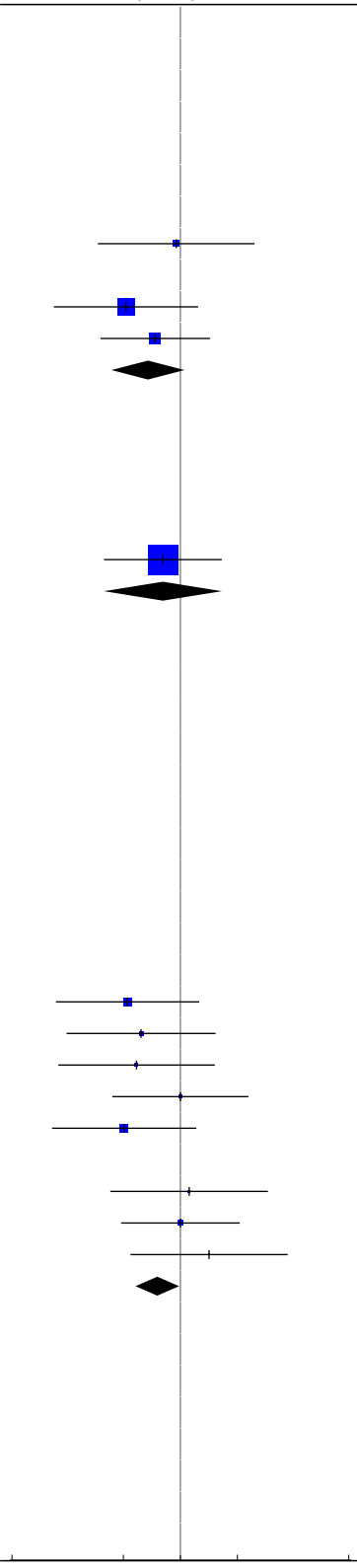
Analysis 2.4. Comparison 2 Antibiotic versus no antibiotic - subgroup by class of antibiotic, Outcome 4 Maternal serious infectious complications.

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.4.1 Natural penicillins					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.4.2 Aminopenicillins (ampicillin)					
Dashow 1986	1/70	0/19		9.57%	0.85[0.04,19.96]
Duff 1982	0/42	0/40			Not estimable
Miller 1968	0/150	4/150		55.19%	0.11[0.01,2.05]
Padilla 1983	1/34	3/37		35.24%	0.36[0.04,3.32]
Subtotal (95% CI)	**296**	**246**		**100%**	**0.27[0.06,1.18]**
Total events: 2 (Antibiotic), 7 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=0.93, df=2(P=0.63); I^2=0%					
Test for overall effect: Z=1.74(P=0.08)					
2.4.3 Extended-spectrum penicillins					
Lewis 1990	1/76	2/75		100%	0.49[0.05,5.33]
Subtotal (95% CI)	**76**	**75**		**100%**	**0.49[0.05,5.33]**
Total events: 1 (Antibiotic), 2 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.58(P=0.56)					
2.4.4 Beta-lactamase inhibitor combinations					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.4.5 First generation cephalosporin					
Dashow 1986	0/70	0/19			Not estimable
Gall 1979	0/46	4/49		25.68%	0.12[0.01,2.14]
Kreutner 1978	0/48	2/49		14.57%	0.2[0.01,4.14]
Levin 1983	0/44	1/22		11.69%	0.17[0.01,4.02]
Phelan 1979	1/61	1/61		5.89%	1[0.06,15.63]
Polk 1982	0/138	4/128		27.48%	0.1[0.01,1.9]
Rouzi 2000	0/121	0/109			Not estimable
Stiver 1983	1/119	0/56		3.99%	1.43[0.06,34.44]
Witt 2011	2/741	1/371		7.85%	1[0.09,11.01]
Wong 1978	1/48	0/51		2.86%	3.18[0.13,76.31]
Subtotal (95% CI)	**1436**	**915**		**100%**	**0.39[0.16,0.95]**
Total events: 5 (Antibiotic), 13 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=5.24, df=7(P=0.63); I^2=0%					
Test for overall effect: Z=2.08(P=0.04)					
2.4.6 Second generation cephalosporin					
Bourgeois 1985	0/73	0/75			Not estimable
Dashow 1986	0/64	0/19			Not estimable
Dillon 1981	0/46	0/55			Not estimable



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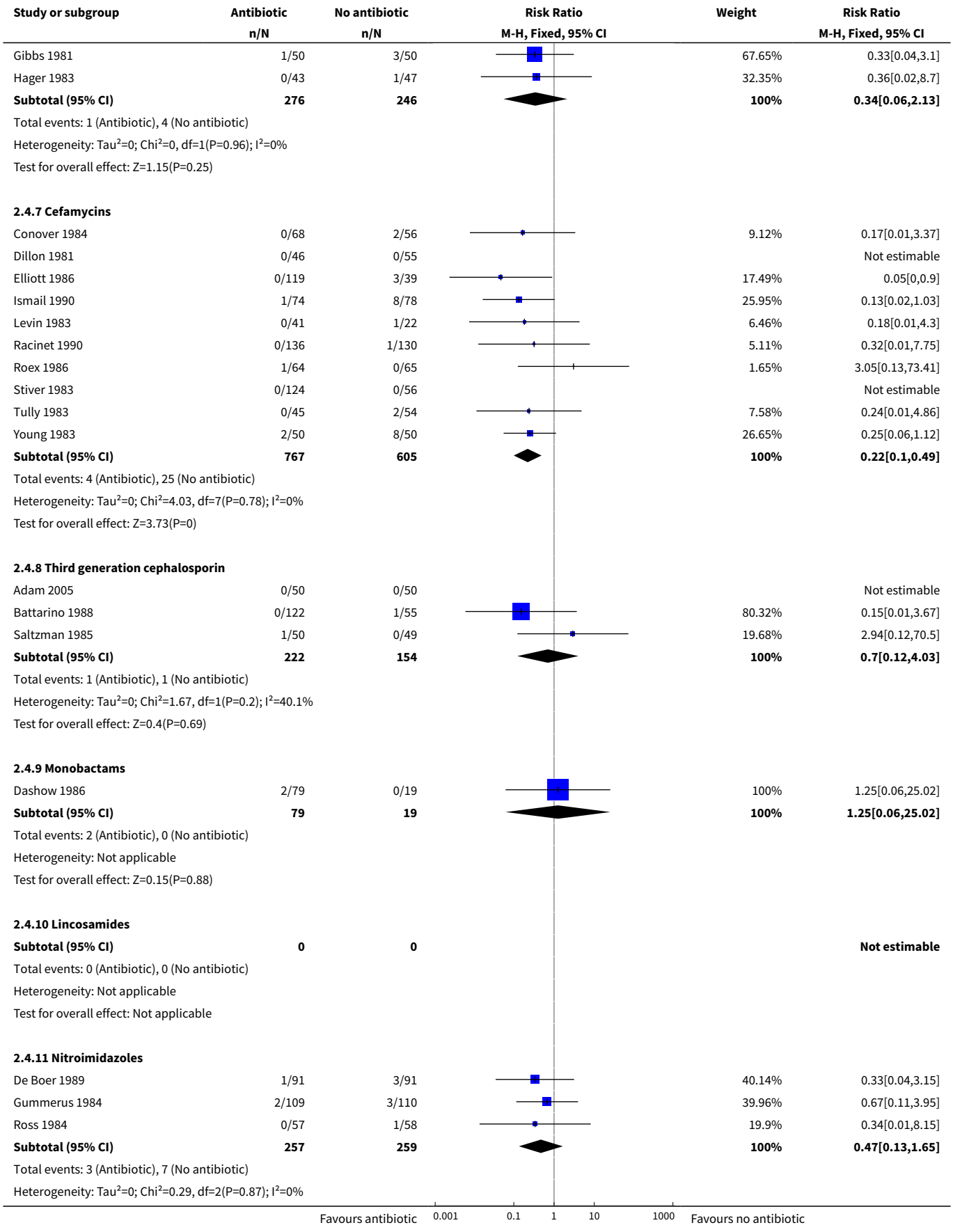

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Gibbs 1981	1/50	3/50		67.65%	0.33[0.04,3.1]
Hager 1983	0/43	1/47		32.35%	0.36[0.02,8.7]
Subtotal (95% CI)	**276**	**246**		**100%**	**0.34[0.06,2.13]**
Total events: 1 (Antibiotic), 4 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=0, df=1(P=0.96); I²=0%					
Test for overall effect: Z=1.15(P=0.25)					
2.4.7 Cefamycins					
Conover 1984	0/68	2/56		9.12%	0.17[0.01,3.37]
Dillon 1981	0/46	0/55			Not estimable
Elliott 1986	0/119	3/39		17.49%	0.05[0,0.9]
Ismail 1990	1/74	8/78		25.95%	0.13[0.02,1.03]
Levin 1983	0/41	1/22		6.46%	0.18[0.01,4.3]
Racinet 1990	0/136	1/130		5.11%	0.32[0.01,7.75]
Roex 1986	1/64	0/65		1.65%	3.05[0.13,73.41]
Stiver 1983	0/124	0/56			Not estimable
Tully 1983	0/45	2/54		7.58%	0.24[0.01,4.86]
Young 1983	2/50	8/50		26.65%	0.25[0.06,1.12]
Subtotal (95% CI)	**767**	**605**		**100%**	**0.22[0.1,0.49]**
Total events: 4 (Antibiotic), 25 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=4.03, df=7(P=0.78); I²=0%					
Test for overall effect: Z=3.73(P=0)					
2.4.8 Third generation cephalosporin					
Adam 2005	0/50	0/50			Not estimable
Battarino 1988	0/122	1/55		80.32%	0.15[0.01,3.67]
Saltzman 1985	1/50	0/49		19.68%	2.94[0.12,70.5]
Subtotal (95% CI)	**222**	**154**		**100%**	**0.7[0.12,4.03]**
Total events: 1 (Antibiotic), 1 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=1.67, df=1(P=0.2); I²=40.1%					
Test for overall effect: Z=0.4(P=0.69)					
2.4.9 Monobactams					
Dashow 1986	2/79	0/19		100%	1.25[0.06,25.02]
Subtotal (95% CI)	**79**	**19**		**100%**	**1.25[0.06,25.02]**
Total events: 2 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.15(P=0.88)					
2.4.10 Lincosamides					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.4.11 Nitroimidazoles					
De Boer 1989	1/91	3/91		40.14%	0.33[0.04,3.15]
Gummerus 1984	2/109	3/110		39.96%	0.67[0.11,3.95]
Ross 1984	0/57	1/58		19.9%	0.34[0.01,8.15]
Subtotal (95% CI)	**257**	**259**		**100%**	**0.47[0.13,1.65]**
Total events: 3 (Antibiotic), 7 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=0.29, df=2(P=0.87); I²=0%					

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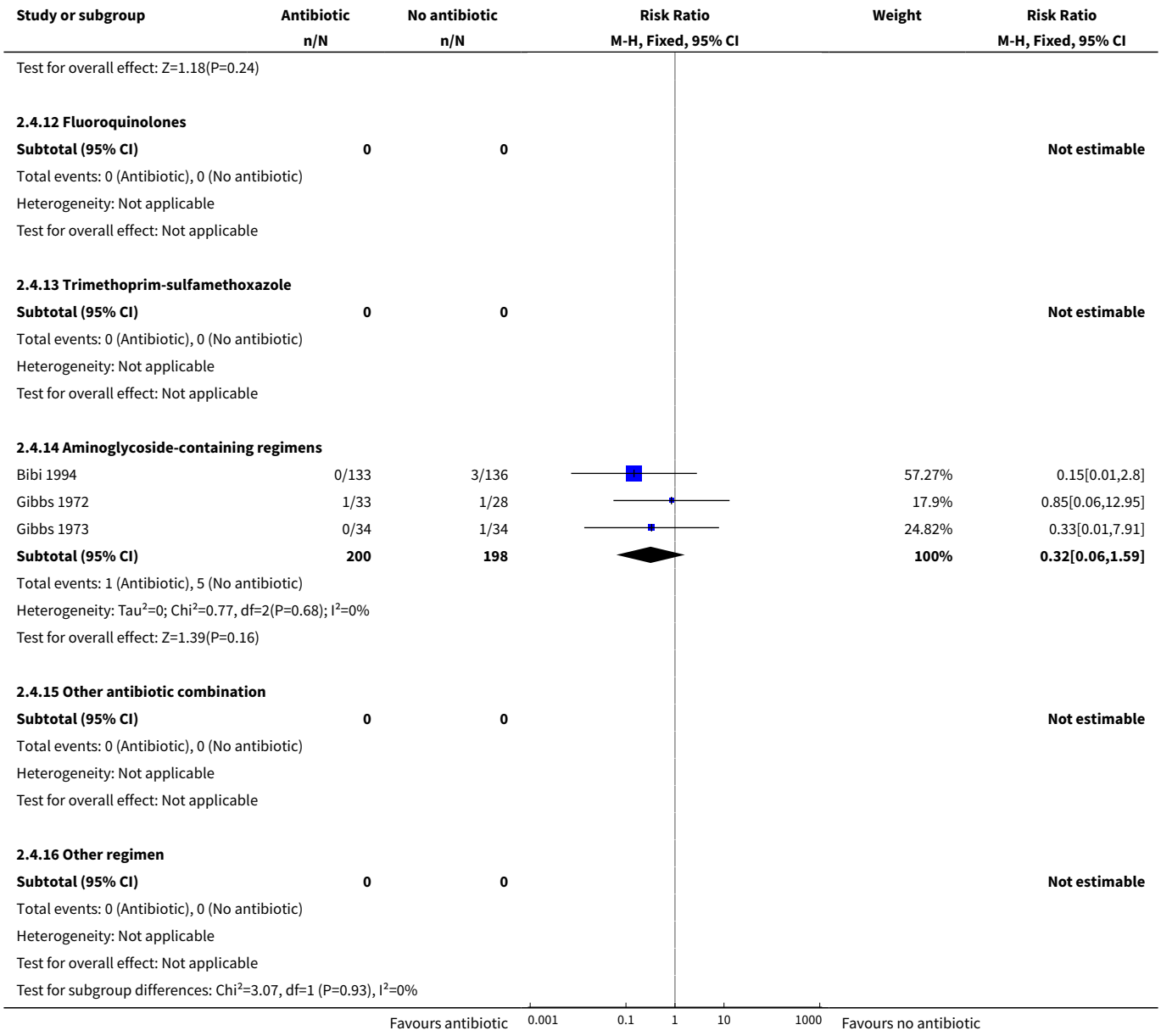
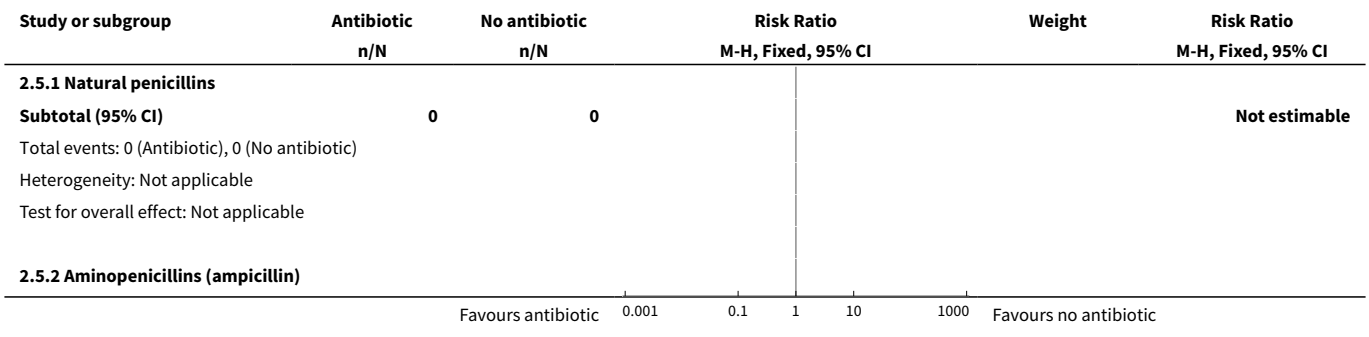


Analysis 2.5. Comparison 2 Antibiotic versus no antibiotic - subgroup by class of antibiotic, Outcome 5 Maternal urinary tract infection.



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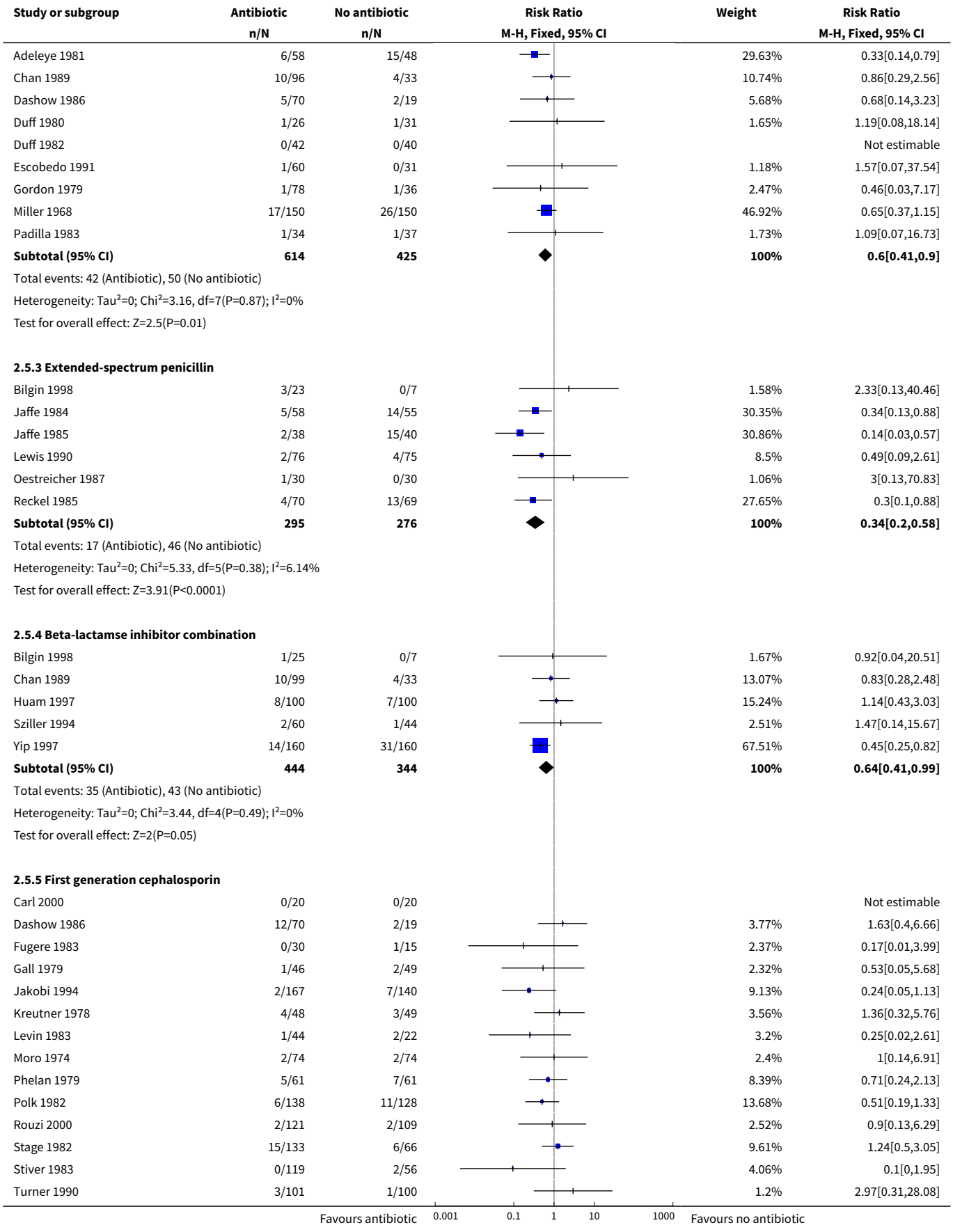

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Adeleye 1981	6/58	15/48		29.63%	0.33[0.14,0.79]
Chan 1989	10/96	4/33		10.74%	0.86[0.29,2.56]
Dashow 1986	5/70	2/19		5.68%	0.68[0.14,3.23]
Duff 1980	1/26	1/31		1.65%	1.19[0.08,18.14]
Duff 1982	0/42	0/40			Not estimable
Escobedo 1991	1/60	0/31		1.18%	1.57[0.07,37.54]
Gordon 1979	1/78	1/36		2.47%	0.46[0.03,7.17]
Miller 1968	17/150	26/150		46.92%	0.65[0.37,1.15]
Padilla 1983	1/34	1/37		1.73%	1.09[0.07,16.73]
Subtotal (95% CI)	**614**	**425**		**100%**	**0.6[0.41,0.9]**
Total events: 42 (Antibiotic), 50 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=3.16, df=7(P=0.87); I^2=0%					
Test for overall effect: Z=2.5(P=0.01)					
2.5.3 Extended-spectrum penicillin					
Bilgin 1998	3/23	0/7		1.58%	2.33[0.13,40.46]
Jaffe 1984	5/58	14/55		30.35%	0.34[0.13,0.88]
Jaffe 1985	2/38	15/40		30.86%	0.14[0.03,0.57]
Lewis 1990	2/76	4/75		8.5%	0.49[0.09,2.61]
Oestreicher 1987	1/30	0/30		1.06%	3[0.13,70.83]
Reckel 1985	4/70	13/69		27.65%	0.3[0.1,0.88]
Subtotal (95% CI)	**295**	**276**		**100%**	**0.34[0.2,0.58]**
Total events: 17 (Antibiotic), 46 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=5.33, df=5(P=0.38); I^2=6.14%					
Test for overall effect: Z=3.91(P<0.0001)					
2.5.4 Beta-lactamse inhibitor combination					
Bilgin 1998	1/25	0/7		1.67%	0.92[0.04,20.51]
Chan 1989	10/99	4/33		13.07%	0.83[0.28,2.48]
Huam 1997	8/100	7/100		15.24%	1.14[0.43,3.03]
Sziller 1994	2/60	1/44		2.51%	1.47[0.14,15.67]
Yip 1997	14/160	31/160		67.51%	0.45[0.25,0.82]
Subtotal (95% CI)	**444**	**344**		**100%**	**0.64[0.41,0.99]**
Total events: 35 (Antibiotic), 43 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=3.44, df=4(P=0.49); I^2=0%					
Test for overall effect: Z=2(P=0.05)					
2.5.5 First generation cephalosporin					
Carl 2000	0/20	0/20			Not estimable
Dashow 1986	12/70	2/19		3.77%	1.63[0.4,6.66]
Fugere 1983	0/30	1/15		2.37%	0.17[0.01,3.99]
Gall 1979	1/46	2/49		2.32%	0.53[0.05,5.68]
Jakobi 1994	2/167	7/140		9.13%	0.24[0.05,1.13]
Kreutner 1978	4/48	3/49		3.56%	1.36[0.32,5.76]
Levin 1983	1/44	2/22		3.2%	0.25[0.02,2.61]
Moro 1974	2/74	2/74		2.4%	1[0.14,6.91]
Phelan 1979	5/61	7/61		8.39%	0.71[0.24,2.13]
Polk 1982	6/138	11/128		13.68%	0.51[0.19,1.33]
Rouzi 2000	2/121	2/109		2.52%	0.9[0.13,6.29]
Stage 1982	15/133	6/66		9.61%	1.24[0.5,3.05]
Stiver 1983	0/119	2/56		4.06%	0.1[0,1.95]
Turner 1990	3/101	1/100		1.2%	2.97[0.31,28.08]

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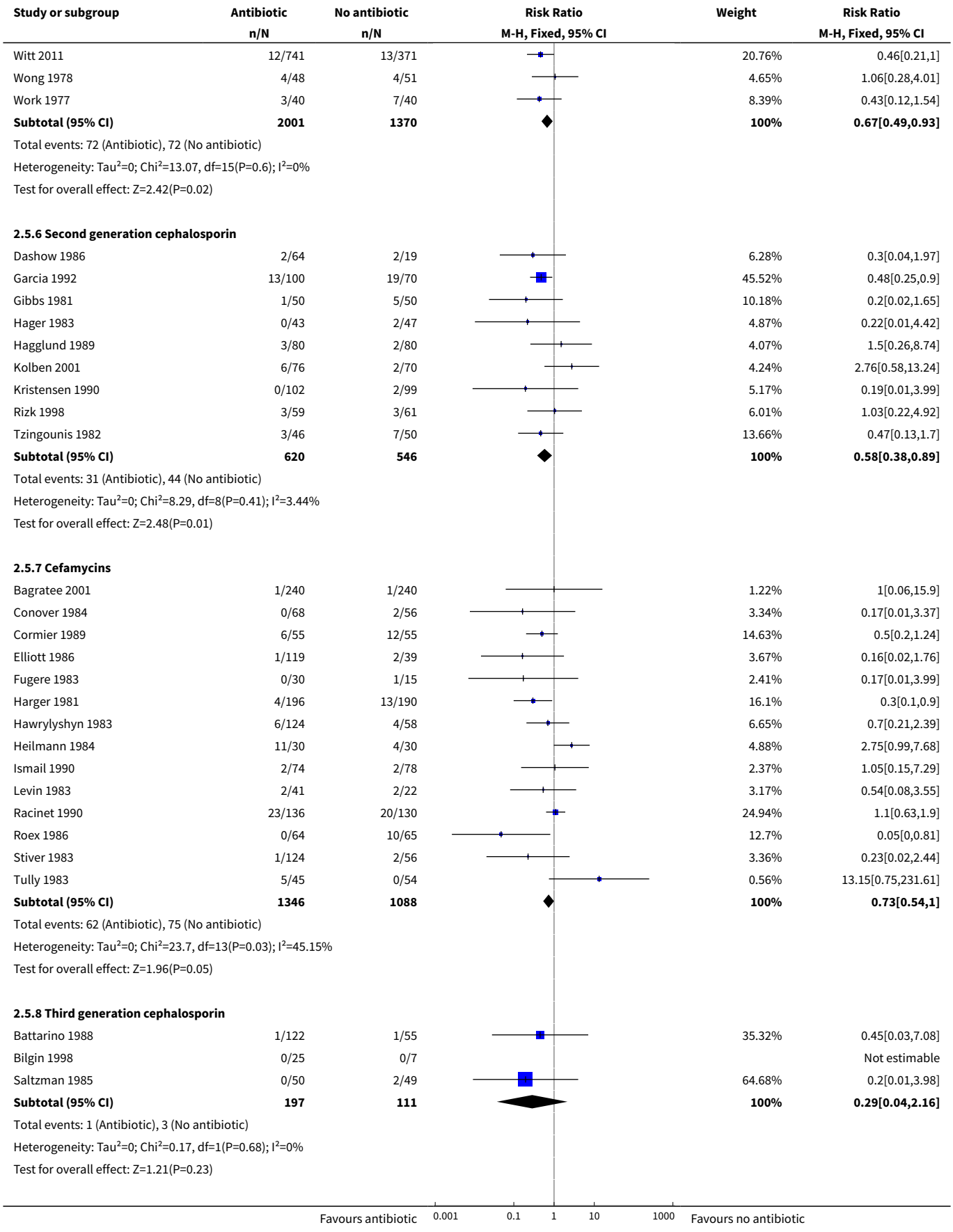

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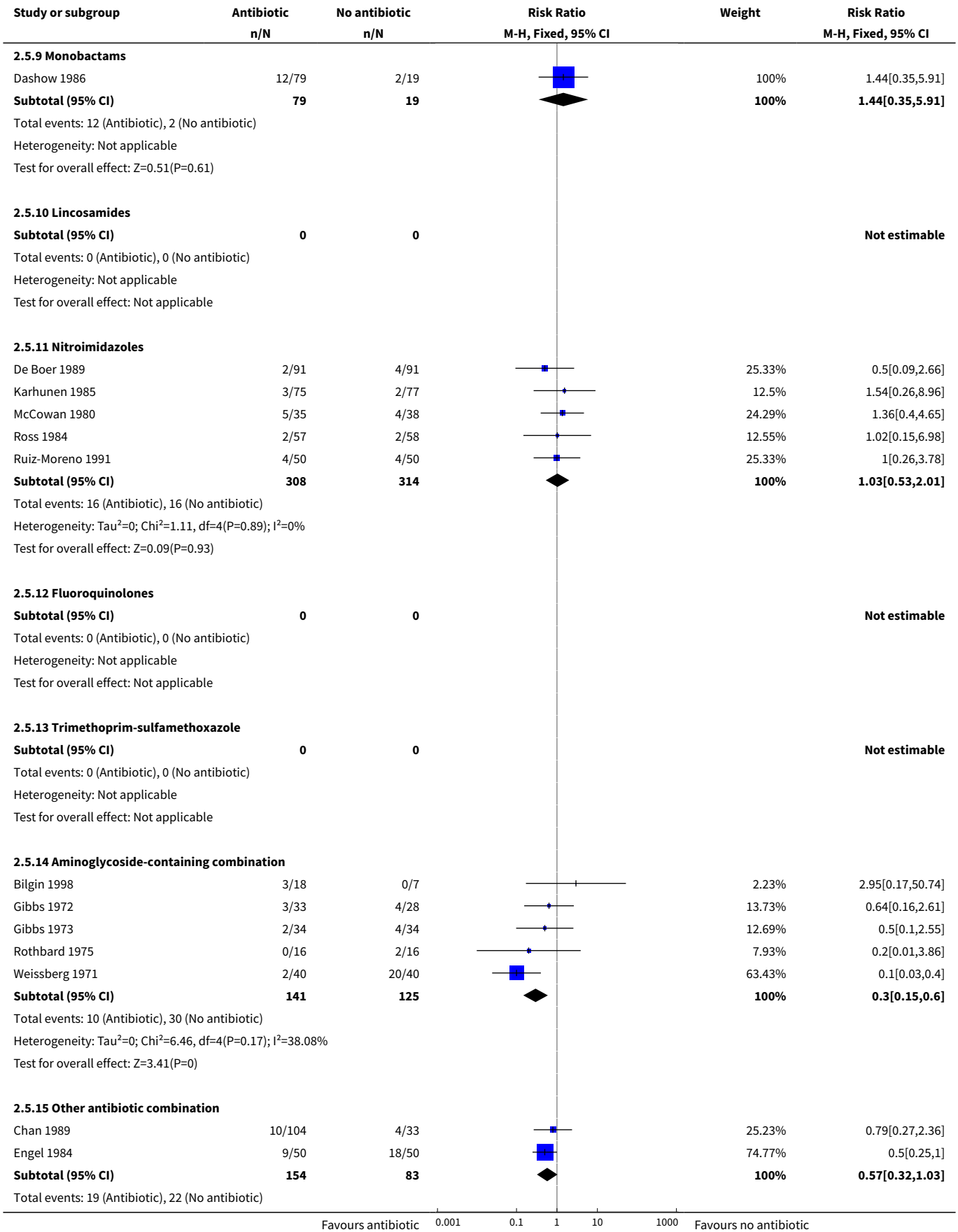

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.5.9 Monobactams					
Dashow 1986	12/79	2/19		100%	1.44[0.35,5.91]
Subtotal (95% CI)	**79**	**19**		**100%**	**1.44[0.35,5.91]**
Total events: 12 (Antibiotic), 2 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.51(P=0.61)					
2.5.10 Lincosamides					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.5.11 Nitroimidazoles					
De Boer 1989	2/91	4/91		25.33%	0.5[0.09,2.66]
Karhunen 1985	3/75	2/77		12.5%	1.54[0.26,8.96]
McCowan 1980	5/35	4/38		24.29%	1.36[0.4,4.65]
Ross 1984	2/57	2/58		12.55%	1.02[0.15,6.98]
Ruiz-Moreno 1991	4/50	4/50		25.33%	1[0.26,3.78]
Subtotal (95% CI)	**308**	**314**		**100%**	**1.03[0.53,2.01]**
Total events: 16 (Antibiotic), 16 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=1.11, df=4(P=0.89); I^2=0%					
Test for overall effect: Z=0.09(P=0.93)					
2.5.12 Fluoroquinolones					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.5.13 Trimethoprim-sulfamethoxazole					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.5.14 Aminoglycoside-containing combination					
Bilgin 1998	3/18	0/7		2.23%	2.95[0.17,50.74]
Gibbs 1972	3/33	4/28		13.73%	0.64[0.16,2.61]
Gibbs 1973	2/34	4/34		12.69%	0.5[0.1,2.55]
Rothbard 1975	0/16	2/16		7.93%	0.2[0.01,3.86]
Weissberg 1971	2/40	20/40		63.43%	0.1[0.03,0.4]
Subtotal (95% CI)	**141**	**125**		**100%**	**0.3[0.15,0.6]**
Total events: 10 (Antibiotic), 30 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=6.46, df=4(P=0.17); I^2=38.08%					
Test for overall effect: Z=3.41(P=0)					
2.5.15 Other antibiotic combination					
Chan 1989	10/104	4/33		25.23%	0.79[0.27,2.36]
Engel 1984	9/50	18/50		74.77%	0.5[0.25,1]
Subtotal (95% CI)	**154**	**83**		**100%**	**0.57[0.32,1.03]**
Total events: 19 (Antibiotic), 22 (No antibiotic)					

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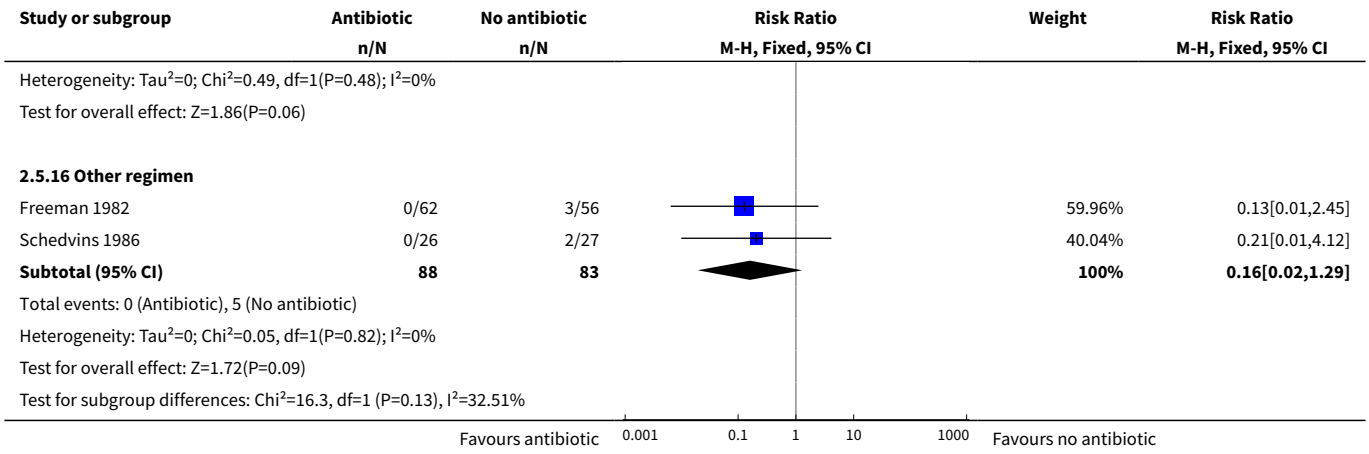
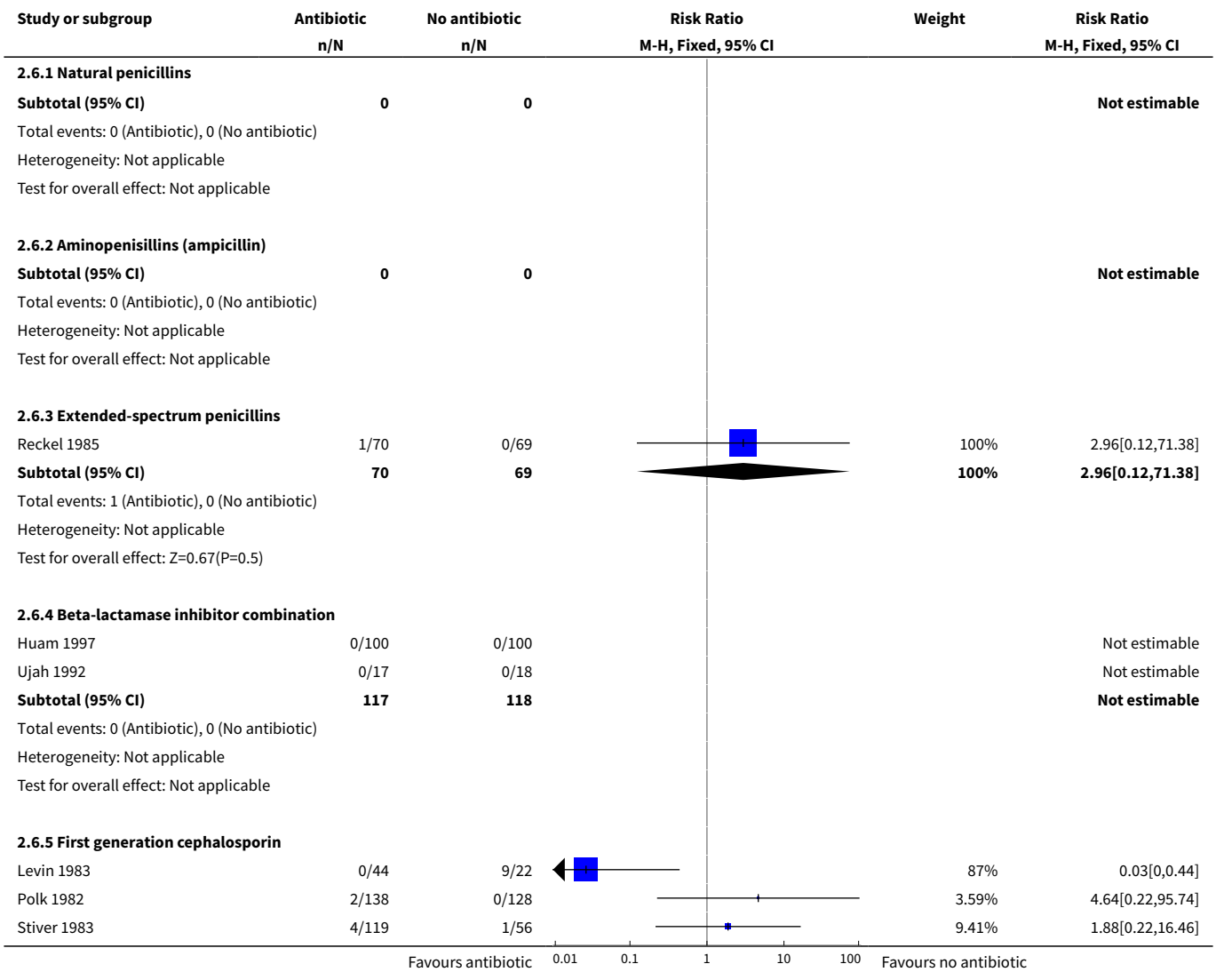


Analysis 2.6. Comparison 2 Antibiotic versus no antibiotic - subgroup by class of antibiotic, Outcome 6 Maternal adverse effects.



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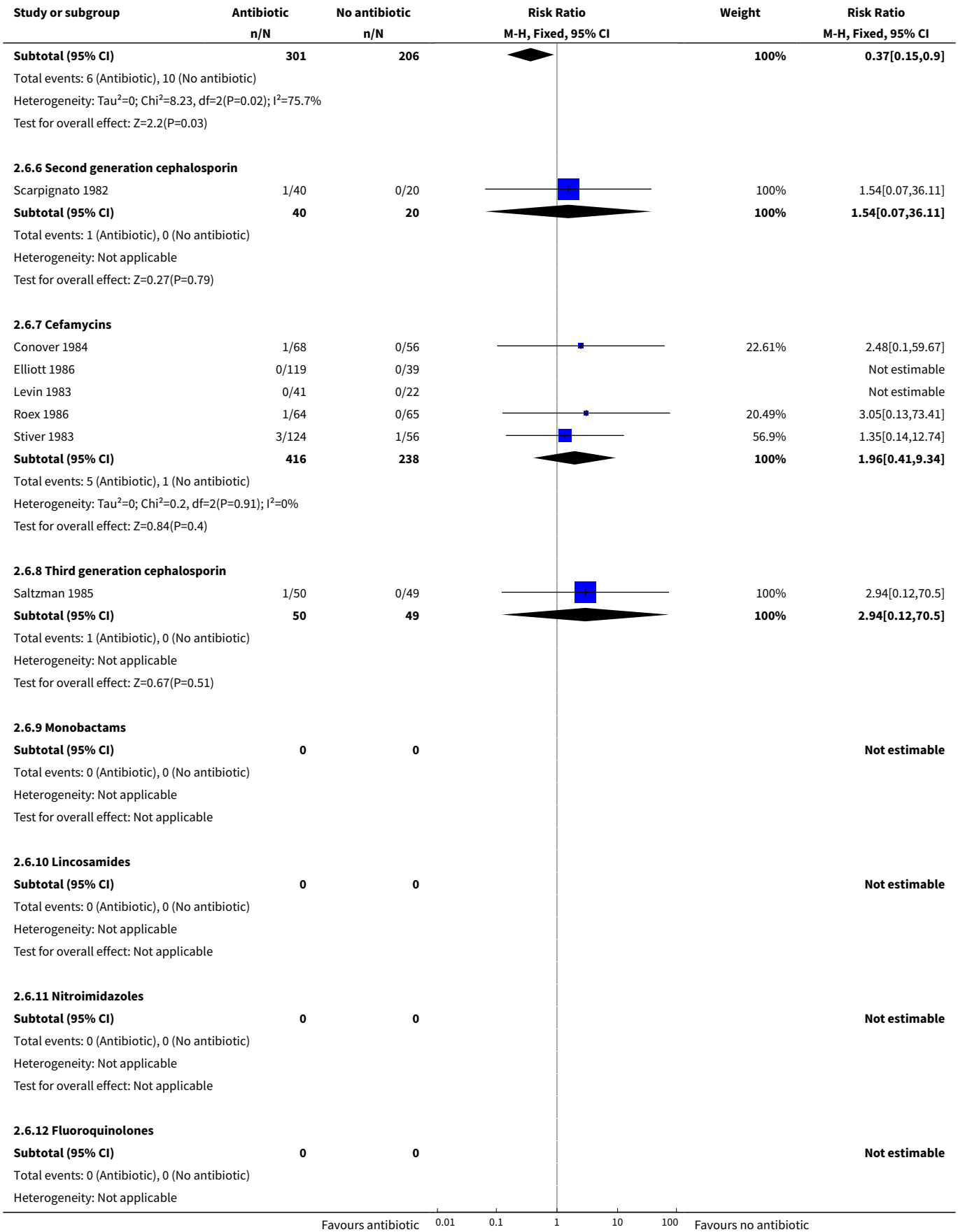

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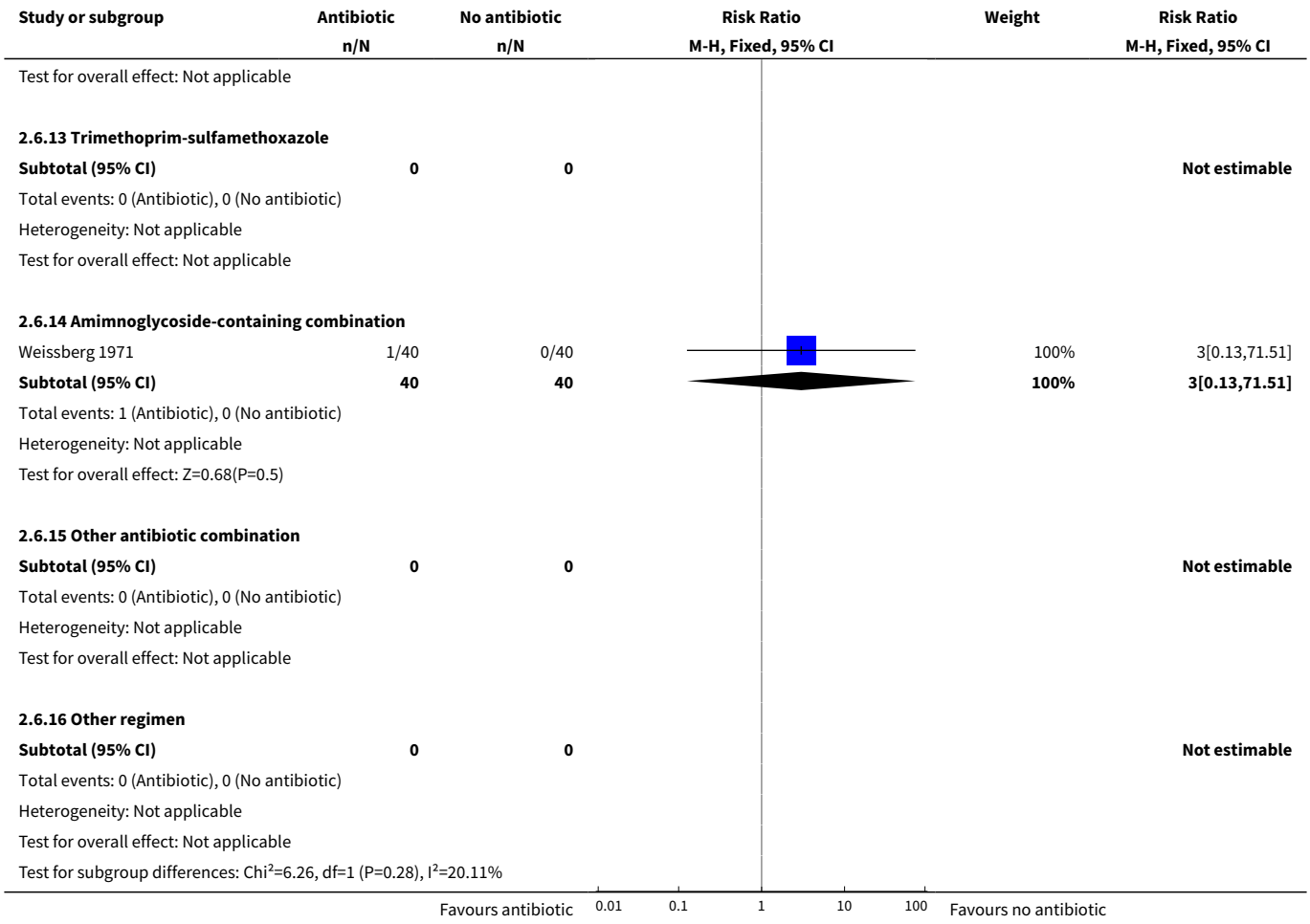
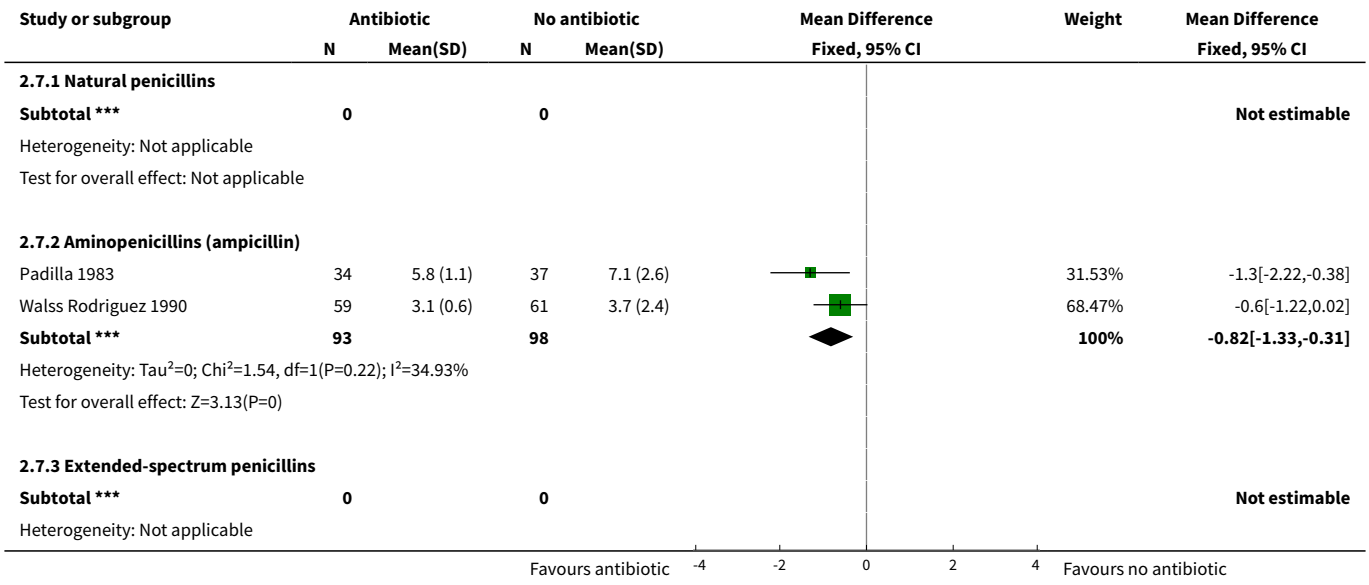


Analysis 2.7. Comparison 2 Antibiotic versus no antibiotic - subgroup by class of antibiotic, Outcome 7 Maternal days in hospital.



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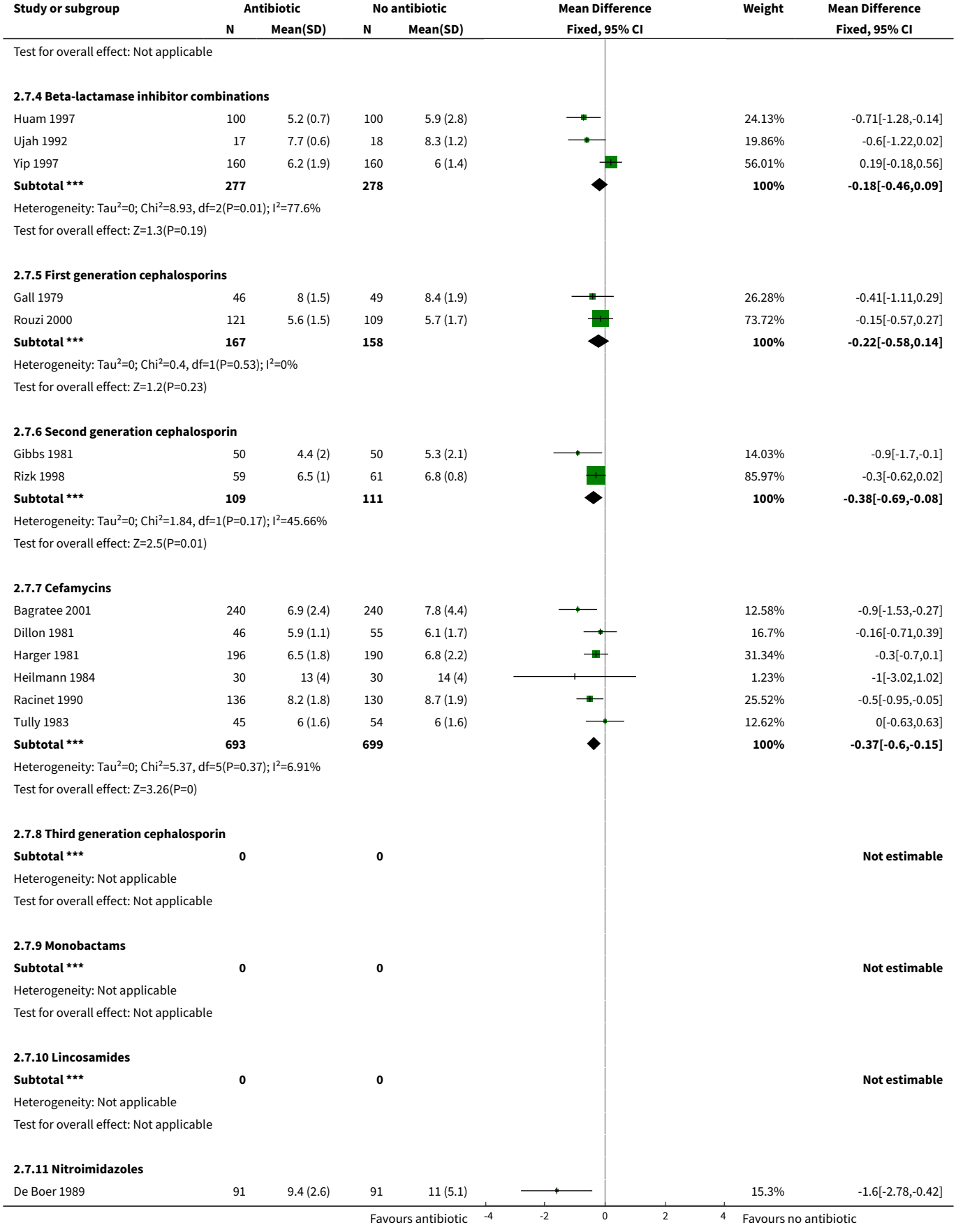

Study or subgroup	Antibiotic N	Antibiotic Mean(SD)	No antibiotic N	No antibiotic Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Test for overall effect: Not applicable							
2.7.4 Beta-lactamase inhibitor combinations							
Huam 1997	100	5.2 (0.7)	100	5.9 (2.8)		24.13%	-0.71[-1.28,-0.14]
Ujah 1992	17	7.7 (0.6)	18	8.3 (1.2)		19.86%	-0.6[-1.22,0.02]
Yip 1997	160	6.2 (1.9)	160	6 (1.4)		56.01%	0.19[-0.18,0.56]
Subtotal ***	**277**		**278**			**100%**	**-0.18[-0.46,0.09]**
Heterogeneity: Tau^2=0; Chi^2=8.93, df=2(P=0.01); I^2=77.6%							
Test for overall effect: Z=1.3(P=0.19)							
2.7.5 First generation cephalosporins							
Gall 1979	46	8 (1.5)	49	8.4 (1.9)		26.28%	-0.41[-1.11,0.29]
Rouzi 2000	121	5.6 (1.5)	109	5.7 (1.7)		73.72%	-0.15[-0.57,0.27]
Subtotal ***	**167**		**158**			**100%**	**-0.22[-0.58,0.14]**
Heterogeneity: Tau^2=0; Chi^2=0.4, df=1(P=0.53); I^2=0%							
Test for overall effect: Z=1.2(P=0.23)							
2.7.6 Second generation cephalosporin							
Gibbs 1981	50	4.4 (2)	50	5.3 (2.1)		14.03%	-0.9[-1.7,-0.1]
Rizk 1998	59	6.5 (1)	61	6.8 (0.8)		85.97%	-0.3[-0.62,0.02]
Subtotal ***	**109**		**111**			**100%**	**-0.38[-0.69,-0.08]**
Heterogeneity: Tau^2=0; Chi^2=1.84, df=1(P=0.17); I^2=45.66%							
Test for overall effect: Z=2.5(P=0.01)							
2.7.7 Cefamycins							
Bagratee 2001	240	6.9 (2.4)	240	7.8 (4.4)		12.58%	-0.9[-1.53,-0.27]
Dillon 1981	46	5.9 (1.1)	55	6.1 (1.7)		16.7%	-0.16[-0.71,0.39]
Harger 1981	196	6.5 (1.8)	190	6.8 (2.2)		31.34%	-0.3[-0.7,0.1]
Heilmann 1984	30	13 (4)	30	14 (4)		1.23%	-1[-3.02,1.02]
Racinet 1990	136	8.2 (1.8)	130	8.7 (1.9)		25.52%	-0.5[-0.95,-0.05]
Tully 1983	45	6 (1.6)	54	6 (1.6)		12.62%	0[-0.63,0.63]
Subtotal ***	**693**		**699**			**100%**	**-0.37[-0.6,-0.15]**
Heterogeneity: Tau^2=0; Chi^2=5.37, df=5(P=0.37); I^2=6.91%							
Test for overall effect: Z=3.26(P=0)							
2.7.8 Third generation cephalosporin							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.7.9 Monobactams							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.7.10 Lincosamides							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.7.11 Nitroimidazoles							
De Boer 1989	91	9.4 (2.6)	91	11 (5.1)		15.3%	-1.6[-2.78,-0.42]

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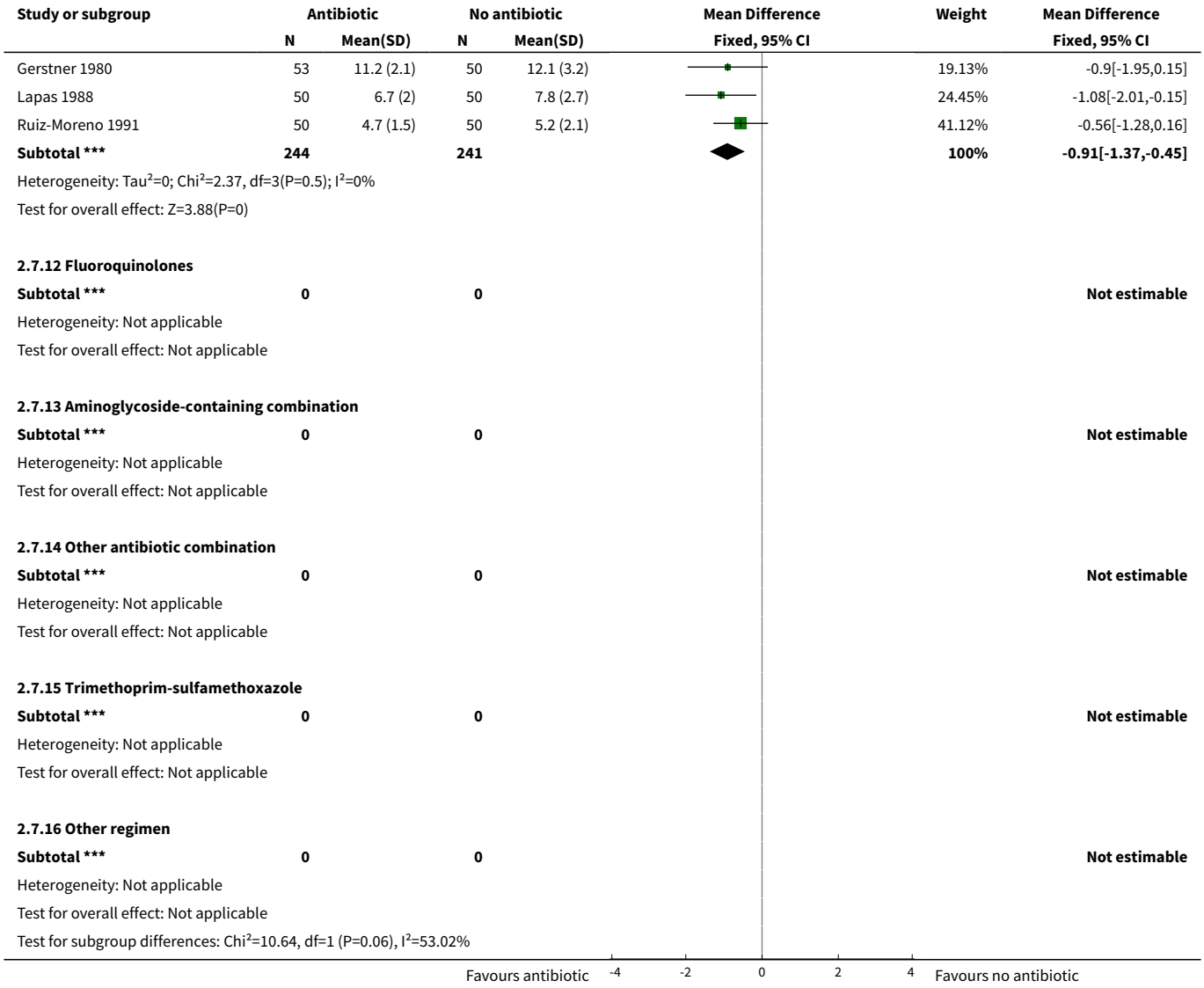

Comparison 3. Antibiotics versus no antibiotics - subgroup by type of cesarean section

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maternal febrile morbidity/fever	56		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Elective cesarean section	16	2537	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.38, 0.61]
1.2 Non-elective cesarean section	15	1784	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.37, 0.51]
1.3 Both elective and non-elective, or undefined cesarean section	29	4725	Risk Ratio (M-H, Fixed, 95% CI)	0.45 [0.40, 0.50]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Maternal wound infection	82		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Elective cesarean section	17	3537	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.47, 0.82]
2.2 Non-elective cesarean section	20	2291	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.27, 0.58]
2.3 Both elective and non-elective, or undefined cesarean section	49	8579	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.28, 0.40]
3 Maternal endometritis	83		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Elective cesarean section	15	2502	Risk Ratio (M-H, Fixed, 95% CI)	0.38 [0.24, 0.61]
3.2 Non-elective cesarean section	20	2310	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.33, 0.47]
3.3 Both elective and non-elective, or undefined cesarean section	52	8776	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.32, 0.42]
4 Maternal serious infectious complications	32		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Elective cesarean section	4	545	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.04, 24.21]
4.2 Non-elective cesarean section	6	696	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.12, 0.65]
4.3 Both elective and non-elective, or undefined cesarean section	24	4918	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.19, 0.54]
5 Maternal urinary tract infection	66		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Elective cesarean section	12	1936	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.57, 1.50]
5.2 Non-elective cesarean section	17	1981	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.31, 0.60]
5.3 Both elective and non-elective, or undefined cesarean section	41	7043	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.49, 0.70]
6 Maternal adverse effects	13		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Elective cesarean section	2	235	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

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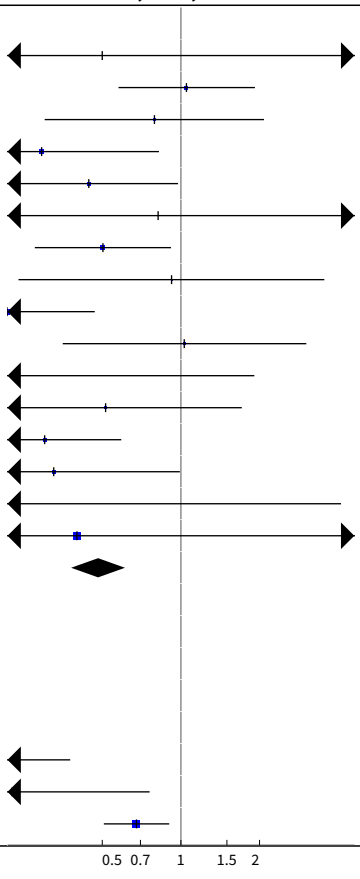
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.2 Non-elective cesarean section	5	808	Risk Ratio (M-H, Fixed, 95% CI)	2.86 [0.61, 13.31]
6.3 Both elective and non-elective, or undefined cesarean section	6	1088	Risk Ratio (M-H, Fixed, 95% CI)	2.23 [0.75, 6.63]
7 Maternal days in hospital	19		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Elective cesarean section	5	1065	Mean Difference (IV, Fixed, 95% CI)	-0.41 [-0.62, -0.21]
7.2 Non-elective cesarean section	4	646	Mean Difference (IV, Fixed, 95% CI)	-0.46 [-0.78, -0.14]
7.3 Both elective and non-elective, or undefined cesarean section	11	1668	Mean Difference (IV, Fixed, 95% CI)	-0.39 [-0.57, -0.21]

Analysis 3.1. Comparison 3 Antibiotics versus no antibiotics - subgroup by type of cesarean section, Outcome 1 Maternal febrile morbidity/fever.

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 Elective cesarean section					
Adam 2005	1/50	2/50		1.12%	0.5[0.05,5.34]
Bagratee 2001	20/240	19/240		10.6%	1.05[0.58,1.92]
Dashow 1986	12/100	5/33		4.19%	0.79[0.3,2.08]
Duff 1982	4/42	13/40		7.43%	0.29[0.1,0.82]
Huam 1997	8/100	18/100		10.04%	0.44[0.2,0.97]
Jaffe 1984	2/22	2/18		1.23%	0.82[0.13,5.25]
Jakobi 1994	15/167	25/140		15.17%	0.5[0.28,0.92]
Kolben 2001	4/76	4/70		2.32%	0.92[0.24,3.54]
Mahomed 1988	7/115	33/117		18.25%	0.22[0.1,0.47]
Rizk 1998	6/59	6/61		3.29%	1.03[0.35,3.02]
Rothbard 1975	0/16	4/16		2.51%	0.11[0.01,1.91]
Rouzi 2000	4/121	7/109		4.11%	0.51[0.15,1.71]
Shah 1998	13/139	14/45		11.8%	0.3[0.15,0.59]
Sziller 1994	4/60	9/44		5.79%	0.33[0.11,0.99]
Ujah 1992	0/17	2/18		1.36%	0.21[0.01,4.1]
Wu 1991	1/80	1/32		0.8%	0.4[0.03,6.2]
Subtotal (95% CI)	**1404**	**1133**		**100%**	**0.48[0.38,0.61]**
Total events: 101 (Antibiotic), 164 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=19.42, df=15(P=0.2); I^2=22.75%					
Test for overall effect: Z=6.03(P<0.0001)					
3.1.2 Non-elective cesarean section					
Elliott 1986	7/119	14/39		6.44%	0.16[0.07,0.38]
Freeman 1982	3/62	12/56		3.85%	0.23[0.07,0.76]
Harger 1981	53/196	76/190		23.56%	0.68[0.51,0.9]



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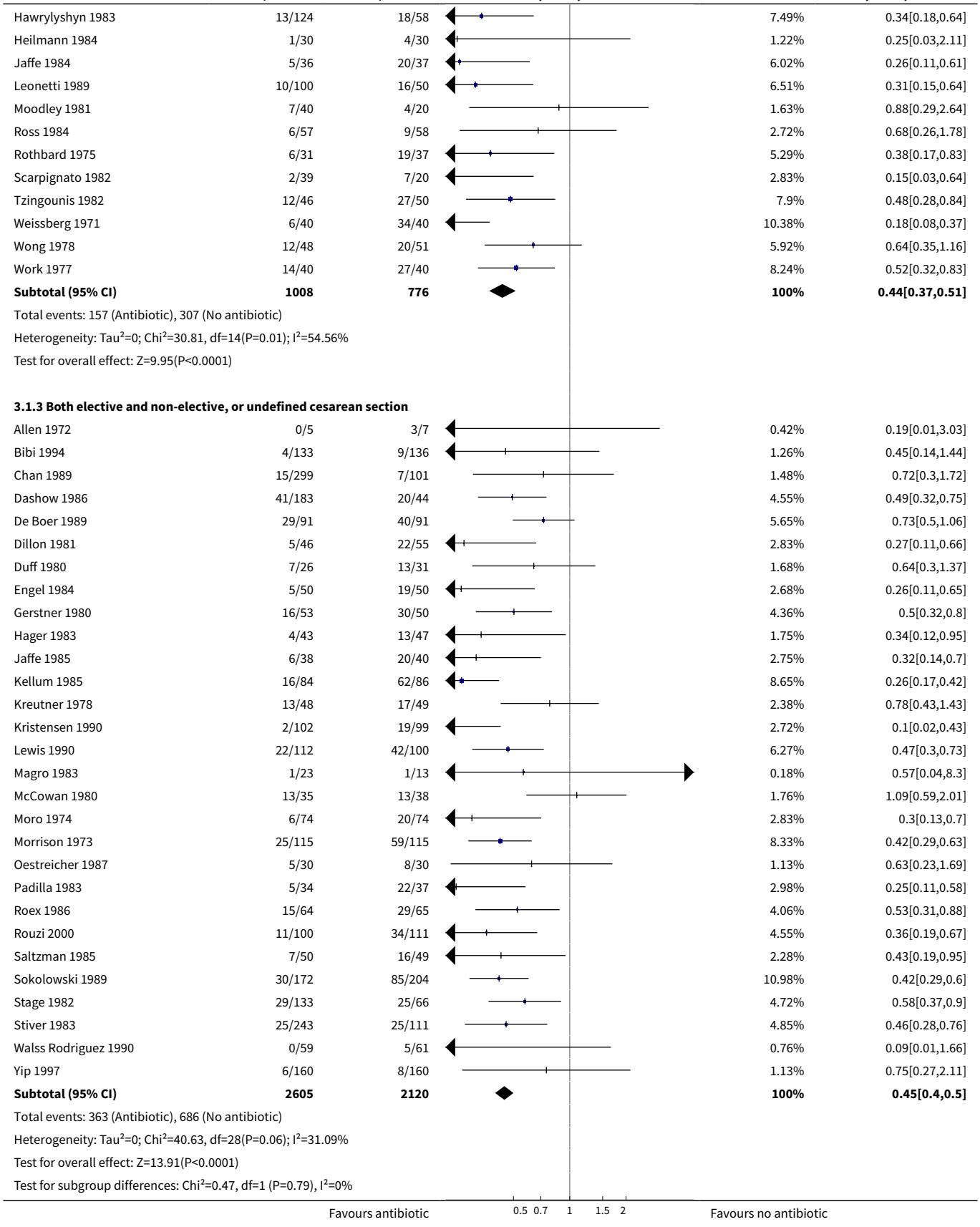

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Hawrylyshyn 1983	13/124	18/58		7.49%	0.34[0.18,0.64]
Heilmann 1984	1/30	4/30		1.22%	0.25[0.03,2.11]
Jaffe 1984	5/36	20/37		6.02%	0.26[0.11,0.61]
Leonetti 1989	10/100	16/50		6.51%	0.31[0.15,0.64]
Moodley 1981	7/40	4/20		1.63%	0.88[0.29,2.64]
Ross 1984	6/57	9/58		2.72%	0.68[0.26,1.78]
Rothbard 1975	6/31	19/37		5.29%	0.38[0.17,0.83]
Scarpignato 1982	2/39	7/20		2.83%	0.15[0.03,0.64]
Tzingounis 1982	12/46	27/50		7.9%	0.48[0.28,0.84]
Weissberg 1971	6/40	34/40		10.38%	0.18[0.08,0.37]
Wong 1978	12/48	20/51		5.92%	0.64[0.35,1.16]
Work 1977	14/40	27/40		8.24%	0.52[0.32,0.83]
Subtotal (95% CI)	**1008**	**776**		**100%**	**0.44[0.37,0.51]**
Total events: 157 (Antibiotic), 307 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=30.81, df=14(P=0.01); I²=54.56%					
Test for overall effect: Z=9.95(P<0.0001)					
3.1.3 Both elective and non-elective, or undefined cesarean section					
Allen 1972	0/5	3/7		0.42%	0.19[0.01,3.03]
Bibi 1994	4/133	9/136		1.26%	0.45[0.14,1.44]
Chan 1989	15/299	7/101		1.48%	0.72[0.3,1.72]
Dashow 1986	41/183	20/44		4.55%	0.49[0.32,0.75]
De Boer 1989	29/91	40/91		5.65%	0.73[0.5,1.06]
Dillon 1981	5/46	22/55		2.83%	0.27[0.11,0.66]
Duff 1980	7/26	13/31		1.68%	0.64[0.3,1.37]
Engel 1984	5/50	19/50		2.68%	0.26[0.11,0.65]
Gerstner 1980	16/53	30/50		4.36%	0.5[0.32,0.8]
Hager 1983	4/43	13/47		1.75%	0.34[0.12,0.95]
Jaffe 1985	6/38	20/40		2.75%	0.32[0.14,0.7]
Kellum 1985	16/84	62/86		8.65%	0.26[0.17,0.42]
Kreutner 1978	13/48	17/49		2.38%	0.78[0.43,1.43]
Kristensen 1990	2/102	19/99		2.72%	0.1[0.02,0.43]
Lewis 1990	22/112	42/100		6.27%	0.47[0.3,0.73]
Magro 1983	1/23	1/13		0.18%	0.57[0.04,8.3]
McCowan 1980	13/35	13/38		1.76%	1.09[0.59,2.01]
Moro 1974	6/74	20/74		2.83%	0.3[0.13,0.7]
Morrison 1973	25/115	59/115		8.33%	0.42[0.29,0.63]
Oestreicher 1987	5/30	8/30		1.13%	0.63[0.23,1.69]
Padilla 1983	5/34	22/37		2.98%	0.25[0.11,0.58]
Roex 1986	15/64	29/65		4.06%	0.53[0.31,0.88]
Rouzi 2000	11/100	34/111		4.55%	0.36[0.19,0.67]
Saltzman 1985	7/50	16/49		2.28%	0.43[0.19,0.95]
Sokolowski 1989	30/172	85/204		10.98%	0.42[0.29,0.6]
Stage 1982	29/133	25/66		4.72%	0.58[0.37,0.9]
Stiver 1983	25/243	25/111		4.85%	0.46[0.28,0.76]
Walss Rodriguez 1990	0/59	5/61		0.76%	0.09[0.01,1.66]
Yip 1997	6/160	8/160		1.13%	0.75[0.27,2.11]
Subtotal (95% CI)	**2605**	**2120**		**100%**	**0.45[0.4,0.5]**
Total events: 363 (Antibiotic), 686 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=40.63, df=28(P=0.06); I²=31.09%					
Test for overall effect: Z=13.91(P<0.0001)					
Test for subgroup differences: Chi²=0.47, df=1 (P=0.79), I²=0%					

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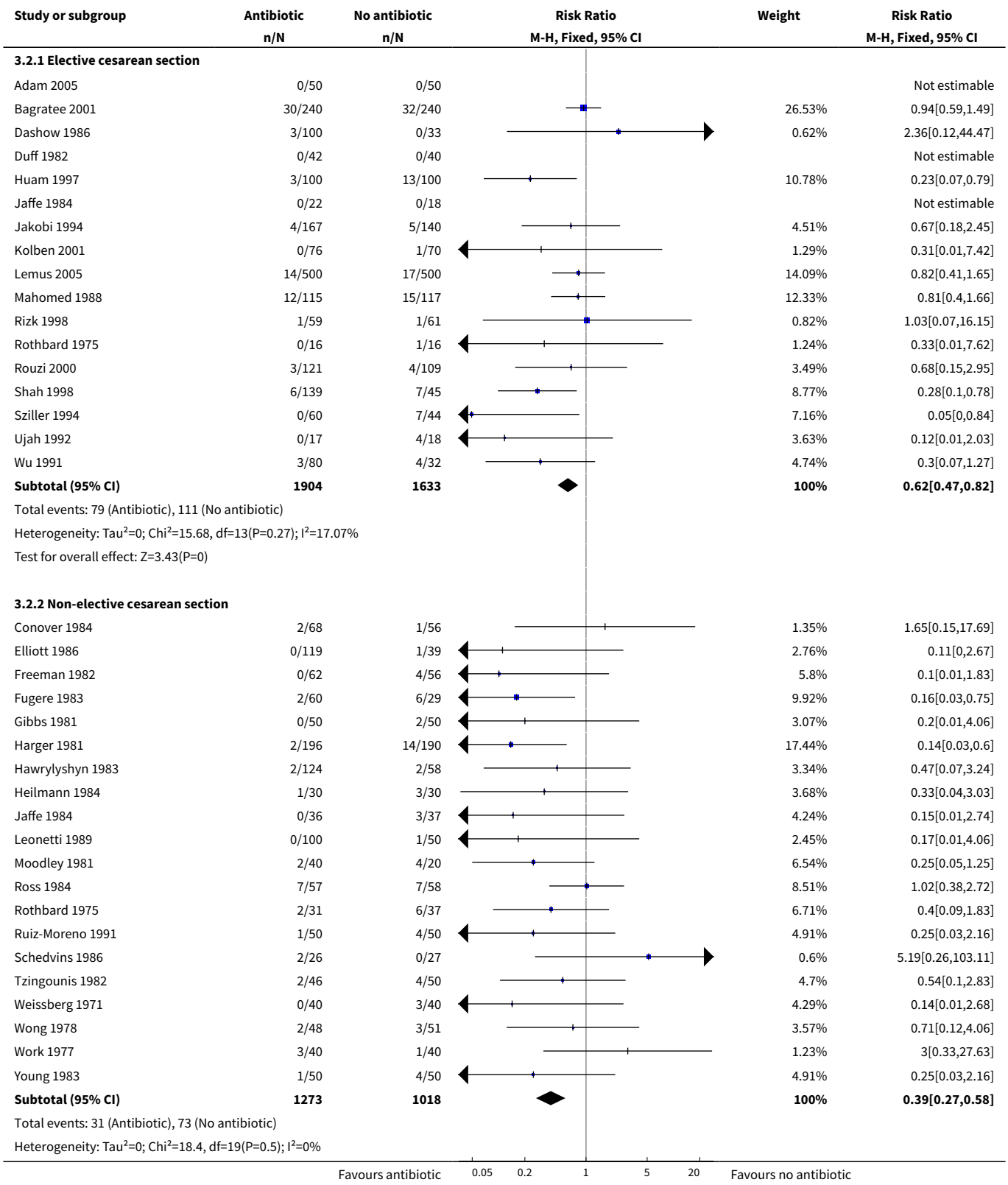
Analysis 3.2. Comparison 3 Antibiotics versus no antibiotics - subgroup by type of cesarean section, Outcome 2 Maternal wound infection.



Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.2.1 Elective cesarean section					
Adam 2005	0/50	0/50			Not estimable
Bagratee 2001	30/240	32/240		26.53%	0.94[0.59,1.49]
Dashow 1986	3/100	0/33		0.62%	2.36[0.12,44.47]
Duff 1982	0/42	0/40			Not estimable
Huam 1997	3/100	13/100		10.78%	0.23[0.07,0.79]
Jaffe 1984	0/22	0/18			Not estimable
Jakobi 1994	4/167	5/140		4.51%	0.67[0.18,2.45]
Kolben 2001	0/76	1/70		1.29%	0.31[0.01,7.42]
Lemus 2005	14/500	17/500		14.09%	0.82[0.41,1.65]
Mahomed 1988	12/115	15/117		12.33%	0.81[0.4,1.66]
Rizk 1998	1/59	1/61		0.82%	1.03[0.07,16.15]
Rothbard 1975	0/16	1/16		1.24%	0.33[0.01,7.62]
Rouzi 2000	3/121	4/109		3.49%	0.68[0.15,2.95]
Shah 1998	6/139	7/45		8.77%	0.28[0.1,0.78]
Sziller 1994	0/60	7/44		7.16%	0.05[0,0.84]
Ujah 1992	0/17	4/18		3.63%	0.12[0.01,2.03]
Wu 1991	3/80	4/32		4.74%	0.3[0.07,1.27]
Subtotal (95% CI)	**1904**	**1633**		**100%**	**0.62[0.47,0.82]**
Total events: 79 (Antibiotic), 111 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=15.68, df=13(P=0.27); I^2=17.07%					
Test for overall effect: Z=3.43(P=0)					
3.2.2 Non-elective cesarean section					
Conover 1984	2/68	1/56		1.35%	1.65[0.15,17.69]
Elliott 1986	0/119	1/39		2.76%	0.11[0,2.67]
Freeman 1982	0/62	4/56		5.8%	0.1[0.01,1.83]
Fugere 1983	2/60	6/29		9.92%	0.16[0.03,0.75]
Gibbs 1981	0/50	2/50		3.07%	0.2[0.01,4.06]
Harger 1981	2/196	14/190		17.44%	0.14[0.03,0.6]
Hawrylyshyn 1983	2/124	2/58		3.34%	0.47[0.07,3.24]
Heilmann 1984	1/30	3/30		3.68%	0.33[0.04,3.03]
Jaffe 1984	0/36	3/37		4.24%	0.15[0.01,2.74]
Leonetti 1989	0/100	1/50		2.45%	0.17[0.01,4.06]
Moodley 1981	2/40	4/20		6.54%	0.25[0.05,1.25]
Ross 1984	7/57	7/58		8.51%	1.02[0.38,2.72]
Rothbard 1975	2/31	6/37		6.71%	0.4[0.09,1.83]
Ruiz-Moreno 1991	1/50	4/50		4.91%	0.25[0.03,2.16]
Schedvins 1986	2/26	0/27		0.6%	5.19[0.26,103.11]
Tzingounis 1982	2/46	4/50		4.7%	0.54[0.1,2.83]
Weissberg 1971	0/40	3/40		4.29%	0.14[0.01,2.68]
Wong 1978	2/48	3/51		3.57%	0.71[0.12,4.06]
Work 1977	3/40	1/40		1.23%	3[0.33,27.63]
Young 1983	1/50	4/50		4.91%	0.25[0.03,2.16]
Subtotal (95% CI)	**1273**	**1018**		**100%**	**0.39[0.27,0.58]**
Total events: 31 (Antibiotic), 73 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=18.4, df=19(P=0.5); I^2=0%					

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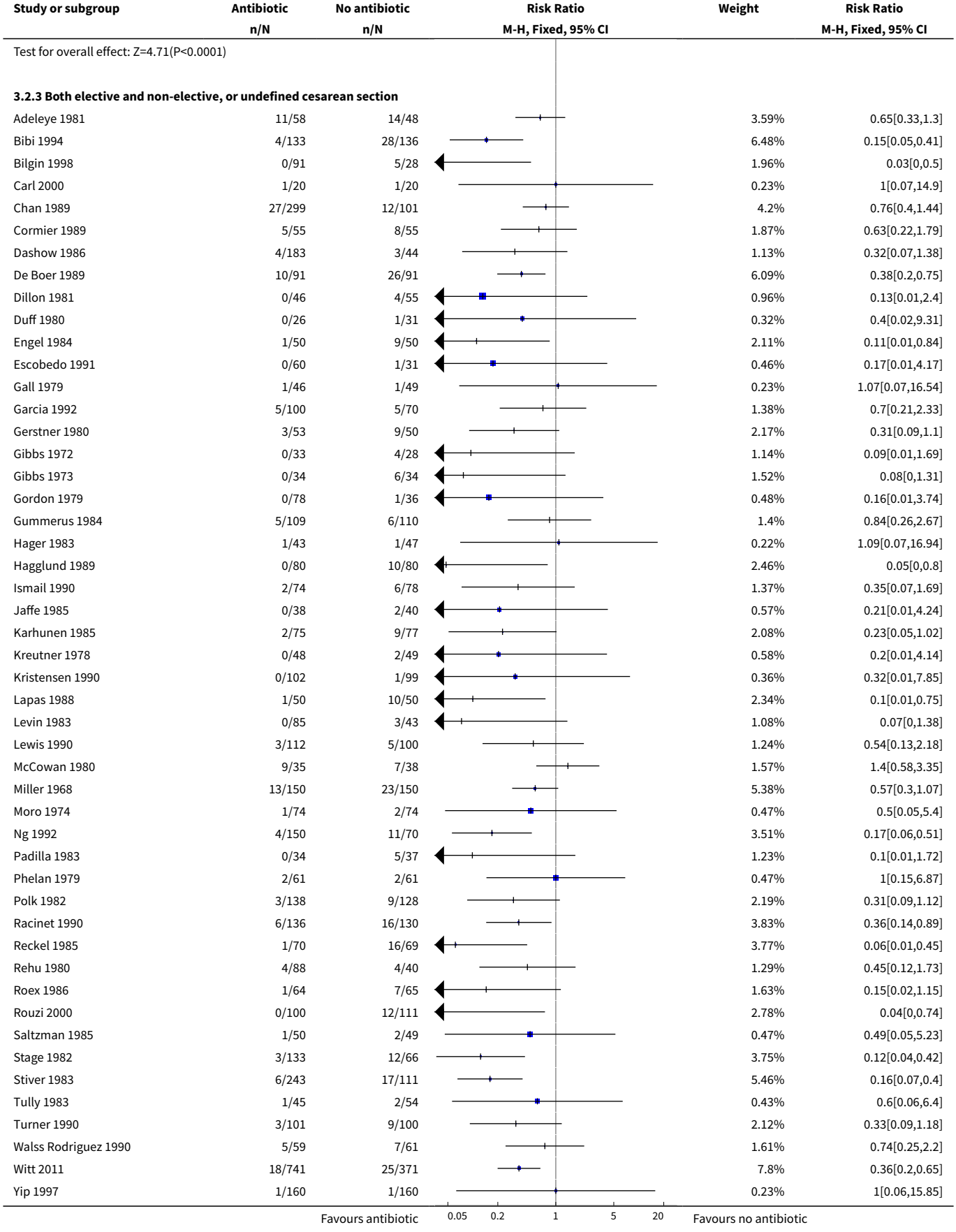

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Test for overall effect: Z=4.71(P<0.0001)					
3.2.3 Both elective and non-elective, or undefined cesarean section					
Adeleye 1981	11/58	14/48		3.59%	0.65[0.33,1.3]
Bibi 1994	4/133	28/136		6.48%	0.15[0.05,0.41]
Bilgin 1998	0/91	5/28		1.96%	0.03[0,0.5]
Carl 2000	1/20	1/20		0.23%	1[0.07,14.9]
Chan 1989	27/299	12/101		4.2%	0.76[0.4,1.44]
Cormier 1989	5/55	8/55		1.87%	0.63[0.22,1.79]
Dashow 1986	4/183	3/44		1.13%	0.32[0.07,1.38]
De Boer 1989	10/91	26/91		6.09%	0.38[0.2,0.75]
Dillon 1981	0/46	4/55		0.96%	0.13[0.01,2.4]
Duff 1980	0/26	1/31		0.32%	0.4[0.02,9.31]
Engel 1984	1/50	9/50		2.11%	0.11[0.01,0.84]
Escobedo 1991	0/60	1/31		0.46%	0.17[0.01,4.17]
Gall 1979	1/46	1/49		0.23%	1.07[0.07,16.54]
Garcia 1992	5/100	5/70		1.38%	0.7[0.21,2.33]
Gerstner 1980	3/53	9/50		2.17%	0.31[0.09,1.1]
Gibbs 1972	0/33	4/28		1.14%	0.09[0.01,1.69]
Gibbs 1973	0/34	6/34		1.52%	0.08[0,1.31]
Gordon 1979	0/78	1/36		0.48%	0.16[0.01,3.74]
Gummerus 1984	5/109	6/110		1.4%	0.84[0.26,2.67]
Hager 1983	1/43	1/47		0.22%	1.09[0.07,16.94]
Hagglund 1989	0/80	10/80		2.46%	0.05[0,0.8]
Ismail 1990	2/74	6/78		1.37%	0.35[0.07,1.69]
Jaffe 1985	0/38	2/40		0.57%	0.21[0.01,4.24]
Karhunen 1985	2/75	9/77		2.08%	0.23[0.05,1.02]
Kreutner 1978	0/48	2/49		0.58%	0.2[0.01,4.14]
Kristensen 1990	0/102	1/99		0.36%	0.32[0.01,7.85]
Lapas 1988	1/50	10/50		2.34%	0.1[0.01,0.75]
Levin 1983	0/85	3/43		1.08%	0.07[0,1.38]
Lewis 1990	3/112	5/100		1.24%	0.54[0.13,2.18]
McCowan 1980	9/35	7/38		1.57%	1.4[0.58,3.35]
Miller 1968	13/150	23/150		5.38%	0.57[0.3,1.07]
Moro 1974	1/74	2/74		0.47%	0.5[0.05,5.4]
Ng 1992	4/150	11/70		3.51%	0.17[0.06,0.51]
Padilla 1983	0/34	5/37		1.23%	0.1[0.01,1.72]
Phelan 1979	2/61	2/61		0.47%	1[0.15,6.87]
Polk 1982	3/138	9/128		2.19%	0.31[0.09,1.12]
Racinet 1990	6/136	16/130		3.83%	0.36[0.14,0.89]
Reckel 1985	1/70	16/69		3.77%	0.06[0.01,0.45]
Rehu 1980	4/88	4/40		1.29%	0.45[0.12,1.73]
Roex 1986	1/64	7/65		1.63%	0.15[0.02,1.15]
Rouzi 2000	0/100	12/111		2.78%	0.04[0,0.74]
Saltzman 1985	1/50	2/49		0.47%	0.49[0.05,5.23]
Stage 1982	3/133	12/66		3.75%	0.12[0.04,0.42]
Stiver 1983	6/243	17/111		5.46%	0.16[0.07,0.4]
Tully 1983	1/45	2/54		0.43%	0.6[0.06,6.4]
Turner 1990	3/101	9/100		2.12%	0.33[0.09,1.18]
Walss Rodriguez 1990	5/59	7/61		1.61%	0.74[0.25,2.2]
Witt 2011	18/741	25/371		7.8%	0.36[0.2,0.65]
Yip 1997	1/160	1/160		0.23%	1[0.06,15.85]

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Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Subtotal (95% CI)	**4904**	**3675**	◆	**100%**	**0.34[0.28,0.4]**
Total events: 168 (Antibiotic), 382 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=60.98, df=48(P=0.1); I^2=21.28%					
Test for overall effect: Z=12.09(P<0.0001)					
Test for subgroup differences: Chi^2=13.53, df=1 (P=0), I^2=85.22%					

Favours antibiotic 0.05 0.2 1 5 20 Favours no antibiotic

Analysis 3.3. Comparison 3 Antibiotics versus no antibiotics - subgroup by type of cesarean section, Outcome 3 Maternal endometritis.

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.3.1 Elective cesarean section					
Adam 2005	1/50	1/50		1.89%	1[0.06,15.55]
Bagratee 2001	2/240	4/240		7.56%	0.5[0.09,2.7]
Dashow 1986	2/100	3/33		8.53%	0.22[0.04,1.26]
Duff 1982	1/42	6/40		11.62%	0.16[0.02,1.26]
Huam 1997	0/100	0/100			Not estimable
Jaffe 1984	0/22	0/18			Not estimable
Jakobi 1994	3/167	3/140		6.17%	0.84[0.17,4.09]
Kolben 2001	2/76	1/70		1.97%	1.84[0.17,19.87]
Mahomed 1988	0/115	6/117		12.18%	0.08[0,1.37]
Rizk 1998	3/59	2/61		3.72%	1.55[0.27,8.95]
Rothbard 1975	0/16	0/16			Not estimable
Rouzi 2000	0/121	1/109		2.98%	0.3[0.01,7.3]
Shah 1998	7/139	7/45		20%	0.32[0.12,0.87]
Sziller 1994	3/60	7/44		15.27%	0.31[0.09,1.15]
Wu 1991	1/80	3/32		8.1%	0.13[0.01,1.23]
Subtotal (95% CI)	**1387**	**1115**	◆	**100%**	**0.38[0.24,0.61]**
Total events: 25 (Antibiotic), 44 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=8.98, df=11(P=0.62); I^2=0%					
Test for overall effect: Z=4(P<0.0001)					
3.3.2 Non-elective cesarean section					
Conover 1984	8/68	11/56		3.98%	0.6[0.26,1.39]
D'Angelo 1980	12/49	19/31		7.68%	0.4[0.23,0.7]
Elliott 1986	6/119	13/39		6.46%	0.15[0.06,0.37]
Freeman 1982	3/62	5/56		1.73%	0.54[0.14,2.16]
Fugere 1983	2/60	2/29		0.89%	0.48[0.07,3.26]
Gibbs 1981	8/50	24/50		7.92%	0.33[0.17,0.67]
Harger 1981	20/196	38/190		12.73%	0.51[0.31,0.84]
Hawrylyshyn 1983	9/124	17/58		7.64%	0.25[0.12,0.52]
Jaffe 1984	0/36	6/37		2.12%	0.08[0,1.35]
Leonetti 1989	10/100	12/50		5.28%	0.42[0.19,0.9]
Ross 1984	2/57	2/58		0.65%	1.02[0.15,6.98]
Rothbard 1975	1/31	8/37		2.41%	0.15[0.02,1.13]
Ruiz-Moreno 1991	7/50	15/50		4.95%	0.47[0.21,1.05]
Scarpignato 1982	2/39	6/20		2.62%	0.17[0.04,0.77]
Schedvins 1986	3/26	9/27		2.91%	0.35[0.11,1.14]

Favours antibiotic 0.1 0.2 0.5 1 2 5 10 Favours no antibiotic

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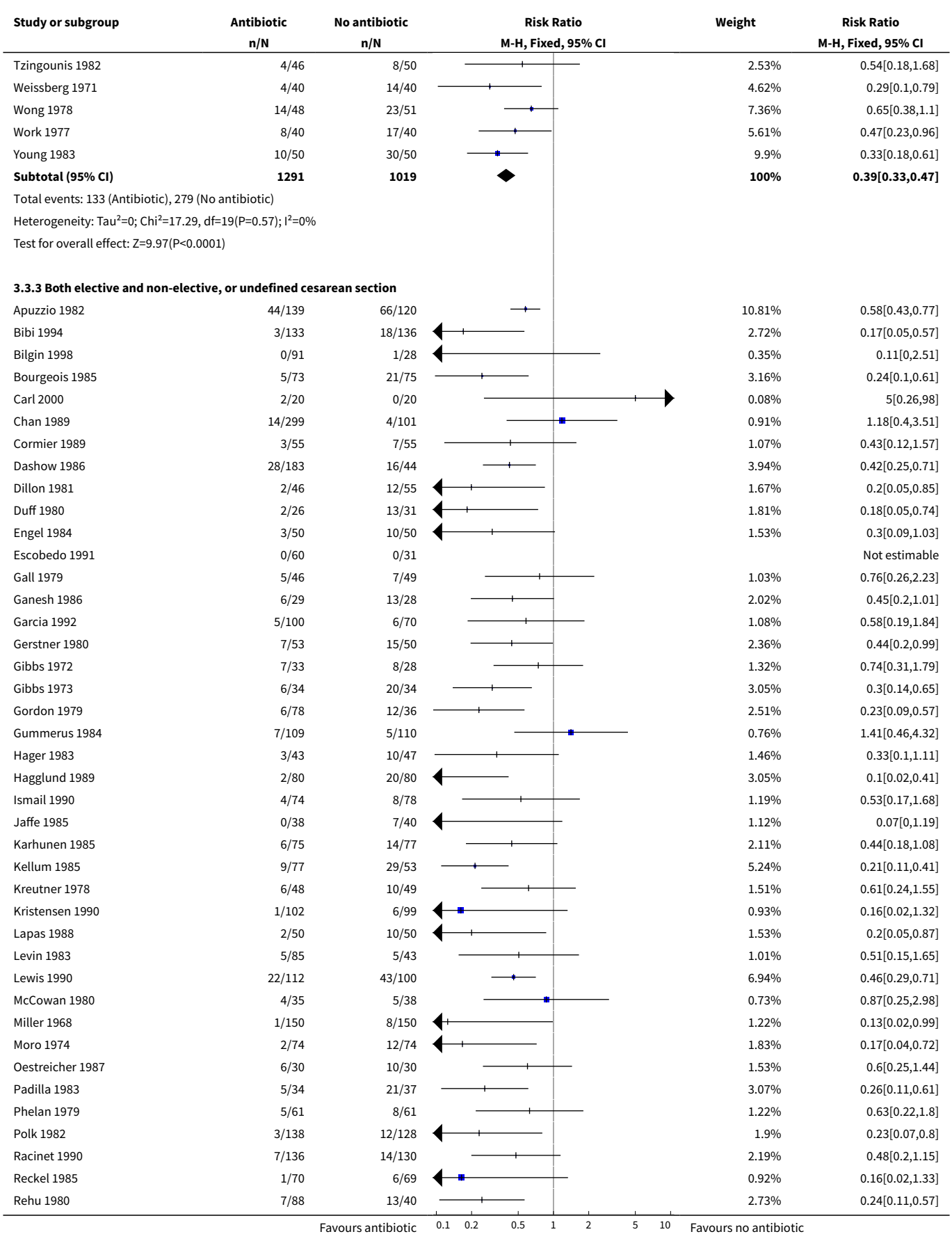

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Tzingounis 1982	4/46	8/50		2.53%	0.54[0.18,1.68]
Weissberg 1971	4/40	14/40		4.62%	0.29[0.1,0.79]
Wong 1978	14/48	23/51		7.36%	0.65[0.38,1.1]
Work 1977	8/40	17/40		5.61%	0.47[0.23,0.96]
Young 1983	10/50	30/50		9.9%	0.33[0.18,0.61]
Subtotal (95% CI)	**1291**	**1019**		**100%**	**0.39[0.33,0.47]**
Total events: 133 (Antibiotic), 279 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=17.29, df=19(P=0.57); I^2=0%					
Test for overall effect: Z=9.97(P<0.0001)					
3.3.3 Both elective and non-elective, or undefined cesarean section					
Apuzzio 1982	44/139	66/120		10.81%	0.58[0.43,0.77]
Bibi 1994	3/133	18/136		2.72%	0.17[0.05,0.57]
Bilgin 1998	0/91	1/28		0.35%	0.11[0,2.51]
Bourgeois 1985	5/73	21/75		3.16%	0.24[0.1,0.61]
Carl 2000	2/20	0/20		0.08%	5[0.26,98]
Chan 1989	14/299	4/101		0.91%	1.18[0.4,3.51]
Cormier 1989	3/55	7/55		1.07%	0.43[0.12,1.57]
Dashow 1986	28/183	16/44		3.94%	0.42[0.25,0.71]
Dillon 1981	2/46	12/55		1.67%	0.2[0.05,0.85]
Duff 1980	2/26	13/31		1.81%	0.18[0.05,0.74]
Engel 1984	3/50	10/50		1.53%	0.3[0.09,1.03]
Escobedo 1991	0/60	0/31			Not estimable
Gall 1979	5/46	7/49		1.03%	0.76[0.26,2.23]
Ganesh 1986	6/29	13/28		2.02%	0.45[0.2,1.01]
Garcia 1992	5/100	6/70		1.08%	0.58[0.19,1.84]
Gerstner 1980	7/53	15/50		2.36%	0.44[0.2,0.99]
Gibbs 1972	7/33	8/28		1.32%	0.74[0.31,1.79]
Gibbs 1973	6/34	20/34		3.05%	0.3[0.14,0.65]
Gordon 1979	6/78	12/36		2.51%	0.23[0.09,0.57]
Gummerus 1984	7/109	5/110		0.76%	1.41[0.46,4.32]
Hager 1983	3/43	10/47		1.46%	0.33[0.1,1.11]
Hagglund 1989	2/80	20/80		3.05%	0.1[0.02,0.41]
Ismail 1990	4/74	8/78		1.19%	0.53[0.17,1.68]
Jaffe 1985	0/38	7/40		1.12%	0.07[0,1.19]
Karhunen 1985	6/75	14/77		2.11%	0.44[0.18,1.08]
Kellum 1985	9/77	29/53		5.24%	0.21[0.11,0.41]
Kreutner 1978	6/48	10/49		1.51%	0.61[0.24,1.55]
Kristensen 1990	1/102	6/99		0.93%	0.16[0.02,1.32]
Lapas 1988	2/50	10/50		1.53%	0.2[0.05,0.87]
Levin 1983	5/85	5/43		1.01%	0.51[0.15,1.65]
Lewis 1990	22/112	43/100		6.94%	0.46[0.29,0.71]
McCowan 1980	4/35	5/38		0.73%	0.87[0.25,2.98]
Miller 1968	1/150	8/150		1.22%	0.13[0.02,0.99]
Moro 1974	2/74	12/74		1.83%	0.17[0.04,0.72]
Oestreicher 1987	6/30	10/30		1.53%	0.6[0.25,1.44]
Padilla 1983	5/34	21/37		3.07%	0.26[0.11,0.61]
Phelan 1979	5/61	8/61		1.22%	0.63[0.22,1.8]
Polk 1982	3/138	12/128		1.9%	0.23[0.07,0.8]
Racinet 1990	7/136	14/130		2.19%	0.48[0.2,1.15]
Reckel 1985	1/70	6/69		0.92%	0.16[0.02,1.33]
Rehu 1980	7/88	13/40		2.73%	0.24[0.11,0.57]

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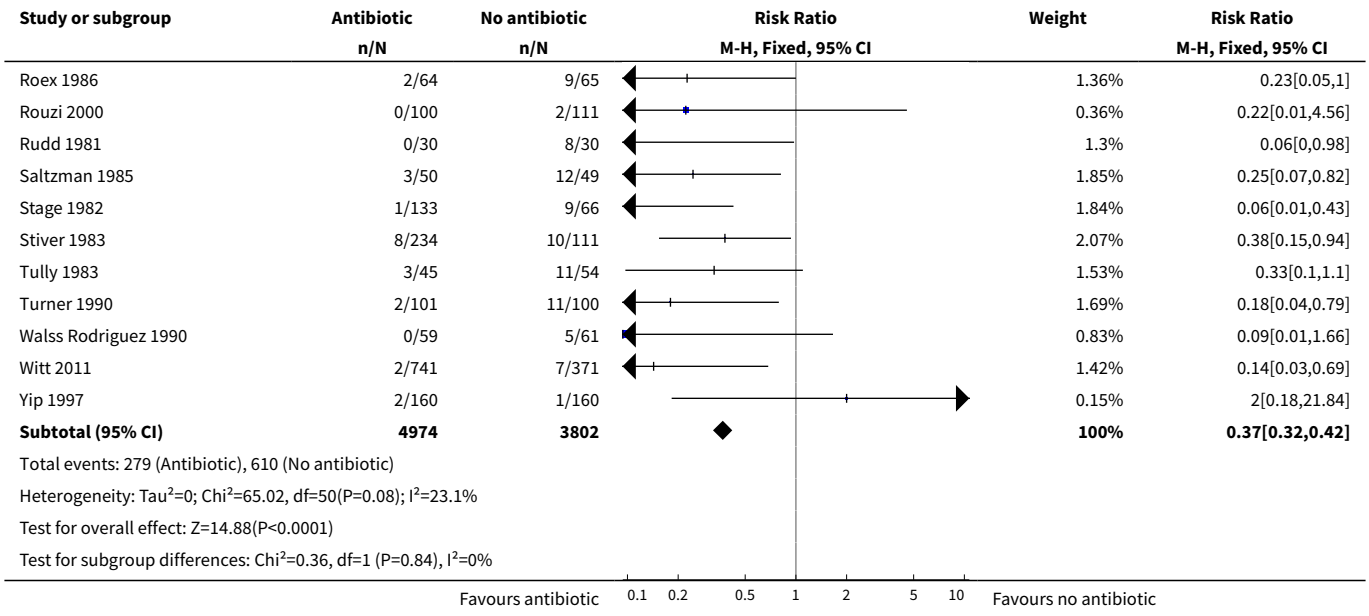
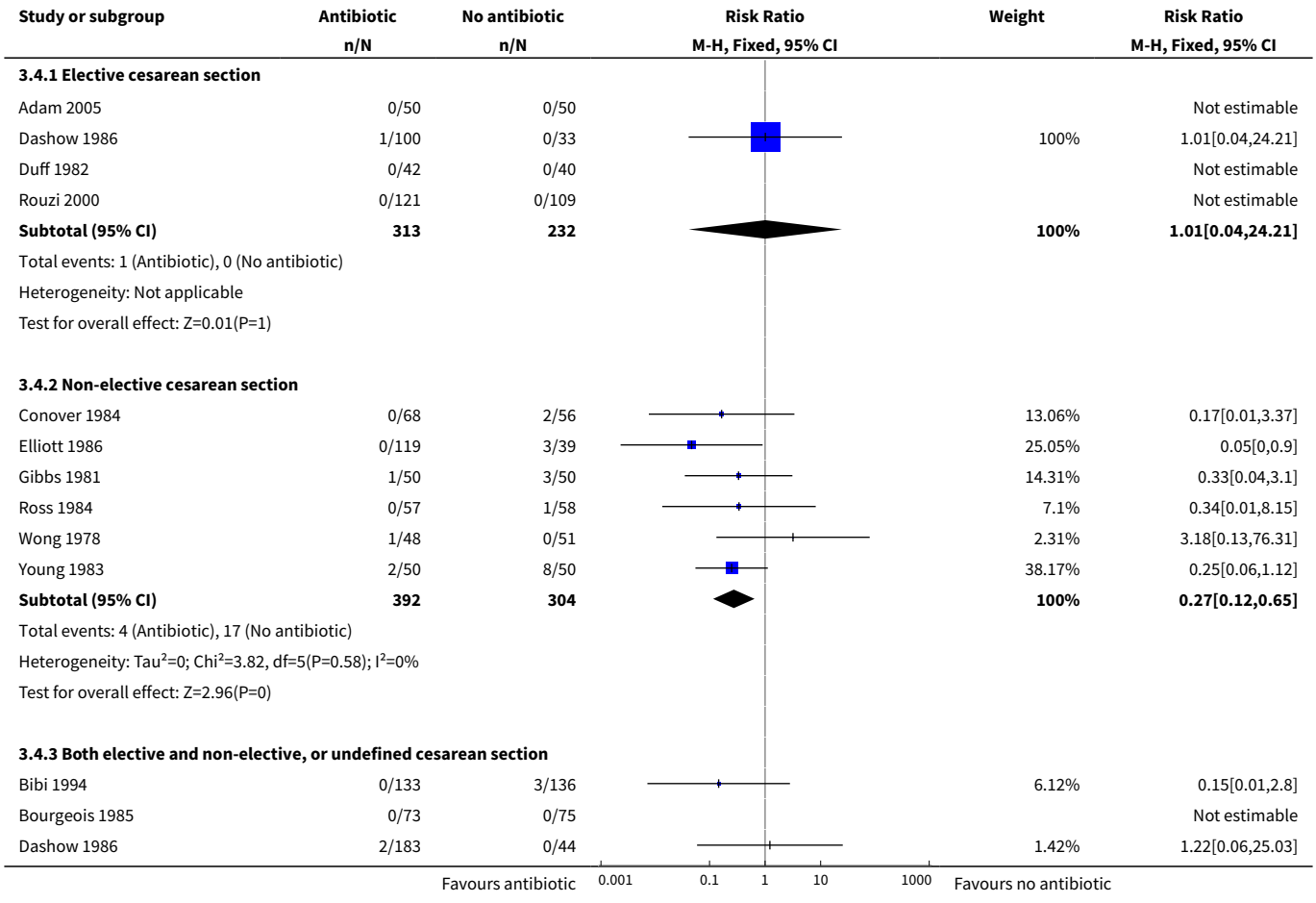


Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Roex 1986	2/64	9/65		1.36%	0.23[0.05,1]
Rouzi 2000	0/100	2/111		0.36%	0.22[0.01,4.56]
Rudd 1981	0/30	8/30		1.3%	0.06[0,0.98]
Saltzman 1985	3/50	12/49		1.85%	0.25[0.07,0.82]
Stage 1982	1/133	9/66		1.84%	0.06[0.01,0.43]
Stiver 1983	8/234	10/111		2.07%	0.38[0.15,0.94]
Tully 1983	3/45	11/54		1.53%	0.33[0.1,1.1]
Turner 1990	2/101	11/100		1.69%	0.18[0.04,0.79]
Walss Rodriguez 1990	0/59	5/61		0.83%	0.09[0.01,1.66]
Witt 2011	2/741	7/371		1.42%	0.14[0.03,0.69]
Yip 1997	2/160	1/160		0.15%	2[0.18,21.84]
Subtotal (95% CI)	**4974**	**3802**		**100%**	**0.37[0.32,0.42]**
Total events: 279 (Antibiotic), 610 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=65.02, df=50(P=0.08); I²=23.1%					
Test for overall effect: Z=14.88(P<0.0001)					
Test for subgroup differences: Chi²=0.36, df=1 (P=0.84), I²=0%					

Analysis 3.4. Comparison 3 Antibiotics versus no antibiotics - subgroup by type of cesarean section, Outcome 4 Maternal serious infectious complications.



Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.4.1 Elective cesarean section					
Adam 2005	0/50	0/50			Not estimable
Dashow 1986	1/100	0/33		100%	1.01[0.04,24.21]
Duff 1982	0/42	0/40			Not estimable
Rouzi 2000	0/121	0/109			Not estimable
Subtotal (95% CI)	**313**	**232**		**100%**	**1.01[0.04,24.21]**
Total events: 1 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.01(P=1)					
3.4.2 Non-elective cesarean section					
Conover 1984	0/68	2/56		13.06%	0.17[0.01,3.37]
Elliott 1986	0/119	3/39		25.05%	0.05[0,0.9]
Gibbs 1981	1/50	3/50		14.31%	0.33[0.04,3.1]
Ross 1984	0/57	1/58		7.1%	0.34[0.01,8.15]
Wong 1978	1/48	0/51		2.31%	3.18[0.13,76.31]
Young 1983	2/50	8/50		38.17%	0.25[0.06,1.12]
Subtotal (95% CI)	**392**	**304**		**100%**	**0.27[0.12,0.65]**
Total events: 4 (Antibiotic), 17 (No antibiotic)					
Heterogeneity: Tau²=0; Chi²=3.82, df=5(P=0.58); I²=0%					
Test for overall effect: Z=2.96(P=0)					
3.4.3 Both elective and non-elective, or undefined cesarean section					
Bibi 1994	0/133	3/136		6.12%	0.15[0.01,2.8]
Bourgeois 1985	0/73	0/75			Not estimable
Dashow 1986	2/183	0/44		1.42%	1.22[0.06,25.03]

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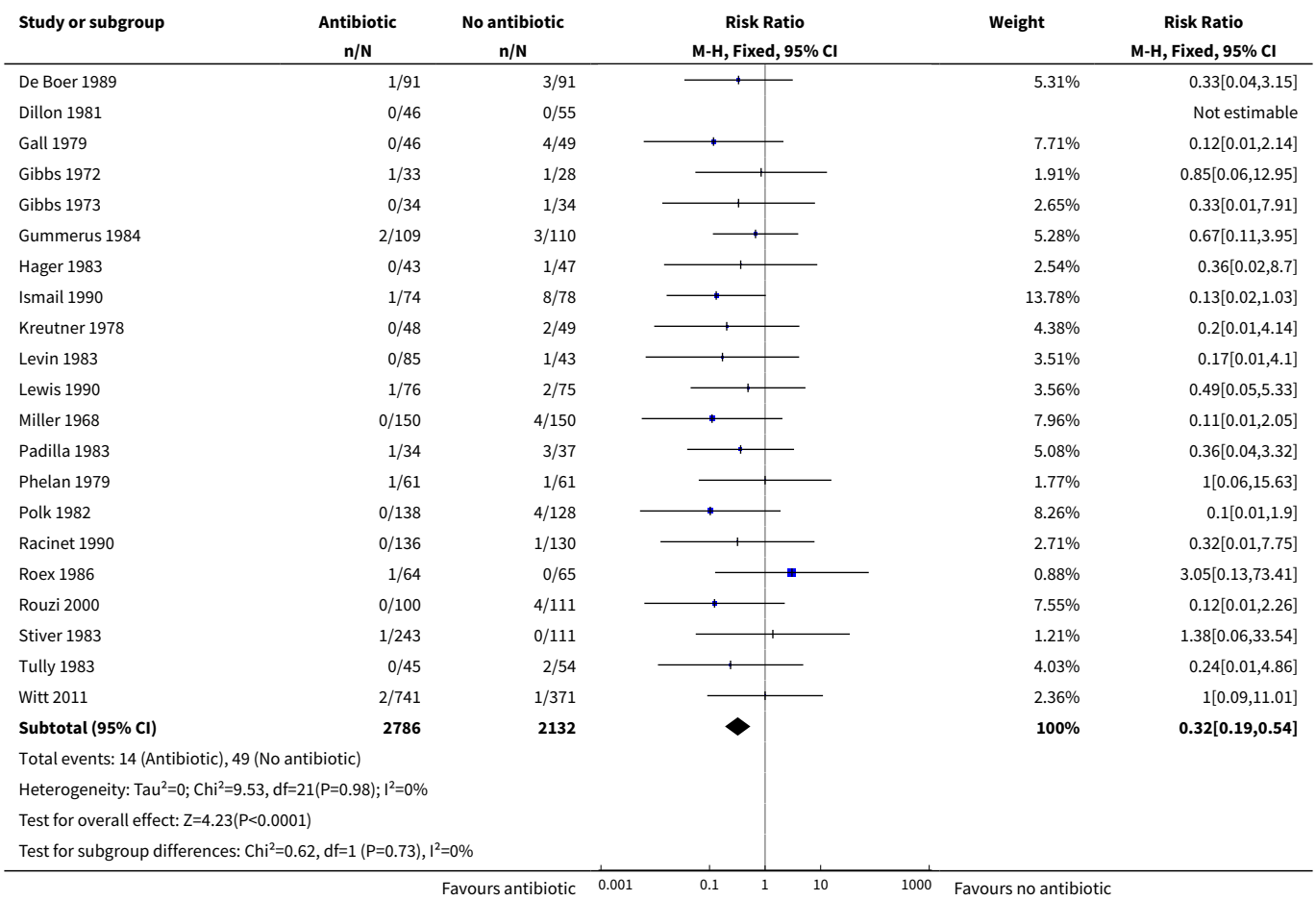
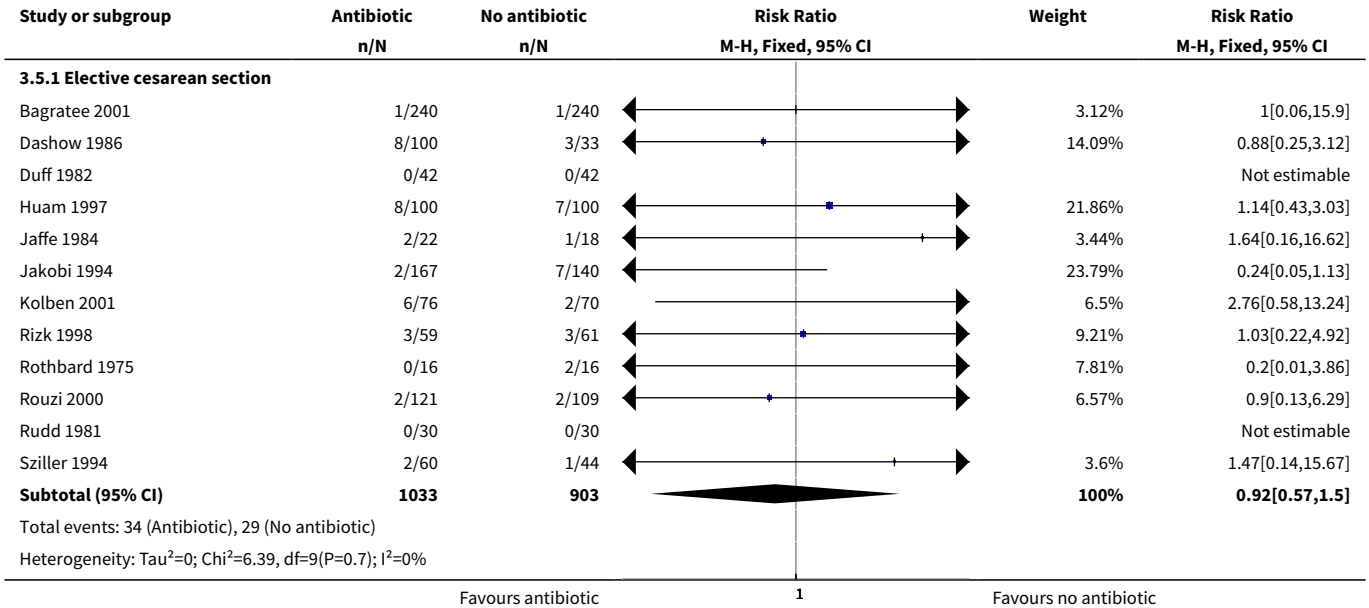


Analysis 3.5. Comparison 3 Antibiotics versus no antibiotics - subgroup by type of cesarean section, Outcome 5 Maternal urinary tract infection.



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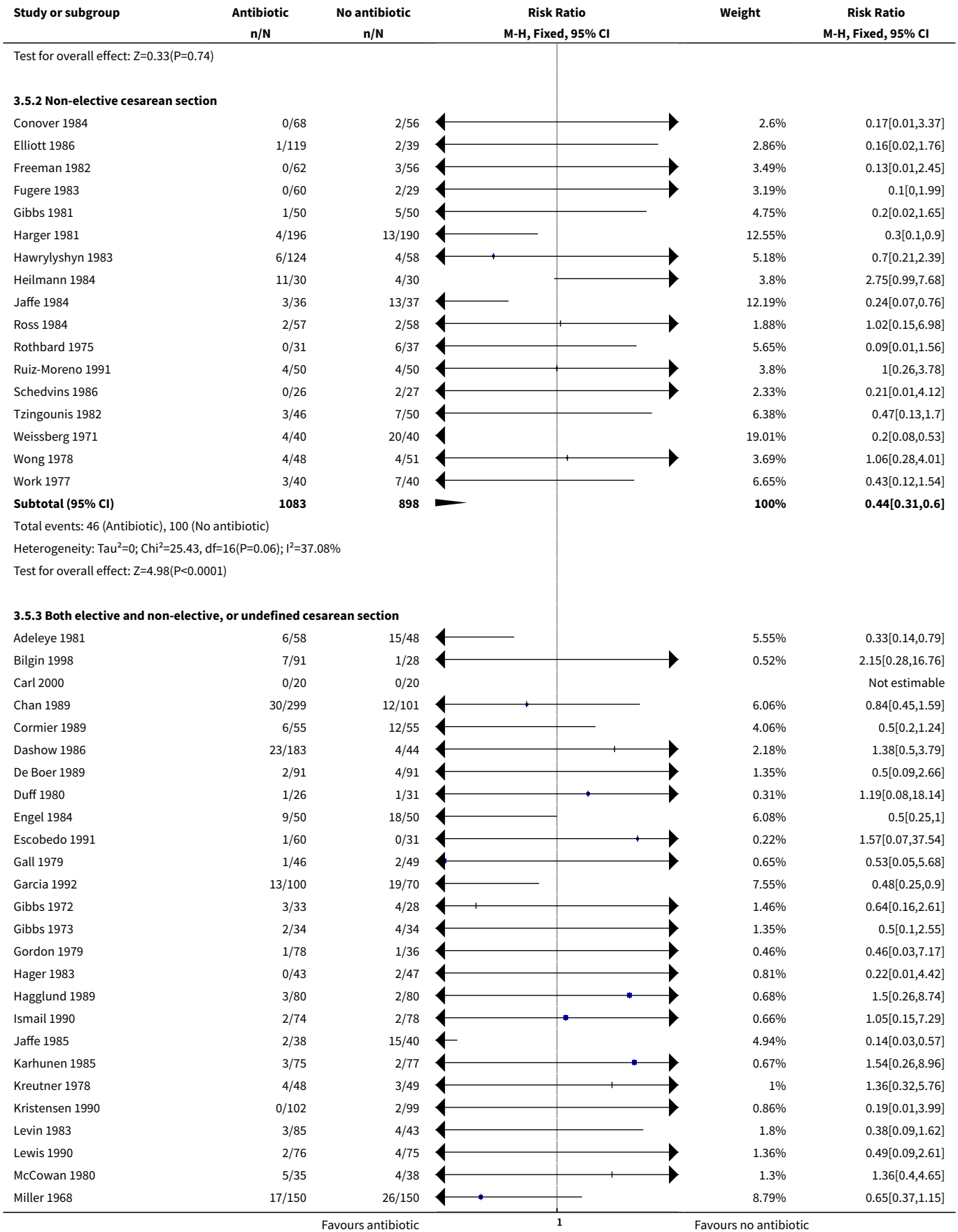

Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Test for overall effect: Z=0.33(P=0.74)					
3.5.2 Non-elective cesarean section					
Conover 1984	0/68	2/56		2.6%	0.17[0.01,3.37]
Elliott 1986	1/119	2/39		2.86%	0.16[0.02,1.76]
Freeman 1982	0/62	3/56		3.49%	0.13[0.01,2.45]
Fugere 1983	0/60	2/29		3.19%	0.1[0,1.99]
Gibbs 1981	1/50	5/50		4.75%	0.2[0.02,1.65]
Harger 1981	4/196	13/190		12.55%	0.3[0.1,0.9]
Hawrylyshyn 1983	6/124	4/58		5.18%	0.7[0.21,2.39]
Heilmann 1984	11/30	4/30		3.8%	2.75[0.99,7.68]
Jaffe 1984	3/36	13/37		12.19%	0.24[0.07,0.76]
Ross 1984	2/57	2/58		1.88%	1.02[0.15,6.98]
Rothbard 1975	0/31	6/37		5.65%	0.09[0.01,1.56]
Ruiz-Moreno 1991	4/50	4/50		3.8%	1[0.26,3.78]
Schedvins 1986	0/26	2/27		2.33%	0.21[0.01,4.12]
Tzingounis 1982	3/46	7/50		6.38%	0.47[0.13,1.7]
Weissberg 1971	4/40	20/40		19.01%	0.2[0.08,0.53]
Wong 1978	4/48	4/51		3.69%	1.06[0.28,4.01]
Work 1977	3/40	7/40		6.65%	0.43[0.12,1.54]
Subtotal (95% CI)	**1083**	**898**		**100%**	**0.44[0.31,0.6]**
Total events: 46 (Antibiotic), 100 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=25.43, df=16(P=0.06); I^2=37.08%					
Test for overall effect: Z=4.98(P<0.0001)					
3.5.3 Both elective and non-elective, or undefined cesarean section					
Adeleye 1981	6/58	15/48		5.55%	0.33[0.14,0.79]
Bilgin 1998	7/91	1/28		0.52%	2.15[0.28,16.76]
Carl 2000	0/20	0/20			Not estimable
Chan 1989	30/299	12/101		6.06%	0.84[0.45,1.59]
Cormier 1989	6/55	12/55		4.06%	0.5[0.2,1.24]
Dashow 1986	23/183	4/44		2.18%	1.38[0.5,3.79]
De Boer 1989	2/91	4/91		1.35%	0.5[0.09,2.66]
Duff 1980	1/26	1/31		0.31%	1.19[0.08,18.14]
Engel 1984	9/50	18/50		6.08%	0.5[0.25,1]
Escobedo 1991	1/60	0/31		0.22%	1.57[0.07,37.54]
Gall 1979	1/46	2/49		0.65%	0.53[0.05,5.68]
Garcia 1992	13/100	19/70		7.55%	0.48[0.25,0.9]
Gibbs 1972	3/33	4/28		1.46%	0.64[0.16,2.61]
Gibbs 1973	2/34	4/34		1.35%	0.5[0.1,2.55]
Gordon 1979	1/78	1/36		0.46%	0.46[0.03,7.17]
Hager 1983	0/43	2/47		0.81%	0.22[0.01,4.42]
Hagglund 1989	3/80	2/80		0.68%	1.5[0.26,8.74]
Ismail 1990	2/74	2/78		0.66%	1.05[0.15,7.29]
Jaffe 1985	2/38	15/40		4.94%	0.14[0.03,0.57]
Karhunen 1985	3/75	2/77		0.67%	1.54[0.26,8.96]
Kreutner 1978	4/48	3/49		1%	1.36[0.32,5.76]
Kristensen 1990	0/102	2/99		0.86%	0.19[0.01,3.99]
Levin 1983	3/85	4/43		1.8%	0.38[0.09,1.62]
Lewis 1990	2/76	4/75		1.36%	0.49[0.09,2.61]
McCowan 1980	5/35	4/38		1.3%	1.36[0.4,4.65]
Miller 1968	17/150	26/150		8.79%	0.65[0.37,1.15]

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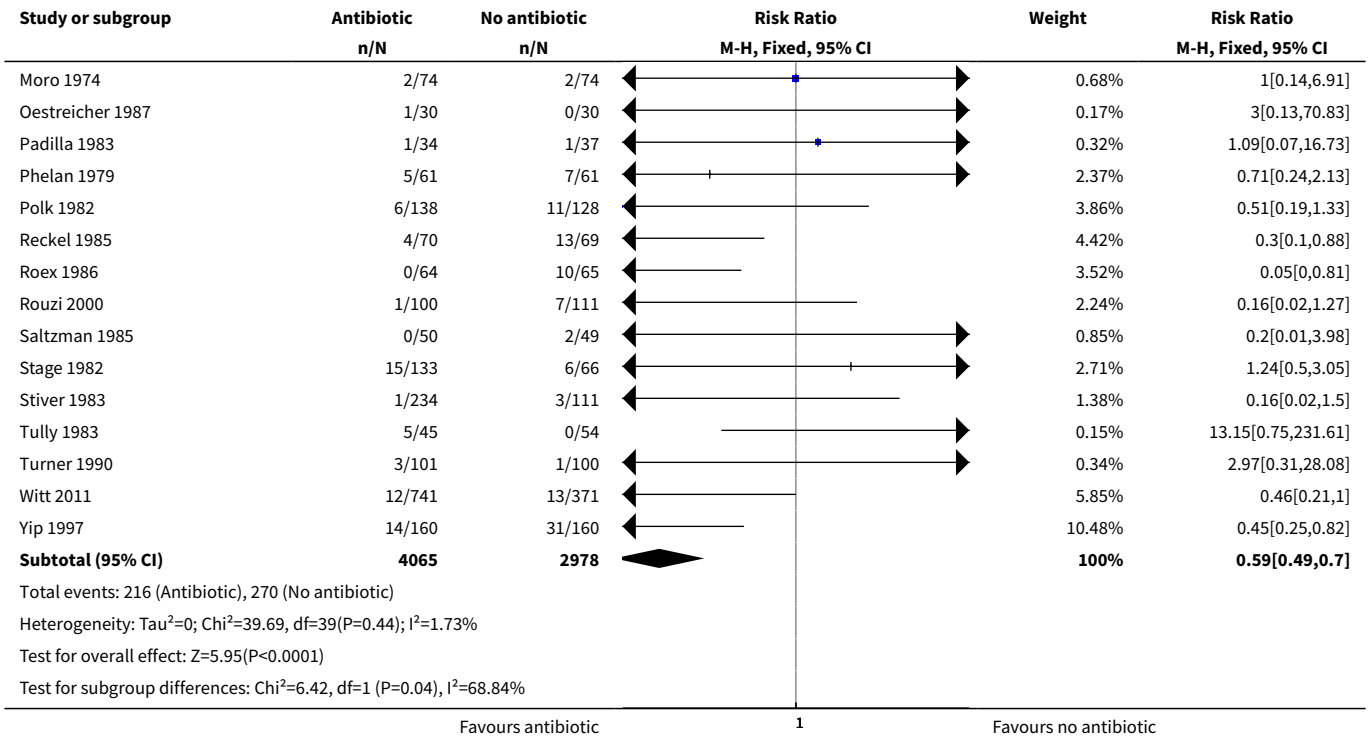
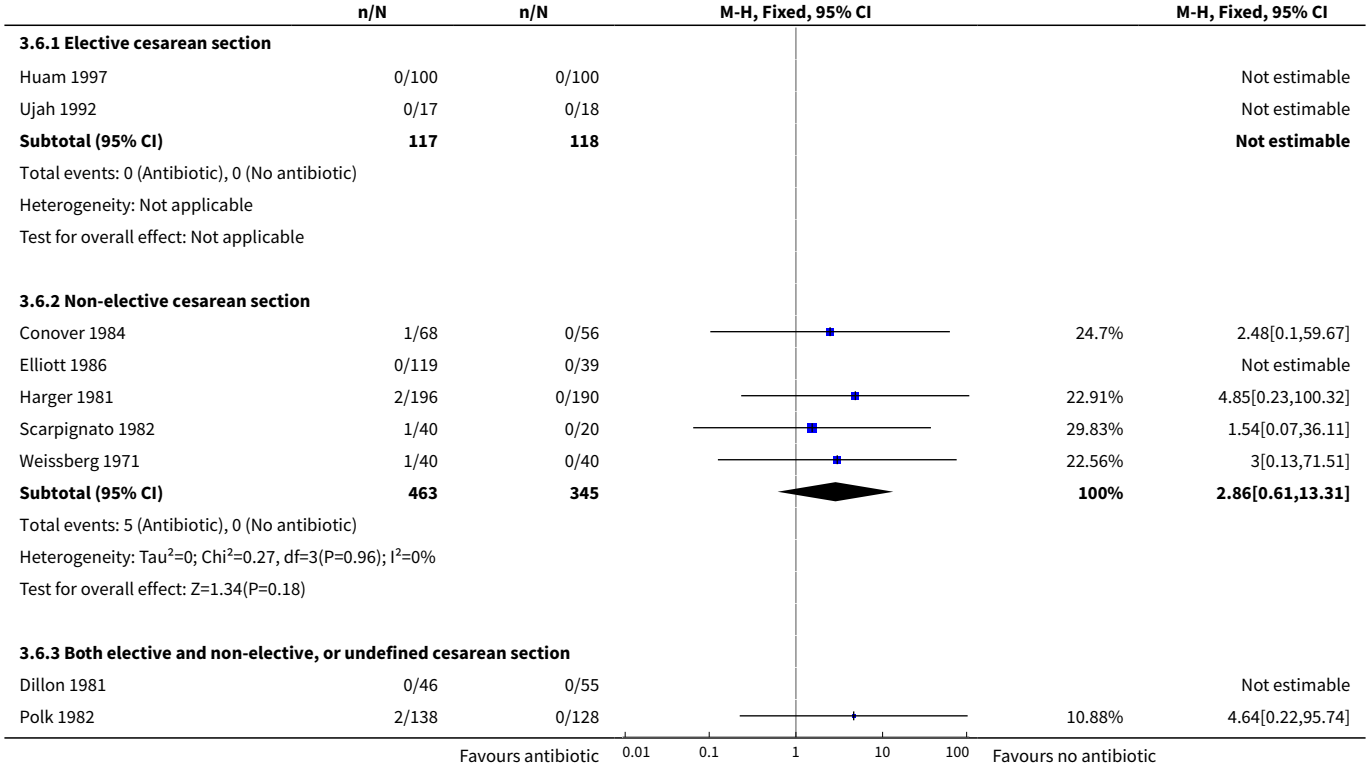


Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Moro 1974	2/74	2/74		0.68%	1[0.14,6.91]
Oestreicher 1987	1/30	0/30		0.17%	3[0.13,70.83]
Padilla 1983	1/34	1/37		0.32%	1.09[0.07,16.73]
Phelan 1979	5/61	7/61		2.37%	0.71[0.24,2.13]
Polk 1982	6/138	11/128		3.86%	0.51[0.19,1.33]
Reckel 1985	4/70	13/69		4.42%	0.3[0.1,0.88]
Roex 1986	0/64	10/65		3.52%	0.05[0,0.81]
Rouzi 2000	1/100	7/111		2.24%	0.16[0.02,1.27]
Saltzman 1985	0/50	2/49		0.85%	0.2[0.01,3.98]
Stage 1982	15/133	6/66		2.71%	1.24[0.5,3.05]
Stiver 1983	1/234	3/111		1.38%	0.16[0.02,1.5]
Tully 1983	5/45	0/54		0.15%	13.15[0.75,231.61]
Turner 1990	3/101	1/100		0.34%	2.97[0.31,28.08]
Witt 2011	12/741	13/371		5.85%	0.46[0.21,1]
Yip 1997	14/160	31/160		10.48%	0.45[0.25,0.82]
Subtotal (95% CI)	**4065**	**2978**		**100%**	**0.59[0.49,0.7]**
Total events: 216 (Antibiotic), 270 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=39.69, df=39(P=0.44); I^2=1.73%					
Test for overall effect: Z=5.95(P<0.0001)					
Test for subgroup differences: Chi^2=6.42, df=1 (P=0.04), I^2=68.84%					

Analysis 3.6. Comparison 3 Antibiotics versus no antibiotics - subgroup by type of cesarean section, Outcome 6 Maternal adverse effects.



Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.6.1 Elective cesarean section					
Huam 1997	0/100	0/100			Not estimable
Ujah 1992	0/17	0/18			Not estimable
Subtotal (95% CI)	**117**	**118**			**Not estimable**
Total events: 0 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.6.2 Non-elective cesarean section					
Conover 1984	1/68	0/56		24.7%	2.48[0.1,59.67]
Elliott 1986	0/119	0/39			Not estimable
Harger 1981	2/196	0/190		22.91%	4.85[0.23,100.32]
Scarpignato 1982	1/40	0/20		29.83%	1.54[0.07,36.11]
Weissberg 1971	1/40	0/40		22.56%	3[0.13,71.51]
Subtotal (95% CI)	**463**	**345**		**100%**	**2.86[0.61,13.31]**
Total events: 5 (Antibiotic), 0 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=0.27, df=3(P=0.96); I^2=0%					
Test for overall effect: Z=1.34(P=0.18)					
3.6.3 Both elective and non-elective, or undefined cesarean section					
Dillon 1981	0/46	0/55			Not estimable
Polk 1982	2/138	0/128		10.88%	4.64[0.22,95.74]

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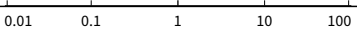
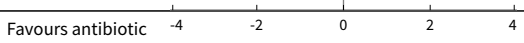
Study or subgroup	Antibiotic n/N	No antibiotic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Reckel 1985	1/70	0/69		10.56%	2.96[0.12,71.38]
Roex 1986	1/64	0/65		10.4%	3.05[0.13,73.41]
Saltzman 1985	1/50	0/49		10.59%	2.94[0.12,70.5]
Stiver 1983	6/243	2/111		57.57%	1.37[0.28,6.68]
Subtotal (95% CI)	**611**	**477**		**100%**	**2.23[0.75,6.63]**
Total events: 11 (Antibiotic), 2 (No antibiotic)					
Heterogeneity: Tau^2=0; Chi^2=0.68, df=4(P=0.95); I^2=0%					
Test for overall effect: Z=1.45(P=0.15)					
Test for subgroup differences: Chi^2=0.07, df=1 (P=0.8), I^2=0%					



Analysis 3.7. Comparison 3 Antibiotics versus no antibiotics - subgroup by type of cesarean section, Outcome 7 Maternal days in hospital.

Study or subgroup	Antibiotic N	Antibiotic Mean(SD)	No antibiotic N	No antibiotic Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
3.7.1 Elective cesarean section							
Bagratee 2001	240	6.9 (2.4)	240	7.8 (4.4)		10.6%	-0.9[-1.53,-0.27]
Huam 1997	100	5.2 (0.7)	100	5.9 (2.8)		13.32%	-0.71[-1.28,-0.14]
Rizk 1998	59	6.5 (1)	61	6.8 (0.8)		40.43%	-0.3[-0.62,0.02]
Rouzi 2000	121	5.6 (1.5)	109	5.7 (1.7)		24.69%	-0.15[-0.57,0.27]
Ujah 1992	17	7.7 (0.6)	18	8.3 (1.2)		10.96%	-0.6[-1.22,0.02]
Subtotal ***	**537**		**528**			**100%**	**-0.41[-0.62,-0.21]**
Heterogeneity: Tau^2=0; Chi^2=5.68, df=4(P=0.22); I^2=29.52%							
Test for overall effect: Z=3.93(P<0.0001)							
3.7.2 Non-elective cesarean section							
Gibbs 1981	50	4.4 (2)	50	5.3 (2.1)		15.58%	-0.9[-1.7,-0.1]
Harger 1981	196	6.5 (1.8)	190	6.8 (2.2)		62.4%	-0.3[-0.7,0.1]
Heilmann 1984	30	13 (4)	30	14 (4)		2.46%	-1[-3.02,1.02]
Ruiz-Moreno 1991	50	4.7 (1.5)	50	5.2 (2.1)		19.56%	-0.56[-1.28,0.16]
Subtotal ***	**326**		**320**			**100%**	**-0.46[-0.78,-0.14]**
Heterogeneity: Tau^2=0; Chi^2=2.11, df=3(P=0.55); I^2=0%							
Test for overall effect: Z=2.85(P=0)							
3.7.3 Both elective and non-elective, or undefined cesarean section							
De Boer 1989	91	9.4 (2.6)	91	11 (5.1)		2.39%	-1.6[-2.78,-0.42]
Dillon 1981	46	5.9 (1.1)	55	6.1 (1.7)		10.94%	-0.16[-0.71,0.39]
Gall 1979	46	8 (1.5)	49	8.4 (1.9)		6.84%	-0.41[-1.11,0.29]
Gerstner 1980	53	11.2 (2.1)	50	12.1 (3.2)		2.99%	-0.9[-1.95,0.15]
Lapas 1988	50	6.7 (2)	50	7.8 (2.7)		3.83%	-1.08[-2.01,-0.15]
Padilla 1983	34	5.8 (1.1)	37	7.1 (2.6)		3.95%	-1.3[-2.22,-0.38]
Racinet 1990	136	8.2 (1.8)	130	8.7 (1.9)		16.71%	-0.5[-0.95,-0.05]
Rouzi 2000	100	5.7 (1.5)	111	6.6 (2.4)		11.46%	-0.86[-1.4,-0.32]
Tully 1983	45	6 (1.6)	54	6 (1.6)		8.27%	0[-0.63,0.63]
Walss Rodriguez 1990	59	3.1 (0.6)	61	3.7 (2.4)		8.58%	-0.6[-1.22,0.02]
Yip 1997	160	6.2 (1.9)	160	6 (1.4)		24.03%	0.19[-0.18,0.56]
Subtotal ***	**820**		**848**			**100%**	**-0.39[-0.57,-0.21]**
Heterogeneity: Tau^2=0; Chi^2=25.99, df=10(P=0); I^2=61.53%							



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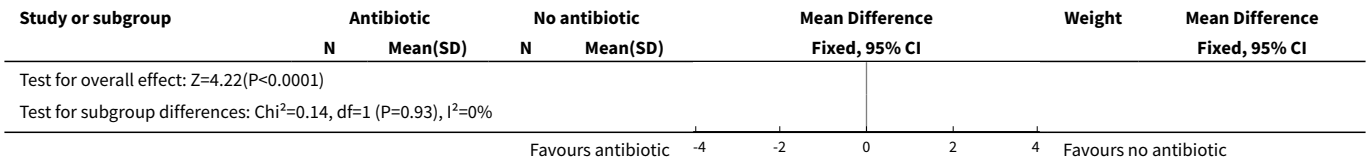

Comparison 4. Antibiotics versus no antibiotics - subgroup by timing of administration

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maternal febrile morbidity/fever	56		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Before cord clamping	26	3560	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.42, 0.56]
1.2 After cord clamping	25	5095	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.39, 0.50]
1.3 Timing not defined	5	391	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.15, 0.38]
2 Maternal wound infection	82		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Before cord clamping	37	5593	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.32, 0.47]
2.2 After cord clamping	42	8428	Risk Ratio (M-H, Fixed, 95% CI)	0.41 [0.34, 0.50]
2.3 Timing not defined	5	385	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.11, 0.85]
3 Maternal endometritis	83		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Before cord clamping	32	4965	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.26, 0.40]
3.2 After cord clamping	48	8213	Risk Ratio (M-H, Fixed, 95% CI)	0.40 [0.36, 0.46]
3.3 Timing not defined	5	409	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.18, 0.50]
4 Maternal serious infectious complications	32		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Before cord clamping	13	2194	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.12, 0.64]
4.2 After cord clamping	19	3893	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.19, 0.55]
4.3 Timing not defined	1	71	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.04, 3.32]
5 Maternal urinary tract infections	66		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Before cord clamping	30	4443	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.50, 0.74]
5.2 After cord clamping	34	6166	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.43, 0.68]
5.3 Timing not defined	4	350	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.18, 0.75]

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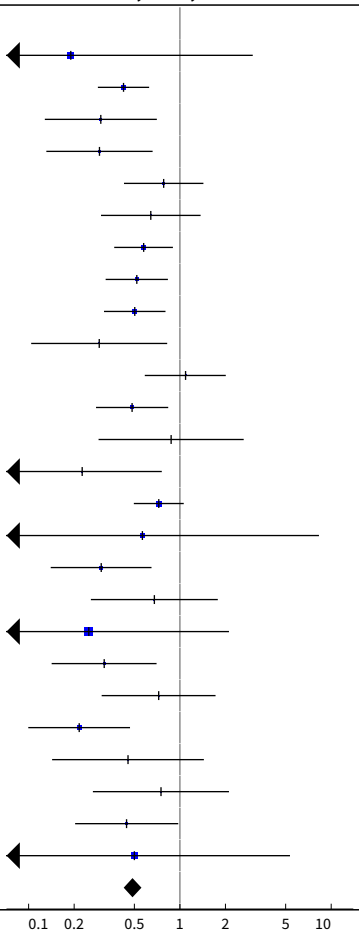
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Maternal adverse effects	13		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Before cord clamping	2	339	Risk Ratio (M-H, Fixed, 95% CI)	2.96 [0.12, 71.38]
6.2 After cord clamping	8	1617	Risk Ratio (M-H, Fixed, 95% CI)	2.44 [0.88, 6.75]
6.3 Timing not defined	3	175	Risk Ratio (M-H, Fixed, 95% CI)	2.17 [0.24, 19.70]
7 Maternal days in hospital	19		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Before cord clamping	7	1060	Mean Difference (IV, Fixed, 95% CI)	-0.33 [-0.59, -0.08]
7.2 After cord clamping	10	2213	Mean Difference (IV, Fixed, 95% CI)	-0.40 [-0.55, -0.25]
7.3 Timing not defined	2	106	Mean Difference (IV, Fixed, 95% CI)	-0.82 [-1.34, -0.31]

Analysis 4.1. Comparison 4 Antibiotics versus no antibiotics - subgroup by timing of administration, Outcome 1 Maternal febrile morbidity/fever.

Study or subgroup	Antibiotics n/N	No antibiotics n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
4.1.1 Before cord clamping					
Allen 1972	0/5	3/7		0.64%	0.19[0.01,3.03]
Morrison 1973	25/115	59/115		12.57%	0.42[0.29,0.63]
Moro 1974	6/74	20/74		4.26%	0.3[0.13,0.7]
Rothbard 1975	6/47	23/53		4.6%	0.29[0.13,0.66]
Kreutner 1978	13/48	17/49		3.58%	0.78[0.43,1.43]
Duff 1980	7/26	13/31		2.53%	0.64[0.3,1.37]
Stage 1982	29/133	25/66		7.12%	0.58[0.37,0.9]
Work 1977	14/40	27/40		5.75%	0.52[0.32,0.83]
Gerstner 1980	16/53	30/50		6.58%	0.5[0.32,0.8]
Duff 1982	4/42	13/40		2.84%	0.29[0.1,0.82]
McCowan 1980	13/35	13/38		2.65%	1.09[0.59,2.01]
Tzingounis 1982	12/46	27/50		5.51%	0.48[0.28,0.84]
Moodley 1981	7/40	4/20		1.14%	0.88[0.29,2.64]
Freeman 1982	3/62	12/56		2.69%	0.23[0.07,0.76]
De Boer 1989	29/91	40/91		8.52%	0.73[0.5,1.06]
Magro 1983	1/23	1/13		0.27%	0.57[0.04,8.3]
Jaffe 1984	7/58	22/55		4.81%	0.3[0.14,0.65]
Ross 1984	6/57	9/58		1.9%	0.68[0.26,1.78]
Heilmann 1984	1/30	4/30		0.85%	0.25[0.03,2.11]
Jaffe 1985	6/38	20/40		4.15%	0.32[0.14,0.7]
Chan 1989	15/299	7/101		2.23%	0.72[0.3,1.72]
Mahomed 1988	7/115	33/117		6.97%	0.22[0.1,0.47]
Bibi 1994	4/133	9/136		1.9%	0.45[0.14,1.44]
Yip 1997	6/160	8/160		1.7%	0.75[0.27,2.11]
Huam 1997	8/100	18/100		3.83%	0.44[0.2,0.97]
Adam 2005	1/50	2/50		0.43%	0.5[0.05,5.34]
Subtotal (95% CI)	**1920**	**1640**		**100%**	**0.49[0.42,0.56]**



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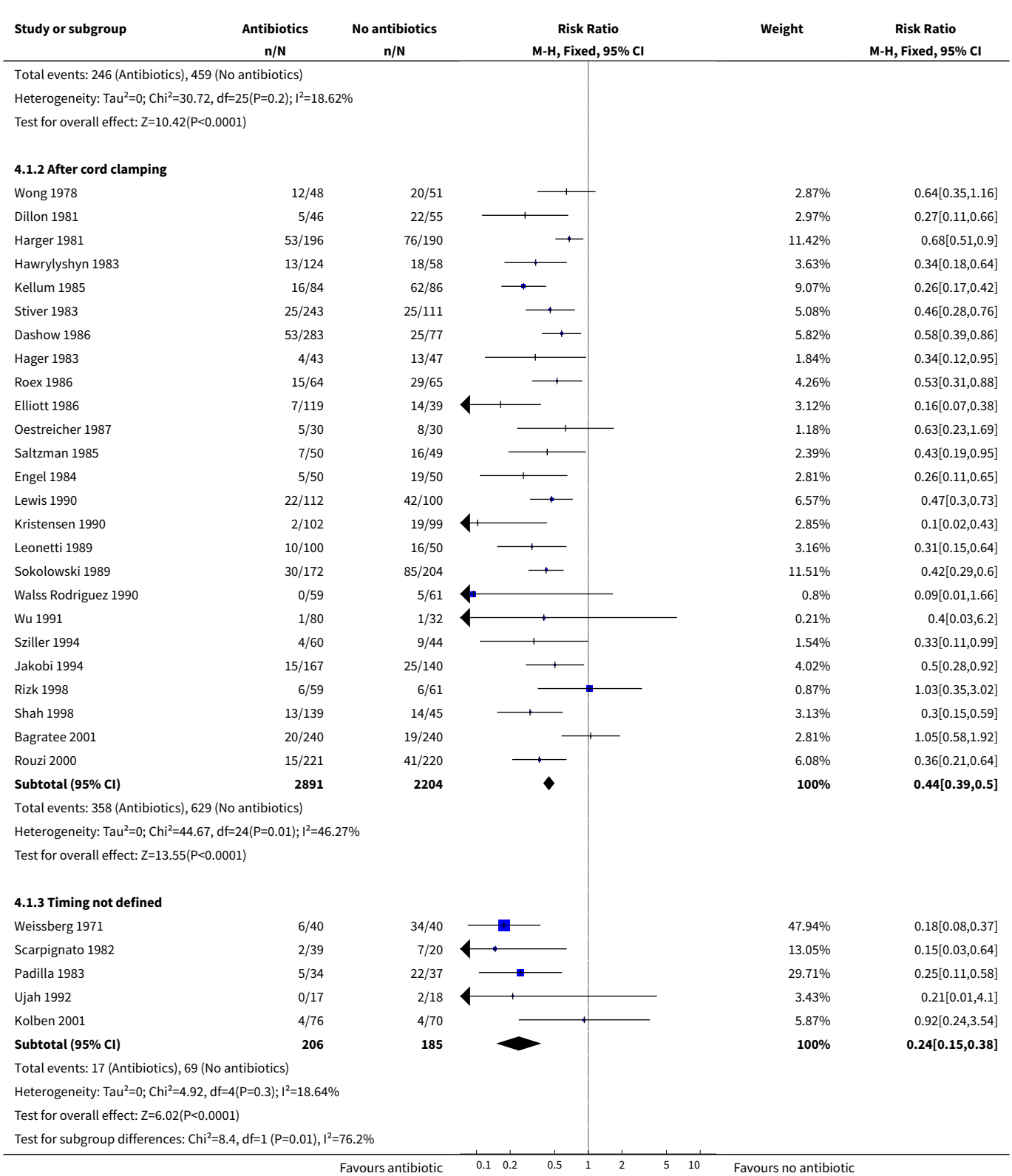

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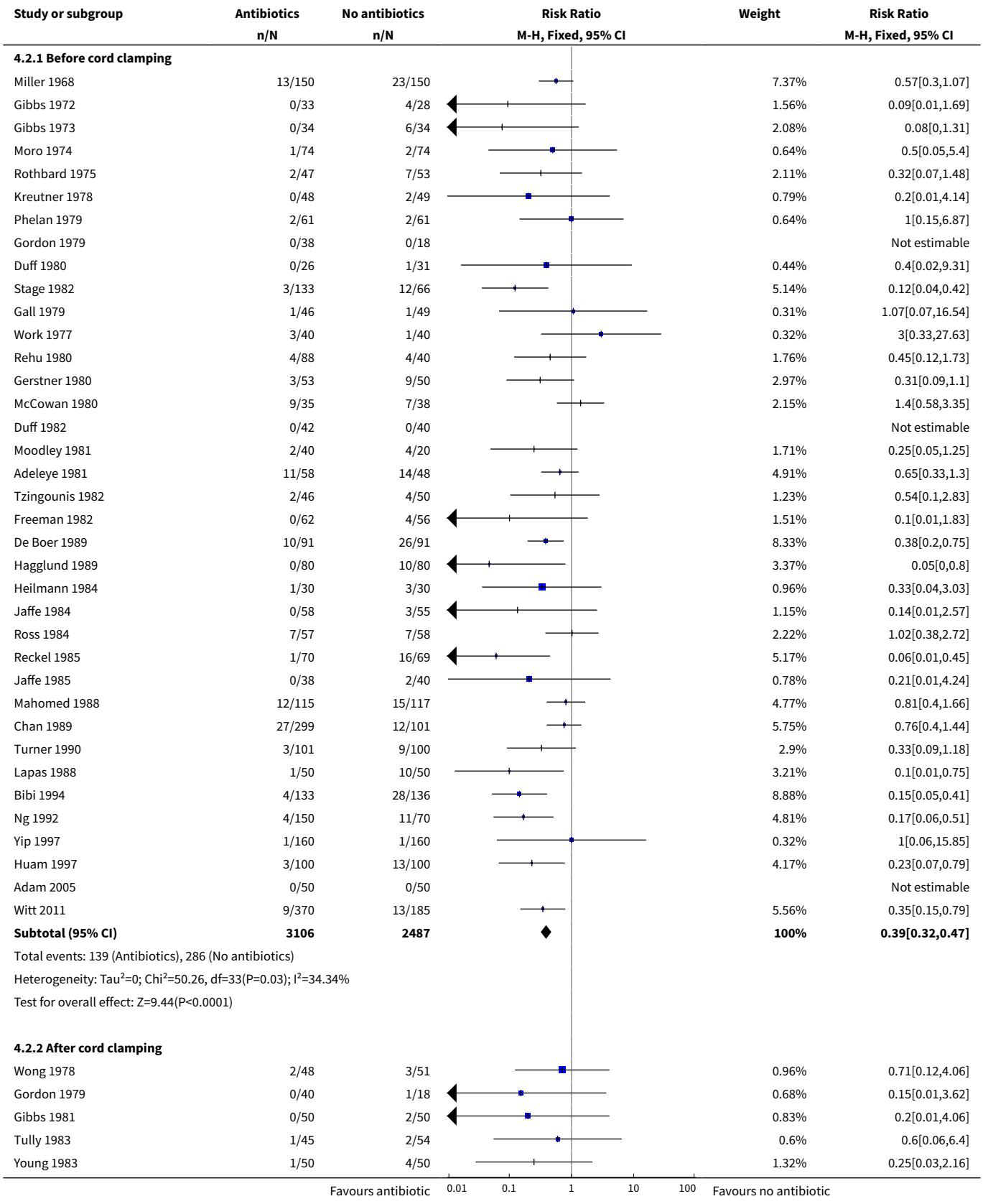
Analysis 4.2. Comparison 4 Antibiotics versus no antibiotics - subgroup by timing of administration, Outcome 2 Maternal wound infection.



Study or subgroup	Antibiotics n/N	No antibiotics n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
4.2.1 Before cord clamping					
Miller 1968	13/150	23/150		7.37%	0.57[0.3,1.07]
Gibbs 1972	0/33	4/28		1.56%	0.09[0.01,1.69]
Gibbs 1973	0/34	6/34		2.08%	0.08[0,1.31]
Moro 1974	1/74	2/74		0.64%	0.5[0.05,5.4]
Rothbard 1975	2/47	7/53		2.11%	0.32[0.07,1.48]
Kreutner 1978	0/48	2/49		0.79%	0.2[0.01,4.14]
Phelan 1979	2/61	2/61		0.64%	1[0.15,6.87]
Gordon 1979	0/38	0/18			Not estimable
Duff 1980	0/26	1/31		0.44%	0.4[0.02,9.31]
Stage 1982	3/133	12/66		5.14%	0.12[0.04,0.42]
Gall 1979	1/46	1/49		0.31%	1.07[0.07,16.54]
Work 1977	3/40	1/40		0.32%	3[0.33,27.63]
Rehu 1980	4/88	4/40		1.76%	0.45[0.12,1.73]
Gerstner 1980	3/53	9/50		2.97%	0.31[0.09,1.1]
McCowan 1980	9/35	7/38		2.15%	1.4[0.58,3.35]
Duff 1982	0/42	0/40			Not estimable
Moodley 1981	2/40	4/20		1.71%	0.25[0.05,1.25]
Adeleye 1981	11/58	14/48		4.91%	0.65[0.33,1.3]
Tzingounis 1982	2/46	4/50		1.23%	0.54[0.1,2.83]
Freeman 1982	0/62	4/56		1.51%	0.1[0.01,1.83]
De Boer 1989	10/91	26/91		8.33%	0.38[0.2,0.75]
Hagglund 1989	0/80	10/80		3.37%	0.05[0,0.8]
Heilmann 1984	1/30	3/30		0.96%	0.33[0.04,3.03]
Jaffe 1984	0/58	3/55		1.15%	0.14[0.01,2.57]
Ross 1984	7/57	7/58		2.22%	1.02[0.38,2.72]
Reckel 1985	1/70	16/69		5.17%	0.06[0.01,0.45]
Jaffe 1985	0/38	2/40		0.78%	0.21[0.01,4.24]
Mahomed 1988	12/115	15/117		4.77%	0.81[0.4,1.66]
Chan 1989	27/299	12/101		5.75%	0.76[0.4,1.44]
Turner 1990	3/101	9/100		2.9%	0.33[0.09,1.18]
Lapas 1988	1/50	10/50		3.21%	0.1[0.01,0.75]
Bibi 1994	4/133	28/136		8.88%	0.15[0.05,0.41]
Ng 1992	4/150	11/70		4.81%	0.17[0.06,0.51]
Yip 1997	1/160	1/160		0.32%	1[0.06,15.85]
Huam 1997	3/100	13/100		4.17%	0.23[0.07,0.79]
Adam 2005	0/50	0/50			Not estimable
Witt 2011	9/370	13/185		5.56%	0.35[0.15,0.79]
Subtotal (95% CI)	**3106**	**2487**		**100%**	**0.39[0.32,0.47]**
Total events: 139 (Antibiotics), 286 (No antibiotics)					
Heterogeneity: Tau^2=0; Chi^2=50.26, df=33(P=0.03); I^2=34.34%					
Test for overall effect: Z=9.44(P<0.0001)					
4.2.2 After cord clamping					
Wong 1978	2/48	3/51		0.96%	0.71[0.12,4.06]
Gordon 1979	0/40	1/18		0.68%	0.15[0.01,3.62]
Gibbs 1981	0/50	2/50		0.83%	0.2[0.01,4.06]
Tully 1983	1/45	2/54		0.6%	0.6[0.06,6.4]
Young 1983	1/50	4/50		1.32%	0.25[0.03,2.16]

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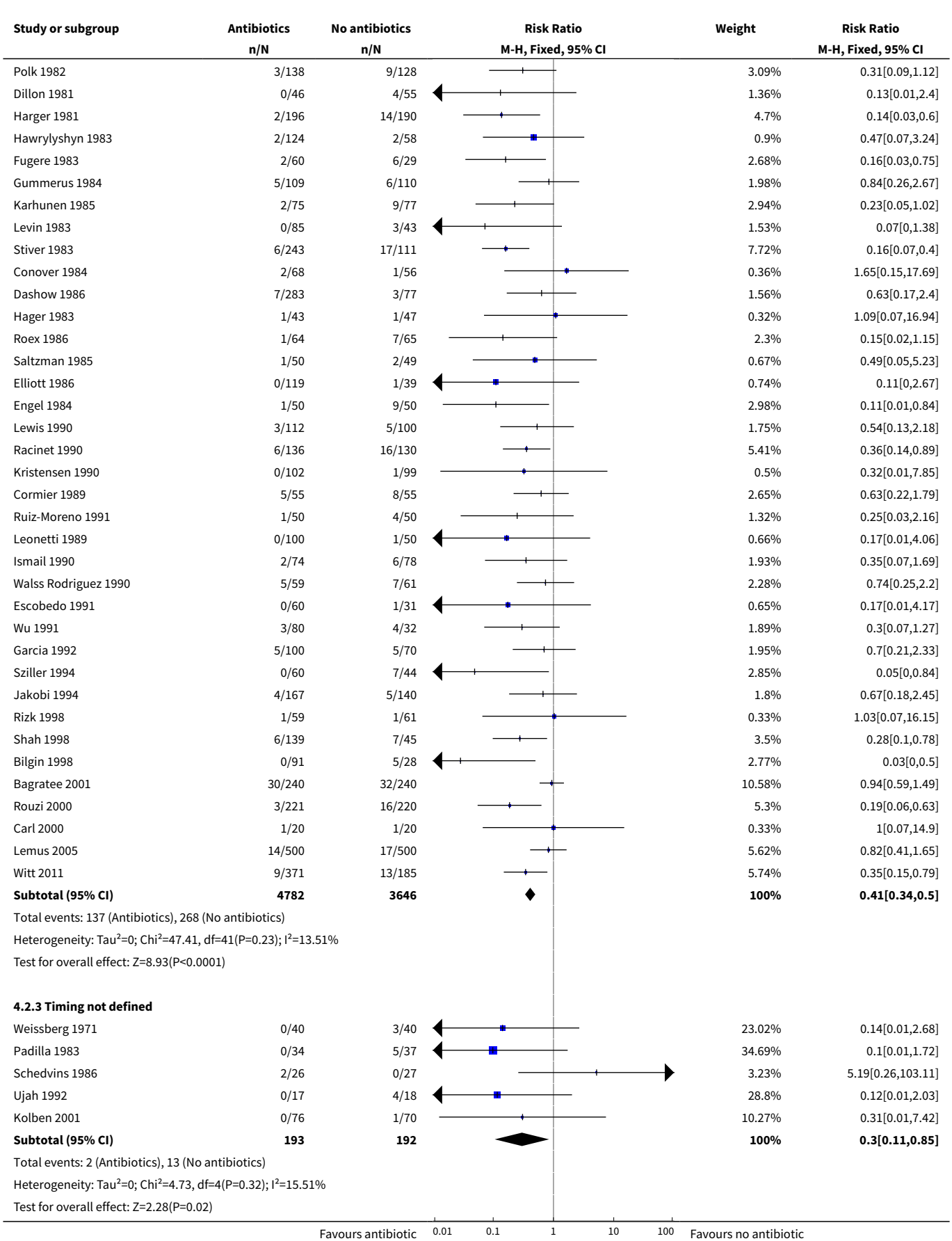

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Study or subgroup	Antibiotics n/N	No antibiotics n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Test for subgroup differences: Chi²=0.43, df=1 (P=0.81), I²=0%					

Favours antibiotic 0.01 0.1 1 10 100 Favours no antibiotic

Analysis 4.3. Comparison 4 Antibiotics versus no antibiotics - subgroup by timing of administration, Outcome 3 Maternal endometritis.

Study or subgroup	Antibiotics n/N	No antibiotics n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
4.3.1 Before cord clamping					
Miller 1968	1/150	8/150		2.78%	0.13[0.02,0.99]
Gibbs 1972	7/33	8/28		3.01%	0.74[0.31,1.79]
Gibbs 1973	6/34	20/34		6.95%	0.3[0.14,0.65]
Moro 1974	2/74	12/74		4.17%	0.17[0.04,0.72]
Rothbard 1975	1/47	8/53		2.61%	0.14[0.02,1.09]
Kreutner 1978	6/48	10/49		3.44%	0.61[0.24,1.55]
Duff 1980	2/26	13/31		4.12%	0.18[0.05,0.74]
Phelan 1979	5/61	8/61		2.78%	0.63[0.22,1.8]
Gordon 1979	4/38	6/18		2.83%	0.32[0.1,0.98]
Stage 1982	1/133	9/66		4.18%	0.06[0.01,0.43]
Rehu 1980	7/88	13/40		6.21%	0.24[0.11,0.57]
Gall 1979	5/46	7/49		2.36%	0.76[0.26,2.23]
Work 1977	8/40	17/40		5.91%	0.47[0.23,0.96]
Duff 1982	1/42	6/40		2.14%	0.16[0.02,1.26]
Gerstner 1980	7/53	15/50		5.37%	0.44[0.2,0.99]
McCowan 1980	4/35	5/38		1.67%	0.87[0.25,2.98]
Tzingounis 1982	4/46	8/50		2.67%	0.54[0.18,1.68]
Freeman 1982	3/62	5/56		1.83%	0.54[0.14,2.16]
Hagglund 1989	2/80	20/80		6.95%	0.1[0.02,0.41]
Jaffe 1984	0/58	6/55		2.32%	0.07[0,1.27]
Ross 1984	2/57	2/58		0.69%	1.02[0.15,6.98]
Reckel 1985	1/70	6/69		2.1%	0.16[0.02,1.33]
Jaffe 1985	0/38	7/40		2.54%	0.07[0,1.19]
Mahomed 1988	0/115	6/117		2.24%	0.08[0,1.37]
Chan 1989	14/299	4/101		2.08%	1.18[0.4,3.51]
Turner 1990	2/101	11/100		3.84%	0.18[0.04,0.79]
Lapas 1988	2/50	10/50		3.48%	0.2[0.05,0.87]
Bibi 1994	3/133	18/136		6.19%	0.17[0.05,0.57]
Yip 1997	2/160	1/160		0.35%	2[0.18,21.84]
Huam 1997	0/100	0/100			Not estimable
Adam 2005	1/50	1/50		0.35%	1[0.06,15.55]
Witt 2011	1/370	4/185		1.85%	0.13[0.01,1.11]
Subtotal (95% CI)	**2737**	**2228**		**100%**	**0.33[0.26,0.4]**
Total events: 104 (Antibiotics), 274 (No antibiotics)					
Heterogeneity: Tau²=0; Chi²=39.74, df=30(P=0.11); I²=24.52%					
Test for overall effect: Z=10.16(P<0.0001)					
4.3.2 After cord clamping					
Wong 1978	14/48	23/51		3.32%	0.65[0.38,1.1]
Gordon 1979	2/40	6/18		1.23%	0.15[0.03,0.67]

Favours antibiotic 0.01 0.1 1 10 100 Favours no antibiotic

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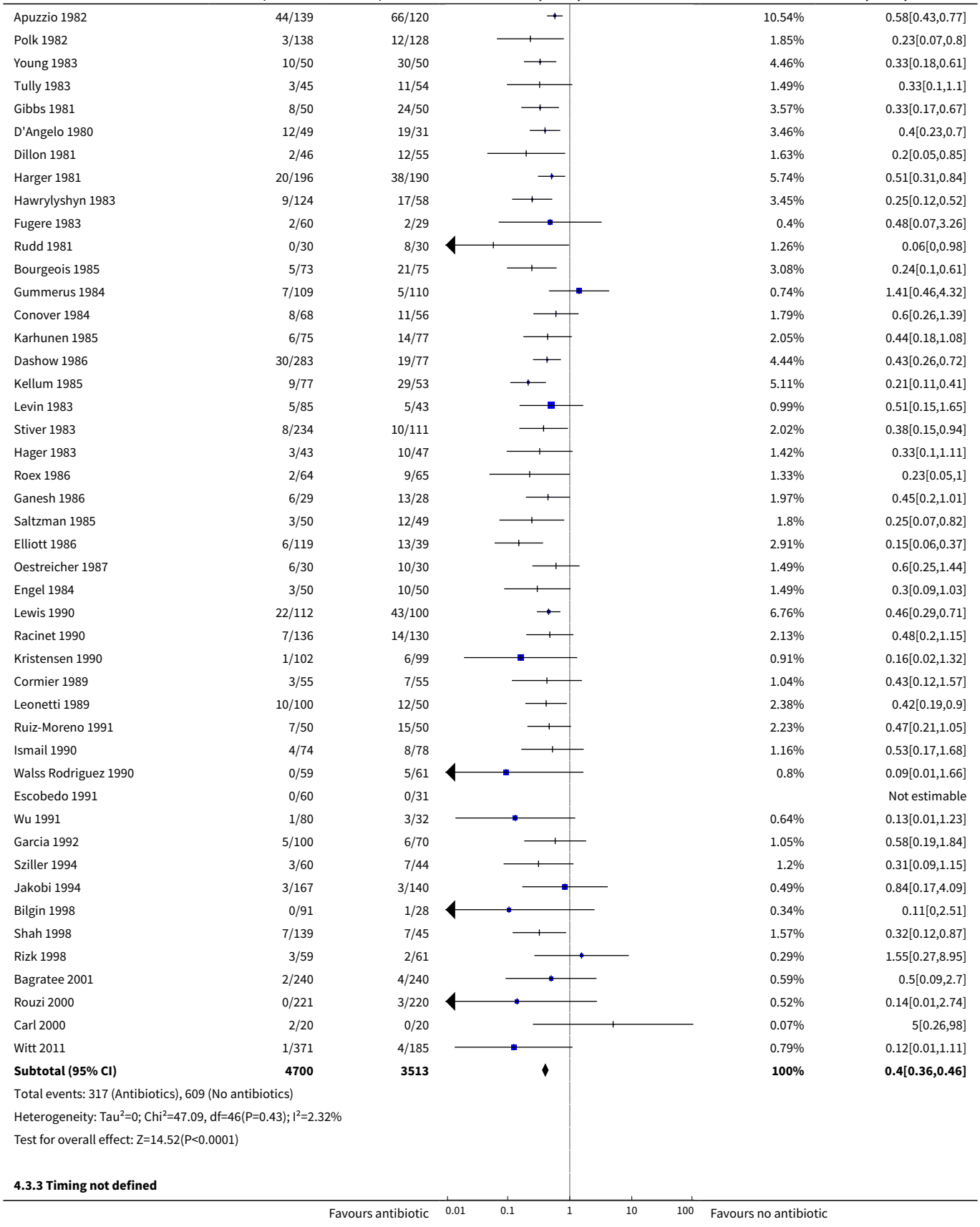

Study or subgroup	Antibiotics n/N	No antibiotics n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Apuzzio 1982	44/139	66/120		10.54%	0.58[0.43,0.77]
Polk 1982	3/138	12/128		1.85%	0.23[0.07,0.8]
Young 1983	10/50	30/50		4.46%	0.33[0.18,0.61]
Tully 1983	3/45	11/54		1.49%	0.33[0.1,1.1]
Gibbs 1981	8/50	24/50		3.57%	0.33[0.17,0.67]
D'Angelo 1980	12/49	19/31		3.46%	0.4[0.23,0.7]
Dillon 1981	2/46	12/55		1.63%	0.2[0.05,0.85]
Harger 1981	20/196	38/190		5.74%	0.51[0.31,0.84]
Hawrylyshyn 1983	9/124	17/58		3.45%	0.25[0.12,0.52]
Fugere 1983	2/60	2/29		0.4%	0.48[0.07,3.26]
Rudd 1981	0/30	8/30		1.26%	0.06[0,0.98]
Bourgeois 1985	5/73	21/75		3.08%	0.24[0.1,0.61]
Gummerus 1984	7/109	5/110		0.74%	1.41[0.46,4.32]
Conover 1984	8/68	11/56		1.79%	0.6[0.26,1.39]
Karhunen 1985	6/75	14/77		2.05%	0.44[0.18,1.08]
Dashow 1986	30/283	19/77		4.44%	0.43[0.26,0.72]
Kellum 1985	9/77	29/53		5.11%	0.21[0.11,0.41]
Levin 1983	5/85	5/43		0.99%	0.51[0.15,1.65]
Stiver 1983	8/234	10/111		2.02%	0.38[0.15,0.94]
Hager 1983	3/43	10/47		1.42%	0.33[0.1,1.11]
Roex 1986	2/64	9/65		1.33%	0.23[0.05,1]
Ganesh 1986	6/29	13/28		1.97%	0.45[0.2,1.01]
Saltzman 1985	3/50	12/49		1.8%	0.25[0.07,0.82]
Elliott 1986	6/119	13/39		2.91%	0.15[0.06,0.37]
Oestreicher 1987	6/30	10/30		1.49%	0.6[0.25,1.44]
Engel 1984	3/50	10/50		1.49%	0.3[0.09,1.03]
Lewis 1990	22/112	43/100		6.76%	0.46[0.29,0.71]
Racinet 1990	7/136	14/130		2.13%	0.48[0.2,1.15]
Kristensen 1990	1/102	6/99		0.91%	0.16[0.02,1.32]
Cormier 1989	3/55	7/55		1.04%	0.43[0.12,1.57]
Leonetti 1989	10/100	12/50		2.38%	0.42[0.19,0.9]
Ruiz-Moreno 1991	7/50	15/50		2.23%	0.47[0.21,1.05]
Ismail 1990	4/74	8/78		1.16%	0.53[0.17,1.68]
Walss Rodriguez 1990	0/59	5/61		0.8%	0.09[0.01,1.66]
Escobedo 1991	0/60	0/31			Not estimable
Wu 1991	1/80	3/32		0.64%	0.13[0.01,1.23]
Garcia 1992	5/100	6/70		1.05%	0.58[0.19,1.84]
Sziller 1994	3/60	7/44		1.2%	0.31[0.09,1.15]
Jakobi 1994	3/167	3/140		0.49%	0.84[0.17,4.09]
Bilgin 1998	0/91	1/28		0.34%	0.11[0,2.51]
Shah 1998	7/139	7/45		1.57%	0.32[0.12,0.87]
Rizk 1998	3/59	2/61		0.29%	1.55[0.27,8.95]
Bagratee 2001	2/240	4/240		0.59%	0.5[0.09,2.7]
Rouzi 2000	0/221	3/220		0.52%	0.14[0.01,2.74]
Carl 2000	2/20	0/20		0.07%	5[0.26,98]
Witt 2011	1/371	4/185		0.79%	0.12[0.01,1.11]
Subtotal (95% CI)	**4700**	**3513**		**100%**	**0.4[0.36,0.46]**
Total events: 317 (Antibiotics), 609 (No antibiotics)					
Heterogeneity: Tau^2=0; Chi^2=47.09, df=46(P=0.43); I^2=2.32%					
Test for overall effect: Z=14.52(P<0.0001)					
4.3.3 Timing not defined					

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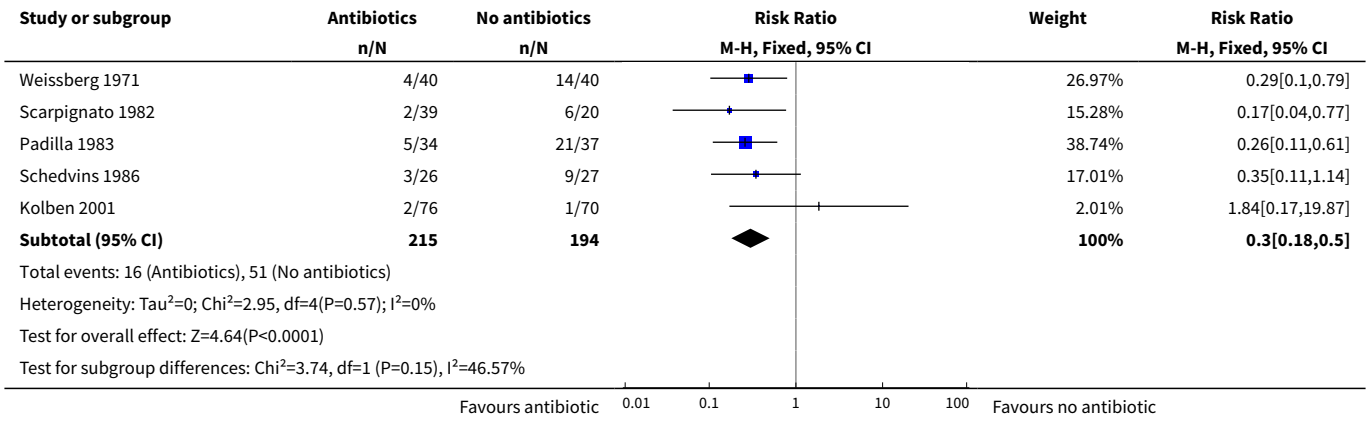
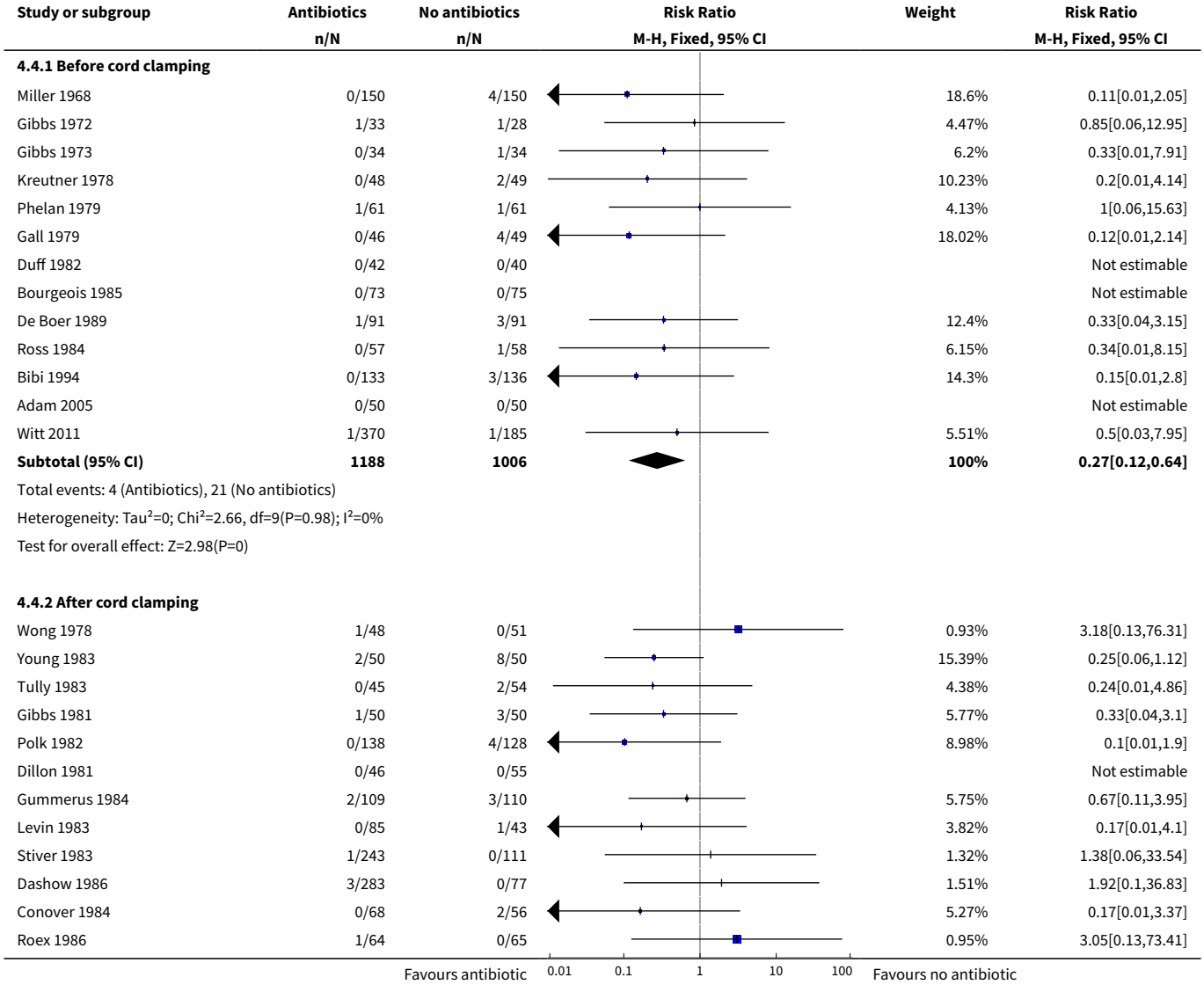


Analysis 4.4. Comparison 4 Antibiotics versus no antibiotics - subgroup by timing of administration, Outcome 4 Maternal serious infectious complications.



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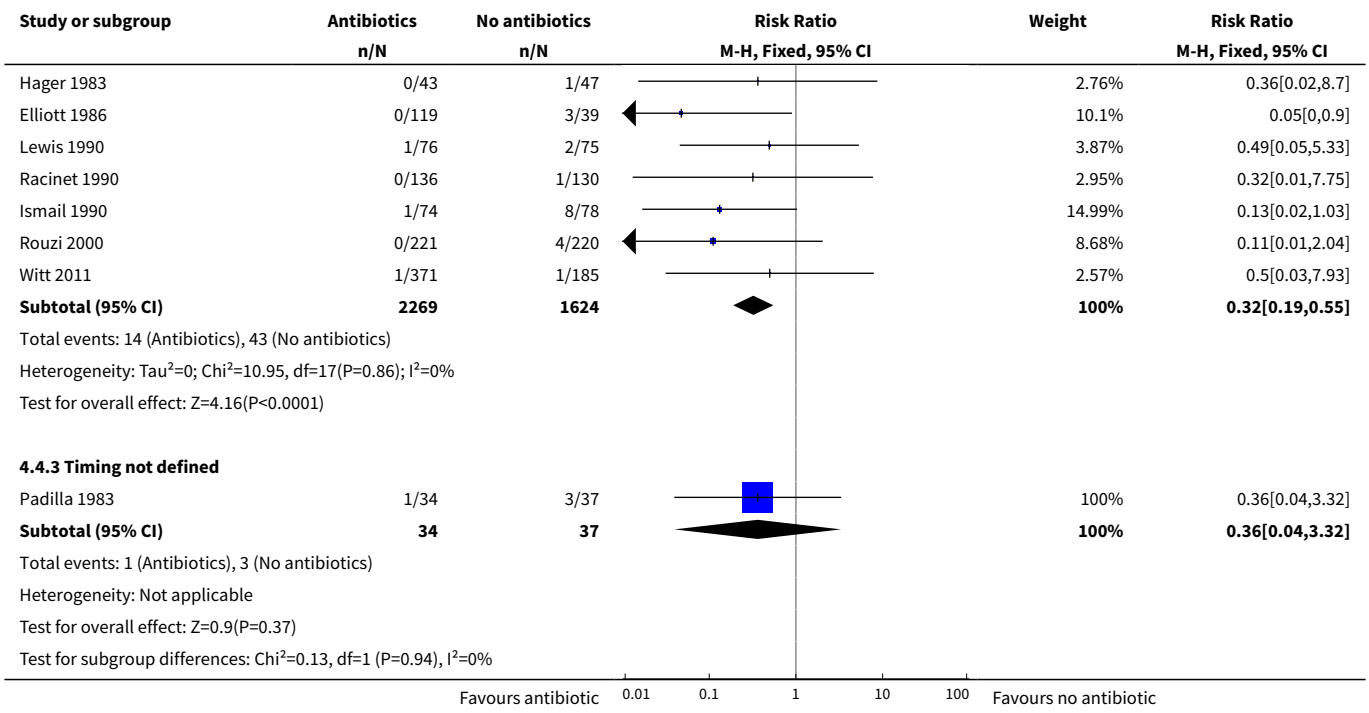
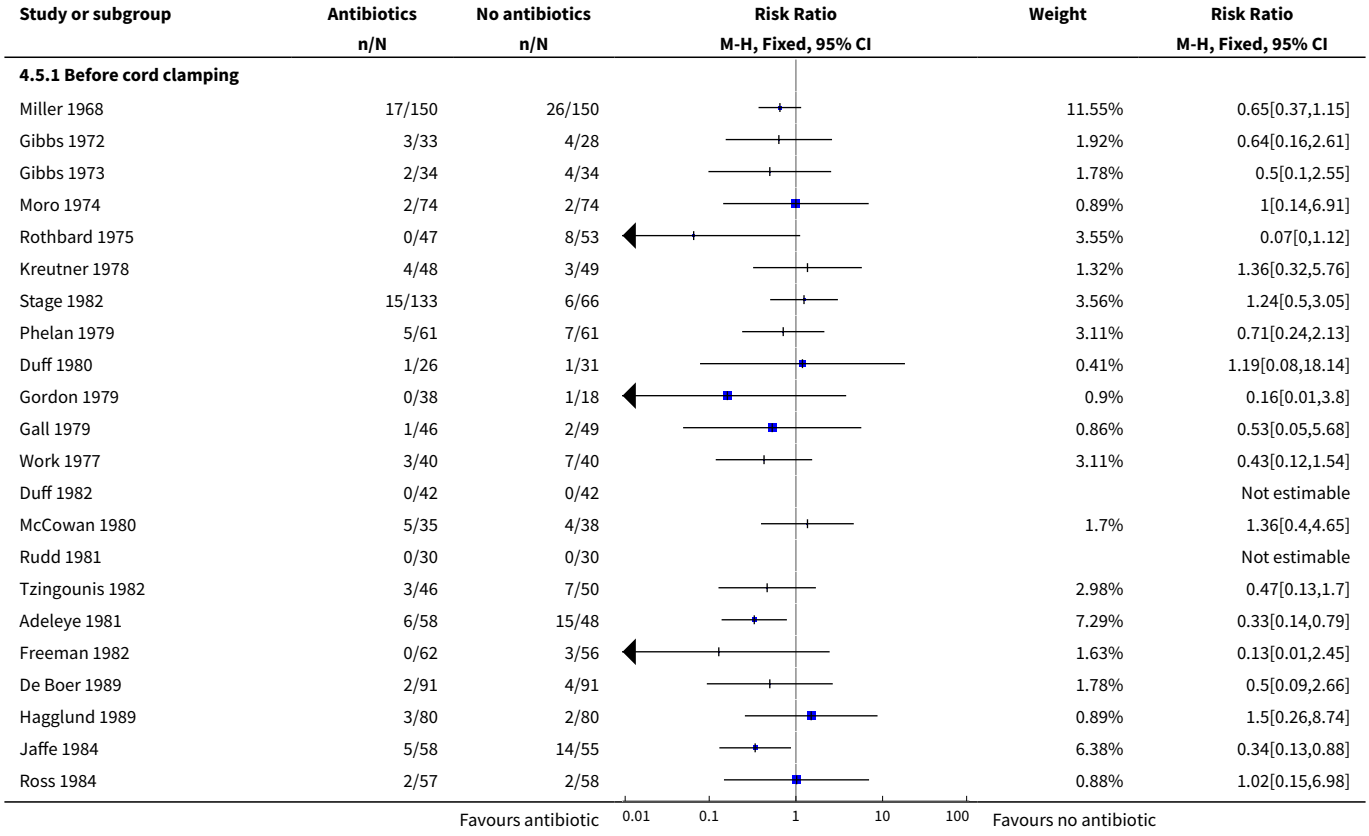


Study or subgroup	Antibiotics n/N	No antibiotics n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Hager 1983	0/43	1/47		2.76%	0.36[0.02,8.7]
Elliott 1986	0/119	3/39		10.1%	0.05[0,0.9]
Lewis 1990	1/76	2/75		3.87%	0.49[0.05,5.33]
Racinet 1990	0/136	1/130		2.95%	0.32[0.01,7.75]
Ismail 1990	1/74	8/78		14.99%	0.13[0.02,1.03]
Rouzi 2000	0/221	4/220		8.68%	0.11[0.01,2.04]
Witt 2011	1/371	1/185		2.57%	0.5[0.03,7.93]
Subtotal (95% CI)	**2269**	**1624**		**100%**	**0.32[0.19,0.55]**
Total events: 14 (Antibiotics), 43 (No antibiotics)					
Heterogeneity: Tau^2=0; Chi^2=10.95, df=17(P=0.86); I^2=0%					
Test for overall effect: Z=4.16(P<0.0001)					
4.4.3 Timing not defined					
Padilla 1983	1/34	3/37		100%	0.36[0.04,3.32]
Subtotal (95% CI)	**34**	**37**		**100%**	**0.36[0.04,3.32]**
Total events: 1 (Antibiotics), 3 (No antibiotics)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.9(P=0.37)					
Test for subgroup differences: Chi^2=0.13, df=1 (P=0.94), I^2=0%					

Analysis 4.5. Comparison 4 Antibiotics versus no antibiotics - subgroup by timing of administration, Outcome 5 Maternal urinary tract infections.



Study or subgroup	Antibiotics n/N	No antibiotics n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
4.5.1 Before cord clamping					
Miller 1968	17/150	26/150		11.55%	0.65[0.37,1.15]
Gibbs 1972	3/33	4/28		1.92%	0.64[0.16,2.61]
Gibbs 1973	2/34	4/34		1.78%	0.5[0.1,2.55]
Moro 1974	2/74	2/74		0.89%	1[0.14,6.91]
Rothbard 1975	0/47	8/53		3.55%	0.07[0,1.12]
Kreutner 1978	4/48	3/49		1.32%	1.36[0.32,5.76]
Stage 1982	15/133	6/66		3.56%	1.24[0.5,3.05]
Phelan 1979	5/61	7/61		3.11%	0.71[0.24,2.13]
Duff 1980	1/26	1/31		0.41%	1.19[0.08,18.14]
Gordon 1979	0/38	1/18		0.9%	0.16[0.01,3.8]
Gall 1979	1/46	2/49		0.86%	0.53[0.05,5.68]
Work 1977	3/40	7/40		3.11%	0.43[0.12,1.54]
Duff 1982	0/42	0/42			Not estimable
McCowan 1980	5/35	4/38		1.7%	1.36[0.4,4.65]
Rudd 1981	0/30	0/30			Not estimable
Tzingounis 1982	3/46	7/50		2.98%	0.47[0.13,1.7]
Adeleye 1981	6/58	15/48		7.29%	0.33[0.14,0.79]
Freeman 1982	0/62	3/56		1.63%	0.13[0.01,2.45]
De Boer 1989	2/91	4/91		1.78%	0.5[0.09,2.66]
Hagglund 1989	3/80	2/80		0.89%	1.5[0.26,8.74]
Jaffe 1984	5/58	14/55		6.38%	0.34[0.13,0.88]
Ross 1984	2/57	2/58		0.88%	1.02[0.15,6.98]

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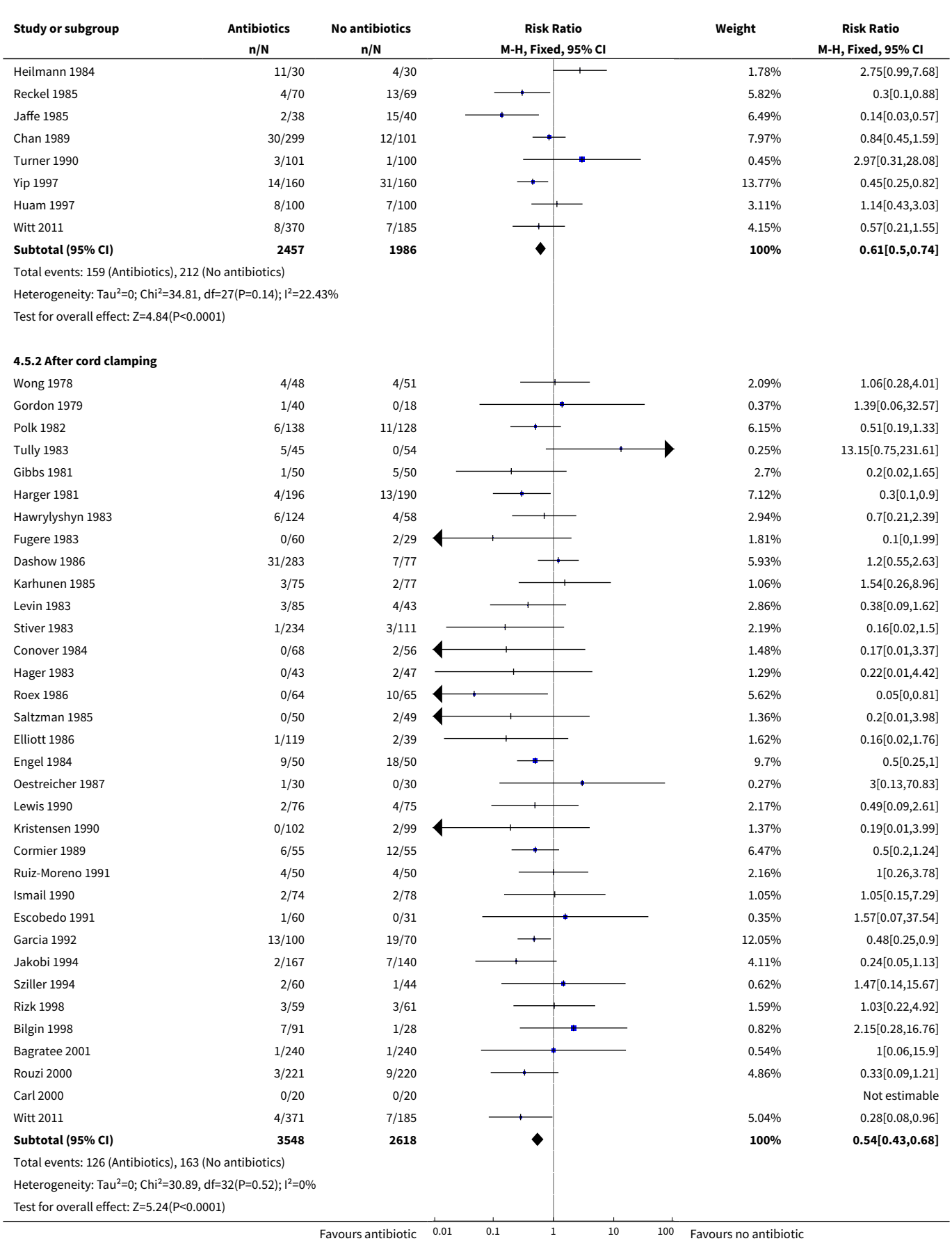

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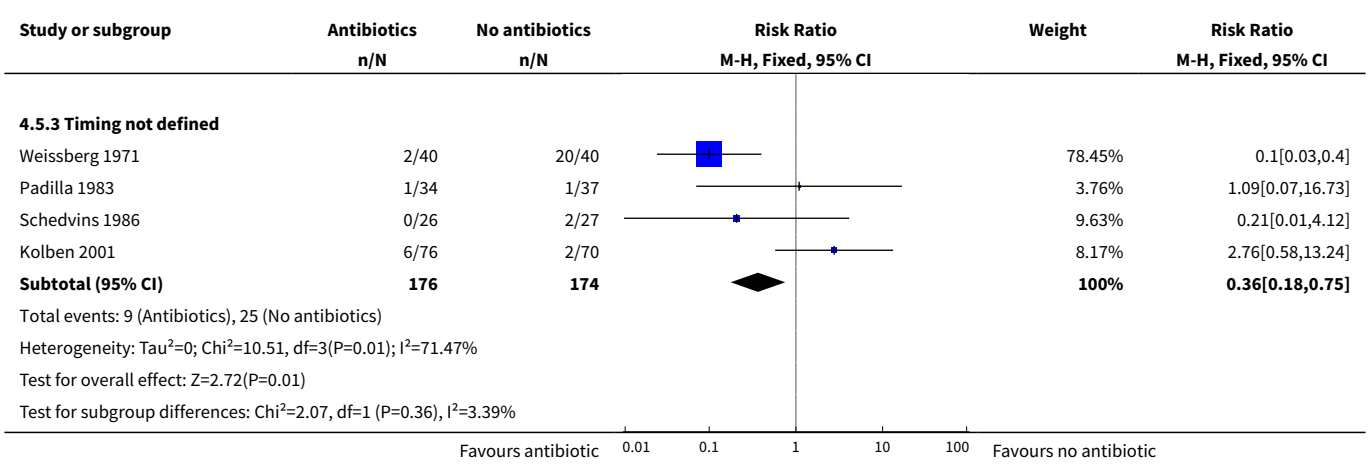
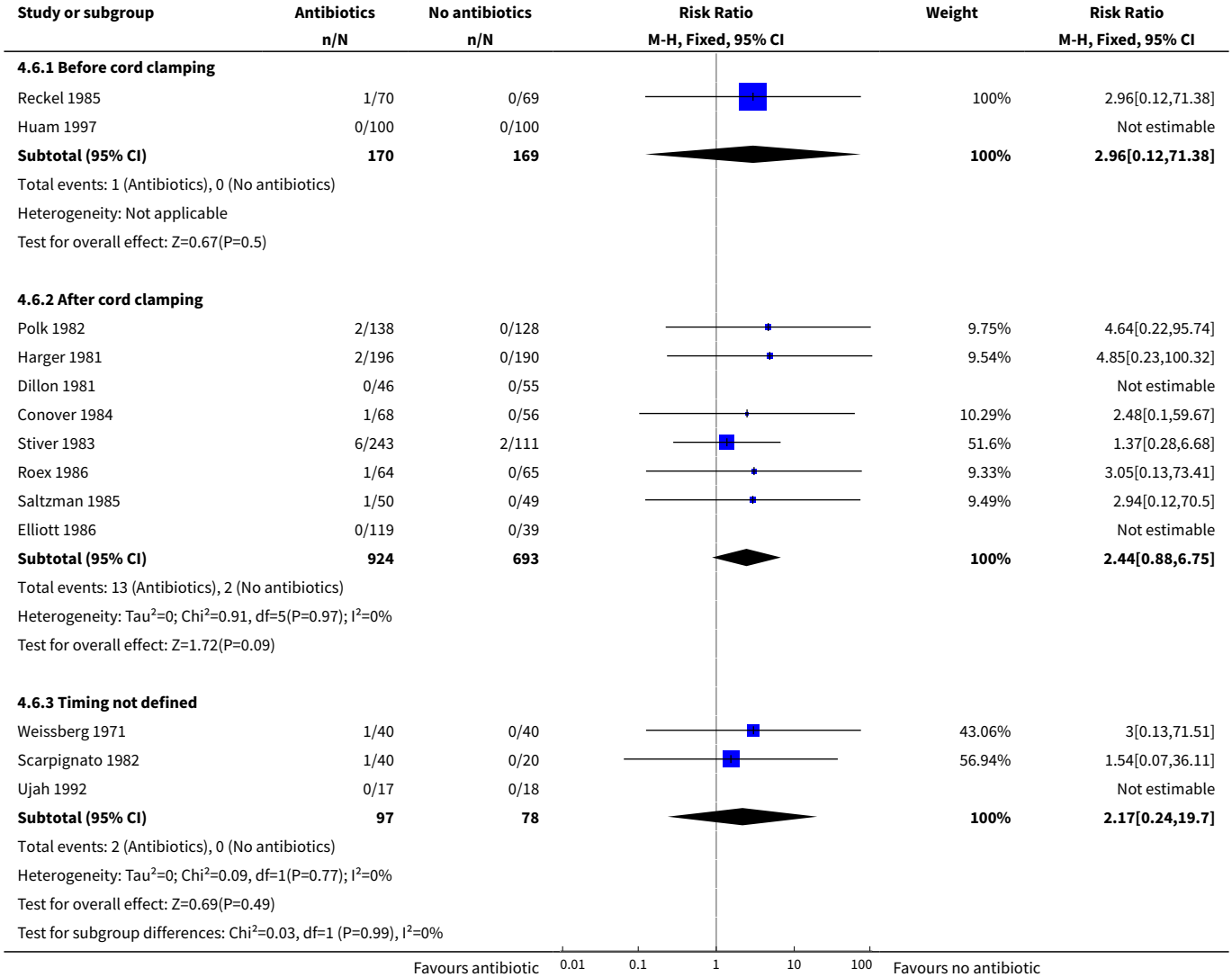


Analysis 4.6. Comparison 4 Antibiotics versus no antibiotics - subgroup by timing of administration, Outcome 6 Maternal adverse effects.



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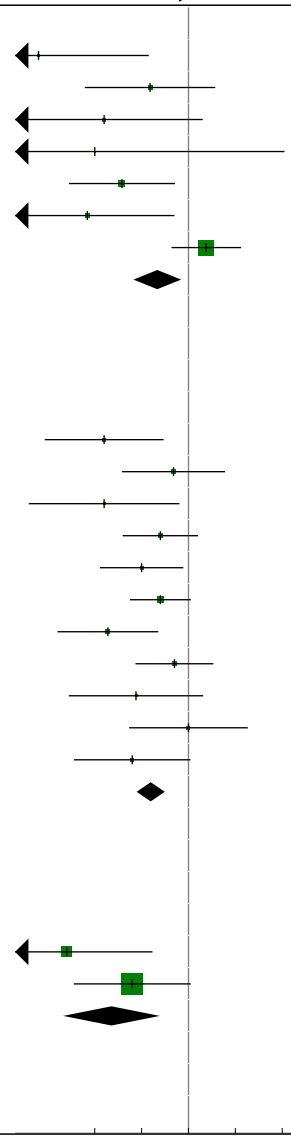
Analysis 4.7. Comparison 4 Antibiotics versus no antibiotics - subgroup by timing of administration, Outcome 7 Maternal days in hospital.

Study or subgroup	Antibiotics N	Antibiotics Mean(SD)	No antibiotics N	No antibiotics Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
4.7.1 Before cord clamping							
De Boer 1989	91	9.4 (2.6)	91	11 (5.1)		4.67%	-1.6[-2.78,-0.42]
Gall 1979	46	8 (1.5)	49	8.4 (1.9)		13.35%	-0.41[-1.11,0.29]
Gerstner 1980	53	11.2 (2.1)	50	12.1 (3.2)		5.84%	-0.9[-1.95,0.15]
Heilmann 1984	30	13 (4)	30	14 (4)		1.58%	-1[-3.02,1.02]
Huam 1997	100	5.2 (0.7)	100	5.9 (2.8)		20.2%	-0.71[-1.28,-0.14]
Lapas 1988	50	6.7 (2)	50	7.8 (2.7)		7.47%	-1.08[-2.01,-0.15]
Yip 1997	160	6.2 (1.9)	160	6 (1.4)		46.89%	0.19[-0.18,0.56]
Subtotal ***	**530**		**530**			**100%**	**-0.33[-0.59,-0.08]**
Heterogeneity: Tau^2=0; Chi^2=17.84, df=6(P=0.01); I^2=66.38%							
Test for overall effect: Z=2.57(P=0.01)							
4.7.2 After cord clamping							
Bagratee 2001	240	6.9 (2.4)	240	7.8 (4.4)		5.61%	-0.9[-1.53,-0.27]
Dillon 1981	46	5.9 (1.1)	55	6.1 (1.7)		7.45%	-0.16[-0.71,0.39]
Gibbs 1981	50	4.4 (2)	50	5.3 (2.1)		3.49%	-0.9[-1.7,-0.1]
Harger 1981	196	6.5 (1.8)	190	6.8 (2.2)		13.97%	-0.3[-0.7,0.1]
Racinet 1990	136	8.2 (1.8)	130	8.7 (1.9)		11.38%	-0.5[-0.95,-0.05]
Rizk 1998	59	6.5 (1)	61	6.8 (0.8)		21.39%	-0.3[-0.62,0.02]
Rouzi 2000	100	5.7 (1.5)	111	6.6 (2.4)		7.8%	-0.86[-1.4,-0.32]
Rouzi 2000	121	5.6 (1.5)	109	5.7 (1.7)		13.06%	-0.15[-0.57,0.27]
Ruiz-Moreno 1991	50	4.7 (1.5)	50	5.2 (2.1)		4.38%	-0.56[-1.28,0.16]
Tully 1983	45	6 (1.6)	54	6 (1.6)		5.63%	0[-0.63,0.63]
Walss Rodriguez 1990	59	3.1 (0.6)	61	3.7 (2.4)		5.84%	-0.6[-1.22,0.02]
Subtotal ***	**1102**		**1111**			**100%**	**-0.4[-0.55,-0.25]**
Heterogeneity: Tau^2=0; Chi^2=11.73, df=10(P=0.3); I^2=14.72%							
Test for overall effect: Z=5.26(P<0.0001)							
4.7.3 Timing not defined							
Padilla 1983	34	5.8 (1.1)	37	7.1 (2.6)		31.67%	-1.3[-2.22,-0.38]
Ujah 1992	17	7.7 (0.6)	18	8.3 (1.2)		68.33%	-0.6[-1.22,0.02]
Subtotal ***	**51**		**55**			**100%**	**-0.82[-1.34,-0.31]**
Heterogeneity: Tau^2=0; Chi^2=1.53, df=1(P=0.22); I^2=34.8%							
Test for overall effect: Z=3.13(P=0)							
Test for subgroup differences: Chi^2=2.81, df=1 (P=0.24), I^2=28.92%							



ADDITIONAL TABLES

Table 1. Classification of antibiotics

Penicillins	
	Natural penicillins

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Table 1. Classification of antibiotics *(Continued)*

	Penicillinase-resistant penicillin	Cloxacillin	Extended spectrum of activity compared with natural penicillin
	Aminopenicillins	Ampicillin	
	Extended-spectrum penicillins	Ticarcillin, pipericillin, carbenicillin, mezlocillin	
	Beta-lactamase inhibitor combination	Sulbactam Augmentin	
Cephalosporins			
	1st generation	Cefazolin	
	2nd generation	Cefamandole, cefuroxime	
	Cefamycins (2nd generation)	Cefoxitin, cefotetan	
	3rd generation		
	4th generation		
Carbapenems and monobactams			
Tetracyclines			
Macrolides			
Aminoglycosides	Gentamicin		
Lincosamides	Clindamycin, lincomycin		
Nitroimidazole	Metronidazole		
Fluoroquinolones			
Trimethoprim-sulfamethoxazole			
Aminoglycoside containing combination			
Other antibiotic combination			
Other regimens			

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FEEDBACK

Griffin, July 1999

Summary

It has been stated that manual removal of the placenta during cesarean section increases the risk of endometritis, when compared to cord traction for placental delivery. Occlusive dressings also increase wound healing and decrease the risk of wound infection. Would it be better to adopt these simple measures first and then trial antibiotic therapy again?

Summary of comments from Chris Griffin, July 1999.

Reply

Infection following cesarean section may be reduced by the use of cord traction to remove the placenta and occlusive wound dressings. Most trials of prophylactic antibiotic therapy do not specify the methods of placental removal and wound care, and may represent a mixture of various methods. Given the clinically important reduction of infection with antibiotic use in general, support for a policy of not using antibiotics would require evidence from randomized trials that in the context of placental removal by cord traction and occlusive wound dressings, antibiotic therapy confers no additional benefit.

Contributors

Summary of response from Fiona Smaill and Justus Hofmeyr, October 1999.

WHAT'S NEW

Date	Event	Description
31 July 2014	New citation required but conclusions have not changed	95 trials included (9 new trials included), 25 trials excluded. Conclusions remain unchanged.
31 July 2014	New search has been performed	Search updated. Please note that blinding has now been divided into two assessments: 1. Blinding of participants and personnel (performance bias); and 2. Blinding of outcome assessors (detection bias) - tables have been updated. 'Summary of findings' tables have been incorporated for this update.

HISTORY

Protocol first published: Issue 4, 2008
Review first published: Issue 1, 2010

Date	Event	Description
31 May 2009	New search has been performed	Search updated. Five new trials included (Adam 2005; Freeman 1982; Huam 1997; Jaffe 1984; Kolben 2001).
18 May 2009	New citation required but conclusions have not changed	New review team substantially updated this review.
3 January 2008	Amended	Converted to new review format. Added a note about the updating of the review.
5 March 2002	New search has been performed	Fifteen additional trials have been added to the review. The overall conclusion remains unchanged. Antibiotic prophylaxis will

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Date	Event	Description
		reduce infectious complications following both an elective and non-elective cesarean section.
30 June 1999	Feedback has been incorporated	Added feedback from Chris Griffin and response from authors.

CONTRIBUTIONS OF AUTHORS

The initial draft of the 2014 updated review was prepared by F Smaill. R Grivell helped with identifying new trials and data entry and commented on the text of the review and 'Summary of findings' tables.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- University of the Witwatersrand, South Africa.
- The University of Liverpool, UK.

External sources

- UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Department of Reproductive Health and Research (RHR), World Health Organization, Switzerland.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have used fixed-effect Mantel-Haenszel meta-analysis for combining data because the *Cochrane Handbook for Systematic Reviews of Interventions* suggests it is more commonly used (Higgins 2008) (2009 update).

We have modified the wording in the methods sections for Assessment of heterogeneity, Assessment of reporting biases and Data synthesis to update them with the new methods being used by the group, developed in conjunction with the Group's Statistician, Simon Gates, and Richard Riley. We have used these new methods in the review (2009 update).

The quality of the evidence was assessed using the GRADE approach (Schunemann 2009) in order to assess the quality of the body of evidence relating key outcomes. We have included subgroup analyses based on type of antibiotic, type of cesarean section and timing of administration (2014 update).

INDEX TERMS

Medical Subject Headings (MeSH)

Antibiotic Prophylaxis [*adverse effects]; Bacterial Infections [*prevention & control]; Cesarean Section [*adverse effects]; Endometritis [*prevention & control]; Postoperative Complications [*prevention & control]; Randomized Controlled Trials as Topic; Surgical Wound Infection [prevention & control]; Urinary Tract Infections [prevention & control]

MeSH check words

Female; Humans; Pregnancy

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