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Different classes of antibiotics given to women routinely for preventing infection at caesarean section (Review)

Gyte GML, Dou L, Vazquez JC

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TABLE OF CONTENTS

HEADER 1
ABSTRACT 1
PLAIN LANGUAGE SUMMARY 2
SUMMARY OF FINDINGS 3
BACKGROUND 6
OBJECTIVES 7
METHODS 7
Figure 1. 12
RESULTS 13
Figure 2. 17
Figure 3. 18
Figure 4. 19
Figure 5. 20
DISCUSSION 24
AUTHORS' CONCLUSIONS 25
ACKNOWLEDGEMENTS 25
REFERENCES 26
CHARACTERISTICS OF STUDIES 34
DATA AND ANALYSES 89
Analysis 1.1. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 1 Maternal sepsis. 96
Analysis 1.2. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 2 Maternal endometritis. 97
Analysis 1.5. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 5 Maternal fever (febrile morbidity). 98
Analysis 1.6. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 6 Maternal wound infection. 99
Analysis 1.7. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 7 Maternal urinary tract infection. 100
Analysis 1.9. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 9 Maternal composite serious infectious complication. 101
Analysis 1.10. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 10 Maternal composite adverse effects. 102
Analysis 1.11. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 11 Maternal allergic reactions. 102
Analysis 1.12. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 12 Maternal nausea. 103
Analysis 1.13. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 13 Maternal vomiting. 104
Analysis 1.14. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 14 Maternal diarrhoea. 104
Analysis 1.15. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 15 Maternal skin rash. 105
Analysis 1.21. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 21 Maternal length of hospital stay. 106
Analysis 2.1. Comparison 2 Cephalosporins versus penicillins - by type of caesarean, Outcome 1 Maternal sepsis. 107
Analysis 2.2. Comparison 2 Cephalosporins versus penicillins - by type of caesarean, Outcome 2 Maternal endometritis. 108
Analysis 3.1. Comparison 3 Cephalosporins versus penicillins - by timing of administration, Outcome 1 Maternal sepsis. 110
Analysis 3.2. Comparison 3 Cephalosporins versus penicillins - by timing of administration, Outcome 2 Maternal endometritis. 111
Analysis 4.1. Comparison 4 Cephalosporins versus penicillins - by route of administration, Outcome 1 Maternal sepsis. 112
Analysis 4.2. Comparison 4 Cephalosporins versus penicillins - by route of administration, Outcome 2 Maternal endometritis. 113
Analysis 5.2. Comparison 5 Cephalosporin (1st generation B1) versus penicillins (extended spectrum A3), Outcome 2 Maternal endometritis. 115
Analysis 5.5. Comparison 5 Cephalosporin (1st generation B1) versus penicillins (extended spectrum A3), Outcome 5 Maternal fever (febrile morbidity). 116
Analysis 5.6. Comparison 5 Cephalosporin (1st generation B1) versus penicillins (extended spectrum A3), Outcome 6 Maternal wound infection. 116
Analysis 5.10. Comparison 5 Cephalosporin (1st generation B1) versus penicillins (extended spectrum A3), Outcome 10 Maternal composite adverse effects. 116
Analysis 6.2. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 2 Maternal endometritis. 118
Analysis 6.5. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 5 Maternal fever (febrile morbidity). 118

Analysis 6.6. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 6 Maternal wound infection. 119
Analysis 6.7. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 7 Maternal urinary tract infection. 119
Analysis 6.10. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 10 Maternal composite adverse effects. 119
Analysis 6.11. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 11 Maternal allergic reactions. 120
Analysis 6.15. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 15 Maternal skin rash. 120
Analysis 6.21. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 21 Maternal length of hospital stay. 120
Analysis 7.1. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 1 Maternal sepsis. 122
Analysis 7.2. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 2 Maternal endometritis. 122
Analysis 7.5. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 5 Maternal fever (febrile morbidity). 123
Analysis 7.6. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 6 Maternal wound infection. 123
Analysis 7.7. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 7 Maternal urinary tract infection. 123
Analysis 7.10. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 10 Maternal composite adverse effects. 124
Analysis 7.15. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 15 Maternal skin rash. 124
Analysis 8.1. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 1 Maternal sepsis. 125
Analysis 8.2. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 2 Maternal endometritis. 126
Analysis 8.5. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 5 Maternal fever (febrile morbidity). 126
Analysis 8.6. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 6 Maternal wound infection. 127
Analysis 8.7. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 7 Maternal urinary tract infection. 127
Analysis 8.10. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 10 Maternal composite adverse effects. 127
Analysis 8.11. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 11 Maternal allergic reactions. 128
Analysis 8.15. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 15 Maternal skin rash. 128
Analysis 9.1. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 1 Maternal sepsis. 129
Analysis 9.2. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 2 Maternal endometritis. 130
Analysis 9.6. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 6 Maternal wound infection. 130
Analysis 9.7. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 7 Maternal urinary tract infection. 130
Analysis 9.9. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 9 Maternal composite serious infectious complication. 131
Analysis 9.10. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 10 Maternal composite adverse effects. 131
Analysis 9.11. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 11 Maternal allergic reactions. 131

Analysis 9.12. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 12 Maternal nausea. 132
Analysis 9.13. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 13 Maternal vomiting. 132
Analysis 9.14. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 14 Maternal diarrhoea. 132
Analysis 9.15. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 15 Maternal skin rash. 133
Analysis 10.2. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 2 Maternal endometritis. 134
Analysis 10.5. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 5 Maternal fever (febrile morbidity). 135
Analysis 10.6. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 6 Maternal wound infection. 135
Analysis 10.7. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 7 Maternal urinary tract infection. 135
Analysis 10.9. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 9 Maternal composite serious infectious complication. 136
Analysis 10.10. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 10 Maternal composite adverse effects. 136
Analysis 10.11. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 11 Maternal allergic reactions. 136
Analysis 10.13. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 13 Maternal vomiting. 137
Analysis 10.15. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 15 Maternal skin rash. 137
Analysis 10.21. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 21 Maternal length of hospital stay. 137
Analysis 11.1. Comparison 11 Fluoroquinolones (C) vs penicillins (A), Outcome 1 Maternal sepsis. 139
Analysis 11.2. Comparison 11 Fluoroquinolones (C) vs penicillins (A), Outcome 2 Maternal endometritis. 139
Analysis 11.6. Comparison 11 Fluoroquinolones (C) vs penicillins (A), Outcome 6 Maternal wound infection. 139
Analysis 11.7. Comparison 11 Fluoroquinolones (C) vs penicillins (A), Outcome 7 Maternal urinary tract infection. 140
Analysis 12.1. Comparison 12 Fluoroquinolones (C) vs cephalosporins (B), Outcome 1 Maternal sepsis. 141
Analysis 12.2. Comparison 12 Fluoroquinolones (C) vs cephalosporins (B), Outcome 2 Maternal endometritis. 141
Analysis 12.6. Comparison 12 Fluoroquinolones (C) vs cephalosporins (B), Outcome 6 Maternal wound infection. 142
Analysis 12.7. Comparison 12 Fluoroquinolones (C) vs cephalosporins (B), Outcome 7 Maternal urinary tract infection. 142
Analysis 13.2. Comparison 13 Other antibiotic regimens (D to I) versus penicillins (A), Outcome 2 Maternal endometritis. 145
Analysis 13.6. Comparison 13 Other antibiotic regimens (D to I) versus penicillins (A), Outcome 6 Maternal wound infection. 145
Analysis 14.2. Comparison 14 Other antibiotic regimens (D to I) versus cephalosporins (B), Outcome 2 Maternal endometritis. 150
Analysis 14.5. Comparison 14 Other antibiotic regimens (D to I) versus cephalosporins (B), Outcome 5 Maternal fever (febrile morbidity). 150
Analysis 14.6. Comparison 14 Other antibiotic regimens (D to I) versus cephalosporins (B), Outcome 6 Maternal wound infection. 151
Analysis 14.7. Comparison 14 Other antibiotic regimens (D to I) versus cephalosporins (B), Outcome 7 Maternal urinary tract infection. 151
Analysis 15.2. Comparison 15 Other antibiotic regimens versus different antibiotic regimens, Outcome 2 Maternal endometritis. 154
Analysis 15.6. Comparison 15 Other antibiotic regimens versus different antibiotic regimens, Outcome 6 Maternal wound infection. 155
Analysis 15.7. Comparison 15 Other antibiotic regimens versus different antibiotic regimens, Outcome 7 Maternal urinary tract infection. 155
Analysis 15.27. Comparison 15 Other antibiotic regimens versus different antibiotic regimens, Outcome 27 Stillbirth (not-prespecified). 155
ADDITIONAL TABLES 156
APPENDICES 157

WHAT'S NEW 158
HISTORY 158
CONTRIBUTIONS OF AUTHORS 158
DECLARATIONS OF INTEREST 158
SOURCES OF SUPPORT 158
DIFFERENCES BETWEEN PROTOCOL AND REVIEW 158
NOTES 159
INDEX TERMS 159

[Intervention Review]

Different classes of antibiotics given to women routinely for preventing infection at caesarean section

Gillian ML Gyte[1], Lixia Dou[1], Juan C Vazquez[2]

[1]Cochrane Pregnancy and Childbirth Group, Department of Women's and Children's Health, The University of Liverpool, Liverpool, UK. [2]Departamento de Salud Reproductiva, Instituto Nacional de Endocrinologia (INEN), Habana, Cuba

Contact address: Lixia Dou, Cochrane Pregnancy and Childbirth Group, Department of Women's and Children's Health, The University of Liverpool, First Floor, Liverpool Women's NHS Foundation Trust, Crown Street, Liverpool, L8 7SS, UK. lillydou@hotmail.com.

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ABSTRACT

Background

Caesarean section increases the risk of postpartum infection for women and prophylactic antibiotics have been shown to reduce the incidence; however, there are adverse effects. It is important to identify the most effective class of antibiotics to use and those with the least adverse effects.

Objectives

To determine, from the best available evidence, the balance of benefits and harms between different classes of antibiotic given prophylactically to women undergoing caesarean section.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 September 2014) and reference lists of retrieved papers.

Selection criteria

We included randomised controlled trials comparing different classes of prophylactic antibiotics given to women undergoing caesarean section. We excluded trials that compared drugs with placebo or drugs within a specific class; these are assessed in other Cochrane reviews.

Data collection and analysis

Two review authors independently assessed the studies for inclusion, assessed risk of bias and carried out data extraction.

Main results

We included 35 studies of which 31 provided data on 7697 women. For the main comparison between cephalosporins versus penicillins, there were 30 studies of which 27 provided data on 7299 women. There was a lack of good quality data and important outcomes often included only small numbers of women.

For the comparison of a single cephalosporin versus a single penicillin (Comparison 1 subgroup 1), we found no significant difference between these classes of antibiotics for our chosen most important seven outcomes namely: maternal sepsis - there were no women with sepsis in the two studies involving 346 women; maternal endometritis (risk ratio (RR) 1.11, 95% confidence interval (CI) 0.81 to 1.52, nine studies, 3130 women, random effects, *moderate quality of the evidence*); maternal wound infection (RR 0.83, 95% CI 0.38 to 1.81, nine studies, 1497 women, random effects, *low quality of the evidence*), maternal urinary tract infection (RR 1.48, 95% CI 0.89 to 2.48, seven

studies, 1120 women, *low quality of the evidence*) and maternal composite adverse effects (RR 2.02, 95% CI 0.18 to 21.96, three studies, 1902 women, *very low quality of the evidence*). None of the included studies looked for infant sepsis nor infant oral thrush.

This meant we could only conclude that the current evidence shows no overall difference between the different classes of antibiotics in terms of reducing maternal infections after caesarean sections. However, none of the studies reported on infections diagnosed after the initial postoperative hospital stay. We were unable to assess what impact, if any, the use of different classes of antibiotics might have on bacterial resistance.

Authors' conclusions

Based on the best currently available evidence, cephalosporins and penicillins have similar efficacy at caesarean section when considering immediate postoperative infections. We have no data for outcomes on the baby, nor on late infections (up to 30 days) in the mother. Clinicians need to consider bacterial resistance and women's individual circumstances.

PLAIN LANGUAGE SUMMARY

Comparing different types of antibiotics given routinely to women at caesarean section to prevent infections

Background

Women undergoing caesarean section have an increased likelihood of infection compared with women who give birth vaginally. These infections can be in the urine, surgical incision, or the lining of the womb (endometritis). The infections can become serious, causing, for example, an abscess in the pelvis or infection in the blood, and very occasionally can lead to the mother's death. Sound surgical techniques are important for reducing infections, along with skin antiseptics and antibiotics. However, antibiotics can cause adverse effects such as nausea, vomiting, skin rash and rarely allergic reactions in the mother, and the risk of thrush (candida) for the mother and the baby. Antibiotics, given to women around the time of giving birth, can also change the baby's gut flora and thus may interfere with the baby's developing immune system.

Our review question

We asked if cephalosporin antibiotics were better than penicillins for women having a caesarean section. We also looked to see how other groups of antibiotics compared.

What we found

When comparing cephalosporins against penicillins, we found 27 studies, involving 7299 women as of September 2014. The quality of the studies was generally unclear and three studies reported drug company funding. Cephalosporins and penicillins had similar effects in reducing infections after caesareans and similar adverse effects. However, none of the studies considered infections after the women left hospital. None of the studies looked at outcomes on the babies. Other evidence show tetracyclines can cause discolouration of teeth in children and are best avoided. Consideration also needs to be given to antibiotics compatible with breastfeeding. We were unable to assess bacterial resistance, and this is crucial when considering which antibiotic might be used.

What our results mean

At caesarean sections, cephalosporins and penicillins have similar benefits and side effects for mothers when considering infections immediately following the operation but there is no information on babies. Clinicians need to consider bacterial resistance and women's individual circumstances.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Cephalosporins versus penicillins - all women for preventing infection at caesarean section

Cephalosporins versus penicillins - all women for preventing infection at caesarean section

Population: Women undergoing caesarean section.
Settings: Hospitals in Sudan, US, Thailand, Italy, Zimbabwe, Mozanbique, Switzerland, South Africa, Canada, Rwanda, Malaysia, Finland, United Arab Emirates, Netherlands, Argentina, UK, Greece.
Intervention: Cephalosporins versus penicillins - all women.

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	Cephalosporins versus penicillins - all women				
Maternal sepsis - Single cephalosporin vs single penicillin	See comment	See comment	Not estimable	346 (2 studies)	See comment	The outcome was reported with no events.
Maternal endometritis - Single cephalosporin vs single penicillin	**Study population**		**RR 1.11** (0.81 to 1.52)	3130 (9 studies)	⊕⊕⊕⊖ **moderate** [1]	
	109 per 1000	**121 per 1000** (88 to 165)				
	Moderate					
	86 per 1000	**95 per 1000** (70 to 131)				
Infant sepsis - Single cephalosporin vs single penicillin	See comment	See comment	Not estimable	0 (0)	See comment	This outcome was not reported in any of the included studies.
Infant oral thrush - Single cephalosporin vs single penicillin	See comment	See comment	Not estimable	0 (0)	See comment	This outcome was not reported in any of the included studies.

Maternal wound infection - Single cephalosporin vs single penicillin	**Study population**		**RR 0.83** (0.38 to 1.81)	1497 (9 studies)	⊕⊕⊖⊖ **low** [1,2]
	33 per 1000	**27 per 1000** (12 to 59)			
	Moderate				
	34 per 1000	**28 per 1000** (13 to 62)			
Maternal urinary tract infection - Single cephalosporin vs single penicillin	**Study population**		**RR 1.48** (0.89 to 2.48)	1120 (7 studies)	⊕⊕⊖⊖ **low** [1,2]
	49 per 1000	**72 per 1000** (43 to 121)			
	Moderate				
	37 per 1000	**55 per 1000** (33 to 92)			
Maternal composite adverse effects - Single cephalosporin vs single penicillin	**Study population**		**RR 2.02** (0.18 to 21.96)	1902 (3 studies)	⊕⊖⊖⊖ **very low** [3,4]
	2 per 1000	**4 per 1000** (0 to 47)			
	Moderate				
	0 per 1000	**0 per 1000** (0 to 0)			

*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] Most studies contributing data had design limitations.
[2] Wide confidence interval crossing the line of no effect & small sample size.
[3] One study with design limitations.

4 Wide confidence interval crossing the line of no effect & few events.

BACKGROUND

Women undergoing caesarean section have an increased risk of postoperative infection and infectious morbidity compared with women giving birth vaginally (Declercq 2007). Since caesarean section rates are in excess of 20% in many high-income countries, these infections are a major concern.

Description of the condition

Caesarean sections have been shown to have nearly five times the risk of postpartum infection as vaginal births (and this is with a policy of antibiotics at caesarean section) and just over 75% occur after hospital discharge (Leth 2009). The infectious complications that can occur after caesarean birth include infections of the wound/incision, endometritis (infection of the lining of the uterus) and urinary tract infection, although fever can occur after any operation and is not necessarily an indicator of infection (MacLean 1990). However, there can occasionally be more serious infectious complications such as pelvic abscess (collection of pus in the pelvis), bacteraemia (bacterial infection in the blood), septic shock (reduced blood volume due to infection), necrotising fasciitis (tissue destruction in the abdominal wall) and septic pelvic vein thrombophlebitis (inflammation and infection of the veins in the pelvis). These more serious infectious complications can lead to maternal mortality.

Description of the intervention

The potential for prophylactic antibiotics to reduce the incidence of maternal infectious morbidity following caesarean section has now been systematically investigated (Smaill 2002; Smaill 2008). Although evidence has existed for some time to support this practice (Pedersen 1996), it is not clear whether any one particular agent, dose or route of administration is superior. Many different drug regimens have been reported to be effective in decreasing immediate postoperative infectious morbidity. To date, various penicillins (ampicillin, ticarcillin, mezlocillin, piperacillin), cephalosporins (cefazolin, cephalothin, ceforanide, cefonicid, cefuroxime, ceftazidime, cefoxitin, cefamandole, cephradine, cefotetan, cefotaxime), fluoroquinolones etc. have been used for caesarean section prophylaxis and overall they have demonstrated some efficacy either alone or in combination with another drug (Smaill 2008). Some of these drugs have activity against a narrow range of potential pathogens (e.g. metronidazole, gentamicin), others have additional specific anaerobic activity (e.g. cefoxitin and cefotetan), and yet others have very broad-spectrum coverage (imipenem). Their pharmacokinetic properties (e.g. serum half-life) also differ. Some drugs used in the past are now associated with bacterial resistance.

In addition to the choice of drug there are differences in the route of administration and the timing of administration of prophylactic antibiotics. As well as systemic administration (intravenous and intramuscular), use of intra-operative irrigation of the uterus and peritoneal cavity with an antibiotic solution has been reported. While some guidelines recommend multiple doses of antibiotics, a single dose at the time of the procedure may be adequate. These considerations will be covered in other Cochrane reviews - see Differences between protocol and review for details.

How the intervention might work

Since penicillin was introduced during the 1940s, scientists have developed numerous other antibiotics. Today, over 100 different antibiotics are available. For the prevention of surgical infections it is generally considered that sound surgical technique is important along with skin antiseptics and the use of antibiotics (Owen 1994). Antibiotics act by either killing bacteria (bacteriocidal) or inhibiting bacterial replication (bacteriostatic) but the large variety of different types of bacteria mean a large variety of possible antibiotics may be used.

Classification of antibiotics

Antibiotics can be classified in a number of ways, but classifying by chemical structure is useful because antibiotics within a structural class will generally have similar patterns of effectiveness, toxicity and allergic potential (Bayarski 2006; eMedExpert 2009; Goodman 2008). The most commonly used types of antibiotics are penicillins, cephalosporins, fluoroquinolones, tetracyclines and macrolides, with each class including many drugs (Table 1). Penicillins have a common structure which they share with cephalosporins. Both classes of antibiotics are bactericidal, acting through inhibiting cell wall synthesis. Penicillins are grouped into four types and cephalosporins are grouped into four generations with each newer generation having a broader spectrum of activity (eMedExpert 2009). Fluoroquinolones are the newest class of antibiotics and are synthetic rather than derived from bacteria. These newer fluoroquinolones are broad-spectrum bacteriocidal drugs chemically unrelated to penicillins or cephalosporins. They interfere with the ability of bacteria to make DNA. Tetracyclines are derived from streptomyces bacteria and are broad-spectrum bacteriostatic antibiotics. Macrolides are also derived from streptomyces bacteria and are also bacteriostatic in action, binding to bacterial ribosomes. Aminoglycosides are used to treat gram-negative bacteria and may be used alongside penicillins and cephalosporins (eMedExpert 2009).

Potential adverse effects of antibiotics

On the mother

The benefits of antibiotics are well-known, but there are potential adverse effects which also need to be considered. Antibiotic use is associated with some gastrointestinal symptoms (nausea, vomiting or diarrhoea), skin rashes, thrush/candidiasis (infection with candida which can affect both mother and baby), and joint pain (Dancer 2004). Occasionally there can also be blood problems, or kidney or liver damage (Dancer 2004; Westphal 1994), and very occasionally anaphylaxis (a hypersensitivity reaction leading to pallor, shock and collapse, which is sometimes fatal). Possible interactions with other drugs the mother may be taking also need to be considered.

On the infant

Some antibiotics can reach the baby during labour or through breastfeeding, and these may upset the pattern of friendly bacterial flora being established in the baby's gut as part of the baby's immune system (Bedford Russell 2006; Penders 2006). There is evidence that this impact can continue for up to six months after birth (Grolund 1999) and the consequences of this may occasionally be late-onset serious bacterial infections (Glasgow 2005). It has been proposed that perinatal exposure to certain agents can cause irreversible changes to health conditions in adulthood through

impact on hormonal imprinting (Csaba 2007; Tchernitchin 1999). It is also possible that babies born prematurely, with less mature immune systems, may be affected more.

Drug-resistant strains of antibiotics

Resistance of bacteria to antibiotics is spreading and develops when a strain of bacteria evolves which is not destroyed by the antibiotic. The antibiotic kills off the non-resistant bacteria allowing the resistant ones to colonise and spread. Widespread use of antibiotics can contribute to the development of drug-resistant strains of bacteria, which means that these antibiotics become ineffective because of bacterial resistance (Dancer 2004). At a population level this is a critical problem which may cause increase in serious morbidity from hospital-acquired drug-resistant infections (Dancer 2004). The use of antibiotics in other areas of maternity care, e.g. anti-Group B streptococcus prophylaxis, contribute further to this problem. This drug resistance is unlikely to be detected in randomised controlled trials and other types of research are needed to assess the potential problem of drug-resistant strains (e.g. MRSA (Methicillin-resistant *Staphylococcus aureus*), *C difficile)* in hospitals. The dose and number of antibiotic administrations given are a major consideration in relation to antibiotic resistance. These issues will be addressed in the other reviews - *see* Differences between protocol and review for details.

Why it is important to do this review

Since there are an overwhelming number of effective drugs available, attempts to define an antibiotic regimen of choice have been problematic. Ideally, such a drug regimen should be: (1) proven to be effective in well-designed prospective, randomised, double-blind clinical trials, (2) active against the majority of pathogens likely to be involved, (3) able to attain adequate serum and tissue levels throughout the procedure, (4) not associated with the development of antimicrobial resistance, (5) inexpensive, and (6) well-tolerated. In many respects penicillins and cephalosporins meet these criteria. Many investigators have used these drugs and have recommended that drugs from these classes represent the antibiotics of choice for caesarean section prophylaxis (Cartwright 1984). However, current knowledge of bacterial resistance may challenge these recommendations.

The past several decades have seen an increase in the incidence of caesarean section, associated with an increase in maternal postoperative infection. Studies indicate that wound infection can be as high as 30% and endometritis as high as 60% where prophylactic antibiotics have not been utilised (Smaill 2002). Therefore, infectious complications that occur following caesarean section are an important contributor to maternal morbidity and mortality (Henderson 1995). Such complications are also an important source of increased hospital stay and consumption of financial resources. Prophylactic antibiotics for caesarean section can be expected to result in a major reduction in postoperative infectious morbidity. The question that remains, therefore, is which regimen to use.

OBJECTIVES

To determine, from the best available evidence, the balance of benefits and harms between different class of antibiotic given prophylactically to women undergoing caesarean section, considering the effectiveness in reducing infectious complications for women and adverse effects on both mother and infant.

Other Cochrane reviews will address: effectiveness against placebo (Smaill 2008), dosage by the various classes of antibiotics, different routes of administration and various timings of administration.

We will consider factors that may affect antibiotic resistance in a future update of this review.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) where the intention was to allocate participants randomly to one of at least two alternative classes of regimens of antibiotic prophylaxis for caesarean section. We excluded quasi-RCTs. Cluster-RCTs were eligible for inclusion but none were identified. Cross-over trials were not eligible for inclusion.

Types of participants

Women undergoing caesarean section, both elective and non-elective.

Types of interventions

Prophylactic antibiotic regimens comparing different classes of antibiotics. We included studies where there was a comparison between two or more antibiotics from the different classes of antibiotics.

We excluded comparisons of different drugs within the same class of antibiotics as these will be assessed in other Cochrane reviews.

- Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section
- Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section

Assessment of the appropriate timing and route of administration of prophylactic antibiotics will also be considered in further reviews.

- Timing of prophylactic antibiotics for preventing infectious morbidity in women undergoing caesarean section
- Routes of administration for antibiotic given to women routinely for preventing infection after caesarean section

Types of outcome measures

Primary outcomes

Maternal

1. Maternal sepsis (suspected or proven)
2. Endometritis

Infant

1. Infant sepsis (suspected or proven)
2. Oral thrush

Secondary outcomes

Maternal

1. Fever (febrile morbidity)
2. Wound infection
3. Urinary tract infection
4. Thrush
5. Serious infectious complication (such as bacteraemia, septic shock, septic thrombophlebitis, necrotising fasciitis, or death attributed to infection)
6. Adverse effects of treatment on the woman (e.g. allergic reactions, nausea, vomiting, diarrhoea, skin rashes)
7. Maternal length of hospital stay
8. Infections - post-hospital discharge to 30 days postoperatively (not pre-specified in the protocol)
9. Readmissions (not pre-specified in the protocol)

Infant

1. Immediate adverse effects of antibiotics on the infant (unsettled, diarrhoea, rashes)
2. Infant length of hospital stay
3. Long-term adverse effects (e.g. general health, frequency of visits to hospital)
4. Infant's immune system development (using a validated scoring assessment)

Additional outcomes

1. Development of bacterial resistance
2. Costs

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 searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (30 September 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 or date restrictions.

Data collection and analysis

For methods used in the previous version of this review, please see Alfirevic 2010.

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

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 or, if required, we consulted the third review author.

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 or, if required, we consulted the third review author. Data were entered into Review Manager software (RevMan 2014) and checked for accuracy.

When information regarding any of the above was unclear, we planned 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 or by involving a third assessor.

(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.

We 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 assessed the methods as:

- low risk of bias (e.g. telephone or central randomisation; 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.

We 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.

We 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 randomised 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 planned to re-include missing data in the analyses which we undertook.

We assessed the 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 randomisation);
- 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 described for each included study any important concerns we had about other possible sources of bias.

(7) Overall risk of bias

We made explicit judgements about whether studies were at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we planned to assess the likely magnitude and direction of the bias and whether we considered it is likely to impact on the findings. In future updates, we will explore the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

For this update the quality of the evidence 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 first subgroup, single cephalosporins versus single penicillins:

1. Maternal sepsis
2. Maternal endometritis
3. Infant sepsis
4. Infant oral thrush
5. Wound infection
6. Maternal urinary tract infection
7. Maternal composite adverse effects (e.g. allergic reactions; nausea, vomiting, diarrhoea, skin rashes)

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.

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 standardised mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials

Had we identified any cluster-RCTs we would have included them in the analyses along with individually-randomised trials, following the methods described in Higgins 2009 and the *Handbook* [Section 16.3.4 or 16.3.6] 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 use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. In future updates, if we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will 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 randomisation unit is considered to be unlikely.

We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity subgroup analysis to investigate the effects of the randomisation unit.

Other unit of analysis issues

No special methods were used for trials with more than one treatment group.

Dealing with missing data

For included studies, levels of attrition were noted. In future updates, if more eligible studies are included, the impact of including studies with high levels of missing data in the overall assessment of treatment effect will be explored by using sensitivity 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 randomised to each group in the analyses. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the Tau^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if the Tau^2 was greater than zero or the I^2 was greater than 30% and there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity. Had we identified substantial heterogeneity (above 30%), we planned to explore it by pre-specified subgroup analysis.

Assessment of reporting biases

Where there were 10 or more studies in the meta-analysis, we investigated reporting biases (such as publication bias) using funnel plots. We assessed funnel plot asymmetry visually. If asymmetry was suggested by a visual assessment, we explored possible reasons for this.

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.

Where there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials was considered clinically meaningful. The random-effects summary was treated as the average range of possible treatment effects and we discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we did not combine trials. If 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 analysed separately, for all outcomes, penicillins and cephalosporins given alone as opposed to when they were given in combination with other drugs, for the main comparison of cephalosporins versus penicillins (Comparison 1).

We carried out the following subgroup analyses for the main comparison between penicillins and cephalosporins only and for primary outcomes only.

1. By type of surgery: elective caesarean section versus non-elective caesarean section versus mixed or not defined. (Rupture of membranes for more than six hours or the presence of labour was used to differentiate a non-elective caesarean section from an elective procedure.)
2. By time of administration: before cord clamping versus after cord clamping versus not defined.
3. By route of administration: systemic versus lavage.

We intended to undertake a subgroup analysis by the number of doses given but feel this is better assessed in other reviews (*Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section* and *Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section)*. There will also be a review or reviews on the timing and routes of administration of the antibiotics where studies exist which compare directly, for example, before and after cord clamping (*Timing of prophylactic antibiotics for preventing infectious morbidity in women undergoing caesarean section* and *Routes of administration for antibiotic given to women routinely for preventing infection after caesarean section)*.

We assessed subgroup differences by interaction tests (Deeks 2001) available within RevMan (RevMan 2014). We reported the results of subgroup analyses quoting the Chi^2 statistic and P value, and the interaction test I^2 value.

Sensitivity analysis

We planned to carry out sensitivity analysis to explore the effect of trial quality for important outcomes in the review. Where there was a high risk of bias associated with a particular aspect of study quality, for example, inadequate sequence generation and allocation concealment (Schultz 1995), we planned to explore this by sensitivity analysis (Higgins 2009) but we felt there were insufficient high-quality trials (only three identified Figure 1) for a meaningful analysis.

Figure 1. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

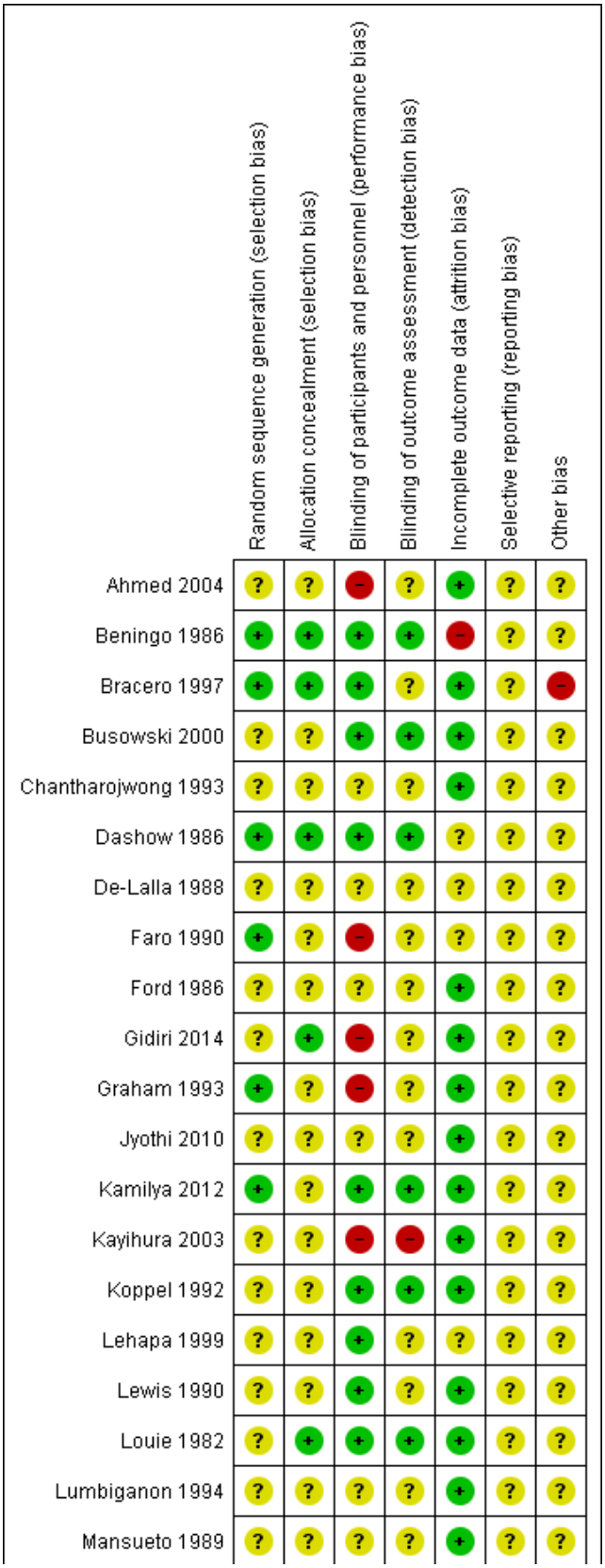
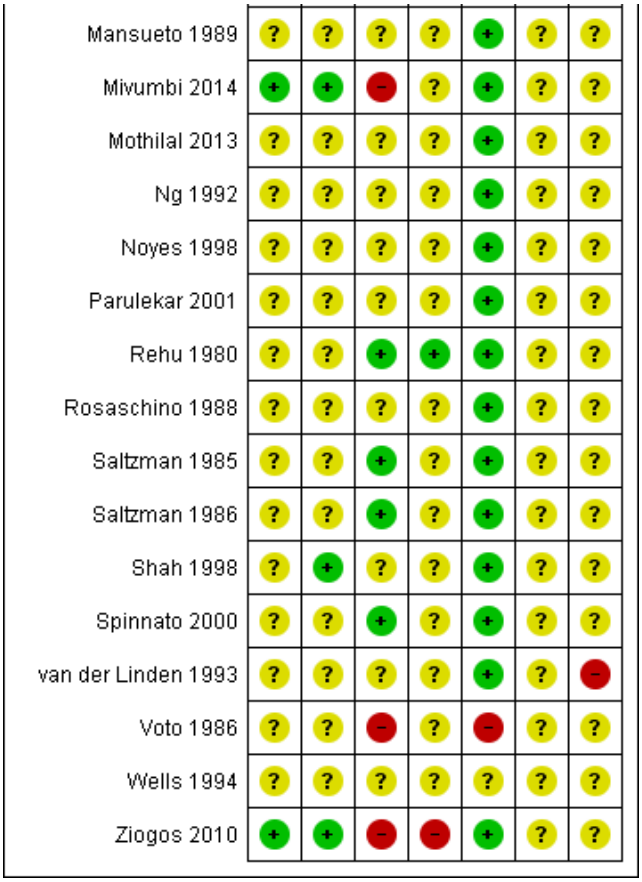


Figure 1. (Continued)



RESULTS

Description of studies

Results of the search

We identified 136 reports for 133 studies. For a detailed description of studies *see* Characteristics of included studies, Characteristics of excluded studies and Characteristics of studies awaiting classification.

The 35 trials included in the review were conducted mostly in industrialised countries, for example, United States, Canada, Israel, Italy, Switzerland or The Netherlands (see Characteristics of included studies).. Criteria listed to define the presence of outcome variables of interest (e.g. endometritis) were remarkably consistent across trials.

Two studies await data extraction, either because they are being translated or we are awaiting information from the authors (see Studies awaiting classification).

Included studies

We included 35 studies, of which 31 provided data involving 7697 women and we undertook 37 meta-analyses. Four studies were reported as conference abstracts only (De-Lalla 1988; Lehapa 1999; Lumbiganon 1994; Wells 1994). Four studies did not provide data: two full papers (Graham 1993; Voto 1986) and two of the conference abstracts (De-Lalla 1988; Wells 1994). Antibiotics for prophylaxis were administered after the cord was clamped in all but five of the studies, where four administered the prophylaxis before cord clamping (Ahmed 2004; Mivumbi 2014; Parulekar 2001; Rosaschino 1988) and one study did not provide the information (Gidiri 2014).

Cephalosporins versus penicillins

We included 30 studies, of which 27 provided data on 7299 women, where cephalosporins were compared with penicillins for prophylaxis at caesarean section (Ahmed 2004; Beningo 1986; Bracero 1997; Busowski 2000; Chantharojwong 1993; Dashow 1986; Faro 1990; Ford 1986; Gidiri 2014; Jyothi 2010; Kamilya 2012; Koppel 1992; Lehapa 1999; Lewis 1990; Louie 1982; Lumbiganon 1994; Mivumbi 2014; Ng 1992; Noyes 1998; Parulekar 2001; Rosaschino 1988; Saltzman 1985; Saltzman 1986; Shah 1998; Spinnato 2000; van der Linden 1993; Ziogos 2010). Four studies were included though they provide no usable data on the outcomes listed in the review (De-Lalla 1988; Graham 1993; Voto 1986).

We looked at comparisons of the subgroups of :

1. single cephalosporins versus single penicillins
2. single cephalosporins versus penicillin combinations (e.g. co-amoxyclav)
3. cephalosporin combinations versus single penicillins
4. cephalosporin combinations versus penicillin combinations

Other antibiotic classes

We found three studies comparing a cephalosporin or penicillin with another class of antibiotics (Busowski 2000; Mothilal 2013; Wells 1994).

Mixed antibiotics regimens that did not include cephalosporins versus penicillins

We included a further five studies that assessed other combined antibiotic regimens against penicillins or cephalosporins for prophylaxis at caesarean section (Kayihura 2003; Mansueto 1989; Mothilal 2013; Rehu 1980; Shah 1998) and one study already included which also compared a combination of other antibiotics with a cephalosporin (Parulekar 2001).

Excluded studies

We excluded 96 studies that compared different antibiotics within the same class, either singly or in combination (*see* Characteristics of excluded studies).

Risk of bias in included studies

See Figure 1 for a summary of 'Risk of bias' assessments.

Allocation

Five studies were considered to have adequate sequence generation and allocation concealment (Beningo 1986; Bracero 1997; Dashow 1986; Mivumbi 2014; Ziogos 2010). Three further studies were assessed as low risk of bias for sequence generation but were unclear on allocation concealment (Faro 1990; Graham 1993; Kamilya 2012). The remaining studies were unclear about how adequately they had addressed these aspects to minimise bias.

Blinding

Thirteen studies were assessed as low risk of bias for performance bias (Beningo 1986; Bracero 1997; Busowski 2000; Dashow 1986; Kamilya 2012; Koppel 1992; Lehapa 1999; Lewis 1990; Louie 1982; Rehu 1980; Saltzman 1985; Saltzman 1986; Spinnato 2000), eight were assessed as high risk (Ahmed 2004; Faro 1990; Gidiri 2014; Graham 1993; Kayihura 2003; Mivumbi 2014; Voto 1986; Ziogos 2010) and the remainder were unclear.

For detection bias, we assessed seven studies as low risk (Beningo 1986; Busowski 2000; Dashow 1986; Kamilya 2012; Koppel 1992; Louie 1982; Rehu 1980), two as high risk (Kayihura 2003; Ziogos 2010) and the remainder as unclear.

Incomplete outcome data

Twenty-eight studies were assessed as low risk of attrition bias (Ahmed 2004; Bracero 1997; Busowski 2000; Chantharojwong 1993; Ford 1986; Gidiri 2014; Graham 1993; Jyothi 2010; Kamilya 2012; Kayihura 2003; Koppel 1992; Lewis 1990; Louie 1982; Lumbiganon 1994; Mansueto 1989; Mivumbi 2014; Mothilal 2013; Ng 1992; Noyes 1998; Parulekar 2001; Rehu 1980; Rosaschino 1988; Saltzman 1985; Saltzman 1986; Shah 1998; Spinnato 2000; van der Linden 1993; Ziogos 2010).

Selective reporting

This was unclear on all the included studies as we were not able to assess the trial protocols.

Other potential sources of bias

This was assessed as unclear for all but two of the included studies; many of the studies were quite old and it was difficult to assess if there were other biases. The two studies assessed as having high risk of other bias were studies funded by drug companies (Bracero 1997; van der Linden 1993). In one study the antibiotic drugs were donated by the drug company but this was considered not to necessarily increase the likelihood of bias (Ahmed 2004). The other included studies gave no mention of drug company involvement.

Effects of interventions

See: **Summary of findings for the main comparison** Cephalosporins versus penicillins - all women for preventing infection at caesarean section

The search identified 35 studies of which 31 provided data in a format that could be included in this review (Ahmed 2004; Beningo 1986; Bracero 1997; Busowski 2000; Chantharojwong 1993; Dashow 1986; Faro 1990; Ford 1986; Gidiri 2014; Jyothi 2010; Kamilya 2012; Kayihura 2003; Koppel 1992; Lehapa 1999; Lewis 1990; Louie 1982; Lumbiganon 1994; Mansueto 1989; Mivumbi 2014; Mothilal 2013; Ng 1992; Noyes 1998; Parulekar 2001; Rehu 1980; Rosaschino 1988; Saltzman 1985; Saltzman 1986; Shah 1998; Spinnato 2000; van der Linden 1993; Ziogos 2010). These studies included 7697 women. A further four studies also addressed the comparisons in this review but did not provide data that could be included in the meta-analyses (De-Lalla 1988; Graham 1993; Voto 1986; Wells 1994).

The classification of antibiotics is set out in Additional tables.

1. Cephalosporins (B) versus penicillins (A) - all women, 27 studies, 7299 women

Twenty-seven studies provided data for inclusion in this comparison (Ahmed 2004; Beningo 1986; Bracero 1997; Busowski 2000; Chantharojwong 1993; Dashow 1986; Faro 1990; Ford 1986; Gidiri 2014; Jyothi 2010; Kamilya 2012; Koppel 1992; Lehapa 1999; Lewis 1990; Louie 1982; Lumbiganon 1994; Mivumbi 2014; Ng 1992; Noyes 1998; Parulekar 2001; Rosaschino 1988; Saltzman 1985; Saltzman 1986; Shah 1998; Spinnato 2000; van der Linden 1993; Ziogos 2010). A further four studies addressed this comparison but did not provide data in a format suitable for inclusion (De-Lalla 1988; Graham 1993; Voto 1986; Wells 1994).

Overall, the quality of studies was generally unclear for the critical aspects of selection bias, probably reflecting that they were mostly older studies undertaken in the 1980s and 1990s. Only five studies met the criteria for low risk of bias in terms of sequence generation and allocation concealment (Beningo 1986; Bracero 1997; Dashow 1986; Mivumbi 2014; Ziogos 2010). Three studies had adequate sequence generation but allocation concealment was unclear (Faro 1990; Graham 1993; Kamilya 2012;). The remainder were unclear on both sequence generation and allocation concealment (Figure 1).

For this comparison we have pooled any cephalosporin or any penicillin, at any dose or doses and by any route of administration. Different cephalosporins, different penicillins and different doses will be assessed in other reviews on *Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section* and *Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section*.

Subgroup 1: A single cephalosporin (B) versus a single penicillin (A)

Of the included studies with data, 13 assessed a single cephalosporin versus a single penicillin and involved 4010 women (Beningo 1986; Chantharojwong 1993; Dashow 1986; Faro 1990; Ford 1986; Lehapa 1999; Lewis 1990; Louie 1982; Mivumbi 2014; Ng 1992; Rosaschino 1988; Saltzman 1986; Spinnato 2000).

The quality of these studies was generally unclear on selection bias. Three studies were assessed at low risk of bias for both sequence generation and allocation concealment (Beningo 1986; Dashow 1986; Mivumbi 2014). One study had adequate sequence generation but allocation concealment was unclear (Faro 1990).

Primary outcomes

There was no maternal sepsis identified in the 346 women involved in two studies which looked at this outcome (Analysis 1.1). There was no significant difference identified in the incidence of endometritis between cephalosporins and penicillins, average risk ratio (RR) 1.11, and 95% confidence interval (CI) 0.81 to 1.52, nine studies, 3130 women, random effects (Tau^2 = 0.05; Chi^2 = 10.67, P = 0.22; I^2 = 25%, Analysis 1.2).

None of the included studies assessed either infant sepsis or infant oral thrush.

Secondary outcomes

There was no significant difference identified for the following:

- maternal fever (average RR 0.89, 95% CI 0.61 to 1.30, seven studies, 1344 women, random effects Tau^2 = 0.09; Chi^2 = 9.75, P = 0.14; I^2 = 38%, Analysis 1.5);
- maternal wound infection (average RR 0.83 95% CI 0.38 to 1.81, nine studies, 1497 women, random effects (Tau^2 = 0.29; Chi^2 = 9.11, P = 0.24; I^2 = 23%, Analysis 1.6) ;
- maternal urinary tract infection (average RR 1.48; 95% CI 0.89 to 2.48, seven studies, 1120 women, random effects (Tau^2 = 0.00; Chi^2 = 3.90, P = 0.56, I^2 = 0%, Analysis 1.7);
- maternal composite adverse effects (RR 2.02, 95% CI 0.18 to 21.96, three studies, 1902 women, Analysis 1.10);
- maternal skin rash (RR 1.45, 95% CI 0.06 to 35.38, two studies, 351 women, Analysis 1.15).

For the remaining outcomes, either there were no events or the studies did not asses the outcomes.

See Analysis 1.1 to Analysis 1.28.

Subgroup 2: A single cephalosporin (B) versus a penicillin combination (A+)

Twelve studies involving 2875 women compared a single cephalosporin with a penicillin combination. Six studies compared a cephalosporin alone with co-amoxyclav (Ahmed 2004; Jyothi 2010; Kamilya 2012; Koppel 1992; Lumbiganon 1994; Saltzman 1985); five studies compared a cephalosporin alone with a penicillin plus sulbactam (Bracero 1997; Busowski 2000; Noyes 1998; Spinnato 2000; Ziogos 2010). One study compared a cephalosporin alone with a cocktail of drugs including a penicillin (Parulekar 2001).

The quality of these studies was generally unclear. The studies were all unclear for sequence generation and allocation concealment.

Primary outcomes

There was no significant difference identified between single cephalosporins and penicillin combinations in sepsis (RR 2.37, 95% CI 0.10 to 56.41, one study, 75 women, Analysis 1.1), nor in endometritis (average RR 0.90, 95% CI 0.60 to 1.35, ten studies, 2134 women, random effects Tau^2 = 0.00, Chi^2 = 5.21, P = 0.74, I^2 = 0%, Analysis 1.2).

None of the studies assessed infant sepsis or infant oral thrush.

Secondary outcomes

There was no significant difference identified between single cephalosporins and penicillin combinations for:

- maternal fever (average RR 0.92, 95% CI 0.56 to 1.49, six studies, 1824 women, random effects, Tau^2 = 0.15; Chi^2 = 8.75, P = 0.12; I^2 = 43%, Analysis 1.5);
- maternal wound infection (average RR 0.72, (95% CI 0.40 to 1,30, seven studies, 1608 women, random effects Tau^2 = 0.00; Chi^2 = 2.04, P = 0.92; I^2 = 0%, Analysis 1.6);
- maternal urinary tract infection (average RR 0.66, 95% CI 0.17 to 2.55, six studies, 1361 women, random effects Tau^2 = 0.95, Chi^2 = 6.25, P= 0.10; I^2 = 52%, Analysis 1.7);
- maternal composite adverse effects (RR 0.96, 95% CI 0.09 to 10.50, four studies, 1333 women, Analysis 1.10);
- maternal vomiting (RR 7.00, 95% CI 0.37 to 133.78, two studies, 319 women, Analysis 1.13);
- maternal skin rash (RR 1.26, 95% CI 0.34 to 4.67, four studies, 618 women, Analysis 1.15).

For the remaining outcomes, either there were no events or the studies did not asses the outcomes.

See Analysis 1.1 to Analysis 1.28.

Subgroup 3: A cephalosporin combination (B+) versus a single penicillin (A)

One study with 147 women compared a cephalosporin combination versus a single penicillin (Shah 1998).

The study was unclear about how the randomisation sequence was generated but was considered at low risk of bias for allocation concealment.

Primary outcomes

We found no significant difference between cephalosporin combination and single penicillins for maternal endometritis (RR 2.70, 95% CI 0.63 to 11.55, one study, 139 women, Analysis 1.2).

The study did not assess maternal sepsis, infant sepsis nor infant oral thrush.

Secondary outcomes

There was no significant difference identified between cephalosporin combination and single penicillins for:

- maternal fever (RR 2.36, 95% CI 0.84 to 6.62, one study, 139 women, Analysis 1.5);

- maternal wound infection (RR 2.02, 95% CI 0.42 to 9.63, one study, 139 women, Analysis 1.6).

For the remaining outcomes, either there were no events or the study did not assess the outcomes.

See Analysis 1.1 to Analysis 1.26.

Subgroup 4: A cephalosporin combination (B+) versus a penicillin combination (A+)

Two studies with 363 women compared a cephalosporin combination versus a penicillin combination (Gidiri 2014; van der Linden 1993).

In terms of quality, one study was generally unclear for most of the aspects of assessment of bias of these studies (van der Linden 1993) the other study was unclear on sequence generation and allocation concealment and was considered at high risk of bias for blinding (Gidiri 2014).

Primary outcomes

There was no significant difference identified between cephalosporins combinations and penicillins combinations for maternal sepsis (RR 3.21, 95% CI 0.34 to 30.45, one study, 232 women, Analysis 1.1) or endometritis (RR 0.33, 95% CI 0.01 to 7.77, one study, 83 women, Analysis 1.2).

The study did not assess infant sepsis nor infant oral thrush.

Secondary outcomes

There was no significant difference identified between cephalosporins combinations and penicillins combinations for:

- maternal fever (RR 1.57, 95% CI 0.69 to 3.60, two studies, 315 women, Analysis 1.5);
- maternal wound infection (RR 1.23, 95% CI 0.42 to 3.58, two studies, 315 women, Analysis 1.6).

For the remaining outcomes, either there were no events or the study did not assess the outcomes.

See Analysis 1.1 to Analysis 1.28.

Publication bias

We identified possible publication bias in the assessment of maternal endometritis (Figure 2) and urinary tract infection (Figure 3). However, there appeared to be no publication bias for maternal fever (Figure 4) nor wound infections (Figure 5). However, as we found no overall difference this is probably of little significance.

Figure 2. Funnel plot of comparison: 1 Cephalosporins versus penicillins - all women, outcome: 1.2 Maternal endometritis.

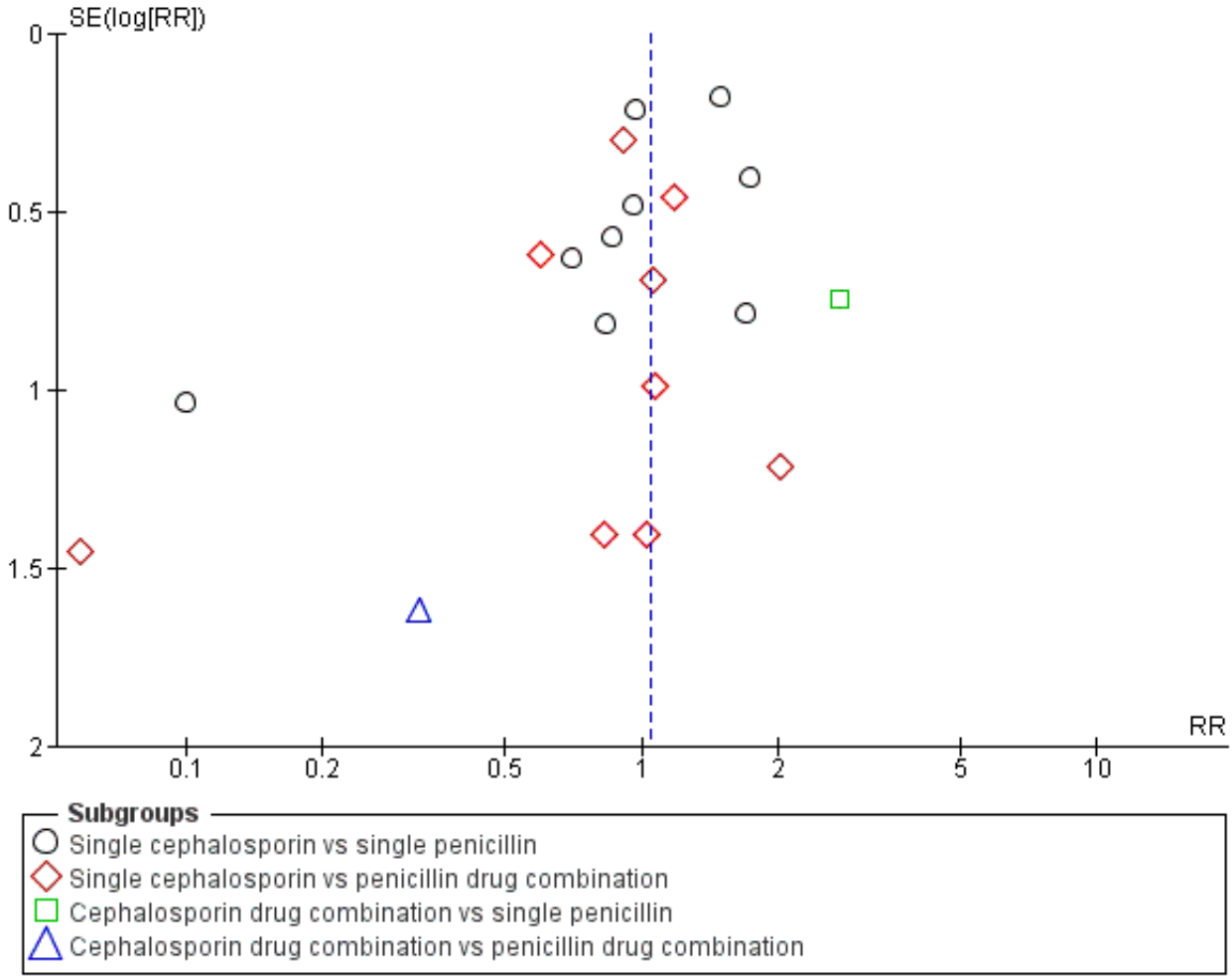


Figure 3. Funnel plot of comparison: 1 Cephalosporins versus penicillins - all women, outcome: 1.7 Maternal urinary tract infection.

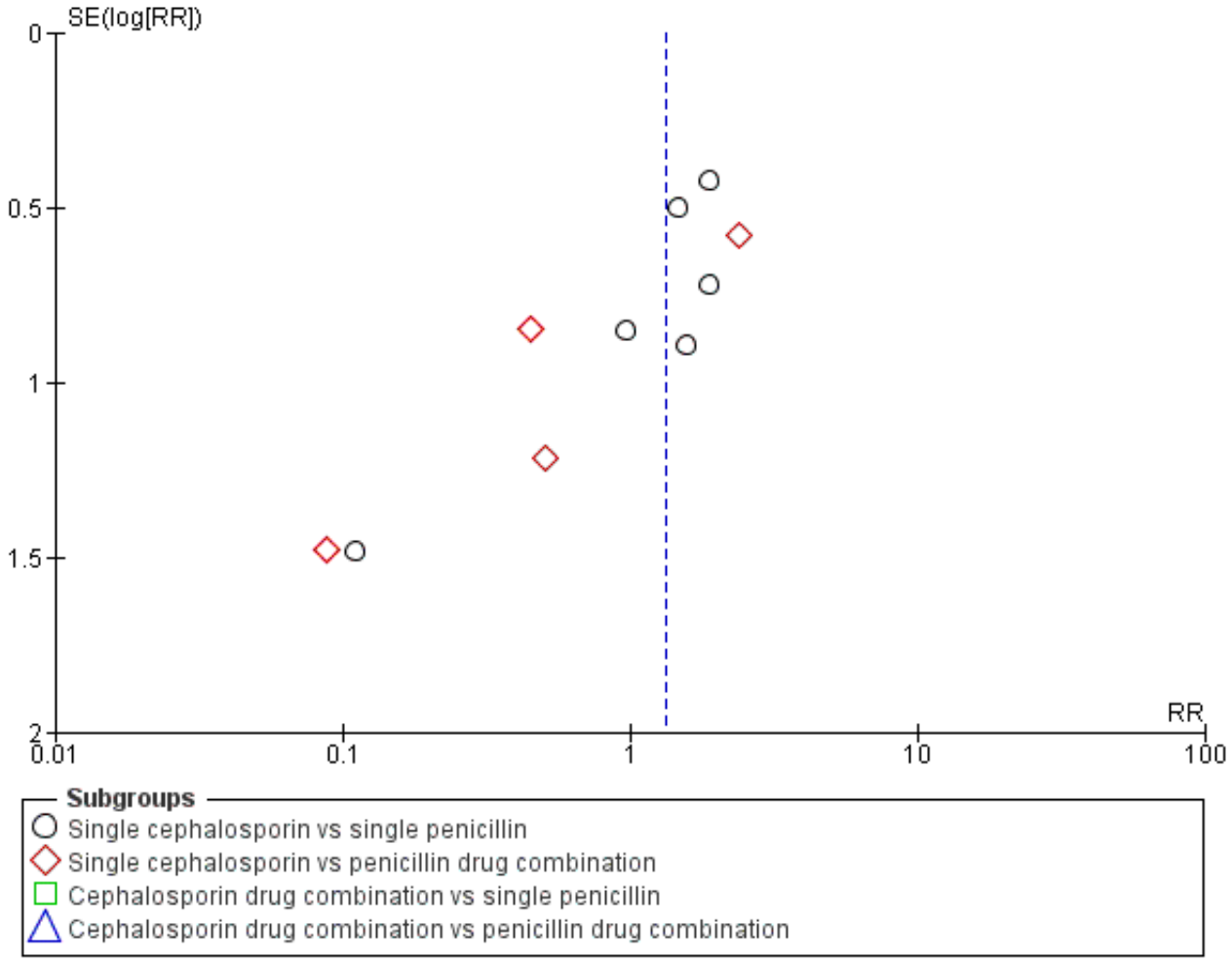


Figure 4. Funnel plot of comparison: 1 Cephalosporins versus penicillins - all women, outcome: 1.5 Maternal fever (febrile morbidity).

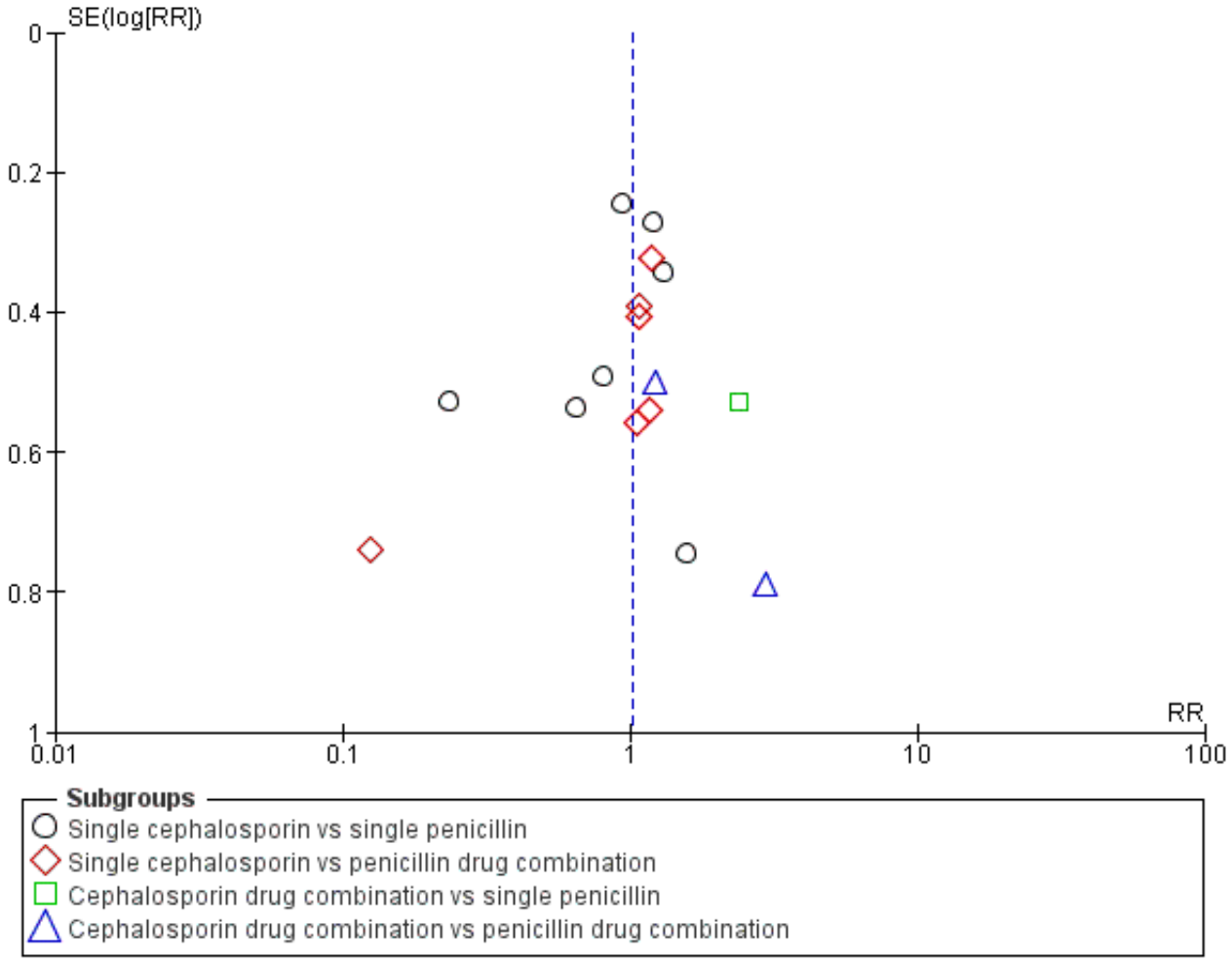
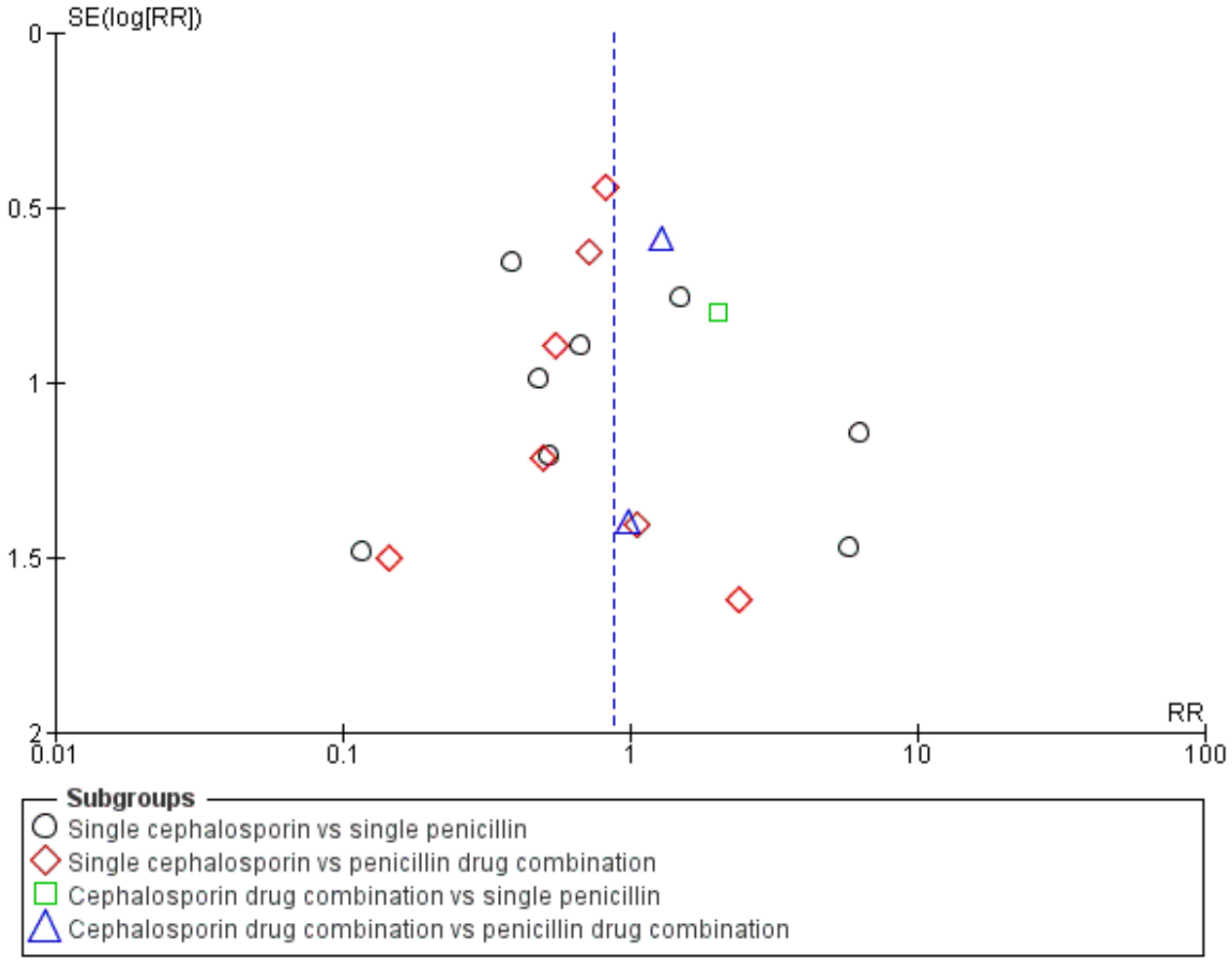


Figure 5. Funnel plot of comparison: 1 Cephalosporins versus penicillins - all women, outcome: 1.6 Maternal wound infection.



2. Cephalosporins (B) versus penicillins (A) - comparison by type of caesarean section, 22 studies, 5788 women

Twenty-two studies provided data on at least one primary outcome for this subgroup comparison (*see* Characteristics of included studies. Three studies included women having an elective caesarean section (Ahmed 2004; Jyothi 2010; Shah 1998), five studies included women having a non-elective caesarean section (Busowski 2000; Faro 1990; Louie 1982; Saltzman 1986; van der Linden 1993) and 14 studies included women having elective or non-elective caesarean section or the studies did not specify the type of caesarean section (Bracero 1997; Chantharojwong 1993; Dashow 1986; Gidiri 2014; Kamilya 2012; Koppel 1992; Lewis 1990; Mivumbi 2014; Noyes 1998; Parulekar 2001; Rosaschino 1988; Saltzman 1985; Spinnato 2000; Ziogos 2010). A further five studies specified the type of caesarean section but did not provide data on at least one primary outcome (Beningo 1986; Ford 1986; Lehapa 1999; Lumbiganon 1994; Ng 1992).

Four studies were assessed as having low risk of bias in terms of adequate sequence generation and adequate allocation concealment (Bracero 1997; Dashow 1986; Mivumbi 2014; Ziogos 2010). Two studies had adequate sequence generation (Faro 1990; Kamilya 2012) but unclear allocation concealment;. The remainder of the studies were unclear for both sequence generation and allocation concealment (Figure 1).

We identified no real differences between the two groups of drugs in relation to the different types of caesarean section for maternal sepsis (RR 2.91, 95% CI 0.47 to 18.10, four studies, 653 women, Analysis 2.1) or endometritis (average RR 1.11, 95% CI 0.90 to 1.37, 20 studies, 5390 women, random effects Tau^2 = 0.01, Chi^2 = 18.60, P = 0.42, I^2 = 3%, Analysis 2.2). However, in the subgroup analysis for endometritis we found differences between groups of type of caesarean section (interaction test, Chi^2 = 5.18, P = 0.08, I^2 = 61.4%). Penicillins were more effective than cephalosporins for reducing endometritis among women undergoing non-elective caesarean section (average RR 1.33, 95% CI 1.01 to 1.75, 6 studies, 2362 women, random effects Tau^2 = 0.00, Chi^2 = 3.68, P = 0.60, I^2 = 0%, Analysis 2.2).

None of the studies assessed infant sepsis nor infant oral thrush.

3. Cephalosporins (B) versus penicillins (A) - comparison by timing of administration, 22 studies, 5788 women

Twenty-two studies provided data on at least one primary outcome for inclusion in this subgroup comparison (*see* Characteristics of included studies). Two studies administered antibiotics before cord clamping (Ahmed 2004; Mivumbi 2014) and 19 studies administered the antibiotics after cord clamping (Bracero 1997; Busowski 2000; Chantharojwong 1993; Faro 1990; Jyothi 2010; Kamilya 2012; Koppel 1992; Lewis 1990; Louie 1982; Mivumbi 2014; Noyes 1998; Parulekar 2001; Rosaschino 1988; Saltzman 1985; Saltzman 1986; Shah 1998; Spinnato 2000; van der Linden 1993; Ziogos 2010) and two studies did not report the timing of administration with relation to cord clamping (Dashow 1986; Gidiri 2014). A further five studies addressed this comparison but did not provide data in a format suitable for inclusion (Beningo 1986; Ford 1986; Lehapa 1999; Lumbiganon 1994; Ng 1992).

Four studies were assessed as having low risk of bias in terms of adequate sequence generation and adequate allocation concealment (Bracero 1997; Dashow 1986; Mivumbi 2014; Ziogos 2010). Two studies had adequate sequence generation but unclear allocation concealment (Faro 1990; Kamilya 2012) The remainder of the studies were unclear for both sequence generation and allocation concealment (Figure 1).

We identified no real differences between the two groups of drugs for maternal sepsis (RR 2.91, 95% CI 0.47 to 18.10, four studies, 653 women, Analysis 3.1) or endometritis (average RR 1.11, 95% CI 0.90 to 1.37, 20 studies, 5390 women, random effects $Tau^2 = 0.01$, $Chi^2 = 18.6$, P = 0.42, $I^2 = 3\%$, Analysis 3.2) in relation to the timing of administration. A separate review will be undertaken where studies have compared directly the antibiotic being given before versus after cord clamping ('*Timing of prophylactic antibiotics for preventing infectious morbidity in women undergoing caesarean section*').

The interaction test for endometritis showed no significant difference between the groups (P = 0.75) and this was also the case visually.

None of the studies assessed infant sepsis nor infant oral thrush.

4. Cephalosporins (B) versus penicillins (A) - comparison by route of administration, 22 studies, 5788 women

Twenty-two studies provided data on at least one primary outcome for inclusion in this subgroup comparison. Twenty studies compared the antibiotics when given by intravenous administration (Ahmed 2004; Bracero 1997; Busowski 2000; Chantharojwong 1993; Faro 1990; Gidiri 2014; Jyothi 2010; Kamilya 2012; Koppel 1992; Louie 1982; Mivumbi 2014; Noyes 1998; Parulekar 2001; Rosaschino 1988; Saltzman 1985; Saltzman 1986; Shah 1998; Spinnato 2000; van der Linden 1993; Ziogos 2010). Two studies compared the antibiotics when administered as a lavage/irrigation (Dashow 1986; Lewis 1990). A further five studies addressed this comparison but did not provide data in a format suitable for inclusion (Beningo 1986; Ford 1986; Lehapa 1999; Lumbiganon 1994; Ng 1992).

Four studies were assessed as having low risk of bias in terms of adequate sequence generation and adequate allocation concealment (Bracero 1997; Dashow 1986; Mivumbi 2014; Ziogos 2010). Two studies had adequate sequence generation but unclear allocation concealment (Faro 1990; Kamilya 2012). The remainder of the studies were unclear for both sequence generation and allocation concealment (Figure 1).

We identified no real differences between the two groups of drugs for maternal sepsis (average RR 2.90, 95% CI 0.46 to 18.17, four studies, 653 women, random effects $Tau^2 = 0.00$, $Chi^2 = 0.02$, P = 0.88, $I^2 = 0\%$, Analysis 4.1) or endometritis (RR 1.12, 95% CI 0.92 to 1.37, 20 studies, 5390 women, Analysis 4.2) in relation to the route of administration. A separate review will be undertaken where studies have compared directly the different routes of antibiotic administration ('*Routes of administration for antibiotic given to women routinely for preventing infection after caesarean section*').

The interaction test for endometritis showed no significant difference between the groups (P = 0.38) and this was also the case visually.

None of the studies assessed infant sepsis nor infant oral thrush.

5. First generation cephalosporins (B1) versus extended spectrum penicillins (A3) - all women, two studies, 822 women

Two studies provided data for inclusion in this comparison (Faro 1990; Shah 1998). Cephalosporins included cefazolin (Faro 1990), cephazoline, (Faro 1990) and cephradine plus metronidazole (Shah 1998). Penicillins included only piperacillin (Faro 1990; Shah 1998). Both studies were of unclear quality, with one being unclear about the sequence generation (Shah 1998) and the other being unclear about concealment allocation (Faro 1990). (Figure 1).

Primary outcomes

There was a significantly higher incidence of maternal endometritis with first generation cephalosporins compared with extended spectrum penicillins (RR 2.18, 95% CI 1.30 to 3.66, two studies, 814 women, Analysis 5.2). None of the other primary outcomes (maternal sepsis, infant sepsis and infant thrush) were assessed in either of these studies.

Secondary outcomes

There was no statistically significant difference identified in maternal fever (RR 2.36, 95% CI 0.84 to 6.62, one study, 139 women, Analysis 5.5) nor maternal wound infection (RR 2.02, 95% CI 0.42 to 9.63, one study, 139 women, Analysis 5.6). None of the other secondary outcomes were assessed in this comparisons.

Neither study assessed any outcomes on the infant, nor post-discharge infections or readmissions for the mother.

6. First generation cephalosporins (B1) versus aminopenicillins (A4) - all women, eight studies, 1882 women

Eight studies provided data for inclusion in this comparison (Chantharojwong 1993; Dashow 1986; Faro 1990; Jyothi 2010; Louie 1982; Lumbiganon 1994; Mivumbi 2014; Noyes 1998). Cephalosporins included cefazolin (Chantharojwong 1993; Faro 1990; Jyothi 2010; Louie 1982; Lumbiganon 1994; Noyes 1998; Mivumbi 2014) and cephapirin (Dashow 1986). Penicillins included ampicillin (Chantharojwong 1993; Dashow 1986; Faro 1990; Louie 1982; Mivumbi 2014), amoxicillin/clavulanic acid (Lumbiganon 1994) and ampicillin/sulbactam (Noyes 1998). A further study addressed this comparison but did not provide data in a format suitable for inclusion (Graham 1993). Two studies were assessed

as adequate on sequence generation and allocation concealment (Dashow 1986; Mivumbi 2014) and one study was adequate on allocation concealment but because sequence generation was unclear overall uncertainty remains (Lumbiganon 1994). The remainder were assessed as unclear for allocation concealment (Figure 1).

Primary outcomes

There was no significant difference identified in maternal endometritis (average RR 1.09, 95% CI 0.69 to 1.71, seven studies, 1487 women, random effects, $Tau^2 = 0.08$, $Chi^2 = 7.66$, P = 0.26, $I^2 = 22\%$, Analysis 6.2). None of the other primary outcomes (maternal sepsis, infant sepsis and infant thrush) were assessed in any of these studies.

Secondary outcomes

There was no statistically significant difference identified in maternal fever (average RR 0.78, 95% CI 0.40 to 1.51, five studies, 883 women, random effects $Tau^2 = 0.35$, $Chi^2 = 10.37$, P = 0.03, $I^2 = 61\%$, Analysis 6.5), wound infection (RR 0.85, 95% CI 0.36 to 2.01, five studies, 626 women, Analysis 6.6), urinary tract infections (average RR 1.41, 95% CI 0.54 to 3.70, five studies, 626 women, random effects $Tau^2 = 0.28$, $Chi^2 = 4.17$, P = 0.24, $I^2 = 28\%$, Analysis 6.7), nor maternal composite adverse outcomes (RR 0.32, 95% CI 0.01 to 7.84, two studies, 861 women, Analysis 6.10). There was a significant reduction in the mothers' hospital stay with the cephalosporins (mean difference (MD) -1.50, 95% CI -2.46 to -0.54, one study, 132 women, Analysis 6.21). There were no events in the assessments of maternal allergic reactions not skin rashes. None of the other secondary outcomes were assessed in any of the studies.

None of the studies assessed any outcomes on the infant, nor post-discharge infections or readmissions for the mother.

7. Second generation cephalosporins (B2) versus extended spectrum penicillins (A3) - all women, six studies, 2077 women

Six studies provided data for inclusion in this comparison (Beningo 1986; Faro 1990; Ford 1986; Lewis 1990; Saltzman 1985; Saltzman 1986). Cephalosporins included cefoxitin (Beningo 1986; Faro 1990; Ford 1986; Lewis 1990; Saltzman 1985; Saltzman 1986), cefonicid (Faro 1990) and cefotetan (Faro 1990). Penicillins included piperacillin (Beningo 1986; Faro 1990; Ford 1986), ticarcillin (Lewis 1990; Saltzman 1985) and mezlocillin (Saltzman 1986). A further study addressed this comparison but did not provide data in a format suitable for inclusion (De-Lalla 1988). Only one study was assessed as adequate on sequence generation and allocation concealment (Beningo 1986). One study was adequate for sequence generation but unclear on allocation concealment (Faro 1990) and the remainder were unclear on both criteria (Figure 1).

Primary outcomes

There was no sepsis in the 287 women included in the one study that reported it (Lewis 1990). We found no significant difference identified for maternal endometritis (average RR 1.10, 95% CI 0.78 to 1.54, four studies, 1334 women, random effects $Tau^2 = 0.01$, $Chi^2 = 3.19$, P = 0.36, $I^2 = 6\%$, Analysis 7.2). None of the other primary outcomes (infant sepsis and infant thrush) were assessed in either of these studies.

Secondary outcomes

There was no significant difference identified for maternal fever (RR 1.08, 95% CI 0.79 to 1.47, four studies, 850 women, Analysis 7.5), wound infection (average RR 2.37, 95% CI 0.64 to 8.73, two studies, 438 women, random effects $Tau^2 = 0.08$, $Chi^2 = 2.37$, P = 0.30, $I^2 = 8\%$, Analysis 7.6), urinary tract infection (average RR 1.43, 95% CI 0.67 to 3.07, three studies, 567 women, random effects $Tau^2 = 0.09$, $Chi^2 = 2.42$, P = 0.30, $I^2 = 17\%$, Analysis 7.7), maternal composite adverse effects (RR 2.02, 95% CI 0.18 to 21.96, two studies, 1030 women, Analysis 7.10) and skin rash (RR 2.70, 95% CI 0.11 to 64.96, one study, 129 women, Analysis 7.15).

Three studies looked at infection rates after discharge (Beningo 1986; Saltzman 1985; Saltzman 1986). Two other studies reported no infections up to six weeks postoperatively based on 305 women participating in the studies (Saltzman 1985; Saltzman 1986).

None of the studies assessed any outcomes on the infant.

8. Second generation cephalosporins (B2) versus aminopenicillins (A4) - all women, eight studies, 1921 women

Eight studies provided data for inclusion in this comparison (Bracero 1997; Busowski 2000; Dashow 1986; Faro 1990; Noyes 1998; Spinnato 2000; van der Linden 1993; Ziogos 2010). Cephalosporins included cefotetan (Bracero 1997; Busowski 2000; Faro 1990; Noyes 1998; Spinnato 2000; Ziogos 2010), cefamandole (Dashow 1986), cefonicid (Faro 1990), cefoxitin (Faro 1990) and cefuroxime (van der Linden 1993). Penicillins included ampicillin (Bracero 1997; Dashow 1986; Faro 1990; Spinnato 2000), ampicillin/sulbactam (Busowski 2000; Noyes 1998; Spinnato 2000) and amoxicillin/clavulanic acid (van der Linden 1993). A further study addressed this comparison but did not provide data in a format suitable for inclusion (Voto 1986). Two studies were assessed as adequate on sequence generation and allocation concealment (Bracero 1997; Dashow 1986). One study was assessed as adequate on sequence generation but unclear on allocation concealment (Faro 1990) and the remainder were unclear on both criteria (Figure 1).

Primary outcomes

There was no significant difference identified in maternal sepsis (RR 2.37, 95% CI 0.10 to 56.41, one study, 75 women, Analysis 8.1) nor endometritis (RR 1.01, 95% CI 0.75 to 1.35, eight studies, 1890 women, Analysis 8.2). None of the other primary outcomes (infant sepsis and infant thrush) were assessed in any of these studies.

Secondary outcomes

There was no significant difference identified for maternal fever (RR 1.17, 95% CI 0.64 to 2.15, three studies, 387 women, Analysis 8.5), wound infection (RR 1.14, 95% CI 0.47 to 2.78, five studies, 638 women, Analysis 8.6), urinary tract infection (average RR 0.63, 95% CI 0.11 to 3.66, four studies, 462 women, random effects $Tau^2 = 1.56$, $Chi^2 = 6.10$; P = 0.05, $I^2 = 67\%$, Analysis 8.7), maternal composite adverse effects (RR 1.92, 95% CI 0.18 to 20.82, three studies, 1130 women, Analysis 8.10), nor skin rash (RR 1.02, 95% CI 0.23 to 4.46, two studies, 364 women, Analysis 8.15). For urinary tract infection there was high heterogeneity and studies showed effects in different directions but no overall difference was identified Analysis 8.7). None of the other secondary outcomes were assessed in any of the included studies.

None of the studies assessed any outcomes on the infants, nor post-discharge infections or readmissions for the mother.

9. Third generation cephalosporins (B3) versus extended-spectrum penicillins (A3) - all women, two studies, 359 women

Two studies provided data for inclusion in this comparison (Faro 1990; Rosaschino 1988). Cephalosporins included ceftizoxime (Faro 1990) and ceftriaxone (Rosaschino 1988). Penicillins included piperacillin (Faro 1990) and mezlocillin (Rosaschino 1988). Neither study was assessed as adequate on both sequence generation and allocation concealment. Only the Faro study (Faro 1990) had adequate sequence generation and all other criteria were assessed as unclear (Figure 1).

Primary outcomes

There was no sepsis in the 287 women included in the one study that reported it (Rosaschino 1988). We found significantly more women with endometritis when third generation cephalosporins were used compared with extended spectrum penicillin (RR 2.14, 95% CI 1.14 to 4.00, one study, 300 women, Analysis 9.2). None of the other primary outcomes were assessed.

Secondary outcomes

Although some secondary outcomes were assessed, there were no events in the included studies.

Neither study assessed any outcomes on the infants, nor post-discharge infections or readmissions for the mother.

10. Third generation cephalosporins (B3) versus aminopenicillins (A4) - all women, seven studies, 1904 women

Seven studies provided data for inclusion in this comparison (Ahmed 2004; Faro 1990; Kamilya 2012; Koppel 1992; Lehapa 1999; Louie 1982; Ng 1992). Cephalosporins included ceftriaxone (Ahmed 2004; Lehapa 1999), ceftizoxime (Faro 1990), cefotamine (Kamilya 2012; Koppel 1992), cefotaxime (Louie 1982) and cefoperazone (Ng 1992). Penicillins ampicillin/cloxacillin (Ahmed 2004), amoxicillin/clavulanic acid (Koppel 1992) and ampicillin (Faro 1990; Lehapa 1999; Louie 1982; Ng 1992). None of the six studies were assessed as adequate on both sequence generation and allocation concealment. Only the Faro study (Faro 1990) had adequate sequence generation and all other criteria were assessed as unclear for the studies (Figure 1).

Primary outcomes

There was no significant difference identified for maternal endometritis (RR 1.47, 95% CI 0.89 to 2.42, five studies, 1472 women, Analysis 10.2). The other primary outcomes were not assessed in any of the studies.

Secondary outcomes

There was a significant reduction in maternal wound infection with third generation cephalosporins (B3) compared with aminopenicillins (A4) (RR 0.49, 95% CI 0.27 to 0.90, six studies, 1556 women, Analysis 10.6).

We identified no significant difference in maternal fever (RR 1.12, 95% CI 0.69 to 1.83, three studies, 1060 women, Analysis 10.5), urinary tract infection (RR 0.52, 95% CI 0.10 to 2.80, two studies, 233 women, Analysis 10.7), maternal vomiting (RR 7.00, 95% CI 0.37 to 133.78, one study, 200 women, Analysis 10.13) or maternal skin rash (RR 3.00, 95% CI 0.12 to 72.77, one study, 200 women, Analysis 10.15). The other secondary outcomes were not assessed in any of the included studies. There was no significant difference identified in the length of hospital stay (MD -0.03, 95% CI -0.14 to 0.08, one study, 746 women, Analysis 10.21).

None of the studies assessed any outcomes on the infant, nor post-discharge infections or readmissions for the mother.

11. Fluoroquinolones (C) versus penicillins (A) - all women, one study, 72 women

One study provided data for inclusion in this comparison (Busowski 2000). This study compared the second generation fluoroquinolone (C2) ciprofloxacin with the ampicillin/sulbactam (A4). This study was of questionable quality as it provided no information on the sequence generation or allocation concealment.

There were insufficient data to provide good evidence on the only outcomes assessed (maternal sepsis, endometritis, wound infection and urinary tract infection) in this comparison (Analysis 11.1; Analysis 11.2; Analysis 11.6; Analysis 11.7).

This study did not address any outcomes on the infant, nor post-discharge infections or readmissions for the mother.

12. Fluoroquinolones (C) versus cephalosporins (B) - all women, one study, 81 women

One study provided data for inclusion in this comparison (Busowski 2000). This study compared the second generation fluoroquinolone (C2) ciprofloxacin with the second generation cephalosporin cefotetan (B2). This study was of questionable quality as it provided no information on the sequence generation or allocation concealment.

There were insufficient data to provide good evidence on the only outcomes assessed (maternal sepsis, endometritis, wound infection and urinary tract infection) in this comparison (Analysis 12.1; Analysis 12.2; Analysis 11.6; Analysis 12.7).

This study did not address any outcomes on the infant, nor post-discharge infections or readmissions for the mother.

13. Other antibiotic regimens (D - I) versus penicillins (A)

13.1 Lincosamide (H) plus aminoglycoside (G) versus penicillin (A) - all women, one study, 88 women

One study involving 88 women provided data for this comparison (Rehu 1980). This study compared clindamicin (a lincosamide - group H) plus gentamicin (an aminoglycoside - group G) against benzylpenicillin penicillin (a penicillin - group A). The sequence generation and allocation concealment was unclear.

There were insufficient data to provide good evidence on the only outcomes assessed (maternal endometritis and wound infection) in this comparison (Analysis 13.2; Analysis 13.6).

This study did not address any outcomes on the infant, nor post-discharge infections or readmissions for the mother.

14. Other antibiotic regimens (D to I) versus cephalosporins (B)

14.1 Beta-lactam (F) versus cephalosporin (B) - all women, two studies, 118 women

Two studies involving 118 women provided data for this comparison (Mansueto 1989; Mothilal 2013). These studies compared azithromycin (a macrolide - group E) against cefazolin (a cephalosporin - group B1) (Mothilal 2013) and imipenem (a beta-lactam - group F) against cefotamine (a cephalosporin - group B3) (Mansueto 1989). The sequence generation and allocation concealment were unclear in both studies.

There were insufficient data to provide good evidence on the only outcomes assessed (maternal endometritis, fever, wound infection and urinary tract infection) in this comparison (Analysis 14.2; Analysis 14.5; Analysis 14.6; Analysis 12.7).

This study did not address any outcomes on the infant, nor post-discharge infections or readmissions for the mother.

15. Other antibiotic regimens versus different antibiotic regimens

15.1 Aminoglycoside (G) plus nitroimidazole (I) versus standard antibiotic cocktail - all women, one study, 241 women

One study involving 241 women provided data for this comparison (Kayihura 2003). This study compared gentamicin (an aminoglycoside - group G) plus metronidazole (a nitroimidazole - group I) versus a standard cocktail of antibiotics. The sequence generation and allocation concealment was unclear.

There were no differences identified in maternal endometritis (RR 0.81, 95% CI 0.29 to 2.26, one study, 241 women, Analysis 15.2), wound infection (RR 3.23, 95% CI 0.34 to 30.64, one study 241 women, Analysis 15.6) and urinary tract infection (RR 1.08, 95% CI 0.07 to 17.03, one study 241 women, Analysis 15.7).

This study did not address any outcomes on the infant, nor post-discharge infections or readmissions for the mother.

Sensitivity analyses

There were insufficient data from high-quality studies for an meaningful sensitivity analyses.

DISCUSSION

Antibiotic prophylaxis can be expected to produce a significant reduction in the incidence of maternal infectious morbidity (Smaill 2008). The type of antibiotic used prophylactically, as well as the optimal timing of administration, have been widely studied and discussed in the literature. Here we have addressed the comparisons between the different classes of antibiotics.

Summary of main results

There was no conclusive evidence identified of any difference between cephalosporins and penicillins in the outcomes of maternal sepsis, endometritis, fever, wound infection, urinary tract infection and adverse effects. Endometritis seemed less common when extended-spectrum penicillins were used rather than first or third generation cephalosporins, but more data are required to be sure of this.

Nor was there any difference identified between fluoroquinolones and penicillins or cephalosporins for maternal sepsis, endometritis, wound infection or urinary tract infection. However, there are clearly insufficient data on the comparisons with fluoroquinolones and further trials are needed.

None of the studies assessed any outcomes on the baby. This is a serious omission as women will want to know if this intervention has any adverse effect on their babies. There are also concerns about this lack of information even for studies where the antibiotic was given after the cord had been clamped and cut, as these drugs may pass to the baby through breastfeeding. In addition, none of the studies assessed readmissions and only three considered post-discharge infections. This is a limitation of this analysis as late infections appear to constitute the majority of infections after caesarean section (Leth 2009). We have no information on whether prophylactic antibiotics impact on these infections and whether one class of antibiotic is better than another.

We also identified no overall differences between cephalosporins and penicillins by the subgroup analyses of type of caesarean, timing of administration (before or after cord clamping), nor route of administration. Other Cochrane reviews to be undertaken will address specifically the timing and routes of administration (*Timing of prophylactic antibiotics for preventing infectious morbidity in women undergoing caesarean section* and *Routes of administration for antibiotic given to women routinely for preventing infection after caesarean section*).

In terms of subsidiary drug classifications, there seemed to be no overall difference identified, except that there may be less wound infection with third generation cephalosporins compared with ampicillins and less endometritis with extended-spectrum penicillins compared with first or third generation cephalosporins. However, since these are all likely to be underpowered, further studies are needed. The comparisons between the specific subclasses of penicillins and cephalosporins will also be addressed in further Cochrane reviews (*Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section* and *Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section*).

Overall completeness and applicability of evidence

There is uncertainty around the quality of the evidence and for the subclassification of the antibiotics there were insufficient data to draw any firm conclusions. Development of bacterial resistance is an important consideration which we plan to address as best we can in a subsequent update of this review.

Quality of the evidence

The quality of the evidence was generally unclear for most of the studies, possibly reflecting the lack of knowledge about the important criteria for minimising bias when many of the studies were undertaken back in the 1980s and 1990s. The quality of the evidence using GRADE was moderate for maternal endometritis, low for wound infection and maternal urinary tract infection, and very low for maternal composite adverse effects (Summary of findings for the main comparison). The outcomes were downgraded due to design limitations or wide confidence

interval crossing the line of no effect, small sample sizes and few events.

Potential biases in the review process

We attempted to minimise bias in a number of ways: two review authors assessed eligibility for inclusion and carried out data extraction, and three authors assessed risk of bias. Each worked independently. Nevertheless, the process of assessing risk of bias, for example, is not an exact science and includes many personal judgements.

Agreements and disagreements with other studies or reviews

The previous version of this review concluded that there was no difference in efficacy between ampicillin and first generation cephalosporins and that the more costly extended-spectrum penicillins and second and third generation cephalosporins had not been demonstrated to be any more effective (Hopkins 1999). This previous version of the review also found no benefit from multiple doses but this aspect will be addressed in the remaining two reviews to be undertaken (*Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section* and *Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section*). There is a published review on the timing of administration of the antibiotic that suggests that further studies are needed also assessing neonatal outcomes (Tita 2009). This question needs to be addressed in a Cochrane review so that it can be updated as new data come along (*Timing of prophylactic antibiotics for preventing infectious morbidity in women undergoing caesarean section*).

AUTHORS' CONCLUSIONS

Implications for practice

Best current evidence suggests that both cephalosporins and penicillins represent good choices for prophylaxis in women undergoing caesarean section, although the impact on post-discharge infections and on the infant are unknown, as is the impact on bacterial resistance. All are critical to decision-making. The use of any antibiotic needs to be made on an individual basis, taking into account other medication the mother may be on. Impact on the baby, for which there is no formal evidence, also needs to be considered, as does bacterial resistance. More costly extended-spectrum penicillins, second or third generation cephalosporins and combination regimens have not been demonstrated to be more effective but there are few data upon which to make a clear judgement.

Considering that all the antibiotic regimens have shown similar efficacy in terms of the measured outcomes, the decision of what antibiotic to use will depend on the woman's sensitivity to specific antibiotics, the physician's experience, the adverse events, the prevalence of pathogenic organisms according to previous epidemiological studies (if available), the availability and the costs in the different scenarios.

Implications for research

There is a need for good-quality trials to assess the most effective antibiotic to use at caesarean section and it is critical that outcomes on the babies are assessed. Trials should include the outcomes identified for this review, in particular outcomes on the baby and post-discharge infections for the mother. There will continue to be debate both in the literature and in clinical practice regarding the optimal time for administration of prophylactic antibiotics and there is a need for a Cochrane review on this aspect of care. The impact of routine antibiotics at caesarean section on bacterial resistance needs to be investigated with some urgency.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Ahmed 2004

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women having elective CS for various reasons. • N = 200. Exclusion criteria • Women who had received antibiotics within previous 2 weeks; had visible signs of infection; elevated temperature; allergic to the antimicrobials used.
Interventions	Intervention: cephalosporin (B3). • Ceftriaxone. • 1 g single dose. • N = 100. Comparison: penicillin (A4) combination. • Ampicillin + cloxacillin. • 1 g - every 8 hours (3 doses). • N = 100.

Ahmed 2004 *(Continued)*

Outcomes	Post-operative febrile morbidity; post-operative infection; endometritis; wound infection; pelvic abscess; peritonitis; other febrile morbidity.
Notes	Dates: January to June 2001 Setting: Wad Medani Teaching Hospital, Central Sudan. Subgroups 1. Elective CS. 2. Before cord clamping. 3. IV administration. 4. Single dose cephalosporin vs multiple dose penicillin. • Comparisons: 1 (subgroup 2); 2; 3; 4; 10. • "The drugs were donated by Alhikma Company, Wad Medani, Sudan."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...were randomised..."
Allocation concealment (selection bias)	Unclear risk	"...were randomised..."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded and the drug regimens were different, one a single dose, the other 3 doses.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	No statistical differences in admission variables between the two groups. Data and P values provided on temperature, weight, gestational age, pre-operative Hb. However, other aspects of bias unclear. · "The drugs were donated by Alhikma Company, Wad Medani, Sudan." but it seems unclear whether this might give the company any influence or not.

Beningo 1986

Methods	RCT. Individual women. Multi-centre (6 centres). 2-arm study.
Participants	Inclusion criteria • Women undergoing primary or repeat CS. • N = 346.

Beningo 1986 *(Continued)*

	Exclusion criteria • Use of antimicrobial therapy within previous 7 days; sensitivity to cephalosporins or penicillin; abnormal renal or hepatic laboratory tests; intention to breastfeed within 24 hours of birth; infection at the time of enrolment.
Interventions	Intervention: cephalosporin (B2). • Cefoxitin. • 6 g total. 3 IV doses of 2 g each at 4-hour intervals starting immediately after cord clamping. • N = 177 but 147 analysed. Comparison: penicillin (A3). • Piperacillin. • 6 g total. 3 IV doses of 2 g each at 4-hour intervals starting immediately after cord clamping. • N = 169 but 136 analysed.
Outcomes	Satisfactory prophylactic response; febrile morbidity (temperature > 38 °C x 2 occasions, 6 hours apart, not included first 24 hours post-operation; wound infection).
Notes	Setting: Women from hospitals and universities of San Francisco, Atlanta, Memphis, Los Angeles, Phoenix, New York. Subgroups 1. Type of CS not defined. 2. After cord clamping. 3. IV administration. 4. Multiple doses. • Comparison 1 (subgroup 1); 7. • This study included some long-term follow-up. 'Unsatisfactory prophylaxis - bacterial infection within 3-10 weeks' was 11/147 with cephalosporin and 15/136 with penicillin (RR 0.68, 95% CI 0.23 to 1.43). • No information on funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"...a computer-generated randomization schedule..."
Allocation concealment (selection bias)	Low risk	"...a computer-generated randomization schedule maintained by each hospital pharmacy..."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"The investigator and his (or her) staff were blinded as to antibiotic assignment. The code was not broken by the investigator until the last patient had been evaluated for prophylactic response."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	· "The investigator and his (or her) staff were blinded as to antibiotic assignment. The code was not broken by the investigator until the last patient had been evaluated for prophylactic response."
Incomplete outcome data (attrition bias) All outcomes	High risk	Excluded after randomisation: cephalosporin group 30/177 (16.9%) and penicillin group 33/119 (19.5%). Also differential loss from two groups.

Beningo 1986 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	Study not stopped early; similar baseline characteristics for weight; height & race, but significant difference in mean age - though not considered important. Other aspects of bias were unclear. No information on funding source of study.

Bracero 1997

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women undergoing CS and at high risk of developing post-operative infection. • Criteria for high risk: > 4 pre-operative vaginal examinations; internal fetal monitoring; obesity; ruptured membranes for > 30 minutes; meconium-stained amniotic fluid; labour of any duration before the operation. • 16 to 48 years. • N = 196 but 26 excluded for protocol violations = 170 analysed. Exclusion criteria • Women with hypersensitivity to penicillins or cephalosporins; those with required concomitant antibiotic therapy; or had received antibiotics during 72 hrs preceding enrolment; those in another drug study; women with immunological, renal or hepatic impairment or who had concomitant infections that might confuse the interpretation of the results.
Interventions	Intervention: cephalosporin (B2). • Cefotetan. • 1 g, single dose, IV, at time of cord clamping. • N = 83. Comparison: penicillin (A4) combination. • Ampicillin + sulbactam (0.5 g). • 1 g, single dose, IV, at time of cord clamping. • N = 87.
Outcomes	Treatment success; incision site infection; endometritis; UTI; febrile morbidity; peak recorded temperature; days in hospital.
Notes	Setting: Westchester County Medical Center, US. Subgroups 1. Type of CS not defined. 2. After cord clamping. 3. IV administration. 4. Single dose. • Comparisons: 1 (subgroup 2); 2; 3; 4; 8. • "This work was supported by a grant (89-S-0591, R-0102) from The Reorig Division of Pfizer Inc."

Risk of bias

Bias	Authors' judgement	Support for judgement

Bracero 1997 *(Continued)*

Random sequence generation (selection bias)	Low risk	“A computer was used to generate a list of random numbers for two groups.”
Allocation concealment (selection bias)	Low risk	“Treatment assignments were placed in numbered, sealed and opaque envelopes."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	“Neither patient nor obstetrician was informed of the antibiotic assignment. The study drugs were administered by the anaesthesiologist in the operating room immediately after the umbilical cord was clamped”
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	“Neither patient nor obstetrician was informed of the antibiotic assignment"
Incomplete outcome data (attrition bias) All outcomes	Low risk	26/196 (13%) women were excluded because of protocol violations.
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	High risk	"This work was supported by a grant (89-S-0591, R-0102) from The Reorig Division of Pfizer Inc." Not stopped early; no imbalance in baseline characteristics assessed on: on age; race; weight; height; BP; temperature and pulse but other aspects of bias were unclear.

Busowski 2000

Methods	RCT. Individual women. 3-arm study.
Participants	Inclusion criteria • Women undergoing CS following labour for > 2 hours without evidence of infection. • N = 114. Exclusion criteria • Inability to understand or give consent; oral temperature > 100^0F; antibiotic treatment within 72 hours prior to birth; allergies to study antibiotics; intention to breastfeed. • Requirement of additional antibiotics during or after CS - this may contribute to high risk of bias through exclusion after randomisation.
Interventions	Intervention: cephalosporin (B2). • Cefotetan. • 1 g, single dose, IV. • N = 42. Comparison 1: penicillin (A4) combination • Ampicillin +sulbactam. • 1.5 g. • N = 33.

Busowski 2000 *(Continued)*

	Comparison 2 • Ciprofloxacin - fluoroquinolone - 2nd generation (C2). • N = 39.
Outcomes	Endometritis; pneumonia; bacteraemia; UTI; would infection; postpartum stay > 6 days.
Notes	Setting: Tampa General Hospital, US. Subgroups 1. Non-elective CS. 2. After cord clamping. 3. IV administration. 4. Single dose. • Comparisons: 1(subgroup 2); 2; 3; 4; 11; 12. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"... prospectively randomised..."
Allocation concealment (selection bias)	Unclear risk	"... prospectively randomised..."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	· "Investigators were blinded to treatment."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	· "Investigators were blinded to treatment."
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	We did not asses trial protocol.
Other bias	Unclear risk	Baseline characteristics similar for: primaparous; weight; gestation; race; repeat CS; Hb but there was a statistically significant difference in age considered not to be clinically important. Other aspects of bias were unclear. No information about funding source of study.

Chantharojwong 1993

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women undergoing CS. All considered at risk of infection.

Chantharojwong 1993 *(Continued)*

- Rupture of membranes > 6 hours; labour > 12 hours; cervical effacement and dilatation > 4 cm; > 4 vaginal examinations.
- N = 109.

Exclusion criteria

- History of allergies to penicillin or cephalosporin; not co-operative; oral temperature > 38 °C within period 24 hours prior to operation; received antibiotics within 7 days prior to CS.

Interventions	Intervention: cephalosporin (B1). • Cefazolin. • 3 g total; 1 g every 6 hours up to 3 doses; IV; just after cord clamping. • N = 53 randomised. 1 woman could not be evaluated because she was febrile in the labour room and so was excluded, leaving N = 52. Comparison: penicillin (A4). • Ampicillin. • 3 g total; 1 g every 6 hours up to 3 doses; IV; just after cord clamping. • N = 56 randomised - 2 women could not be evaluated because they were febrile in the labour room and so were excluded, leaving N = 54.
Outcomes	Febrile morbidity; endometritis; parametritis; UTI; wound infection.
Notes	Dates: 1st January 1990 to 31 December 1992. Setting: Inburi Hospital, Thailand. Subgroups 1. Type of CS not defined. 2. After cord clamping. 3. IV administration. 4. Multiple doses. • Comparisons: 1(subgroup 1);2; 3; 4. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"... assigned randomly..."
Allocation concealment (selection bias)	Unclear risk	"... assigned randomly..."
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias)	Low risk	Only 3 women excluded.

Chantharojwong 1993 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Unclear risk	Baseline characteristics similar between groups on: age; height; weight; gravidity; gestation; preoperative haematocrit. However, other aspects of bias unclear. No information about funding source of study.

Dashow 1986

Methods	RCT. Individual women. 5-arm study.
Participants	Inclusion criteria • Women undergoing CS. • N = 204 in this review (though 360 in study which included a placebo group). Exclusion criteria • Women with a history of penicillin or cephalosporin allergy, those taking antibiotics, those with known infectious process at the time of operation (e.g. chorioamnionitis or UTI).
Interventions	Intervention 1: cephalosporin (B1). • Cephapirin. • 2 g; lavage. • N = 70 - reported in Table 4 Post-operative morbidity (but 70 reported in Table 2 Risk factors). Intervention 2: cephalosporin (B2). • Cefamandole. • 2 g; lavage. • N = 64 - reported in Table 4 Post-operative morbidity (but 70 reported in Table 2 Risk factors). Comparison: penicillin (A4). • Ampicillin. • 2g; lavage. • N = 70. 4th group - moxalactam disodium (1-oxa-beta-lactam antibiotic: N = 64 in Table 4 (but 79 in Table 2). 5th group - placebo (N = 77). Vitamin added to each solution for disguise.
Outcomes	Endometritis (temperature > 37.8 °C, uterine tenderness, pelvic irritation without other localizing signs); wound infection (breakdown, positive culture and/or cellulitis): febrile morbidity (temperature > 100.4 x 2. 6 hour apart, excluded first 24 hours); mean duration of hospital stay.
Notes	Dates: 1 December 1982 to 31 May 1984. Setting: Madigan Army Medical Center, US. Subgroups 1. Type of CS not defined. 2. Not defined with respect to timing of cord clamping.

Dashow 1986 *(Continued)*

3. Lavage during operation.
4. Not relevant for irrigation.

- Comparisons 1(subgroup 1); 2; 3; 4.
- The numbers of women reported in each group differed in the Tables. We will write to the authors to check the figures and in the meantime we have used the data from Table 4 'Post-operative morbidity outcomes: All patients'.
- No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"A computer-generated table of pseudo-random numbers using the mixed congruential method was used by the pharmacy to assign each patient to one of five groups."
Allocation concealment (selection bias)	Low risk	"A computer-generated table of pseudo-random numbers using the mixed congruential method was used by the pharmacy to assign each patient to one of five groups."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Patients and physicians were unaware of the group assignment until after completion of the study..."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Patients and physicians were unaware of the group assignment until after completion of the study..."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No explanation for differences between the numbers of the initially randomised groups and the groups included in the morbidity analysis (cephapirin 79 vs 70, cefamandole 70 vs 64, moxalactam 64 vs 79. The total of women included is the same (360); therefore we can assume that women originally assigned to one group received other treatment and they were not analysed by intention to treat. The uneven numbers may be due to lack of block-randomisation.
Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	Baseline characteristics similar on: age; parity; gestation. Small difference on gravidity but not considered clinically important. However, other aspects of bias unclear. No information about funding source of study.

De-Lalla 1988

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women undergoing CS. • N = 300. Exclusion criteria • Not documented.

De-Lalla 1988 *(Continued)*

Interventions	Intervention: cephalosporin (B2). • Cefotetan. • 2 g; IV; when the cord is clamped. • N = 106. Comparison: penicillin (A3). • Mezlocillin. • 2 g; IV; when the cord is clamped. • N = 194.
Outcomes	Fever > 38 °C; endometritis; wound infection; UTIs; asymptomatic bacteriuria.
Notes	Setting: Obstetric and Gynecologic department of UCSC, Como, Italy. Subgroups 1. Type of CS not defined. 2. After cord clamping. 3. IV administration. 4. Single dose. • No information about funding source of study. • Conference abstract only. The study did not provide any data on the outcomes in the review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information provided.
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Unclear risk	No information provided. Also no information about funding source of study.

Faro 1990

Methods	RCT. Individual women. 10-arm study.
Participants	Inclusion criteria • Women in labour giving birth by CS. • Labour > 2 hours; afebrile. • N = 1580. Exclusion criteria • Antibiotics within previous 7 days.
Interventions	Interventions: cephalosporins (B1, B2, B3). 1. Cefazolin (B1), 1 g x 3 doses (N = 142). 2. Cefazolin (B1), 1 g (N = 217). 3. Cefazolin (B1), 2 g (N = 161). 4. Ceftizoxime (B3), 1 g (N = 145). 5. Cefonicid (B2), 1 g (N = 147). 6. Cefotetan (B2), 1 g (N = 148). 7. Cefoxitin (B2), 1 g (N = 155). 8. Cefoxitin (B2), 2 g (N = 162). Total N = 1277. Comparisons: penicillins (A3, A4). 1. Ampicillin (A4), 2 g (N = 148). 2. Piperacillin (A3), 4 g (N = 155). Total N = 303.
Outcomes	Endometritis (defined as temperature > 37.8 °C x 2, 4 hours apart, excluding 24 hours after delivery plus tachycardia, white blood count > 14, uterine tenderness).
Notes	Dates: 7 December 1989 to 1 July 1989. Setting: Harris County Hospital, US. Mixed ethnic population. Subgroups 1. Non-elective CS. 2. After cord clamping. 3. IV administration. 4. Mostly single dose, only 1 multiple dose. • Comparisons 1 (subgroup 1); 2; 3; 4; 5; 6; 7; 8; 9; 10. • Study reported as 'ongoing' and so randomisation was not complete and 1 group had a many more women than the others. This is likely to contribute to high risk of bias. • No information on funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"...randomised...according to a computer-generated schedule."

Faro 1990 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Prospective, open, randomised study.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Prospective, open, randomised study but assessors may have been blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No loss to follow-up as yet but study still on-going at time of publication.
Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	The difference in the numbers allocated to groups (ranging from 142 to 217) is reported as likely to be due to the study being on-going and the randomisation schedule not complete or to some statistical issue, this si unclear. No information on funding source of study.

Ford 1986

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women undergoing CS. • N = 263. Exclusion criteria • Women with drug allergies, antibiotics within 7 days, infection at time of enrolment, renal or hepatic dysfunction.
Interventions	Intervention: cephalosporin (B2). • Cefoxitin. • 2 g; after cord clamped; plus 2 additional doses (2 g) at 4 hours apart. • N = 131. Comparison: penicillin (A3). • Piperacillin. • 2 g; after cord clamped; plus 2 additional doses (2 g) at 4 hours apart. • N = 132.
Outcomes	Febrile morbidity; duration of hospitalisation; administration of systematic antibiotics post-operatively; wound healing; infection at operation site.
Notes	Setting: UCLA Medical Center, US. Subgroups

Ford 1986 *(Continued)*

1. Type of CS not defined.
2. After cord clamping.
3. Route of administration not specified.
4. Multiple doses.

- Comparison 1 (subgroup 1); 7.
- No information on funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...randomly assigned...".
Allocation concealment (selection bias)	Unclear risk	"...randomly assigned...".
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There appeared to be no loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	No baseline imbalances on: age; weight; duration of surgery. However, other aspects of possible bias were unclear. No information on funding source of study.

Gidiri 2014

Methods	RCT. 2-arm parallel study. Women randomised individually.
Participants	Inclusion criteria • Women undergoing CS, elective and emergency. • N = 280. Exclusion criteria Women who declined to participate in the study; severe immunosuppression of any cause; stage 3 and 4 HIV infection; prolonged rupture of membranes more than 12 hours; surgery longer than 3 hours; chorioamnionitis diagnosed preoperatively and obvious concurrent infection that requires therapeutic antibiotics.
Interventions	Intervention: Cephalosporin (B3) and metronidazole (I) combination. • Single dose of ceftriaxone 1 g IV plus metronidazole 500 mg IV preoperatively and no further antibiotics postoperatively, except for treatment of infection.

Gidiri 2014 *(Continued)*

	• Total number randomised: N = 136 randomised, analysis on 112. Comparison: Penicillin (A1) + chloramphenicol + amoxicillin (A4) + metronidazole (I) combination. • Antibiotics for 1 week as follows: preoperatively benzyl penicillin 5 MU IV and chloramphenicol 1g IV Postoperatively within 24 hours of the operation: IV benzyl penicillin 2.5 MU 6-hourly for three doses and IV chloramphenicol 500 mg 6-hourly for three doses. From day 1 postoperatively, amoxicillin 500mg t.d.s. for 7 days, metronidazole 400mg t.d.s. for 7 days. • Total number randomised: N = 144, analysis on 120.
Outcomes	Pyrexia; admission with puerperal sepsis; wound sepsis; death; duration of hospital stay; laparotomy for pelvic abscess.
Notes	Dates: 2 February 2012 to 30 May 2012. Setting: Parirenyatwa and Harare (tertiary) hospitals, Zimbabwe. Subgroups 1. Mixed, elective and emergency CS. 2. Cephalosporin given before cord clamping vs penicillin given both before and after cord clamping. 3. Systemic - IV. 4. Single dose vs multiple doses. • Comparisons 1 (subgroup 4); 2; 3; 4. • Authors report 'No conflict of interest' and they alone are responsible for the content and writing of the paper. So appears to have no drug company involvement.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Low risk	Randomisation was by taking a ticket from a box. There was an A4 envelope of tickets at each of the two maternity units. Each envelope contained 75 tickets marked Arm 1 and 75 marked Arm 2. The ticket for Arm 1 was identical to that of Arm 2 in size, shape and material.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not really possible to blind as one group had a single dose and the other had a weeks prescription.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information so most likely assessors were not blinded either.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Women lost to follow-up were 24 in each group.
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Unclear risk	Baseline data showed no imbalance on: age; marital status; education; occupation; booking status; HIV. Otherwise unclear. Authors report 'No conflict of interest' and they alone are responsible for the content and writing of the paper. So appears to have no drug company involvement.

Graham 1993

Methods	RCT. Individual women. Multi-centre. 2-arm study.
Participants	Inclusion criteria • Women who were in labour or had ruptured membranes and were about to have an indicated CS (repeat procedure, malpresentation, arrest of the active phase of labour). • N = 84. Exclusion criteria • Women who had received antibiotics within 7 days of the CS or who had a diagnosis of intra-amniotic infection.
Interventions	Intervention: cephalosporin (B1). • Cefazolin. • 1 g; IV; after cord clamped. • N = unclear. Comparison: penicillin (A4). • Ampicillin. • 2 g; IV; after cord clamped. • N = unclear.
Outcomes	Genital tract cultures.
Notes	Setting: University Medical Centre, Lubbock & LBJ General Hospital, Houston, Texas, US. Subgroups 1. Non-elective CS. 2. After cord clamping. 3. IV administration. 4. Single dose. • No information about funding source of study. • The study did not provide any data on the outcomes in the review. It assessed eradication of rates using before and after data.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"...computer-generated number..."
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Antibiotic administration was not blinded.
Blinding of outcome assessment (detection bias)	Unclear risk	Antibiotic administration was not blinded but outcome assessor could have been blinded.

Graham 1993 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	No exclusions of women were reported.
Selective reporting (reporting bias)	Unclear risk	We did not asses trial protocol.
Other bias	Unclear risk	Baseline characteristics across groups not reported and other aspects of possible bias unclear. No information about funding source of study.

Jyothi 2010

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • "Women who were scheduled to undergo hysterectomy for benign disease and elective cesarean delivery were enrolled in this trial". However, only women underwent CS will be included in the review. • N = 122 women having elective CS (60 having hysterectomy) Exclusion criteria • "We excluded patients who gave history of hypersensitivity to penicillin or cephalosporin; or signs of pre-existing infections and those who had received antibiotic therapy within the last seven days prior to surgery."
Interventions	Intervention: cephalosporin (B1). • Cefazolin 2 g, administered IV. • Medication was administered as a single dose. • Immediately after clamping the umbilical cord. • Total number randomised: N = 67. Comparison: penicillin (A4) combination. • Amoxycillin-clavulanic acid 2.4 g (co-amoxyclav) - administered IV. • Medication was administered as a single dose. • Immediately after clamping the umbilical cord. • Total number randomised: N = 55
Outcomes	Outcomes: fever and infection, endometritis. Reported outcomes: postoperative hospital stay, wound infection, asymptomatic bacteriuria, total infection, postoperative urinary infection.
Notes	Setting: Kasturba Hospital, Manipal, Karnataka, India, April 2004 to September 2005. Subgroups 1. Elective CS. 2. After cord clamping. 3. Systemic - IV administration. 4. Single dose. • Comparisons 1 (subgroup 2); 2; 3; 4; 6.

Jyothi 2010 *(Continued)*

- No information about funding source for study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss of follow-up was reported.
Selective reporting (reporting bias)	Unclear risk	The study protocol is unavailable.
Other bias	Unclear risk	Baseline characteristics were similar for: age; BMI; associated disease; type of surgery (primary CS or not). Other possible biases were unclear. No information about funding source for study.

Kamilya 2012

Methods	RCT two parallel treatment groups, women randomised individually.
Participants	Inclusion criteria • Women undergoing CS, elective or emergency. • N = 760 randomised with 746 analysed. Exclusion criteria • Women known to be hypersensitive to any of the trial drugs; any antibiotic treatment 2 weeks prior to surgery; presence of chorioamnionitis; diabetes; malnutrition; obesity, >85 kg; immuno-compromised state; > 3 times per vaginal examination for intrapartum cases; prolonged preoperative hospitalisation and duration of labor > 6 hours.
Interventions	Intervention: cephalosporin (B3). • Cefotaxime 1 g single dose intravenous. • Just after clamping the umbilical cord. • Total number randomised: N = 380 but 372 analysed. Comparison: penicillin (A4) combination. • Amoxicillin–clavulanic acid combination 1.2 g single dose IV.

Kamilya 2012 *(Continued)*

- Just after clamping the umbilical cord.
- Total number randomised: N = 380 but 374 analysed.

Outcomes	Febrile morbidity, wound healing, endometritis, side effects of antibiotics. Reported outcomes: "fever, mild or moderate wound infection, endometritis, UTI or any serious infection, fever in the 5th post-operative period, adverse reactions, duration of hospital stay. "
Notes	Setting Tertiary care teaching hospital in Kolkata, India. Subgroups 1. Both elective and emergency CS. 2. After cord clamping. 3. Systemic - IV. 4. Single dose. • Comparisons 1 (subgroup 2); 2; 3; 4; 10. • No information about funding source of trial.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomization was done a priori by computer in blocks of 40."
Allocation concealment (selection bias)	Unclear risk	"The randomization list remained in the custody of the principal investigator."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Being a double blind study, the nature or medication being received by individual trial subjects was not known to the subject or the project clinician".
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Being a double blind study, the nature or medication being received by individual trial subjects was not known to the subject or the project clinician". It seemed most likely considering the outcomes assessed that assessors were blinded as well.
Incomplete outcome data (attrition bias) All outcomes	Low risk	"A total of 760 patients were recruited for the study. Eight patients in the cefotaxime group and six patients in the amoxicillin–clavulanic acid group had to be excluded from final analysis for various reasons".
Selective reporting (reporting bias)	Unclear risk	The study protocol is unavailable.
Other bias	Unclear risk	Baseline characteristics were similar for: age; parity; gestation. Other possible biases were unclear. No information about funding source of trial.

Kayihura 2003

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women having an emergency CS. • N = 288 but data on 241. Exclusion criteria • Women with allergies to antibiotics; use of antibiotics within previous 24 hours; pathology that should be treated with antibiotics; chorioamnionitis; fever on admission; need of transfusion before or during the CS; ruptured membranes > 24 hrs; body weight > 132 kg; elective CS.
Interventions	Intervention: aminoglycoside (G) + nitroimidazole (I) combination. • 160 mg gentamicin (G) and metronidazole (I) IV. • IV before operation starts, so before cord clamping. • No more antibiotics given post-operatively. • N = 143 randomised but 116 in analysis. Comparison: penicillins (A1) + nitroimidazole (I) + macrolide (E) combination. • Penicillin 4,000,000 UI IV for 6 hrs and metronidazole 500 mg IV 8 hours during 1st 24 hrs. Then erythromycin 500 mg 6-hourly orally and metronidazole 500 mg 8-hourly orally during 6 days. • IV for 1st 24 hours then orally for 6 days. • No other antibiotics given. • N = 145 randomised but 125 in analysis.
Outcomes	Maternal endometritis; would infection; UTI; peritonitis; evisceration; post-operative infection; stillbirth.
Notes	Dates: January to June 2000. Setting: Maternity Unit, Hospital Central de Maputo, Mozambique. Quaternary level care. Subgroups 1. Non-elective CS. 2. Mixed: before cord clamping for intervention vs after cord clamping for comparison. 3. IV administration vs combination of IV and oral administration. 4. Single dose of intervention vs multiple dose of comparison. • Comparison 15. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...randomly constituted...".
Allocation concealment (selection bias)	Unclear risk	"The anaesthetist administered the antibiotics according to the code written in the exercise book in the sequential order of admission to the theatre...the code was then written on the patient's file so that the surgeon could prescribe...the doctor on duty was not aware of the group to which the patient was allocated. The principle investigator was not allowed either to select cases to be enrolled in the study or to follow the patients in the ward."

Kayihura 2003 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Non-blinded comparative study. Although the doctor on duty was reported as not aware of the group to which the woman was allocated, the anaesthetist and surgeon were aware and overall the study was described as not blinded.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Non-blinded comparative study. "Medical doctors allowing the patients to leave the maternity ward knew the regimen followed by the patients in order to not modify the antibiotics given…".
Incomplete outcome data (attrition bias) All outcomes	Low risk	288 women randomised and analysis on 241 so 47/288 (16.3%) loss.
Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	Baseline characteristics similar for:age; parity; gestation. However, other possible biases are unclear. No information about funding source of study.

Koppel 1992

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women having a CS. • N = 119. Exclusion criteria • Women were excluded if they were allergic to penicillin or cephalosporin, or if they had been given a pre-operative antibiotic treatment within 2 weeks prior to CS.
Interventions	Intervention: cephalosporin (B3). • Cefotaxime. • 1 g IV with 20 mL NaCl. • N = 59. Comparison: penicillin (A4) combination. • Amoxicillin plus clavulanic acid. • 1.2 g IV with 20 mL NaCl. • N = 60.
Outcomes	Endometritis (temperature > 37.5 °C, uterine tenderness); UTI; wound infection.
Notes	Dates: 17 October 1987 to 24 February 1989. Setting: Kantonspital Hospital, Winterthur, Switzerland. Translation: from German. Subgroups 1. Type of CS not defined. 2. After cord clamping.

Koppel 1992 *(Continued)*

3. IV administration.
4. Single dose.

- Comparisons: 1 (subgroup 2): 2; 3; 4; 10.
- No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The translation reports: "A midwife not involved in the study pulled the names from a randomised list and provided the medications in neutral syringes in the operating room." It is unclear if a 'randomised list', is the same as a 'random table' and until we are able to check this we are reporting this as unclear.
Allocation concealment (selection bias)	Unclear risk	A midwife who was not part of the study divided the women into 2 treatment groups, cefotaxim and amoxicillin/clavulanic acid, according to a randomised list.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind trial.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind trial.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	Baseline characteristics similar for age. However, other possible biases unclear. No information about funding source of study.

Lehapa 1999

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women who underwent emergency CS. • N = 233. Exclusion criteria • No information provided.
Interventions	Intervention: cephalosporin (B3). • Ceftriaxone. • 1 g, IV, followed by 4 × 6-hourly doses of a placebo (physiological saline). • N = 108. Comparison: penicillin (A4).

Lehapa 1999 *(Continued)*

- Ampicillin.
- 1 g, IV, plus 4 × 6-hourly doses of 500 mg of ampicillin.
- N = 125.

Outcomes	Abdominal and/or wound sepsis; febrile morbidity; hospital stay; antibiotic and consumable costs.
Notes	Setting: Ga-Rankuwa Hospital, South Africa. Subgroups 1. Non-elective CS. 2. Unclear when given in relation to cord clamping. 3. IV administration. 4. Single dose cephalosporin vs multiple doses penicillin. • Comparison 1 (subgroup 1); 10. • No information about funding source of study. Conference abstract only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind study.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind study although it is unclear whether assessors might have known allocation of not.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	None reported, but there is no information on the denominators in either group for us to be sure there was no loss of participants.
Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	Two groups reported as similar in baseline characteristics on: age; gestation; type of incision; length of surgery, but no data provided. Other aspects of potential bias were unclear. No information about funding source of study.

Lewis 1990

Methods	RCT. Individual women. Study in 2 parts. Study 1: compared a penicillin vs placebo (so not included in this review). Study 2: compared a cephalosporin vs a penicillin.

Lewis 1990 *(Continued)*

Participants	Inclusion criteria • Women having CS. • N = 396, 9 excluded as charts not available, leaving 383 for analysis. Exclusion criteria • Women who had antibiotics within 2 weeks of CS and those allergic to penicillin.
Interventions	Intervention: cephalosporin (B2). • Cefoxitin. • 2 g in 1.5 L, by irrigation. • N = 186. Comparison: penicillin (A3). • Ticarcillin. • 5 g in 1.2 L, by irrigation. • N = 197.
Outcomes	Endometritis; wound infection (criteria not specified): UTI (criteria not specified): sepsis.
Notes	Setting: Louisiana State University Hospital, US. Subgroups 1. Both elective and non-elective CS. Data reported separately but randomisation not stratified. 2. After cord clamping. 3. Irrigation/lavage. 4. Single lavage dose but • Comparisons: 1 (subgroup 1): 2; 3; 4; 7. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...random double-blind fashion...".
Allocation concealment (selection bias)	Unclear risk	"...random double-blind fashion...".
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind study.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Although a double-blind study, it is unclear whether the outcome assessors might have not know allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	396 women were reported to be included with 383 providing data, 186 in cephalosporin group and 197 in penicillin group (loss of 13/396 = 3.3%).

Lewis 1990 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	Baseline characteristics were similar for age; gestation; gravidity; parity; length of labour. However, other potential biases were unclear. No information about funding source of study.

Louie 1982

Methods	RCT. Individual women. 3-arm study.
Participants	Inclusion criteria • All women undergoing emergency CS. • Women in active labour with membrane rupture prior to surgery; rectal temperature < 37.8 °C ; no history of penicillin or cephalosporin allergy; no antibiotic therapy in previous 2 weeks. • N = 195 but data on 188. Exclusion criteria • None specified.
Interventions	Intervention 1: cephalosporin (B1). • Cefazolin. • 1g IV after cord clamped and 2 further doses at 6 and 12 hours post-operation. • N = 70. Intervention 2: cephalosporin (B3). • Cefotaxime. • 1 g IV after cord clamped and 2 further doses at 6 and 12 hours post-operation. • N = 58. Comparison: penicillin (A4). • Ampicillin. • 1 g IV after cord clamped and 2 further doses at 6 and 12 hours post-operation. • N = 60. • For the purposes of this review we have pooled the data for cefazolin and cefotaxime. Any differences between these 2 cephalosporins will be assessed in the review on 'Different regimens of cephalosporin antibiotic prophylaxis at caesarean section for reducing maternal morbidity'.
Outcomes	Endometritis (temperature > 38 °C, foul lochia, uterine tenderness); UTI; wound infection; febrile morbidity (temp > 38 °C x 2, 6 hours apart, excluding first 24 hours).
Notes	Dates: December 1979 to December 1981. Setting: Women's Centre at the Health Sciences Winnipeg, Canada. Subgroups 1. Non-elective CS. 2. After cord clamping. 3. IV administration. 4. Multiple doses. • Comparisons: 1 (subgroup 1); 2; 3; 4; 6; 10.

Louie 1982 *(Continued)*

- No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...randomised...".
Allocation concealment (selection bias)	Low risk	"..unlabelled but number-coded, previously randomised vials...".
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind trial.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Only pharmacist was aware of the drug code."
Incomplete outcome data (attrition bias) All outcomes	Low risk	7/195 (3.6%) lost to follow-up. Similar across groups.
Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	Baseline characteristics similar for age and race. However, other possible biases were unclear. No information about funding source of study.

Lumbiganon 1994

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women undergoing emergency CS. • N = 400 but 379 analysed. Exclusion criteria • No information provided.
Interventions	Intervention: cephalosporin (B1). • Cefazolin. • 1g after clamping the umbilical cord. • N = 191. Comparison: penicillin (A4) combination. • Amoxicillin plus clavulanic acid. • 1.2 g after clamping the umbilical cord. • N = 188.

Lumbiganon 1994 *(Continued)*

Outcomes	Febrile and infectious morbidity.
Notes	Setting: Department of Obstetric and Gynecology, Khon Kaen University, Thailand. Subgroups 1. Non-elective CS. 2. After cord clamping. 3. Route of administration not specified. 4. Single dose. • Comparison 1 (subgroup 2); 6. • No information about funding source of study. • Conference abstract only.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided.
Allocation concealment (selection bias)	Unclear risk	Although the published abstract provided no information, the registration of the study with the Oxford Database of Perinatal Trials reported allocation was "by sealed, numbered envelopes" but it is unclear if these had to be used in sequential order.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	'Partially blinded'.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	'Partially blinded'.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up reported.
Selective reporting (reporting bias)	Unclear risk	Trial protocol not available and trial registration form only asks for principle outcomes (febrile morbidity & infectious morbidity) both of which are reported in the Conference abstract.
Other bias	Unclear risk	No baseline data provided and other possible biases unclear. No information about funding source of study.

Mansueto 1989

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women undergoing non-elective CS. • N = 48. Exclusion criteria

Mansueto 1989 *(Continued)*

	• Allergy to penicillin or cephalosporin; impaired renal and/or liver function; fever (> 38 °C and/or clinical signs of infection); antibiotic therapy 48 hours prior to the surgical procedure.
Interventions	Intervention: B-lactam (F). • Imipenem. • 500 mg IV after cord clamped. • N = 22. Comparison: cephalosporin (B3). • Cefotamine. • 1 g IV after cord clamped and 3 additional doses every 12 hours. • N = 26.
Outcomes	Infective complications after the CS (endometritis, infection of the wound, peritonitis, urinary infections, other causes, fever morbidity).
Notes	Dates: 1 January 1988 to 30 September 1988. Setting: Umberto I Hospital, Frosinone, Italy. Subgroups 1. Non-elective CS. 2. After cord clamping. 3. Systemic - IV. 4. Single dose vs multiple doses. • Comparison 14. • Translated from Italian. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Women reported to be divided randomly into two groups.
Allocation concealment (selection bias)	Unclear risk	No information.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up.
Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.

Mansueto 1989 *(Continued)*

Other bias	Unclear risk	No differences in baseline characteristics for: age, parity, length of PROM and number of vaginal examination between two groups. Other possible biases were unclear. No information about funding source of study.

Mivumbi 2014

Methods	A prospective, randomised, open-label, single-site study,with two parallel arms. Women randomised individually.
Participants	Inclusion criteria • Women undergoing CS for any indication at a gestation of 37 weeks 0 days or more. • N = 132. Exclusion criteria • Preoperative clinical diagnosis of chorioamnionitis, a fever of 38° or higher at any point during admission, prior antibiotic use within 2 weeks, known HIV-positive status, known allergy to penicillin or cephalosporin, and insulin-dependent diabetes.
Interventions	Intervention: cephalosporin (B1). • Cefazolin 1 g. • Administered intravenously no more than 60 minutes prior to skin incision. • Single dose. • Postoperative antibiotics were administered only if there was a diagnosis of infection, and were not given routinely. • Total number randomised: N = 66. Comparison (usual care): aminopenicillin (A4). • Ampicillin 2 g (usual care group). • Administered intravenously no more than 60 minutes prior to skin incision. • Single dose. • Postoperative antibiotics were administered only if there was a diagnosis of infection, and were not given routinely. • Total number randomised: N = 66.
Outcomes	Outcomes: The primary outcome variable was postoperative febrile morbidity. Secondary outcomes were infection-related complications defined as endometritis, wound infection, UTI, fever with unexplained source, need for therapeutic antibiotics, and length of postoperative days in hospital (starting the day after surgery and including the day of discharge). Reported outcomes: Febrile morbidity, endometritis, wound infection, UTI, unexplained fever(febrile morbidity), required therapeutic antibiotics, length of postoperative stay, allergic reactions.
Notes	Dates: March 1 to May 31, 2012. Setting: The Centre Hospitalier Universitaire de Kigali/University Teaching Hospital of Kigali (CHUK), which is located in Kigali, the capital of Rwanda, is 1 of 3 tertiary care referral hospitals in the Rwandan healthcare system and, compared with district hospitals, receives a disproportionate number of women needing CS. Subgroups 1. Both elective and emergency CS. 2. Before cord clamping.

Mivumbi 2014 *(Continued)*

3. Systemic.
4. Single dose.

- Comparisons: 1 (subgroup 1); 2; 3; 4; 6.
- Reported that authors have no conflict of interest. Funding source of study not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The cards inside the envelopes were randomized by the principle investigator using a random integer generator."
Allocation concealment (selection bias)	Low risk	“The women were preoperatively randomized to 1 of 2 study groups via numerically ordered cards in sealed envelopes...The allocated envelopes were opened by clinicians only after the decision for cesarean delivery was made."
Blinding of participants and personnel (performance bias) All outcomes	High risk	“...open-label...”.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	As open-label RCT the investigators were not blinded but the assessors could have been blinded. .
Incomplete outcome data (attrition bias) All outcomes	Low risk	"No women were lost to follow-up”.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Unclear risk	Not known. Reported that authors have no conflict of interest. Funding source of study not reported.

Mothilal 2013

Methods	A randomised prospective study with two parallel arms. Women randomised individually.
Participants	Inclusion criteria • Women undergoing CS - elective, non-elective in labour and emergency. • N = 70. Exclusion criteria • Women who had signs of obvious infection, suspected renal impairment by history or lab evidence, who has known drug hypersensitivity to Azithromycin or Cephalosporin, who were recently administered with antibiotics, diabetic and anaemic pregnant women.
Interventions	Intervention: macrolide (E). • 500 mg of Azithromycin. • Half an hour prior to the surgery. • Total number randomised: N = 35.

Mothilal 2013 *(Continued)*

	Comparison: cephalosporin (B1). • 1 g of Cefazolin. • Half an hour prior to the surgery. • Total number randomised: N = 35.
Outcomes	Reported outcomes: post-operative fever, wound healing duration (healing within 10 days, healing within 20 days), pain for 6 days, pain for 7-9 days, infection, PV discharge.
Notes	Study dates: September 2011 to February 2012. Follow-up of the cases were finished in March 2012. Setting: Department of Obstetrics & Gynaecology, SRM Medical Research Centre and Hospital in Kattankulathur, Kancheepuram District, India. Subgroups 1. Both elective and non-elective CS. 2. Before cord clamping. 3. Systemic. 4. Single dose. • Comparison 14. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	“The pregnant women were randomly given either Azithromycin or cefazolinas prophylactic antibiotics” and "(Antibiotics) were given ... in a random order ...”.
Allocation concealment (selection bias)	Unclear risk	"The pregnant women were randomly given either Azithromycin or Cefazolinas prophylactic antibiotics".
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information on this.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information on this.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses of follow-up were reported.
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available.
Other bias	Unclear risk	Not known. No information about funding source of study.

Ng 1992

Methods	RCT. Individual women. 3-arm study.
Participants	Inclusion criteria

Ng 1992 *(Continued)*

- Women undergoing emergency CS.
- N = 145 in the cephalosporin vs penicillin comparison (though 222 in the whole study which included 'No antibiotic' group).

Exclusion criteria

- Known hypersensitivity to either antibiotic, the presence of infection or fever before the operation, women already on antibiotics for any reason and women with multiple pregnancies.

Interventions	Intervention 1: cephalosporin (B3). • Cefoperazone. • 3 doses of 1g at 12-hourly intervals. • First dose given at induction of anaesthesia and the total number of doses of antibiotics given was calculated to give coverage for the first 24 hours after surgery. • N = 71, then 1 excluded. Intervention 2: penicillin (A4). • Ampicillin. • 4 doses of 500 mg at 6-hourly intervals. • First dose given at induction of anaesthesia and the total number of doses of antibiotics given was calculated to give coverage for the first 24 hours after surgery. • N = 74. Comparison • No antibiotics. • No data included in this review. • N = 77, then 1 excluded.
Outcomes	Febrile morbidity; wound infection.
Notes	Dates: March to August 1991. Setting: Ipoh General Hospital, Ipoh, Perak Darul Ridzuan. Subgroups 1. Non-elective CS. 2. Before cord clamping. 3. Systemic. 4. Multiple doses. • Comparison 1 (subgroup 1); 10. • No information about funding source of study. Inconsistency in data. There was inconsistency in the number of women reported in each group between the table and the text. We took the data from the tables and will write to the authors to seek clarification.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	A randomised trial.
Allocation concealment (selection bias)	Unclear risk	No information provided.

Ng 1992 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women excluded - 1 from each group.
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Unclear risk	Baseline characteristics similar for: age; race; parity; gestation. Other possible biases were unclear. No information about funding source of study.

Noyes 1998

Methods	RCT. Individual women. 3-arm study.
Participants	Inclusion criteria • Women undergoing CS. • Gravid women in labour or having had rupture of membranes for 6 hours. • N = 300, but analysis on 292. Exclusion criteria • < 18 years of age, known allergy to penicillin or cephalosporin antibiotics, antibiotic therapy within 72 hours prior to hospital admission, history of group B streptococcal infection, prophylactic antibiotic therapy for underlying medical illness or enhancement of fetal lung maturity, or clinical evidence of chorioamnionitis at the time of CS.
Interventions	Intervention 1: cephalosporin (B1). • Cefazolin. • 1 g, IV, single dose. • N = 98. Intervention 2: cephalosporin (B2). • Cefotetan. • 1 g, IV, single dose. • N = 99. Comparison: penicillin (A4) combination. • Ampicillin + sulbactam. • 1.5 g, IV, single dose. • N = 95.
Outcomes	Endometritis.
Notes	Dates: July 1988 to November 1990.

Noyes 1998 *(Continued)*

Setting: New York Hospital, university-based, US.

Subgroups

1. Non-elective CS.
2. After cord clamping.
3. IV administration.
4. Single dose.

- Comparison: 1 (subgroup 2); 2; 3; 4; 6; 8.
- No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Prospective randomized trial".
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	8 out of 300 women (2.7%) were excluded from the analysis.
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Unclear risk	There was insufficient information to assess other possible biases. No information about funding source of study.

Parulekar 2001

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion • Women undergoing CS. • N = 200. Exclusion • Hypersensitivity to drugs being used; any antibiotic treatment 2 weeks prior to surgery; chorioamnionitis.
Interventions	Intervention: cephalosporin (B3). • Cefotoxime.

Parulekar 2001 *(Continued)*

	• 1 g IV. • N = 100. Comparison: penicillin (A2) + aminoglycoside (G) combination. • Cloxacillin (1 g, 8-hourly for 48 hours) followed by oral cloxacillin (500 mg, 8-hourly for 72 hours. Also gentamycin (80 mg IV/IM 12-hourly for 5 days). • N = 100.
Outcomes	Postpartum infection; wound infection; fever; duration in hospital.
Notes	Setting: Naval Hospital INHS Asvini Colaba, Mumbai, India. Subgroups 1. Type of CS not defined. 2. After cord clamping. 3. IV administration. 4. Single dose vs multiple long-term post-operative antibiotics. • Comparison 1 (subgroup 2); 2; 3; 4; 14. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...randomly assigned...".
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up was reported.
Selective reporting (reporting bias)	Unclear risk	Study protocol unavailable.
Other bias	Unclear risk	Insufficient information to assess other possible biases. No information about funding source of study.

Rehu 1980

Methods	RCT. Individual women. 4 groups.
Participants	Inclusion

Rehu 1980 *(Continued)*

	• Women undergoing CS in labour. • N = 130 but only include 90 in this review as remainder given placebo. Exclusion • None stated.
Interventions	Intervention 1: penicillin (A1). • Benzyl penicillin (A1) $10x10^6$ units in 1000 mlLof 5% glucose IV. • N = 48. Intervention 2: lincosamide antibiotic (H) + aminoglycoside (G). • Clindamicin (H) (500 mg in 1000 ml of 5% glucose IV) + gentamicin (G) (80 mg IM). • N = 42. Comparison 1: placebo 1 (not included in this review). • 100 mL 5% glucose without antibiotics. • N = 40. Comparison 2: placebo 2 (not included in this review). • 100 mL 5% glucose without antibiotics. • N = 17.
Outcomes	Endometritis; wound infection; duration of hospital stay; number of women receiving post-operative treatment.
Notes	Dates: September 1977 and January 1978. Setting: State/maternity hospital, Helsinki, Finland. Subgroups 1. Non-elective CS. 2. Before cord clamping. 3. IV administration. 4. Multiple dose IV + IM) vs single dose and continued until 4 hours after operation. • Comparison 13. • Study compared a penicillin (benzyl penicillin) vs a macrolide (clindamycin) plus a aminoglycoside (gentamicin). Solutions of benzyl penicillin and clindamycin were infused starting 30 minutes prior to CS and the gentamicin was given by IM injection 30 minutes prior to the procedure. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...assigned at random...".
Allocation concealment (selection bias)	Unclear risk	Antibiotic preparations for intravenous use were supplied in solution in bottles carrying code numbers. Still unclear if there was allocation concealment.
Blinding of participants and personnel (performance bias)	Low risk	"The code was kept secret for persons performing the operations and observing the patients in the postoperative period."

Rehu 1980 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"The code was kept secret for persons performing the operations and observing the patients in the postoperative period".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Two out of the 147 women receiving antibiotics of other reasons during the preoperative period were later excluded from the series.
Selective reporting (reporting bias)	Unclear risk	We did not assess the trial protocol.
Other bias	Unclear risk	There was no information on baseline characteristics of the women in the groups, and other possible biases were unclear. No information about funding source of study.

Rosaschino 1988

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women having a CS. • N = 59. Exclusion criteria • Women with certain or presumed hypersensitivity to β lactamine.
Interventions	Intervention: cephalosporin (B3). • Ceftriaxone. • 1 g IV bolus; pre-operative. • N = 27. Comparison: penicillin (A3). • Mezlocillin. • 2 g IV bolus; pre-operative. • N = 32.
Outcomes	Tolerability, wound infections, urinary or respiratory infections, complications, side effects.
Notes	Setting: Bolognini di Seriate (BG) hospital, obstetric and gynaecological clinic, Italy. Translation: paper in Italian with summary in English. We had information extracted for us in English. Subgroups 1. Type of CS not defined. 2. Before cord clamping. English abstract says preoperative, translation of main text says immediately after operation but the Italian words is 'preoperatorio'. 3. IV administration. 4. Single dose. • Comparison: 1(subgroup 1); 2 ;3; 4; 9. • No information about funding source of study.

Rosaschino 1988 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised controlled trial.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up reported.
Selective reporting (reporting bias)	Unclear risk	Study protocol unavailable.
Other bias	Unclear risk	Unable to assess other possible biases. No information about funding source of study.

Saltzman 1985

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women who underwent primary CS for cephalopelvic disproportion. • N = 147 with data on 129. Exclusion criteria • Women with clinical signs of active infection, an oral temperature of 100.4 ºF (38.0 ºC) or more within 24 hours preceding surgery, systemic antimicrobial use within 3 days prior to CS, or known hypersensitivity to penicillin or cephalosporins.
Interventions	Intervention: cephalosporin (B2). • Cefoxitin. • 2 g each dose, with 3 doses given. • First dose of each drug was given immediately after the umbilical cord was clamped, with the second and third doses administered 4 and 8 hours afterward. • N = 68. Comparison: penicillin (A3) combination. • Ticarcillin + clavulanic acid. • 3 g of ticarcillin and 100 mg of clavulanic acid, 3 doses given.

Saltzman 1985 *(Continued)*

	• First dose of each drug was given immediately after the umbilical cord was clamped, with the second and third doses administered 4 and 8 hours afterward. • N = 61.
Outcomes	Febrile morbidity; endometritis; UTI.
Notes	Setting: Virginia, US. Subgroups 1. Type of CS not defined. 2. After cord clamping. 3. IV administration. Although route of administration not specified the administration of doses 4 and 8 hours after birth indicated lavage was not used. 4. Multiple doses. • Comparison: 1 (subgroup 2); 2; 3; 4; 7. • Long-term follow-up: reported no infections at 6 weeks post-operatively. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...randomly assigned...".
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind study.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind study but no mention about whether assessors were blinded or not.
Incomplete outcome data (attrition bias) All outcomes	Low risk	18 out of 147 women (12.2%) were excluded from the analysis.
Selective reporting (reporting bias)	Unclear risk	Study protocol unavailable.
Other bias	Unclear risk	No information on baseline characteristics. Other possible biases were unclear. No information about funding source of study.

Saltzman 1986

Methods	RCT. Individual women. 3-arm study.
Participants	Inclusion criteria • Women undergoing primary CS at high risk of developing post-operative infectious morbidity.

Saltzman 1986 *(Continued)*

	• In active labour and/or had had membrane rupture > 6 hours; predominately women receiving private practice care. • N = 158 but data on 151. Exclusion criteria • Women with clinical signs of active infection; oral temp > 38 °C within 24 hours; systemic antimicrobial used within 3 days prior to CS; known hypersensitivity to penicillin or cephalosporin.
Interventions	Intervention: cephalosporin (B2). • Cefoxitin. • 12 mg total, 4 mg each dose, 3 doses, at cord clamping and at 4 hours and 8 hours. • N = 49. Comparison 1: penicillin (A3). • Mezlocillin. • 4 mg, 1 dose, at cord clamping. • N = 51. Comparison 2: penicillin (A3). • Mezlocillin. • 6 mg total, 3 doses, 2 mg every 4 hours from cord clamping. • N = 51.
Outcomes	Febrile morbidity (temperature > 38 x 2, 8 hours apart, excluding first 24 hours post-operatively; endometritis (temperature > 38 plus foul lochia or uterine tenderness); wound infection (wound surrounded by cellulitis and/or draining purulent material); UTI.
Notes	Dates: October 1982 to April 1983. Setting: Virginia, US. Subgroups 1. Non-elective CS. 2. After cord clamping. 3. IV administration. Although route of administration not specified the administration of doses 4 and 8 hours after birth indicated lavage was not used. 4. Mixture of single and multiple doses. • Comparisons: 1 (subgroup 1); 2; 3; 4; 7. • Single and multiple doses were pooled for the comparison between B2 and A3 (Comparison 7). • Long-term follow-up: reported no infections at 6 weeks post-operatively. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...randomly assigned...".
Allocation concealment (selection bias)	Unclear risk	"...randomly assigned...".

Saltzman 1986 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	"...double-blind study...".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind study but no mention of whether assessors were blinded or not.
Incomplete outcome data (attrition bias) All outcomes	Low risk	7 out of 158 women (4.4%) were removed for failure to fulfil the study criteria.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable.
Other bias	Unclear risk	Baseline characteristics similar on: age; parity; gestation. However other aspects of potential bias were unclear. No information about funding source of study.

Shah 1998

Methods	RCT. Individual women. 4-arm study.
Participants	Inclusion criteria • Women undergoing elective CS. • N = 147 in the cephalosporin comparisons (198 in total). Exclusion criteria • Women who gave history of hypersensitivity to penicillin or cephalosporin and those having received antibiotic therapy within the last 3 days prior to surgery; women with severe hepato-renal insufficiency (total bilirubin > 3 mg/100 ml and/or serum creatinine > 2.5 mg/100 ml); women with positive cultures prior to operation; definite clinical or laboratory evidence of infection where sampling for culture was not possible.
Interventions	Intervention: cephalosporin (B1) combination. • Cephradine + metronidazole. • 3 doses of 500 mg cephradine + 500 mg metronidazole; IV. • N = 47. Comparison 1: penicillin (A3). • Piperacillin - single dose. • 4 g; IV. • N = 48. Comparison 2: penicillin (A3). • Piperacillin - multiple doses. • 3 doses of 2 g each; IV. • N = 52. Comparison 3: Data not included in this review. • No antibiotics.

Shah 1998 *(Continued)*

- Did not receive any prophylactic antibiotic and served as the control group. No other antibiotic was administered to any of these women during the study period.
- N = 51.

Outcomes	Post-operative febrile morbidity; metritis with pelvic cellulitis; wound infection.
Notes	Dates: January 1995 to mid-1996. Setting: Abu-Dhabi, United Arab Emirates. Subgroups 1. Elective CS. 2. After cord clamping. 3. IV administration. 4. Single and multiple doses. • Comparisons: 1 (subgroup 3); 2; 3; 4; 5. • Single and multiple doses were pooled for the comparison between B1 and A3 (Comparison 5). • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Reports women were randomised and no further details.
Allocation concealment (selection bias)	Low risk	'...consecutively numbered sealed envelopes...'.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	11 out of 198 women (5.6%) were excluded during the course of the study.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable.
Other bias	Unclear risk	No information on the baseline characteristics of women in each group. Also other aspects of possible bias were unclear. No information about funding source of study.

Spinnato 2000

Methods	RCT. Individual women. 3-arm study.
Participants	Inclusion criteria

Spinnato 2000 *(Continued)*

- Women requiring CS.
- N = 301, data available on 298.

Exclusion criteria

- Known hypersensitivity to any study antibiotic, preoperative diagnosis of chorioamnionitis, antibiotic therapy within the previous 24 hours, known HIV-positive serology, and women who refused to participate in the study. During the study period, women known to be group B beta haemolytic streptococcus carriers were treated intrapartally with antibiotics and thus were excluded from the study.

Interventions	Intervention: cephalosporin (B2). • Cefotetan. • 2 g; IV; immediately after the umbilical cord was clamped. • N = 96. Comparison 1: penicillin (A4). • Ampicillin. • 2 g; IV; immediately after the umbilical cord was clamped. • N = 101. Comparison 2: penicillin (A4) combination. • Ampicillin + sulbactam. • 3 g; IV; immediately after the umbilical cord was clamped. • N = 101.
Outcomes	Endomyometritis; wound complications.
Notes	Dates: 24 January 1994 to 12 December 1996. Setting: University of Louisville Hospital, US. Subgroups 1. Mixed types of CS, both elective and non-elective. 2. After cord clamping. 3. IV administration. 4. Single doses. • Comparisons: 1 (subgroups 1 & 2); 2; 3; 4; 8. • Authors report "Owing to the absence of endometritis among patients undergoing elective, nonlabouring cesarean delivery (n = 92), the data were also analysed after excluding these patients." We have not reported on this subgroup of women as the randomisation appears not to have been stratified by type of CS. • We have pooled data from ampicillin and ampicillin/sulbactam. Authors report that "Ampicillin/sulbactam combines a B lactam antibiotic with a B lactamase inhibitor extending its antibacterial spectrum". This data will be considered for inclusion in the review 'Different regimens of penicillin antibiotic prophylaxis at caesarean section for reducing maternal morbidity'. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...patients were randomized...".

Spinnato 2000 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"...double-blinded...".
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blinded but unclear if the outcome assessors were blinded or not.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Three out of 301 women (1.0%) were not evaluated due to incomplete information data that restricted chart retrieval.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable.
Other bias	Unclear risk	Baseline characteristics were similar on: age; gestational age; height and weight. Other possible biases were unclear. No information about funding source of study.

van der Linden 1993

Methods	RCT. Individual women. 2-arm study, stratified by type of operation, CS or hysterectomy. We only report on women having CS here.
Participants	Inclusion criteria • Women undergoing vaginal hysterectomy without cysto/rectocoele repair or secondary CS. • Secondary CS is defined as CS performed after onset of labour. • N = 83 in CS group. Exclusion criteria • Hypersensitivity to any of the study drugs, antibiotic treatment within 48 hours prior to surgery, previously scheduled antibiotic treatment during the post-operative period of 72 hours or longer, impaired renal function, hepatic dysfunction, haematological and neurological disorders, or the presence of serious underlying disease or infection.
Interventions	Intervention: cephalosporin (B2) combination. • Cefuroxime (750 mg) plus metronidazole (500 mg, which gives anaerobic cover). • The first dose was given IV at the induction of anaesthesia, followed by the same dose 8 and 16 hours later. • In women undergoing CS, medication was started immediately after clamping the umbilical cord. • N = 42. Comparison: penicillin (A4) combination. • Amoxicillin + clavulanic acid (which gives anaerobic cover). • Single dose of 2200 mg IV at the induction of anaesthesia. • In women undergoing CS, medication was started immediately after clamping the umbilical cord. • N = 41.

van der Linden 1993 *(Continued)*

Outcomes	UTI; febrile temperature; abdominal wound infection; endometritis and infiltrates at the top of the vaginal vault.
Notes	Dates: 1 August 1988 to 15 December 1989. Setting: Leyenburg Hospital, Netherlands. Subgroups 1. Non-elective CS. 2. After cord clamping. 3. IV administration. 4. Single and multiple doses. • Comparisons: 1 (subgroup 4); 2; 3; 4; 8. • "This study was sponsored by Smith Kline and Beecham Pharmaceuticals."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Women were “randomly allocated to one of two treatment regimes”.
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Low risk	16 out of 215 (7.4%) women were excluded from the analysis.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable.
Other bias	High risk	Baseline characteristics were similar on: age and weight. Other possible biases were unclear. The study was sponsored by Smith Kline and Beecham Pharmaceuticals.

Voto 1986

Methods	RCT. Individual women. 2-arm study.
Participants	Inclusion criteria • Women requiring a CS. • N = 80. Exclusion criteria

Voto 1986 *(Continued)*

	• None specified.
Interventions	Intervention: cephalosporin (B2). • Cefoxitin. • 2 g, IV, every 4 hours, after cord clamping. • N = 39 with analysis on 37 (95%) Comparison: penicillin (A4). • Ampicillin. • 2 g orally with daily doses divided into 4 doses, for 7 days. • N = 40 with analysis on 17 (42%).
Outcomes	Analyses of cultures at endocervix, skin and tissue and urine.
Notes	Setting: maternity ward, the Hospital Juan A. Fernandez, Buenos Aires, Argentina. Translation: from Portuguese. Subgroups 1. Type of CS not defined. 2. After cord clamping. 3. IV administration of cephalosporin and oral administration of penicillin. 4. Multiple doses. • We have not included data from this study because of the high loss of data from the penicillin group (58%). The authors concluded that the use of cefoxitin was efficacious in preventing infection after CS. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Women were divided, at random, into two groups of which one was administered cefoxitin and the other ampicillin."
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	High risk	Of the 80 women included (GpA = 39 and GpB = 40) authors only report data on GpA = 37 and GpB = 17. Suggest loss too high and very uneven, so groups are not randomised groups. We have not used data in the meta-analyses.
Selective reporting (reporting bias)	Unclear risk	The study protocol was unavailable.
Other bias	Unclear risk	No information on baseline characteristics and other possible biases unclear. No information about funding source of study.

Wells 1994

Methods	RCT. Individual women. 3-arm study.
Participants	Inclusion criteria • Women undergoing emergency CS. • N = 84. Exclusion criteria • No information provided.
Interventions	Intervention 1: cephalosporin (B) + nitroimidazole (I). • Cefuroxime plus metronidazole. • N = ?. Intervention 2: nitroimidazole (I). • Metronidazole. • N = ?. Comparison: placebo. • Placebo. • N = ?.
Outcomes	Temperature; wound infection; offensive lochia; UTI.
Notes	Setting: authors from Grey's Hospital, London, UK. Subgroups 1. Non-elective CS. 2. After cord clamping. 3. IV administration. 4. Single dose. • We have not included data from this study because no denominator data were provided. We are attempting to contact the authors. • Conference abstract only, no published version of this study has been identified. • No information about funding source of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...were randomised...".
Allocation concealment (selection bias)	Unclear risk	No information provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No information provided.

Wells 1994 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information provided.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information provided.
Selective reporting (reporting bias)	Unclear risk	We did not assess trial protocol.
Other bias	Unclear risk	No baseline data and other aspects of possible bias were unclear. No information about funding source of study.

Ziogos 2010

Methods	Prospective RCT - 2 parallel arms - women randomised individually.
Participants	Inclusion criteria • Women undergoing CS. • N = 176. Exclusion criteria • Women with known hypersensitivity to penicillin, cephalosporins, those who required concomitant antibiotic therapy or had received antibiotics during the 72 hours immediately preceding their enrolment.
Interventions	Intervention: cephalosporin (B2). • Cefuroxime (1.5 g). • IV. • After the time the umbilical cord was clamped. • Total number randomised: n = 85. Comparison: penicillin (A4) combination. • Ampicillin/sulbactam 3 g. • IV. • after the time the umbilical cord was clamped. • Total number randomised: n = 91.
Outcomes	Outcomes: The primary outcome was development of an infection either at the surgical site or elsewhere e.g. UTI. Endometritis, Reported outcomes: postoperative infections, surgical site infection (SSI), endometritis, Duration of hospitalisation in days median (IQR), Duration of hospitalisation post-operatively in days median (IQR), adverse drug reactions.
Notes	Study dates July 2004 to December 2008 Setting Major tertiary care hospital, Nikaia's Regional General Hospital "Agios Panteleimon", Athens, Greece.

Ziogos 2010 *(Continued)*

Subgroups

1. Mixed elective and emergency CS.
2. After cord clamping.
3. Systemic - IV.
4. Single dose.

- Comparison: 1 (subgroup 2); 2; 3; 4; 8.
- Authors reported that had no competing interests.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Using a random-number generator".
Allocation concealment (selection bias)	Low risk	"The sequence was obtained using a central telephone number and it was concealed until interventions were assigned."
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Participants ... were blinded to the intervention, however the physician administering the intervention and assessing the outcomes was not."
Blinding of outcome assessment (detection bias) All outcomes	High risk	"Participants ... were blinded to the intervention, however the physician administering the intervention and assessing the outcomes was not."
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss of follow-up were reported
Selective reporting (reporting bias)	Unclear risk	The study protocol is unavailable.
Other bias	Unclear risk	Not known. Authors reported that had no competing interests.

BP: blood pressure
CI: confidence interval
CS: caesarean section
Hb: haemoglobin
IM: intramuscular
IV: intravenous
PROM: premature rupture of membranes
RCT: randomised controlled trial
RR: risk ratio
t.d.s.: three times daily
UTI: urinary tract infection
vs: versus

A. Penicillins
A1. Natural penicillins
A2. Penicillinase-resistant penicillins
A3. Extended-spectrum penicillins
A4. Aminopenicillins

B. Cephalosporins
B1. First generation cephalosporins
B2. Second generation cephalosporins
B3. Third generation cephalosporins

B4. Fourth generation cephalosporins
C. Fluoroquinolones
D. Tetracyclines
E. Macrolides
F. Beta-lactams/carbapenems
G. Aminoglycosides
H. Lincosamides
I. Nitroimidazoles

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

Study	Reason for exclusion
Andrews 2003	Study compared 2 different 2nd generation cephalosporins. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Baheraie 1997	Compares single vs multiple doses of same class of antibiotic (cephalosporin). Study will be considered in the review 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Beksac 1989	Quasi-RCT - "...randomly assigned according to the last number of her hospital notes..."
Berkeley 1990	Study compared a cephalosporin (cefotaxime) by 2 different routes of administration, IV and lavage.
Bernstein 1994	Study compared 2 different cephalosporins, cefotetan versus cefoxitin. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Bilgin 1998	Quasi-RCT, allocated women to groups according to last digit of hospital number.
Boothby 1984	Study compared a cephalosporin (cefoxitin) by 2 different routes of administration, IV and lavage.
Carlson 1990	Study compared 2 different cephalosporins, cefazolin versus cefotetan. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Chamberlain 1993	Study compared ampicillins plus sulbactam versus ampicillin alone. Study will be considered in the review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Chittacharoen 1998	Study compared 2 different ampicillins (augmentin vs ampicillin). Study will be considered in the review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Conover 1984	Study compared a cephalosporin (cefoxitin) by 2 different routes of administration, IV and irrigation.
Crombleholme 1987	Study compared 2 versus 3 doses of a penicillin (mezlocillin). Study will be considered in review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Crombleholme 1989	Study compared 2 different 2nd generation cephalosporins. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.

Study	Reason for exclusion
Cunningham 1983	Study compared 2 differing timings of giving the prophylactic antibiotics, before and after cord clamping.
D'Angelo 1980	Comparison of short- versus long-course prophylactic antibiotic treatment. Authors do not list dose of drug at time of first administration, nor do they indicate the time of administration (pre-operative, cord clamp). The authors are not even clear about the identity of the drug which begins the prophylactic regimen. They state that it is a random study but provide no details of mechanism.
De Palma 1980	At the start of the study 2 arms: 1 a no treatment arm, the other composed of women given either cefamandole or penicillin plus gentamicin. It would have been possible to try and dissect important information from the study except that they changed the antibiotic regimen after treating 57/105 women in the cefamandole subgroup. A co-intervention (addition of chloramphenicol) was also applied to 3/105 women in the cefamandole subgroup and 4/104 women in the penicillin/gentamicin arm.
De Palma 1982	Timing of delivery of antibiotics for prophylaxis not specified. Authors state antibiotics given within 90 minutes of delivery with no indication as to whether these might have been given pre-, post- or intra-operatively. Mechanism of randomisation clearly inadequate.
Digumarthi 2008	Quasi-RCT, allocated women to groups alternatively.
Ding 2000	Study compared 2 different cephalosporins from 1st and 2nd generations. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Donnenfeld 1986	Study compared a cephalosporin (cefazolin) by 2 different routes of administration, IV and lavage.
Duff 1987	Study compared 2 different cephalosporins, cefazolin versus cefonicid; 1 g after cord clamped. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Elliot 1982	Study compared a penicillin, ampicillin, given in differing multiple doses. Study will be considered in review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Elliot 1986	Study compared a cephalosporin, cefoxitin, given in different ways, IV or lavage, or a combination of IV plus lavage.
Fejgin 1993	This study compared 2 different cephalosporins from 2nd and 3rd generations. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Flaherty 1983	Comparison of pharmacokinetics of cefoxitin when administered by intravenous versus intraperitoneal lavage. Outcome variable of interest: concentration of drug in decidua. No outcomes of interest in our review are listed or were collected (i.e. febrile morbidity, endometritis, etc).
Fugere 1983	Study compared 2 different cephalosporins, cefoxitin (2 g) versus cefazolin (1g). Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Galask 1988	Study compared 2 different cephalosporins, cefotetan (2 g, single dose, IV dose) versus cefoxitin (6 g, multiple doses (2 g each dose), IV); after cord clamped. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.

Study	Reason for exclusion
Galask 1989	Study compared 2 different 2nd generation cephalosporins. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Gall 1987	Study compared a penicillin, piperacillin (4 g, IV, after cord clamped) single dose versus multiple doses. Study will be considered in review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Gonen 1986	Study compared a cephalosporin, cefamandole, by 2 different routes of administration, lavage and multiple doses IV.
Gonik 1985	Study compared a cephalosporin, cefotaxime (IV, after cord clamped) single dose (1 g) versus multiple doses (3 x 1 g). Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Gonik 1994	Study compared 2 different 2nd generation cephalosporins. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Gordon 1982	Study compared 2 different cephalosporins from 2nd and 3rd generations. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Grujic 2009	Study not randomised, authors report that women weer allocated to groups according to the type of antibiotics prophylaxis administered as a single dose.
Gul 1999	Study compared different timings of the antibiotic prophylaxis (before versus after cord clamping).
Hager 1991	Study compared 3 cephalosporins, cefazolin (1 g) versus cefoxitin (2 g) versus cefotaxime (1 g); IV; after cord clamped. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Hartert 1987	Study compared 2 cephalosporins, single dose cefonicid (1 g) versus multiple doses cefoxitin (2 g each); IV; after cord clamped. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Hawrylyshyn 1983	Study compared a cephalosporin, cefoxitin, single dose (2 g) versus multiple dosed (2 g each); IV; after cord clamped. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Ijarotimi 2012	Comparing the same antibiotics but using different time scales (24 hours vs 48 hours + oral for 5 days). Study may be considered for possible inclusion in another review.
Itskovitz 1979	Quasi-RCT. Women were assigned to each of the 2 wings of the department according to the day of their admission.
Jakobi 1988	Study compared a cephalosporin, cefazolin, single dose (1 g) versus multiple doses (2 g each); IV; after cord clamped. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Kreutner 1979	Study compared 2 cephalosporins, cephalothin versus cefamandole; 1 g; IV at differing times of administration. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.

Study	Reason for exclusion
Lavery 1986	Study compared penicillin (mezlocillin) by differing routes of administration and single versus multiple doses. Study will be considered in review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Leonetti 1989	Study compared penicillin (piperacillin, IV after cord clamping) single (4 g) versus multiple doses (4 g each). Study will be considered in review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Leveno 1984	Study compared a cephalosporin (cefamandole 2 g) by 2 routes of administration, lavage versus IV.
Levin 1983	Study compared 2 different cephalosporins, cefoxitin versus cephapirin (2 g/L by irrigation). Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Luttkus 1997	Compares different doses of the same cephalosporin. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section (0732)'.
Lyimo 2012	Compares different doses of the same combination of antibiotics. Study may be considered for possible inclusion in another review.
Macones 2008	Study compared different timings of giving the prophylactic antibiotic.
Maggioni 1998	Study compared 2 different B-lactams (F).
Major 1999	Study compared 2 different cephalosporins from 1st and 2nd generations. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Mansani 1984	Study on antibiotics for women undergoing hysterectomy.
Masse 1988	Study compared a cephalosporin, cefoxitin (2 g IV after cord clamped) single dose versus multiple doses. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Mathelier 1992	Study compared a cephalosporin, cefazolin, by different routes of administration, '2 g IV after cord clamped and saline irrigation of abdomen' versus '1 g IV after cord clamped and 1 g in 500 ml normal saline by irrigation'.
McGregor 1986	Study compared 2 cephalosporins, cefotetan (2 g IV after cord clamped) versus cefoxitin (2 g IV and 2 further doses at 4 and 8 hours post-operatively).
McGregor 1988	Study compared 2 cephalosporins, cefotetan (2 g IV after cord clamped) versus cefoxitin (2 g IV and 2 further doses at 4 and 8 hours post-operatively).
Meyer 2000	This study compared a cephalosporin versus the same cephalosporin plus another antibiotic. More specifically, cefazolin versus cefalozin-metronidazole. So this study compared B1 versus B1 + I and will be considered in the review 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Meyer 2003	Study compared 2 different 1st generation cephalosporins 1 in combination with metronidazole versus the antibiotic alone.
Neuman 1990	Study comparing penicillin G (10 million units IV after cord clamped) plus tetracycline (250 mg IM after cord clamped) versus ampicillin (2 g) plus tetracycline (1.5 g per day, to complete 3 days).

Study	Reason for exclusion
	Study will be considered in review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
O'Leary 1986	Study compared a penicillin (ampicillin 2 g IV intraoperatively and 7 further doses) versus the same penicillin regime plus another antibiotic (gentamicin 2 g IV after cord clamping and 6 further doses). So the study compared A4 versus A4 + G and will be considered in the review 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Ovalle 1996	Quasi-RCT as “Patients were distributed strictly by order of admission in five groups:”.
Parsons 1985	Study compared 2 cephalosporins, cefonicid (1 g IV after cord clamped) versus cefoxitin (2 g IV after cord clamped and 4 additional doses). Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Patacchiola 2000	Study compared 2 3rd generation penicillins at differing doses. Study will be considered in the review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Periti 1988	Study compared 2 different cephalosporins from 1st and 2nd generations. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Peterson 1990	Study compared 2 different cephalosporins by 2 different routes of administration. Cefazolin (2 g IV after cord clamped) versus cefamandole (2 g IV after cord clamped) versus cefazolin (2 g in 1 L in normal saline by lavage) versus cefamandole (2 g in 1 L normal saline by lavage). Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Pevzner 2009	Compares giving prophylactic antibiotics before or after cord clamping. Study will be considered for review on 'Timing of prophylactic antibiotics for preventing infectious morbidity in women undergoing caesarean section'.
Prasuna 2011	Quasi-RCT, allocated women to groups alternately.
Puri 1991	Quasi-RCT, allocated women to groups alternately.
Rayburn 1985	Study compared a 1st and 3rd generation cephalosporins. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Rijhsinghani 1995	This study compares a single penicillin with a penicillin combination so should be considered for review ‘Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section’.
Rodriguez 1990	Study compared different timings of giving prophylactic antibiotics.
Roex 1987	Study compared a cephalosporin, cefoxitin (2 g IV after cord clamped) single dose versus multiple doses. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Roy 2003	Study looked at women with acute pelvic infections.
Saravolatz 1985	Study compared cephalosporin (ceforanide) by 2 routes of administration, 2 g IV after cord clamped versus 2 g in 1 L normal saline by irrigation.

Study	Reason for exclusion
Scarpignato 1982	Study compared a cephalosporin (cefuroxime) by different length of administration, 750 mg IM 30 to 60 minutes pre-operatively and again post-operatively at 8 and 16 hours versus 750 mg IM to complete 5 days of therapy, first dose post-operatively after return of woman to the ward.
Seton 1996	Study looked at different timings of giving 3rd generation cephalosporins.
Shakya 2010	Stuudy is unclear how women were allocated to groups and also compared single dose (Cefazolin + Metronidazole) vs multiple doses antibiotics
Stiver 1983	Study compared a cephalosporin (cefoxitin) at different doses, 1 g IV after cord clamped versus 2 g IV after cord clamped. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Stiver 1984	Study compared 2 different cephalosporins from 1st and 2nd generations. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Sullivan 2006	Study looked at different timings of giving 1st generation cephalosporins for prophylaxis. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Sullivan 2007	Study looked at different timings of giving 1st generation cephalosporins for prophylaxis.
Tassi 1987	Study compared a cephalosporin (ceftazidime) by single (2 g IM 1 hour pre-operative) versus multiple doses (2 g IM 1 hour pre-operative plus 2 additional doses). Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Teansutikul 1993	Study compared different doses of ampicillins. Study will be considered in the review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Thigpen 2005	Study looked at different timings of giving 1st generation cephalosporins for prophylaxis.
van Beekhuizen 2008	Study looked at single dose of ampicillin plus metronidazole versus multiple doses in low-income setting.
van Velzen 2009	Study compared a single dose of ampicillin + metronidazole versus multiple doses.
Varner 1986	Study compared a cephalosporin (cefotetan) by single (2 g IV after cord clamping) versus multiple doses (2 g IV after cord clamping plus 2 additional doses). Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
von Mandach 1993	Study compared 2 cephalosporins, ceftriaxone 1 g IV after cord clamped versus cefoxitin 1 g IV after cord clamped and 2 additional doses at 8 and 16 hours after first dose. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.
Wagner 2006	Study compared 2 different 3rd generation cephalosporins. Study will be considered in the review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section'.

Study	Reason for exclusion
Warnecke 1982	Study compares prophylactic antibiotics with what we presume is 'no treatment' as the English summary only refers to the 'control group'. Study will be considered for review on 'Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section'.
Watts 1991	Study looked at upper genital isolates at birth as predictors of infection.
Wax 1997	Study looked at different timings of cephalosporin administration (before and after cord clamping).
Wu 1991	Study compared a penicillin versus the same penicillin plus another antibiotic. More specifically, ampicillin versus ampicillin-gentamicin. So the study compared A4 versus A4 + G and will be considered in the review on 'Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section'.
Xu 1997	Study looked at cephalosporins versus penicillins but the penicillins were sometimes given with other classes of antibiotics and the data could not be separated.
Yildirim 2009	Study compares administration of antibiotics before and after cord clamping. Study will be considered for review on 'Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section.
Zutshi 2008	Compared different dosage regimens of the same antibiotic, but the specific antibiotic is not given in this conference abstract.

IM: intramuscular
IV: intravenous
RCT: randomised controlled trial
vs: versus

Characteristics of studies awaiting assessment *[ordered by study ID]*

Deng 2007

Methods	RCT. 2 parallel-arm study. Women randomised individually.
Participants	Inclusion criteria • Women undergoing CS. • N = 100. Exclusion criteria • Not documented.
Interventions	Intervention: cephalosporin (B1) + metronidazole (I). • Cefazolin + metronidazole. • Cefazolin sodium 2 g + 0.5% metronidazole 200ml, IV, during and after operation. • Total number randomised: N = 48. Comparison: penicillins (A1 + A4) + metronidazole (I). • Ampicillin + benzylpenicillin + metronidazole. • Ampicillin sodium 3 g + 0.5% metronidazole 200 mL, IV during CS. • Then 0.5% metronidazole 200 mL + ampicillin sodium 3 g + benzylpenicillin sodium 4x10^{6}U after CS. • Total number randomised: N = 52.

Deng 2007 *(Continued)*

Outcomes	Infection, duration of medication and cost.
Notes	Dates: No information. Setting: Central Hospital of Changnin District of Shanghai, China. Subgroups: 1. Type of CS not specified. 2. Timing in relation to cord clamping not specified - just says during and after operation. 3. Systemic - IV. 4. Multiple doses. Paper in Chinese with abstract only in English. No data provided in abstract. Translation on main paper sought/we will write to authors for data.

Ijarotimi 2013

Methods	
Participants	
Interventions	
Outcomes	
Notes	Seeking full text.

CS: caesarean section
IV: intravenous
RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1. Cephalosporins versus penicillins - all women

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maternal sepsis	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Single cephalosporin vs single penicillin	2	346	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Single cephalosporin vs penicillin drug combination	1	75	Risk Ratio (M-H, Fixed, 95% CI)	2.37 [0.10, 56.41]
1.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.4 Cephalosporin drug combination vs penicillin drug combination	1	232	Risk Ratio (M-H, Fixed, 95% CI)	3.21 [0.34, 30.45]
2 Maternal endometritis	20		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 Single cephalosporin vs single penicillin	9	3130	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.81, 1.52]
2.2 Single cephalosporin vs penicillin drug combination	10	2134	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.60, 1.35]
2.3 Cephalosporin drug combination vs single penicillin	1	139	Risk Ratio (M-H, Random, 95% CI)	2.70 [0.63, 11.55]
2.4 Cephalosporin drug combination vs penicillin drug combination	1	83	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.77]
3 Infant sepsis	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Single cephalosporin vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Single cephalosporin vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Single cephalosporin vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Single cephalosporin vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	16		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 Single cephalosporin vs single penicillin	7	1344	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.61, 1.30]
5.2 Single cephalosporin vs penicillin drug combination	6	1824	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.56, 1.49]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.3 Cephalosporin drug combination vs single penicillin	1	139	Risk Ratio (M-H, Random, 95% CI)	2.36 [0.84, 6.62]
5.4 Cephalosporin drug combination vs penicillin drug combination	2	315	Risk Ratio (M-H, Random, 95% CI)	1.57 [0.69, 3.60]
6 Maternal wound infection	19		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Single cephalosporin vs single penicillin	9	1497	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.38, 1.81]
6.2 Single cephalosporin vs penicillin drug combination	7	1608	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.40, 1.30]
6.3 Cephalosporin drug combination vs single penicillin	1	139	Risk Ratio (M-H, Random, 95% CI)	2.02 [0.42, 9.63]
6.4 Cephalosporin drug combination vs penicillin drug combination	2	315	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.42, 3.58]
7 Maternal urinary tract infection	14		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 Single cephalosporin vs single penicillin	7	1120	Risk Ratio (M-H, Random, 95% CI)	1.48 [0.89, 2.48]
7.2 Single cephalosporin vs penicillin drug combination	6	1361	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.17, 2.55]
7.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.4 Cephalosporin drug combination vs penicillin drug combination	1	83	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 Maternal thrush	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 Single cephalosporin vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Single cephalosporin vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Maternal composite serious infectious complication	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.1 Single cephalosporin vs single penicillin	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.2 Single cephalosporin vs penicillin drug combination	1	746	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	7		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
10.1 Single cephalosporin vs single penicillin	3	1902	Risk Ratio (M-H, Fixed, 95% CI)	2.02 [0.18, 21.96]
10.2 Single cephalosporin vs penicillin drug combination	4	1333	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.09, 10.50]
10.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Maternal allergic reactions	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
11.1 Single cephalosporin vs single penicillin	2	191	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 Single cephalosporin vs penicillin drug combination	3	1041	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Maternal nausea	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
12.1 Single cephalosporin vs single penicillin	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.2 Single cephalosporin vs penicillin drug combination	1	119	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.1 Single cephalosporin vs single penicillin	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.2 Single cephalosporin vs penicillin drug combination	2	319	Risk Ratio (M-H, Fixed, 95% CI)	7.0 [0.37, 133.78]
13.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
14.1 Single cephalosporin vs single penicillin	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 Single cephalosporin vs penicillin drug combination	1	119	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
15.1 Single cephalosporin vs single penicillin	2	351	Risk Ratio (M-H, Fixed, 95% CI)	1.45 [0.06, 35.38]
15.2 Single cephalosporin vs penicillin drug combination	4	618	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [0.34, 4.67]
15.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Immediate infant adverse effects	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
16.1 Single cephalosporin vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.2 Single cephalosporin vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

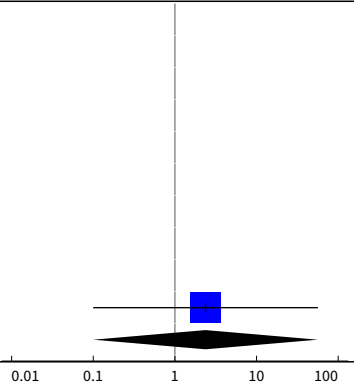
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
17 Infant unsettled	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
17.1 Single cephalosporin vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 Single cephalosporin vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
18.1 Single cephalosporin vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.2 Single cephalosporin vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
19.1 Single cephalosporin vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.2 Single cephalosporin vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
20.1 Single cephalosporin vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.2 Single cephalosporin vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.3 Cephalosporin drug combination vs single penicillin	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

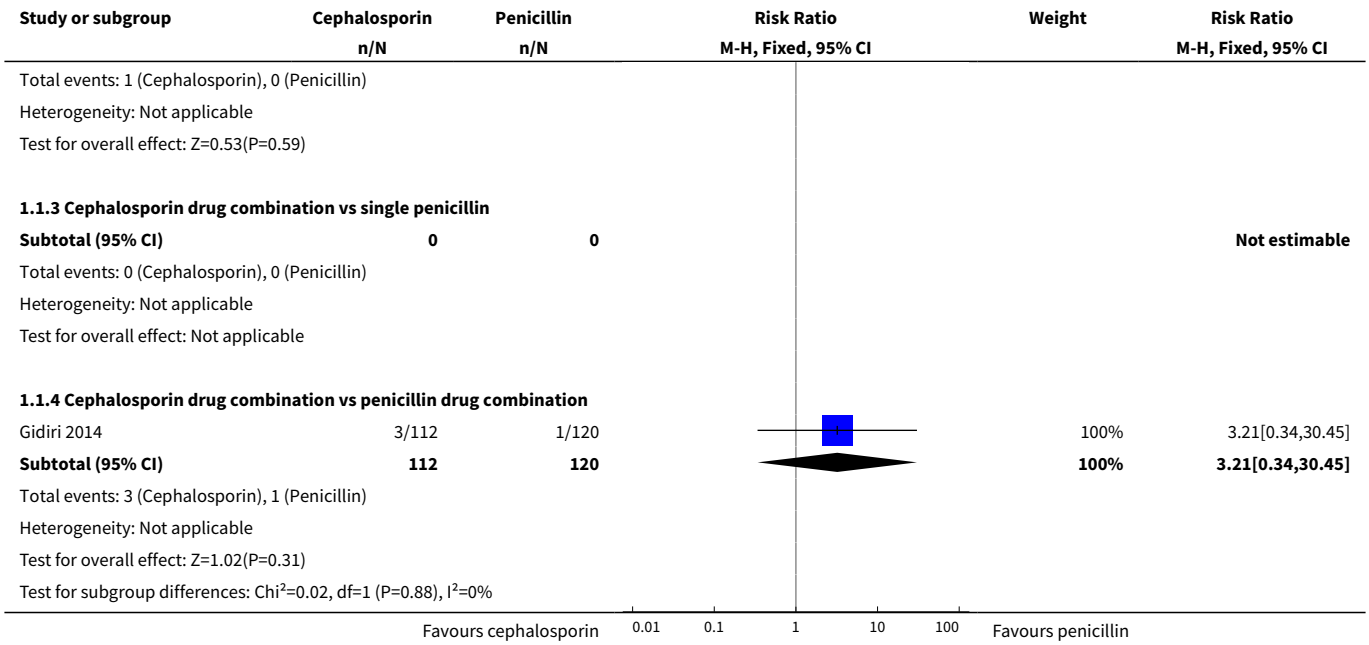
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
20.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
21.1 Single cephalosporin vs single penicillin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.2 Single cephalosporin vs penicillin drug combination	1	746	Mean Difference (IV, Fixed, 95% CI)	-0.03 [-0.14, 0.08]
21.3 Cephalosporin drug combination vs single penicillin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Infant length of hospital stay	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
22.1 Single cephalosporin vs single penicillin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 Single cephalosporin vs penicillin drug combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.3 Cephalosporin drug combination vs single penicillin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
23.1 Single cephalosporin vs single penicillin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 Single cephalosporin vs penicillin drug combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.3 Cephalosporin drug combination vs single penicillin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Infant general health	0		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
24.1 Single cephalosporin vs single penicillin	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.2 Single cephalosporin vs penicillin drug combination	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
24.3 Cephalosporin drug combination vs single penicillin	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
25.1 Single cephalosporin vs single penicillin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.2 Single cephalosporin vs penicillin drug combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.3 Cephalosporin drug combination vs single penicillin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
26.1 Single cephalosporin vs single penicillin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26.2 Single cephalosporin vs penicillin drug combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26.3 Cephalosporin drug combination vs single penicillin	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26.4 Cephalosporin drug combination vs penicillin drug combination	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

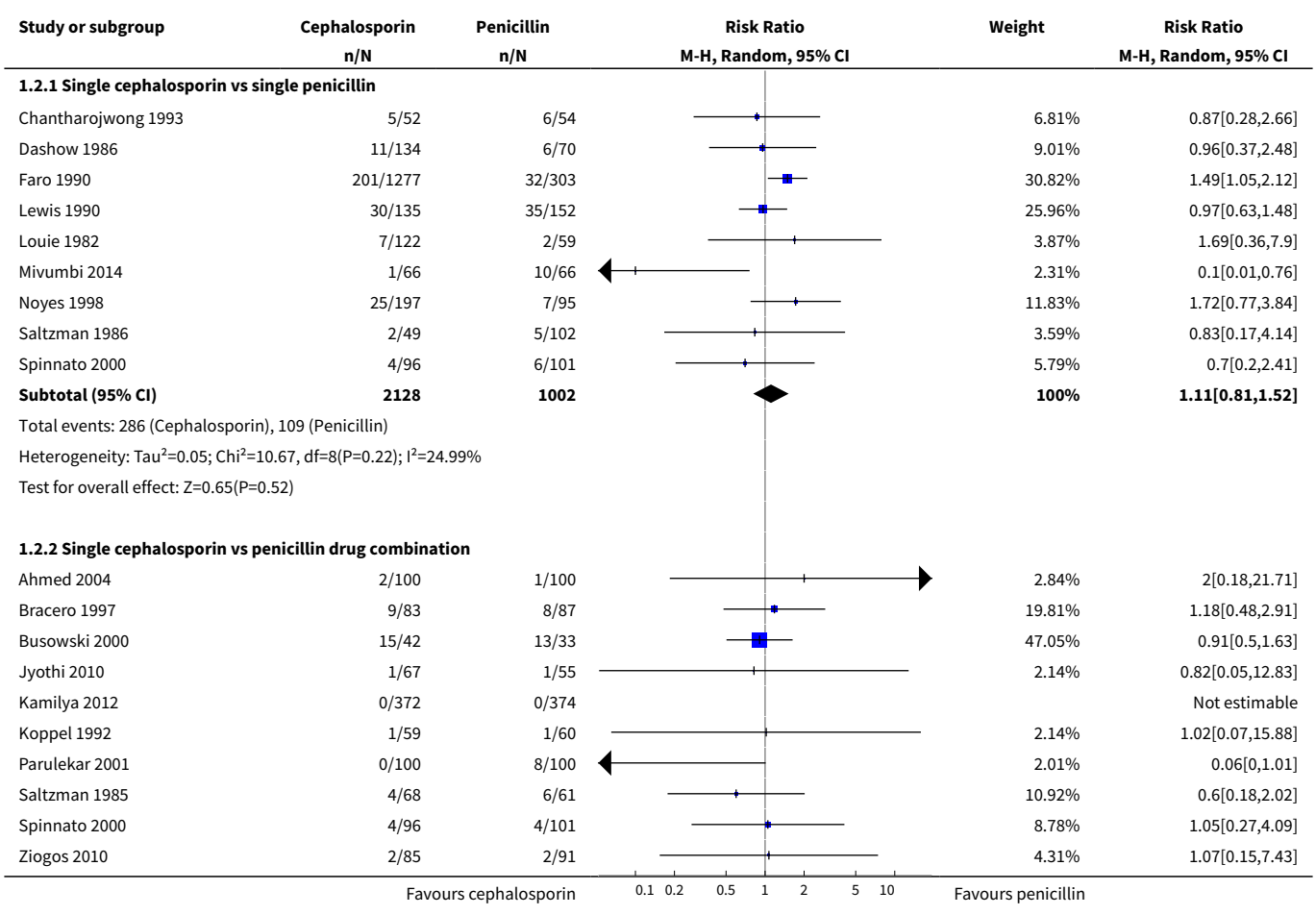
Analysis 1.1. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 1 Maternal sepsis.

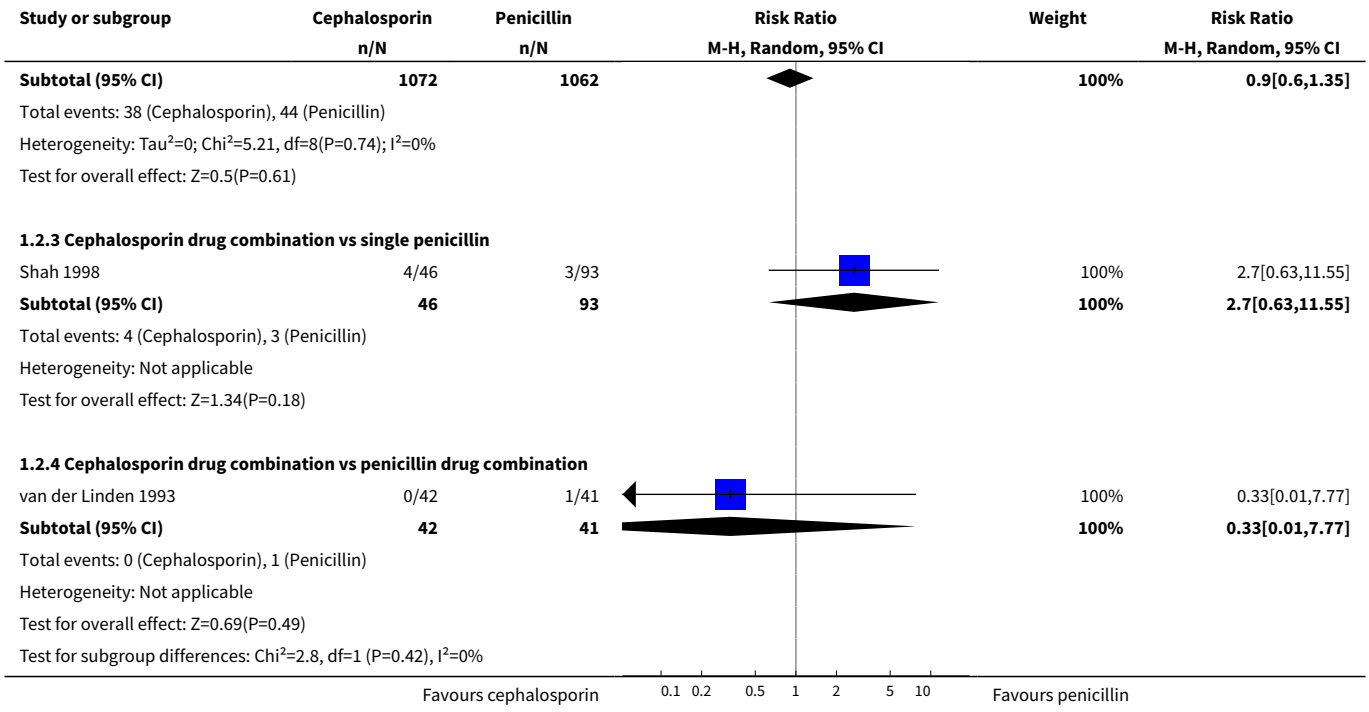
Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Single cephalosporin vs single penicillin					
Lewis 1990	0/135	0/152			Not estimable
Rosaschino 1988	0/27	0/32			Not estimable
Subtotal (95% CI)	**162**	**184**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.1.2 Single cephalosporin vs penicillin drug combination					
Busowski 2000	1/42	0/33		100%	2.37[0.1,56.41]
Subtotal (95% CI)	**42**	**33**		**100%**	**2.37[0.1,56.41]**



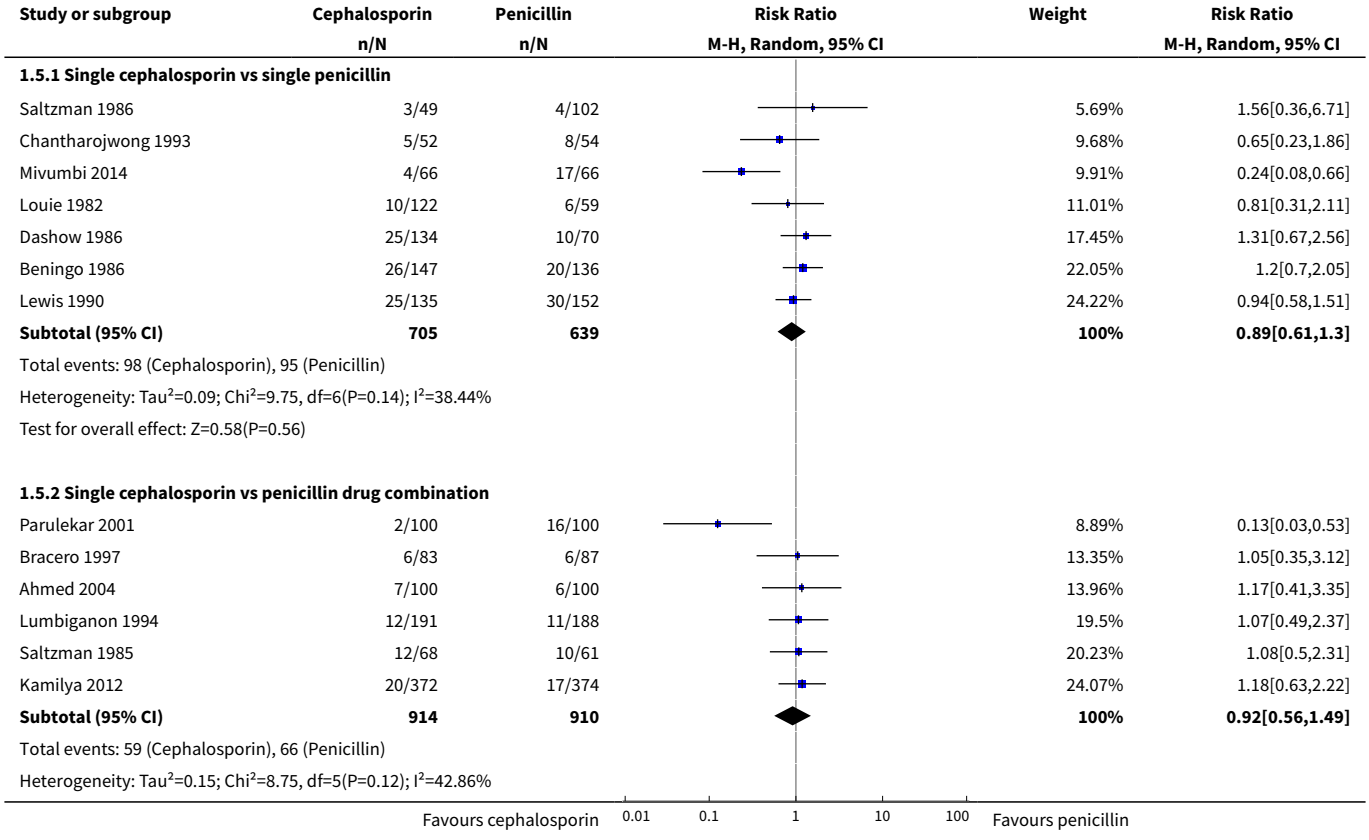


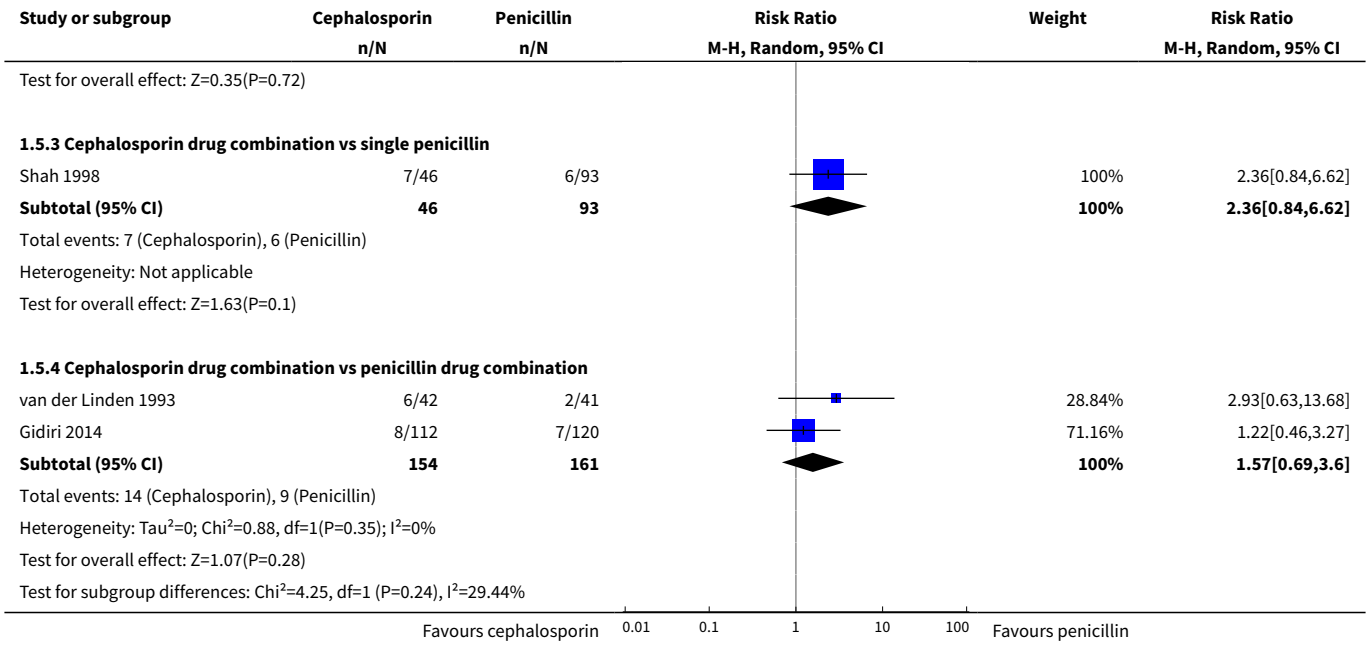
Analysis 1.2. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 2 Maternal endometritis.



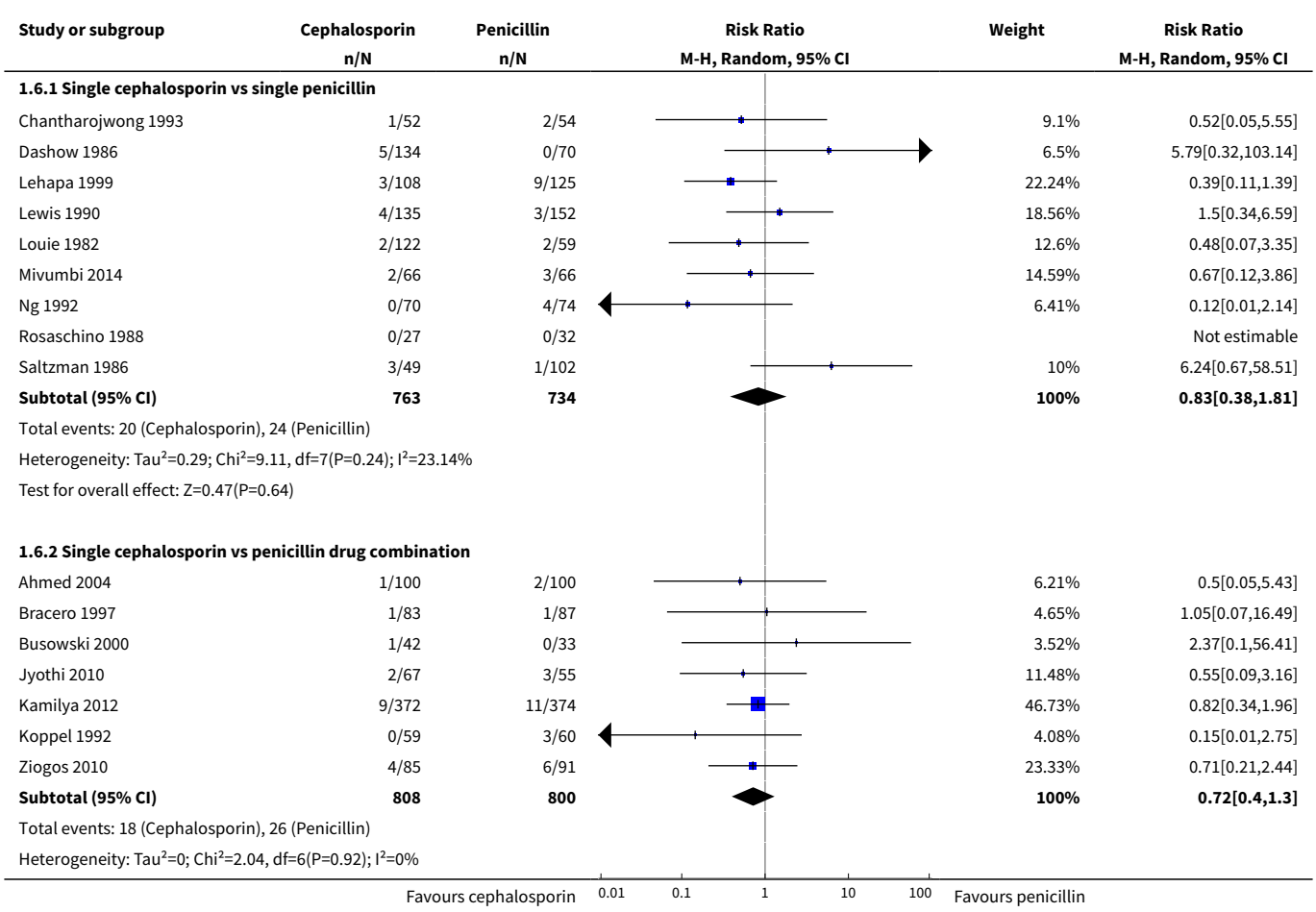


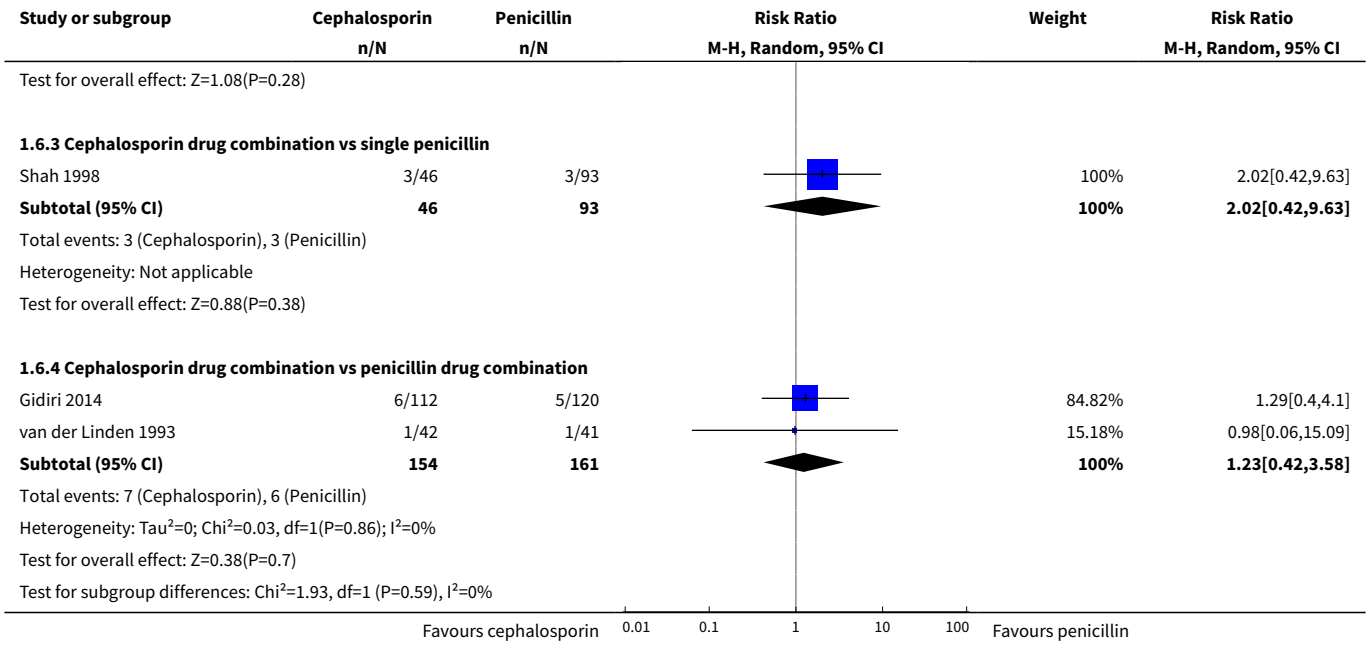
Analysis 1.5. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 5 Maternal fever (febrile morbidity).



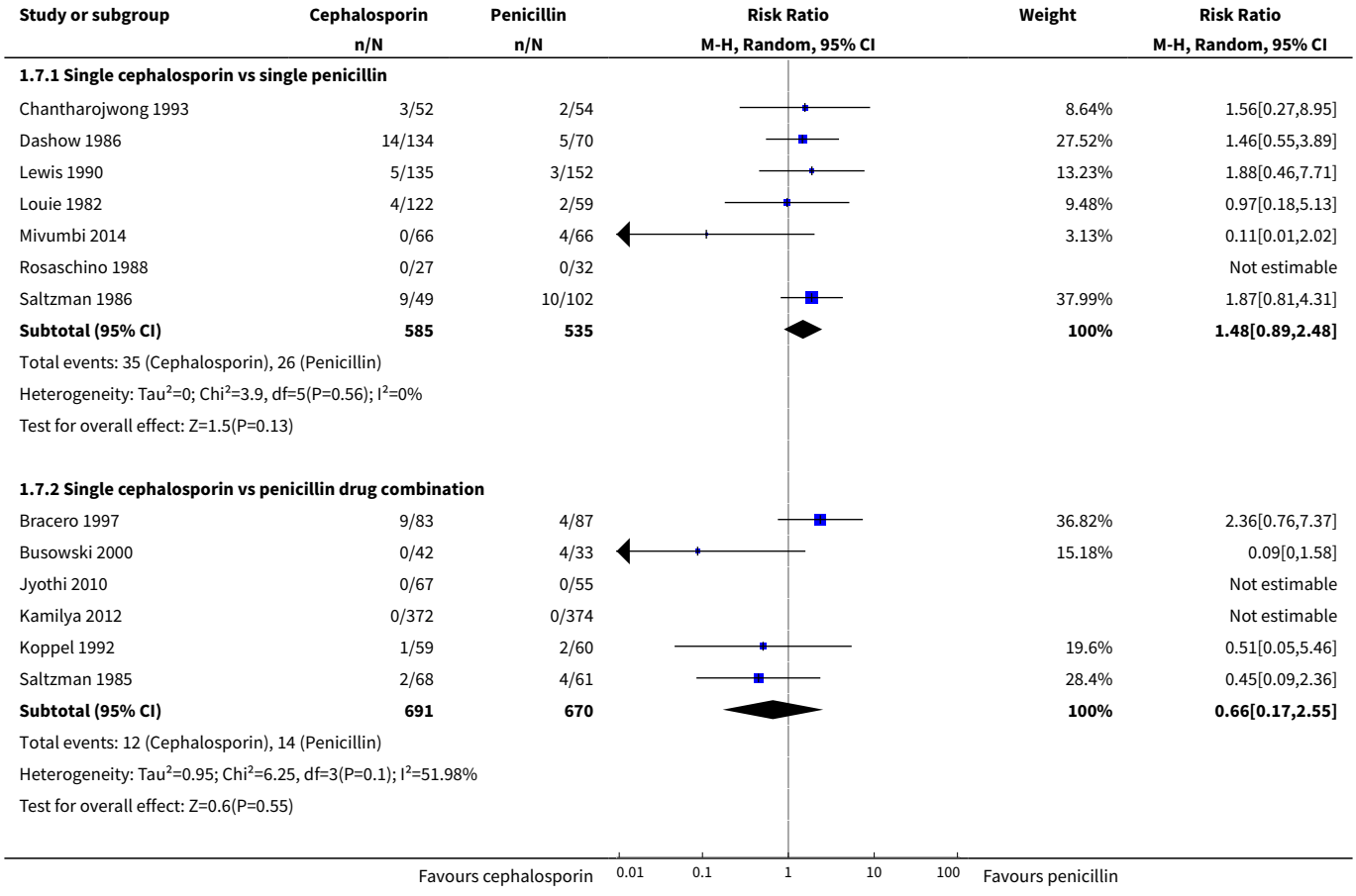


Analysis 1.6. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 6 Maternal wound infection.





Analysis 1.7. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 7 Maternal urinary tract infection.



Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.7.3 Cephalosporin drug combination vs single penicillin					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.7.4 Cephalosporin drug combination vs penicillin drug combination					
van der Linden 1993	0/42	0/41			Not estimable
Subtotal (95% CI)	**42**	**41**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Chi^2=1.2, df=1 (P=0.27), I^2=16.62%					

Favours cephalosporin 0.01 0.1 1 10 100 Favours penicillin

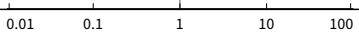
Analysis 1.9. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 9 Maternal composite serious infectious complication.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.9.1 Single cephalosporin vs single penicillin					
Rosaschino 1988	0/27	0/32			Not estimable
Subtotal (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.9.2 Single cephalosporin vs penicillin drug combination					
Kamilya 2012	0/372	0/374			Not estimable
Subtotal (95% CI)	**372**	**374**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.9.3 Cephalosporin drug combination vs single penicillin					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.9.4 Cephalosporin drug combination vs penicillin drug combination					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					

Favours cephalosporin 0.01 0.1 1 10 100 Favours penicillin

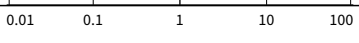
Analysis 1.10. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 10 Maternal composite adverse effects.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.10.1 Single cephalosporin vs single penicillin					
Faro 1990	0/1277	0/303			Not estimable
Ford 1986	2/131	1/132		100%	2.02[0.18,21.96]
Rosaschino 1988	0/27	0/32			Not estimable
Subtotal (95% CI)	**1435**	**467**		**100%**	**2.02[0.18,21.96]**
Total events: 2 (Cephalosporin), 1 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.58(P=0.57)					
1.10.2 Single cephalosporin vs penicillin drug combination					
Kamilya 2012	0/372	0/374			Not estimable
Koppel 1992	0/59	0/60			Not estimable
Noyes 1998	2/197	1/95		100%	0.96[0.09,10.5]
Ziogos 2010	0/85	0/91			Not estimable
Subtotal (95% CI)	**713**	**620**		**100%**	**0.96[0.09,10.5]**
Total events: 2 (Cephalosporin), 1 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.03(P=0.98)					
1.10.3 Cephalosporin drug combination vs single penicillin					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.10.4 Cephalosporin drug combination vs penicillin drug combination					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Chi^2=0.18, df=1 (P=0.67), I^2=0%					



Analysis 1.11. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 11 Maternal allergic reactions.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.11.1 Single cephalosporin vs single penicillin					
Mivumbi 2014	0/66	0/66			Not estimable
Rosaschino 1988	0/27	0/32			Not estimable
Subtotal (95% CI)	**93**	**98**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.11.2 Single cephalosporin vs penicillin drug combination					
Kamilya 2012	0/372	0/374			Not estimable



Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Koppel 1992	0/59	0/60			Not estimable
Ziogos 2010	0/85	0/91			Not estimable
Subtotal (95% CI)	**516**	**525**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.11.3 Cephalosporin drug combination vs single penicillin					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.11.4 Cephalosporin drug combination vs penicillin drug combination					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					

Favours cephalosporin 0.01 0.1 1 10 100 Favours penicillin

Analysis 1.12. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 12 Maternal nausea.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.12.1 Single cephalosporin vs single penicillin					
Rosaschino 1988	0/27	0/32			Not estimable
Subtotal (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.12.2 Single cephalosporin vs penicillin drug combination					
Koppel 1992	0/59	0/60			Not estimable
Subtotal (95% CI)	**59**	**60**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.12.3 Cephalosporin drug combination vs single penicillin					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.12.4 Cephalosporin drug combination vs penicillin drug combination					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					

Favours cephalosporin 0.01 0.1 1 10 100 Favours penicillin

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					

Favours cephalosporin 0.01 0.1 1 10 100 Favours penicillin

Analysis 1.13. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 13 Maternal vomiting.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.13.1 Single cephalosporin vs single penicillin					
Rosaschino 1988	0/27	0/32			Not estimable
Subtotal (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.13.2 Single cephalosporin vs penicillin drug combination					
Ahmed 2004	3/100	0/100		100%	7[0.37,133.78]
Koppel 1992	0/59	0/60			Not estimable
Subtotal (95% CI)	**159**	**160**		**100%**	**7[0.37,133.78]**
Total events: 3 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.29(P=0.2)					
1.13.3 Cephalosporin drug combination vs single penicillin					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.13.4 Cephalosporin drug combination vs penicillin drug combination					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					

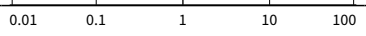
Favours cephalosporin 0.01 0.1 1 10 100 Favours penicillin

Analysis 1.14. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 14 Maternal diarrhoea.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.14.1 Single cephalosporin vs single penicillin					
Rosaschino 1988	0/27	0/32			Not estimable
Subtotal (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

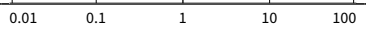
Favours cephalosporin 0.01 0.1 1 10 100 Favours penicillin

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.14.2 Single cephalosporin vs penicillin drug combination					
Koppel 1992	0/59	0/60			Not estimable
Subtotal (95% CI)	**59**	**60**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.14.3 Cephalosporin drug combination vs single penicillin					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.14.4 Cephalosporin drug combination vs penicillin drug combination					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					



Analysis 1.15. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 15 Maternal skin rash.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.15.1 Single cephalosporin vs single penicillin					
Noyes 1998	1/197	0/95		100%	1.45[0.06,35.38]
Rosaschino 1988	0/27	0/32			Not estimable
Subtotal (95% CI)	**224**	**127**		**100%**	**1.45[0.06,35.38]**
Total events: 1 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.23(P=0.82)					
1.15.2 Single cephalosporin vs penicillin drug combination					
Ahmed 2004	1/100	0/100		12.64%	3[0.12,72.77]
Bracero 1997	2/83	3/87		74.05%	0.7[0.12,4.08]
Koppel 1992	0/59	0/60			Not estimable
Saltzman 1985	1/68	0/61		13.31%	2.7[0.11,64.96]
Subtotal (95% CI)	**310**	**308**		**100%**	**1.26[0.34,4.67]**
Total events: 4 (Cephalosporin), 3 (Penicillin)					
Heterogeneity: Tau^2=0; Chi^2=0.93, df=2(P=0.63); I^2=0%					
Test for overall effect: Z=0.34(P=0.73)					
1.15.3 Cephalosporin drug combination vs single penicillin					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.15.4 Cephalosporin drug combination vs penicillin drug combination					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Test for subgroup differences: Chi²=0.01, df=1 (P=0.93), I²=0%					

Favours cephalosporin 0.01 0.1 1 10 100 Favours penicillin

Analysis 1.21. Comparison 1 Cephalosporins versus penicillins - all women, Outcome 21 Maternal length of hospital stay.

Study or subgroup	Cephalosporin N	Mean(SD)	Penicillin N	Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.21.1 Single cephalosporin vs single penicillin							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.21.2 Single cephalosporin vs penicillin drug combination							
Kamilya 2012	372	6.7 (0.8)	374	6.7 (0.8)		100%	-0.03[-0.14,0.08]
Subtotal ***	**372**		**374**			**100%**	**-0.03[-0.14,0.08]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%							
Test for overall effect: Z=0.52(P=0.6)							
1.21.3 Cephalosporin drug combination vs single penicillin							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
1.21.4 Cephalosporin drug combination vs penicillin drug combination							
Subtotal ***	**0**		**0**				**Not estimable**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							

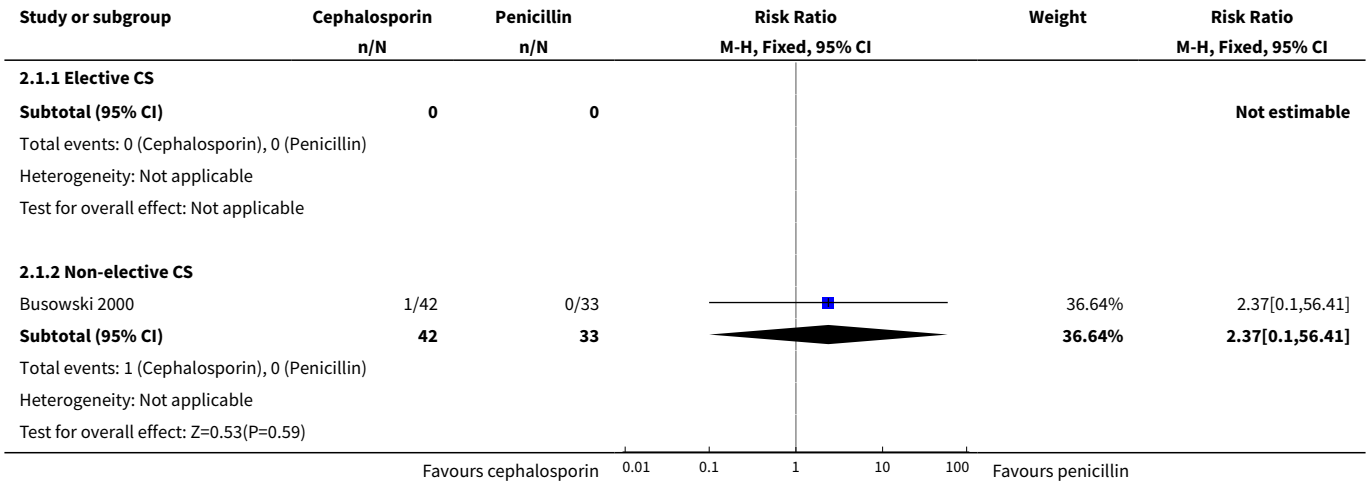
Favours cephalosporin -100 -50 0 50 100 Favours penicillin

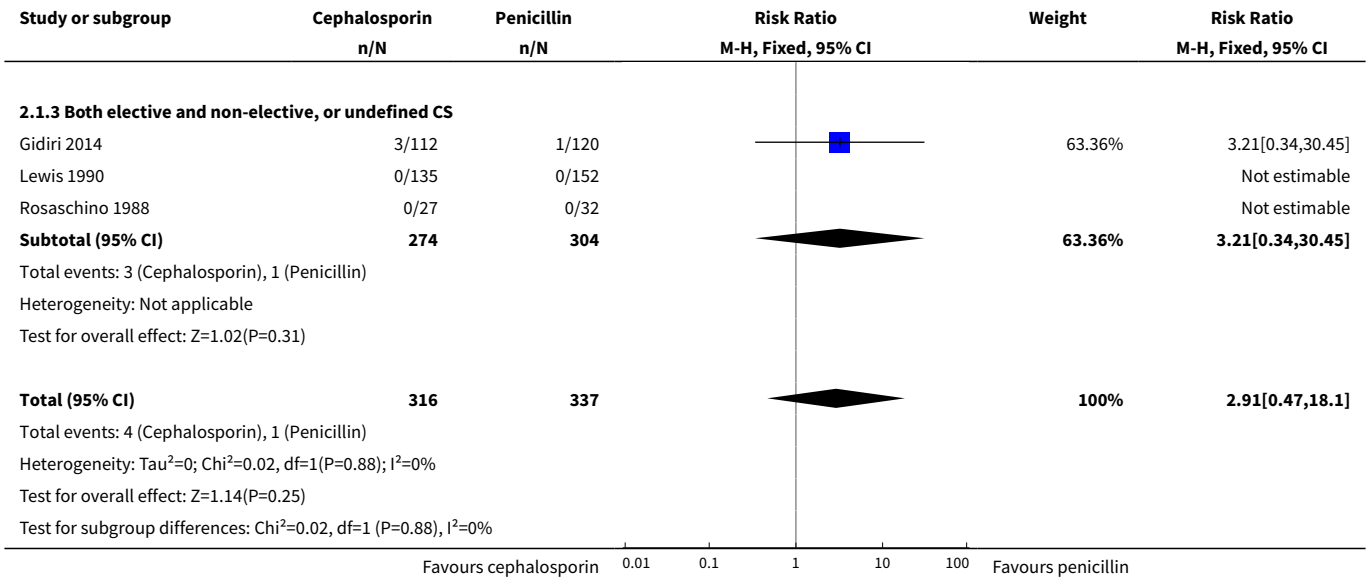
Comparison 2. Cephalosporins versus penicillins - by type of caesarean

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maternal sepsis	4	653	Risk Ratio (M-H, Fixed, 95% CI)	2.91 [0.47, 18.10]
1.1 Elective CS	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Non-elective CS	1	75	Risk Ratio (M-H, Fixed, 95% CI)	2.37 [0.10, 56.41]

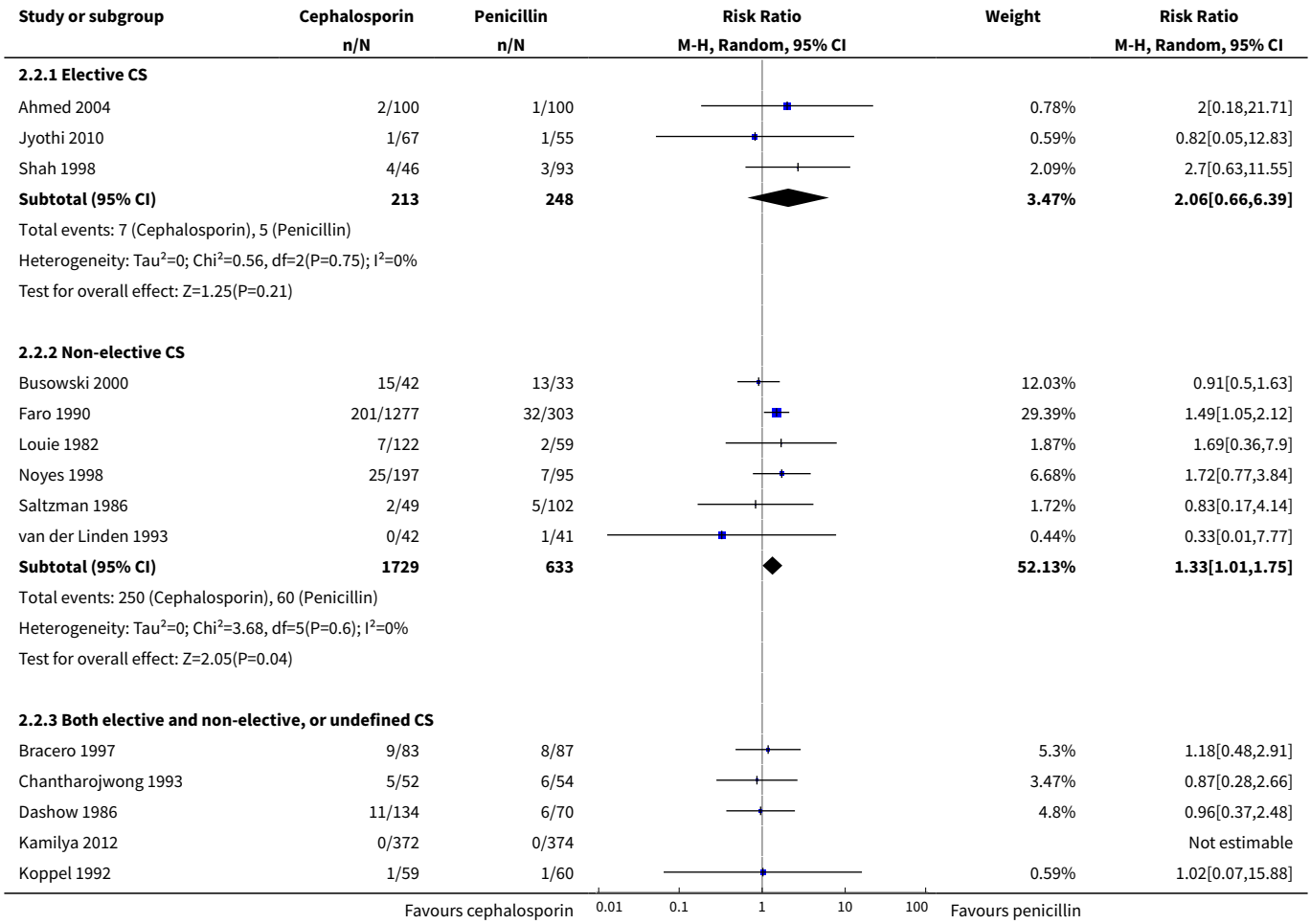
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1.3 Both elective and non-elective, or un-defined CS	3	578	Risk Ratio (M-H, Fixed, 95% CI)	3.21 [0.34, 30.45]
2 Maternal endometritis	20	5390	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.90, 1.37]
2.1 Elective CS	3	461	Risk Ratio (M-H, Random, 95% CI)	2.06 [0.66, 6.39]
2.2 Non-elective CS	6	2362	Risk Ratio (M-H, Random, 95% CI)	1.33 [1.01, 1.75]
2.3 Both elective and non-elective, or un-defined CS	11	2567	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.60, 1.19]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.1 Elective CS	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Non-elective CS	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Both elective and non-elective, or un-defined CS	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.1 Elective CS	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Non-elective CS	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Both elective and non-elective, or un-defined CS	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

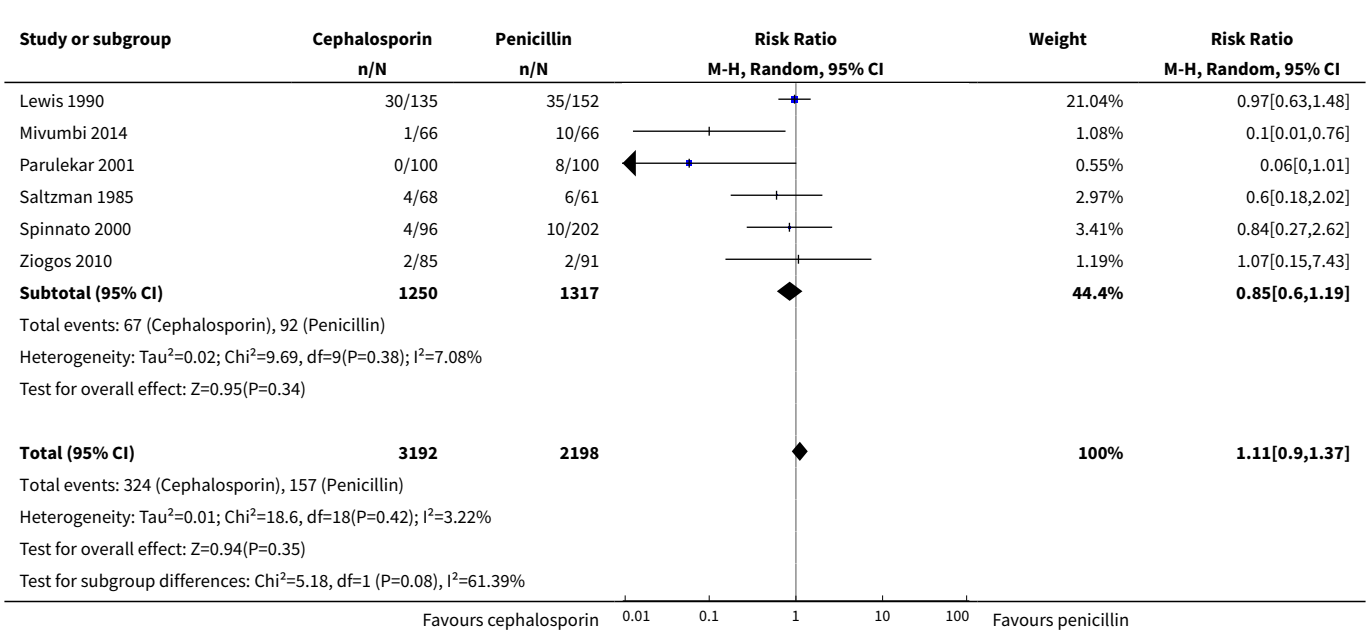
Analysis 2.1. Comparison 2 Cephalosporins versus penicillins - by type of caesarean, Outcome 1 Maternal sepsis.





Analysis 2.2. Comparison 2 Cephalosporins versus penicillins - by type of caesarean, Outcome 2 Maternal endometritis.





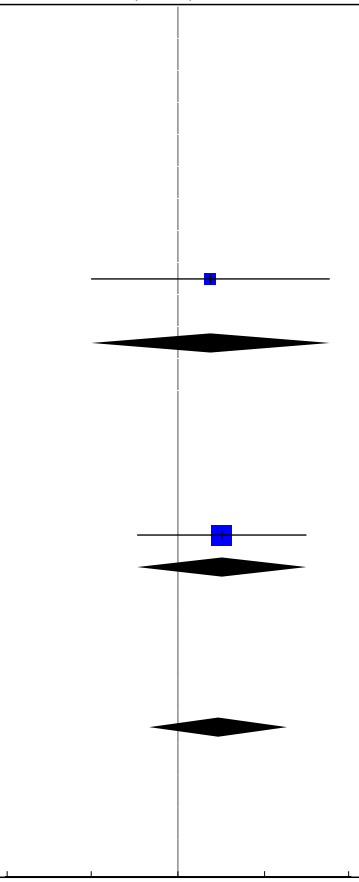
Comparison 3. Cephalosporins versus penicillins - by timing of administration

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Maternal sepsis	4	653	Risk Ratio (M-H, Fixed, 95% CI)	2.91 [0.47, 18.10]
1.1 Before cord clamping	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 After cord clamping	2	362	Risk Ratio (M-H, Fixed, 95% CI)	2.37 [0.10, 56.41]
1.3 Timing of administration not reported or both used	1	232	Risk Ratio (M-H, Fixed, 95% CI)	3.21 [0.34, 30.45]
2 Maternal endometritis	20	5390	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.90, 1.37]
2.1 Before cord clamping	2	332	Risk Ratio (M-H, Random, 95% CI)	0.42 [0.02, 8.20]
2.2 After cord clamping	17	4854	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.94, 1.42]
2.3 Timing of administration nor reported	1	204	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.37, 2.48]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.1 Before cord clamping	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 After cord clamping	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Timing of administration nor reported	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.1 Before cord clamping	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 After cord clamping	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Timing of administration nor reported	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

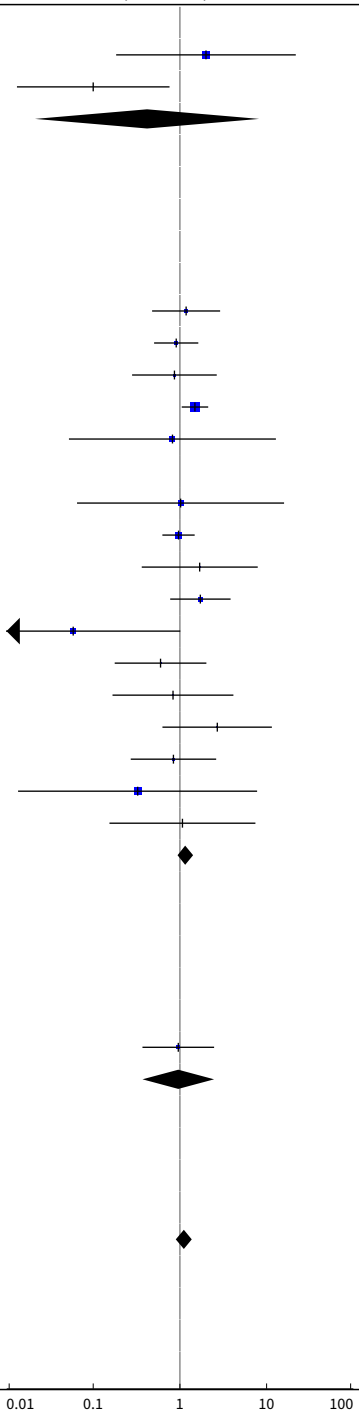
Analysis 3.1. Comparison 3 Cephalosporins versus penicillins - by timing of administration, Outcome 1 Maternal sepsis.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.1.1 Before cord clamping					
Rosaschino 1988	0/27	0/32			Not estimable
Subtotal (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.1.2 After cord clamping					
Busowski 2000	1/42	0/33		36.64%	2.37[0.1,56.41]
Lewis 1990	0/135	0/152			Not estimable
Subtotal (95% CI)	**177**	**185**		**36.64%**	**2.37[0.1,56.41]**
Total events: 1 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.53(P=0.59)					
3.1.3 Timing of administration not reported or both used					
Gidiri 2014	3/112	1/120		63.36%	3.21[0.34,30.45]
Subtotal (95% CI)	**112**	**120**		**63.36%**	**3.21[0.34,30.45]**
Total events: 3 (Cephalosporin), 1 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.02(P=0.31)					
Total (95% CI)	**316**	**337**		**100%**	**2.91[0.47,18.1]**
Total events: 4 (Cephalosporin), 1 (Penicillin)					
Heterogeneity: Tau²=0; Chi²=0.02, df=1(P=0.88); I²=0%					
Test for overall effect: Z=1.14(P=0.25)					
Test for subgroup differences: Chi²=0.02, df=1 (P=0.88), I²=0%					



Analysis 3.2. Comparison 3 Cephalosporins versus penicillins - by timing of administration, Outcome 2 Maternal endometritis.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
3.2.1 Before cord clamping					
Ahmed 2004	2/100	1/100		0.78%	2[0.18,21.71]
Mivumbi 2014	1/66	10/66		1.08%	0.1[0.01,0.76]
Subtotal (95% CI)	**166**	**166**		**1.87%**	**0.42[0.02,8.2]**
Total events: 3 (Cephalosporin), 11 (Penicillin)					
Heterogeneity: Tau^2=3.34; Chi^2=3.62, df=1(P=0.06); I^2=72.4%					
Test for overall effect: Z=0.57(P=0.57)					
3.2.2 After cord clamping					
Bracero 1997	9/83	8/87		5.3%	1.18[0.48,2.91]
Busowski 2000	15/42	13/33		12.03%	0.91[0.5,1.63]
Chantharojwong 1993	5/52	6/54		3.47%	0.87[0.28,2.66]
Faro 1990	201/1277	32/303		29.39%	1.49[1.05,2.12]
Jyothi 2010	1/67	1/55		0.59%	0.82[0.05,12.83]
Kamilya 2012	0/372	0/374			Not estimable
Koppel 1992	1/59	1/60		0.59%	1.02[0.07,15.88]
Lewis 1990	30/135	35/152		21.04%	0.97[0.63,1.48]
Louie 1982	7/122	2/59		1.87%	1.69[0.36,7.9]
Noyes 1998	25/197	7/95		6.68%	1.72[0.77,3.84]
Parulekar 2001	0/100	8/100		0.55%	0.06[0,1.01]
Saltzman 1985	4/68	6/61		2.97%	0.6[0.18,2.02]
Saltzman 1986	2/49	5/102		1.72%	0.83[0.17,4.14]
Shah 1998	4/46	3/93		2.09%	2.7[0.63,11.55]
Spinnato 2000	4/96	10/202		3.41%	0.84[0.27,2.62]
van der Linden 1993	0/42	1/41		0.44%	0.33[0.01,7.77]
Ziogos 2010	2/85	2/91		1.19%	1.07[0.15,7.43]
Subtotal (95% CI)	**2892**	**1962**		**93.33%**	**1.15[0.94,1.42]**
Total events: 310 (Cephalosporin), 140 (Penicillin)					
Heterogeneity: Tau^2=0; Chi^2=12.6, df=15(P=0.63); I^2=0%					
Test for overall effect: Z=1.36(P=0.17)					
3.2.3 Timing of administration nor reported					
Dashow 1986	11/134	6/70		4.8%	0.96[0.37,2.48]
Subtotal (95% CI)	**134**	**70**		**4.8%**	**0.96[0.37,2.48]**
Total events: 11 (Cephalosporin), 6 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.09(P=0.93)					
Total (95% CI)	**3192**	**2198**		**100%**	**1.11[0.9,1.37]**
Total events: 324 (Cephalosporin), 157 (Penicillin)					
Heterogeneity: Tau^2=0.01; Chi^2=18.6, df=18(P=0.42); I^2=3.22%					
Test for overall effect: Z=0.94(P=0.35)					
Test for subgroup differences: Chi^2=0.58, df=1 (P=0.75), I^2=0%					

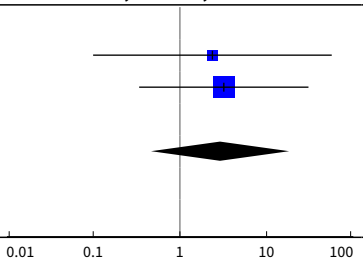


Comparison 4. Cephalosporins versus penicillins - by route of administration

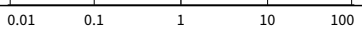
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Maternal sepsis	4	653	Risk Ratio (M-H, Random, 95% CI)	2.90 [0.46, 18.17]
1.1 Intravenous administration	3	366	Risk Ratio (M-H, Random, 95% CI)	2.90 [0.46, 18.17]
1.2 Lavage/infiltration	1	287	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Route of administration not specified	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2 Maternal endometritis	20	5390	Risk Ratio (IV, Fixed, 95% CI)	1.12 [0.92, 1.37]
2.1 Intravenous administration	18	4899	Risk Ratio (IV, Fixed, 95% CI)	1.18 [0.94, 1.49]
2.2 Lavage/infiltration	2	491	Risk Ratio (IV, Fixed, 95% CI)	0.96 [0.65, 1.43]
2.3 Route of administration not specified	0	0	Risk Ratio (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.1 Intravenous administration	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Lavage/infiltration	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Route of administration not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.1 Intravenous administration	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Lavage/infiltration	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 Route of administration not specified	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 4.1. Comparison 4 Cephalosporins versus penicillins - by route of administration, Outcome 1 Maternal sepsis.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
4.1.1 Intravenous administration					
Busowski 2000	1/42	0/33		33.49%	2.37[0.1,56.41]
Gidiri 2014	3/112	1/120		66.51%	3.21[0.34,30.45]
Rosaschino 1988	0/27	0/32			Not estimable
Subtotal (95% CI)	**181**	**185**		**100%**	**2.9[0.46,18.17]**
Total events: 4 (Cephalosporin), 1 (Penicillin)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.88); I^2=0%					

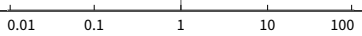


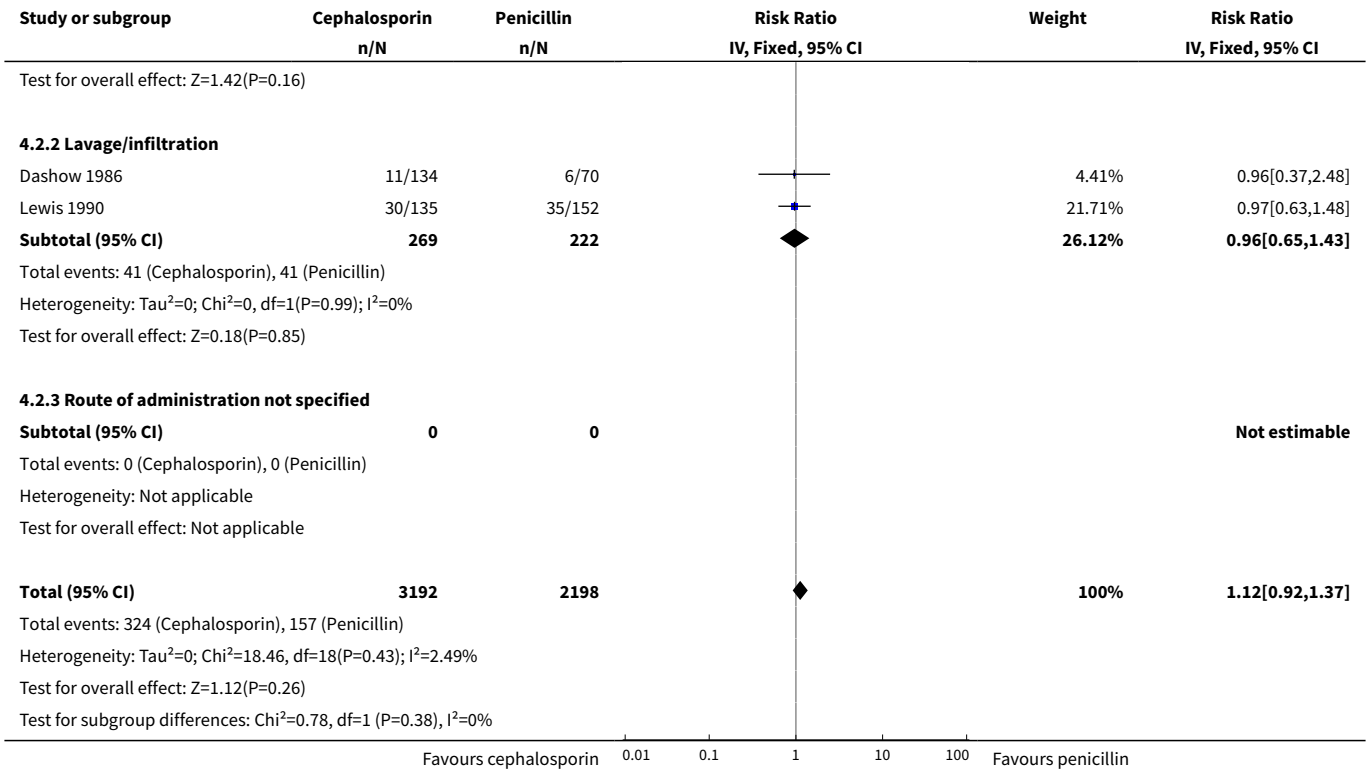
Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Test for overall effect: Z=1.14(P=0.25)					
4.1.2 Lavage/infiltration					
Lewis 1990	0/135	0/152			Not estimable
Subtotal (95% CI)	**135**	**152**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
4.1.3 Route of administration not specified					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Cephalosporin), 0 (Penicillin)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**316**	**337**		**100%**	**2.9[0.46,18.17]**
Total events: 4 (Cephalosporin), 1 (Penicillin)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.88); I^2=0%					
Test for overall effect: Z=1.14(P=0.25)					
Test for subgroup differences: Not applicable					



Analysis 4.2. Comparison 4 Cephalosporins versus penicillins - by route of administration, Outcome 2 Maternal endometritis.

Study or subgroup	Cephalosporin n/N	Penicillin n/N	Risk Ratio IV, Fixed, 95% CI	Weight	Risk Ratio IV, Fixed, 95% CI
4.2.1 Intravenous administration					
Ahmed 2004	2/100	1/100		0.7%	2[0.18,21.71]
Bracero 1997	9/83	8/87		4.89%	1.18[0.48,2.91]
Busowski 2000	15/42	13/33		11.62%	0.91[0.5,1.63]
Chantharojwong 1993	5/52	6/54		3.16%	0.87[0.28,2.66]
Faro 1990	201/1277	32/303		32.36%	1.49[1.05,2.12]
Jyothi 2010	1/67	1/55		0.53%	0.82[0.05,12.83]
Kamilya 2012	0/372	0/374			Not estimable
Koppel 1992	1/59	1/60		0.53%	1.02[0.07,15.88]
Louie 1982	7/122	2/59		1.68%	1.69[0.36,7.9]
Mivumbi 2014	1/66	10/66		0.97%	0.1[0.01,0.76]
Noyes 1998	25/197	7/95		6.22%	1.72[0.77,3.84]
Parulekar 2001	0/100	8/100		0.5%	0.06[0,1.01]
Saltzman 1985	4/68	6/61		2.7%	0.6[0.18,2.02]
Saltzman 1986	2/49	5/102		1.55%	0.83[0.17,4.14]
Shah 1998	4/46	3/93		1.89%	2.7[0.63,11.55]
Spinnato 2000	4/96	10/202		3.11%	0.84[0.27,2.62]
van der Linden 1993	0/42	1/41		0.4%	0.33[0.01,7.77]
Ziogos 2010	2/85	2/91		1.06%	1.07[0.15,7.43]
Subtotal (95% CI)	**2923**	**1976**		**73.88%**	**1.18[0.94,1.49]**
Total events: 283 (Cephalosporin), 116 (Penicillin)					
Heterogeneity: Tau^2=0; Chi^2=17.68, df=16(P=0.34); I^2=9.5%					





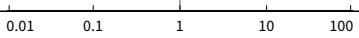
Comparison 5. Cephalosporin (1st generation B1) versus penicillins (extended spectrum A3)

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Maternal sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Maternal endometritis	2	814	Risk Ratio (M-H, Fixed, 95% CI)	2.18 [1.30, 3.66]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	1	139	Risk Ratio (M-H, Fixed, 95% CI)	2.36 [0.84, 6.62]
6 Maternal wound infection	1	139	Risk Ratio (M-H, Fixed, 95% CI)	2.02 [0.42, 9.63]
7 Maternal urinary tract infection	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Maternal thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Maternal composite serious infectious complication	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	1	675	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Maternal allergic reactions	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
12 Maternal nausea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Immediate infant adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Infant unsettled	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Infant length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Infant general health	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

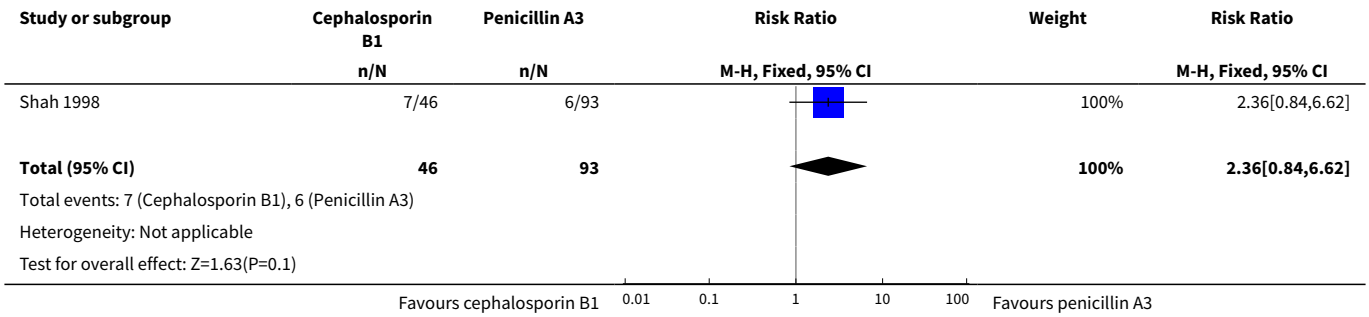
Analysis 5.2. Comparison 5 Cephalosporin (1st generation B1) versus penicillins (extended spectrum A3), Outcome 2 Maternal endometritis.

Study or subgroup	Cephalosporin B1 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Faro 1990	93/520	13/155		90.98%	2.13[1.23,3.7]
Shah 1998	4/46	3/93		9.02%	2.7[0.63,11.55]
Total (95% CI)	**566**	**248**		**100%**	**2.18[1.3,3.66]**
Total events: 97 (Cephalosporin B1), 16 (Penicillin A3)					
Heterogeneity: Tau^2=0; Chi^2=0.09, df=1(P=0.77); I^2=0%					
Test for overall effect: Z=2.96(P=0)					

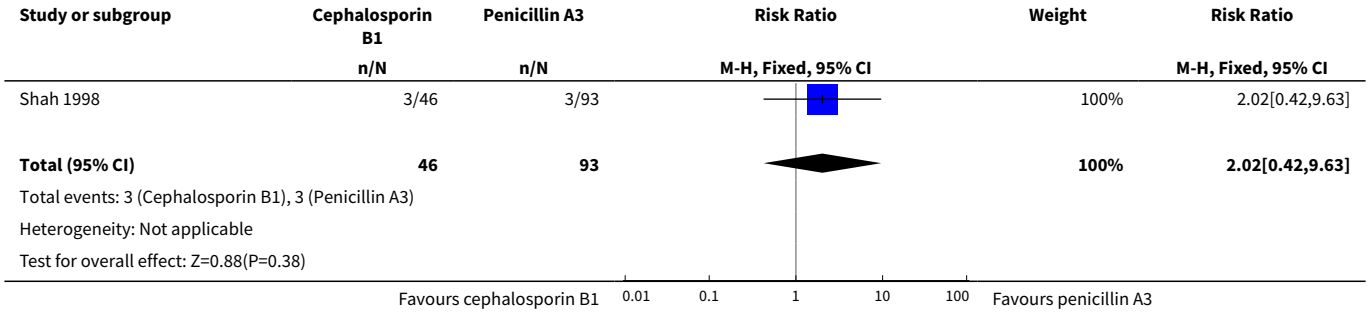


Favours cephalosporin B1 — Favours penicillin A3

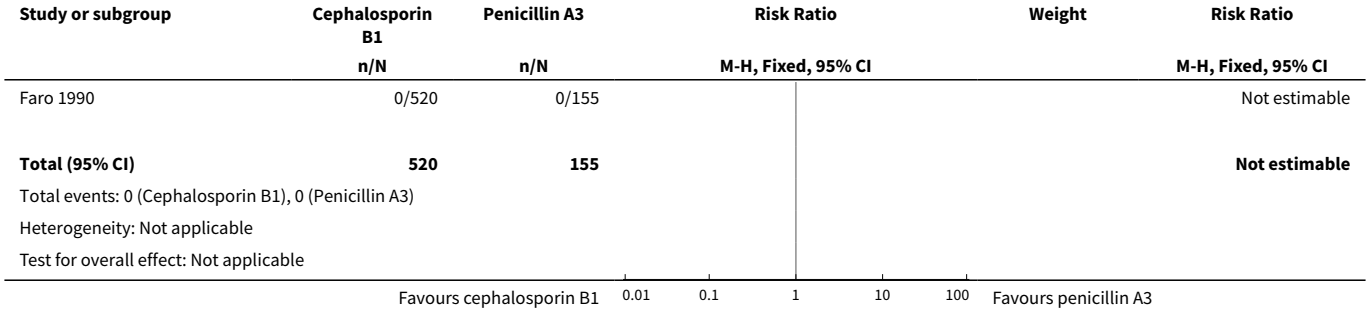
Analysis 5.5. Comparison 5 Cephalosporin (1st generation B1) versus penicillins (extended spectrum A3), Outcome 5 Maternal fever (febrile morbidity).



Analysis 5.6. Comparison 5 Cephalosporin (1st generation B1) versus penicillins (extended spectrum A3), Outcome 6 Maternal wound infection.



Analysis 5.10. Comparison 5 Cephalosporin (1st generation B1) versus penicillins (extended spectrum A3), Outcome 10 Maternal composite adverse effects.



Comparison 6. Cephalosporin (1st generation B1) versus penicillins (ampicillin A4)

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Maternal sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Maternal endometritis	7	1487	Risk Ratio (M-H, Random, 95% CI)	1.09 [0.69, 1.71]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	5	883	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.40, 1.51]
6 Maternal wound infection	5	626	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.36, 2.01]
7 Maternal urinary tract infection	5	626	Risk Ratio (M-H, Random, 95% CI)	1.41 [0.54, 3.70]
8 Maternal thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Maternal composite serious infectious complication	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	2	861	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.01, 7.84]
11 Maternal allergic reactions	1	132	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Maternal nausea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	1	193	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Immediate infant adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Infant unsettled	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	1	132	Mean Difference (IV, Fixed, 95% CI)	-1.50 [-2.46, -0.54]
22 Infant length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
24 Infant general health	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

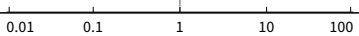
Analysis 6.2. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 2 Maternal endometritis.

Study or subgroup	Cephalosporin B1 n/N	Penicillin A4 n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Chantharojwong 1993	5/52	6/54		13.02%	0.87[0.28,2.66]
Dashow 1986	8/70	6/70		15.53%	1.33[0.49,3.64]
Faro 1990	71/520	19/148		38.7%	1.06[0.66,1.71]
Jyothi 2010	1/67	1/55		2.6%	0.82[0.05,12.83]
Louie 1982	3/67	2/59		6.04%	1.32[0.23,7.64]
Mivumbi 2014	1/66	10/66		4.63%	0.1[0.01,0.76]
Noyes 1998	14/98	7/95		19.48%	1.94[0.82,4.59]
Total (95% CI)	**940**	**547**		**100%**	**1.09[0.69,1.71]**
Total events: 103 (Cephalosporin B1), 51 (Penicillin A4)					
Heterogeneity: Tau^2=0.08; Chi^2=7.66, df=6(P=0.26); I^2=21.72%					
Test for overall effect: Z=0.36(P=0.72)					

Favours cephalosporin B1 — Favours penicillin A4

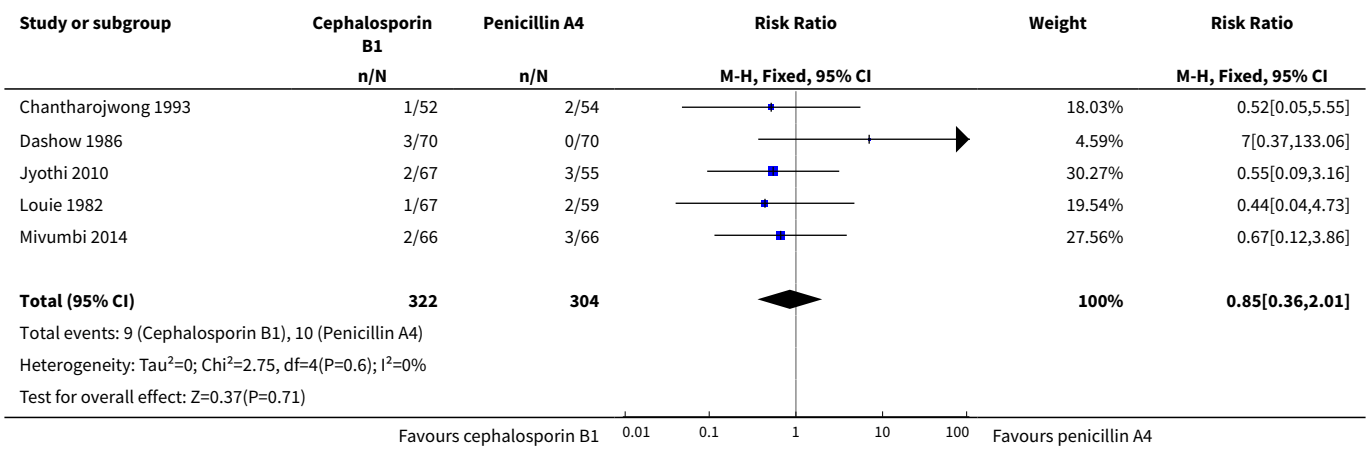
Analysis 6.5. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 5 Maternal fever (febrile morbidity).

Study or subgroup	Cephalosporin B1 n/N	Penicillin A4 n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Chantharojwong 1993	5/52	8/54		18.13%	0.65[0.23,1.86]
Dashow 1986	17/70	10/70		24.1%	1.7[0.84,3.45]
Louie 1982	5/67	6/59		16.86%	0.73[0.24,2.28]
Lumbiganon 1994	12/191	11/188		22.52%	1.07[0.49,2.37]
Mivumbi 2014	4/66	17/66		18.38%	0.24[0.08,0.66]
Total (95% CI)	**446**	**437**		**100%**	**0.78[0.4,1.51]**
Total events: 43 (Cephalosporin B1), 52 (Penicillin A4)					
Heterogeneity: Tau^2=0.35; Chi^2=10.37, df=4(P=0.03); I^2=61.41%					
Test for overall effect: Z=0.75(P=0.46)					

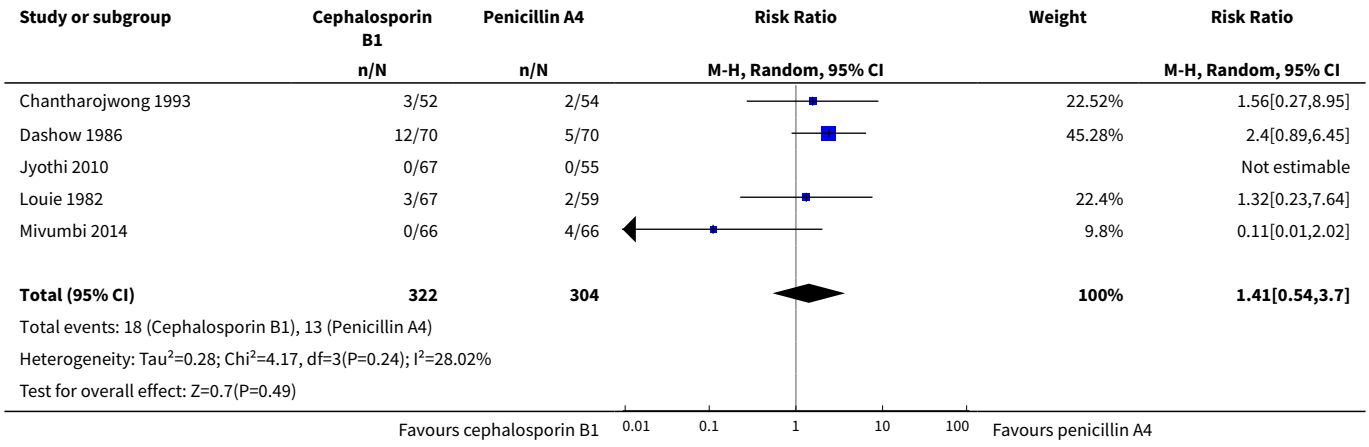


Favours cephalosporin B1 — Favours penicillin A4

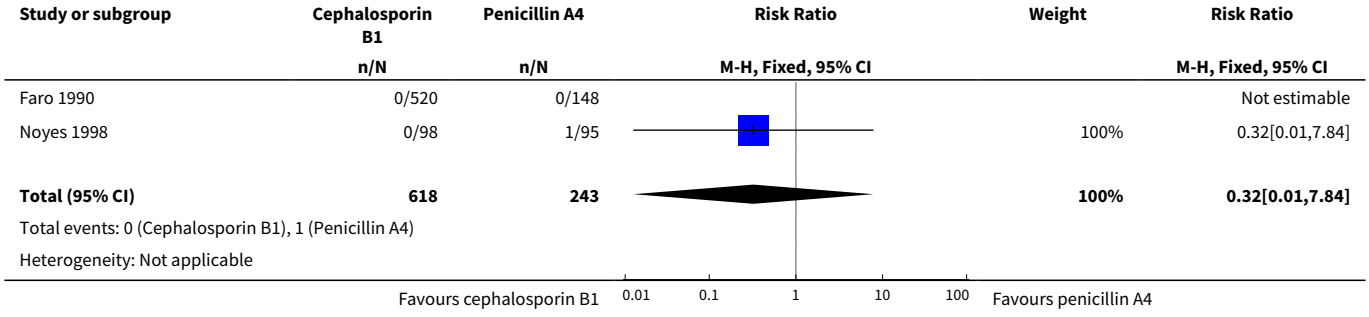
Analysis 6.6. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 6 Maternal wound infection.

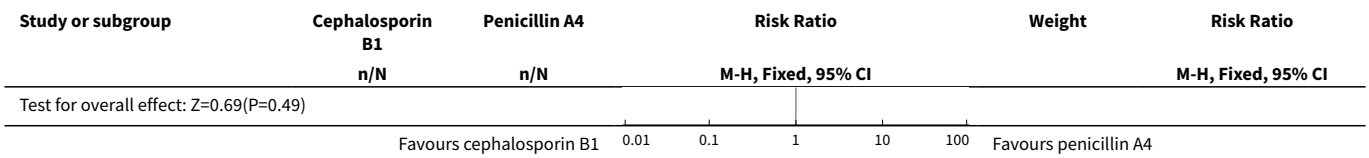


Analysis 6.7. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 7 Maternal urinary tract infection.

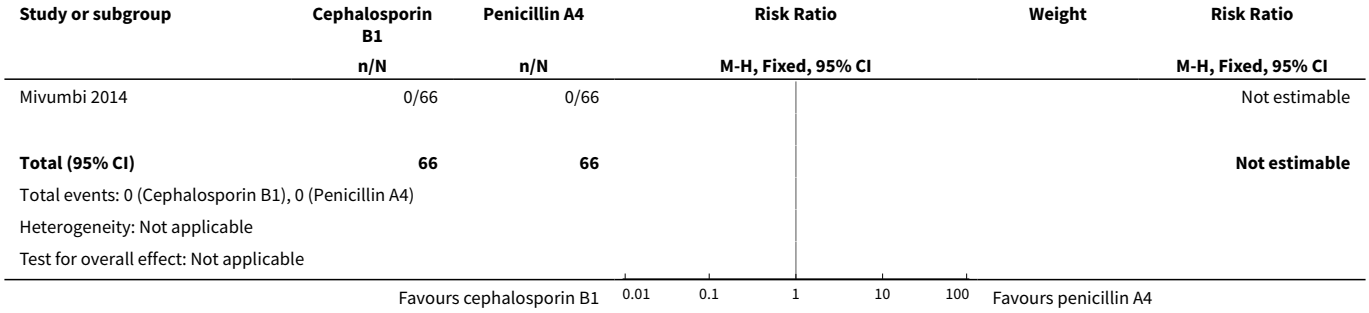


Analysis 6.10. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 10 Maternal composite adverse effects.

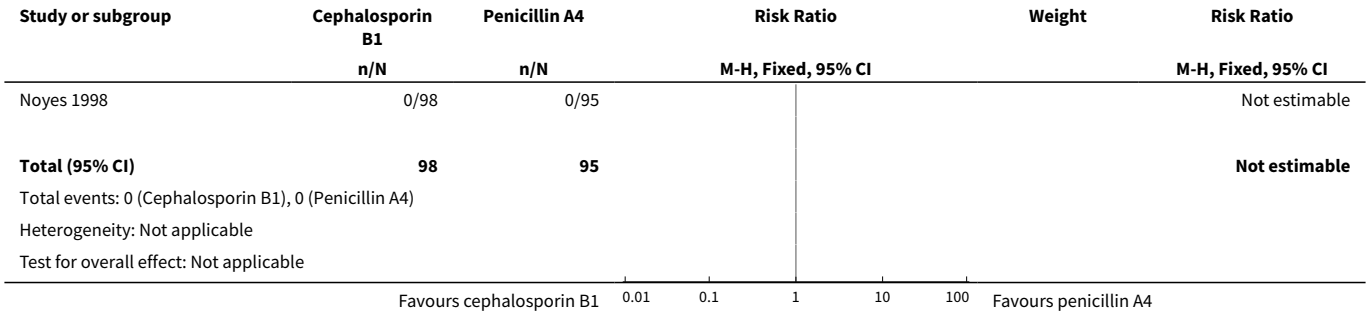




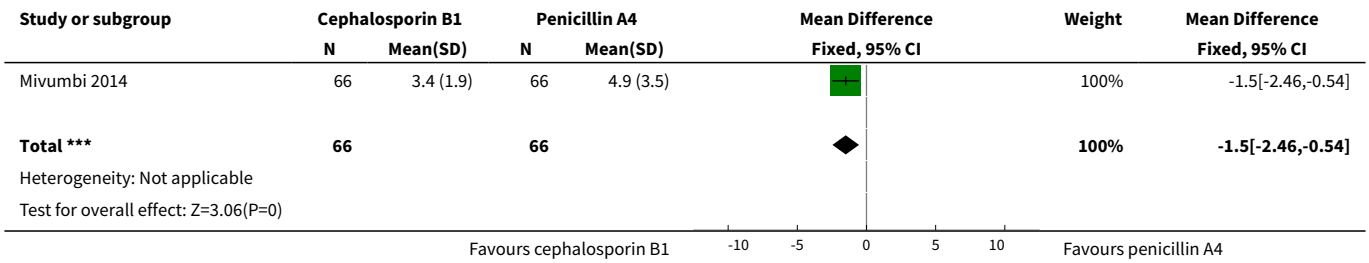
Analysis 6.11. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 11 Maternal allergic reactions.



Analysis 6.15. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 15 Maternal skin rash.



Analysis 6.21. Comparison 6 Cephalosporin (1st generation B1) versus penicillins (ampicillin A4), Outcome 21 Maternal length of hospital stay.



Comparison 7. Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3)

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Maternal sepsis	1	287	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Maternal endometritis	4	1334	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.78, 1.54]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	4	850	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.79, 1.47]
6 Maternal wound infection	2	438	Risk Ratio (M-H, Random, 95% CI)	2.37 [0.64, 8.73]
7 Maternal urinary tract infection	3	567	Risk Ratio (M-H, Random, 95% CI)	1.43 [0.67, 3.07]
8 Maternal thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Maternal composite serious infectious complication	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	2	1030	Risk Ratio (M-H, Fixed, 95% CI)	2.02 [0.18, 21.96]
11 Maternal allergic reactions	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Maternal nausea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	1	129	Risk Ratio (M-H, Fixed, 95% CI)	2.70 [0.11, 64.96]
16 Immediate infant adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Infant unsettled	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Infant length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
24 Infant general health	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 7.1. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 1 Maternal sepsis.

Study or subgroup	Cephalosporin B2 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Lewis 1990	0/135	0/152			Not estimable
Total (95% CI)	**135**	**152**			**Not estimable**
Total events: 0 (Cephalosporin B2), 0 (Penicillin A3)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours cephalosporin B2 — Favours penicillin A3

Analysis 7.2. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 2 Maternal endometritis.

Study or subgroup	Cephalosporin B2 n/N	Penicillin A3 n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Faro 1990	82/612	13/155		33.96%	1.6[0.91,2.79]
Lewis 1990	30/135	35/152		53.81%	0.97[0.63,1.48]
Saltzman 1985	4/68	6/61		7.73%	0.6[0.18,2.02]
Saltzman 1986	2/49	5/102		4.49%	0.83[0.17,4.14]
Total (95% CI)	**864**	**470**		**100%**	**1.1[0.78,1.54]**
Total events: 118 (Cephalosporin B2), 59 (Penicillin A3)					
Heterogeneity: Tau^2=0.01; Chi^2=3.19, df=3(P=0.36); I^2=5.85%					
Test for overall effect: Z=0.53(P=0.6)					

Favours cephalosporin B2 — Favours penicillin A3

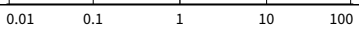
Analysis 7.5. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 5 Maternal fever (febrile morbidity).

Study or subgroup	Cephalosporin B2 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Beningo 1986	26/147	20/136		33.44%	1.2[0.7,2.05]
Lewis 1990	25/135	30/152		45.42%	0.94[0.58,1.51]
Saltzman 1985	12/68	10/61		16.97%	1.08[0.5,2.31]
Saltzman 1986	3/49	4/102		4.18%	1.56[0.36,6.71]
Total (95% CI)	**399**	**451**		**100%**	**1.08[0.79,1.47]**
Total events: 66 (Cephalosporin B2), 64 (Penicillin A3)					
Heterogeneity: Tau^2=0; Chi^2=0.73, df=3(P=0.87); I^2=0%					
Test for overall effect: Z=0.46(P=0.65)					

Favours cephalosporin B2 — Favours penicillin A3

Analysis 7.6. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 6 Maternal wound infection.

Study or subgroup	Cephalosporin B2 n/N	Penicillin A3 n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Lewis 1990	4/135	3/152		68.02%	1.5[0.34,6.59]
Saltzman 1986	3/49	1/102		31.98%	6.24[0.67,58.51]
Total (95% CI)	**184**	**254**		**100%**	**2.37[0.64,8.73]**
Total events: 7 (Cephalosporin B2), 4 (Penicillin A3)					
Heterogeneity: Tau^2=0.08; Chi^2=1.09, df=1(P=0.3); I^2=8.05%					
Test for overall effect: Z=1.3(P=0.2)					



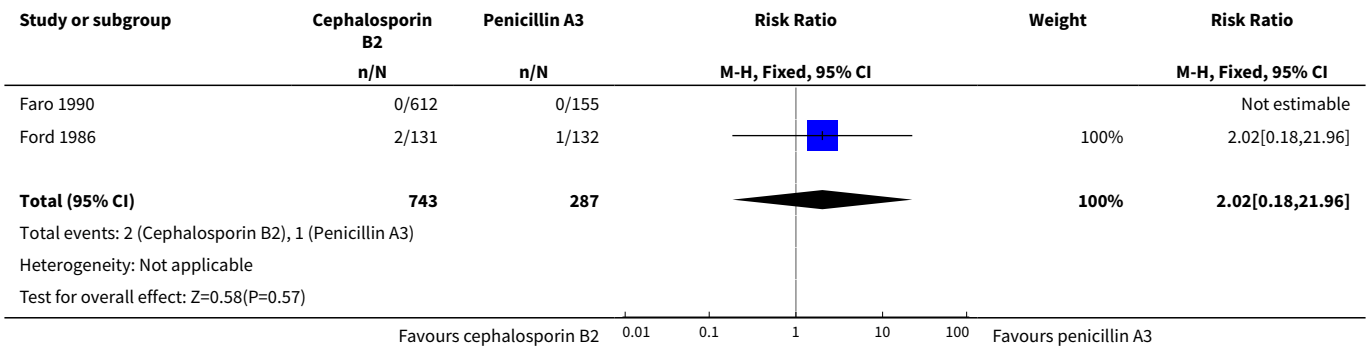
Favours cephalosporin B2 — Favours penicillin A3

Analysis 7.7. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 7 Maternal urinary tract infection.

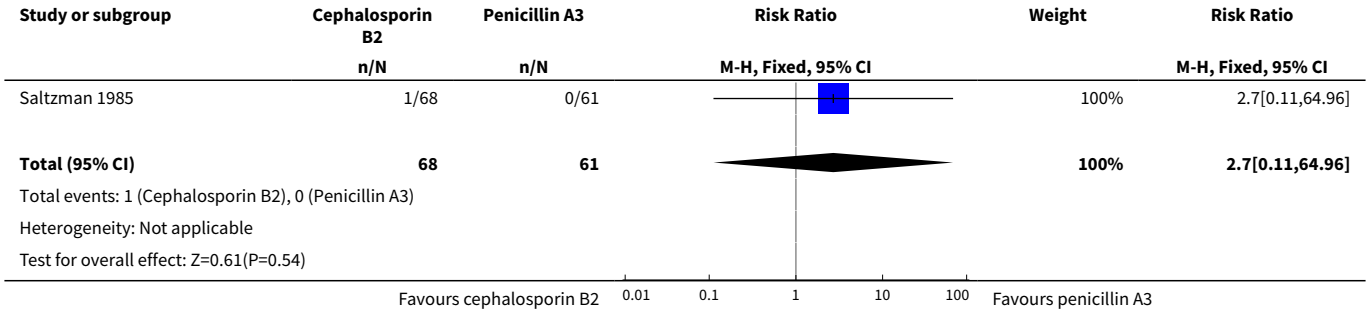
Study or subgroup	Cephalosporin B2 n/N	Penicillin A3 n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Lewis 1990	5/135	3/152		24.91%	1.88[0.46,7.71]
Saltzman 1985	2/68	4/61		18.75%	0.45[0.09,2.36]
Saltzman 1986	9/49	10/102		56.34%	1.87[0.81,4.31]
Total (95% CI)	**252**	**315**		**100%**	**1.43[0.67,3.07]**
Total events: 16 (Cephalosporin B2), 17 (Penicillin A3)					
Heterogeneity: Tau^2=0.09; Chi^2=2.42, df=2(P=0.3); I^2=17.2%					
Test for overall effect: Z=0.93(P=0.35)					

Favours cephalosporin B2 — Favours penicillin A3

Analysis 7.10. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 10 Maternal composite adverse effects.



Analysis 7.15. Comparison 7 Cephalosporin (2nd generation B2) versus penicillins (extended-spectrum A3), Outcome 15 Maternal skin rash.



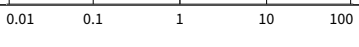
Comparison 8. Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maternal sepsis	1	75	Risk Ratio (M-H, Fixed, 95% CI)	2.37 [0.10, 56.41]
2 Maternal endometritis	8	1890	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.75, 1.35]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	3	387	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.64, 2.15]
6 Maternal wound infection	5	638	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.47, 2.78]
7 Maternal urinary tract infection	4	462	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.11, 3.66]
8 Maternal thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

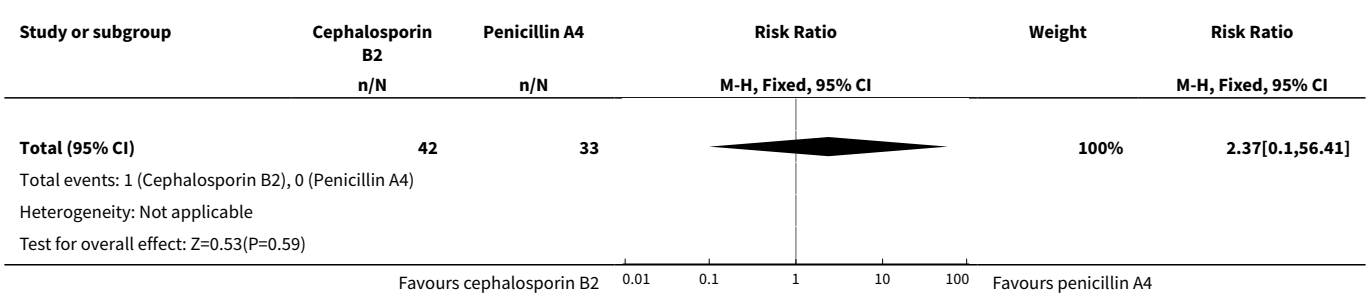
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
9 Maternal composite serious infectious complication	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	3	1130	Risk Ratio (M-H, Fixed, 95% CI)	1.92 [0.18, 20.82]
11 Maternal allergic reactions	1	176	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Maternal nausea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	2	364	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.23, 4.46]
16 Immediate infant adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Infant unsettled	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Infant length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Infant general health	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 8.1. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 1 Maternal sepsis.

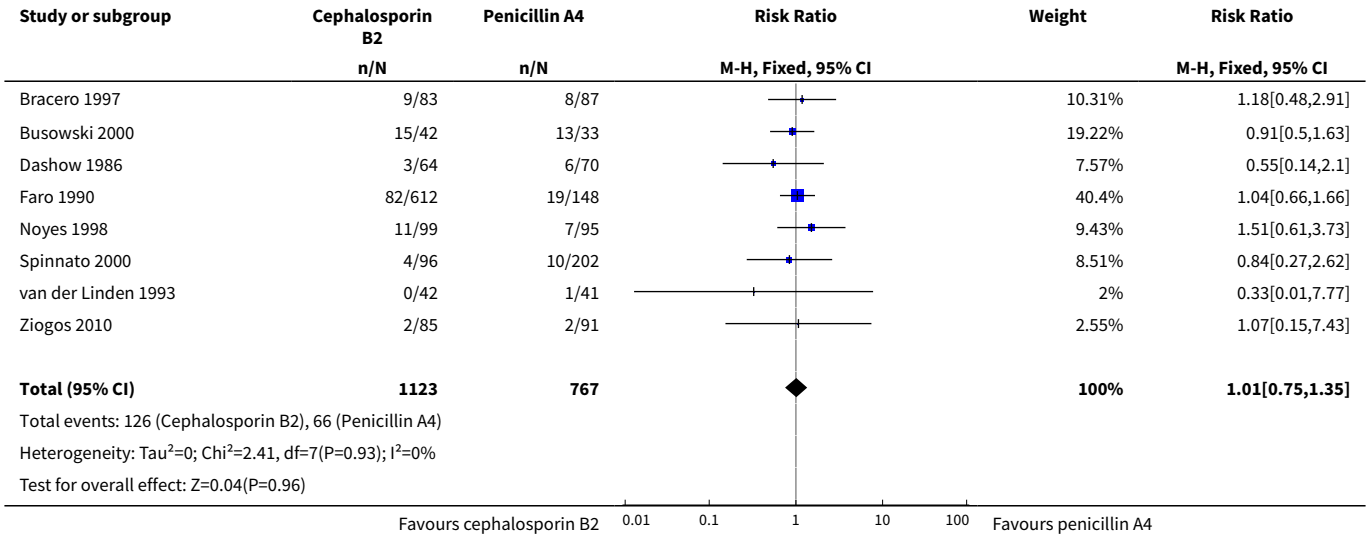
Study or subgroup	Cephalosporin B2 n/N	Penicillin A4 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Busowski 2000	1/42	0/33		100%	2.37[0.1,56.41]



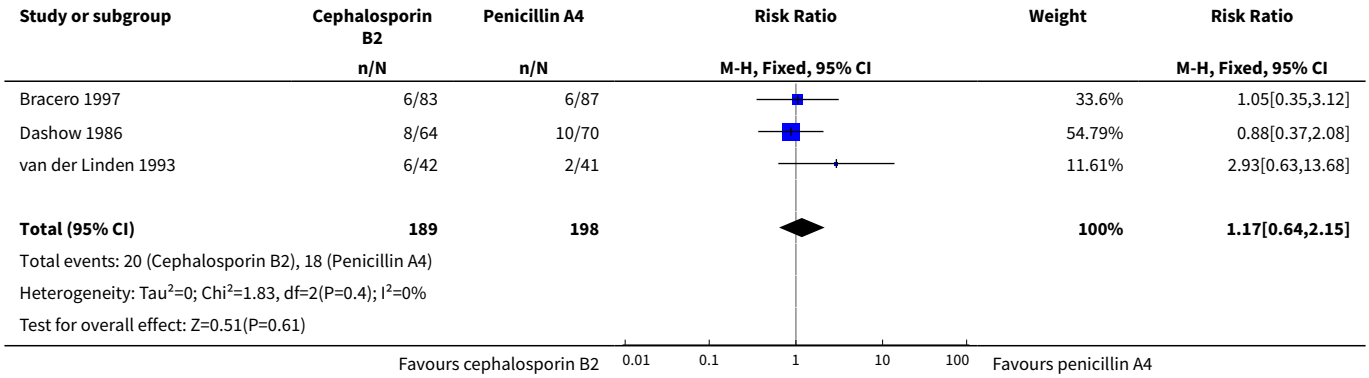
Favours cephalosporin B2 — Favours penicillin A4



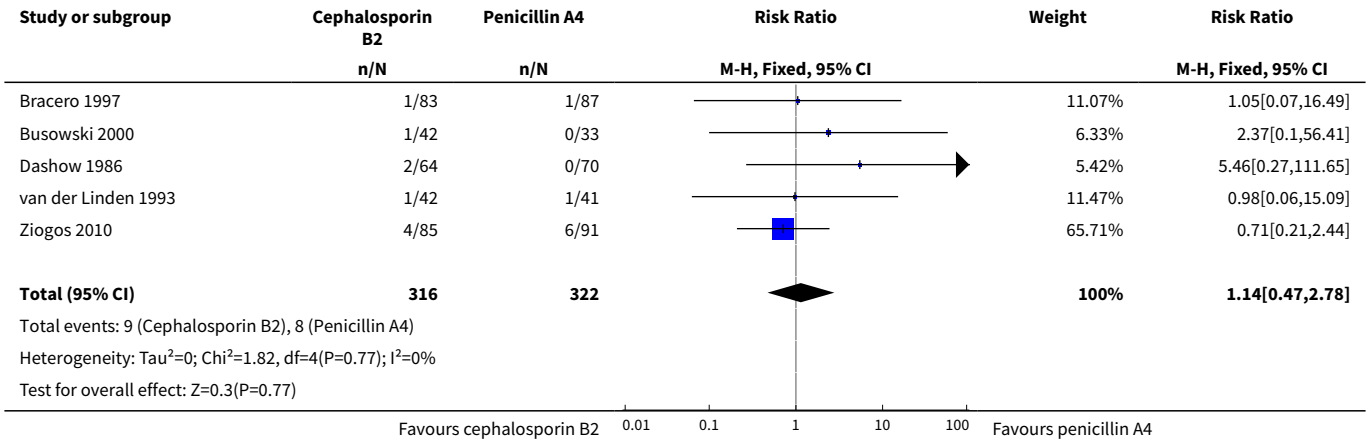
Analysis 8.2. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 2 Maternal endometritis.



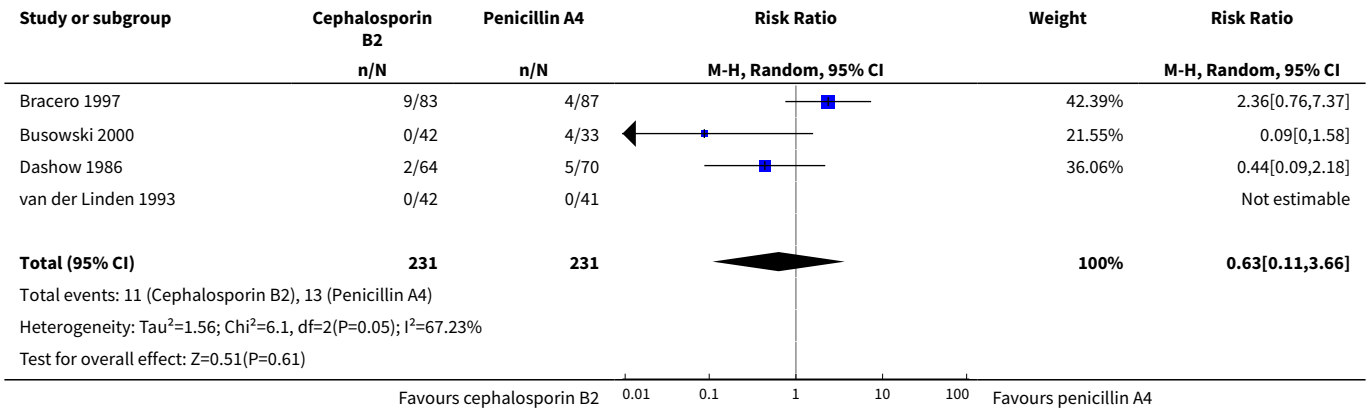
Analysis 8.5. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 5 Maternal fever (febrile morbidity).



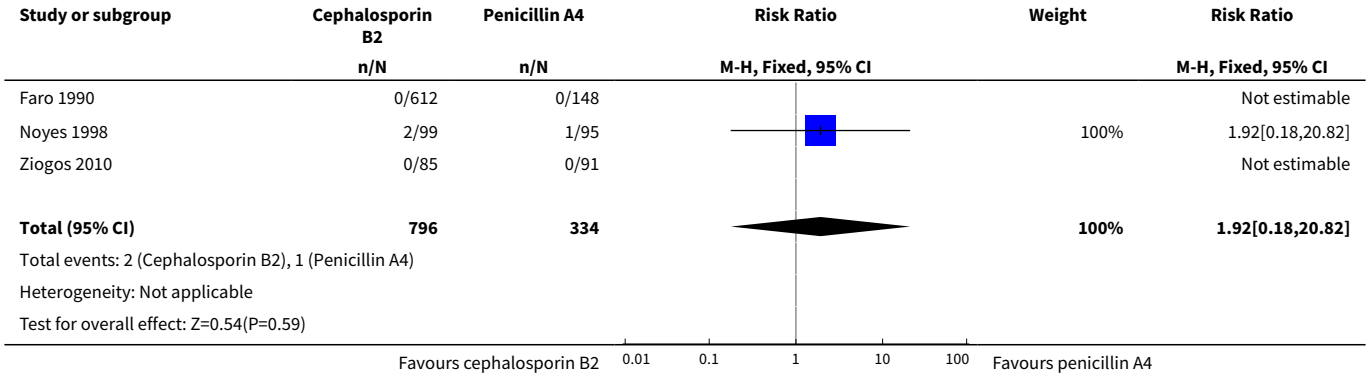
Analysis 8.6. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 6 Maternal wound infection.



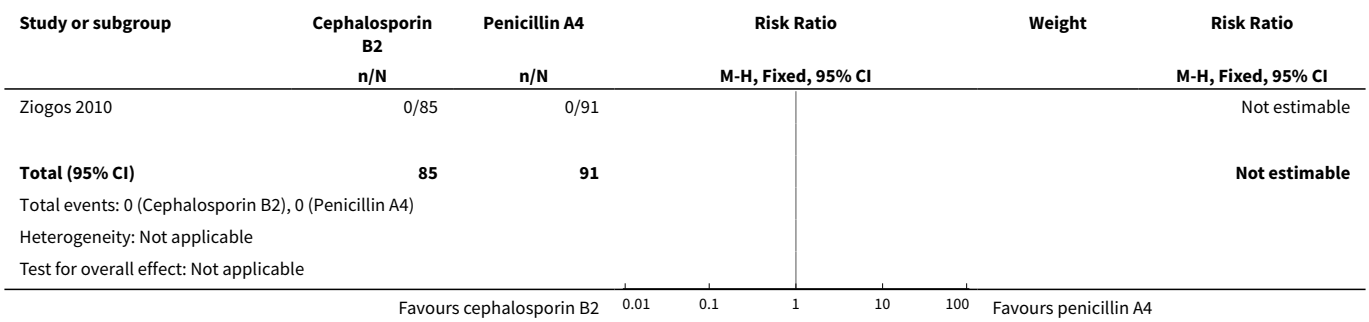
Analysis 8.7. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 7 Maternal urinary tract infection.



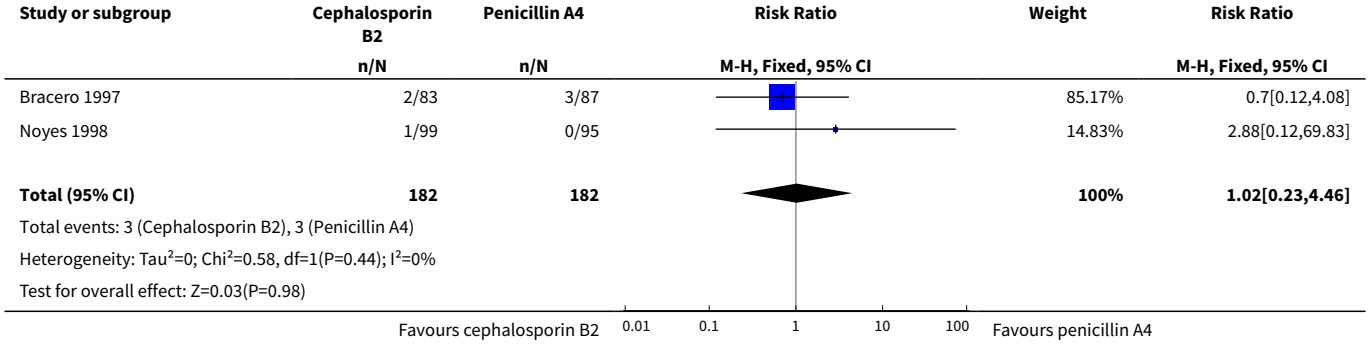
Analysis 8.10. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 10 Maternal composite adverse effects.



Analysis 8.11. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 11 Maternal allergic reactions.



Analysis 8.15. Comparison 8 Cephalosporin (2nd generation B2) versus penicillins (ampicillin A4), Outcome 15 Maternal skin rash.



Comparison 9. Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3)

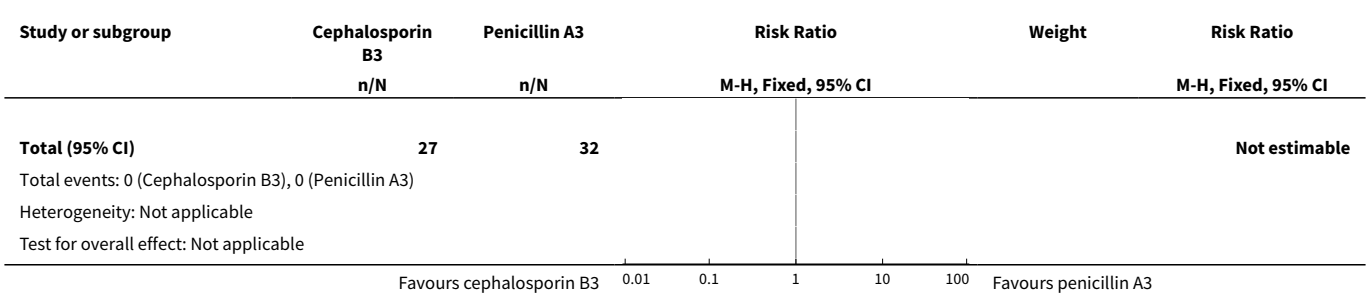
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maternal sepsis	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Maternal endometritis	1	300	Risk Ratio (M-H, Fixed, 95% CI)	2.14 [1.14, 4.00]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Maternal wound infection	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Maternal urinary tract infection	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Maternal thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
9 Maternal composite serious infectious complication	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	2	359	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Maternal allergic reactions	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Maternal nausea	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	1	59	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Immediate infant adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Infant unsettled	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Infant length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Infant general health	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

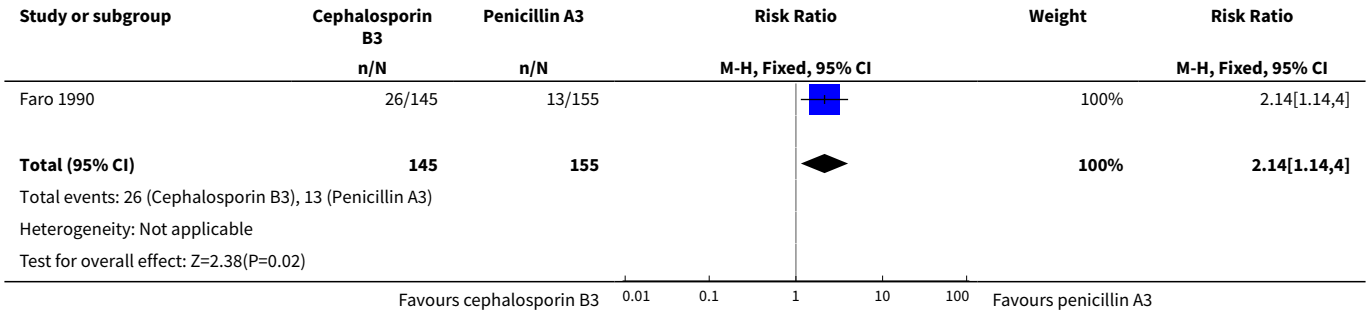
Analysis 9.1. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 1 Maternal sepsis.

Study or subgroup	Cephalosporin B3	Penicillin A3	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
Rosaschino 1988	0/27	0/32			Not estimable

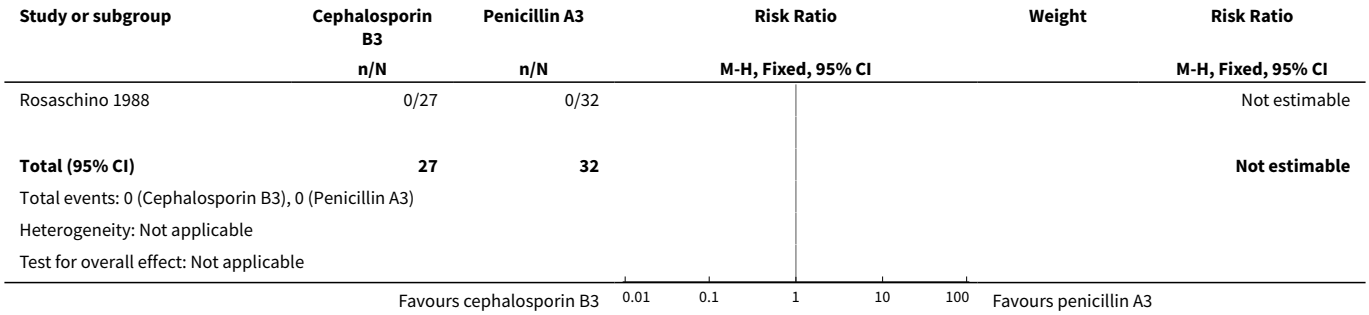
Favours cephalosporin B3 — 0.01 — 0.1 — 1 — 10 — 100 — Favours penicillin A3



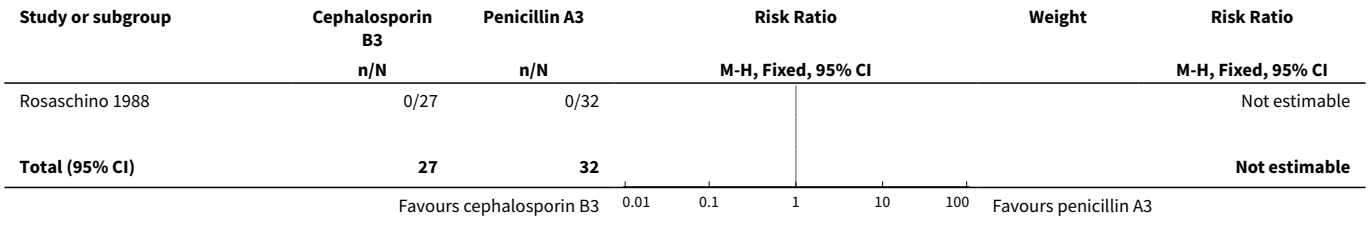
Analysis 9.2. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 2 Maternal endometritis.



Analysis 9.6. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 6 Maternal wound infection.



Analysis 9.7. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 7 Maternal urinary tract infection.



Study or subgroup	Cephalosporin B3 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Total events: 0 (Cephalosporin B3), 0 (Penicillin A3)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours cephalosporin B3 0.01 0.1 1 10 100 Favours penicillin A3

Analysis 9.9. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 9 Maternal composite serious infectious complication.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rosaschino 1988	0/27	0/32			Not estimable
Total (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin B3), 0 (Penicillin A3)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours cephalosporin B3 0.01 0.1 1 10 100 Favours penicillin A3

Analysis 9.10. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 10 Maternal composite adverse effects.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Faro 1990	0/145	0/155			Not estimable
Rosaschino 1988	0/27	0/32			Not estimable
Total (95% CI)	**172**	**187**			**Not estimable**
Total events: 0 (Cephalosporin B3), 0 (Penicillin A3)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours cephalosporin B3 0.01 0.1 1 10 100 Favours penicillin A3

Analysis 9.11. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 11 Maternal allergic reactions.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rosaschino 1988	0/27	0/32			Not estimable
Total (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin B3), 0 (Penicillin A3)					

Favours cephalosporin B3 0.01 0.1 1 10 100 Favours penicillin A3

Study or subgroup	Cephalosporin B3 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours cephalosporin B3 0.01 0.1 1 10 100 Favours penicillin A3

Analysis 9.12. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 12 Maternal nausea.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rosaschino 1988	0/27	0/32			Not estimable
Total (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin B3), 0 (Penicillin A3)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours cephalosporin B3 0.01 0.1 1 10 100 Favours penicillin A3

Analysis 9.13. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 13 Maternal vomiting.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rosaschino 1988	0/27	0/32			Not estimable
Total (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin B3), 0 (Penicillin A3)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours cephalosporin B3 0.01 0.1 1 10 100 Favours penicillin A3

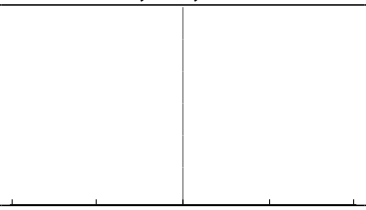
Analysis 9.14. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 14 Maternal diarrhoea.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rosaschino 1988	0/27	0/32			Not estimable
Total (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin B3), 0 (Penicillin A3)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

Favours cephalosporin B3 0.01 0.1 1 10 100 Favours penicillin A3

Analysis 9.15. Comparison 9 Cephalosporin (3rd generation B3) versus penicillins (extended-spectrum A3), Outcome 15 Maternal skin rash.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A3 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rosaschino 1988	0/27	0/32			Not estimable
Total (95% CI)	**27**	**32**			**Not estimable**
Total events: 0 (Cephalosporin B3), 0 (Penicillin A3)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



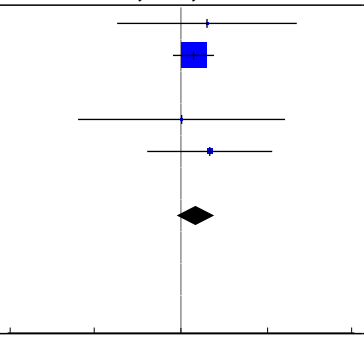
Comparison 10. Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maternal sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Maternal endometritis	5	1472	Risk Ratio (M-H, Fixed, 95% CI)	1.47 [0.89, 2.42]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	3	1060	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.69, 1.83]
6 Maternal wound infection	6	1556	Risk Ratio (M-H, Fixed, 95% CI)	0.49 [0.27, 0.90]
7 Maternal urinary tract infection	2	233	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.10, 2.80]
8 Maternal thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Maternal composite serious infectious complication	1	746	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	2	1039	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Maternal allergic reactions	1	746	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Maternal nausea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	1	200	Risk Ratio (M-H, Fixed, 95% CI)	7.0 [0.37, 133.78]
14 Maternal diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	1	200	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.12, 72.77]
16 Immediate infant adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
17 Infant unsettled	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	1	746	Mean Difference (IV, Fixed, 95% CI)	-0.03 [-0.14, 0.08]
22 Infant length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Infant general health	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

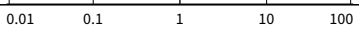
Analysis 10.2. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 2 Maternal endometritis.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A4 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Ahmed 2004	2/100	1/100		4.4%	2[0.18,21.71]
Faro 1990	26/145	19/148		82.75%	1.4[0.81,2.41]
Kamilya 2012	0/372	0/374			Not estimable
Koppel 1992	1/59	1/60		4.36%	1.02[0.07,15.88]
Louie 1982	4/55	2/59		8.49%	2.15[0.41,11.25]
Total (95% CI)	**731**	**741**		**100%**	**1.47[0.89,2.42]**
Total events: 33 (Cephalosporin B3), 23 (Penicillin A4)					
Heterogeneity: Tau^2=0; Chi^2=0.37, df=3(P=0.95); I^2=0%					
Test for overall effect: Z=1.52(P=0.13)					



Analysis 10.5. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 5 Maternal fever (febrile morbidity).

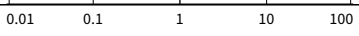
Study or subgroup	Cephalosporin B3 n/N	Penicillin A4 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Ahmed 2004	7/100	6/100		20.87%	1.17[0.41,3.35]
Kamilya 2012	20/372	17/374		58.98%	1.18[0.63,2.22]
Louie 1982	5/55	6/59		20.14%	0.89[0.29,2.76]
Total (95% CI)	**527**	**533**		**100%**	**1.12[0.69,1.83]**
Total events: 32 (Cephalosporin B3), 29 (Penicillin A4)					
Heterogeneity: Tau^2=0; Chi^2=0.19, df=2(P=0.91); I^2=0%					
Test for overall effect: Z=0.46(P=0.65)					



Favours cephalosporin B3 — Favours penicillin A4

Analysis 10.6. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 6 Maternal wound infection.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A4 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Ahmed 2004	1/100	2/100		6.43%	0.5[0.05,5.43]
Kamilya 2012	9/372	11/374		35.28%	0.82[0.34,1.96]
Koppel 1992	0/59	3/60		11.16%	0.15[0.01,2.75]
Lehapa 1999	3/108	9/125		26.83%	0.39[0.11,1.39]
Louie 1982	1/55	2/59		6.21%	0.54[0.05,5.75]
Ng 1992	0/70	4/74		14.08%	0.12[0.01,2.14]
Total (95% CI)	**764**	**792**		**100%**	**0.49[0.27,0.9]**
Total events: 14 (Cephalosporin B3), 31 (Penicillin A4)					
Heterogeneity: Tau^2=0; Chi^2=3.08, df=5(P=0.69); I^2=0%					
Test for overall effect: Z=2.29(P=0.02)					



Favours cephalosporin B3 — Favours penicillin A4

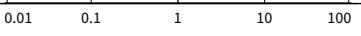
Analysis 10.7. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 7 Maternal urinary tract infection.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A4 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Koppel 1992	1/59	2/60		50.68%	0.51[0.05,5.46]
Louie 1982	1/55	2/59		49.32%	0.54[0.05,5.75]
Total (95% CI)	**114**	**119**		**100%**	**0.52[0.1,2.8]**
Total events: 2 (Cephalosporin B3), 4 (Penicillin A4)					
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=0.98); I^2=0%					
Test for overall effect: Z=0.76(P=0.45)					

Favours cephalosporin B3 — Favours penicillin A4

Analysis 10.9. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 9 Maternal composite serious infectious complication.

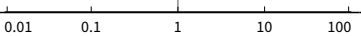
Study or subgroup	Cephalosporin B3 n/N	Penicillin A4 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kamilya 2012	0/372	0/374			Not estimable
Total (95% CI)	**372**	**374**			**Not estimable**
Total events: 0 (Cephalosporin B3), 0 (Penicillin A4)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



Favours cephalosporin B3 — Favours penicillin A4

Analysis 10.10. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 10 Maternal composite adverse effects.

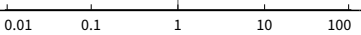
Study or subgroup	Cephalosporin B3 n/N	Penicillin A4 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Faro 1990	0/145	0/148			Not estimable
Kamilya 2012	0/372	0/374			Not estimable
Total (95% CI)	**517**	**522**			**Not estimable**
Total events: 0 (Cephalosporin B3), 0 (Penicillin A4)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					



Favours cephalosporin B3 — Favours penicillin A4

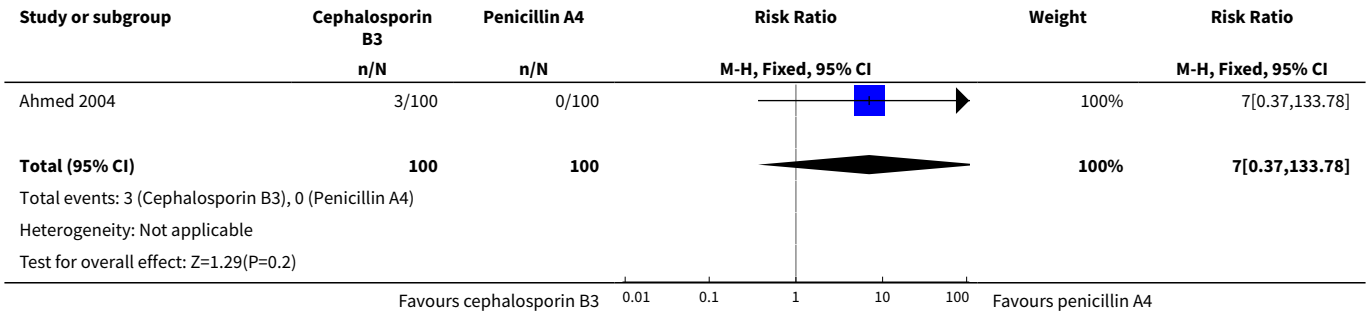
Analysis 10.11. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 11 Maternal allergic reactions.

Study or subgroup	Cephalosporin B3 n/N	Penicillin A4 n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kamilya 2012	0/372	0/374			Not estimable
Total (95% CI)	**372**	**374**			**Not estimable**
Total events: 0 (Cephalosporin B3), 0 (Penicillin A4)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					

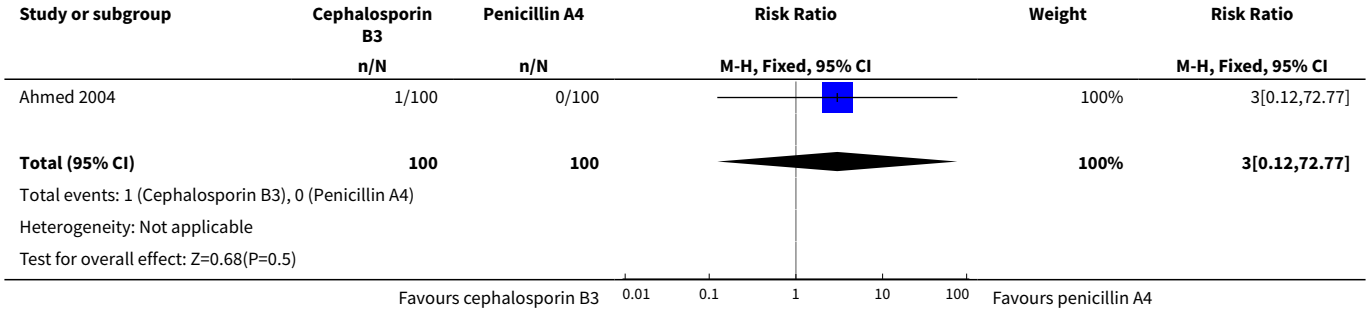


Favours cephalosporin B3 — Favours penicillin A4

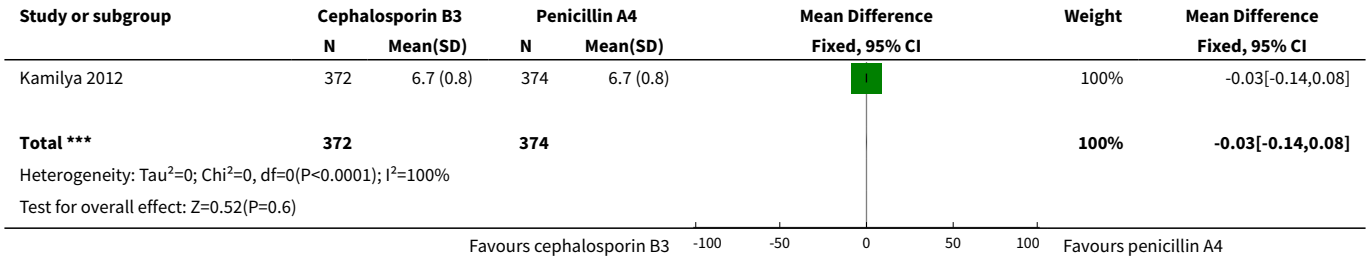
Analysis 10.13. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 13 Maternal vomiting.



Analysis 10.15. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 15 Maternal skin rash.



Analysis 10.21. Comparison 10 Cephalosporin (3rd generation B3) versus penicillins (ampicillins A4), Outcome 21 Maternal length of hospital stay.



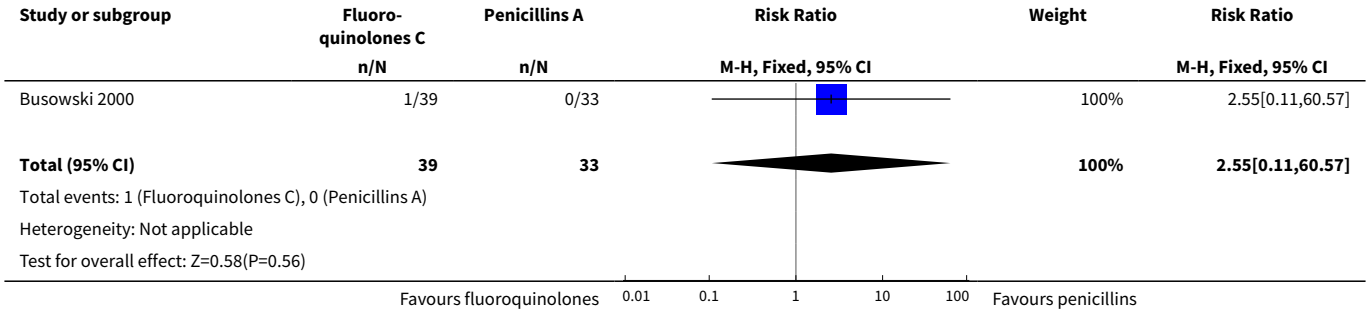
Comparison 11. Fluoroquinolones (C) vs penicillins (A)

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Maternal sepsis	1	72	Risk Ratio (M-H, Fixed, 95% CI)	2.55 [0.11, 60.57]

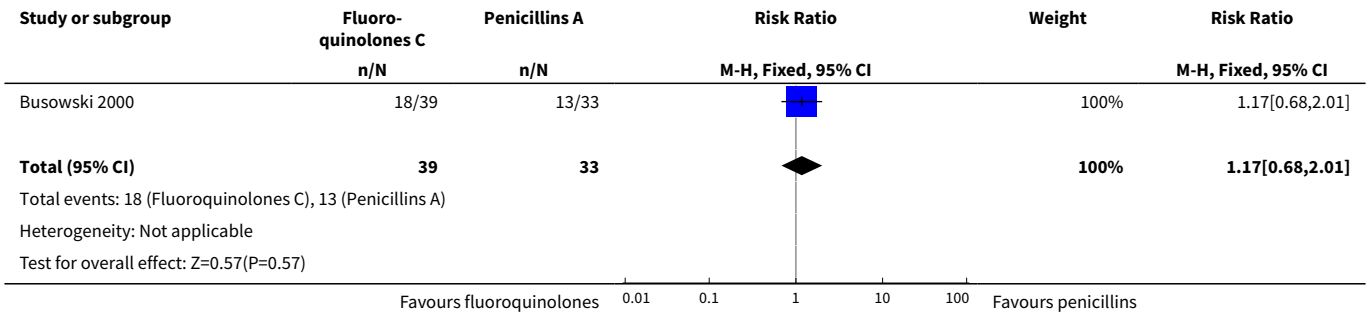
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
2 Maternal endometritis	1	72	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.68, 2.01]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Maternal wound infection	1	72	Risk Ratio (M-H, Fixed, 95% CI)	4.25 [0.21, 85.51]
7 Maternal urinary tract infection	1	72	Risk Ratio (M-H, Fixed, 95% CI)	0.09 [0.01, 1.69]
8 Maternal thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Maternal composite serious infectious complication	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Maternal allergic reactions	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Maternal nausea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Immediate infant adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Infant unsettled	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Infant length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Infant general health	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
26 Costs	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

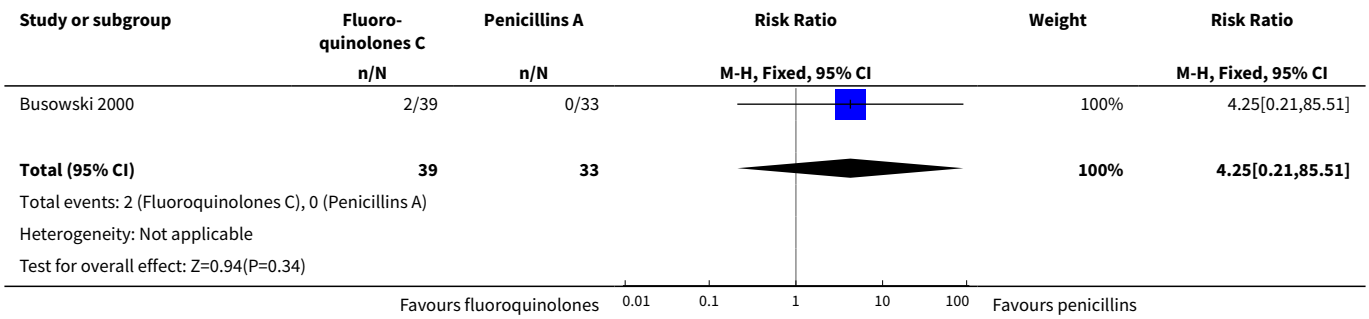
Analysis 11.1. Comparison 11 Fluoroquinolones (C) vs penicillins (A), Outcome 1 Maternal sepsis.



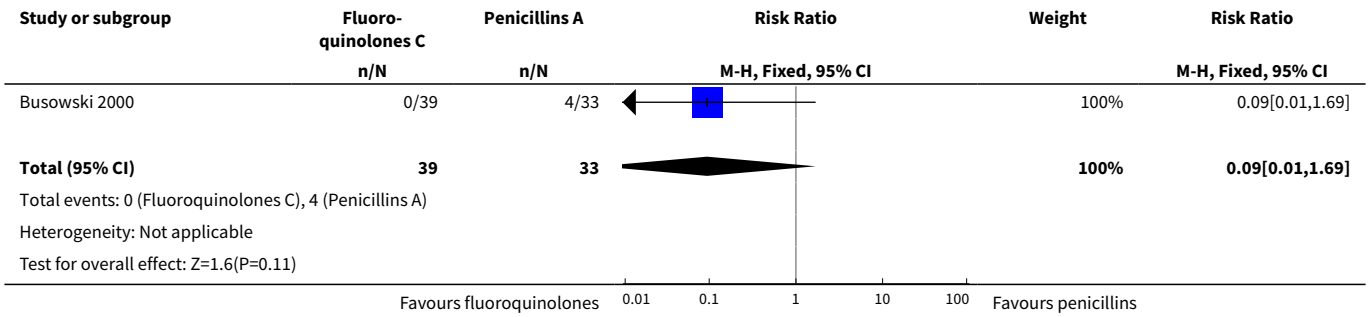
Analysis 11.2. Comparison 11 Fluoroquinolones (C) vs penicillins (A), Outcome 2 Maternal endometritis.



Analysis 11.6. Comparison 11 Fluoroquinolones (C) vs penicillins (A), Outcome 6 Maternal wound infection.



Analysis 11.7. Comparison 11 Fluoroquinolones (C) vs penicillins (A), Outcome 7 Maternal urinary tract infection.

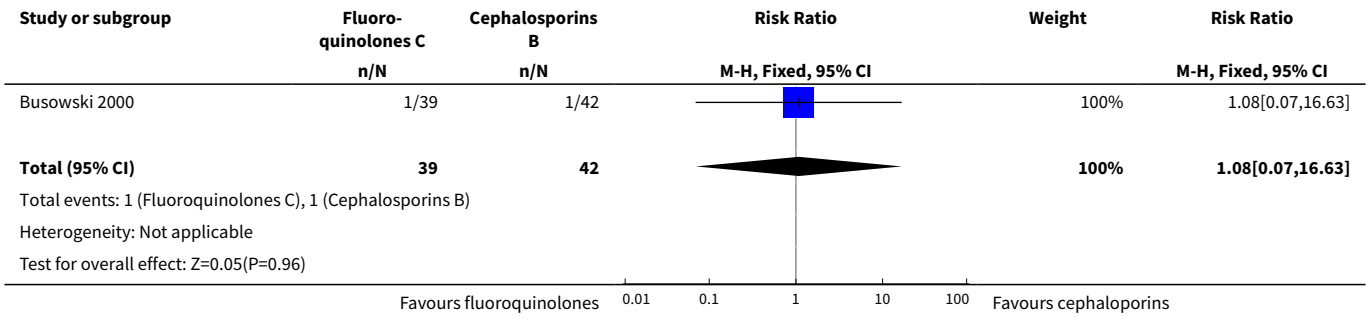


Comparison 12. Fluoroquinolones (C) vs cephalosporins (B)

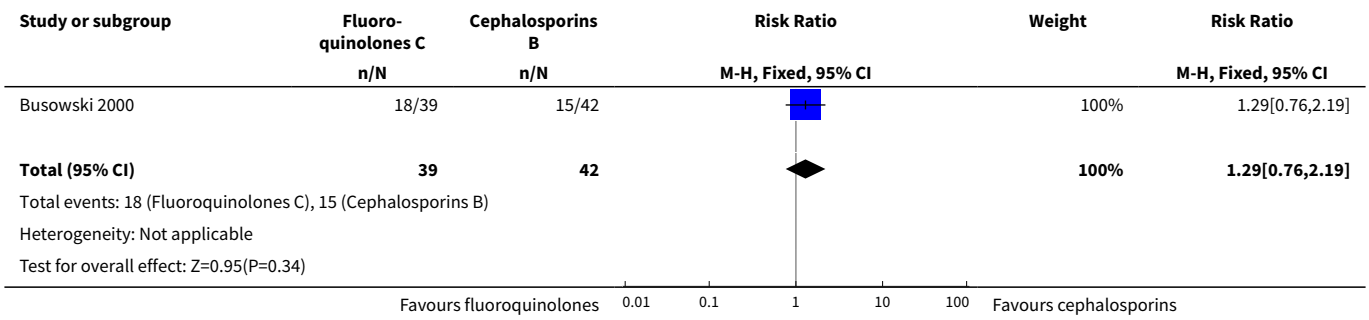
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Maternal sepsis	1	81	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.07, 16.63]
2 Maternal endometritis	1	81	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.76, 2.19]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Maternal wound infection	1	81	Risk Ratio (M-H, Fixed, 95% CI)	2.15 [0.20, 22.82]
7 Maternal urinary tract infection	1	81	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Maternal thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Maternal composite serious infectious complication	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Maternal allergic reactions	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Maternal nausea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Immediate infant adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Infant unsettled	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
19 Infant skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Infant length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Infant general health	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

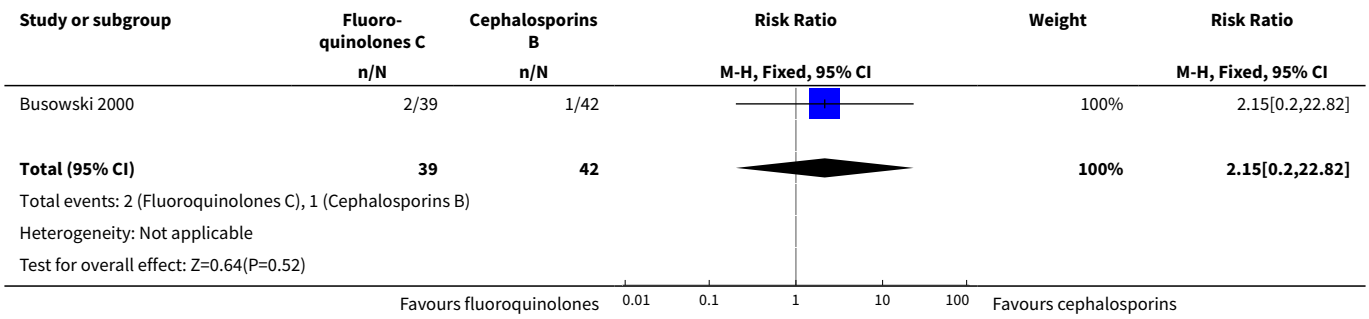
Analysis 12.1. Comparison 12 Fluoroquinolones (C) vs cephalosporins (B), Outcome 1 Maternal sepsis.



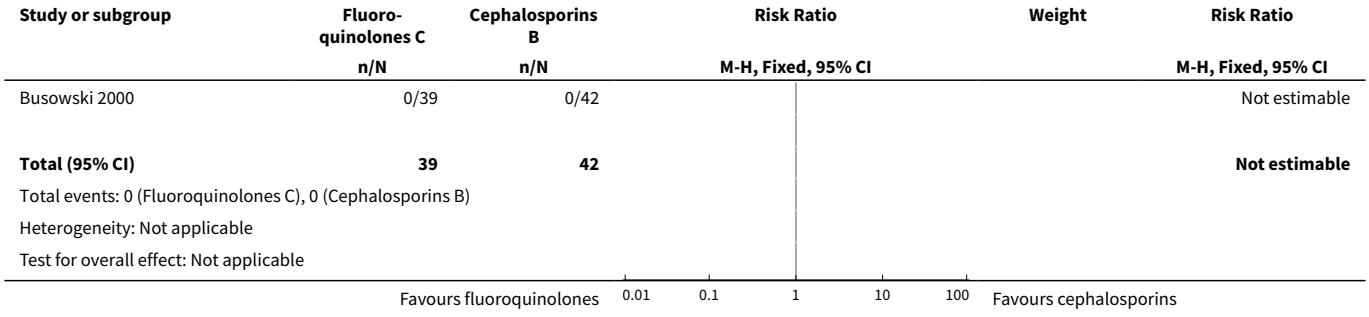
Analysis 12.2. Comparison 12 Fluoroquinolones (C) vs cephalosporins (B), Outcome 2 Maternal endometritis.



Analysis 12.6. Comparison 12 Fluoroquinolones (C) vs cephalosporins (B), Outcome 6 Maternal wound infection.



Analysis 12.7. Comparison 12 Fluoroquinolones (C) vs cephalosporins (B), Outcome 7 Maternal urinary tract infection.



Comparison 13. Other antibiotic regimens (D to I) versus penicillins (A)

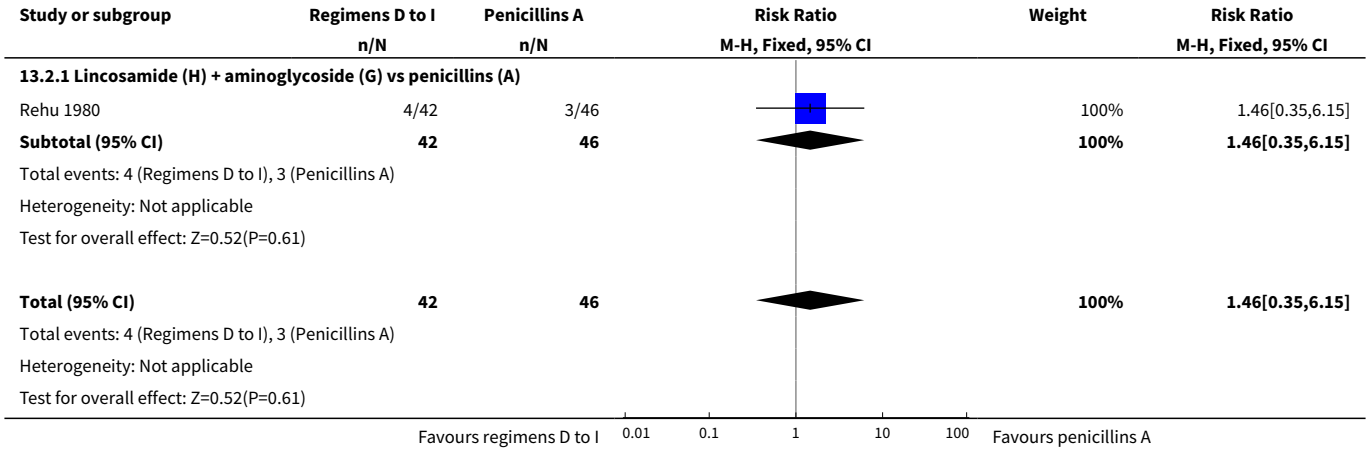
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Maternal sepsis	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Lincosamide (H) + aminoglyco-side (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Maternal endometritis	1	88	Risk Ratio (M-H, Fixed, 95% CI)	1.46 [0.35, 6.15]
2.1 Lincosamide (H) + aminoglyco-side (G) vs penicillins (A)	1	88	Risk Ratio (M-H, Fixed, 95% CI)	1.46 [0.35, 6.15]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.1 Lincosamide (H) + aminoglyco-side (G) vs penicillins (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Lincosamide (H) + aminoglycoside (G) vs penicillins (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.1 Lincosamide (H) + aminoglycoside (G) vs penicillins (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Maternal wound infection	1	88	Risk Ratio (M-H, Fixed, 95% CI)	0.55 [0.11, 2.84]
6.1 Lincosamide (H) + aminoglycoside (G) vs penicillins (A)	1	88	Risk Ratio (M-H, Fixed, 95% CI)	0.55 [0.11, 2.84]
7 Maternal urinary tract infection	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Maternal thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Maternal composite serious infectious complication	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Maternal allergic reactions	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Maternal nausea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

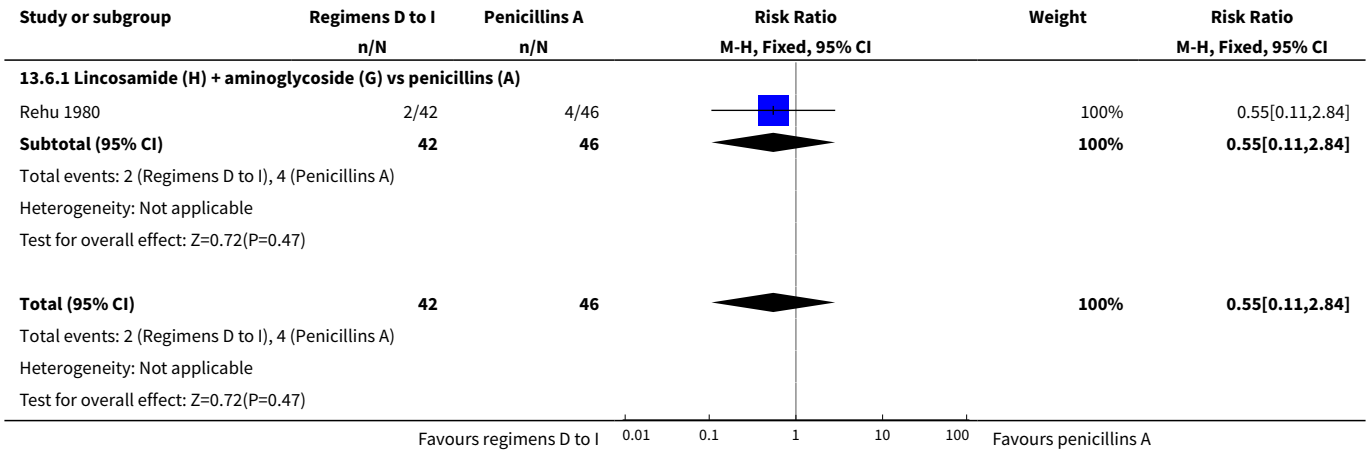
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15 Maternal skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Immediate infant adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Infant unsettled	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Infant length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Infant general health	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
25.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26.1 Lincosamide (H) + aminoglycoside (G) vs penicillin (A)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 13.2. Comparison 13 Other antibiotic regimens (D to I) versus penicillins (A), Outcome 2 Maternal endometritis.



Analysis 13.6. Comparison 13 Other antibiotic regimens (D to I) versus penicillins (A), Outcome 6 Maternal wound infection.



Comparison 14. Other antibiotic regimens (D to I) versus cephalosporins (B)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Maternal sepsis	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Maternal endometritis	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Beta-lactams (F) versus cephalosporins (B)	1	48	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.08, 17.82]
3 Infant sepsis	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Macrolides (E) versus cephalosporins (B)	1	70	Risk Ratio (M-H, Fixed, 95% CI)	7.0 [0.37, 130.69]
5.2 Beta-lactams (F) versus cephalosporins (B)	1	48	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.06, 6.09]
6 Maternal wound infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Beta-lactams (F) versus cephalosporins (B)	1	48	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.02, 9.15]
7 Maternal urinary tract infection	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 Beta-lactams (F) versus cephalosporins (B)	1	48	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Maternal thrush	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Maternal composite serious infectious complication	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
10.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Maternal allergic reactions	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
11.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Maternal nausea	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
12.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
13.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

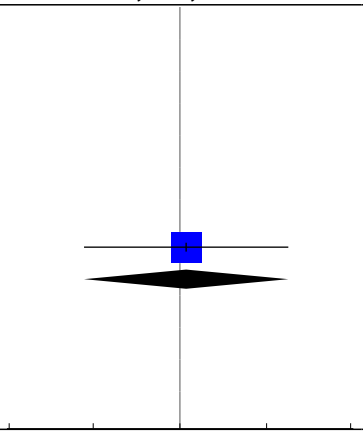
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
14.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
15.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Immediate infant adverse effects	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
16.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Infant unsettled	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
18.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
19.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
20.1 Macrolides (E) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
21.1 Macrolides (E) versus cephalosporins (B)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Infant length of hospital stay	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
22.1 Macrolides (E) versus cephalosporins (B)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Infant's immune system development	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
23.1 Macrolides (E) versus cephalosporins (B)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Infant general health	0		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
24.1 Macrolides (E) versus cephalosporins (B)	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
25.1 Macrolides (E) versus cephalosporins (B)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
26.1 Macrolides (E) versus cephalosporins (B)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
26.2 Beta-lactams (F) versus cephalosporins (B)	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

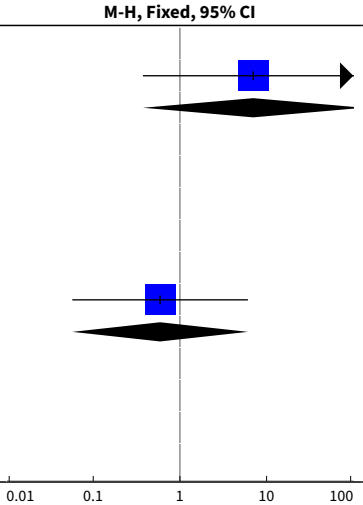
Analysis 14.2. Comparison 14 Other antibiotic regimens (D to I) versus cephalosporins (B), Outcome 2 Maternal endometritis.

Study or subgroup	Regimens D to I n/N	Cephalosporins B n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
14.2.1 Macrolides (E) versus cephalosporins (B)					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Regimens D to I), 0 (Cephalosporins B)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
14.2.2 Beta-lactams (F) versus cephalosporins (B)					
Mansueto 1989	1/22	1/26		100%	1.18[0.08,17.82]
Subtotal (95% CI)	**22**	**26**		**100%**	**1.18[0.08,17.82]**
Total events: 1 (Regimens D to I), 1 (Cephalosporins B)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.12(P=0.9)					
Test for subgroup differences: Not applicable					

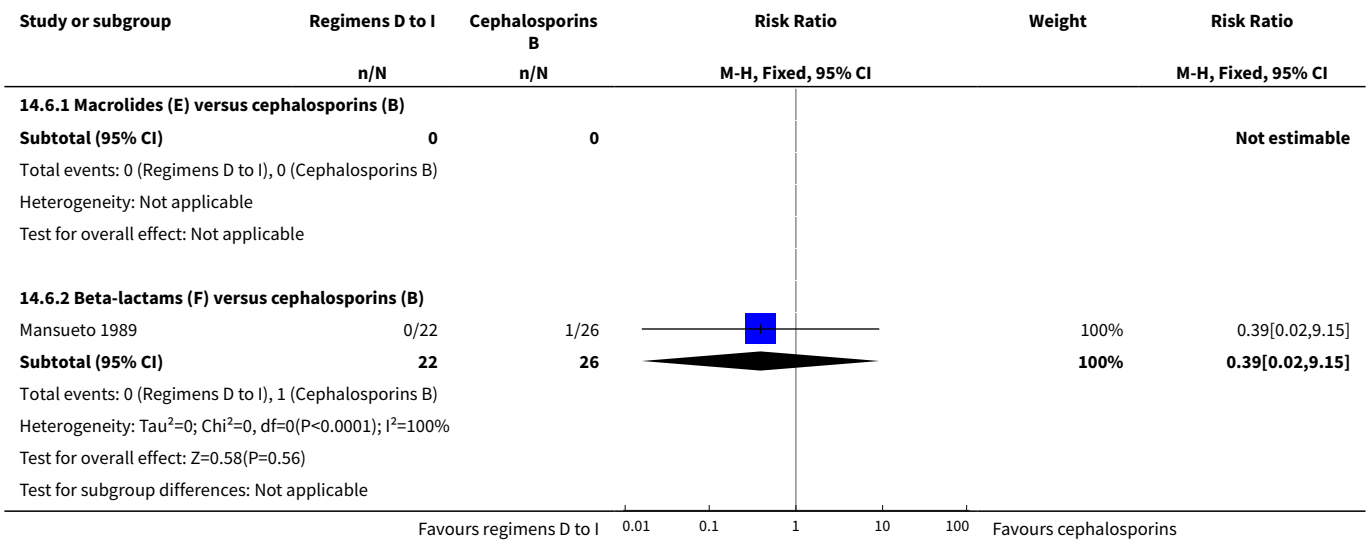


Analysis 14.5. Comparison 14 Other antibiotic regimens (D to I) versus cephalosporins (B), Outcome 5 Maternal fever (febrile morbidity).

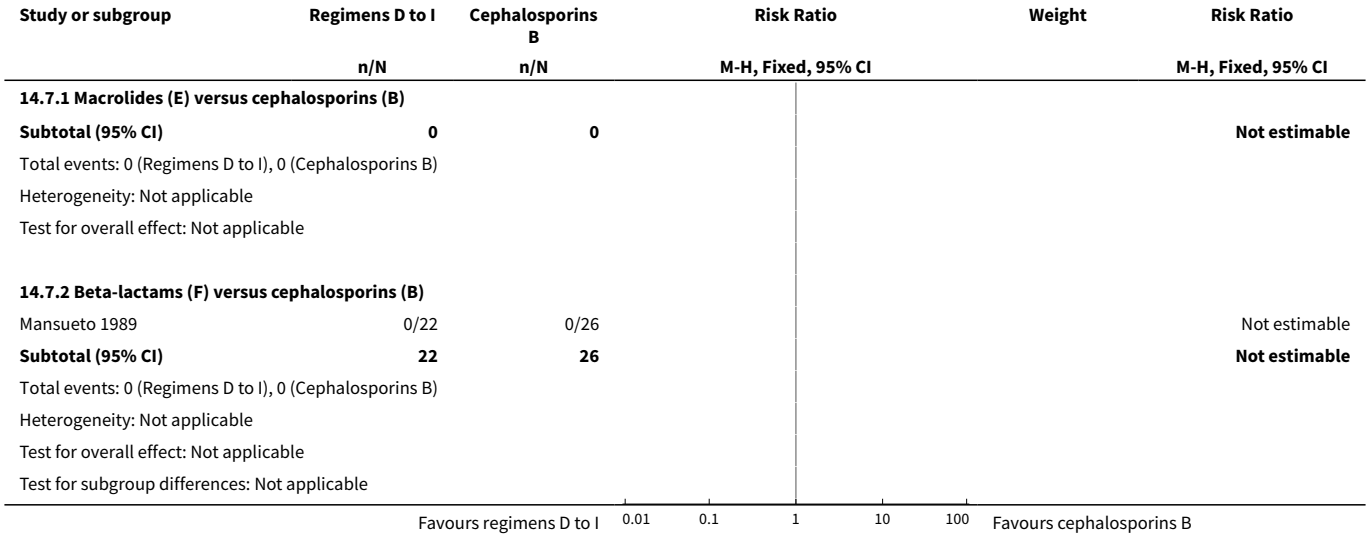
Study or subgroup	Regimens D to I n/N	Cephalosporins B n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
14.5.1 Macrolides (E) versus cephalosporins (B)					
Mothilal 2013	3/35	0/35		100%	7[0.37,130.69]
Subtotal (95% CI)	**35**	**35**		**100%**	**7[0.37,130.69]**
Total events: 3 (Regimens D to I), 0 (Cephalosporins B)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.3(P=0.19)					
14.5.2 Beta-lactams (F) versus cephalosporins (B)					
Mansueto 1989	1/22	2/26		100%	0.59[0.06,6.09]
Subtotal (95% CI)	**22**	**26**		**100%**	**0.59[0.06,6.09]**
Total events: 1 (Regimens D to I), 2 (Cephalosporins B)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.44(P=0.66)					
Test for subgroup differences: Chi^2=1.68, df=1 (P=0.2), I^2=40.33%					



Analysis 14.6. Comparison 14 Other antibiotic regimens (D to I) versus cephalosporins (B), Outcome 6 Maternal wound infection.



Analysis 14.7. Comparison 14 Other antibiotic regimens (D to I) versus cephalosporins (B), Outcome 7 Maternal urinary tract infection.



Comparison 15. Other antibiotic regimens versus different antibiotic regimens

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Maternal sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

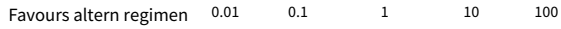
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Maternal endometritis	1	241	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.29, 2.26]
2.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	1	241	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.29, 2.26]
3 Infant sepsis	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Infant oral thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Maternal fever (febrile morbidity)	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Maternal wound infection	1	241	Risk Ratio (M-H, Fixed, 95% CI)	3.23 [0.34, 30.64]
6.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	1	241	Risk Ratio (M-H, Fixed, 95% CI)	3.23 [0.34, 30.64]
7 Maternal urinary tract infection	1	241	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.07, 17.03]
7.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	1	241	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.07, 17.03]
8 Maternal thrush	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Maternal composite serious infectious complication	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Maternal composite adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Maternal allergic reactions	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12 Maternal nausea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
12.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13 Maternal vomiting	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Maternal diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15 Maternal skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Immediate infant adverse effects	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
17 Infant unsettled	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
17.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18 Infant diarrhoea	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
18.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19 Infant skin rash	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
19.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Development of bacterial resistance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 Maternal length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
21.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Infant length of hospital stay	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

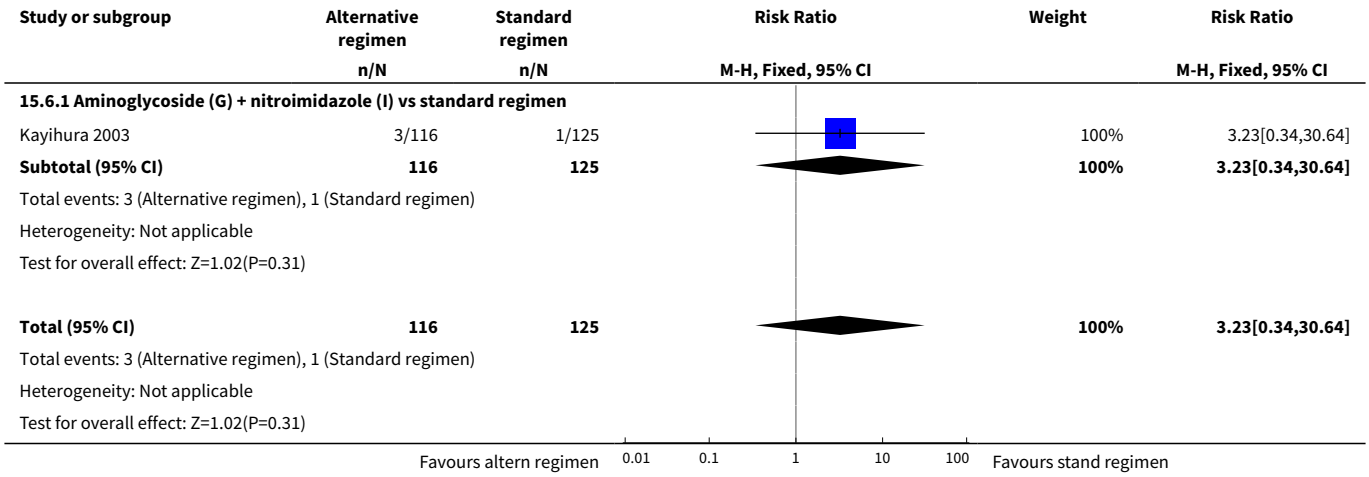
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
23 Infant's immune system development	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
23.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24 Infant general health	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
24.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Infant frequency of hospital visits	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26 Costs	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
26.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
27 Stillbirth (not-prespecified)	1	241	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.03, 2.38]
27.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen	1	241	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.03, 2.38]

Analysis 15.2. Comparison 15 Other antibiotic regimens versus different antibiotic regimens, Outcome 2 Maternal endometritis.

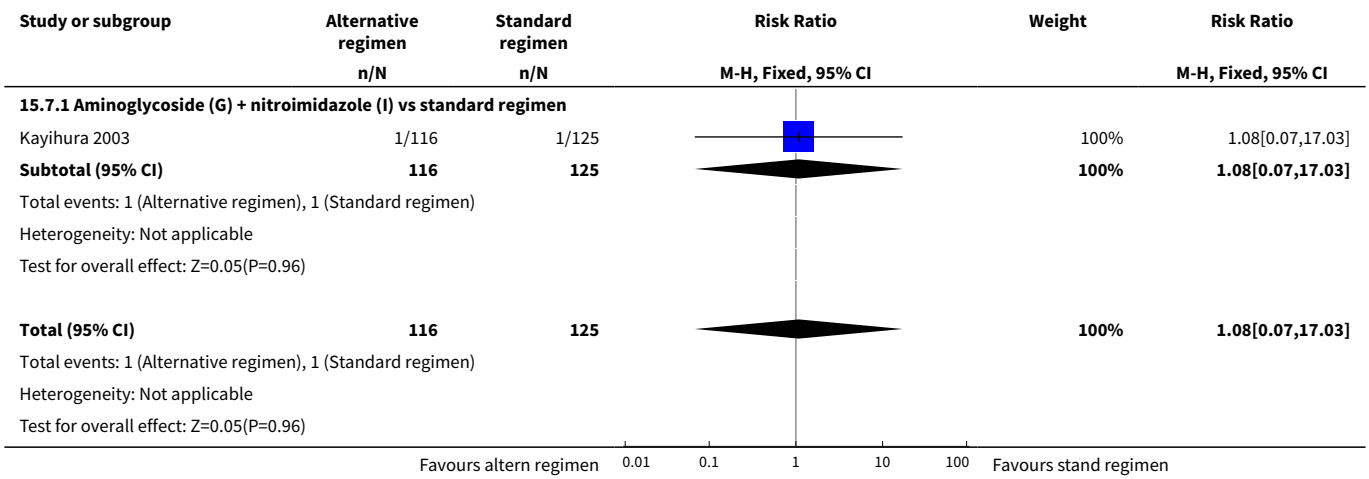
Study or subgroup	Alternative regimen n/N	Stamdard regimen n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
15.2.1 Aminoglycoside (G) + nitroimidazole (I) vs standard regimen					
Kayihura 2003	6/116	8/125		100%	0.81[0.29,2.26]
Subtotal (95% CI)	**116**	**125**		**100%**	**0.81[0.29,2.26]**
Total events: 6 (Alternative regimen), 8 (Stamdard regimen)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.41(P=0.68)					
Total (95% CI)	**116**	**125**		**100%**	**0.81[0.29,2.26]**
Total events: 6 (Alternative regimen), 8 (Stamdard regimen)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.41(P=0.68)					



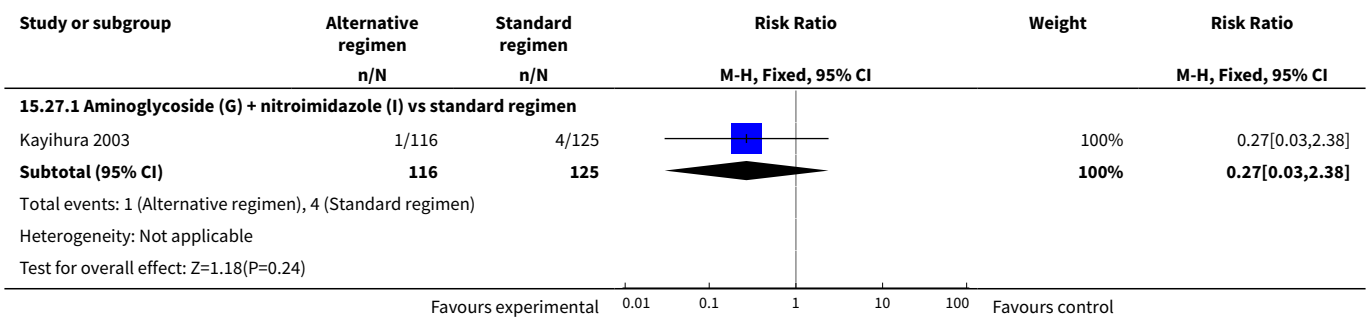
Analysis 15.6. Comparison 15 Other antibiotic regimens versus different antibiotic regimens, Outcome 6 Maternal wound infection.

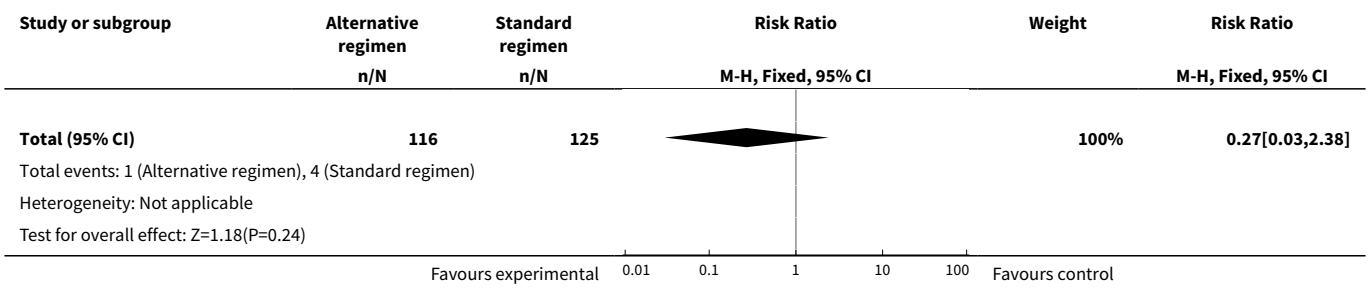


Analysis 15.7. Comparison 15 Other antibiotic regimens versus different antibiotic regimens, Outcome 7 Maternal urinary tract infection.



Analysis 15.27. Comparison 15 Other antibiotic regimens versus different antibiotic regimens, Outcome 27 Stillbirth (not-prespecified).





ADDITIONAL TABLES

Table 1. Classification of antibiotics

A. Penicillins	Penicillins consist of a thiazolidine ring connected to a B-lactam ring to which is attached a side chain. The penicillin nucleus itself is the chief structural requirement for biological activity. Penicillins are the oldest class of antibiotics and function by inhibiting cell wall synthesis (bactericidal). **A1.** Natural penicillins are based on the original penicillin-G structure. Examples include: penicillin G; procaine, penicillin V; benzathine. **A2.** Penicillinase-resistant penicillins are active even in the presence of the bacterial enzyme that inactivates most natural penicillins. Examples include: cloxacillin; dicloxacillin; methicillin; nafcillin; oxacillin. **A3.** Extended spectrum penicillins which are effective against a wider range of bacteria. Examples include: ticarcillin; piperacillin; carbenicillin; timentin. **A4.** Aminopenicillins also have an extended spectrum of action compared with the natural penicillins. Examples include: ampicillin; amoxicillin. **A+**. Penicillin combinations. Examples include: co-amoxyclav = 'ampicillin+ clavulanic acid' (Trade names include: Augmentin; Clavamox; Tyclav); 'ampicillin + sulbactam' (Trade names include: Ampictam; Unasyn).
B. Cephalosporins	Cephalosporins have a similar basic structure to penicillins but with different side chains. They function by inhibiting cell wall synthesis. **B1.** First generation cephalosporins; examples include: cephalothin; cefazolin; cephapirin; cephradine; cephalexin; cefadroxil. **B2.** Second generation cephalosporins; examples include: cefoxitin; cefaclor; cefuroxime; cefotetan; cefprozil; cefamandole, cefonicid; ceforanide, cefotiam. **B3.** Third generation cephalosporins, examples include: cefotaxime; ceftizoxime; ceftriaxon; cefpodoxime; cefditoren; ceftibuten; ceftazidine; cefcapene; cefdaloxime; cefetamet; cefixime; cefmenoxime; cefodizime; cefoperazone; cefpimizole. **B4.** Fourth generation cephalosporins, examples include: cefepime; cefpirome; cefclidine; cefluprenam; cefozopran; cefquinome. **B+**: Cephalosporin combinations. Examples include: 'cephradine + metronidazole'; 'ceftriaxone + metronidazole'; 'cloxacillin + gentamicin'.
C. Fluoroquinolones	The fluoroquinolones target the bacterial DNA gyrase and topoisomerase. They are potent bacteriocidal agents against a broad variety of micro-organisms. Examples include: ciprofloxacin; levofloxacin; lomefloxacin; norfloxacin; sparfloxacin; clinafloxacin; gatifloxacin; ofloxacin; trovafloxacin.

Table 1. Classification of antibiotics *(Continued)*

D. Tetracyclines	Tetracyclines are bacteriostatic antibiotics active against a wide range of aerobes and anaerobic gram-positive and gram-negative bacteria. They inhibit bacterial protein synthesis by binding to the 30S bacterial ribosome. Examples include: tetracycline; doxycycline; minocycline. Tetracyclines should not be used with children under 8 and specifically during teeth development as they can cause a permanent brown discolouration to the teeth. This antibiotic is, therefore, unlikely to be used at caesarean section. Chloramphenicol is considered to have similar action to tetracycline.
E. Macrolides	Macrolide antibiotics inhibit bacterial protein synthesis. Resistance can arise. Examples include: erythromycin; clarithromycin; azithromycin.
F. Other beta-lactams (carbapenems)	Carbapenems are beta-lactams that have a broader spectrum of activity than most other beta-lactam antibiotics. Examples include: imipenem; meropenem; ertapenem; aztreonam, mezlocillin.
G. Aminoglycosides	Aminoglycosides are first-line therapy for a limited number of very specific, often historically prominent infections, such as plague, turaremia and tuberculosis. Examples include: streptomycin; gentamicin, kanamycin.
H. Lincosamides	Lincosamides are protein synthesis inhibitors which bind to the 50s subunit of bacterial ribosomes and inhibit early elongation of peptide chain by inhibiting transpeptidase reaction. Examples include: lincomycin; clindamycin.
I. Nitroimidazoles	Nitroimidazole is an imidazole derivative that contains a nitro group. It is used for the treatment of infection with anaerobic organisms. Examples include: metronidazole, tinidazol.
J. Others	

See Goodman 2008 for more detailed information about the classification and BNF 2009. Also from Wikipedia (http://www.wikipedia.org/)

APPENDICES

Appendix 1. Data collection for studies identified before October 1998

All potential trials were selected for eligibility according to the criteria specified in the protocol and data were extracted from each publication by two reviewers. Any discrepancies were resolved by discussion. In addition to the main outcome measures listed above, information on the setting of the study (country, type of population, socioeconomic status), a detailed description of the antibiotic regimen used (drug, dose, frequency and timing), and definitions of the outcomes (if provided) were collected. An intention-to-treat analysis was performed where possible.

Trials were assessed for methodological quality using the standard Cochrane criteria of adequacy of allocation concealment: adequate (A), unclear (B), inadequate (C), or that allocation concealment was not used (D). Information on blinding of outcome assessment and loss to follow-up were collected.

The main comparison of any treatment versus another treatment was to be stratified according to the indication for caesarean section.

Separate comparisons of different classes of antibiotics and regimens, grouped where appropriate by spectrum of activity, were made. If there were sufficient trials, separate comparisons were made between the timing of antibiotic administration, the number of doses given and the route of administration (whether systemic or lavage).

Summary relative risks were calculated using a fixed-effect model (if there was no significant heterogeneity between trials).

WHAT'S NEW

Date	Event	Description
30 September 2014	New citation required but conclusions have not changed	Six new trials included. Conclusions remain the same.
30 September 2014	New search has been performed	Methods updated to include GRADE. Search updated, 17 new reports identified.

HISTORY

Protocol first published: Issue 3, 1998
Review first published: Issue 10, 2010

Date	Event	Description
13 July 2010	New search has been performed	We have included further studies and re-structured the review to address the comparisons between different classes of antibiotics. Further reviews will be undertaken to address comparisons within classes of antibiotics, including drug doses, and separate reviews will be undertaken on timings and routes of administration - *see* Differences between protocol and review.

CONTRIBUTIONS OF AUTHORS

Gill Gyte (GG) drafted the protocol with Zarko Alfirevic (ZA) and Lixia Dou (LD) providing comments. GG, LD and Juan C Vazquez (JCV) carried out the data extraction and GG entered the data with LD checking the data entry. GG drafted the results and conclusions and both LD and JCV checked and provided amendments.

For the 2014 update, GG, JVC and LD performed the data extraction, GG entered the data with LD and JVC checking the data entry. JCV provided the clinical input to the text of the update.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- 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

From the original protocol, this review has been separated into three reviews as described in the updated protocol sections of this review and a further two reviews will provide information on this topic.

1. Different classes of antibiotics given to women routinely for preventing infection after caesarean section (this review)

2. Different regimens of penicillin antibiotic given to women routinely for preventing infection after caesarean section (Liu 2014)
3. Different regimens of cephalosporin antibiotic given to women routinely for preventing infection after caesarean section (protocol in preparation)
4. Timing of prophylactic antibiotics for preventing infectious morbidity in women undergoing caesarean section (Baxter 2011) (review in preparation)
5. Routes of administration for antibiotic given to women routinely for preventing infection after caesarean section (protocol in preparation)

We have added subgroup analyses for all outcomes for Comparison 1, 'Cephalosporins versus penicillins', according to whether single or combination drugs were used.

We have added two further outcomes 'Post-discharge infections - to 30 days' and 'Maternal readmissions to hospital'.

NOTES

The Hopkins 1999 published review on, *Antibiotic prophylaxis regimens and drugs for caesarean section*, has been subsequently 'withdrawn' from publication in *The Cochrane Library* because it has become out of date. The review has now been split into five separate reviews.

1. Different classes of antibiotics given to women routinely for preventing infection at caesarean section (this review)
2. Different regimens of penicillin antibiotics given to women routinely for preventing infection after caesarean section (Liu 2014)
3. Different regimens of cephalosporin antibiotic prophylaxis at caesarean section for reducing morbidity (protocol in preparation)
4. Timing of prophylactic antibiotics for preventing infectious morbidity in women undergoing caesarean section (Baxter 2011) (review in preparation)
5. Routes of administration of antibiotic prophylaxis for preventing infection after caesarean section (protocol in preparation)

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Bacterial Agents [adverse effects] [classification] [*therapeutic use]; Antibiotic Prophylaxis [methods]; Bacterial Infections [*prevention & control]; Cephalosporins [adverse effects] [*therapeutic use]; Cesarean Section [*adverse effects]; Penicillins [adverse effects] [*therapeutic use]; Postoperative Complications [*prevention & control]; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Infant, Newborn; Pregnancy