

Antibiotic prophylaxis for cesarean section (Review)

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TABLE OF CONTENTS

ABSTRACT	1
PLAIN LANGUAGE SUMMARY	1
BACKGROUND	2
OBJECTIVES	2
CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW	3
SEARCH METHODS FOR IDENTIFICATION OF STUDIES	3
METHODS OF THE REVIEW	3
DESCRIPTION OF STUDIES	3
METHODOLOGICAL QUALITY	4
RESULTS	5
DISCUSSION	5
AUTHORS' CONCLUSIONS	7
FEEDBACK	7
POTENTIAL CONFLICT OF INTEREST	7
ACKNOWLEDGEMENTS	7
SOURCES OF SUPPORT	7
REFERENCES	8
TABLES	14
Characteristics of included studies	14
Characteristics of excluded studies	42
ANALYSES	43
Comparison 01. Prophylactic antibiotics in cesarean section	43
INDEX TERMS	43
COVER SHEET	43
GRAPHS AND OTHER TABLES	44
Analysis 01.01. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 01 Fever	45
Analysis 01.02. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 02 Wound infection	47
Analysis 01.03. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 03 Endometritis	50
Analysis 01.04. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 04 Urinary tract infection	53
Analysis 01.05. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 05 Serious infectious morbidity/ death	56
Analysis 01.06. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 06 Maternal side-effects	58
Analysis 01.07. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 07 Days in hospital (mother)	59

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ABSTRACT

Background

The single most important risk factor for postpartum maternal infection is cesarean delivery.

Objectives

The objective of this review was to assess the effects of prophylactic antibiotic treatment on infectious complications in women undergoing cesarean delivery.

Search strategy

We searched the Cochrane Pregnancy and Childbirth Group trials register (January 2002) and the Cochrane Controlled Trials Register (The Cochrane Library, Issue 4, 2001).

Selection criteria

Randomized trials comparing antibiotic prophylaxis or no treatment for both elective and non-elective cesarean section.

Data collection and analysis

Two reviewers assessed trial quality and extracted data.

Main results

Eighty-one trials were included. Use of prophylactic antibiotics in women undergoing cesarean section substantially reduced the incidence of episodes of fever, endometritis, wound infection, urinary tract infection and serious infection after cesarean section. The reduction in the risk of endometritis with antibiotics was similar across different patient groups: the relative risk (RR) for endometritis for elective cesarean section (number of women = 2037) was 0.38 (95% confidence interval (CI) 0.22 to 0.64); the RR for non-elective cesarean section (n = 2132) was 0.39 (95% CI 0.34 to 0.46); and the RR for all patients (n = 11,937) was 0.39 (95% CI 0.31 to 0.43). Wound infections were also reduced: for elective cesarean section (n = 2015) RR 0.73 (95% CI 0.53 to 0.99); for non-elective cesarean section (n = 2780) RR 0.36 95% CI 0.26 to 0.51]; and for all patients (n = 11,142) RR 0.41 (95% CI 0.29 to 0.43).

Authors' conclusions

The reduction of endometritis by two thirds to three quarters and a decrease in wound infections justifies a policy of recommending prophylactic antibiotics to women undergoing elective or non-elective cesarean section.

PLAIN LANGUAGE SUMMARY

Women taking antibiotics just before, during or just after their cesarean section operation, are much less likely to have infection of their womb (uterus) and wound

Women who have a cesarean section operation (removing the baby by surgery through the mother's abdomen) have an increased risk of infection. This can lead to serious complications, including death. The review of trials found evidence that it is beneficial for women

to take antibiotic drugs (usually by injection) before, during or after their caesarean section, whether they have signs of infection or not (antibiotic prophylaxis). Women taking prophylactic antibiotics are much less likely to have endometritis (infection of the womb's lining) and wound infection. See also the Cochrane Review 'Antibiotic prophylaxis regimens and drugs for caesarean section'.

BACKGROUND

The single most important risk factor for post-partum maternal infection is caesarean delivery (Gibbs 1980). Women undergoing caesarean section have a five to 20-fold greater risk for infection compared with a vaginal delivery. Caesarean section rates average greater than 20% in the developed world and make up a similar percentage of hospital deliveries in developing countries. Infectious complications that occur after caesarean delivery are an important and substantial cause of maternal morbidity and are associated with a significant increase in hospital stay (Henderson 1995).

Infectious complications following caesarean delivery include fever, wound infection, endometritis, bacteremia, other serious infection (including pelvic abscess, septic shock, necrotizing fasciitis and septic pelvic vein thrombophlebitis) and urinary tract infection (Gibbs 1980; Leigh 1990; Boggess 1996). Fever can occur after any operative procedure and a low grade fever following a caesarean delivery may not necessarily be a marker of infection (MacLean 1990). Without prophylaxis, the incidence of endometritis is reported to range from 20 to 85%; rates of wound infection and serious infectious complications as high as 25% have been reported (Enkin 1989). There has been no consistent application of a standard definition for endometritis nor wound infection and surveillance strategies for the ascertainment of infections, especially following hospital discharge, vary widely (Hulton 1992; Baker 1995). Differences in the socioeconomic status of the population studied will explain some of the variability in incidence as will the use of different criteria to diagnose infection.

Factors that have been associated with an increased risk of infection among women who have a caesarean delivery include emergency caesarean section, labor and its duration, ruptured membranes and the duration of rupture, the socioeconomic status of the woman, number of prenatal visits, vaginal examinations during labour and internal fetal monitoring, urinary tract infection, anemia, blood loss, obesity, diabetes, general anesthesia, the skill of the operator and the operative technique (Gibbs 1980; Webster 1988; Magann 1995; Desjardins 1996; Killian 2001). Labor and ruptured membranes appear to be the most important factors, with obesity particularly important for wound infections (Beattie 1994). The association of bacterial vaginosis with an increased incidence of endometritis following caesarean delivery has also been reported (Watts 1990).

The most important source of micro-organisms responsible for post-caesarean section infection is the genital tract, particularly if

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

General principles for the prevention of any surgical infection include sound surgical technique, skin antisepsis and antimicrobial prophylaxis (Owen 1994). Although antibiotic prophylaxis during caesarean section has been extensively studied and generally found to be effective in preventing infection, surveys suggest inconsistent and variable application of recommendations for its use (Pedersen 1996; Huskins 2001). Questions remain about the indications for prophylaxis, the choice of drug (whether a broad spectrum or longer acting agent is better), its route, timing and frequency, the cost-effectiveness of different strategies, adverse effects of antibiotics for the woman and her infant, and the potential for increased use of antimicrobial prophylaxis to be a factor in the development of antimicrobial resistance (Mugford 1989; Mallaret 1990a; Shlaes 1997). Particularly controversial is whether antibiotic treatment should be given to all mothers or only to those at greatest risk of infection (Gilstrap 1988; Suonio 1989; Ehrenkrans 1990; Howey 1990).

OBJECTIVES

To determine, from the best evidence available, whether prophylactic antibiotic treatment compared with placebo or no treatment given to women when undergoing a caesarean delivery decreases the incidence of febrile morbidity, wound infection, endometritis, urinary tract infection or any serious infectious complication (such as bacteremia, septic shock, septic thrombophlebitis, necrotizing fasciitis and death).

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All trials were considered where the intention was to allocate participants randomly to receive antibiotic prophylaxis or no antibiotics for cesarean section.

Types of participants

Women undergoing cesarean delivery, both elective and non-elective. Rupture of membranes for more than six hours or the presence of labour were used to differentiate a non-elective cesarean delivery from an elective procedure.

Types of intervention

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

Types of outcome measures

Trials were considered if any one of the following clinical outcomes, however they were defined by the authors, was reported:

- (i) fever;
- (ii) wound infection;
- (iii) endometritis;
- (iv) urinary tract infection;
- (v) serious infectious complication (such as bacteremia, septic shock, septic thrombophlebitis, necrotizing fasciitis, or death attributed to infection).

In addition, data were collected (where available) on adverse events of treatment (eg allergic reactions, antibiotic-associated diarrhea, development of bacterial resistance), maternal length of stay and costs, and any infant outcomes reported.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

This review has drawn on the search strategy developed for the Pregnancy and Childbirth Group as a whole. The full list of journals and conference proceedings as well as the search strategies for the electronic databases, which are searched by the Group on behalf of its reviewers, are described in detail in the 'Search strategies for the identification of studies section' within the editorial information about the Cochrane Pregnancy and Childbirth Group. Briefly, the Group searches on a regular basis MEDLINE, the Cochrane Controlled Trials Register and reviews the Contents tables of a further 38 relevant journals received via ZETOC, an electronic current awareness service.

Relevant trials, which are identified through the Group's search strategy, are entered into the Group's Specialised Register of

Controlled Trials. Please see Review Group's details for more detailed information. Date of last search: January 2002.

In addition, the Cochrane Controlled Trials Register (The Cochrane Library, Issue 4, 2001) was searched on the terms (ANTIBIOT* or ANTIMICR*) and (CAESAR* or CESAR*).

METHODS OF THE REVIEW

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 were collected. An intent to treat analysis was performed where the data were provided to enable this to be done.

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). Note was made on whether the trials were placebo controlled and information on blinding of outcome assessment and loss to follow-up was collected.

The main comparison of any treatment versus no treatment was stratified by whether the cesarean section was elective, non-elective or a combination of both/unspecified, resulting in four main comparisons:

- (1) Any antibiotic versus placebo/no treatment (elective cesarean deliveries).
- (2) Any antibiotic versus placebo/no treatment (non-elective cesarean deliveries).
- (3) Any antibiotic versus placebo/no treatment (a combination of both elective and non-elective/unspecified cesarean deliveries).
- (4) Any antibiotic versus placebo/no treatment (all cesarean deliveries).

Summary relative risks were calculated using a fixed effects model where there was no significant heterogeneity among trials (chi-squared test for heterogeneity <0.05). A random effects model was used if statistically significant heterogeneity among trials was observed.

DESCRIPTION OF STUDIES

Eighty-one trials, that enrolled close to 12,000 women, were identified that met the inclusion criteria for this review. For a detailed description of studies, see table of 'Characteristics of included studies'. Of those studies excluded from the analysis, most were because either no clinical outcomes were reported or the specific outcomes

of interest were not described. For some studies, although the trial was initially randomized, part-way through the study the placebo arm was dropped. Because results on the initially randomized part of the study were not available, these studies were not included in the analysis (See table of 'Characteristics of excluded studies' for further details).

While the majority (59/81) of the studies included in the review were conducted in industrial countries (40 from the US, 15 from Western Europe and Scandinavia, three from Canada and one from New Zealand) studies were reported from developing countries including Nigeria, Tunisia, Kenya, Zimbabwe, and South Africa as well as Mexico, Greece, Turkey, Israel, the Middle East, China and Malaysia. Many of the studies included a majority of women who were identified as from a low socio-economic group, but other studies enrolled women who were not perceived to be at an increased risk of infection because of socio-economic status. Most studies adequately described the characteristics of the women who were enrolled, including details of the indication for cesarean section, mean duration of labour and membrane rupture and number of repeat sections. The most recent study published (Bagratee 2001) included information on the number of women who were HIV positive. In no study were details on the incidence of bacterial vaginosis provided.

The objective of this review was to study the effect of prophylaxis in both elective and non-elective cesarean sections and strict definitions of an elective and non-elective cesarean section were used by the authors of this review to categorize patients and studies. In thirteen studies, data on patients undergoing an elective cesarean section were available (Rothbard 1975; Duff 1982; Karhunen 1985; Dashow 1986; Mahomed 1988; De Boer 1989; Lewis 1990; Wu 1991; Jakobi 1994; Rizk 1998; Shah 1998; Rouzi 2000; Bagratee 2001). In 24 studies, there were data on non-elective procedures. The remaining and the majority of studies did not differentiate between an elective or non-elective procedure, or the definitions used were not consistent with those used in this review; these have been grouped as 'both' or 'undefined'. Often a repeat section had been classified as elective by the study authors, but it was not always evident that all of these women were indeed not in labour and often the duration of membrane rupture was unclear.

The antimicrobial agents most often used in the trials included ampicillin, a first generation cephalosporin (usually cefazolin), a second generation cephalosporin (cefoxitin, cefotetan or cefuroxime), metronidazole, an extended spectrum penicillin (eg ticarcillin, or a beta-lactamase inhibitor combination) and an aminoglycoside-containing combination. Antibiotics for prophylaxis were usually administered intravenously after the cord was clamped. Nine studies were included where irrigation of the peritoneal or uterine cavity with an antibiotic containing solution was compared with either saline irrigation or no irrigation. The duration of the post-operative treatment course varied from a single dose ($n = 22$) to as long as a week. In 32 studies, antibiotics were

continued for up to 24 hours following the procedure. While most studies were published in the 1980s, new studies have continued to be performed in the 1990s and published as recently as 2001.

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

METHODOLOGICAL QUALITY

For detailed information on methods, see table of 'Characteristics of included studies'.

The methodological quality of the trials on the whole was reasonably good and in only five studies was the method of randomization clearly inadequate (C) (Morrison 1973; Rothbard 1975; Bilgin 1998; Kellum 1985; Turner 1990). Only those where there was a central randomization process/computer generated randomization with the code held at a remote site (usually the pharmacy) was the randomization classified as adequate (A) ($n = 22$). For two thirds of the studies, details on the method of randomization were not clearly stated and allocation concealment could not be ensured; these have been categorized as unclear (B).

Approximately two thirds (57/81) of the studies were placebo-controlled (which included the use of saline irrigation). In most studies, all women who were initially randomized were included in the outcomes and an intent to treat analysis was performed. Dropouts were reported in 23 studies; for nine of these, it was possible to include them in an intent to treat analysis but in the fourteen others, insufficient data were provided on dropouts for them to be included in the analysis. Where the group allocation of dropouts was not provided, there was the possibility that there may have been selective withdrawals from one or other of the groups. There were some studies where a discrepancy in the numbers allocated to the randomized groups, unlikely to have occurred

by chance, was not accounted for. In most cases (Adeleye 1981; Apuzzio 1982; Conover 1984; Jakobi 1994) the numbers in the placebo group were smaller than those in the treatment group, raising the possibility of selective withdrawals not mentioned in the published report.

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

RESULTS

The women included in these 81 trials varied greatly in their baseline risk of infection. For the outcome of endometritis, the average rate of infection in the control groups in those women undergoing an elective cesarean section was 7.03% [standard deviation (SD) 7.14], range 0 to 24%. For those women undergoing non-elective or emergency section, the incidence of endometritis in the control groups was 30.14% [SD 15.22], range 3 to 61%; and in those studies where the indication for cesarean section was not defined or included both groups the incidence of endometritis was 19.9% [SD 14.4], range 0 to 59%. Similar wide variability in the baseline incidence of the other outcomes (fever, wound infection, urinary tract infection) in the group receiving no treatment was seen among the studies.

The results of the trials included in this review are, however, remarkably consistent, both in direction of effect and in effect size. Overall, the use of prophylactic antibiotics with cesarean section results in a major, clinically important, and statistically significant reduction in the incidence of episodes of fever, endometritis, wound infection, urinary tract infection and serious infection after cesarean section. Only in nine studies that reported the incidence of urinary tract infection in women undergoing an elective cesarean section were the differences in the rate of urinary tract infections not statistically significant and there were too few serious infectious outcomes in women undergoing an elective cesarean section to analyse.

Whether considering only elective cesarean sections (number of studies = 12; number of women = 2037), non-elective cesarean section (number of studies = 23; number of women = 2132), the undefined group (number of studies = 48; number of women = 6788) or all women together (n = 11,957), the relative risks (RR) for the effect of antibiotics is remarkably similar for the outcome of endometritis: 0.38 (95% confidence interval (CI) 0.22 to 0.64]; 0.39 (0.34 to 0.46); 0.36 (0.30 to 0.44) and 0.39 (0.31 to 0.43) respectively. There is a similar close clustering of relative risks for the outcome for fever (number of studies = 45; number of women = 7180) among the three subgroups. Seventy-five studies reported on the outcome of wound infection. The rate of wound infections in the elective, non-elective and both or undefined control groups

were quite similar (8.51%, 7.61% and 10.6% respectively). Antibiotic treatment was associated with a reduction in wound infections: for non-elective cesarean sections (n = 2780) the relative risk was 0.36 95% CI 0.26 to 0.51] and for all patients (n = 11,142) the RR was 0.41 (95% CI 0.29 to 0.43). The reduction in wound infection after an elective cesarean section (n = 2015) just reached statistical significance (RR 0.73 (95% CI 0.53 to 0.99)]).

Using an episode of bacteremia and any other serious infectious morbidity as defined by the authors (except a prolonged febrile episode) as the definition of a serious outcome, antibiotic treatment was associated with relative risks of 0.28 (95% CI 0.13 to 0.61) for non-elective deliveries, 0.54 (0.32 to 0.92) for the undefined group, and 0.44 (0.29 to 0.68) for all women together (number of studies = 31; total number of women = 4760). There were no deaths reported in either group. Maternal side effects were not consistently collected. Overall there were three episodes in the placebo or untreated group (0.4%), compared with 16 in the treated groups (1.5%). There were no serious drug-related adverse events reported. The most common side-effect was rash, followed by phlebitis at the site of the intravenous infusion. Data were available on maternal length of stay for 15 studies. Hospital stay was reduced in the treated group by 0.47 days (95% CI 0.88 to 0.19). Duration of stay in the group receiving treatment ranged from 4.4 to 11.2 days, and for the no treatment group 5.2 to 12.1 days. Overall there was insufficient information presented to be able to compare the costs of antibiotic treatment with no treatment.

Despite the large number of trials, different populations and different antibiotic regimens, there was no statistically significant heterogeneity among the results of the studies for most outcomes. However, heterogeneity was present for 'fever', 'endometritis' and 'days in hospital (mother)' and for these outcomes, a random effects model was used.

Given the strength of the association between antibiotics and the outcomes, a sensitivity analysis incorporating a measure of study quality would not be expected to change the conclusions.

DISCUSSION

No conclusions can be made from this review about the relative effectiveness of different antibiotic regimens (see review: Antibiotic prophylaxis regimens and drugs for cesarean section (Hopkins 2002)).

Although serious complications (such as bacteremia) were uncommon following an elective cesarean section, the overall rate of febrile morbidity in the untreated control groups included in this review for an elective section was 15.6%, for wound infection 8.51% and for endometritis 4.62%. The National Nosocomial Infections Surveillance (NNIS) System reports rates of surgical site infection for cesarean section of 3.35% when there are no risk factors present for infection (risk index 0) (NNIS 2000). The

rate of surgical site infection following a high risk cesarean section (risk index category two and three) from the NNIS database is 8.11%. These rates, when compared with infection rates following other surgical procedures that are collected as part of the NNIS system, are high. Given the number of operative deliveries performed, these rates translate into very large numbers of women with an infectious complication following delivery and significant costs and morbidity.

Some obstetrical units may perceive they have a very low rate of infection after elective procedures and do not consider routine prophylaxis is necessary. These units should ensure they have carefully followed up all women after discharge to ensure all late infections have been included, especially important given the early discharge policy of many units. Only in this situation, where the rate is known to be low and where no specific high risk factors have been identified, would it be acceptable for a unit to decide not to administer antibiotics to any particular group of women.

Because the estimate of the number of women needed to treat to prevent one infection will depend on the baseline risk of infection, fewer women undergoing an emergency section, where the risk of infection is higher, are needed to be treated to prevent an infectious outcome than women undergoing an elective procedure. Generally the side effects of a single antibiotic dose are minor, but rarely serious allergic reactions can occur and be fatal. Although the risk of side-effects reported in these studies was low, these data were incompletely collected, making it difficult to know accurately the incidence of the adverse effects of treatment. There are also unknown and unquantified effects of antibiotic use that include changing the normal maternal flora, effects on the presentation of infection in the infant, and the development of antimicrobial resistance. There is evidence that the cervicovaginal flora is altered in patients undergoing cesarean section, whether antibiotics are used or not, but in the past no problem with managing resistant organisms in this setting was recognized (Galask 1987). While increased use of antimicrobial prophylaxis may be one factor in increasing antimicrobial resistance (Shlaes 1997), there are no data supporting the contention that appropriate use of short course antimicrobial prophylaxis will cause significant bacterial resistance nor evidence that a policy of antibiotic prophylaxis for cesarean section has harmful effects that outweigh its benefits, even in those women perceived to be at low risk. Optimizing the choice and the duration of prophylactic antibiotic therapy is recommended as one strategy to prevent antimicrobial resistance (Shlaes 1997). Trends in antibiotic resistance should be monitored, reported and used to establish practice guidelines and monitor institutional policies. Susceptibility testing of significant bacterial isolates should guide antimicrobial therapy of individual women who develop infection despite prophylaxis.

While febrile morbidity is common after cesarean section, few of these women will have positive bacterial cultures or a specific indication for antimicrobial treatment, but these women are often

investigated further. Specimens for bacterial culture may be collected and empiric antibiotic therapy started. This review could not address the cost of this strategy. In those studies, however, that did report the rate of the additional use of antibiotics and/or costs, there were significant differences with more days of antibiotics being prescribed to the women who had not received prophylaxis. The cost impact of the difference in fever between the two groups cannot, therefore, be ignored.

This review included in its definition of an elective cesarean section those patients not in labour but with ruptured membranes for less than six hours, included studies that did not have a placebo arm and included studies that used antibiotic irrigation as well as systemic agents. A recent published meta-analysis (Chelmow 2001) that used an expanded search strategy to identify additional relevant studies, and included only placebo controlled studies of systemic antibiotics in women undergoing elective cesarean section who were nonlaboring with intact membranes, clearly showed a reduction in infections in this low risk population relative risk (RR) for endometritis 0.05 (95% confidence interval (CI) 0.01 to 0.38) and supports the conclusion of this review.

Inconsistent adherence to policies for administering antibiotic prophylaxis are reported (Pedersen 1996; Huskins 2001; Mah 2001) but simple quality improvement methods have been demonstrated to improve adherence with overall and timely administration of prophylaxis and reduce the infection rate (Weinberg 2001). It was also shown in this study that a program that introduced a policy of universal prophylaxis for all women undergoing a cesarean section was more effective than one that required the obstetrician to decide whether a woman was high risk and mandated prophylaxis only for the high-risk women. In a recent prospective cohort study from a high risk obstetrical unit in New York state, absence of antibiotic prophylaxis was identified by multiple logistic regression analysis as being independently associated with surgical site infection after cesarean section for both high risk women (RR 1.7; 95% CI 1.1-2.5) and low risk women (RR 2.1; 95% CI 1.3-3.3) and was identified as one of two modifiable factors (the other being fewer prenatal visits) (Killian 2001).

In all but a couple of the studies included in this review, antibiotics were administered after the cord was clamped in an attempt to reduce antibiotic exposure in the infant. It has, however, been shown that the lowest risk of surgical wound infection is associated with antibiotics administered in the pre-operative period as compared with the perioperative or postoperative period (Classen 1992). Although an increase in infectious outcomes when the antibiotic is administered after the cord was clamped has not been shown in the studies that have compared preoperative administration with antibiotics administered after cord clamping, these studies have been small with too few outcomes to exclude a clinically important difference (Gordon 1979; Cunningham 1983; Wax 1997). In the absence of evidence showing a difference in maternal in-

fections or harmful effects in the infant, either approach can be recommended.

AUTHORS' CONCLUSIONS

Implications for practice

Prophylactic antibiotics will reduce the incidence of endometritis following both elective and non-elective cesarean section by two thirds to three quarters and the incidence of wound infection by up to three quarters. Post-partum febrile morbidity and the incidence of urinary tract infections are also decreased. Fewer serious complications will occur. All units should have a policy that recommends the administration of prophylactic antibiotics for women undergoing cesarean section. Obstetrical units should collect information on infection rates following cesarean section as an important quality indicator.

Implications for research

Further placebo controlled trials of the effectiveness of antibiotics with cesarean section are not ethically justified. Research should concentrate on methods to implement effective policies of routine prophylaxis for women undergoing cesarean section. Rates of infection following cesarean section are higher than for many other surgical procedures, even with a policy of uniform prophylaxis. Future research should look at interventions to reduce further the incidence of infection from that achieved with our current approach to antibiotic prophylaxis, eg the topical vaginal administration of metronidazole (Pitt 2001) and determine the role of surgical technique, pre- and intra-operative preparation and infection control policies on infection rates.

There is the potential opportunity for a cost-effective analysis to be performed in a unit where routine prophylactic antibiotics are not administered to women undergoing an elective cesarean section and where the risk of infection is very low, in an attempt to identify women at increased risk of infection in whom prophylaxis may be cost-effective. However, there is currently no evidence to support such a strategy. Because of local variation in practice and patients, the results of such research will likely only be applicable to an individual unit and not generalizable.

Better data on the safety of the intervention for the mother and infant are needed. Studies should be undertaken to determine what role antimicrobial prophylactic regimens have in the development of antimicrobial resistance. Research into the perceptions of the advantages and disadvantages of the intervention from the perspective of the woman and the healthcare provider will help define educational and research needs.

There is a need for more information about the role of bacterial vaginosis and infectious complications following cesarean section and whether this has implications for current prophylactic recommendations.

FEEDBACK

Griffin, July 1999

Summary

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

Summary of comments from Chris Griffin, July 1999.

Author's reply

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

Contributors

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

POTENTIAL CONFLICT OF INTEREST

None known.

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**Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	Adeleye 1981
Methods	'Divided randomly into two groups'; not placebo-controlled. Imbalance in group size not accounted for (58 vs 48).
Participants	Both elective and non-elective cesarean deliveries. Exclusion criteria: fever or obvious infection before operation. Setting: University College Hospital, Ibadan, Nigeria. Majority of patients from low socio-economic class.
Interventions	Ampicillin 500mg before operation and 250mg 6 hourly for at least 7 days (intramuscularly until able to take orally) (n = 58) versus no antibiotics unless temperature 38 degrees C after the third postoperative day (n = 48). Both groups received curative doses of chloroquine.
Outcomes	Wound infection; urinary tract infection (not defined further); 'genital sepsis' (not defined further).
Notes	Episodes of 'genital sepsis' classified as endometritis. Prophylaxis continued for 7 days.
Allocation concealment	B – Unclear

Study	Allen 1972
Methods	Randomized list of placebo or drug, kept in hospital pharmacy; code not broken until after patient classified as 'morbid' or 'non-morbid'; placebo-controlled.
Participants	Women undergoing cesarean section (criteria not specified). Exclusion: evidence of clinical infection, history of penicillin allergy. Setting: Johns Hopkins University, Baltimore, US; August 1970 - January 1971.

Characteristics of included studies (Continued)

Interventions	Cephalothin 1g IV on call to operating room, further 2g IV intra-operatively and every 6 hours for 48 hours, then 500mg IM for additional 72 hours (n = 5) versus placebo (n = 7).
Outcomes	Morbidity (temperature > 100.9 degrees fahrenheit twice, 6 hours apart after first 48 hours or other clinical signs of infection); not separated. For this review, the authors' definition of morbidity has been classified as fever.
Notes	Part of a larger randomized trial of prophylactic antibiotics in gynecologic surgery; most patients (87%) were undergoing hysterectomy; only 12/300 patients enrolled underwent cesarean section.
Allocation concealment	A – Adequate

Study	Apuzzio 1982
Methods	Double blind, placebo controlled. 'Randomly divided into 2 groups'. Discrepancy in group numbers (139 vs 120) not accounted for.
Participants	Both elective and non-elective cesarean deliveries. Exclusion criteria: antibiotics within 2 weeks; pyrexia; any visible infection; penicillin allergy; known medical illness that might cause pyrexia; internal fetal scalp or uterine monitoring. Setting: College Hospital, New Jersey, October 1977 to June 1980. Women 'predominantly black (90%) and socioeconomically disadvantaged'.
Interventions	Ticarcillin 6g intravenously within 15 minutes of cord clamping (n = 139) versus saline placebo (n = 120). Subset of 22 in each group received ticarcillin 3g/saline 6-8 hours postoperatively (results similar so authors combined results with single dose group). No postoperative antibiotics unless pyrexial >38 degrees C after day 1.
Outcomes	Endomyometritis (pyrexia, uterine tenderness and no evidence of other infection).
Notes	Authors' definition of low and high risk not comparable to definitions for elective/non-elective used in this review. Results for adolescent group (aged 15-18) reported in J Adolescent Health Care 1984;5:163-166. In that study, incidence of endomyometritis in elective section: 0% for treatment vs 43% for placebo (numbers not given).
Allocation concealment	B – Unclear

Study	Bagratee 2001
Methods	Randomized (computer-based allocation), double-blind, placebo controlled. All patients accounted for; intent to treat analysis performed.
Participants	Women undergoing elective cesarean delivery. Exclusion: prior antibiotics within 2 weeks, allergy to penicillin or cephalosporin, rupture of membranes. Setting: Durban, South Africa.
Interventions	Cefoxitin (2g IV after cord clamping) (n = 237) vs matching placebo (n = 238).
Outcomes	Febrile morbidity (oral temperature >38 degrees C twice 6 hours apart after first 24 hours); wound infection (wound cellulitis, erythema, discharge with or without fever); endometritis (fever, uterine tenderness, mal-odorous lochia); urinary tract infection (fever and positive urine culture); pneumonia; duration of hospital stay.
Notes	11% were HIV positive; Staphylococcus aureus most common pathogen (43%) isolated.
Allocation concealment	A – Adequate

Study	Bibi 1994
Methods	Allocation using random number table; not placebo controlled.
Participants	Women undergoing elective cesarean section or labour <12 hours.

Characteristics of included studies (Continued)

	Exclusion criteria: diagnosed amniotic infection; pyrexia >38 degrees C; antibiotics within 3 days; allergy to beta lactam antibiotics; cardiac disease; diabetes. Setting: Sousse Hospital, Tunisia, February to July 1991.
Interventions	Cephapirine 1g IV with induction of anaesthesia and 6 hours after operation, gentamycin 80mg IM with induction, metronidazole 500mg IV with induction (n = 133), versus no treatment (n = 136).
Outcomes	Endometritis; wound infection; pyrexia only (>38 degrees C 48 hours after surgery): antibiotic 4/133 vs control 9/136; septicemia (0/133 vs 3/136, included as serious morbidity); duration of hospital stay (antibiotic 5.36 days vs control 6.21, p = 0.03, variance not given).
Notes	
Allocation concealment	B – Unclear

Study	Bilgin 1998
Methods	Allocated using last digit of patient's file number to treatment or no treatment. No dropouts.
Participants	Women undergoing cesarean section due to acute fetal distress. Setting: Bursa, Turkey.
Interventions	Ceftriaxone 1g (n = 25) vs mezlocillin 2g (n = 23) vs clindamycin 600mg and amikacin 500mg (n = 18) vs sulbactam ampicillin 1g (n = 25) intravenously after clamping of the cord vs no treatment (n = 28).
Outcomes	Wound infection (redness, tenderness, pain and purulent discharge); urinary tract infection (renal angle tenderness, fever, dysuria and pyuria); endometritis (vaginal spotting, purulent discharge with fever and pain) plus positive cultures.
Notes	
Allocation concealment	C – Inadequate

Study	Bourgeois 1985
Methods	Randomized (computer-generated), partially double blind placebo-controlled (3 groups: antibiotic irrigation, saline placebo irrigation, no irrigation). As the objective of this review is to compare antibiotic with no antibiotic, rather than the effect of irrigation, only the first 2 groups are compared (double blind comparison).
Participants	Both 'low risk' (labor < 6 hours) and 'high risk' (>6 hours) women undergoing cesarean section. Exclusion criteria: allergy to penicillin or cephalosporin; antibiotic use within 7 days; antibiotics required for other reasons; pyrexia >38 degrees C; foul amniotic fluid. Setting: Charlottesville, Virginia, USA, initiated March 1981; almost all were indigent women.
Interventions	Irrigation of the uterus and peritoneal cavity with 2g cefamandole in 1000ml normal saline (n = 73), versus saline placebo (n = 75).
Outcomes	Metritis (pyrexia >38 degrees C twice 8 hours apart, after 24 hours plus abnormal uterine tenderness, without another apparent source); duration of maternal stay (treatment 5.29 days vs placebo 6.32 days, variance could not be calculated).
Notes	Authors' definition of low and high risk do not correspond to those used for elective/non-elective in this review. No treated patients developed evidence of drug reaction. There were no serious infections (pelvic abscess or phlebitis) in either group.
Allocation concealment	A – Adequate

Study	Carl 2000
Methods	Randomly allocated (abstract only; no further details).
Participants	Women undergoing high-risk cesarean section.

Characteristics of included studies (Continued)

	Setting: Texas, USA.
Interventions	Cefazolin 2g in 1000ml irrigation (n = 20) vs normal saline 1000ml irrigation (n = 20).
Outcomes	Wound infection, endometritis, urinary tract infection.
Notes	Follow up 4-6 weeks post-operatively.
Allocation concealment	B – Unclear

Study	Chan 1989
Methods	'Double blind' randomized trial (the anaesthetist was not blind); list of random numbers consulted by nurse.
Participants	All women undergoing cesarean section. Exclusion criteria: receiving antibiotics; pyrexia >37.4 degrees C; diagnosed infection; increased risk of infection, eg diabetes; known sensitivity to the antibiotics. Mostly suburban or rural Chinese women of lower or middle class. Setting: Prince of Wales Hospital, Hong Kong; October 1986 to February 1987.
Interventions	Intravenous therapy at time of induction of anaesthesia: ampicillin 1g (n = 96); ampicillin 1g and metronidazole 500mg (n = 104); ampicillin 1g and salbactam 500mg (n = 99), versus placebo (normal saline) (n = 101). Results of the three treatment groups combined.
Outcomes	Febrile morbidity (oral temperature of more than 38 degrees C at least twice after day 1); wound infection (induration, serosanguinous discharge or dehiscence with purulent discharge); urinary tract infection (positive culture); genital tract infection (pain and uterine tenderness, purulent uterine discharge with microbiological confirmation); any infection anywhere (antibiotic 75/299 vs placebo 28/101); post-operative antibiotic use (22/299 vs 9/101).
Notes	Only moderate or prolonged febrile morbidity (as defined) included.
Allocation concealment	B – Unclear

Study	Conover 1984
Methods	Double blind placebo controlled, computer generated sequence. Allocation to irrigation or intravenous route according to social security number. Imbalance in randomized groups not accounted for (irrigation: cefoxitin 37 vs saline 23; overall 68 vs 56).
Participants	Women at increased risk of post-cesarean section endometritis (in labor or with ruptured membranes). Classified as non-elective for this review. Exclusion criteria: allergy to penicillin or cephalosporins; antibiotic use within 48 hours; separate indication for use of antibiotics; temperature >38 degrees C; chorioamnionitis; pyuria. Setting: Naval Hospital, San Diego, California; March to November 1982.
Interventions	Administration by irrigation of uterus and peritoneal cavity with 2g cefoxitin in 500ml saline (n = 37), versus 500ml normal saline (n = 23), or intravenously after clamping of the umbilical cord, cefoxitin 2g (n = 31) versus saline (n = 33). Irrigation and intravenous groups combined for this review.
Outcomes	Endometritis (febrile morbidity and uterine tenderness); total infection-related morbidity (cefoxitin 10/68 vs saline 14/56); fever index; duration of intravenous antibiotics; additional antibiotics; days in hospital (no difference, variance not given).
Notes	One woman developed an allergic reaction to cefoxitin (acute pruritic rash). There were two episodes of bacteremia (both in placebo groups); there were no episodes of septic pelvic thrombophlebitis nor drainage of pelvic abscess in either group.
Allocation concealment	A – Adequate

Study	Cormier 1989
Methods	Allocated by sealed envelopes; not blinded or placebo controlled.

Characteristics of included studies (Continued)

Participants	Women undergoing cesarean section; both elective and non-elective deliveries. Exclusion criteria: allergy to beta-lactam antibiotics; pyrexia; indication for antibiotics. Setting: Hopital Pellegrin, Bordeaux, France.
Interventions	Cefotetan 2g after clamping of umbilical cord (n = 55) versus no antibiotic (n = 55).
Outcomes	Endometritis; urinary infection; local complications; fever only (cefotetan 0/55 vs control 6/55); antibiotic therapy (10/55 vs 25/55); mean days in hospital (10.0 vs 10.2, no variance given).
Notes	
Allocation concealment	B – Unclear

Study D'Angelo 1980

Methods	'Randomly assigned', no details given; not placebo-controlled.
Participants	Women in labour with ruptured membranes requiring internal monitoring (non-elective delivery). Exclusion criteria: evidence of infection; penicillin or cephalosporin allergy. Setting: Cleveland, Ohio, USA.
Interventions	Short course keftol (1g intravenously 6 hourly for 24 hours, n = 24); long course (keftol 1g intravenously for 8 or more doses and keftol 500mg orally 6 hourly for 5 days, n = 25); versus no prophylactic antibiotics. Short and long courses combined for this review.
Outcomes	Endometritis and/or wound infection (antibiotic 12/49 vs control 20/31).
Notes	It was possible to deduce the rate of endometritis alone, but not wound infection, for this review. One late infectious complication (wound dehiscence) in control group.
Allocation concealment	B – Unclear

Study Dashow 1986

Methods	Double blind placebo controlled trial. Computer-generated numbers using the mixed congruential method.
Participants	All women undergoing cesarean section. Exclusion criteria: penicillin or cephalosporin allergy; antibiotic therapy; known infectious process. Setting: Madigan Army Medical Centre, Tacoma, Washington, USA. December 1982 to May 1984.
Interventions	Irrigation during cesarean section with 2g of either cephalixin sodium (n = 79), cefamandole nafate (n = 70), moxalactam disodium (n = 64) or ampicillin sodium (n = 70), versus saline (n = 77). A vitamin was added to each solution for disguise. The antibiotic groups have been considered together in this review.
Outcomes	Fever (>38 degrees C twice 6 hours apart, excluding the first 24 hours); endomyometritis (pyrexia >37.8 degrees C, uterine tenderness and pelvic peritoneal irritation without other localising signs of irritation; urinary tract infection (positive culture); wound infection; fever index; all infection-related morbidity; therapeutic antibiotics; mean postoperative days (variance not given).
Notes	Three episodes of pelvic thrombophlebitis (all in treated groups). Results were given for all women and women in labour, both high risk (corresponding to the category of non-elective deliveries) and all labour. The data for elective deliveries were deduced from these.
Allocation concealment	A – Adequate

Study De Boer 1989

Methods	Randomized, double blind, placebo-controlled. 7/189 patients initially randomized were not included in analysis.
Participants	All patients undergoing cesarean section. Exclusion criteria: clinical infection. Setting: Chogoria Hospital, Kenya; December 1983 to June 1985.

Characteristics of included studies (Continued)

Interventions	Metronidazole 1g rectal suppository 10-45 minutes before and 8 hours after procedure (n = 91) versus placebo suppository (n = 91).
Outcomes	Fever (>37.9 degrees C on at least one occasion); wound infection; mean febrile days (0.56 for treatment vs 1.23 for control), hospital days, any antibiotic use (18/91 vs 23/91).
Notes	Elective cesarean section not defined. No adverse events on mother or babies noted. There was one grade 3 wound (defined as deep pelvic abscess or evidence of local or generalized peritonitis) in the treatment group as compared with three in the placebo group (classified as serious infectious morbidity).
Allocation concealment	B – Unclear

Study Dillon 1981

Methods	Double-blind, placebo-controlled; numbered packages randomized by pharmacy; 9/110 'packages' not included (either damaged or patients failed to meet inclusion criteria); imbalance in group size (46-placebo vs 55-cefoxitin) not explained.
Participants	All women undergoing cesarean section (one third elective). Exclusion: evidence of active infection, penicillin or cephalosporin allergy; recent antibiotic treatment. Setting: Children's Hospital of Buffalo, USA; women enrolled between September 1979 and April 1980.
Interventions	Cefoxitin 2g IV (n = 46) versus saline placebo (n = 55) after clamping the umbilical cord and at 4 and 10 hours post-operatively.
Outcomes	Febrile morbidity (temperature >38 degrees C twice 6 hours apart after first 24 hours); endometritis (fever, uterine tenderness, leukocytosis); wound infection (fever, cellulitis, exudate); maternal length of stay.
Notes	No serious life-threatening infection in either group; no drug-related side-effects.
Allocation concealment	A – Adequate

Study Duff 1980

Methods	Double-blind, randomized, prepared by hospital pharmacy; placebo-controlled. 23/80 excluded because of errors in dispensation of medication.
Participants	All women undergoing either primary or repeat cesarean section (44% elective). Exclusion: penicillin allergy; chorioamnionitis prior to surgery. Setting: Walter Reed Army Medical Center, Washington DC; October 1976 and March 1977.
Interventions	Ampicillin 1g IV prior to surgery and 6 and 12 hours post-operatively (n = 26) versus placebo (n = 31).
Outcomes	Febrile morbidity (>100.3 degrees fahrenheit twice 6 hours apart after first 24 hours); endomyometritis (fever, uterine and abdominal tenderness, purulent lochia); urinary tract infection (positive culture); wound infection (induration, erythema and warmth with purulent drainage); need for antibiotics (treatment 3/26 vs placebo 13/31); maternal hospital stay (6.03 vs 6.9; no variance given).
Notes	
Allocation concealment	A – Adequate

Study Duff 1982

Methods	Randomized in double-blind fashion; placebo-controlled.
Participants	Women undergoing cesarean section who were not in labor and did not have ruptured membranes (elective). Setting: Washington, DC. US From January 1970 to June 1980.
Interventions	Ampicillin 1g 30 min prior to surgery and at 4 and 8 hours post-operatively (n = 42) versus placebo solution (n = 40).

Characteristics of included studies (Continued)

Outcomes	Febrile morbidity (>100.4 degrees fahrenheit twice 6 hours apart after the first 24 hours); endomyometritis (fever, uterine and adnexal tenderness, purulent lochia); urinary tract infection; wound infection (induration, erythema and warmth with purulent drainage); need for antibiotics (treatment 1/42 vs placebo 6/40); maternal hospital stay (4.3 vs 4.6; no variance given).
Notes	No life-threatening infection related complications nor bacteremic episodes in either group.
Allocation concealment	B – Unclear

Study Elliott 1986

Methods	Randomized, using a table of random numbers; not placebo-controlled. Allocated to either intravenous antibiotic, antibiotic irrigation, both routes or no treatment.
Participants	Women in active labor or ruptured membranes and at least one digital vaginal examination (categorized as non-elective in this review although duration of membrane rupture not stated). Exclusion: allergy to penicillin or cephalosporin, fever >37.7 degrees C with suspicion of chorioamnionitis; antibiotic use within two weeks. Setting: Letterman Army Medical Center, California; Womack Army Community Hospital, North Carolina.
Interventions	Cefoxitin 2g IV after clamping the cord, repeated every six hours for 48 hours (n = 39) versus uterine and peritoneal lavage with 2g cefoxitin after delivery of the placenta (n = 42) versus irrigation plus intravenous therapy (n = 38) versus no therapy (n = 39). The three treatment groups have been combined in this review.
Outcomes	Febrile morbidity (>37.9 degrees C twice 6 hours apart after first 24 hours); endometritis (fever and uterine tenderness); urinary tract infection (positive culture); wound infection (including fever, cellulitis and exudate); hospital stay (treatment 4.86 vs control 5.2; variance could not be calculated).
Notes	3 episodes of septicemia reported in control group vs none in treatment groups. No antibiotic reactions reported.
Allocation concealment	B – Unclear

Study Engel 1984

Methods	Assigned at random to either a control group or the study group by computer-generated list of random numbers; not placebo-controlled.
Participants	Women undergoing cesarean section. Exclusion criteria: severe penicillin allergy, renal insufficiency, antibiotic use, amniotic infection. Setting: Nordwest Hospital, Frankfurt, West Germany.
Interventions	Mezlocillin 4g and oxacillin 2g every 8 hours after clamping of the cord for three doses (n = 50) vs no treatment (n = 50).
Outcomes	Endometritis, urinary tract infections, wound infections.
Notes	Detailed pre- and post- antibiotic microbiological cultures were performed; there were fewer gram positive cocci and more gram negative rods in cervical cultures of the treated group; more break-through infections in the treated group were with mezlocillin-resistant organisms.
Allocation concealment	A – Adequate

Study Escobedo 1991

Methods	Double blind, randomized by computerized tables; matching placebo doses; 3 patients excluded for inadequate follow-up (group allocation not provided).
Participants	Women undergoing cesarean section (labor <12 hours, membrane rupture <12 hours, <7 vaginal exams). Exclusion: any antibiotic within 2 weeks, fever, clinical evidence of infection. Setting: Mexico.

Characteristics of included studies (Continued)

Interventions	Ampicillin 1g intravenously every six hours x 3 then 1g every 6 hours x 7 days (n = 23) vs ampicillin 1g every 6 hours x 3 doses then placebo (n = 37) vs placebo (n = 31).
Outcomes	Fever >38 degrees C x 2 at least 6 hours apart after first 24 hours; endometritis (temperature >38 degrees C, purulent lochia, pain on internal examination); wound infection (increased warmth, size or colour of wound, or purulent secretions); urine infection (dysuria and positive culture).
Notes	No explanation provided for unequal size groups.
Allocation concealment	A – Adequate

Study	Fugere 1983
Methods	Randomized (number allocated randomly to each of 90 boxes) placebo-controlled (coloured vitamin added to placebo solution), double blind.
Participants	Women undergoing non-elective cesarean section. Exclusion: not in labour with intact membranes, allergy to cephalosporins, antibiotic use within 48 hours, fever, ruptured membranes for >36 hours. Setting: Hopital Saint-Luc, Montreal, Canada; September 1980 to November 1981.
Interventions	Cefoxitin 2g IV (n = 30) versus cefazolin 1g IV (n = 30) versus placebo (n = 30) at clamping of the cord and at 6 and 12 hours later. Both treatment groups have been combined.
Outcomes	Endometritis, wound infection, urinary tract infection (symptoms or two successive positive cultures) septicemia, pelvic abscess, pelvic thrombophlebitis. Follow-up at 6 weeks. No side effects observed.
Notes	There were no serious infections in any of the groups. In the placebo and cefazolin groups there was no increase in aerobic bacterial colonization of the cervix after 4 days but there was an increase in colonization by anaerobes; the opposite occurred in the group receiving cefoxitin.
Allocation concealment	B – Unclear

Study	Gall 1979
Methods	Randomized, double-blind, placebo-controlled.
Participants	All women undergoing either a repeat cesarean section or in labor. Exclusion: clinical infection, ruptured membranes for >12 hours, prior antibiotics within 48 hours, renal or hepatic disease. Setting: North Carolina, US.
Interventions	Cefazolin 1g intramuscularly pre-operatively and cephalothin 2g intravenously at 6, 12, and 24 hours after first dose (n = 46) versus placebo (n = 49).
Outcomes	Wound infection (cellulitis, purulent exudate, intraperitoneal abscess or peritonitis); endometritis; urinary tract infection; maternal hospital stay.
Notes	No minor side-effects (rash or pruritus) or major reactions (anaphylaxis) observed. 4 patients (all in control group) had septicemia [counted as serious morbidity].
Allocation concealment	B – Unclear

Study	Ganesh 1986
Methods	'Randomly divided'; no further details; placebo-controlled.
Participants	Women < 21 years old undergoing cesarean section. Exclusion: antibiotic use within 2 weeks; active infection or fever at delivery; penicillin or sulfa allergy; internal fetal monitoring. Setting: University Hospital, New Jersey; November 1983 and December 1984; lower socioeconomic class (90% black).

Characteristics of included studies (Continued)

Interventions	Trimethoprim 240mg and sulfamethoxazole 1200mg intravenously after clamping of cord (n = 29) versus placebo (n = 28).
Outcomes	Endomyometritis (fever >100.3 degrees fahrenheit twice within 24 hours after first day), uterine tenderness, absence of another focus); urinary tract infection (fever and positive culture); wound infection (fever, abnormal appearing wound with cellulitis or a wound draining purulent material).
Notes	Authors' definition of high risk not comparable with that used in this review. The incidence of urinary tract infection and wound infection was similar between the groups (numbers not given).
Allocation concealment	B – Unclear

Study Gerstner 1980

Methods	Women randomized (no further details provided in translation); not placebo-controlled.
Participants	Women undergoing cesarean section. Setting: Universitats-Frauenklinik Wien, Austria; August 1979 and April 1980.
Interventions	Metronidazole (n = 53) versus no treatment (n = 50).
Outcomes	Fever (>38 degrees C on two subsequent days); wound infection; endometritis; additional use of antibiotics (treatment 13/53 vs control 22/50); maternal hospital days.
Notes	Full translation pending.
Allocation concealment	B – Unclear

Study Gibbs 1972

Methods	Random allocation is presumed although method not described; placebo-controlled; antibiotics prepared in coded identical vials by pharmacy; 17 patients initially randomized not included in outcome (? all in the treatment group).
Participants	Women undergoing primary cesarean section or repeat section. Exclusion: penicillin allergy, fever in labor. Setting: University of Pennsylvania; November 1971 and April 1972.
Interventions	Ampicillin 1g, methicillin 1g and kanamycin 0.5g intramuscularly 15 - 30 minutes before, and at 2 and 8 hours after delivery (n = 33) versus placebo (n = 28).
Outcomes	Endometritis (fever and uterine tenderness or fever and pathogenic organism without other cause); urinary tract infection; wound infection (fever, cellulitis and exudate); morbidity [fever >100 degrees fahrenheit in two separate 24 hour periods after first post-partum day or positive post-operative urine culture of >100,000 colonies/ml] (treatment 9/33 vs placebo 17/28); maternal hospital stay (6.5 vs 6.9 days; no variance given).
Notes	Two serious infections: one pelvic abscess in treatment group, one septicemia in placebo group. Authors' definitions of repeat and primary section not comparable to those used for elective/non-elective in this review.
Allocation concealment	B – Unclear

Study Gibbs 1973

Methods	Randomized (although method not described); placebo-controlled; antibiotics prepared in coded identical vials by pharmacy.
Participants	Women undergoing primary cesarean section or repeat section. Exclusion: penicillin allergy, fever in labor, errors in giving medication. Setting: University of Pennsylvania; August 1972 and February 1973.
Interventions	Ampicillin 1g and kanamycin 0.5g intramuscularly 15 to 30 minutes before, and at 2 and 8 hours after delivery (n = 34) versus placebo (n = 34).

Characteristics of included studies (Continued)

Outcomes	Endometritis (fever and uterine tenderness or fever and pathogenic organism without other cause); urinary tract infection; wound infection (fever, cellulitis and exudate; any grade); morbidity [fever >100 degrees fahrenheit in two separate 24 hour periods after first post-partum day or positive post-operative urine culture of >100,000 colonies/ml] (treatment 8/34 vs placebo 22/34).
Notes	One pelvic abscess in placebo group. Authors' definitions of repeat and primary section not comparable to those used for elective/non-elective in this review, categorized as 'both'.
Allocation concealment	B – Unclear

Study	Gibbs 1981
Methods	'Randomized, double-blind', details not specified; placebo-controlled.
Participants	Women in labor with rupture of membranes (non-elective). Exclusion: infection, antibiotics within prior 3 days, allergy to penicillin or cephalosporin; no consent. Setting: Robert B Green Memorial Hospital, Texas, US; October 1978 and July 1979; patients indigent and predominantly Mexican-American.
Interventions	Cefamandole 2 g IV after cord clamping, and at 4 and 8 hours post-operatively (n = 50) versus identical appearing placebo (n = 50).
Outcomes	Endomyo(para)metritis; wound infection; maternal hospital stay; records reviewed 6 weeks to 6 months after discharge. Four episodes of bacteremia (1 in treatment group, 3 in placebo) have been categorized as serious outcomes.
Notes	No incidence of pelvic abscess or septic thrombophlebitis in either group. Increase in Enterobacteriaceae and enterococci and decrease in gram positive anaerobes and nonpathogens in prophylactic group. No adverse clinical or laboratory results attributable to treatment.
Allocation concealment	B – Unclear

Study	Gordon 1979
Methods	'At random'; not placebo-controlled, not double-blind; investigator not intimately involved with post-operative care.
Participants	Women undergoing cesarean section. Exclusion: emergency section, penicillin allergy, fever >38 degrees C, on antibiotics; declined to participate. Setting: San Bernadino county and University of California at Los Angeles Medical Centers; primarily indigent cases; enrolment started November 1976.
Interventions	Ampicillin 1g IV 15-30 minutes before surgery and at 2 and 8 hours post-operatively (n = 38) versus ampicillin 1g IV immediately after cord clamping and at 2 and 8 hours post-operatively (n = 40) versus no antibiotic (n = 36); results for both treatment groups combined.
Outcomes	Endometritis; wound infection; urinary tract infection; maternal hospital stay (5.1 and 4.7 for pre- and post-administration of antibiotics respectively vs 6.0 for no treatment, variance not given).
Notes	Although emergency cesarean sections were excluded, the women enrolled did not conform to our definition of an elective section. Information on neonatal morbidity collected; there were two infants with definite infections in mothers who received no antibiotics and one infection in an infant where antibiotics were given after cord clamping.
Allocation concealment	B – Unclear

Study	Gummerus 1984
Methods	'Randomly divided' (no details provided); placebo-controlled.
Participants	Women undergoing cesarean section; elective cesarean sections not included but definition not provided.

Characteristics of included studies (Continued)

	Exclusion: antibiotics prior to procedure. Setting: School of Midwifery, Helsinki, Finland. Patients enrolled from December 1981 to August 1982.
Interventions	Metronidazole 500mg intravenously after cutting of cord (n = 109) vs placebo (n = 110).
Outcomes	Wound infection, endometritis.
Notes	
Allocation concealment	B – Unclear

Study	Hager 1983
Methods	Randomized, double-blind manner, according to prenumbered envelopes maintained in the central pharmacy; placebo-controlled.
Participants	Women undergoing primary, nonelective cesarean section (while it appears most women were in labour and/or had ruptured membranes it is unclear whether all patients fulfilled our criteria for non-elective). Exclusion: antibiotic use within 7 days, penicillin or cephalosporin allergy. Setting: Central Baptist Hospital, Lexington, Kentucky, US.
Interventions	Cefamandole 500mg IV immediately after the cord was clamped, again in the recovery room and two more doses 6 hours apart (n = 43) versus identical-appearing placebo (n = 47).
Outcomes	Infectious morbidity (fever >100.3 degrees fahrenheit twice 6 hours apart after first 24 hours); endometritis (fever, uterine tenderness, and positive culture from endometrium); wound infection, urinary tract infection; maternal duration of stay (treatment 5.1 days vs placebo 5.4; not significant, no variance given).
Notes	There was one episode of bacteremia in the control group.
Allocation concealment	B – Unclear

Study	Hagglund 1989
Methods	Double-blind, randomized (method not described); placebo-controlled.
Participants	Women undergoing emergency cesarean section (during labor and/or after rupture of membranes). Exclusion: fever >38 degrees C, given antibiotics, chemotherapy or immunosuppressive therapy in prior 3 weeks, allergy to cephalosporins, alcohol or drug abuse, chronic disease of cardiovascular, renal, hepatic or gastrointestinal system, severe anemia. Setting: University Hospital, Lund Sweden, July 1983 and December 1986.
Interventions	Cefuroxime 1.5g IV at the start of the operation and 12 hours later (n = 80) versus saline placebo (n = 80).
Outcomes	Endometritis (fever >38 degrees C twice at least 1 hour apart, after the first post-operative day, and increased tenderness of the uterus); wound infection (redness, tenderness, increased heat and edema of wound); urinary tract infection.
Notes	There were no cases of septicemia or abscess formation observed in either group. Only 55% of women had ruptured membranes (number >6 hours not stated) and 77% were in labor; these definitions do not meet our criteria for non-elective section, categorized as 'both'.
Allocation concealment	B – Unclear

Study	Harger 1981
Methods	Randomized, double-blind, placebo-controlled; 'according to a random schedule'. 10/396 women initially randomized not included in final analysis (errors in protocol, two allergic to penicillin after first dose given and 2, who received cefoxitin, for infusion-related reactions); insufficient data provided to perform intent to treat analysis.
Participants	Women undergoing cesarean section after labor or rupture of membranes (method section unclear as to duration of ruptured membranes; it has been assumed that all women were in labor).

Characteristics of included studies (Continued)

	Exclusion: elective cesarean section without labor; already receiving antibiotics; fever or other evidence of infection; allergy to penicillin or cephalosporins; requiring endocarditis prophylaxis. Setting: Pittsburgh, Pennsylvania, US.
Interventions	Cefoxitin 2g intravenously after cord clamping, and at 6 and 12 hours after initial dose (n = 196) versus matching mannitol and riboflavin placebo (n = 196).
Outcomes	Febrile morbidity (fever >37.9 degrees C twice at least 4 hours apart after first post-operative day); endomyometritis (fever >38 degrees C with uterine tenderness, maternal white blood cell count >15000/cu mm, malodorous lochia and no apparent cause for fever); urinary tract infection; incision infection (purulent drainage with induration and tenderness); additional antibiotic therapy (treatment 26/196 vs placebo 68/190).
Notes	Increase in enterococci and decrease in Staphylococcus aureus, various streptococci, E. coli and a variety of anaerobes from infected sites in prophylactic group compared with placebo.
Allocation concealment	B – Unclear

Study Hawrylyshyn 1983

Methods	Randomized, double-blinded, placebo-controlled. 7 patients initially randomized excluded from analysis: 1 because of an error in drug administration and six because they became febrile and were treated within 8 hours of operation; insufficient data provided to perform intent-to-treat analysis.
Participants	Women undergoing cesarean section (at 'high' risk because of ruptured membranes in active labor); classified as 'non-elective'. Exclusion: febrile, antibiotic use in prior 24 hours; allergy to penicillin or cephalosporin; significant hepatic or renal disease. Setting: Mount Sinai Hospital, Toronto, Canada, July 1980-June 1981. Predominantly private, middle-class and in their late 20s.
Interventions	Cefoxitin 2g intravenously at time of cord clamping (n = 64) versus cefoxitin 2g at time of cord clamping and at 4 and 8 hours post-operatively (n = 60) versus identical-appearing placebo; both treatment groups combined in this analysis.
Outcomes	Febrile morbidity (>38 degrees C twice at least 8 hours apart, after first post-operative day); endometritis (fever, foul, excessive lochia or uterine tenderness); urinary tract infection (fever and positive culture); wound infection (fever, cellulitis or exudate with positive cultures).
Notes	No adverse drug reactions in cefoxitin groups, no septicemia in any group; four patients in placebo group were considered seriously ill (although do not fit the criteria for serious morbidity in this review) compared to none in treatment groups.
Allocation concealment	A – Adequate

Study Ismail 1990

Methods	Double-blind, randomized, placebo-controlled.
Participants	Undergoing cesarean section. Exclusion: preoperative fever, antibiotics within one week, membranes ruptured >36 hours, evidence of chorioamnionitis, penicillin or cephalosporin allergy. Setting: University of Illinois College of Medicine, Chicago, US (large, inner city hospital); majority of subjects black (40%) or Hispanic (60%).
Interventions	Cefoxitin 2g after cord clamped and at 4 and 8 hours (n = 74) versus placebo (n = 78).
Outcomes	Endometritis (fever and uterine tenderness or fever and pathologic organism without other focus); wound infection (fever, cellulitis and exudate); urinary tract infection (fever and symptoms or positive culture).
Notes	In the placebo group there were 8 episodes of serious morbidity (6 cases of sepsis; one pelvic abscess; one episode of pelvic thrombophlebitis) compared with one in the treated group (one episode of sepsis).

Characteristics of included studies (Continued)

Routine post-operative cultures were performed: enterococci were isolated from 30/68 cases who received cefoxitin vs 15/74 who received placebo; there was no change in the rate of cefoxitin resistance in Enterobacteriaceae from the stool after prophylaxis.

Allocation concealment B – Unclear

Study Jaffe 1985

Methods	Randomly assigned (method not stated); placebo controlled. It is unclear whether all patients randomized were included in the analysis.
Participants	Women undergoing cesarean section. Exclusion: women with active infection, allergy to penicillin and antibiotic treatment within 2 weeks. Setting: Kfar-Sava, Israel.
Interventions	Mezlocillin 5g intravenously during 30 minutes prior to surgery (n = 38) vs placebo (n = 40).
Outcomes	Febrile morbidity (>38 degrees C twice at least 4 hours apart after first 24 hours post-operative); endometritis (fever and uterine tenderness); urinary tract infection (single culture of >100,000 bacteria/ml); wound infection (redness, cellulitis, tenderness and exudate from incision).
Notes	Authors' definition of emergency not consistent with definitions used in this review (classified as 'both/undefined').
Allocation concealment	B – Unclear

Study Jakobi 1994

Methods	Randomized by computer program to one of two groups at time of their first antenatal visit; not placebo-controlled. Imbalance in group size not accounted for.
Participants	Low risk women requiring cesarean delivery (elective procedure, duration of membrane rupture <3 hours, no more than two vaginal examinations). Exclusion: required a drug other than cefazolin for prophylaxis, fever, membrane rupture >24 hours. Setting: Rambam Medical Center, Haifa, Israel.
Interventions	Cefazolin 1g after clamping of the cord (n = 167) versus no treatment (n = 140).
Outcomes	Febrile morbidity (fever >37.7 degrees C twice at least 4 hours apart after first 24 hours); endometritis (fever, uterine tenderness and abnormal lochia); urinary tract infection (fever and positive culture); wound infection (fever, cellulitis or exudate with positive culture); therapeutic antibiotic use (treatment group 6.5% versus 20% in control group, p <0.001).
Notes	Although some women were in labour at the time of the procedure (mean duration of labour 53 and 44 minutes in the two groups), the study population so closely resembles the criteria for elective cesarean section used in this review that the results have been included in the 'elective' category.
Allocation concealment	B – Unclear

Study Karhunen 1985

Methods	'Randomized according to a code'; placebo-controlled. 8 women excluded: 4 because they were febrile before the operation, four because of mistakes in administration; data not provided to perform intent to treat analysis.
Participants	Initially all women undergoing cesarean section (n = 80); thereafter women undergoing non-elective (ruptured membranes) section (n = 72). Setting: South Saimaa Central Hospital, Lappeenranta, Finland, May 1982-August 1983.
Interventions	Tinidazole 500mg IV at cord clamping (n = 75) versus identical placebo (n = 77).

Characteristics of included studies (Continued)

Outcomes	Febrile morbidity (>38 degrees C on 2 postoperative days, excluding the first); endometritis (fever, foul lochia or uterine tenderness); wound infection (fever, cellulitis or exudate); urinary tract infection (fever and positive culture).
Notes	Authors' definition of non-elective (ruptured membranes) and elective (unruptured membranes) not consistent with the definitions used in this review; classified in this review as 'both'. Newborn infants observed for effects of tinidazole (although data not given).
Allocation concealment	A – Adequate

Study	Kellum 1985
Methods	Randomized by last digit of hospital admission number to no irrigation, antibiotic irrigation or saline irrigation (placebo-controlled). As the objective of this review is to compare antibiotic with no antibiotic, rather than the effect of irrigation, the two irrigation groups are compared. Follow-up given for only 77/84 of treatment and 53/86 of placebo group for outcome of serious infection, without explanation; intent to treat analysis has been performed.
Participants	Women undergoing nonelective cesarean section (including prolonged ruptured membranes and prolonged labor, as well as general risk factors such as poor nutrition and poverty). Exclusion: current antibiotics, known infectious process, allergy to cephalosporins. Setting: University of Mississippi Medical Center, September 1982-September 1983.
Interventions	Cefamandole 2g in 800ml saline irrigation during the procedure (n = 84) versus saline irrigation (n = 86) versus no treatment (n = 92); only first two groups included.
Outcomes	Febrile morbidity (>100.6 degrees fahrenheit twice 6 hours apart after first post-operative day); serious morbidity (fever and endomyometritis or abscess requiring IV antibiotics for resolution).
Notes	Authors' definition of high risk does not correspond to that used for non-elective in this review, classified as 'both'. The outcome of serious morbidity included endomyometritis and is classified as endometritis in this review.
Allocation concealment	C – Inadequate

Study	Kreutner 1978
Methods	'Random allocation', placebo controlled. 6 women initially randomized not included in analysis (non-adherence or noninfectious complications).
Participants	All women undergoing cesarean section (51/97 not in labor; 61/97 without ruptured membranes). Exclusion: signs of infection, allergy to penicillin or cephalosporin, antibiotics within 2 weeks; lack of consent. Setting: Medical University Hospital of South Carolina; November 1975-June 1976.
Interventions	Cefazolin 1g IV pre-operatively and at 2 and 8 hours post-operatively (n = 48) versus similar volume of placebo (n = 49).
Outcomes	Febrile morbidity (>100.3 degrees fahrenheit twice on any of first 10 post-partum days after the first); endometritis (fever and uterine tenderness, or fever and pathogen from endometrium without other cause); urinary tract infection (fever or positive culture and symptoms); wound infection (fever, cellulitis and/or exudate).
Notes	Aerobic isolates unchanged, fewer anaerobes in patients given placebo; most pathogens isolated were resistant to cefazolin whether treatment or placebo given. There were two episodes of septicemia (both in placebo group).
Allocation concealment	B – Unclear

Study	Kristensen 1990
Methods	'Randomly allocated' using envelope containing empty vial or vial containing treatment; not placebo-controlled; women, attending physicians and study coordinators were 'blind'.

Characteristics of included studies (Continued)

Participants	Women undergoing nonelective cesarean section (58/201 without labour; 65/201 without ruptured membranes). Exclusion: fever, antibiotics within 7 days, penicillin or cephalosporin allergy. Setting: Odense University Hospital, Denmark, February 1987-March 1988.
Interventions	Cefuroxime 750mg IV after cord clamping (n = 102) versus no treatment (n = 99).
Outcomes	Febrile morbidity (>37.9 degrees C twice at least 6 hours apart after first post-operative day); endometritis (fever, uterine tenderness and abnormal lochia); wound infection (fever, cellulitis and/or purulent discharge); urinary tract infection; cost of post-operative antibiotics (treatment \$US0.69 vs control \$US7.47); maternal hospital stay (treatment 8.1 vs control 8.0, no variance given).
Notes	No woman had a severe infection such as pelvic abscess or septic pelvic thrombophlebitis.
Allocation concealment	B – Unclear

Study **Lapas 1988**

Methods	Double blind, placebo controlled.
Participants	Women undergoing elective or non-elective cesarean section. Age range 17-40 years. Exclusion criteria: allergy to metronidazole, amnionitis, and pyrexia. Setting: Athens, Greece.
Interventions	Metronidazole 500mg intravenously 2 hours or immediately preoperatively, 500 mg intraoperatively, 1000mg 8 hours postoperatively (n = 50), versus placebo (n = 50).
Outcomes	Wound infection; endometritis; inadequate wound healing (metronidazole 1/50 vs placebo 8/50); mean temperature (36.8 degrees C SD 1.02 vs 37.6, 1.03); duration of hospital stay.
Notes	Language: Bulgarian. Although the authors are not identical and the presentation of the data makes direct comparisons difficult, the description of the two studies cited is so similar that it is presumed the two citations refer to the same patient population.
Allocation concealment	B – Unclear

Study **Leonetti 1989**

Methods	'Randomly divided'; blinded, placebo-controlled.
Participants	Women undergoing primary cesarean section after onset of labour (corresponds to the definition of non-elective). Exclusion: febrile or infected, allergy to piperacillin. Setting: Jersey City Medical Center, New Jersey; predominantly lower socio-economic indigent women.
Interventions	Piperacillin 4g peri-operatively (n = 50) versus piperacillin 4g peri-operatively and at 4 and 8 hours post-operatively (n = 50) versus placebo (n = 50); both treatment groups combined in analysis.
Outcomes	Febrile morbidity (> 38.0 degrees C twice at least 6 hours apart after first post-operative day); endometritis (fever, tender uterus and purulent lochia); hospital stay (no significant difference, variance not given).
Notes	Use of saline or antibiotic lavage not allowed No adverse reactions reported with treatment.
Allocation concealment	B – Unclear

Study **Levin 1983**

Methods	Randomized (using lottery method), double-blind, placebo-controlled; four women excluded because of protocol deviations.
Participants	All women undergoing cesarean section (39/128 repeat section). Exclusion: fever or infection, allergy to antibiotics.

Characteristics of included studies (Continued)

	Setting: Kaiser-Permanente Medical Center-Santa Clara, California; February-June 1982.
Interventions	Cefoxitin 2g in 1L saline irrigation (n = 41) versus cephalixin 2g in 1L saline irrigation (n = 44) versus identical appearing placebo saline irrigation (n = 43) after delivery of the placenta; both treatment groups combined in the analysis.
Outcomes	Urinary tract infection (positive culture); wound infection (purulent wound discharge with or without wound separation); endometritis (fever >100.4 degrees fahrenheit after first post-operative day, uterine tenderness, foul smelling lochia without other source).
Notes	Follow-up for 8 weeks. One patient in placebo group developed septic pelvic thrombophlebitis and septic pulmonary emboli, classified as a serious complication.
Allocation concealment	A – Adequate

Study **Lewis 1990**

Methods	Random, double-blind, placebo-controlled; results on 15/227 women initially randomized not included in analysis.
Participants	Women undergoing elective and nonelective cesarean section. Exclusion: antibiotic use within 2 weeks, allergy to penicillin. Setting: Louisiana State University Hospital; 90% indigent population, July 1985-January 1986.
Interventions	Ticarcillin 5g in 1200ml saline irrigation (n = 112) versus saline irrigation (n = 100).
Outcomes	Febrile morbidity (>100.3 degrees fahrenheit twice at least 4 hours apart after first post-operative day); endomyometritis, wound infection, urinary tract infection, septicemia, maternal hospital stay (treatment 4.5 vs placebo 5.4, no variance given).
Notes	Definition of elective and nonelective cesarean section not provided. There were 3 episodes of septicemia in those women undergoing emergency section (2 in the control group and one in the placebo group).
Allocation concealment	B – Unclear

Study **Mahomed 1988**

Methods	Randomly allocated (using randomized list of treatment numbers), double-blind, placebo-controlled.
Participants	All women undergoing elective cesarean section (before onset of labour or rupture of membranes; corresponds to our definition of elective). Setting: University of Zimbabwe; patients enrolled between November 1986 and March 1987.
Interventions	Crystalline penicillin 2MU and chloramphenicol 500mg pre-operatively (n = 115) versus matching placebo (n = 117).
Outcomes	Fever (>37.9 degrees C twice at least 4 hours apart after first post-operative day); wound sepsis (graded as abnormal erythema and/or induration, oozing wound without frank pus or pus formation); endomyometritis (fever, uterine tenderness and foul-smelling lochia), pelvic abscess formation, bacteremia; maternal hospital stay (treatment 5.43 vs placebo 6.18, variance not given).
Notes	No woman developed pelvic abscess nor required a laparotomy.
Allocation concealment	A – Adequate

Study **Mallaret 1990**

Methods	Randomized trial 'by drawing of lots', placebo-controlled.
Participants	'Low risk' women, undergoing cesarean section (27% in labour). Exclusion: allergy to beta-lactam antibiotics, receipt of antibiotics within 3 days; ruptured membranes >12 hours; fever, amniotic infection.

Characteristics of included studies (Continued)

	Setting: Grenoble, France, July 1986-December 1987.
Interventions	Cefotetan 1g IV at the time of cord clamping (n = 136) versus placebo injection (n = 130).
Outcomes	Endometritis, wound infection, septicemia; additional antibiotic use (10/136 in treatment group vs 19/130 in placebo); antibiotic costs; maternal hospital stay.
Notes	There was one episode of septicemia in the placebo group.
Allocation concealment	B – Unclear

Study	McCowan 1980
Methods	Randomized, double-blind, placebo-controlled.
Participants	All women undergoing cesarean section (8/73 were repeat). Exclusion: already on antibiotics. Setting: National Women's Hospital, Auckland, New Zealand; June - September 1979.
Interventions	Metronidazole 500mg IV prior to incision and metronidazole 2g suppository at end of surgery (n = 35) versus matching placebo infusion and suppository (n = 38).
Outcomes	Fever (>37.9 degrees C within 14 days of delivery); wound infection, endometritis, urinary tract infection, major complication (return to theatre or hospitalized >10 days because of post-operative morbidity); need for antibiotic therapy (treatment 13 vs placebo 10); fever index (257 degree hours vs 165 hours).
Notes	One major complication (not infectious) in each group (bleeding from lower segment in one, major deep vein thrombosis extending into iliac veins in another).
Allocation concealment	B – Unclear

Study	Miller 1968
Methods	'On a random basis'; partly placebo-controlled.
Participants	All patients undergoing cesarean section. Women with pre-existing urinary tract infection were excluded. Setting: Durban, South Africa.
Interventions	Ampicillin 500mg IM pre-operatively and 8 hourly for 48 hours followed by 500mg orally 8 hourly for 4 days (n = 150) versus no treatment for first 48 hours then oral placebo 8 hourly for 4 days (n = 150).
Outcomes	Urinary tract infection (culture positive), intra-uterine infection not defined further, classified as endometritis), wound infection.
Notes	Fewer post-partum urinary isolates in treated group were sensitive to ampicillin (8/17 vs 18/26). In the control group, three women developed pelvic abscesses (included as serious morbidity) and one patient required hysterectomy for secondary postpartum haemorrhage following severe E. coli intra-uterine infection.
Allocation concealment	B – Unclear

Study	Moodley 1981
Methods	Randomized, double-blind, placebo-controlled (using unmarked code-numbered separate boxes).
Participants	Women undergoing emergency cesarean section (ruptured membranes for >6 hours and <20 hours; corresponds to our definition of non-elective). Exclusion: prior antibiotic therapy, fever >37.2 degrees C, fetal tachycardia of >160/minute. Setting: University of Natal, Durban, South Africa.
Interventions	Lincomycin 600mg (n = 20) versus metronidazole 500mg (n = 20) versus placebo (n = 20) intravenously 2 hours pre-operatively and 8 hourly for 48 hours; both treatment groups are combined for the analysis.
Outcomes	Wound discharge/abscess formation, puerperal sepsis (>37.9 degrees C twice in first 48 hours or >37.5 degrees C from 2nd post-operative day), septicemia, urinary tract infection.

Characteristics of included studies (Continued)

Notes	Authors' definition of puerperal sepsis has been classified as fever. No complications of drug administration reported in mothers or babies; no rash, diarrhoea nor nausea.
Allocation concealment	B – Unclear

Study	Moro 1974
Methods	Randomized (code generated by pharmacy), double-blind, placebo-controlled; code broken when fever developed 14/162 excluded for protocol violations.
Participants	All women undergoing cesarean section (49/148 were repeat procedure; 57/148 were not in labour). Exclusion: membranes ruptured >24 hours. Setting: Norfolk General Hospital, Virginia; both private (n = 70) and clinic (n = 78) women included.
Interventions	Cephalothin 2g IV 15-30 minutes prior to surgery and 1g every 6 hours for 36 hours, then cephalexin 500mg orally every 6 hours until 5th post-operative day (n = 74) versus identical appearing placebo (n = 74).
Outcomes	Fever (>100.3 degrees fahrenheit twice after 48 hours); endometritis (fever, uterine tenderness, foul-smelling or abnormal lochia and positive cultures); urinary tract infection, wound infection; maternal hospital stay (treatment 6.2 vs placebo 7.5, no variance given).
Notes	All bacterial isolates in treatment group were sensitive to cephalothin.
Allocation concealment	A – Adequate

Study	Morrison 1973
Methods	Alternate allocation to treatment or no treatment; not placebo-controlled.
Participants	All women undergoing cesarean section. Exclusion: febrile or infected. Setting: City of Memphis Hospitals, Tennessee; indigent women, many obstetric and metabolic complications.
Interventions	Aqueous penicillin 10 MU every 8 hours and kanamycin 500mg IM every 12 hours pre-operatively and for 3 days post-operatively (n = 115) versus no treatment (n = 115).
Outcomes	Fever (>100.9 degrees fahrenheit after first post-operative day), severe pelvic infection (treatment 27% vs control 7%); 'free of infectious morbidity' (3.6 vs 6.8 days); maternal hospital stay (5.4 vs 8.8 days, no variance given).
Notes	No adverse drug reactions reported; no evidence of development of resistance reported. Unable to ascertain from description of study incidence of endometritis or wound infection; inadequate description of nature of severe pelvic infections (not included as outcome in analysis). Two groups of women were studied retrospectively (n = 75); methods nor results do not specifically describe results of this group and it is unclear whether they have been included in the overall results.
Allocation concealment	C – Inadequate

Study	Ng 1992
Methods	Randomized to treatment or no treatment (method not described). Two patients excluded (one from cefoperazone group, one from no treatment group); intent to treat analysis performed.
Participants	Women undergoing cesarean section. Exclusions: hypersensitivity to one of antibiotics; presence of infection or fever; on antibiotics; multiple pregnancy. Setting: Ipoh, Malaysia.
Interventions	Cefoperazone 1g every 12 hours x 3 (n = 71) vs ampicillin 500mg every 6 hours x 4 (n = 74) vs no treatment (n = 77); both treatment groups combined for data analysis.

Characteristics of included studies (*Continued*)

Outcomes	Wound infection (inflammation over wound with serous or purulent discharge); any antibiotics post-operatively (cefoperazone vs ampicillin vs no treatment: 6.6% vs 16.2% vs 25.7%). Hospital stay: ampicillin vs no treatment 5.57 days (SD 1.43) vs 6.5 days (SD 3.67).
Notes	Author's definition of emergency not consistent with criteria used in this review; classified as both/undefined.
Allocation concealment	B – Unclear

Study **Padilla 1983**

Methods	Randomly assigned, double-blind, placebo-controlled; medication code kept in pharmacy.
Participants	All women undergoing cesarean section (35/71 were a repeat section). The authors definition of primary and repeat are different from those used in this review and have not been analysed separately; most women for repeat section were in early labour at the time the operation was performed. Exclusion: fever, membrane rupture >24 hours, penicillin allergy, lack of consent. Setting: Johns Hopkins Hospital, Baltimore.
Interventions	Ampicillin 2g pre-operatively (n = 34) versus similar-appearing placebo (n = 37).
Outcomes	Fever (>37.0 degrees C twice at least six hours apart after first post-operative day); endometritis, urinary tract infection, wound infection, bacteremia, pelvic abscess, maternal hospital stay.
Notes	There was one pelvic abscess in the placebo group; there were 3 episodes of bacteremia (1 <i>Klebsiella</i> spp. in treatment group, 2 group B streptococcal infections in placebo); combined for outcome of serious morbidity.
Allocation concealment	A – Adequate

Study **Phelan 1979**

Methods	Randomly assigned, case number known only by pharmacy; placebo-controlled. 8 women excluded for mistakes in protocol.
Participants	All women undergoing cesarean section (46/122 were a repeat section). The authors' definition of primary and repeat do not correspond to definitions of elective and nonelective used in this review (repeat sections included women in labor with ruptured membranes). The results for these two categories have been combined in this review. Exclusion: allergy to penicillin or cephalosporin, infection or receiving antibiotics. Setting: Naval Regional Medical Center, Portsmouth, Virginia, US, July-December 1976.
Interventions	Cefazolin 500mg IV 30 minutes before and 500mg at 2 and 1g at 8 hours after delivery (n = 61) versus matching placebo (n = 61).
Outcomes	Endometritis (fever and uterine tenderness or fever and pathogenic organism); urinary tract infection (fever and symptoms, or positive culture); wound infection (fever, cellulitis and exudate); maternal hospital stay (treatment 5.5 days versus placebo 5.7 days, no variance given).
Notes	Two women developed serious complications as stated by the authors: one in treatment group developed septic pelvic thrombophlebitis; one given placebo developed pneumonia and endoparametritis (both included in outcome of serious morbidity).
Allocation concealment	A – Adequate

Study **Polk 1982**

Methods	'Randomly allocated'; double blind; placebo-controlled. 12 participants withdrawn (8 treatment, 4 placebo); intent to treat analysis performed.
Participants	All women undergoing cesarean section (other than repeat section); criteria do not correspond with our definition of non-elective. Exclusion: active infection, fever, membranes ruptured >36 hours, antibiotic therapy within 2 weeks, renal disease, allergy to penicillin or cephalosporin.

Characteristics of included studies (Continued)

	Setting: Brigham and Women's Hospital, Boston, Massachusetts, US, July 1978-October 1980.
Interventions	Cefazolin 2g after cord clamped (n = 146) and at 4 and 8 hours after first dose versus matching placebo (n = 132).
Outcomes	Fever (oral temperature >100.3 degrees fahrenheit on any of 2 of first 10 postoperative days); urinary tract infection, wound infection (only pus-draining included in outcome of wound infection); endometritis (fever, tenderness on pelvic examination, abnormal discharge); pelvic abscess; septic pelvic thrombophlebitis, bacteremia; subsequent antibiotic use (23% for placebo vs 12% for treatment).
Notes	Outcome of fever and minor wound infection combined (11/146 for treatment vs 13/132 for placebo). Four episodes of bacteremia, all in placebo group. One episode of rash and one episode of phlebitis reported in treatment group vs none in control. Data collected at 6 weeks on 259/266 patients; 35% of infections diagnosed after discharge.
Allocation concealment	B – Unclear

Study Reckel 1985

Methods	Randomized to treatment or no treatment. One drop-out (no treatment) included in intent to treat analysis.
Participants	Women undergoing cesarean section. Setting: Hanover, Germany.
Interventions	Mezlocillin 2g intravenously half hour pre-operatively then every eight hours x 4 (n = 70) vs no treatment (n = 70).
Outcomes	Wound infection (inflammation with or without exudation); endometritis (fever and tenderness of the uterus or fever with pathogens from the cervical canal); urinary tract infection (>100,000 bacteria/ml).
Notes	One episode of allergic skin reaction occurred with the injection of mezlocillin.
Allocation concealment	B – Unclear

Study Rehu 1980

Methods	'Assigned at random' to one of three regimens; code kept secret; placebo-controlled; data from a fourth group that consisted of patients allergic to one of the drugs or undergoing an emergency section have not been included. Two women excluded after initial randomization.
Participants	All women undergoing cesarean section. Exclusion: allergic to penicillin, clindamycin or gentamicin; emergency section. Setting: State Maternity Hospital, Helsinki, Finland, September 1977-January 1978.
Interventions	10 million units benzyl penicillin IV (n = 46) versus 500mg clindamycin IV and 80 mg gentamicin IM (n = 42) versus glucose solution placebo (n = 40) IV by infusion starting 30 minutes before operation and stopping 4 hours after. Results of both treatment groups combined.
Outcomes	Endometritis (fever, uterine tenderness and foul-smelling vaginal discharge); wound infection (all grades combined); hospital stay (treatment 7.7 vs 7.7 placebo; no variance given).
Notes	
Allocation concealment	B – Unclear

Study Rizk 1998

Methods	Randomized using computer-generated number screen; not placebo controlled, but patient and study co-ordinators unaware of group allocation.
Participants	Women undergoing elective cesarean section (absence of labor and before rupture of membranes). Exclusion: allergy to penicillin or cephalosporin, prior antibiotic therapy within 7 days. Setting: United Arab Emirates.

Characteristics of included studies (Continued)

Interventions	Cefuroxime 1.5g after clamping of the cord vs no treatment.
Outcomes	Febrile morbidity (temperature of >38 degrees C after first 48 hours); endometritis (uterine tenderness and offensive lochia with fever and no other source); wound infection (erythema, induration or purulent discharge); urinary tract infection (>100,000 bacteria/ml).
Notes	Majority of patients were indigent; follow-up at 6 weeks.
Allocation concealment	A – Adequate

Study **Roex 1986**

Methods	'Randomly allocated'; placebo-controlled. 8 women excluded because of protocol failures and 9 women for intraoperative complications (not defined further).
Participants	All women undergoing cesarean section (77/129 were elective sections). Exclusion: active infection, antibiotics within 7 days, allergy to penicillin or cephalosporin, impaired liver or renal function. Setting: Academisch Ziekenhuis der Vrije Universiteit, Amsterdam, The Netherlands, April 1983-October 1984.
Interventions	Cefoxitin 2g (n = 64) versus matching placebo (n = 65) IV bolus immediately following clamping of the cord and at 6 and 12 hours later.
Outcomes	Febrile morbidity (>38 degrees C for at least 24 hr after first 24 hr); endometritis (fever, fetid lochia and/or uterine tenderness on pelvic examination); wound infection (palpable induration, wound dehiscence and/or pus drained); urinary tract infection (positive culture), bacteremia.
Notes	One episode of Staphylococcus aureus bacteremia (in cefoxitin group) not considered life-threatening (included in outcome of serious morbidity). No serious antibiotic side-effects reported in cefoxitin-treated group; one patient in cefoxitin group developed diarrhoea.
Allocation concealment	B – Unclear

Study **Ross 1984**

Methods	'Randomized, sequential basis'; placebo controlled.
Participants	Women undergoing emergency cesarean section (in active labour with membrane rupture). Exclusion: pyrexia; antibiotic use within 2 weeks. Setting: Addenbrooke's Hospital, Cambridge, UK.
Interventions	Metronidazole 500mg (n = 57) versus placebo (n = 58) IV infusion at start of procedure; postoperatively metronidazole or placebo suppository twice daily for 5 days.
Outcomes	Pyrexia (>38 degrees C twice 4 hours apart after first 24 hours); wound infection; endometritis (heavy, offensive lochia and pyrexia); urinary tract infection; antibiotic use (15/57 in treatment group vs 20/58 in control group).
Notes	One woman in the control group developed a pelvic abscess. Length of admission not significantly different between the two groups (mean 7.4, sd 2.3 days). No adverse reactions occurred.
Allocation concealment	B – Unclear

Study **Rothbard 1975**

Methods	Randomized using last digit of hospital chart: even to treatment, odd to no treatment (not placebo-controlled).
Participants	All women undergoing cesarean section (divided into "no labour" and "labor" groups which correspond to the definitions of elective/non-elective used in this review). Exclusion: fever, antibiotic use within 2 weeks, ruptured membranes >2 hours, major penicillin allergy.

Characteristics of included studies (Continued)

	Setting: New York Medical College, New York, US.
Interventions	Cephalothin 2g IV and kanamycin 1g IM at induction of anesthesia, then cephalothin 2g IV q6hrs x 8 doses and kanamycin 500mg IM q12hr x 4 doses (n = 47) versus no treatment (n = 53).
Outcomes	Endometritis (fever, uterine tenderness and positive culture or fever and pathogenic organism); urinary tract infection, wound infection (fever and cellulitis or exudate). Data available on elective (defined as no labor) and non-elective (defined as presence of labour).
Notes	No difference in average duration of hospital stay between groups (data not shown). One woman (treatment group) developed endometritis with organism resistant to cephalothin and kanamycin.
Allocation concealment	C – Inadequate

Study	Rouzi 2000
Methods	Randomized using computer-generated code, kept confidential, to treatment or identical placebo.
Participants	Women undergoing cesarean section (both elective and emergency). Exclusions: use of antibiotics, fever or signs of infection; allergy to penicillin or cephalosporin. Setting: Jeddah, Saudi Arabia.
Interventions	Cefazolin 1g after clamping of the cord (n = 221) vs matching placebo (n = 220).
Outcomes	Febrile morbidity (>38 degrees C twice 4 hours apart after first 24 hours); endometritis (fever, uterine tenderness and abnormal lochia); wound infection (fever, cellulitis or exudate with positive culture); urinary tract infection (fever and positive urine culture); pneumonia, bacteremia, pelvic abscess, unexplained fever, therapeutic antibiotics, length of post-operative stay.
Notes	Emergency cesarean section not defined, results reported in undefined category. Fetal outcomes reported; no serious side effects with cefazolin.
Allocation concealment	A – Adequate

Study	Rudd 1981
Methods	Randomly allocated using table of random numbers by pharmacy to one of three groups (antibiotic irrigation, placebo irrigation, no irrigation); vitamin solution added to make placebo visually identical; physicians and patients blinded to treatment.
Participants	All women undergoing cesarean section (19/60 women had ruptured membranes >6 hours; 40/60 were in active labour). Exclusion: known infection, currently on antibiotics, allergic to penicillin or cephalosporin. Setting: Tripler Army Medical Center, Honolulu, Hawaii, US.
Interventions	Cefamandole 2g in 800ml normal saline irrigation (n = 30) versus irrigation with 800 ml normal saline (n = 30). Non-irrigation control group (n = 30) not included.
Outcomes	Endomyometritis (fever, unusual uterine and parametrial tenderness without evidence of other source of infection); maternal length of stay.
Notes	Length of hospital stay for the control group included results from both the no irrigation group and the placebo irrigation group (5.37 days vs 4.53 for treatment group).
Allocation concealment	A – Adequate

Study	Ruiz-Moreno 1991
Methods	Randomized, placebo-controlled.
Participants	Women in active labor undergoing cesarean section. Exclusion: Elective cesarean section, evidence of infection, antibiotic use within 8 days, metronidazole intolerance, lack of consent.

Characteristics of included studies (Continued)

	Setting: Hospital Central Militar, Mexico city, Mexico. Women predominantly (78%) of low socioeconomic level.
Interventions	Metronidazole 1g IV (n = 50) versus identical appearing placebo (n = 50) immediately after cord clamping.
Outcomes	Endometritis (purulent and/or foul odor lochia); wound infection (wound edges tender, red and swollen, or frank pus or sanguino-purulent material exuded); urinary tract infection (bacteria seen in sediment) ; maternal hospital stay.
Notes	
Allocation concealment	B – Unclear

Study	Saltzman 1985
Methods	Randomized, double-blind, placebo controlled. One woman initially randomized not included in analysis.
Participants	High risk women undergoing cesarean section (in active labour and/or ruptured membranes >4hours); classified as non-elective in this review. Exclusion: active infection, fever, antibiotic use within 3 days, allergy to penicillin or cephalosporins. Setting: Fairfax Hospital, Virginia, US. Women predominantly private.
Interventions	Ceftizoxime 2g (n = 50) versus placebo (n = 49) IV at time of cord clamping.
Outcomes	Febrile morbidity (oral temperature >37.9 degrees C twice at least 8 hr apart, after first 24 hr); endometritis (fever and foul lochia or uterine tenderness); urinary tract infection (fever and positive culture); wound infection (fever, abnormal-looking wound, surrounded by cellulitis and/or draining purulent material).
Notes	Ceftizoxime is a third generation cephalosporin with broad aerobic and anaerobic activity. There was one drug reaction (maculopapular rash) in the treatment group. Women followed up at 6 weeks.
Allocation concealment	A – Adequate

Study	Sanchez-Ramos 1999
Methods	Double-blind, randomized, placebo-controlled.
Participants	Women undergoing cesarean deliveries for various indications. Setting: Jacksonville, Florida, USA.
Interventions	Metronidazole gel 5g intravaginally (n = 31) vs matching placebo (n = 32).
Outcomes	Endometritis.
Notes	Abstract only.
Allocation concealment	B – Unclear

Study	Scarpignato 1982
Methods	Randomly assigned; not placebo controlled. One woman was excluded because of an allergic reaction to cefuroxime (included in intent to treat analysis).
Participants	Women undergoing emergency cesarean section (58/60 women in spontaneous labor; classified as non-elective). Exclusion: allergy to penicillin or cephalosporins; severe renal disease, history of pelvic infections. Setting: University of Parma, Parma, Italy, November 1981-March 1982.
Interventions	Cefuroxime 750mg IM 30-60 minutes before surgery and 8 and 16 hours after (short term)(n = 20) versus 750mg three times a day for five days (first dose being given post-operatively after the woman had returned to the ward) (long term) (n = 20) versus no treatment (n = 20). The results of both treatment groups have been combined.

Characteristics of included studies (Continued)

Outcomes	Fever (>100.3 degrees fahrenheit twice 6 hr apart); endometritis (fever and uterine tenderness); maternal stay (treatment 7.1 vs control 7.9 days, no variance given).
Notes	Note: the group given long-term prophylaxis received the first dose after return to the ward.
Allocation concealment	B – Unclear

Study Schedvins 1986

Methods	'Randomly referred'; not placebo controlled.
Participants	Women with rupture of membranes for >6 hours (equivalent to non-elective group). Exclusion: fever or foul smell of amniotic fluid. Setting: Sodersjukhuset, Stockholm, Sweden, November 1983-October 1984.
Interventions	Cefuroxime 1.5g IV q8hr for 24 hours, starting immediately before or during the operation, followed by oral cefadroxil 500mg twice daily for 6 days (n = 26) versus no treatment (n = 27).
Outcomes	Endometritis (marked uterine tenderness with or without a foul discharge with fever at least twice); wound infection (redness, tenderness, induration and pus in the wound); urinary tract infection (positive culture).
Notes	Data provided (but not included) for a second control group eligible for inclusion but not randomized. Numbers not provided to calculate mean maternal length of stay for the two randomized groups.
Allocation concealment	B – Unclear

Study Shah 1998

Methods	Randomized using consecutively numbered, sealed envelopes to treatment groups or no treatment. 14 patients excluded from study (8/147 from treatment groups, 6/51 from control group); included in intent to treat analysis.
Participants	Women undergoing elective caesarean section. Exclusion: hypersensitivity to penicillin or cephalosporin; prior antibiotic therapy within 3 days; hepatorenal insufficiency; positive cultures or definite evidence of infection. Setting: United Arab Emirates.
Interventions	Piperacillin 4g intravenously after the cord was clamped (n = 48) vs cephadrine 500mg plus metronidazole 500mg both intravenously after the cord was clamped and every 8 hours x 2 (n = 47) vs piperacillin 2g intravenously after clamping of the cord and 2g every 8 hours x 2 (n = 52) vs no treatment (n = 51).
Outcomes	Febrile morbidity (fever >38 degrees C twice 4 hours apart after first day); endometritis (uterine and parametrial tenderness, foul smelling vaginal discharge); wound infection (local induration and tenderness with wound exudate).
Notes	Three patients who developed drug reactions were excluded from study (one from each of the treatment groups). Late morbidity evaluated at 4-6 weeks.
Allocation concealment	B – Unclear

Study Stage 1982

Methods	Randomly allocated (individually randomized block ensuring two-to-one randomization at each centre); placebo-controlled; women and investigators blind to allocation throughout the study. Part of a larger study looking at prophylaxis also in gynecologic surgery; drop-outs in cesarean section women not stated (overall: 11/319 from treated group, 8/172 from placebo group).
Participants	All women undergoing cesarean section (46% in labor). Exclusion: infection, allergy to penicillin or cephalosporins. Setting: 14 US centers, July 1976-June 1978.
Interventions	Cephadrine 1g IV (n = 133) versus placebo (n = 66) within 1 hour prior to surgery, repeated at 4 hours.

Characteristics of included studies (Continued)

Outcomes	Febrile morbidity (oral temperature >37.7 degrees C twice 4 hours apart, after first 48 hours); endometritis (uterine tenderness, fever and purulent discharge), wound infection (increased local tenderness, redness or swelling); urinary tract infection (positive culture); maternal length of stay (treatment 5.8 days vs placebo 7.57 days; $p < 0.05$, variance not given).
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Notes

Allocation concealment B – Unclear

Study Stiver 1983

Methods Randomly assigned, placebo-controlled.
7 women (one in treatment, six in placebo group) initially randomized but results not included, 6 because they failed to receive all 3 doses, one because of hypotensive episode with first dose; intent to treat analysis performed.

Participants All women in labour or with ruptured membranes (duration of ruptured membranes not stated; mean duration 9.97 hours; included in non-elective category).
Setting: 5 centres in Canada.

Interventions Cefoxitin 2g (n = 124) versus cefazolin 1g (n = 120) versus placebo (n = 117) infused intravenously immediately after cord clamped and 6 and 12 hours later. Results of both treatment groups combined.

Outcomes Febrile morbidity (oral temperature >37.9 degrees C twice at least 6 hours apart after first 24 hours); wound infection (redness, induration, tenderness and/or purulent discharge from the incision line); endometritis/parametritis (uterine and/or adnexal tenderness with fever) urinary tract infection (dysuria or pyuria and positive culture); need for antibiotic therapy (11% for treatment groups vs 27% for placebo); maternal length of stay (7.3 and 7.4 days for treatment groups vs 7.9 for placebo).

Notes Side-effects documented: two infusion-related hypotensive episodes (one with cefazolin, one with placebo that necessitated withdrawal from study); six episodes of phlebitis (five in treated, one in placebo group); one episode of angioedema (placebo patient). Data provided on antibiotic resistance in wound isolates and screening cervical cultures. One episode of bacteremia (in placebo group); one episode of septic shock (in cefazolin-treated group); both outcomes included as serious morbidity.
Follow-up at 6 weeks.

Allocation concealment B – Unclear

Study Tully 1983

Methods Randomized as determined by table of random numbers; placebo-controlled; double-blind
14 women (7 in each group) initially randomized were later excluded but have been included in intent to treat analysis.

Participants Women undergoing primary cesarean section (inclusion criteria not consistent with the definition of non-elective cesarean section used in this review).
Exclusion: <18 years of age, membranes ruptured >35 hours, allergy to penicillin or cephalosporin, fever, infection or antibiotic use, significant underlying cardiac, renal or hepatic disease, unable to provide consent.
Setting: Beth Israel Hospital, Boston, Massachusetts, US, September 1978-June 1980.

Interventions Cefoxitin 2g IV immediately after the cord was clamped and at 4 and 8 hours (n = 52) versus matched placebo (mannitol with riboflavin) (n = 61).

Outcomes Febrile morbidity (oral temperature >37.9 degrees C twice at least 6 hours apart after first 24 hours); urinary tract infection (positive culture); wound infection (purulence, cellulitis or dehiscence); endometritis (fever, uterine tenderness, abnormal lochia); septicemia (positive blood culture in a clinically septic patient); additional antibiotic use (8 in treatment group vs 12 in placebo).

Notes Both episodes of septicemia occurred in the placebo group.

Allocation concealment A – Adequate

Characteristics of included studies (Continued)

Study	Turner 1990
Methods	Alternate patients undergoing caesarean section allocated to treatment or no treatment.
Participants	Women undergoing cesarean section (both elective and emergency). Exclusion: on antibiotics, adverse reaction to penicillin or cephalosporin, pyrexia > 37.5 degrees C in labour, known vaginal pathogen, or suspected intrauterine infection. Setting: Hammersmith Hospital (n = 102) and Northwick Park Hospital (n = 99), London, England.
Interventions	Cephadrine 2g intravenously after induction of anesthesia and 1g 6 and 12 hours after the operation (n = 101) vs no treatment (n = 100).
Outcomes	Puerperal infection (temperature >37.5 degrees C after 24 hours); endometritis (pyrexia with uterine or adnexal tenderness); wound infection (purulent discharge or erythema, induration and serous discharge with positive culture); urinary tract infection (>100,000 colony forming units in urine culture); length of hospital stay (7.63 for treatment group, 7.18 for control group [SD not provided]).
Notes	Definitions of elective and emergency procedure, nor separate outcomes for each group, provided. Follow-up completed 1987.
Allocation concealment	C – Inadequate

Study	Tzingounis 1982
Methods	Selected in a random manner; double-blind; placebo-controlled.
Participants	Women in labour (non-elective). Exclusion: acute bleeding due to abruptio placentae, established infection. Setting: Alexandra Maternity Hospital, Athens, Greece.
Interventions	Cefuroxime 750mg IV within 1 hour of surgery and every 8 hours for 72 hours (n = 46) versus matching placebo (comparable in appearance and viscosity) (n = 50).
Outcomes	Febrile morbidity (oral temperature of >100.3 degrees fahrenheit twice 6 hours apart) and infection of endometrium, urinary tract and wound (not defined); results of duration of maternal stay only provided for febrile patients.
Notes	No patients had any major complications from the use of cefuroxime.
Allocation concealment	B – Unclear

Study	Walss Rodriguez 1990
Methods	Allocated 'in random form' using a random table; not placebo-controlled.
Participants	Women undergoing urgent cesarean section. Exclusion: fever, chorioamnionitis, penicillin allergy, antibiotic treatment in prior 2 weeks. Setting: Coah, Mexico.
Interventions	Ampicillin 2g intravenously every 4 hours x 3 after clamping of cord (n = 59) vs no treatment.
Outcomes	Febrile syndrome; wound infection; abdominal wall abscess; endometritis.
Notes	No definitions of outcomes provided.
Allocation concealment	B – Unclear

Study	Weissberg 1971
Methods	'Selected at random'; not placebo-controlled.
Participants	Women undergoing primary cesarean section after the onset of labor. Setting: Miami, Florida, US. Mostly low-income or indigent Negro women from ghetto areas of large metropolitan area.

Characteristics of included studies (Continued)

Interventions	Penicillin G 2 million units IV every 4 hours and kanamycin 500mg IM every 12 hours as soon as it was decided to perform a cesarean section, at the time of operation or immediately post-operatively and continued for a minimum of 3 days post-operatively (n = 40) versus no treatment (n = 40).
Outcomes	Febrile morbidity (temperature of >100.3 degrees fahrenheit on any two days after first 24 hours); urinary tract infection, endometritis and wound infection (not defined); maternal length of stay (treatment 5.8 days vs 8.7 days for control group, no variance given).
Notes	One patient receiving penicillin had a drug rash on the third day.
Allocation concealment	B – Unclear

Study Wong 1978

Methods	Randomized in numbered packages by the pharmacy department; placebo-controlled; blinded. Seven women initially randomized not included in final analysis (allocated group unknown).
Participants	Women with ruptured membranes who underwent internal fetal monitoring (not consistent with the definition of non-elective used in this review). Exclusion: fever, other antibiotic use, penicillin allergy. Setting: Los Angeles County-University of Southern California Medical Center, Los Angeles, California, US, January 1975-January 1977; 87% Hispanic or Black.
Interventions	Cefazolin 1g IV after the cord was clamped and at 4-6 hours and 10-12 hours post-operatively (n = 48) versus placebo (n = 45).
Outcomes	Standard temperature morbidity, endomyometritis, abdominal wound infection, urinary infections (no definitions provided for any outcomes).
Notes	Two women were said to develop a serious infection: one (cefazolin group) developed septic thrombophlebitis and is included as a serious outcome; the other (placebo group) was treated with antibiotics for prolonged fever (judged not to be a serious outcome for this review).
Allocation concealment	A – Adequate

Study Work 1977

Methods	Selected in random, double-blind manner; placebo-controlled.
Participants	Women in labor. Exclusion: acute bleeding due to abruptio placentae, infection on treatment; abnormal renal function, penicillin allergy. Setting: University of Michigan Medical Center, Ann Arbor, Michigan, US.
Interventions	Cephalothin 2g IV within one hour of operation and at 4 and 8 hours after (n = 40) versus comparable appearing placebo (n = 40).
Outcomes	Febrile morbidity (oral temperature >100.3 degrees fahrenheit twice 6 hours apart); infection of endometrium, urinary tract and wound (definitions not provided); fever index (40 degree hours for treatment group vs 83 for placebo group).
Notes	
Allocation concealment	B – Unclear

Study Wu 1991

Methods	Randomized into three groups (irrigation vs systemic treatment vs no treatment).
Participants	Women undergoing both elective (n = 112) and non-elective (n = 105) cesarean section. Only women undergoing an elective cesarean section were randomized to treatment or no treatment and have been included in analysis. Setting: Beijing, China.

Characteristics of included studies (Continued)

Interventions	Local irrigation with ampicillin 6g after delivery of the placenta (n = 39) vs penicillin 5.6 MU and gentamicin 240,000 U intravenously immediately after surgery and penicillin 1.6 MU and gentamicin 160,000 U per day intramuscularly x 3 days (n = 41) vs no treatment (n = 32).
Outcomes	Endometritis (presence of any 2 of following: temperature above 37.5 degrees C, uterine tenderness, foul vaginal discharge); abdominal wound infection (cellulitis with small amount of exudate within 2 months of operation); uterine incision infection (associated with late post-partum haemorrhage); fever index.
Notes	Women undergoing non-elective sections randomized to either treatment group (not included in this review).
Allocation concealment	B – Unclear

Study Yip 1997

Methods	Assigned by the anesthetist in a randomized, double-blind manner; placebo-controlled.
Participants	Women undergoing cesarean section. Exclusion: penicillin allergy, current antibiotic use, fever, receipt of steroid injection. Setting: Prince of Wales Hospital, Hong Kong.
Interventions	Augmentin 1.2g (amoxycillin sodium 1000mg and clavulanate potassium 200mg) in 10ml saline (n = 160) versus saline placebo (n = 160).
Outcomes	Febrile morbidity (2 oral temperatures >37.9 degrees C at least 6 hours apart after first 24 hours); bacteriuria at day 3 (classified in this review as urinary tract infection); wound infection (purulent discharge, cellulitis, tenderness and wound abscess requiring incision and drainage); endometritis (fever, pelvic pain, uterine tenderness, purulent vaginal discharge without signs of infection in the lower genital tract); duration of hospital stay.
Notes	Sub-rectus Redivac drain routinely inserted.
Allocation concealment	B – Unclear

Study Young 1983

Methods	Randomly assigned; placebo-controlled; physician team blinded.
Participants	Women in labour with an intrauterine pressure catheter and fetal scalp electrode (non-elective). Exclusion: fever, significant systemic disease. Setting: Los Angeles County-University of Southern California Medical Center, Los Angeles, California, US. Predominantly (91%) Hispanic or Black.
Interventions	Cefoxitin 1g IV at time of cord clamping and at 4 and 8 hours (n = 50) versus matching placebo (n = 50).
Outcomes	Endomyometritis, abdominal wound infection, serious complications; duration of maternal hospital stay (treatment 5.1 days vs control 5.9 days, not statistically significant, no variance given).
Notes	One case of septic pelvic thrombophlebitis occurred in the treatment group; there were 8 episodes of bacteremia in the control group vs one in the treatment group; both outcomes combined under serious morbidity.
Allocation concealment	B – Unclear

C = centigrade
 hr = hour/hours
 IM = intramuscularly
 IV = intravenously
 MU = million units
 q6hrs = every six hours
 SD/sd = standard deviation
 vs = versus

Characteristics of excluded studies

Study	Reason for exclusion
Cormier 1988	Did not include women undergoing cesarean section.
Creatsas 1980	Not relevant to this review. Ampicillin or gentamycin given prior to cesarean section in women with intrauterine infection, to measure transplacental transfer. No control group, and no clinical outcomes given.
De Palma 1980	High risk women (membranes ruptured for more than six hours) initially were randomized to early treatment (ie prophylactic therapy continued for four days) vs standard treatment (ie treatment only started when infection apparent). When the results were compared midway through the study, standard therapy was abandoned. The results for the two groups prior to abandoning the no treatment group could not be obtained from the paper.
Elliott 1982	Only the first 42 women were randomized to placebo or active treatment; after that a significant difference was observed between the placebo and treated groups and the placebo arms were discontinued. Further women were randomized to two different active treatments. The data for the first part of the study (with only the first 42 women) are not available from the published paper.
Itskovitz 1979	Not all women were randomly allocated to treatment or no treatment. 150 women were assigned at random to each of the two wings of the department according to the day of their admission, each wing receiving women on alternate days. In both wings, of the last 50 women every second woman served as a control. Fifty women in one wing received IV cephalothin or oral cephalexin, 50 women in the other wing received IV or oral ampicillin. The first 50 women enrolled were all treated; separate results for the last 100 women (who were alternately allocated therapy or no treatment) are not available.
Kreutner 1979	After approximately 70% of the planned study population had been randomized to placebo or one of two active treatment groups, an unacceptably high morbidity rate in the placebo group was confirmed and the placebo arm was discontinued. Further women were randomized to two different active treatments. The data for the first part of the study when women were randomized to treatment or placebo are not available from the published paper.
Louie 1982	Eligible women were in active labor with ruptured membranes. While this study initially included a placebo control group, this group was dropped after 30 women had been enrolled on the basis of ethical considerations about assigning women to a nontreatment group in which the likelihood of morbidity was high. Only seven women (out of a total of 195 women entered) were randomized to placebo, separate results on the initial part of the study not available. The placebo (7) and treatment groups (188) were very imbalanced making a meaningful comparison between groups impossible.
Pawelec 1994	Abstract only; unable to confirm random allocation and method of allocation to no treatment group; data for separate outcomes of endometritis and wound infection not provided.
Petersen 1985	No numerical data.
Pitt 2001	Women were randomized to receive intravaginal metronidazole or placebo gel during labour; most, but not all patients also received one prophylactic dose of cefazolin after cord clamping.
Roex 1987	No clinical outcomes.
Sengupta 1976	In this study, in which women were alternately allocated to antibiotic prophylaxis or no treatment, the women enrolled were undergoing both gynaecological and obstetrical surgery. Rates of infectious complications are given for all abdominal surgery (cesarean section, abdominal hysterectomy and laparotomy). Data specifically on the women who underwent cesarean section are, however, not available from the published study.
Skryten 1988	Abstract only. Rates for all post-operative infection morbidity and clinically significant genital tract-related infections (wound infections, endometritis) and abscess formation (septicemia) combined; rates for individual outcomes not provided.
Spreafico 1987	Results combined from three time periods. In only one period did it appear women were randomized to antibiotic therapy or no treatment; results just for this period not available in published report.
Ujah 1992	Abstract only; results given for post-operative sepsis (38.9% in placebo group, 0% in treatment group), but data for separate outcomes not given.

Characteristics of excluded studies (*Continued*)

Voto 1986	All women received antibiotics (randomized to cefoxitin after cord clamping and then every four hours x 2 or oral ampicillin 2g daily x seven days); no clinical outcomes reported.
Wallace 1984	This was not a randomized trial of antibiotic prophylaxis. Three distinct groups of women were studied: one group was part of randomized trial that compared extracorporeal cesarean section with prophylactic antibiotic; the second group received extracorporeal cesarean section and no antibiotics; the third group received extracorporeal cesarean section with antibiotics (the decision to administer antibiotics in the latter two groups was at the discretion of the physician).
Wells 1994	Absolute numbers cannot be calculated from data provided in abstract; no published version of this study identified.

IV = intravenous

ANALYSES

Comparison 01. Prophylactic antibiotics in cesarean section

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Fever	45	7180	Relative Risk (Random) 95% CI	0.45 [0.39, 0.52]
02 Wound infection	75	11142	Relative Risk (Fixed) 95% CI	0.41 [0.35, 0.48]
03 Endometritis	83	11957	Relative Risk (Random) 95% CI	0.39 [0.34, 0.43]
04 Urinary tract infection	61	8857	Relative Risk (Fixed) 95% CI	0.54 [0.46, 0.64]
05 Serious infectious morbidity/death	31	4760	Relative Risk (Fixed) 95% CI	0.42 [0.28, 0.65]
06 Maternal side-effects	12	1976	Relative Risk (Fixed) 95% CI	2.02 [0.91, 4.50]
07 Days in hospital (mother)	16	2964	Weighted Mean Difference (Random) 95% CI	-0.47 [-0.68, -0.26]

INDEX TERMS

Medical Subject Headings (MeSH)

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

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title	Antibiotic prophylaxis for cesarean section
Authors	Smaill F, Hofmeyr GJ
Contribution of author(s)	Both reviewers were responsible for identifying relevant trials and abstracting the data. The initial draft of the text of the review was prepared by F Smaill.
Issue protocol first published	1999/1
Review first published	1999/2
Date of most recent amendment	14 April 2004
Date of most recent SUBSTANTIVE amendment	05 March 2002
What's New	Fifteen additional trials have been added to the review. The overall conclusion remains unchanged. Antibiotic prophylaxis will reduce infectious complications following both an elective and non-elective cesarean section.

Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	31 January 2002
Date authors' conclusions section amended	Information not supplied by author
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Editorial group	Cochrane Pregnancy and Childbirth Group
Editorial group code	HM-PREG

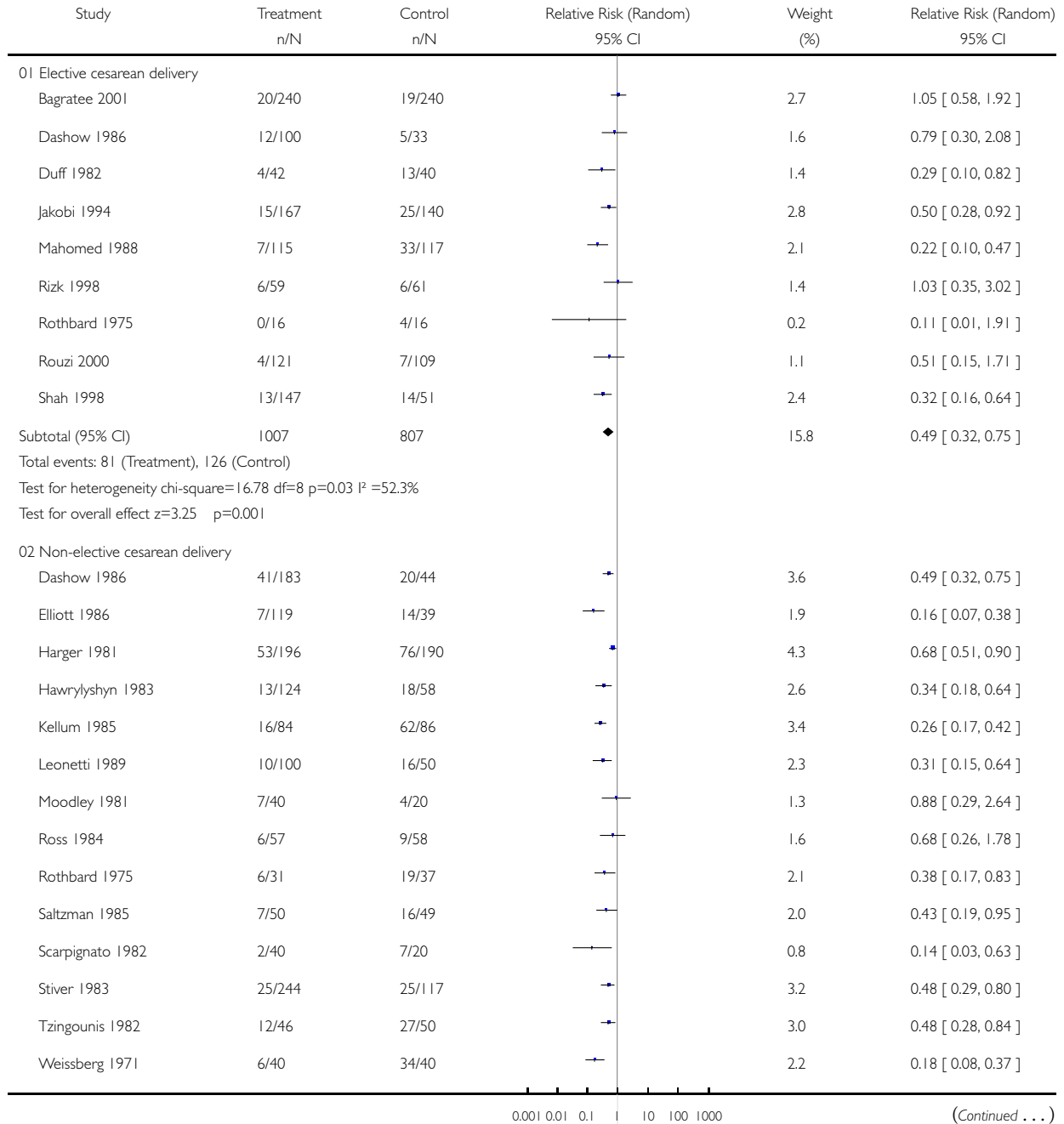
GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 01 Fever

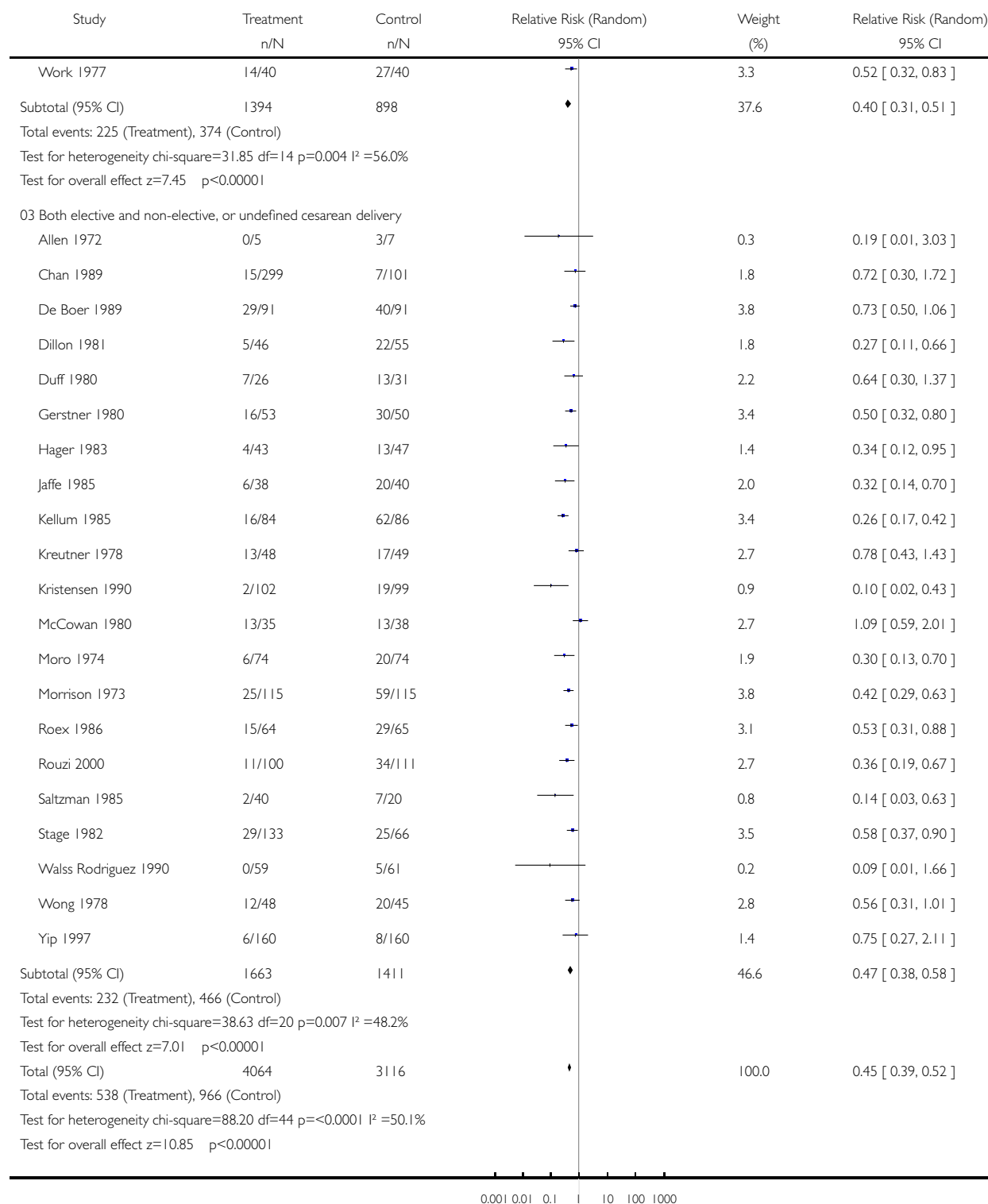
Review: Antibiotic prophylaxis for cesarean section

Comparison: 01 Prophylactic antibiotics in cesarean section

Outcome: 01 Fever



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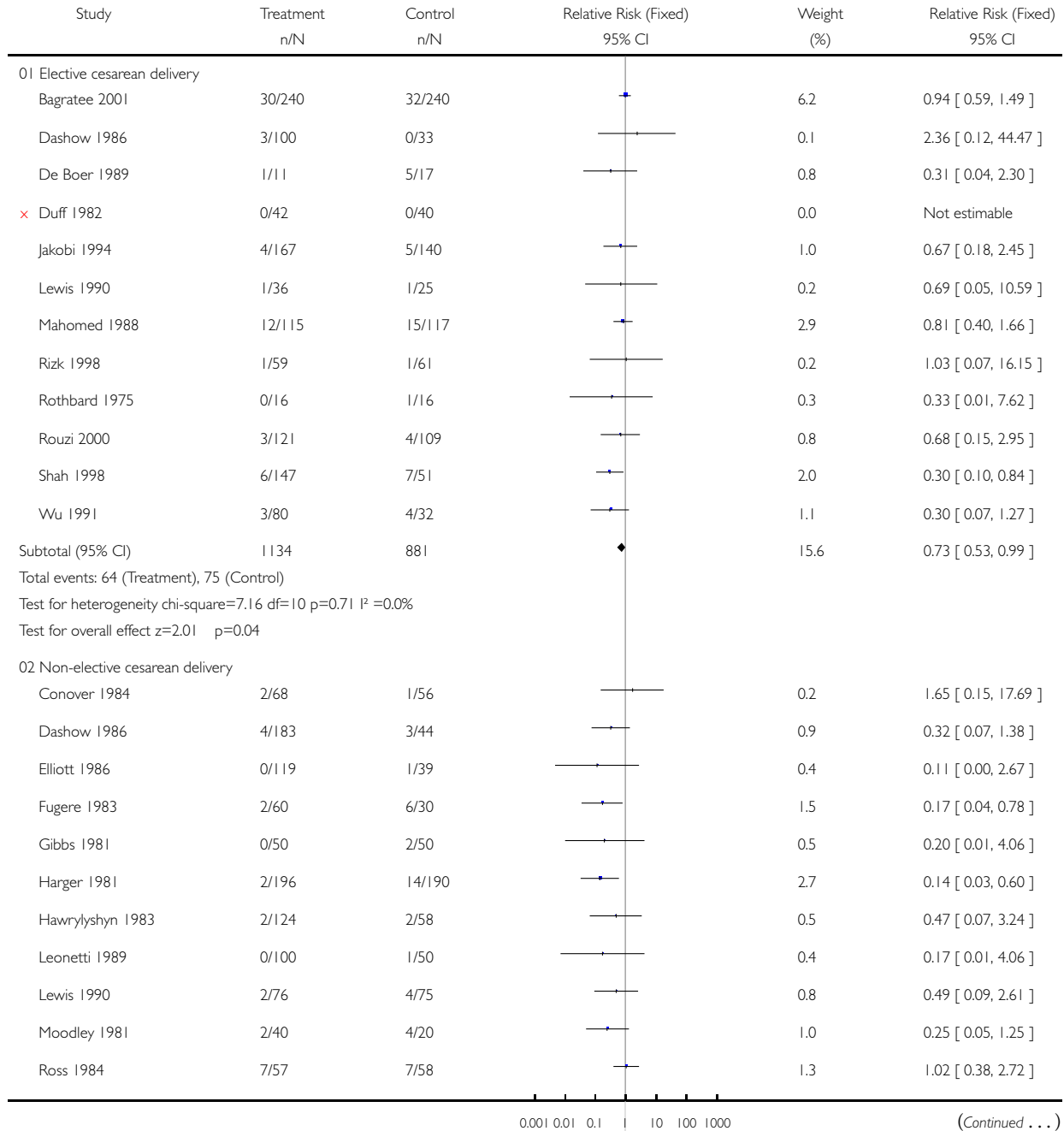


Analysis 01.02. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 02 Wound infection

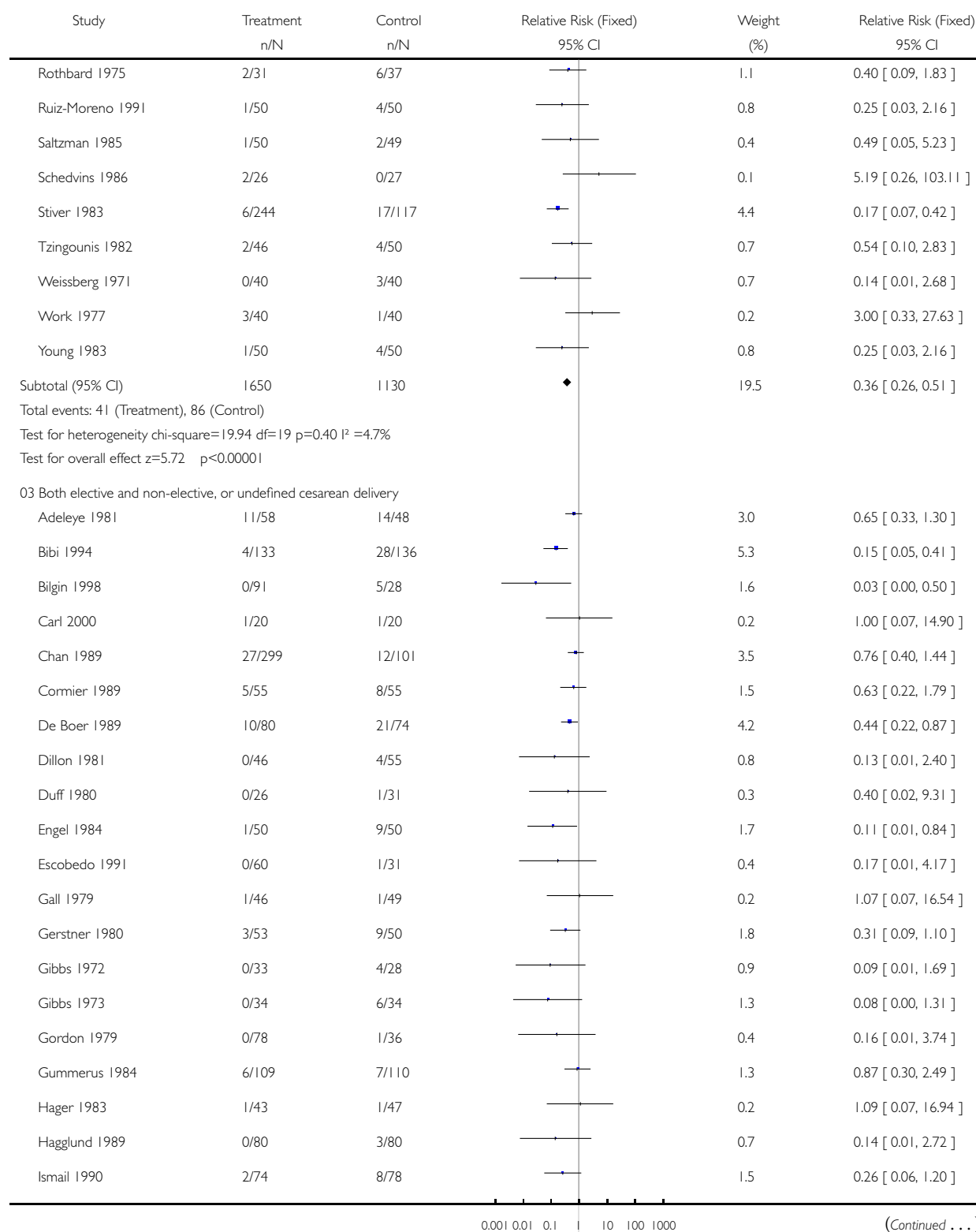
Review: Antibiotic prophylaxis for cesarean section

Comparison: 01 Prophylactic antibiotics in cesarean section

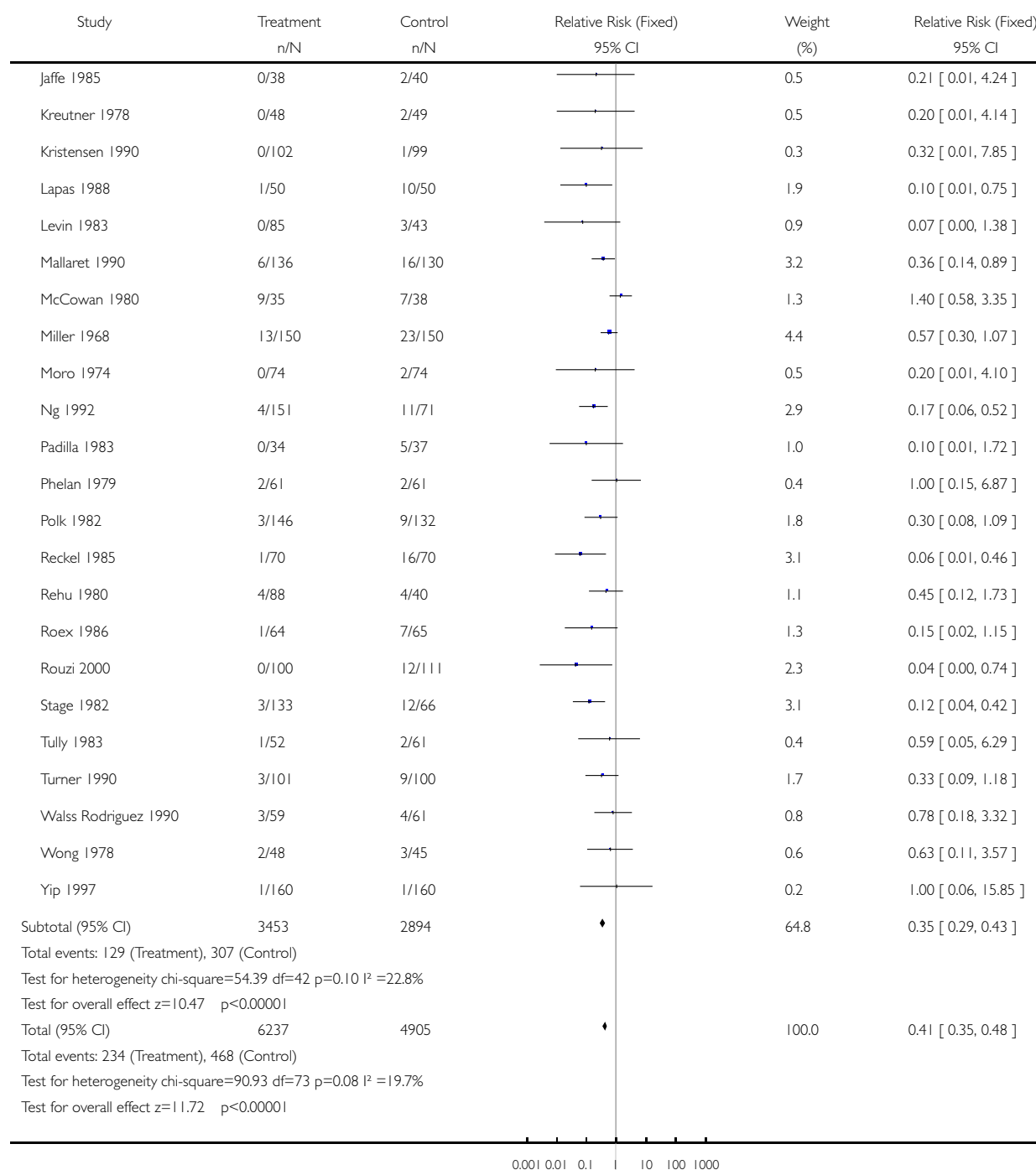
Outcome: 02 Wound infection



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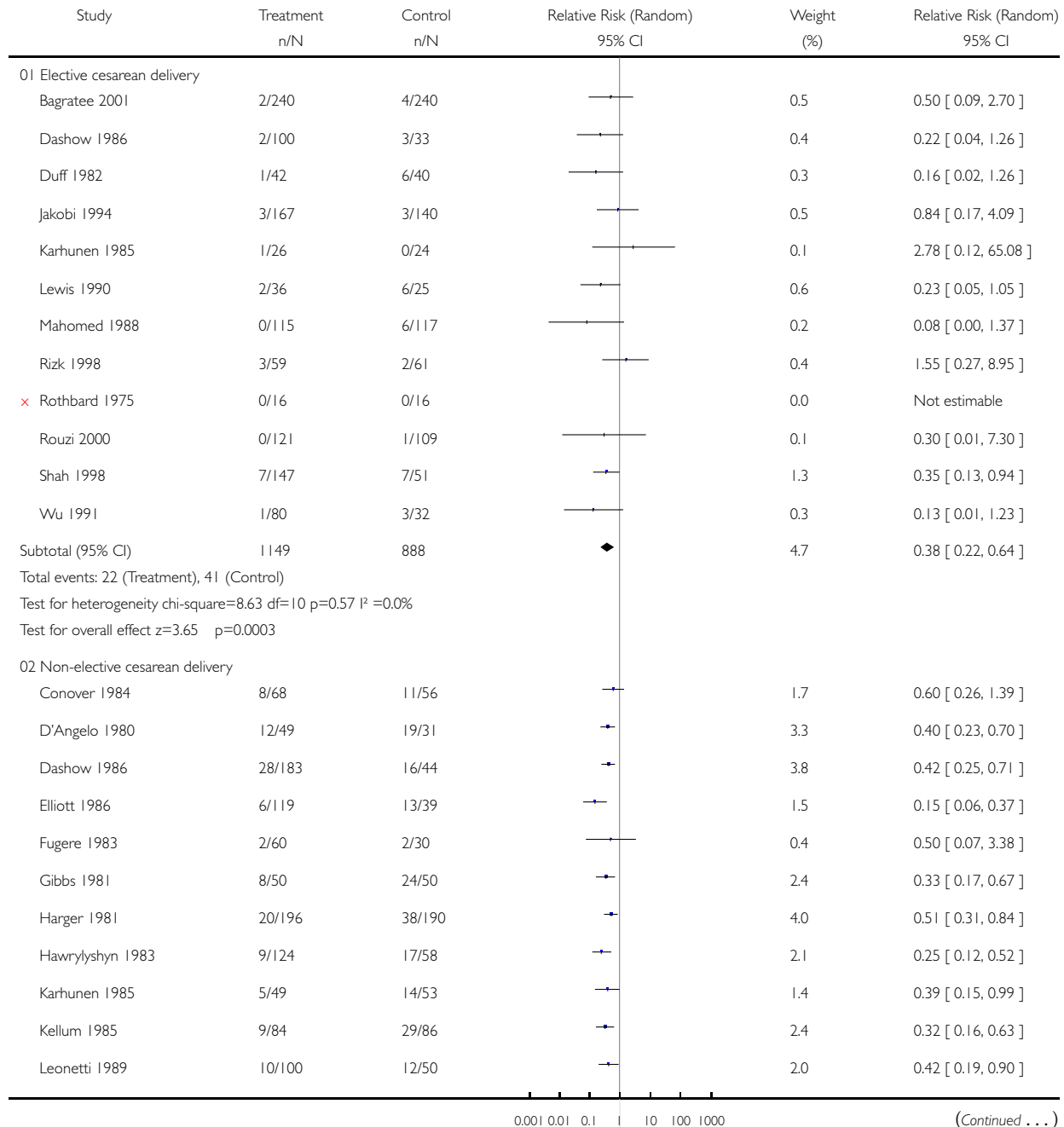


Analysis 01.03. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 03 Endometritis

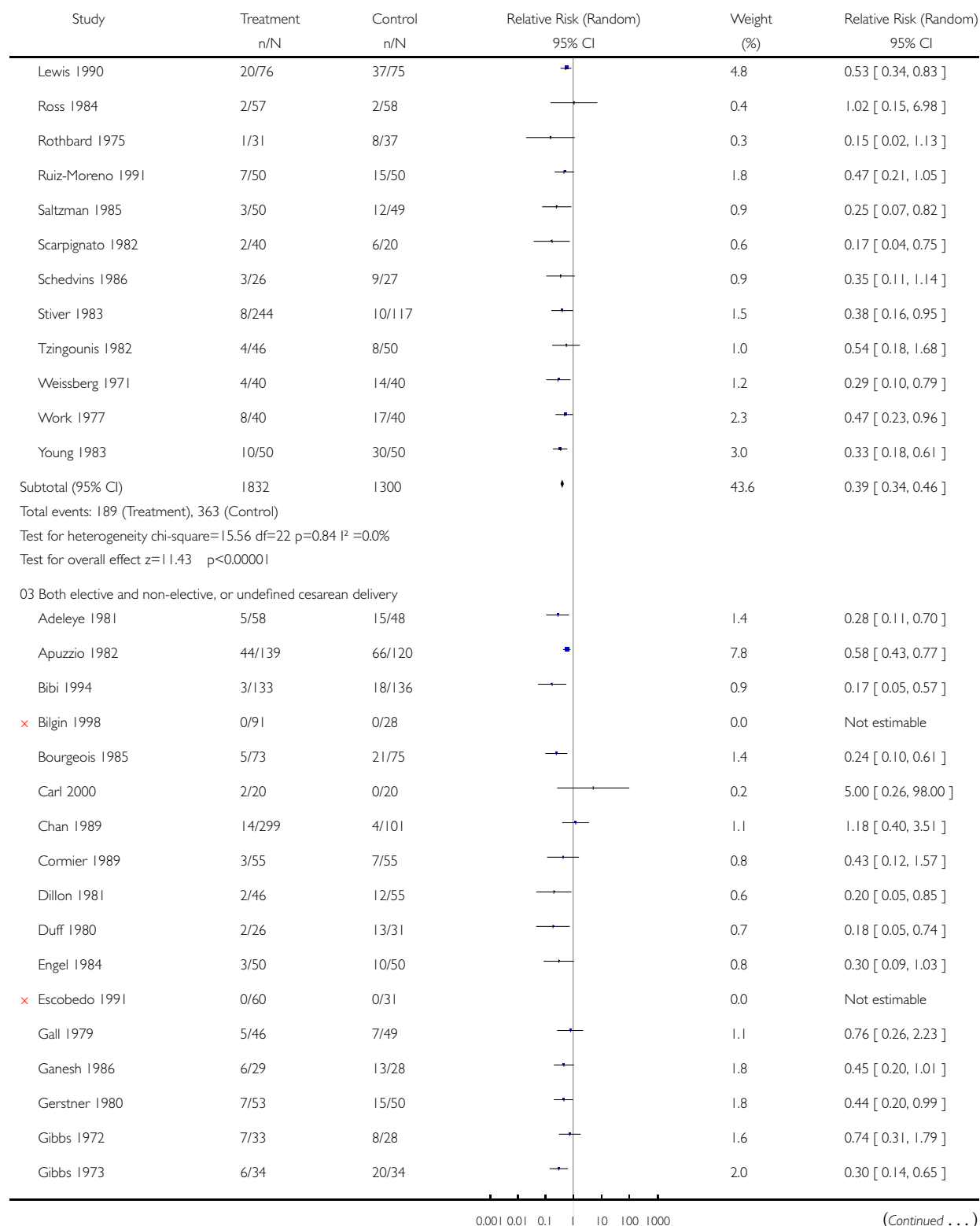
Review: Antibiotic prophylaxis for cesarean section

Comparison: 01 Prophylactic antibiotics in cesarean section

Outcome: 03 Endometritis

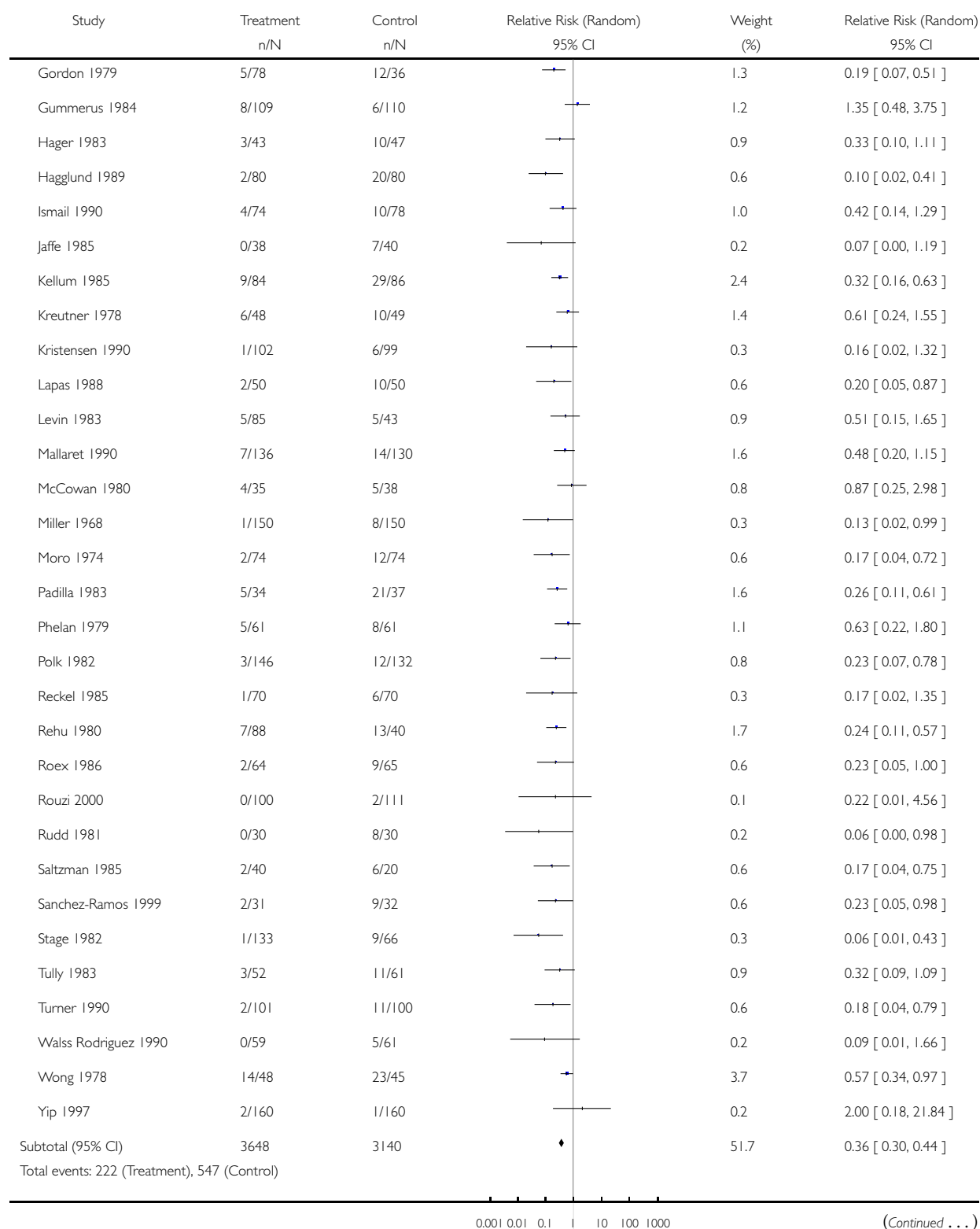


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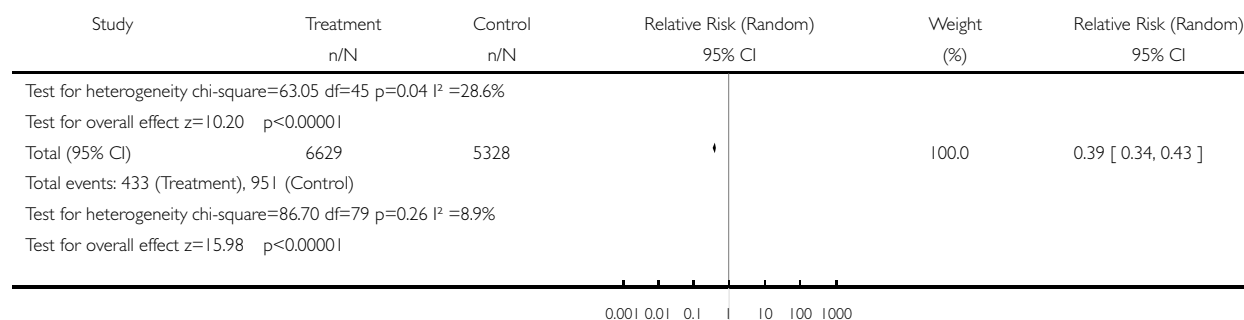


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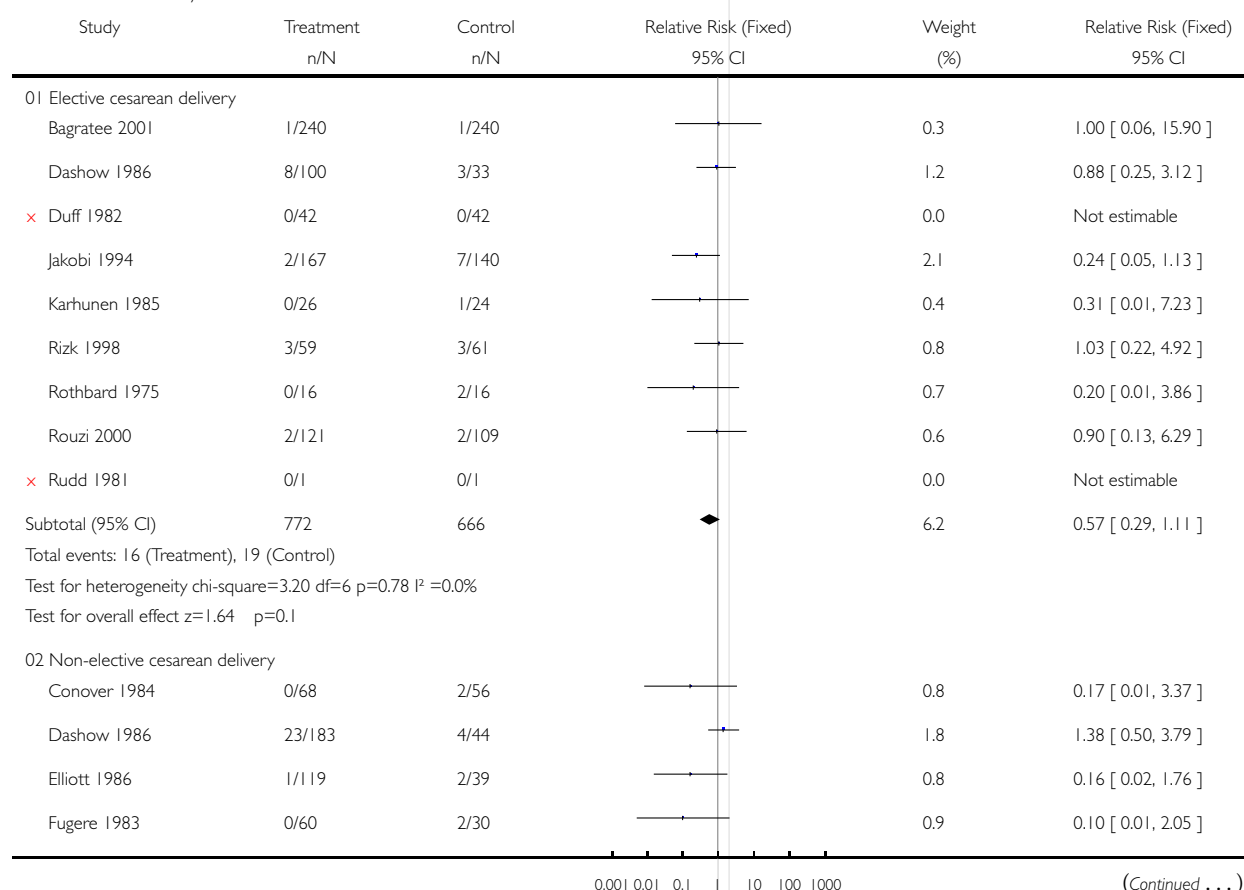


Analysis 01.04. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 04 Urinary tract infection

Review: Antibiotic prophylaxis for cesarean section

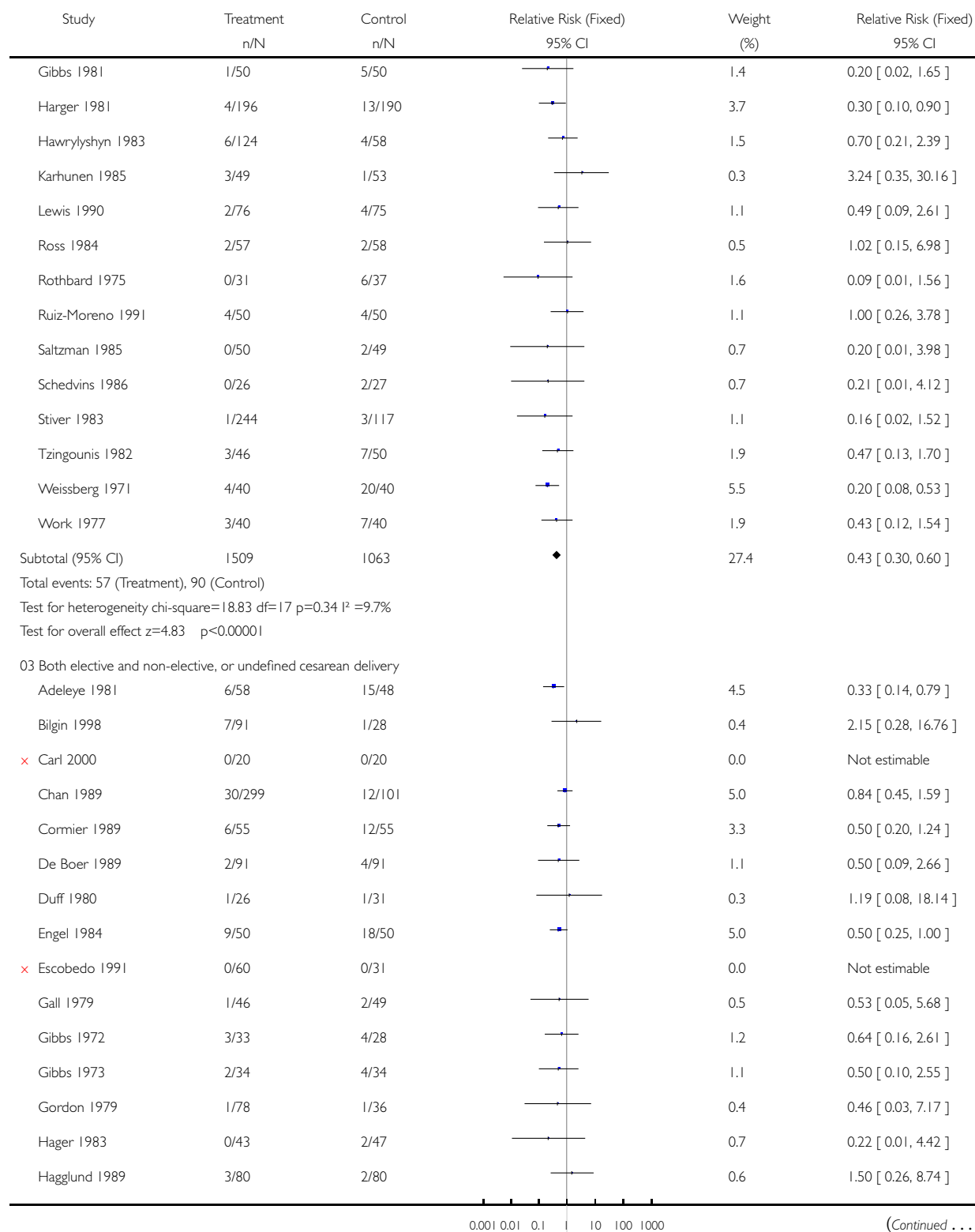
Comparison: 01 Prophylactic antibiotics in cesarean section

Outcome: 04 Urinary tract infection

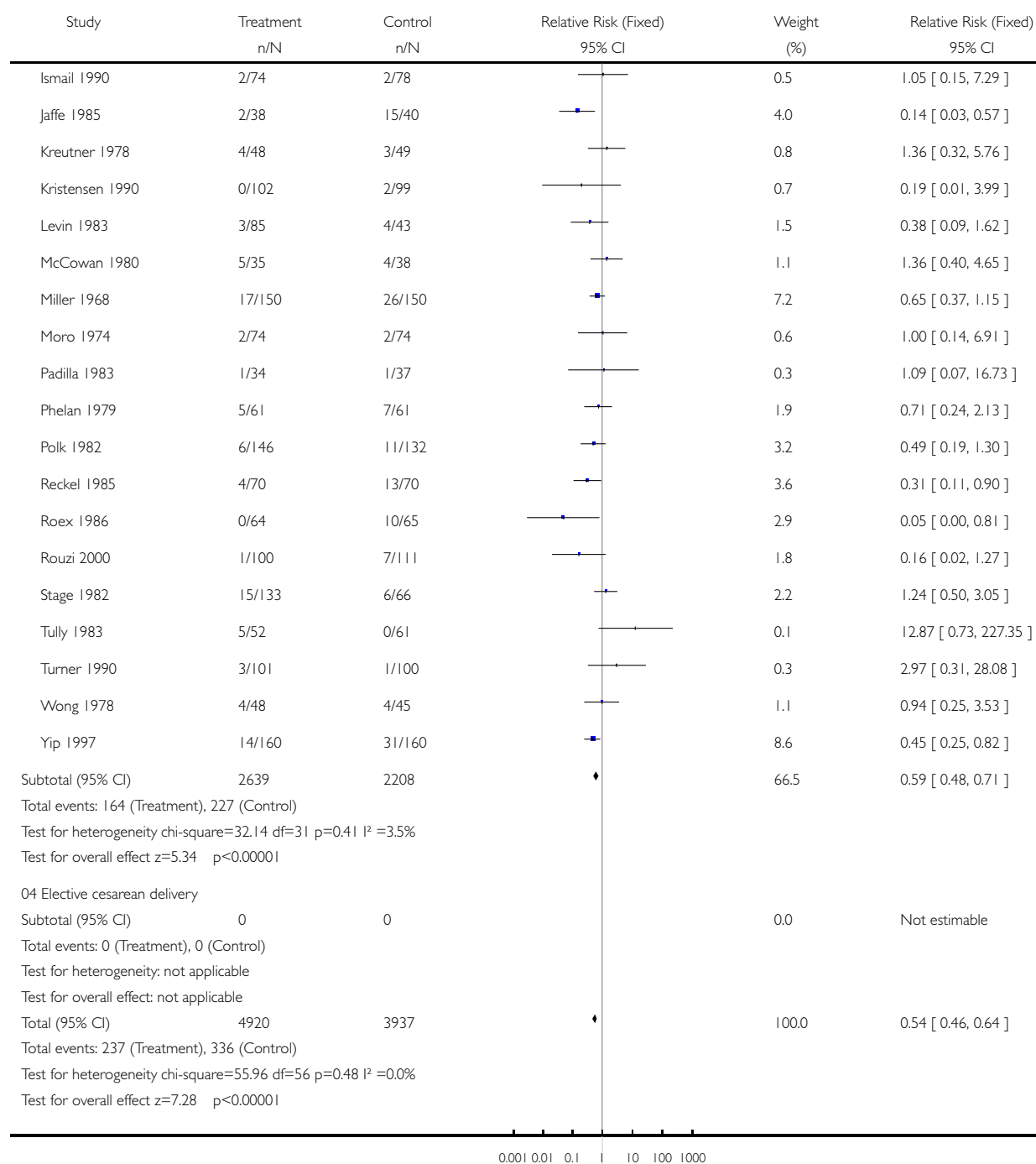


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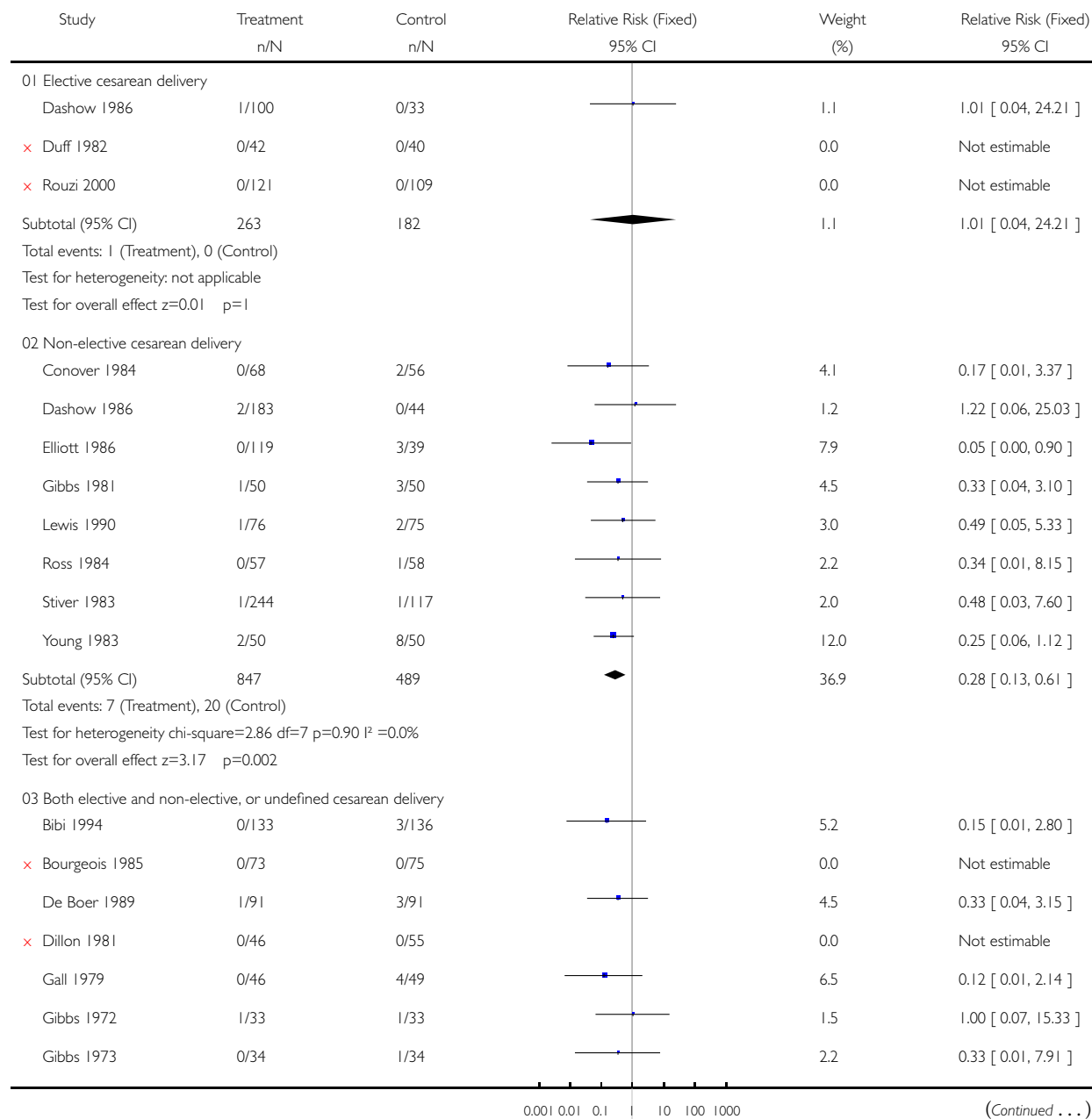


Analysis 01.05. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 05 Serious infectious morbidity/death

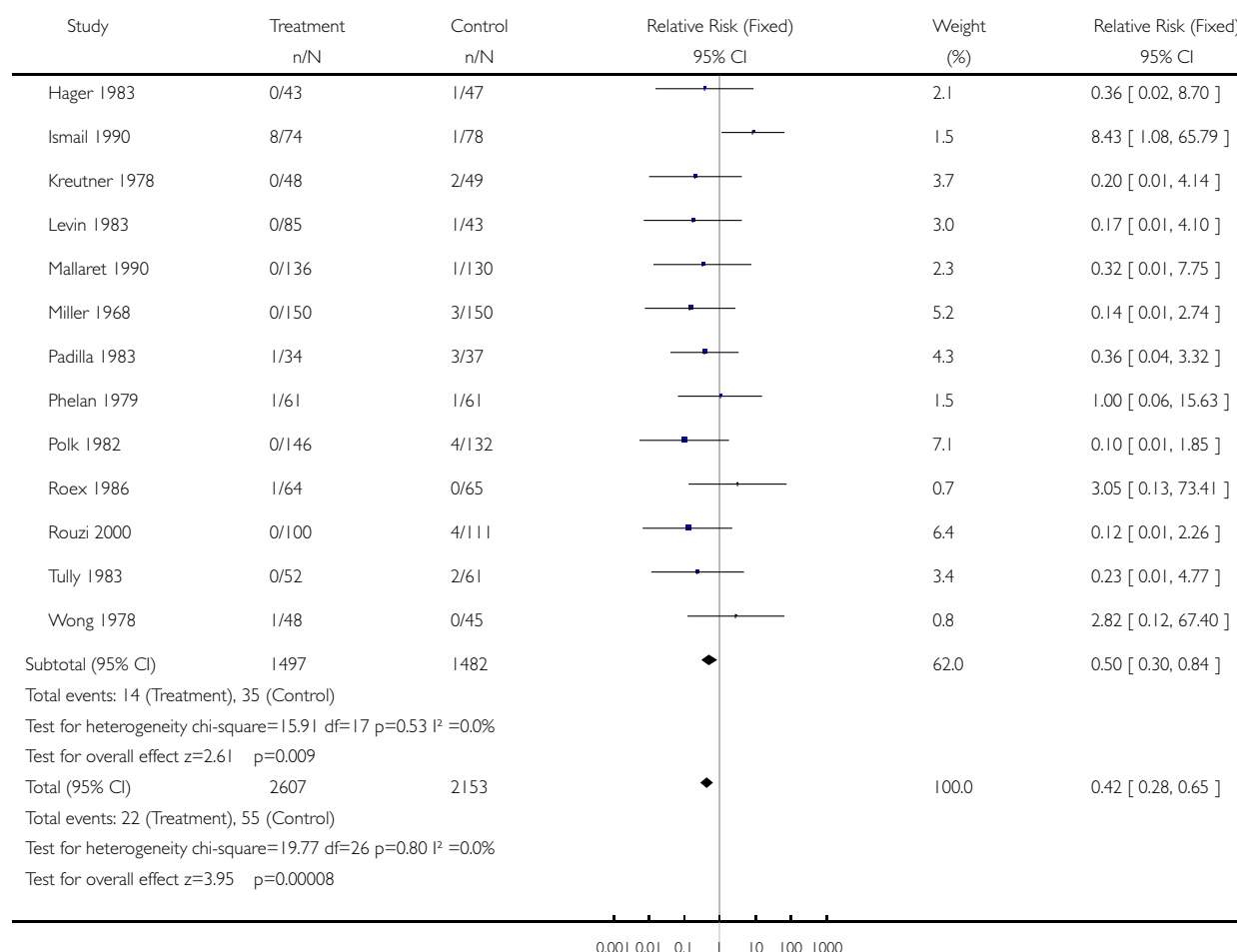
Review: Antibiotic prophylaxis for cesarean section

Comparison: 01 Prophylactic antibiotics in cesarean section

Outcome: 05 Serious infectious morbidity/death



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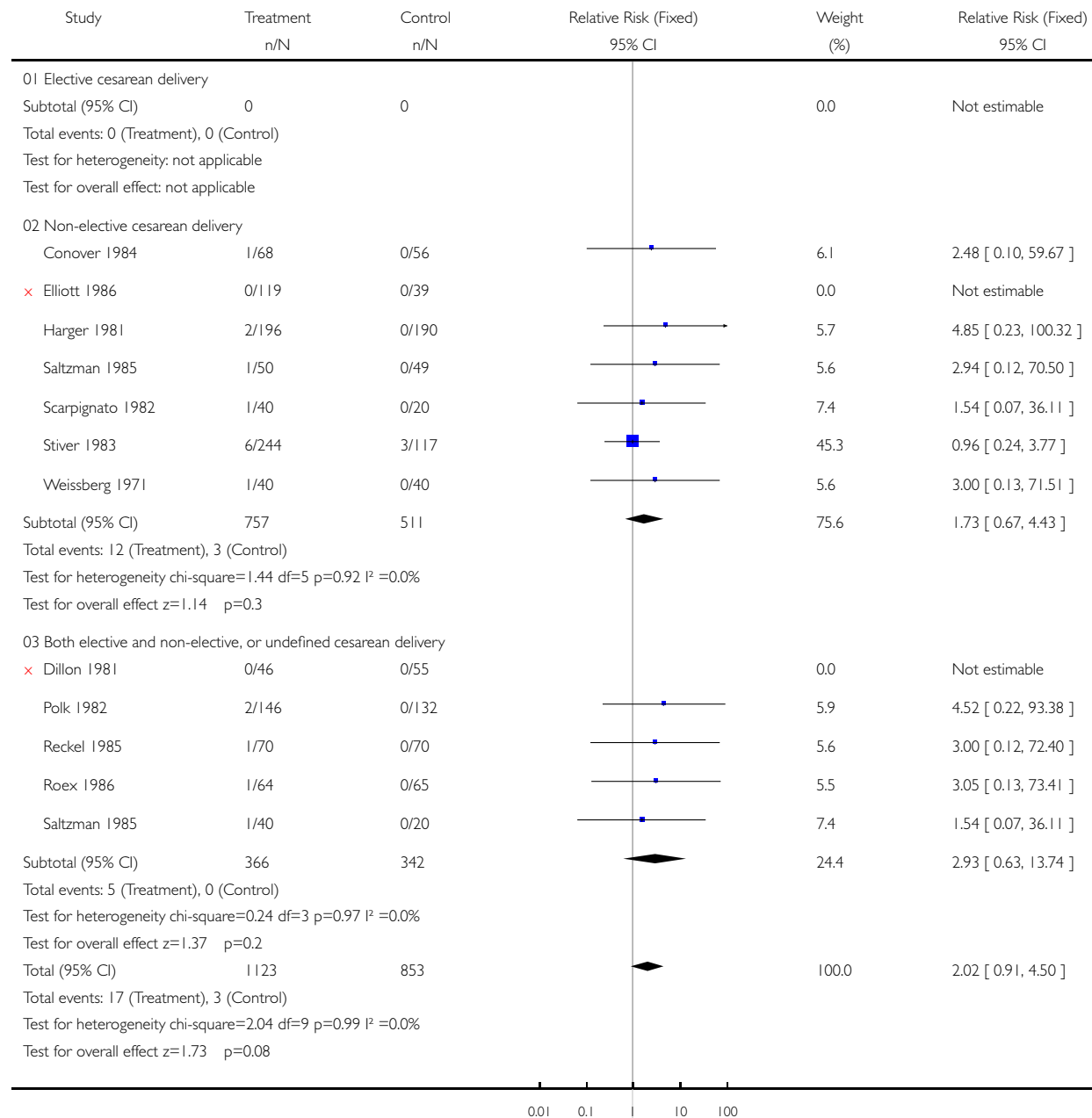


Analysis 01.06. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 06 Maternal side-effects

Review: Antibiotic prophylaxis for cesarean section

Comparison: 01 Prophylactic antibiotics in cesarean section

Outcome: 06 Maternal side-effects



Analysis 01.07. Comparison 01 Prophylactic antibiotics in cesarean section, Outcome 07 Days in hospital (mother)

Review: Antibiotic prophylaxis for cesarean section

Comparison: 01 Prophylactic antibiotics in cesarean section

Outcome: 07 Days in hospital (mother)

