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# Perioperative antibiotics to prevent infection after first-trimester abortion (Review)

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[Intervention Review]

# Perioperative antibiotics to prevent infection after first-trimester abortion

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## ABSTRACT

### Background

There are two main strategies for the prevention of post-abortal upper genital tract infection: antibiotics given around the time of surgery for all women; and 'screen-and-treat', in which all women presenting for abortion are screened for genital infections and those with positive results are treated.

### Objectives

To determine:

1. the effectiveness of antibiotic prophylaxis in preventing post-abortal upper genital tract infection;
2. the most effective antibiotic regimen;
3. the most effective strategy.

### Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE, POPLINE and LILACS. The search was last updated in May 2011.

### Selection criteria

Randomised controlled trials (RCTs) in any language including women undergoing induced first trimester surgical or medical abortion, comparing: 1) any antibiotic regimen to placebo, nothing, or another antibiotic; 2) screen-and-treat versus antibiotics. The primary outcome was the proportion of women diagnosed with post-abortal upper genital tract infection.

### Data collection and analysis

Two reviewers independently selected references and extracted data. We calculated risk ratios (RR) with 95% confidence intervals (CI). We used meta-analysis where appropriate and examined between trial heterogeneity using the $I^2$ statistic. In the presence of between trial heterogeneity we also estimated the 95% prediction interval (PI).

### Main results

A total of 703 unique items was identified. We included 19 RCTs. There was evidence of small study biases (Egger test, P = 0.002). In 15 placebo-controlled RCTs there was an effect of antibiotic prophylaxis (pooled RR 0.59, 95% CI 0.46 to 0.75, 95% PI 0.30 to 1.14, $I^2$ = 39%).

There were insufficient data (three trials) to determine whether one regimen was superior to another. In one trial, the incidence of post-abortal upper genital tract infection was higher in women allocated to the screen-and-treat strategy (RR 1.53, 95% CI 0.99 to 2.36).

**Authors' conclusions**

Antibiotic prophylaxis at the time of first trimester surgical abortion is effective in preventing post-abortal upper genital tract infection. Evidence of between trial heterogeneity suggests that the effect might not apply to all settings, population groups or interventions.

This review did not determine the most effective antibiotic prophylaxis regimen. Antibiotic choice should take into account the local epidemiology of genital tract infections, including sexually transmitted infections.

Further RCTs comparing different antibiotics or combinations of antibiotics with each other would be useful. Such trials could be done in low and middle income countries and where the prevalence of genital tract infections in women presenting for abortion is high.

## PLAIN LANGUAGE SUMMARY

**Antibiotic prophylaxis for first trimester induced abortion**

Infection of the upper genital tract, including the uterus and fallopian tubes, can cause complications after induced abortion. Antibiotics given around the time of the abortion (prophylaxis) could prevent this complication. We found 19 randomised controlled trials that looked at the effect of antibiotic prophylaxis on post-abortal upper genital tract infection amongst women requesting induced abortion in the first trimester of pregnancy. We looked at the effect of any antibiotic prophylaxis regimen on the outcome. Overall, the risk of post-abortal upper genital tract infection in women receiving antibiotics was 59% that of women who received placebo. There were, however, differences between the trial results over and above what would be expected by chance alone. It should be noted that, if the infection is caused by a sexually transmitted organism, antibiotic prophylaxis will not protect the woman from becoming re-infected if her sexual partner has not been treated. None of the trials was done in lower or middle income countries, which is where the risk of post-abortal complications is highest. Further trials are needed to determine whether combinations of antibiotics can prevent more infections than single antibiotics, or whether antibiotic prophylaxis should be restricted to women with positive results of screening tests before the abortion.

## SUMMARY OF FINDINGS

**Summary of findings for the main comparison. Summary table of secondary outcomes in all 19 trials reviewed**

| First author, year | No. of patients analysed for secondary outcome (%, patients analysed for primary outcome as denominator) | Antibiotic treatment within 6 weeks after abortion | Hospitalisation due to infectious complications | Adverse effects of antibiotics |
|---|---|---|---|---|
| *Comparison: antibiotics vs placebo* | | | | |
| Crowley 2001 | n.r. | n.r. | 15 women readmitted in total | n.r. |
| Darj 1987 | 769 (100%) | n.r. | n.r. | Gastrointestinal problems (nausea, vomiting), other (unspecified) |
| Heisterberg 1985b | 532 (100%) | n.r. | n.r. | Gastrointestinal problems (unspecified) |
| Heisterberg 1985c | 12 (12%), only women developing post-abortal upper genital tract infection analysed | Mean amount of antibiotic per patient in intervention arm: 5.9 g (metronidazole) and 8.0 g (ampicillin) and 8.5 IU (penicillin)<br>Mean amount of antibiotic per patient in control arm: 4.1 g (metronidazole) and 13.5 g (ampicillin) and 7.1 IU (penicillin) | Mean hospital days per patient in intervention arm: 6.5 days<br>Mean hospital days per patient in control arm: 6.1 days | n.r. |
| Heisterberg 1987 | 14 (12%), only women developing post-abortal upper genital tract infection analysed | n.r. | n.r. | No adverse events observed. |
| Heisterberg 1988 | 9 (16%), only women developing post-abortal upper genital tract infection analysed | Mean amount of antibiotic per patient in intervention arm: 5.0 g (metronidazole) and 8.3 g (erythromycin)<br>Mean amount of antibiotic per patient in control arm: 5.6 g (metronidazole) and 10.0 g (erythromycin) | Mean hospital days per patient in intervention arm: 6.3 days<br>Mean hospital days per patient in control arm: 7.0 days | n.r. |
| Krohn 1981 | 17 (8%), only women developing post-abortal upper genital tract infection analysed | n.r. | One woman readmitted in each arm | n.r. |
| Krohn 1986 | 285 (100%) | n.r. | n.r. | No adverse events observed. |
| Larsson 1992 | n.r. | n.r. | n.r. | n.r. |

| | | | | |
|---|---|---|---|---|
| Larsson 2000 | n.r. | n.r. | n.r. | n.r. |
| Levallois 1988 | 1077 (100%) | n.r. | n.r. | Gastrointestinal problems (vomiting, nausea, diarrhoea) |
| Nielsen 1993 | 1073 (100%) | n.r. | n.r. | Gastrointestinal problems (vomiting, nausea), hypersensitivity reactions (skin ,rash itching, tongue blisters), pain |
| Sonne-Holm 1981 | 493 (100%) | n.r. | n.r. | Hypersensitivity reactions (rash), gastrointestinal problems (unspecified) |
| Sorensen 1992 | n.r. | n.r. | n.r. | n.r. |
| Westrom 1981 | n.r. | n.r. | n.r. | n.r. |
| *Comparison: antibiotics vs antibiotics* | | | | |
| Caruso 2008 | n.r. | n.r. | n.r. | n.r. |
| Heisterberg 1986 | 13 (16%), only women developing post-abortal upper genital tract infection analysed | Mean amount of antibiotic per patient in intervention arm: 9.6 g (metronidazole) and 10.3 g (ampicillin), 1.6 g (tetracycline) and 1.4 g (erythromycin)<br><br>Mean amount of antibiotic per patient in control arm: 7.3 g (metronidazole) and 7.9 g (ampicillin), 0.8 g (tetracycline) and 0 g (erythromycin) | Mean hospital days per patient in intervention arm: 2.4 days<br><br>Mean hospital days per patient in control arm: 3.9 days | No adverse events observed. |
| Lichtenberg 2003 | n.r. | n.r. | n.r. | n.r. |
| *Comparison: universal antibiotic prophylaxis vs screen-and-treat-policy* | | | | |
| Penney 1998 | 1546 (96%), some women lost to follow up | n.r. | 16 women readmitted in the arm with universal prophylaxis<br><br>1 woman readmitted in the arm with screen-and-treat-policy | n.r. |

n.r.: not reported

## BACKGROUND

Each year 210 million women become pregnant, of whom an estimated 42 million have an induced abortion (WHO 2011). Abortion causes 70,000 deaths and 4,652,171 Disability Adjusted Life Years (DALYs) lost per year worldwide, the vast majority due to unsafe abortions in developing countries. Thirteen percent (47,000) of maternal deaths worldwide are due to unsafe abortion and infections are a major contributor (WHO 2011), Cervical instrumentation can introduce bacteria from the vagina and cervix into the endometrial cavity, leading to post-abortal upper genital tract infection (Sawaya 1996). The terms post-abortal pelvic infection (Levallois 1988) and post-abortal pelvic inflammatory disease (PID) (Heisterberg 1988b), have also been used to describe this condition. Infectious agents associated with post-abortal upper genital tract infection include exogenous bacteria, endogenous vaginal anaerobes associated with bacterial vaginosis, or sexually transmitted cervical pathogens (*Neisseria gonorrhoeae* and *Chlamydia trachomatis*). The prevalence of endocervical *C. trachomatis* in women presenting for abortion has been found to be 13-14% amongst women screened using a nucleic acid amplification test in abortion clinics in England in 1999-2000 (Pimenta 2003) and 2.9% in women undergoing legal abortion in Maputo, Mozambique in 1991-1992, tested using direct immunofluorescence staining (Machungo 2002). Risk factors for post-abortal upper genital tract infection include a history of pelvic inflammatory disease (PID) and the presence of a lower genital tract infection due to *N. gonorrhoeae*, *C. trachomatis* or bacterial vaginosis at the time of abortion (Heisterberg 1988b; Nielsen 1993). Post-abortal upper genital tract infection is associated with short-term morbidity (Cameron 2002) and upper genital tract infections have long-term sequelae in the form of chronic pelvic pain, dyspareunia, infertility and ectopic pregnancy (Soper 2010).

Antibiotics given around the time of abortion should reduce the risk of post-abortal upper genital tract infection. There is, however, ongoing debate about the most effective strategy and antibiotic regimen (Cameron 2002; Penney 1998). The possible approaches that have been investigated so far are described below.

### Antibiotic prophylaxis

Antibiotic prophylaxis is defined as the 'use of antibiotics before, during, or after a diagnostic, therapeutic, or surgical procedure to prevent infectious complications' (National Centre for Biotechnology Information 2010). For women undergoing abortion, this means that they are given antibiotics around the time of surgery even if they are not known to have a vaginal or cervical infection. Universal prophylaxis means that all women are given antibiotics, without carrying out tests for infection. The case in favour of universal antibiotic prophylaxis was first made in a systematic review (Sawaya 1996). Sawaya et al. conducted a meta-analysis of 12 randomised controlled trials (RCTs) published between 1966 and 1994 comparing antibiotics with placebo. They reported a substantial reduction in the risk of post-abortal upper genital tract infection in women receiving antibiotic prophylaxis (relative risk, RR 0.58, 95% confidence intervals, CI 0.47 to 0.71, fixed-effects meta-analysis) but there was substantial between-trial heterogeneity in the results (reported as $P < 0.001$ for homogeneity). The authors concluded that there had been strong evidence that antibiotics reduce the risk of post-abortal infection since 1986 and that further placebo-controlled trials should not be performed (Sawaya 1996). Guidelines about the use of antibiotic prophylaxis for abortion have since been published by several national guideline development groups (Achilles 2011; ACOG 2006; RCOG 2011; SIGN 2008).

### Screen-and-treat

Screen-and-treat means that all women presenting for a termination of pregnancy are screened for genital infections. Those with positive results are treated as soon as the results are known, preferably before the procedure. A screen-and-treat strategy for preventing post-abortal upper genital tract infection due to chlamydia has been evaluated (Giertz 1987; Penney 1998). The major advantage of the screen-and-treat strategy over universal antibiotic prophylaxis is that, if the woman has a sexually transmitted infection, partner notification and treatment can be done to reduce the risk of re-infection from untreated sexual partners (Cameron 2002). In addition, the screen-and-treat strategy avoids the unnecessary administration of antibiotics to non-infected women and provides an opportunity to screen for other sexually transmitted infections and offer counselling (Cameron 2002). However, this strategy is costly and requires more organisation than does universal prophylaxis. Timely provision of results is essential and, even then might delay the procedure if the initial assessment and abortion take place at the same visit. Furthermore, false negative screening test results and infections not screened for can still put women at risk of post-abortal infection (Penney 1998). The infections for which women should be tested differs between settings. The low prevalence of gonorrhoea among women undergoing abortion in the United Kingdom (approximately 0.2%) (Blackwell 1993) makes screening in asymptomatic women controversial (Cameron 2002). In contrast, the prevalence of bacterial vaginosis is high among women requesting abortion, ranging from 17.5% (Penney 1998) to 28% (Blackwell 1993). Furthermore, *C. trachomatis* is detected more often in women with bacterial vaginosis and it may facilitate the carriage of chlamydia to the upper genital tract (Blackwell 1993). Combining preoperative screening with universal antibiotic prophylaxis could prevent both short-term morbidity and allow treatment of sexual partners of infected women, but this would increase costs to the health service even more.

An updated systematic review of the effects of antibiotic prophylaxis in induced abortion provides opportunities to include more recent trials and to address unanswered questions. These may include differences in the effectiveness of antibiotics in trials of women who are not screened for infections preoperatively and those that excluded women with diagnosed infections: determining the optimal antibiotic regimen determining adverse effects and examining the implications for re-infection in women who had a sexually transmitted infection before the abortion.

## OBJECTIVES

1. To determine the effectiveness of antibiotic prophylaxis in preventing post-abortal upper genital tract infection.
2. To determine the most effective antibiotic regimen for preventing post-abortal upper genital tract infection.
3. To determine the most effective strategy for preventing post-abortal upper genital tract infection by comparing universal antibiotic prophylaxis with a screen and treat strategy, or with a combination of screen-and-treat plus universal prophylaxis.

# METHODS

## Criteria for considering studies for this review

### Types of studies

We included all RCTs published by May 2011 in any language.

### Types of participants

All women undergoing induced first trimester surgical or medical abortion with or without a history of PID, or a pre-abortion diagnosis of bacterial vaginosis, *N. gonorrhoeae* or *C. trachomatis.*

### Types of interventions

1. Antibiotic prophylaxis:
a. any antibiotic regimen compared to a placebo or nothing. Both local and systemic antibiotic regimens were included. Antibiotic regimens that included preoperative, perioperative, postoperative doses, or any combination of these were included;
b. any antibiotic regimen compared to another antibiotic regimen. Both local and systemic antibiotic prophylaxis were included.

2. Screen-and-treat strategy:
a. universal antibiotic prophylaxis compared to a screen-and-treat strategy and/or a combination of screen-and-treat and antibiotic prophylaxis.

### Types of outcome measures

1. The primary outcome was the proportion of women diagnosed with post-abortal upper genital tract infection, according to the definition used in the original trials.

2. Secondary outcomes were:
a. other antibiotic treatments provided in the six weeks following the abortion;
b. hospitalisation due to infectious complications;
c. adverse effects of antibiotic prophylaxis or screening;
d. proportion of women undergoing the screen-and-treat strategy who were re-infected with *C. trachomatis*.

## Search methods for identification of studies

A comprehensive literature search was conducted to identify reports describing universal antibiotic prophylaxis, the screen-and-treat strategy and a combination of both strategies for first-trimester abortion. Reference lists of relevant papers were screened for additional, previously unidentified trials. The search was last updated in May 2011. See Appendix 1 for search strategies used.

## Data collection and analysis

### Study identification and data extraction

Two reviewers assessed the titles and abstracts as well as full-text publications to determine eligibility. The same two reviewers used a standardised form to extract data, in duplicate, for characteristics of trials and patients, type of intervention and antibiotic prophylaxis conducted, as well as number of women developing post-abortal upper genital tract infection. Information about trial characteristics that might be associated with bias in the effect estimates, including randomisation sequence generation, concealment of allocation, blinding, and exclusion of participants from analysis after randomisation were also assessed, using criteria from the Cochrane Handbook. Disagreements were resolved by discussion with a third reviewer. We also contacted the trial authors to request clarifications and obtain missing data. Entry of the data in Review Manager software (RevMan 5) was double checked.

### Data synthesis and analysis

We first conducted a descriptive synthesis of the trials and their results and displayed the results in forest plots (RevMan 5).

- For the primary outcome we have used the term 'post-abortal upper genital tract infection', but in the summary of characteristics of included studies we have given the name for the primary outcome used by the trial authors, together with their diagnostic criteria.
- For the intervention, we have used the general term 'antibiotic prophylaxis'. We used the term 'universal antibiotic prophylaxis' only if the trial report did not state that women were tested for genital infections at baseline and that women with positive results would be excluded or treated preoperatively. We did not define a time limit on the duration of the antibiotic regimen.

The results of individual trials are presented as the relative risk (RR) with 95% confidence intervals (95% CI) of post-abortal upper genital tract infection in women in the intervention group compared to those in the control group.

To examine evidence for publication and small study biases we drew funnel plots of log risk ratios against trial size (measured by standard error of the log risk ratio) and did a statistical test for asymmetry (Egger 1997).

Where appropriate, we pooled data using meta-analysis in Stata (version 10, Stata Corporation, Austin, TX). We used the I-squared statistic to estimate the approximate proportion of total variability in point estimates that can be attributed to heterogeneity other than that due to chance (Higgins 2003). We explored possible reasons for heterogeneity by stratifying study results according to the characteristics of the study populations (e.g. history of PID or chlamydia), the interventions (e.g. class of antibiotics used, route of administration, etc.), or methodological characteristics (adequate compared with inadequate random sequence generation, etc.). We also examined the role of methodological characteristics on the effect estimate using meta-regression to estimate the ratio of risk ratios. We used fixed-effects meta-analysis to estimate the common RR (95% CI), assuming that all or most between-trial variability is due to chance if there was little evidence of between-trial heterogeneity ($I^2$ < 25%). In the presence of between-trial heterogeneity ($I^2$ = 25 to 75%) we used random-effects meta-analysis (Der Simonian Laird model) to estimate the average RR. In the text, we present both 95% CI, which express uncertainty around the average effect, which is assumed to be normally distributed, and the 95% prediction interval (PI), which takes into account the whole distribution of the effects (Riley 2011). We did not pool results if there was statistical evidence of severe between-trial heterogeneity ($I^2$ > 75%).

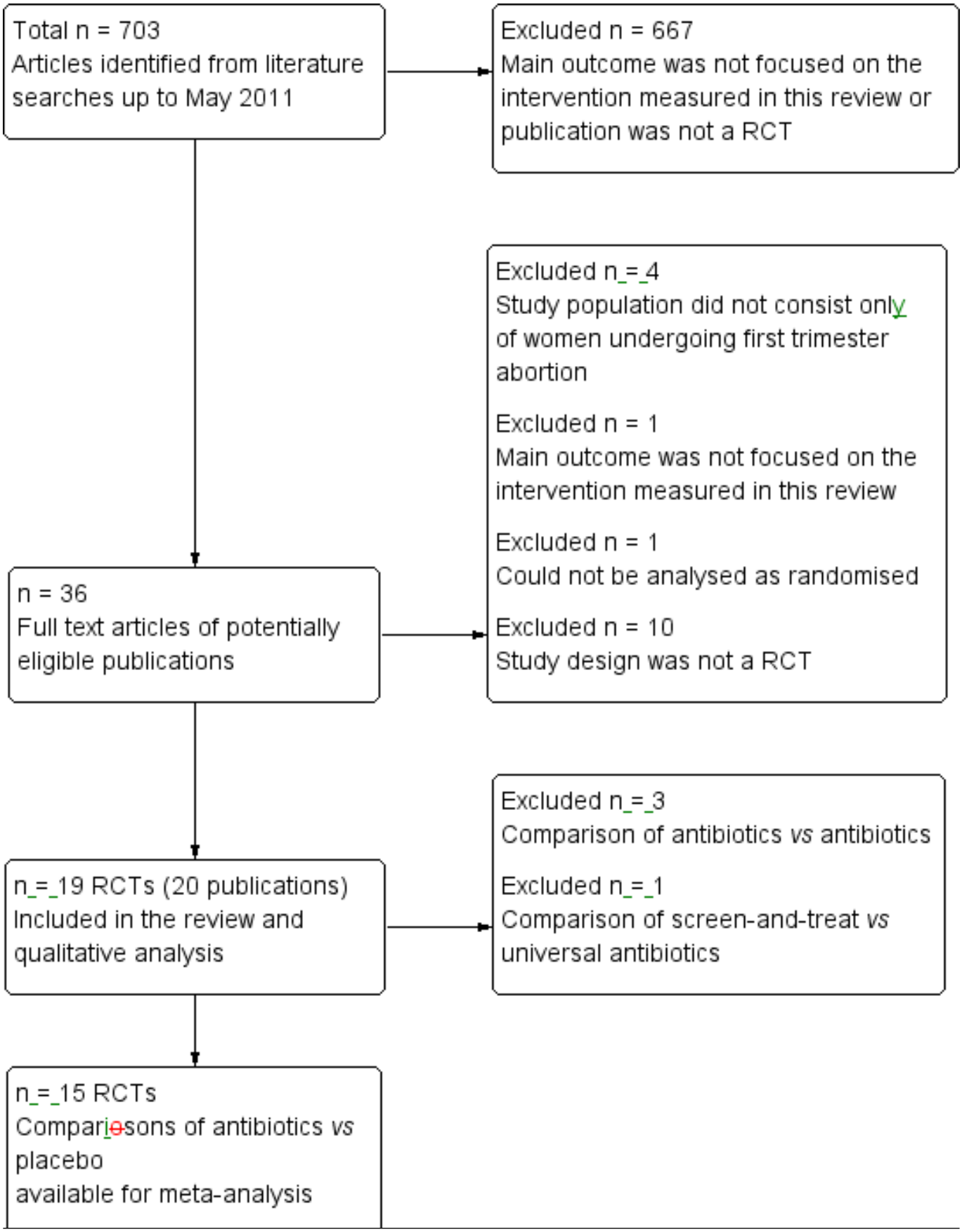
# RESULTS

## Description of studies

Figure 1 shows the flow diagram of studies identified and included in the review. A total of 703 unique items was identified. The full text of 36 potentially eligible publications was read. Sixteen arti-

cles were excluded (Characteristics of excluded studies). Four articles were excluded because the study population was not restricted to women undergoing first-trimester abortion (Cormier 1988; Giertz 1987; Miller 2004; Spence 1982). One study was excluded because the outcome was bacteraemia after abortion and not upper genital tract infection (Heisterberg 1985c). A trial by Henriques et al. (Henriques 1994) was excluded because the women could not be analysed in the groups to which they were randomised; a post-randomisation risk assessment of women in the control group was made and treatment adapted according to this evaluation. We also excluded ten studies that were not RCTs (Bennett 2009; Blackwell 1993; Chen 2007; Faucher 2006; Gemzell-Danielsson 2008; Grossmann 2008; Gupta 2007; May 2007; Nguyen 2009; Prager 2009).

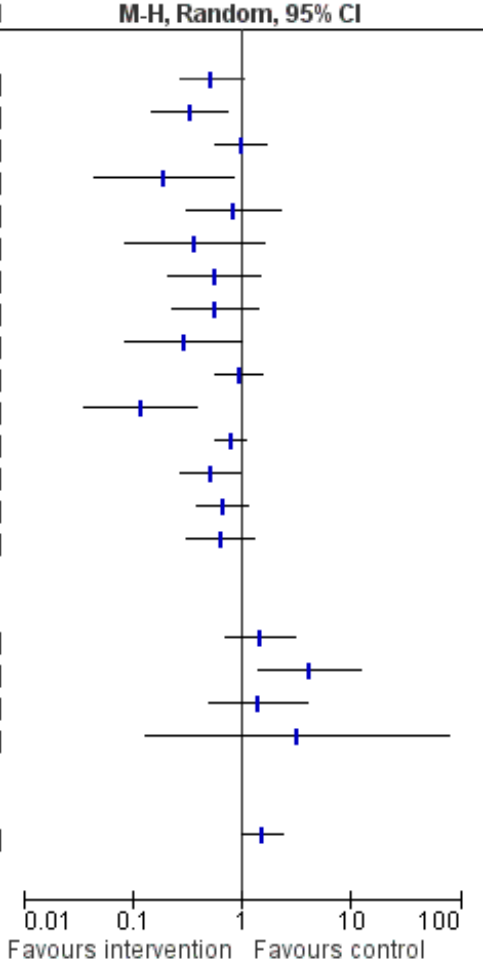
**Figure 1. Flow diagram.**



Nineteen RCTs, reported in 20 publications (see Characteristics of included studies), were included in the main dataset and descriptive assessment of the prophylactic effect of antibiotics to prevent postoperative pelvic infection in women undergoing first-trimester abortion, compared with women receiving placebo, another antibiotic, or a screen-and-treat strategy (Figure 2) (Caruso 2008; Crowley 2001; Darj 1987; Heisterberg 1985a; Heisterberg 1985b; Heisterberg 1986; Heisterberg 1987; Heisterberg 1988; Krohn 1981; Krohn 1986; Larsson 1992; Larsson 2000; Levallois 1988; Lichtenberg 2003; Nielsen 1993; Penney 1998; Sonne-Holm 1981; Sorensen 1992; Westrom 1981). A total of 9715 women was included, 660 of whom developed post-abortal upper genital tract infection. One of the trials by Heisterberg and colleagues was reported with earlier and later results. Both are listed under Heisterberg 1986. We only include the results from the most recent publication.

**Figure 2. Effect of intervention on incidence of post-abortal upper genital tract infection, 19 trials: by comparison**

| Study or Subgroup | Intervention Events | Intervention Total | Control Events | Control Total | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|
| **1.1.1 Antibiotic prophylaxis vs. placebo** | | | | | |
| Crowley 2001 | 12 | 142 | 21 | 131 | 0.53 [0.27, 1.03] |
| Darj 1987 | 8 | 386 | 24 | 383 | 0.33 [0.15, 0.73] |
| Heisterberg 1985a | 25 | 269 | 25 | 263 | 0.98 [0.58, 1.66] |
| Heisterberg 1985b | 2 | 51 | 10 | 49 | 0.19 [0.04, 0.83] |
| Heisterberg 1987 | 7 | 64 | 7 | 54 | 0.84 [0.32, 2.26] |
| Heisterberg 1988 | 2 | 24 | 7 | 31 | 0.37 [0.08, 1.62] |
| Krohn 1981 | 6 | 104 | 11 | 106 | 0.56 [0.21, 1.45] |
| Krohn 1986 | 7 | 145 | 12 | 140 | 0.56 [0.23, 1.39] |
| Larsson 1992 | 3 | 84 | 11 | 90 | 0.29 [0.08, 1.01] |
| Larsson 2000 | 29 | 650 | 30 | 626 | 0.93 [0.57, 1.53] |
| Levallois 1988 | 3 | 536 | 26 | 541 | 0.12 [0.04, 0.38] |
| Nielsen 1993 | 55 | 525 | 73 | 548 | 0.79 [0.57, 1.09] |
| Sonne-Holm 1981 | 14 | 254 | 26 | 239 | 0.51 [0.27, 0.95] |
| Sorensen 1992 | 20 | 189 | 30 | 189 | 0.67 [0.39, 1.13] |
| Westrom 1981 | 10 | 102 | 17 | 110 | 0.63 [0.30, 1.32] |
| **1.1.2 Antibiotic prophylaxis vs. alternative regimen(s)** | | | | | |
| Caruso 2008 | 16 | 153 | 11 | 155 | 1.47 [0.71, 3.07] |
| Caruso 2008 | 16 | 153 | 4 | 158 | 4.13 [1.41, 12.08] |
| Heisterberg 1986 | 8 | 43 | 5 | 38 | 1.41 [0.51, 3.96] |
| Lichtenberg 2003 | 1 | 257 | 0 | 273 | 3.19 [0.13, 77.86] |
| **1.1.3 Screen-and-treat vs. universal antibiotic prophylaxis** | | | | | |
| Penney 1998 | 51 | 836 | 31 | 777 | 1.53 [0.99, 2.36] |




We did not identify any RCTs that included women who had undergone a medical abortion.

Of the 19 included RCTs, 15 compared antibiotic prophylaxis with administration of placebo (Crowley 2001; Darj 1987; Heisterberg 1985a; Heisterberg 1985b; Heisterberg 1987; Heisterberg 1988; Krohn 1981; Krohn 1986; Larsson 1992; Larsson 2000; Levallois 1988; Nielsen 1993; Sonne-Holm 1981; Sorensen 1992; Westrom 1981). Three trials compared antibiotic prophylaxis using one regimen in the intervention arm with an alternative regimen (Heisterberg 1986; Lichtenberg 2003) or regimens (Caruso 2008). One trial compared a screen-and-treat strategy with universal antibiotic prophylaxis (Penney 1998).

The characteristics of included trials are shown below. Most were conducted in Sweden (seven RCTs) (Darj 1987; Krohn 1981; Krohn 1986; Larsson 1992; Larsson 2000; Nielsen 1993; Westrom 1981) and Denmark (seven RCTs) (Heisterberg 1985a; Heisterberg 1985b; Heisterberg 1986; Heisterberg 1987; Heisterberg 1988; Sonne-Holm 1981; Sorensen 1992). One trial took place in each of the following countries: England (Crowley 2001), Scotland (Penney 1998), Italy (Caruso 2008), USA (Lichtenberg 2003) and Canada (Levallois 1988). No studies were conducted in a low or middle income country.

**Reporting of sexually transmitted infections, bacterial vaginosis and history of PID at baseline and exclusions from study population**

In 15 of the 19 trials (Table 1), authors reported that women had laboratory tests for at least one genital infection (Crowley 2001; Heisterberg 1985a; Heisterberg 1985b; Heisterberg 1986; Heisterberg 1987; Heisterberg 1988; Krohn 1981; Krohn 1986; Larsson 1992; Larsson 2000; Levallois 1988; Nielsen 1993; Penney 1998; Sorensen 1992; Westrom 1981). In two trials authors explicitly stated that no preoperative tests for infection were done (Darj 1987; Lichtenberg 2003). In two trials there was no mention of whether tests had been done or not (Caruso 2008; Sonne-Holm 1981).

In 8 of the 19 trials, *C. trachomatis* was tested for in all women at the baseline assessment; the percentage of women with a positive chlamydia test ranged from 1.9% (10/532) (Heisterberg 1985a) to 7.7% (21/273) (Crowley 2001). In two trials, women with chlamydia were treated and excluded (Larsson 1992; Larsson 2000); in one trial, women with chlamydia were treated preoperatively (Crowley 2001); in one trial, in the first part of the trial, women with chlamydia were treated after three weeks and in the second part of the trial women with positive chlamydia tests were excluded (Levallois 1988); in four trials the antibiotic regimens were active against *C. trachomatis* (Heisterberg 1985a; Heisterberg 1988; Penney 1998; Sorensen 1992). In one further trial, some of the women were tested for chlamydia, but the number of women with positive results was not reported (Krohn 1986). In the other 11 trials, testing for *C. trachomatis* was not done.

In 14 trials, *N. gonorrhoeae* was tested for in all women at the baseline visit: in 11 trials, women with gonorrhoea were treated and excluded (Heisterberg 1985a; Heisterberg 1985b; Heisterberg 1986; Heisterberg 1987; Heisterberg 1988; Larsson 1992; Larsson 2000; Levallois 1988; Nielsen 1993; Sorensen 1992; Westrom 1981); in two trials there were no infected women (Crowley 2001; Krohn 1986); in one trial, infected women (3/1613) were included (Penney 1998). In the other five trials, testing for *N. gonorrhoeae* was not done.

In six trials, testing for anaerobic organisms or bacterial vaginosis was done: the percentage of women with bacterial vaginosis in these trials ranged from 17% (220/1276 (Larsson 1992) and 282/1613 (Penney 1998)) to 36% (41/115 (Heisterberg 1987)). In two trials, only women with bacterial vaginosis were included (Crowley 2001; Larsson 1992); in three trials, women with bacterial vaginosis were a part of the study population (Heisterberg 1985b; Heisterberg 1987; Larsson 2000; Penney 1998). In the other 13 trials, testing for bacterial vaginosis was not done.

A history of PID was asked about in seven trials (Crowley 2001; Heisterberg 1985b; Heisterberg 1986; Heisterberg 1988; Nielsen 1993; Sonne-Holm 1981; Sorensen 1992). The criteria for such a diagnosis were reported in only one trial (antibiotics for PID prescribed by a patient's own doctor or a hospital) (Heisterberg 1986). The percentage of women reporting a history of PID was 4% (14/273) in one trial (Crowley 2001) but ranged from 21% (164/769 (Darj 1987) and 105/493 (Sonne-Holm 1981)) to 29% (308/1073 (Nielsen 1993)) in the other trials that recorded this information.

### Reporting of secondary outcomes

Summary of findings for the main comparison shows the studies that assessed secondary outcomes. Three reported antibiotic treatment provided within six weeks following abortion. All were conducted by Heisterberg and colleagues and reported the mean quantity of antibiotics used per infected patient (Heisterberg 1985b; Heisterberg 1986; Heisterberg 1988). None of the studies found statistical evidence of a difference in the amount of antibiotics administered for infection comparing the intervention with the control group. Hospitalisation due to infectious complications was assessed in six studies (Crowley 2001; Heisterberg 1985b; Heisterberg 1986; Heisterberg 1988; Krohn 1981; Penney 1998). Crowley et al. (Crowley 2001) reported the total number of women readmitted to hospital, but did not provide their group allocation. Krohn et al (Krohn 1981) found that in total two women with post-abortal pelvic infection were readmitted to hospital; one in each trial group. Heisterberg and colleagues assessed the mean number of hospital days per infected women for the intervention and control arms in three studies and found no statistical evidence of differences between the two arms (Heisterberg 1985b; Heisterberg 1986; Heisterberg 1988). Penney et al. (Penney 1998) investigated the number of women who were readmitted to hospital within six weeks after abortion. They found that twice as many women randomised to the screen-and-treat arm were readmitted when compared with the prophylactic treatment group.

Adverse events of antibiotic prophylaxis were investigated in eight trials (Darj 1987; Heisterberg 1985a; Heisterberg 1986; Heisterberg 1987; Krohn 1986; Levallois 1988; Nielsen 1993; Sonne-Holm 1981); three did not report any adverse effects (Heisterberg 1986; Heisterberg 1987; Krohn 1986). The most common problems were gastrointestinal symptoms such as nausea, vomiting and diarrhoea, as well as skin rash.

No studies reported the reinfection rate with *C. trachomatis* at follow-up after first-trimester abortion.

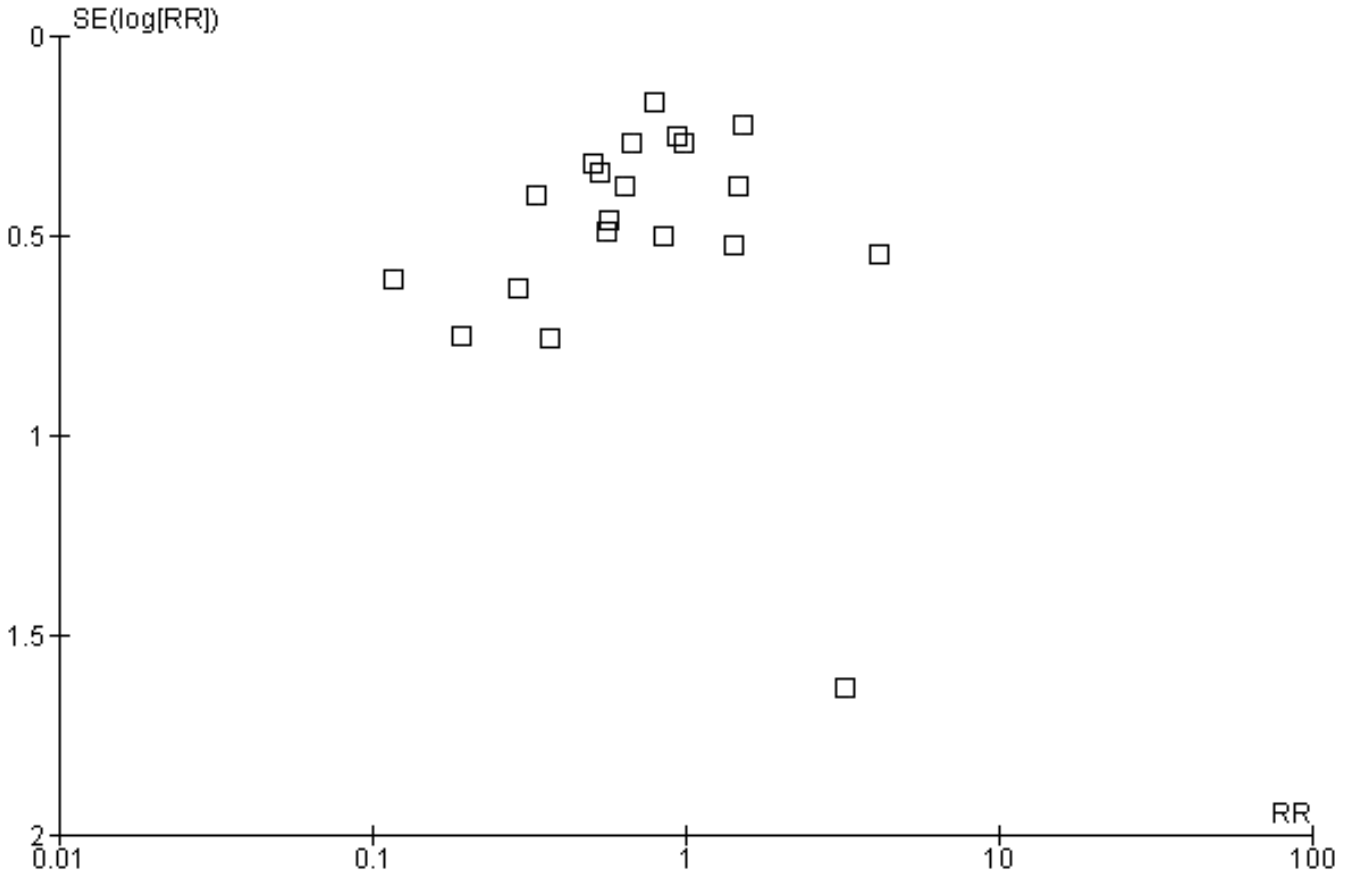
## Risk of bias in included studies

We assessed the risk of bias in all 19 included trials. In stratified analyses, the assessments of trial characteristics were dichotomised, comparing studies with either unclear or inadequate descriptions with those that used adequate methods. Details of the risk of bias assessed in all RCTs are shown with the Characteristics of included studies and summarised in Table 2.

We examined the possible influence of the reporting of methodological characteristics of trials on the observed effect size in stratified analysis of the 15 studies comparing antibiotics with placebo (Crowley 2001; Darj 1987; Heisterberg 1985a; Heisterberg 1985b; Heisterberg 1987; Heisterberg 1988; Krohn 1981; Krohn 1986; Larsson 1992; Larsson 2000; Levallois 1988; Nielsen 1993; Sonne-Holm 1981; Sorensen 1992; Westrom 1981). Table 3 summarises these findings. Table 4 shows the results of meta-regression analysis. In the domains of sequence generation, allocation concealment and blinding, the effect of antibiotics was stronger in trials with adequate reporting than in those with inadequate reporting. Confidence intervals were, however, wide and included the possibility of chance findings. The trial with the most marked effect of the intervention (RR 0.12, 95% CI 0.04 to 0.38) (Levallois 1988) was amongst those with adequate reporting of these methodological features.

Figure 3 shows a funnel plot of all 19 trials. There was strong evidence of small study biases (Egger test P value = 0.002).

**Figure 3. Funnel plot: 19 trials included in the main analysis**




## Effects of interventions

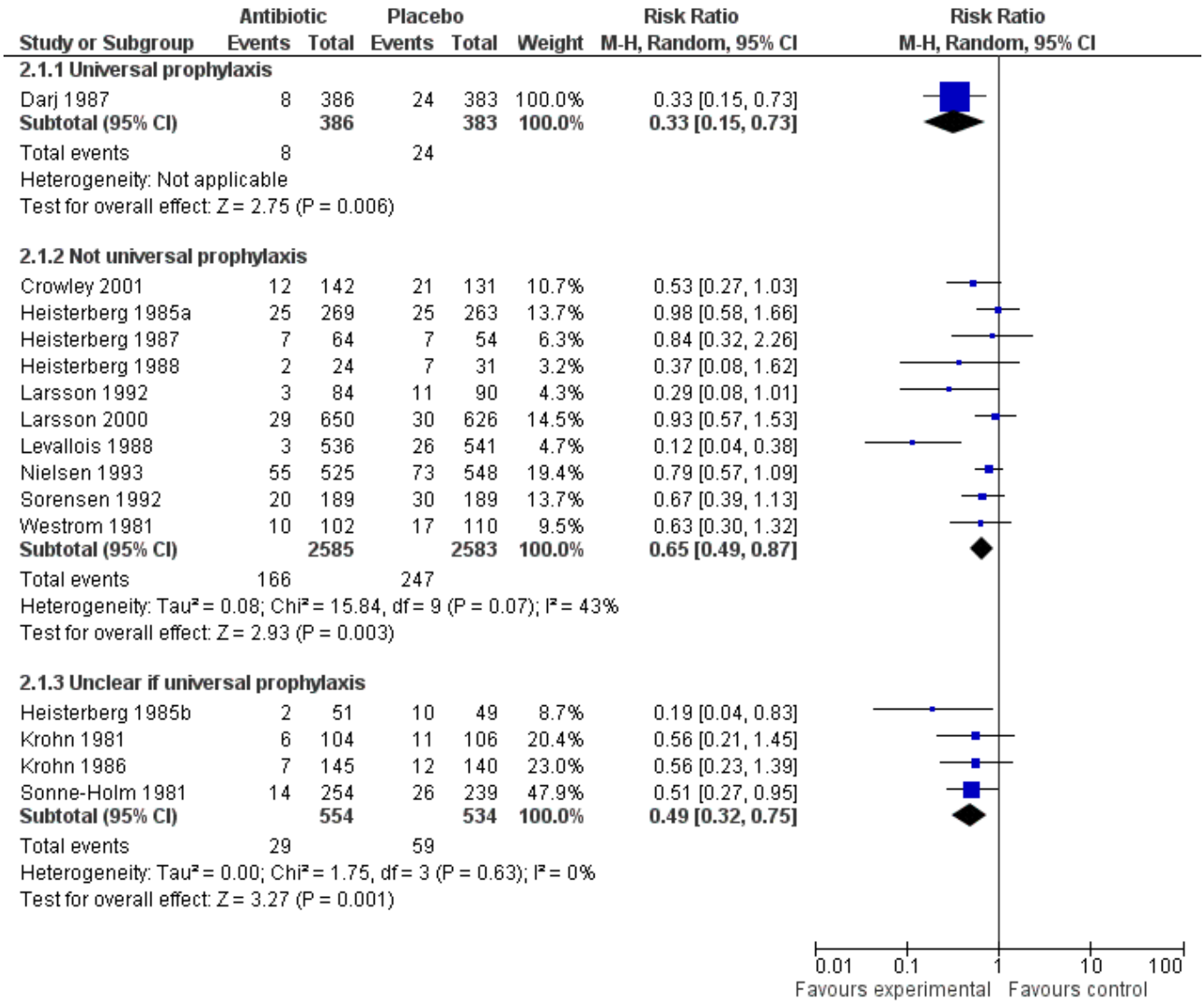
See: **Summary of findings for the main comparison** Summary table of secondary outcomes in all 19 trials reviewed

Figure 2 (Analysis 1.1) shows the results of all individual included trials, according to the particular review objective.

**Objective 1: Effectiveness of antibiotic prophylaxis in preventing post-abortal pelvic infection**

There were 15 trials comparing any antibiotic regimen with placebo (Figure 4, Analysis 2.1) (Crowley 2001; Darj 1987; Heisterberg 1985a; Heisterberg 1985b; Heisterberg 1987; Heisterberg 1988; Krohn 1981; Krohn 1986; Larsson 1992; Larsson 2000; Levallois 1988; Nielsen 1993; Sonne-Holm 1981; Sorensen 1992; Westrom 1981). These trials included a total of 7025 women (median 378 patients, range 55 to 1276). Of these, 3525 women were randomised to the intervention arm receiving antibiotics and 3500 women to the control arm receiving placebo. A total of 203 patients in the intervention arms compared with 330 in the control arms developed upper genital tract infection, according to the authors' definitions.

**Figure 4. Effect of antibiotic prophylaxis on post-abortal upper genital tract infection, 15 trials: by reporting of universal antibiotic prophylaxis.**




*Overall effectiveness of antibiotic prophylaxis*

The pooled RR for all trials of any antibiotic regimen was 0.59 (95% CI 0.46 to 0.75; 95% PI 0.30 to 1.14) in random-effects meta-analysis. There was statistical evidence of heterogeneity between the trial results, with 39% of the variation in results due to factors other than chance. The results of individual trials ranged from: an 88% reduction in the incidence of post-abortal upper genital tract infection in women receiving three perioperative doses of doxycycline on the day of the abortion (3/536) compared with placebo (26/541) (RR 0.12, 95% CI 0.04 to 0.38) (Levallois 1988), to no effect of a seven day course of lymecycline (25/269 women developed post-abortal upper genital tract infection compared with placebo (25/263) (RR 0.98, 95% CI 0.58 to 1.66) (Heisterberg 1985a).

We examined potential reasons for heterogeneity in stratified analyses (Table 3). In general, the magnitude of the effects of antibiotic prophylaxis in all strata was distributed around that of the overall pooled estimate, ranging from RR 0.5 to 0.7, representing a reduction in the risk of post-abortal upper genital tract infection of approximately 30-50%. Considering characteristics of the intervention and study populations, there was no evidence of between-trial heterogeneity ($I^2$ = 0%) in RCTs that examined the effectiveness of nitroimidazole antibiotics (six trials) or penicillins (two trials), in trials using single doses of antibiotics (six trials), or in RCTs in which ≥ 12% of women in the control group developed post-abortal upper genital tract infection (eight trials).

*Universal antibiotic prophylaxis*

No authors of individual trials described the intervention as universal antibiotic prophylaxis. Of the 15 trials, only one explicitly stated that women were included without regard to laboratory diagnoses of *C. trachomatis* or *N. gonorrhoeae* at baseline (Darj 1987). Darj 1987 included 800 women randomised to treatment with a single oral dose of doxycycline or placebo 10-12 hours before the abor-

tion (Analysis 2.1). Baseline cultures for aerobic and anaerobic bacteria were not taken. Amongst women included in analysis, the incidence of post-abortal upper genital tract infection was 2% (8/386) in women receiving doxycycline and 6% (24/383) in women receiving placebo (RR 0.33, 95% CI 0.15 to 0.73).

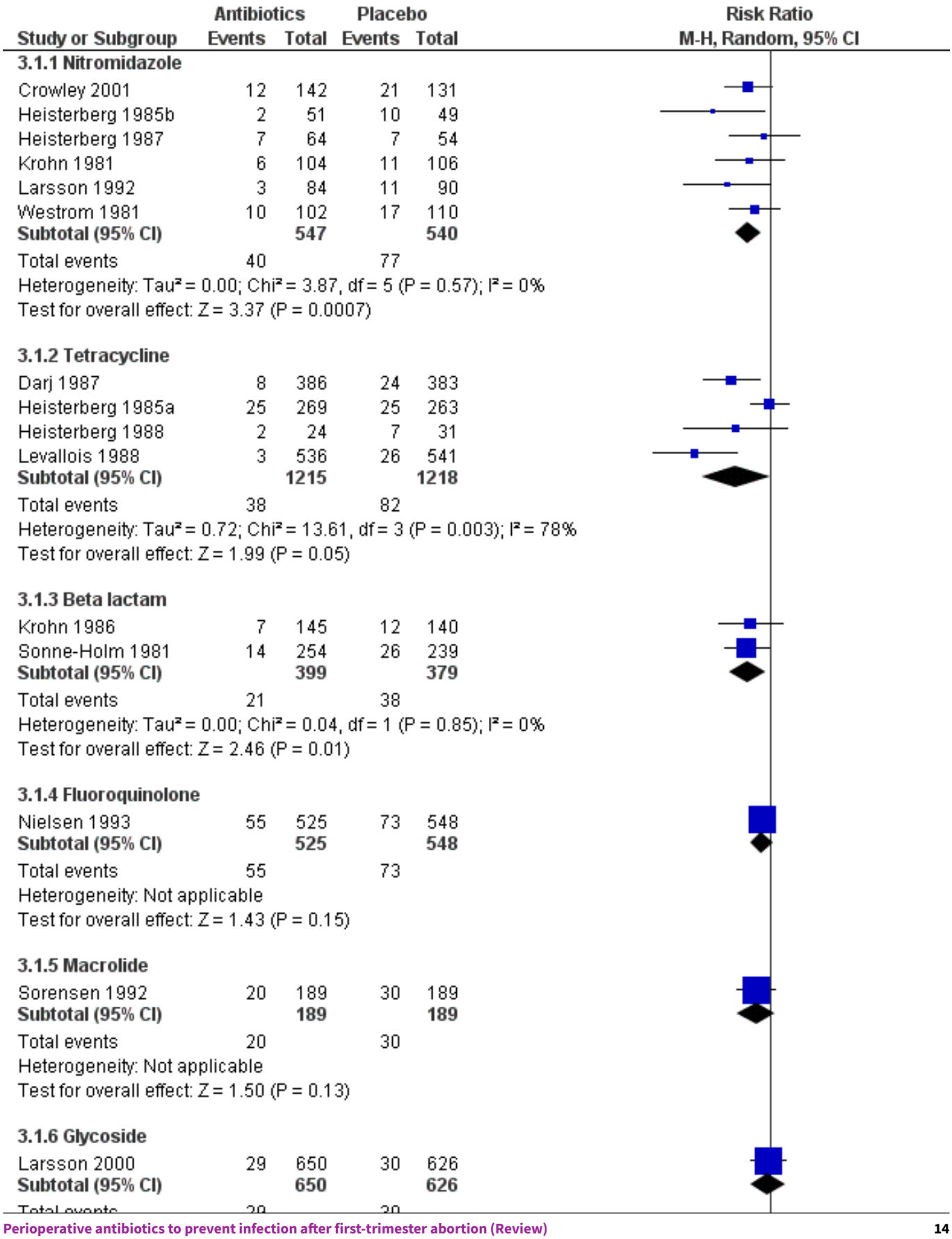
In four further trials (Krohn 1981; Krohn 1986; Sonne-Holm 1981; Heisterberg 1985b) it was unclear if a strategy of universal antibiotic prophylaxis had been followed or not, because exclusion criteria were not explicitly stated (Krohn 1981; Krohn 1986; Sonne-Holm 1981; Heisterberg 1985b), or preoperative tests for infection were not mentioned (Sonne-Holm 1981). In these four trials the pooled RR was 0.49 (95% CI 0.32 to 0.75, $I^2$ = 0%, fixed-effect model).

In all the remaining trials, authors stated that women with laboratory diagnoses of genital infections would be excluded or treated preoperatively (Crowley 2001; Heisterberg 1985a; Heisterberg 1987; Heisterberg 1988; Larsson 1992; Larsson 2000; Levallois 1988; Nielsen 1993; Sorensen 1992; Westrom 1981). There was moderate between-trial heterogeneity ($I^2$ = 43%) with a pooled RR 0.67 (95% CI 0.56 to 0.81, 95% PI 0.32 to 1.36, random-effects model).

Antibiotic class

Figure 5 shows the results of trials according to the class of antibiotic used (Analysis 3.1). Six RCTs compared the effect of nitroimidazoles to placebo and found strong evidence of a prophylactic effect with no evidence of between-trial heterogeneity ($I^2$ = 0%, RR 0.51, 95% CI 0.35 to 0.73, fixed-effect model) (Crowley 2001; Heisterberg 1985b; Heisterberg 1987; Krohn 1981; Larsson 1992; Westrom 1981). All but one of these trials (Krohn 1981) excluded or treated women with gonorrhoea at baseline and two trials excluded or treated women with chlamydia at baseline (Crowley 2001; Larsson 1992).

**Figure 5. Effect of antibiotic prophylaxis on post-abortal upper genital tract infection, 15 trials: by antibiotic class**



Four trials used tetracyclines. There was evidence of severe heterogeneity between trial results ($I^2$ = 78%) and the pooled results were not used (Darj 1987; Heisterberg 1985a; Heisterberg 1988; Levallois 1988). All but one trial (Darj 1987) excluded women with gonorrhoea at baseline. This group included the two trials with the weakest (Heisterberg 1985a) and strongest (Levallois 1988) effects of the interventions. Heisterberg 1985a analysed results from 532 women (118 excluded post randomisation), including 10 (1.9%) with chlamydia. The incidence of post-abortal upper genital tract infection was similar in the group receiving 7 days of lymecycline compared with placebo (RR 0.98, 95% CI 0.58 to 1.66). Chlamydia infection was strongly associated with post-abortal infection (10/48 women with chlamydia vs. 40/481 women without chlamydia, RR 2.5, 95% CI 1.34 to 4.69) but this trial had the lowest percentage of women infected with chlamydia. No testing for bacterial vaginosis was reported. Levallois 1988 analysed 1077 women (23 excluded post randomisation), including 75 (7.0%) with chlamydia. No testing for bacterial vaginosis was reported. Two phases of the trial were reported: in phase 1, women were enrolled, irrespective of chlamydia test results (N = 75); in phase 2, only women with negative chlamydia tests were enrolled (N = 1002). The overall RR was 0.12 (95% CI 0.04 to 0.38).

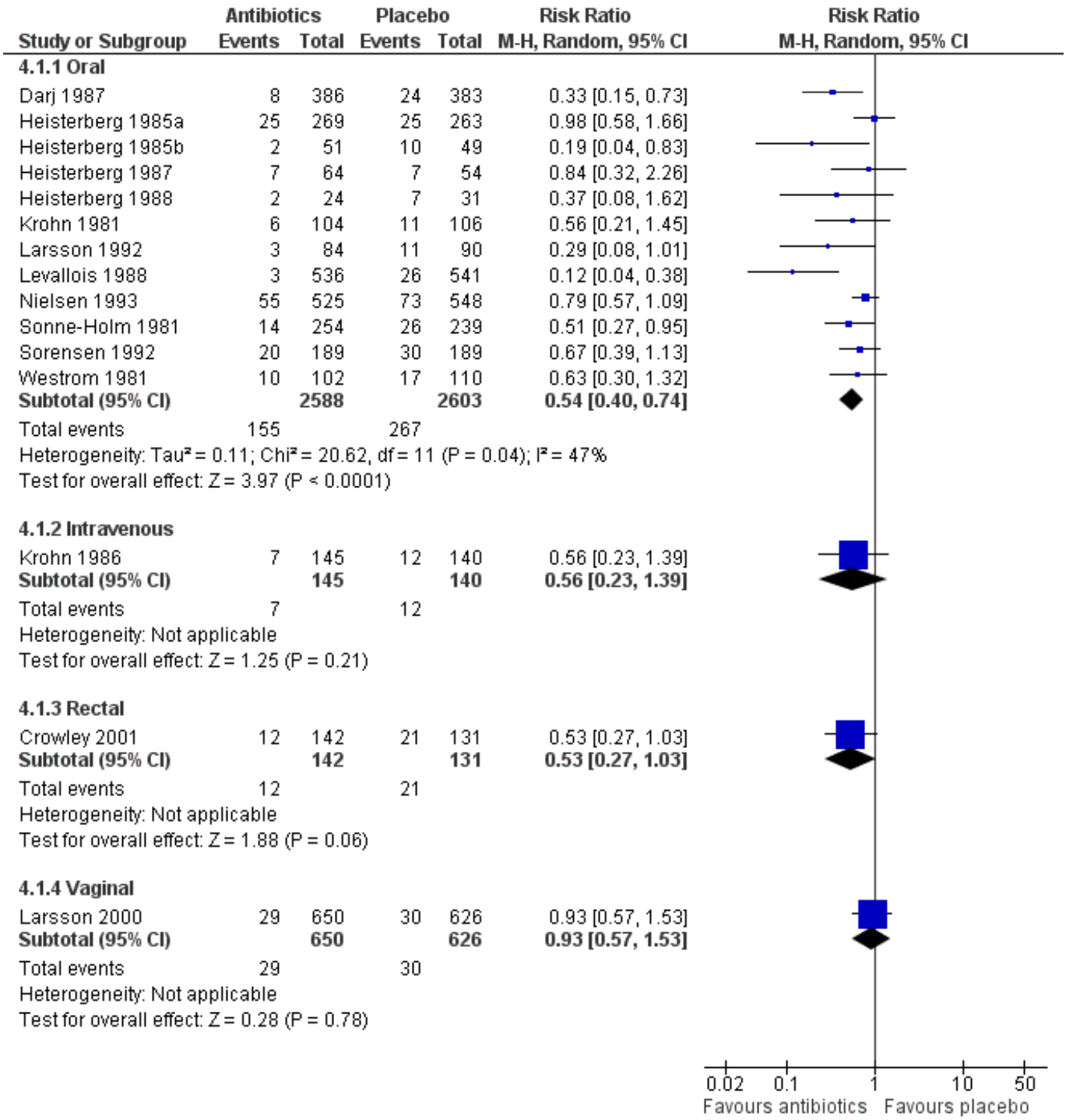
Only two studies compared beta lactam antibiotics to placebo and the results of these trials demonstrated a consistent decrease in post-abortal infection (pooled RR 0.52, 95% CI 0.31 to 0.88, $I^2$ = 0%, fixed-effect model) (Krohn 1986; Sonne-Holm 1981). Women with gonorrhoea were excluded by Sonne-Holm et al. but not Krohn.

Fluoroquinolones (Nielsen 1993), macrolides (Sorensen 1992) and glycosides (Larsson 2000) were examined in only one trial each (Figure 5).

Route of administration

Antibiotics were given orally in 12 of the 15 trials with moderate between-trial heterogeneity (pooled RR 0.54, 95% PI 0.24 to 1.24, random-effect model, $I^2$ = 47%) (Darj 1987; Heisterberg 1985a; Heisterberg 1985b; Heisterberg 1987; Heisterberg 1988; Krohn 1981; Larsson 1992; Nielsen 1993; Sonne-Holm 1981; Sorensen 1992; Westrom 1981) (Analysis 4.1, Figure 6). One trial each examined intravenous (Krohn 1986), intravaginal (Larsson 2000) and rectal (Crowley 2001) routes of administration.

**Figure 6. Effect of antibiotic prophylaxis on post-abortal upper genital tract infection, 15 trials: by route of antibiotic administration**




Timing and frequency of antibiotic administration

Figure 7 (Analysis 5.1) shows trial results stratified by the timing of antibiotic administration. There was between-trial heterogeneity in all strata. Four trials gave antibiotics preoperatively (RR 0.61, 95% PI 0.12 to 3.11, random-effects model, $I^2$ = 39%) (Darj 1987; Krohn 1981; Larsson 2000; Westrom 1981). Six trials used perioperative administration (RR 0.48, 95% PI 0.10 to 2.33, random-effects model, $I^2$ = 62%) (Crowley 2001; Heisterberg 1985b; Heisterberg 1987; Krohn 1986; Levallois 1988; Nielsen 1993); four studies gave antibiotics pre- and postoperatively (RR 0.67, 95% PI 0.16 to 2.89, random-effects model, $I^2$ = 29%) (Heisterberg 1985a; Heisterberg 1988; Larsson 2000; Sorensen 1992) and in one study antibiotics were given peri- and postoperatively (Sonne-Holm 1981).

**Figure 7. Effect of antibiotic prophylaxis on post-abortal upper genital tract infection, 15 trials: by timing of antibiotic administration**

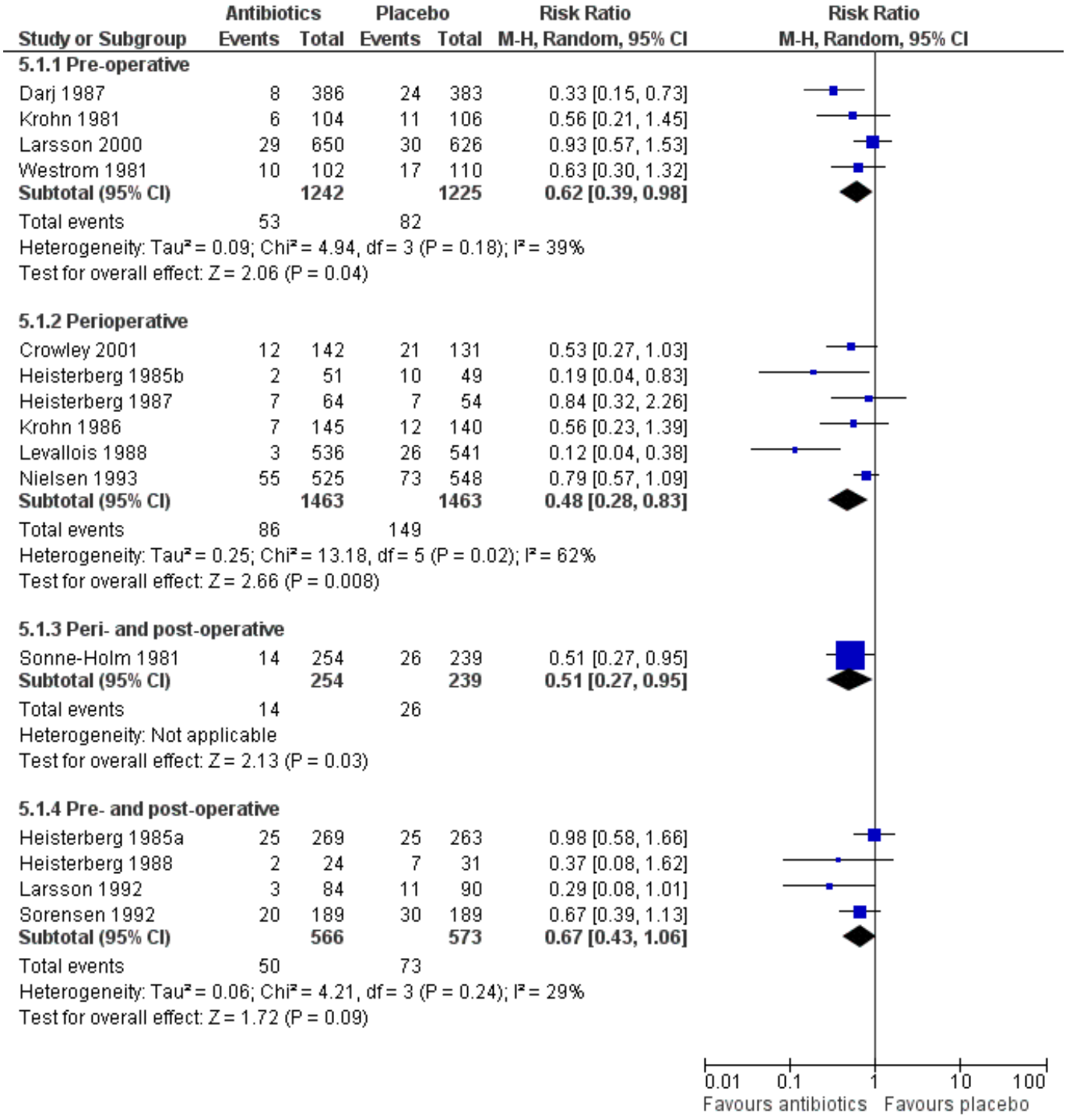
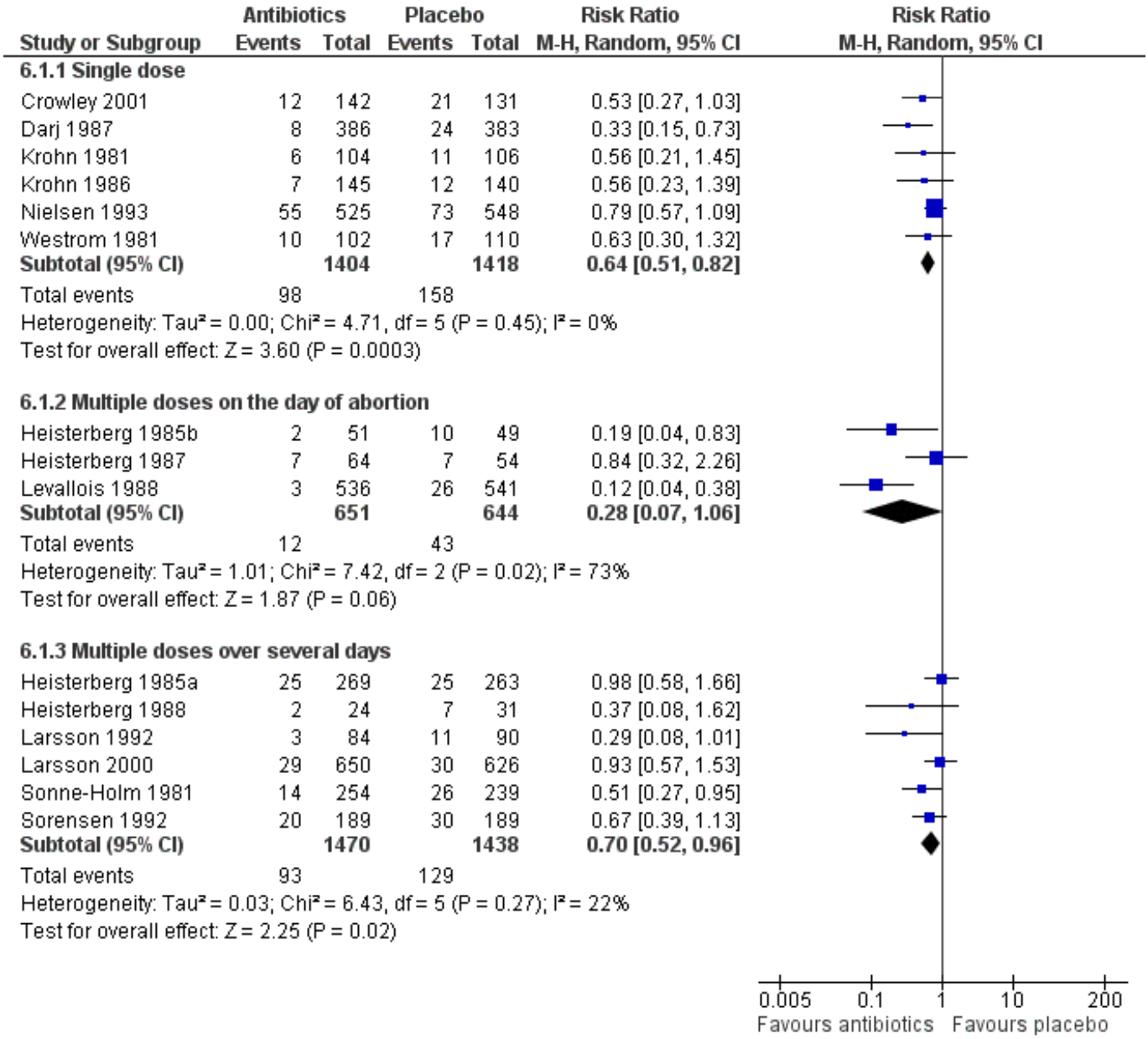



Figure 8 shows trial results stratified by the frequency of the antibiotic regimen (Analysis 6.1). Six studies used a single oral dose of antibiotics, with little between-trial heterogeneity in results (RR 0.63, 95% CI 0.50 to 0.80, fixed-effect model, $I^2 = 0\%$) (Crowley 2001; Darj 1987; Krohn 1981; Krohn 1986; Nielsen 1993; Westrom 1981). The results of six trials using multiple doses of antibiotics given over several days were also reasonably consistent (RR 0.71, 95% CI 0.55 to 0.92, fixed-effect model, $I^2 = 22\%$) (Heisterberg 1985a; Heisterberg 1988; Larsson 1992; Larsson 2000; Sonne-Holm 1981; Sorensen 1992). Trials that involved the use of multiple doses of antibiotic on the same day were very heterogeneous ($I^2 = 73\%$, 3 trials) (Heisterberg 1985b; Heisterberg 1987; Levallois 1988). There were

no trials directly comparing different antibiotics as well as different routes and frequency of antibiotic administration.

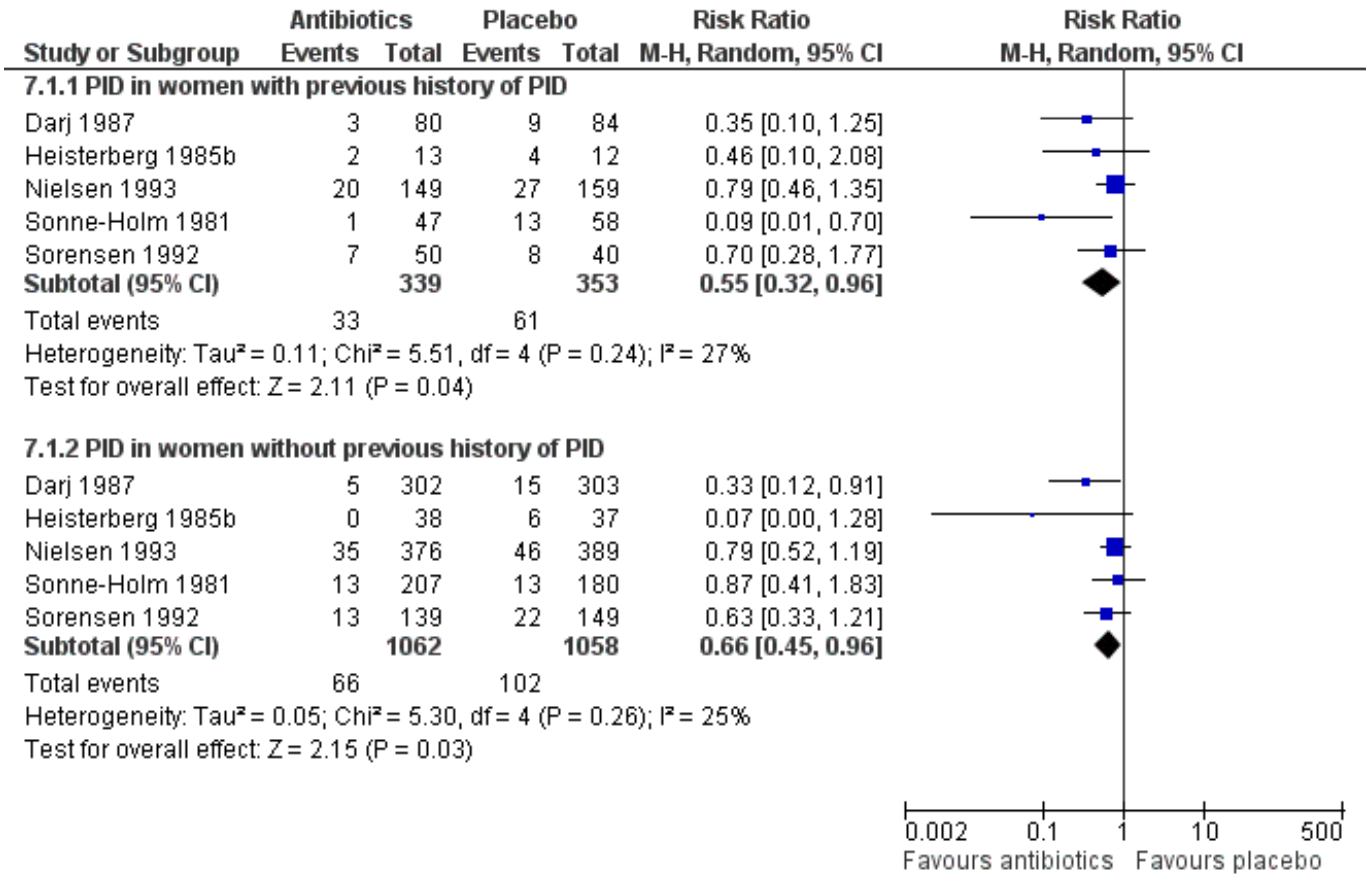
**Figure 8. Effect of antibiotic prophylaxis on post-abortal upper genital tract infection, 15 trials: by antibiotic dosing schedule**




Current or past upper genital tract infection

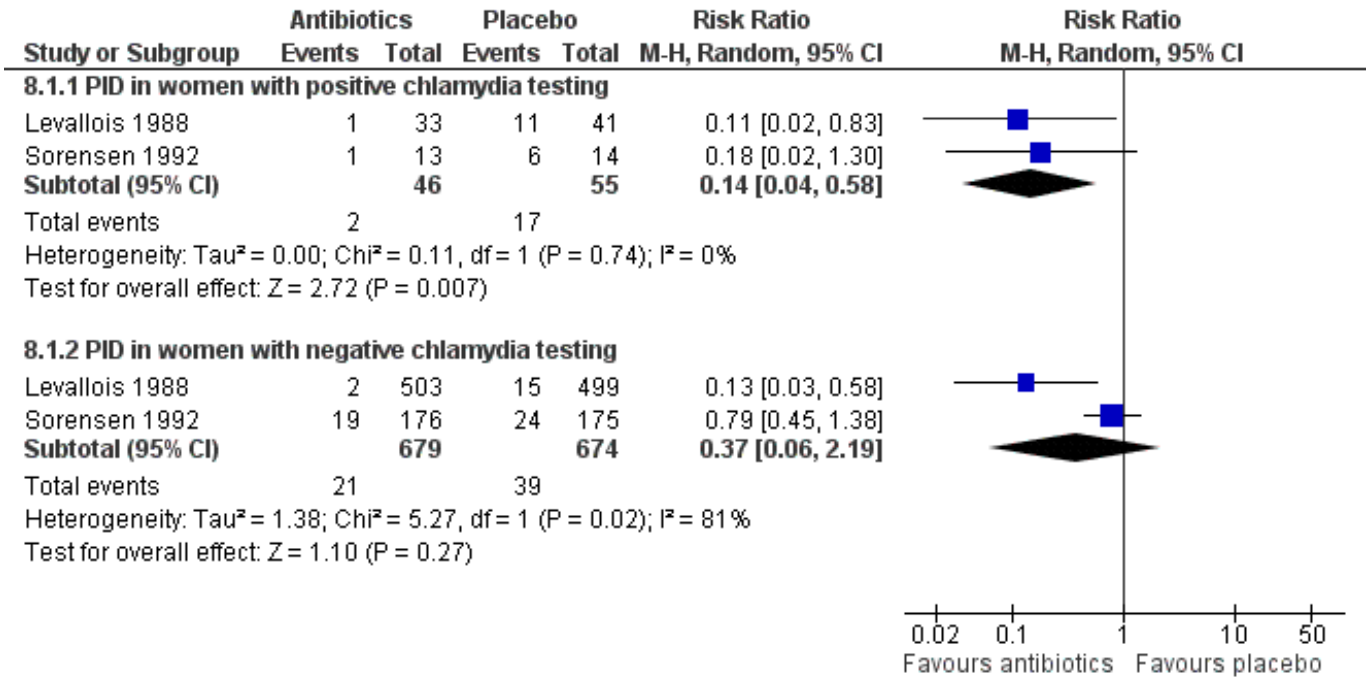
Seven studies reported the number of women with a history of PID (Figure 9, Analysis 7.1) (Darj 1987; Heisterberg 1985b; Heisterberg 1987; Heisterberg 1988; Nielsen 1993; Sonne-Holm 1981; Sorensen 1992). Figure 9 shows results from the five studies that compared the development of post-abortal upper genital tract infection according to the presence or absence of previous PID. Two trials that involved only women with previous PID are not included (Heisterberg 1987; Heisterberg 1988). The magnitude of the effect of prophylactic antibiotics was similar in women with (RR 0.55, 95% CI 0.32 to 0.96, fixed-effect meta-analysis, $I^2$ = 27%) with and without a history of PID (RR 0.66, 95% CI 0.45 to 0.96, random-effects meta-analysis, $I^2$ = 25%).

**Figure 9. Effect of antibiotic prophylaxis on post-abortal upper genital tract infection in women with a history of PID, 5 trials**




Seven studies reported data on chlamydia testing before abortion (Crowley 2001; Heisterberg 1985a; Krohn 1986; Larsson 1992; Larsson 2000; Levallois 1988; Sorensen 1992); two did not test all participants (Heisterberg 1985a; Krohn 1986). Two other trials excluded all chlamydia positive women from participating in the trial (Larsson 1992; Larsson 2000) and Crowley et al. treated all women with chlamydia preoperatively. Two studies were included in a stratified analysis, according to baseline chlamydia status (Levallois 1988; Sorensen 1992) (Figure 10). In women with chlamydia at baseline, both trials showed evidence that prophylactic antibiotics (doxycycline or erythromycin) reduced the incidence of post-abortal upper genital tract infection (pooled RR 0.14, 95% CI 0.03 to 0.57, fixed-effect meta-analysis, $I^2 = 0\%$) (Figure 10; Analysis 8.1). In women without chlamydia at baseline the two trials showed contrasting effects and data were not pooled ($I^2 = 81\%$).

**Figure 10. Effect of antibiotic prophylaxis on post-abortal upper genital tract infection in women with chlamydia at baseline, 2 trials**




All eleven studies testing their participants for gonorrhea excluded women who were found positive (Crowley 2001; Heisterberg 1985a; Heisterberg 1985b; Heisterberg 1987; Heisterberg 1988; Heisterberg 1986; Larsson 1992; Larsson 2000; Levallois 1988; Nielsen 1993; Sorensen 1992). Two trials who tested for bacterial vaginosis included only women with positive testing (Crowley 2001; Krohn 1986).

When the trials were stratified according to the level of upper genital tract infection diagnosed in the control group (Table 3), results were heterogeneous in those with levels below the median for all trials ($I^2$ = 63%) (Darj 1987; Heisterberg 1985a; Krohn 1981; Krohn 1986; Larsson 2000; Sonne-Holm 1981). Amongst trials in women with a high risk of upper genital tract infection the results were more consistent (pooled RR 0.64, 95% CI 0.51 to 0.80, fixed-effect model, $I^2$ = 0%) (Crowley 2001; Heisterberg 1985b; Heisterberg 1987; Heisterberg 1988; Larsson 1992; Nielsen 1993; Sorensen 1992; Westrom 1981).

**Objective 2. To determine the most effective antibiotic regimen for preventing post-abortal upper genital tract infection**

Three trials compared different types of antibiotic regimen: Caruso 2008 and Lichtenberg 2003 compared different durations of the same antibiotic (prulifloxacin and doxycycline, respectively) and Heisterberg 1986 compared two different antibiotics with the same regimen for both. None of the trials was stated to be a non-inferiority trial. In the trials by Heisterberg 1986 and Lichtenberg 2003, there was no statistical evidence of a difference in the incidence of post-abortal upper genital tract infection between groups. Caruso 2008 found that a five day regimen of prulifloxacin starting after the abortion resulted in a higher incidence of post-abortal upper genital tract infection compared with a three day regimen starting the day before the abortion (RR 4.13, 95% CI 1.41 to 12.08). No study compared different antibiotic combinations to a single antibiotic or to another combination of antibiotics.

**Objective 3. To determine the most effective strategy for preventing post-abortal upper genital tract infection by comparing universal antibiotic prophylaxis with a screen-and-treat strategy, or with a combination of screen-and-treat plus universal prophylaxis**

One trial compared the effectiveness of a screen-and-treat strategy with universal prophylaxis (Penney 1998). In the screen-and-treat arm, women were tested preoperatively for chlamydia, gonorrhoea and bacterial vaginosis; those with positive results received appropriate antibiotics for the infection(s) diagnosed (doxycycline, ciprofloxacin and metronidazole, respectively) and were referred to a genitourinary medicine clinic for partner notification. Women with negative screening tests did not receive any antibiotics. Women allocated to universal antibiotic prophylaxis received a single dose of 1 g metronidazole rectally on the day of the abortion followed by doxycycline 100 mg twice daily orally for seven days. A total of 1672 women was randomised but, owing to limited resources, this did not reach the planned number, according to the sample size calculation. The incidence of post-abortal upper genital tract infection was higher in women allocated to the screen-and-treat strategy compared to universal prophylaxis (RR 1.53, 95% CI 0.99 to 2.36) (Penney 1998). Of 45 women in the screen-and-treat group referred to a genitourinary medicine clinic, only 11 attended and only 4 out of 10 partners identified by these women were known to have attended the clinic for treatment.

## DISCUSSION

### Summary of main results

This systematic review included 19 RCTs that examined the effects of perioperative antibiotics to prevent post-abortal upper genital tract infection in women undergoing surgical abortion. In 15 of the 19 trials an antibiotic regimen was compared with placebo and demonstrated a decrease in post-abortal infection; however, only one of these trials appeared to use universal antibiotic prophylaxis without excluding women with genital infections at baseline (RR 0.33, 95% CI 0.15 to 0.73). In four trials where it was unclear whether universal prophylaxis was used, the pooled RR was 0.49 (95% CI 0.32 to 0.75, $I^2$ = 0%, fixed-effect model). In 10 trials that excluded women with infections the protective effect of antibiotics was less pronounced and there was moderate between-trial heterogeneity (pooled RR 0.65, 95% CI 0.32 to 1.36, random-effects model, $I^2$ = 43%).

There were too few trials that compared different antibiotic regimens to determine the most effective regimen. No trials compared different antibiotic combinations to a single antibiotic or to another combination of antibiotics. It was not possible to determine whether a screen-and-treat strategy compared to universal antibiotic prophylaxis was more effective in preventing post-abortal upper genital tract infection as only one trial made this comparison (RR 1.53, 95% CI 0.99 to 2.36). This was the only trial in which partner notification for women with chlamydia or gonorrhoea was carried out; of 91 women with chlamydia, only 4 of 10 notified partners were known to have attended the same genitourinary medicine clinic for treatment.

We did not identify any RCTs examining the effect of antibiotic prophylaxis in women having medical abortion. None of the included RCTs was conducted in a low or middle income country.

### Strengths and weaknesses

The main strengths of this review were that we considered different strategies for preventing post-abortal upper genital tract infection. We examined separately the strategies of universal antibiotic prophylaxis, in which antibiotics are given without taking tests for infections preoperatively and antibiotic prophylaxis in which women with specific infections were excluded or treated preoperatively. In this review, there were many differences between study populations, interventions, inclusion and exclusion criteria and diagnostic criteria so real heterogeneity was expected. We tried to take this into account in the presentation of results when there was evidence of moderate or severe heterogeneity ($I^2$ > 25%), using a strategy suggested by Riley and colleagues (Riley 2011). In these situations we presented 95% CI and a 95% PI, which describe the uncertainty around the intervention effect estimated in random-effects models. The estimate from the random-effects model is the average effect across the trials. Its CI expresses the statistical uncertainty around the average effect, not the potential effect in an individual population or setting, which may differ from the average. The PI reflects the range of effects across the different settings in which the trials were conducted (Riley 2011).

A weakness of the review is the statistical evidence of publication or other small study biases in the 15 trials included in this review. This suggests that there might be trials with results showing no effect or a harmful effect of antibiotic prophylaxis in women presenting for first-trimester surgical abortion. The effect estimated in this review might, therefore, overestimate the prophylactic effect. Limitations of included studies include differences in the diagnostic criteria for both baseline infections (particularly bacterial vaginosis) and for the primary outcome of post-abortal upper genital tract infection (there are no agreed criteria), and duration of follow-up for diagnosing the primary outcome (two to eight weeks).

### Comparison with other studies

This review updates and adds to information in the previous systematic review of antibiotic prophylaxis to prevent post-abortal upper genital tract infection, published by Sawaya 1996 and colleagues. The 12 trials studied by Sawaya 1996 were all identified in our searches and included in our review. Since our search strategy included more databases than that of Sawaya and colleagues, it is unlikely that we missed published trials. In addition to placebo controlled trials we also included trials comparing different antibiotic regimens and different prophylaxis strategies. Therefore, we included the only trial to compare the screen-and-treat strategy with universal antibiotic prophylaxis (Penney 1998). Sawaya 1996 concluded that there has been strong evidence that antibiotics reduce the risk of post-abortal infection in all groups of women. This conclusion was based on a meta-analysis that used a fixed-effect model to estimate a pooled common RR of 0.58 (95% CI 0.47 to 0.71), despite marked between-trial heterogeneity. In this review, we quantify and explore the heterogeneous results between trials.

## AUTHORS' CONCLUSIONS

### Implications for practice

A general strategy of perioperative antibiotics at the time of first-trimester surgical abortion is effective in preventing post-abortal upper genital tract infection, with an average reduction of 41% (95% CI 25 to 54%, random-effects model). The level of between trial heterogeneity suggests that this effect might not, however, apply to all settings, population groups or interventions. To take this into account, we also estimated a 95% PI, which is wider than the 95% CI (RR 0.59, 95% PI 0.30 to 1.14).

There are sub-groups amongst whom antibiotic prophylaxis had a beneficial effect, with no evidence of between trial heterogeneity: women receiving nitroimidazole antibiotics and single dose regimens; and settings in which the rate of post-abortal upper genital tract infection was 12% or more. In this review, there was a beneficial effect both in women with and without a history of PID.

The majority of trials included in the review did not evaluate a strategy of universal antibiotic prophylaxis as it would be applied in practice, i.e. giving prophylaxis to all women without doing tests to screen for existing gonorrhoea and chlamydia. This is because many trials had planned or actual exclusions (or treatment) of women who had infections diagnosed preoperatively. The prophylactic effect of antibiotics was actually weakest in the group of trials that did not use universal prophylaxis, perhaps because the opportunity to prevent post-abortal infections was reduced by the exclusion of those with infections. The antibiotic prophylactic regimen selected in practice should take into account the local epidemiology of lower genital tract infection.

This review did not determine the most effective antibiotic regimen because there were too few trials making such comparisons. In stratified analyses of placebo controlled trials nitroimidazoles prevented post-abortal upper genital tract infections with no evidence of between trial heterogeneity. Anaerobes or organisms as-

sociated with bacterial vaginosis might, therefore, be important aetiologically. In addition, two trials showed an effect of antibiotics active against chlamydia in women who were infected with *C. trachomatis* at baseline. Only one included trial used a combination of antibiotics; Penney 1998 gave metronidazole and doxycycline. This antibiotic combination has been recommended in guidelines as it covers bacterial vaginosis and *C. trachomatis.* In a trial that was not included in the review because only half the women were in the first trimester, Miller 2004 compared a combination of a seven day course of metronidazole and doxycycline with doxycycline alone in women with bacterial vaginosis. They found that the addition of metronidazole did not reduce the incidence of post-abortal infectious complications, defined using a symptom score. Single dose regimens also appeared to be associated with a consistent reduction in the risk of post-abortal upper genital tract infection. Of note, four of these trials assessed the outcome at two weeks or sooner (Krohn 1981; Krohn 1986; Nielsen 1993; Westrom 1981) and three of the trials used nitroimidazoles, which also showed a consistent effect (Crowley 2001; Krohn 1981; Westrom 1981).

The findings of this review are consistent with existing guidelines on antibiotic prophylaxis. In the USA, the American College of Obstetrics and Gynecology (ACOG 2006) did not recommend any particular regimen, whilst the Society of Family Planning states that both nitroimidazoles and tetracyclines are effective (Achilles 2011). Guidance about the duration of the prophylactic regimen differs. The US Society of Family Planning recommends that antibiotics should not be given for more than three days (Achilles 2011). In the UK, Royal College of Obstetrics and Gynaecology guidelines recommend single dose metronidazole with single dose azithromycin or a seven day course of doxycycline (RCOG 2011). The Scottish Intercollegiate Guidelines Network has published general guidelines about antibiotic prophylaxis for surgical procedures and notes that in 'several studies... longer dose duration has no increased benefit' but no specific evidence about abortion was identified (SIGN 2008).

The implications of lower genital tract infections that are sexually transmitted or sexually transmissible for women and their sex partner(s) should be taken into consideration when developing strategies for the prevention of post-abortal upper genital tract infection. If pre-abortion screening tests for infection are not done, practitioners should give women information about the specific infections not covered by the prophylactic regimen, so that they can seek diagnosis, treatment and partner services. If pre-abortion infection screening tests are done, practitioners should provide full treatment and follow-up care for women diagnosed with a sexually transmitted infection. The single trial by Penney 1998 did not determine whether or not there is a difference in the effectiveness of screen-and-treat and universal antibiotic prophylaxis strategies. There were fewer episodes of post-abortal upper genital tract infection in women receiving universal antibiotic prophylaxis, but 95% CI were wide. Furthermore, the authors of the trial tried to ensure treatment for partners to prevent re-infection but very few were known to have attended a clinic for treatment. The implications of this for re-infection are not known; the low partner notification success rate could reflect an inability to reach partners in partnerships that had ended, or a failure to reach ongoing sex partners.

The results of the review cannot be generalised to women having medical abortions because we did not find any relevant trials.

The results of the review cannot be generalised to women in the second trimester of pregnancy because the protocol specified only first-trimester abortion. Future updates should include second-trimester abortion.

Since all included trials were conducted in high income countries where testing is available, the results cannot necessarily be generalised to low and middle income countries, where the prevalence of sexually transmitted and endogenous infections in women requesting abortion might well differ and where screening tests might not be available.

### Implications for research

Further RCTs comparing prophylactic regimens of different antibiotics with each other or combinations of antibiotics with a single antibiotic would be useful. Such trials could be done in low and middle income countries and settings in which the prevalence of lower genital tract infections in women presenting for abortion is high.

Observational cohort studies of women who have had abortions could give valuable information about the risk of re-infection and of upper genital tract damage as longer term consequences of abortion. Follow- up of RCTs could include a time period that is long enough to investigate the incidence of re-infection and the outcomes of partner notification, where appropriate, in women who have received antibiotic prophylaxis.

Further research to improve the accuracy and reproducibility of diagnostic criteria for upper genital tract infection would help to improve objective diagnosis.

## ACKNOWLEDGEMENTS

Carol Manion of Family Health International assisted with the literature searches. We thank Frans Helmerhorst for his contribution to developing the protocol for this review. We thank Marieke Snieders who made important contributions to the earlier stages of this review. She drafted the protocol, conducted the original literature search, selected studies for inclusion, developed the data extraction form and extracted data for some of the included trials.

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* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

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

**Caruso 2008**

| | |
|---|---|
| Methods | - Single centre, Italy<br>- Study period September 2005 - March 2007<br>- Follow-up period 4 weeks |
| Participants | - Number of women randomised unclear, 466 women analysed<br>- Women presenting for surgical abortion in first trimester<br>- Exclusion criteria not reported<br>- Preoperative infections: not tested for |
| Interventions | **Antibiotic prophylaxis compared with alternative regimens of the same antibiotic**<br>- Intervention, arm 1: prulifloxacin 600 mg once daily, oral (postoperative, 5 days)<br>- Intervention, arm 2: prulifloxacin 600 mg once daily, oral (postoperative, 3 days)<br>- Intervention, arm 3: prulifloxacin 600 mg once daily, oral (peri-operative 3 doses, 1 dose preoperatively, 2 doses postoperative) |

**Caruso 2008** *(Continued)*

| | |
|---|---|
| Outcomes | PID diagnosis defined as all of the following: pelvic pain, fever, vaginal discharge. |
| Notes | Unclear if intervention is universal antibiotic prophylaxis according to protocol definition. Number of potentially eligible women excluded and reasons for exclusion not reported. Included in descriptive analysis only because comparison groups also received antibiotics. |

**Crowley 2001**

| | |
|---|---|
| Methods | - Multicentre (3 hospitals), England (Bristol, Taunton)<br>- Study period October 1996 - December 1998<br>- Follow-up period 4 weeks |
| Participants | - 273 women randomised, 273 analysed<br>- Women presenting for surgical abortion in first trimester who had bacterial vaginosis<br>- Exclusion criteria: result of bacterial vaginosis test received after surgery<br>- Preoperative infections:<br>1) History of PID: arm 1: 9/142, arm 2: 5/131<br>2) Chlamydia: arm 1: 10/142, arm 2: 11/131, all treated preoperatively<br>3) Gonorrhoea: none (tested in 2/3 hospitals)<br>4) Bacterial vaginosis: all women |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br>- Intervention, arm 1: metronidazole 2 g single dose, rectal (peri-operative during operation)<br>- Control arm, 2: placebo |
| Outcomes | 1) Upper genital tract infection within 4 weeks, defined as: prescription for antibiotics by general practitioner for at least 2 of the following symptoms:<br>- Fever; lower abdominal pain; heavy vaginal bleeding; offensive or bloody vaginal discharge; OR readmission to hospital with a clinical diagnosis of PID<br>2) Readmission to hospital |
| Notes | Not universal antibiotic prophylaxis according to protocol definition; all women screened for chlamydia and those with positive test results treated preoperatively. |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Allocation concealment (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | Low risk | |

**Darj 1987**

| | |
|---|---|
| Methods | - Single centre, Sweden (Falun)<br>- Study period 18 months, dates not specified<br>- Follow-up visit after 4 weeks |
| Participants | - 800 women randomised, 769 analysed<br>- Women presenting for surgical abortion in first trimester<br>- Exclusion criteria: clinical signs of genital infection; antibiotic treatment within 3 weeks of procedure; allergy to treatment<br>- Preoperative infections:<br>1) History of PID: arm 1: 80/386, arm 2: 84/383<br>2) Chlamydia: not reported (not tested)<br>3) Gonorrhoea: not reported (not tested)<br>4) Bacterial vaginosis: not reported (not tested) |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br>- Intervention, arm 1: doxycycline 400 mg, single dose, oral (preoperative, 12h before)<br>- Control, arm 2: placebo |
| Outcomes | 1) PID defined as lower abdominal pain plus at least 2 of the following: abnormal purulent discharge; temperature > 38 °C; palpable adnexal mass; erythrocyte sedimentation rate > 15 mm/hour; heavy or prolonged bleeding;<br>2) Adverse effect of antibiotic prophylaxis |
| Notes | Universal antibiotic prophylaxis |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Allocation concealment (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | Low risk | |

**Heisterberg 1985a**

| | |
|---|---|
| Methods | - Single centre, Denmark (Copenhagen)<br>- Study period: not reported<br>- Follow-up visit after 2 weeks |

**Heisterberg 1985a** *(Continued)*

| | |
|---|---|
| Participants | - 650 women randomised, 532 analysed<br>- Women presenting for surgical abortion in the first trimester<br>- Exclusion criteria: allergy to treatment; antibiotic treatment at the time of abortion; active haematological or neurological disease; alcohol abuse; positive test for *N. gonorrhoeae*<br>- Infections preoperatively:<br>1) History of PID: not reported in detail<br>2) Chlamydia: arm 1: 29/269 , arm 2: 19/260 (culture not obtained in 3 women)<br>3) Gonorrhoea: all women tested, 6 women with positive result excluded<br>4) Bacterial vaginosis: not reported |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br>- Intervention, arm 1: lymecycline 300 mg twice daily, oral (pre- and postoperative, starting 2 days before, total 7 days)<br>- Control, arm 2: placebo |
| Outcomes | 1) Post-abortal genital infection defined as:<br>a) Patient seen at follow-up visit after 2 weeks, at least 3 of the following: temperature > 38 °C; continued pelvic pain; malaise with tender adnexal mass; pathologic discharge or bleeding<br>b) Patient admitted before scheduled follow-up, at least 2 of the following: temperature > 38 °C; moderate tenderness of the uterus; tender adnexal mass; pathologic discharge or bleeding; OR<br>c) Patient not seen at the follow-up visit, at least 4 of the following: temperature > 38 °C for > 24h; pelvic pain > 5 days; bleeding more than normal menstrual flow for >5 days; foul discharge; infection diagnosed by physician<br>2) Adverse effects of antibiotics |
| Notes | Not universal antibiotic prophylaxis according to protocol definition; study population included only women without gonorrhoea at baseline. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Incomplete outcome data (attrition bias) | Low risk | |

**Heisterberg 1985b**

| | |
|---|---|
| Methods | - Single centre, Denmark (Copenhagen)<br>- Study period March 1982 - August 1982<br>- Follow-up visit after 2 weeks |
| Participants | - 119 women randomised, 100 analysed<br>- Women presenting for surgical abortion in first trimester |

**Heisterberg 1985b** *(Continued)*

| | |
|---|---|
| | - Exclusion criteria: allergy to treatment; treatment with antibiotics at the time of abortion; active haematological or neurological disease; alcohol abuse or treatment with disulfiram (Antabuse); positive test for *N. gonorrhoeae*<br><br>- Preoperative infections:<br><br>1) History of PID: arm 1: 13/ 51, arm 2: 12/49<br><br>2) Chlamydia: not reported<br><br>3) Gonorrhoea: all tested, none positive<br><br>4) Bacterial vaginosis: not reported (culture for *Gardnerella vaginalis*, results not reported by group) |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br><br>- Intervention, arm 1: metronidazole 400 mg, oral (peri-operative 3 doses, 1h before, 4h after, 8h after abortion)<br><br>- Control, arm 2: placebo |
| Outcomes | 1) Post-abortal PID defined as:<br><br>a) Patient seen at follow-up visit after 2 weeks, at least 3 of the following: temperature > 38 °C; continued pelvic pain; malaise with tender adnexal mass; pathologic discharge or bleeding<br><br>b) Patient admitted before scheduled follow-up, at least 2 of the following: temperature > 38 °C; moderate tenderness of the uterus; tender adnexal mass; pathologic discharge or bleeding |
| Notes | Not universal antibiotic prophylaxis according to protocol definition; study population included only women without gonorrhoea at baseline. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | Low risk | |

**Heisterberg 1986**

| | |
|---|---|
| Methods | - Single centre, Denmark (Copenhagen)<br><br>- Study period not reported<br><br>- Follow-up visit after 2 weeks |
| Participants | - 102 women randomised, 81 analysed<br><br>- Women presenting for surgical abortion in first trimester<br><br>- Exclusion criteria: allergy to treatment; treatment with antibiotics at the time of abortion; active haematological or neurological disease; alcohol abuse or treatment with disulfiram (Antabuse); positive test for *N. gonorrhoeae*<br><br>- Preoperative infections: |

**Heisterberg 1986** *(Continued)*

| | |
|---|---|
| | 1) History of PID: all women, 43/43 in arm 1 and 38/38 in arm 2<br><br>2) Chlamydia: not reported<br><br>3) Gonorrhoea: all tested, none positive<br><br>4) Bacterial vaginosis: not reported |
| Interventions | **Antibiotic prophylaxis compared with alternative regimens of the same antibiotic**<br><br>- Intervention, arm 1: metronidazole 400 mg, oral (peri-operative 3 doses, 1h before, 4h after and 8h after abortion)<br><br>- Control, arm 2: pivampicillin 350 mg, oral (peri-operative 3 doses, 1h before, 4h after and 8h after abortion) |
| Outcomes | 1) Post-abortal PID defined as:<br><br>a) Patient seen at follow-up visit after 2 weeks, at least 3 of the following: temperature > 38 °C; continued pelvic pain; malaise with tender adnexal mass; pathologic discharge or bleeding<br><br>b) Patient admitted before scheduled follow-up, at least 2 of the following: temperature > 38 °C; moderate tenderness of the uterus; tender adnexal mass; pathologic discharge or bleeding<br><br>2) Re-admission to hospital |
| Notes | Not universal antibiotic prophylaxis according to protocol definition; study population included only women without gonorrhoea at baseline. All had a history of PID |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | Low risk | |

**Heisterberg 1987**

| | |
|---|---|
| Methods | - Single centre, Denmark (Copenhagen)<br><br>- Study period February 1983 - November 1983<br><br>- Follow-up visit after 2 weeks |
| Participants | - 135 women randomized, 118 analysed<br><br>- Women presenting for surgical abortion in first trimester<br><br>- Exclusion criteria: allergy to treatment; treatment with antibiotics at the time of abortion; active haematological or neurological disease; alcohol abuse or treatment with disulfiram (Antabuse); positive test for *N. gonorrhoeae*<br><br>- Preoperative infections:<br><br>1) History of PID: all women, 64/64 in arm 1, 54/54 in arm 2<br><br>2) Chlamydia: not reported |

**Heisterberg 1987** *(Continued)*

| | |
|---|---|
| | 3) Gonorrhoea: all women tested, 2 women with positive test excluded<br><br>4) Bacterial vaginosis: not reported |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br><br>- Intervention, arm 1: metronidazole 400 mg, oral (peri-operative 3 doses, 1h before, 4h after, 8h after abortion)<br><br>- Control, arm 2: placebo |
| Outcomes | 1) Post-abortal PID defined as:<br><br>a) Patient seen at follow-up visit after 2 weeks, at least 3 of the following: temperature > 38 °C; continued pelvic pain; malaise with tender adnexal mass; pathologic discharge or bleeding<br><br>b) Patient admitted before scheduled follow-up, at least 2 of the following: temperature > 38 °C; moderate tenderness of the uterus; tender adnexal mass; pathologic discharge or bleeding<br><br>2) Readmission to hospital |
| Notes | Not universal antibiotic prophylaxis according to protocol definition; study population included only women without gonorrhoea at baseline. All had a history of PID. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | Low risk | |

**Heisterberg 1988**

| | |
|---|---|
| Methods | - Single centre, Denmark (Copenhagen)<br><br>- Study period not reported<br><br>- Follow-up visit after 2 weeks |
| Participants | - 90 women randomised, 55 analysed<br><br>- Women presenting for surgical abortion in first trimester<br><br>- Exclusion criteria: allergy to treatment; antibiotic treatment at the time of abortion; active haematological or neurological disease; alcohol abuse; positive test for *N. gonorrhoeae*<br><br>- Preoperative infections:<br><br>1) History of PID: all women, 24/24 in arm 1, 31/31 in arm 2<br><br>2) Chlamydia: arm 1: 2/24, arm 2: 1/31<br><br>3) Gonorrhoea: not reported but all women tested and if positive excluded<br><br>4) Bacterial vaginosis: not reported |
| Interventions | **Antibiotic prophylaxis compared to placebo** |

**Heisterberg 1988** *(Continued)*

| | |
|---|---|
| | - Intervention, arm 1: lymecycline 300 mg once daily, oral (pre- and postoperative, starting on the morning of the operation, total 14 days)<br>- Control, arm 2: placebo |
| Outcomes | 1) Post-abortal infection defined as:<br>a) Patient seen at follow-up visit after 2 weeks, at least 3 of the following: temperature > 38 °C; continued pelvic pain; malaise with tender adnexal mass; pathologic discharge or bleeding<br>b) Patient admitted before scheduled follow-up, at least 2 of the following: temperature > 38 °C; moderate tenderness of the uterus; tender adnexal mass; pathologic discharge or bleeding; OR<br>c) Patient not seen at the follow-up visit, at least 4 of the following: temperature > 38 °C for > 24h; pelvic pain > 5 days; bleeding more than normal menstrual flow for > 5 days; foul discharge; infection diagnosed by physician<br>2) Readmission to hospital |
| Notes | Not universal antibiotic prophylaxis according to protocol definition; study population included only women without gonorrhoea at baseline. All had a history of PID. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | Low risk | |

**Krohn 1981**

| | |
|---|---|
| Methods | - Single centre, Sweden (Norrkoping)<br>- Study period not reported<br>- Follow-up visit after 8-10days |
| Participants | - 210 women randomised, 210 analysed<br>- Women presenting for surgical abortion in first trimester<br>- Exclusion criteria: known genitourinary disease (not specified if infections included); antibiotic treatment at time of abortion;<br>- Pre-opertative infections:<br>1) History of PID: not reported<br>2) Chlamydia: not reported<br>3) Gonorrhoea: not reported<br>4) Bacterial vaginosis: not reported, anaerobes cultured |
| Interventions | **Antibiotic prophylaxis compared to placebo** |

**Krohn 1981** *(Continued)*

| | |
|---|---|
| | - Intervention, arm 1: tinidazole 2 g, oral (preoperative single dose, number of hours/days before abortion not stated)<br>- Control, arm 2: Placebo |
| Outcomes | 1) Pelvic infection (endometritis or salpingitis): endometritis defined as temperature > 38 °C; soft and tender uterus and brick-red discharge from cervix; salpingitis, no definition given.<br>2) Readmission to hospital |
| Notes | Unclear if intervention was universal antibiotic prophylaxis according to protocol definition; study population did not exclude women with infections at baseline but excluded women on antibiotics at the time of the abortion. Outcomes poorly defined. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |

**Krohn 1986**

| | |
|---|---|
| Methods | - Single centre, Sweden (Norrkoping)<br>- Study period not reported<br>- Follow-up visit after 1 and 2 weeks |
| Participants | - 305 women randomised, 285 analysed<br>- Women presenting for surgical abortion in first trimester<br>- Exclusion criteria: not reported<br>- Preoperative infections:<br>1) History of PID: not reported<br>2) Chlamydia: 100 of 285 women tested, 8 positive (all in arm 1)<br>3) Gonorrhoea: all women tested, none infected<br>4) Bacterial vaginosis: not reported, anaerobes cultured |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br>- Intervention, arm 1: sulbactam 0.5 g intravenous + ampicillin 1 g intravenous (peri-operative single dose at time of induction)<br>- Control, arm 2: placebo |
| Outcomes | 1) Endometritis defined as: temperature > 38 °C on 2 consecutive days; tender uterus; severe pain or cramps; excessive blood loss; foul vaginal discharge<br>2) Adverse effects of antibiotics administered |
| Notes | Unclear if universal antibiotic prophylaxis according to protocol definition; no exclusion criteria reported but women with chlamydia at baseline were not excluded. |

**Krohn 1986** *(Continued)*

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | High risk | |

**Larsson 1992**

| | |
|---|---|
| Methods | - Multicentre (3 hospitals), Sweden (Gothenburg, Skovde, Gavle)<br>- Study period not reported<br>- Follow-up visit after 4 weeks |
| Participants | - 231 women randomised, 174 analysed<br>- Women presenting for surgical abortion in first trimester<br>- Exclusion criteria: antibiotic treatment before operation; repeat curettage; positive *C. trachomatis* result<br>- Preoperative infections:<br>1) History of PID: not reported<br>2) Chlamydia: all women tested, 23 women with positive results excluded<br>3) Gonorrhoea: unclear how many tested, of those tested all negative<br>4) Bacterial vaginosis: all women, 84/84 in arm 1, 90/90 in arm 2 |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br>- Intervention, arm 1: metronidazole 500 mg 3 times daily, oral (pre-and postoperative, starting up to 1 week before, total 10 days)<br>- Control, arm 2: placebo |
| Outcomes | Post-abortal PID defined as at least 2 of the following: temperature > 38 °C for > 24h; continuous abnormal or purulent vaginal discharge after 1 week; continuous abnormal bleeding after 3 days; palpable adnexal mass; tenderness of uterus or adnexae; erythrocyte sedimentation rate > 30 mm/h |
| Notes | Not universal antibiotic prophylaxis according to protocol definition; study population included only women without chlamydia at baseline. All had bacterial vaginosis. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Incomplete outcome data (attrition bias) | High risk | |

**Larsson 2000**

| | |
|---|---|
| Methods | - Multicentre (7 hospitals), Sweden and Norway<br>- Study period May 1994 - October 1995<br>- Follow-up visit after 4 weeks |
| Participants | - 1655 women randomised, 1276 analysed<br>- Women presenting for surgical abortion in first trimester<br>- Exclusion criteria: allergy to treatment; history of colitis; current PID; current infection with trichomonas, gonorrhoea, chlamydia, candida<br>- Preoperative infections<br>1) History of PID: not reported<br>2) Chlamydia: all women tested, 31 with positive results excluded<br>3) Gonorrhoea: all women tested, unclear how many positive but all excluded<br>4) Bacterial vaginosis: 220/1095 women tested |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br>- Intervention, arm 1: clindamycin cream 2%, intravaginal (preoperative 5 ml applicator for 4-7 days before abortion)<br>- Control, arm 2: placebo |
| Outcomes | Post-abortal infection defined as uterine or adnexal tenderness and at least 1 of the following: temperature > 38 °C for > 24h; abnormal bleeding after 3 days; abnormal discharge after 1 week; palpable adnexal mass |
| Notes | Not universal antibiotic prophylaxis according to protocol definition; study population included only women without chlamydia, gonorrhoea or trichomonas at baseline. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | High risk | |

**Levallois 1988**

| | |
|---|---|
| Methods | - Single centre, Canada (Quebec)<br>- Study period November 1985 - December 1986, split as two phases; phase 1 November 1985 - June 1986, phase 2 July 1986 - December 1986<br>- Follow-up visit at 4-5 weeks |
| Participants | - 1100 women randomised, analysed<br>- Women presenting for surgical abortion in first trimester |

**Levallois 1988** *(Continued)*

| | |
|---|---|
| | - Exclusion criteria before randomisation: allergy to tetracycline; cardiac disease; antibiotic therapy at time of abortion; positive test for *N. gonorrhoeae*; positive test for *C. trachomatis* during second half of trial;<br><br>Preoperative infections<br><br>2) History of PID: not reported<br><br>3) Chlamydia: arm 1: 33/536, arm 2: 42/541<br><br>4) Gonorrhoea: all tested and if positive excluded<br><br>5) Bacterial vaginosis: not reported |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br><br>- Intervention, arm 1: doxycycline 100 mg 3 doses, oral (peri-operative, x 1 1h before, x 2 30 min after abortion)<br><br>- Control, arm 2: placebo |
| Outcomes | 1) Post-abortal pelvic infection defined as: low abdominal pain; uterine, adnexal or motion tenderness; purulent leukorrhoea or temperature > 38 °C or erythrocyte sedimentation rate > 15 mm/h or leukocytosis > 10,000/cubic mm; post-abortal severity score > 10 ('composite score of clinical and biological data', criteria unclear)<br><br>2) Side effects of antibiotic prophylaxis |
| Notes | Not universal antibiotic prophylaxis according to protocol definition; study population included only women without gonorrhoea and, in second half of trial, women without chlamydia. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Allocation concealment (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | High risk | |

**Lichtenberg 2003**

| | |
|---|---|
| Methods | - Single centre, USA (Chicago)<br><br>- Study period November 1995 - May 1996<br><br>- Follow-up visit at 2 weeks |
| Participants | - 800 women randomised, 530 analysed<br><br>- Women presenting for surgical abortion in first trimester<br><br>- Exclusion criteria: breast feeding; allergy to tetracycline; current antibiotic therapy; fever; symptoms of pelvic infection; lives > 50 miles away; non-English speaking<br><br>- Preoperative infections |

**Lichtenberg 2003** *(Continued)*

| | |
|---|---|
| | 1) History of PID: arm 1: 5/257, arm 2:13/273<br>2) Chlamydia: not reported<br>3) Gonorrhoea: not reported<br>4) Bacterial vaginosis: not reported |
| Interventions | **Antibiotic prophylaxis compared with alternative regimens of the same antibiotic**<br>- Intervention, arm 1: doxycycline 100 mg twice daily, oral (postoperative, 7 days)<br>- Control, arm 2: doxycycline 100 mg twice daily, oral (postoperative, 3 days) |
| Outcomes | Pelvic infection defined as: pelvic pain plus temperature > 37.5 °C plus either uterine, adnexal or abdominal tenderness |
| Notes | Unclear if universal antibiotic prophylaxis according to protocol definition; no preoperative screening but women on antibiotics with symptoms of pelvic infection at baseline were excluded. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Allocation concealment (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | Low risk | |

**Nielsen 1993**

| | |
|---|---|
| Methods | - Single centre, Denmark<br>- Study period July 1986 - June 1988<br>- Follow-up visit after 2 weeks and 4 weeks |
| Participants | - 1170 women randomised, 1073 analysed<br>- Women presenting for surgical abortion in first trimester<br>- Exclusion criteria: allergy to treatment; neurological disease; antibiotics at the time of abortion; positive testing for gonorrhoea; re-curettage; patients with insertion of IUD.<br>- Preoperative infections:<br>1) History of PID: arm 1:149/525 , arm 2: 159/548<br>2) Chlamydia: not reported<br>3) Gonorrhoea: all patients tested and 10 women with positive culture excluded<br>4) Bacterial vaginosis: not reported |
| Interventions | **Antibiotic prophylaxis compared to placebo** |

**Nielsen 1993** *(Continued)*

| | |
|---|---|
| | - Intervention, arm 1: ofloxacin 400 mg, oral (peri-operative, single dose)<br>- Control, arm 2: placebo |
| Outcomes | Post-abortal PID defined as:<br>a) Patient seen at the follow-up visit after 2 weeks, 4 of the following: temperature > 38 °C; continued pelvic pain > 5 days; bleeding more than menstrual flow > 5 days; foul discharge; infection diagnosed by general practitioner;<br>b) Patient seen before follow-up visit after 2 weeks, at least 2 of: temperature > 38 °C; moderate tenderness of the uterus; tender adnexal mass; pathologic discharge or bleeding |
| Notes | Not universal antibiotic prophylaxis according to protocol definition; study group included only women without gonorrhoea at baseline. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Incomplete outcome data (attrition bias) | High risk | |

**Penney 1998**

| | |
|---|---|
| Methods | - Multicentre (4 hospitals), Scotland<br>- Study period 1995 - 1996<br>- Follow-up during 8 weeks after surgery |
| Participants | - 1672 women randomised, 1613 analysed (women with screening test results available)<br>- Women presenting for surgical abortion in first trimester<br>- Preoperative infections:<br>1) Chlamydia: all women tested, 91 positive (results according to allocation not available)<br>2) Gonorrhoea: all women tested, 3 positive (results according to allocation not available)<br>3) Bacterial vaginosis: all women tested, 282 positive (results according to allocation not available) |
| Interventions | **Screen and treat compared to universal antibiotic prophylaxis**<br>- Intervention, arm 1: screen and treat preoperatively if positive results for chlamydia (doxycycline 100 mg twice daily, oral, 7 days), gonorrhoea (ciprofloxacin 250 mg single dose, oral), bacterial vaginosis (metronidazole 400 mg twice daily, oral, 7 days)<br>- Intervention, arm 2: universal antibiotic prophylaxis, metronidazole 1 g single dose per rectum peri-operative, immediately before; doxycycline 100 mg twice daily, oral, 7 days, starting immediately after. |
| Outcomes | Suspected PID/endometritis reported by general practitioner: no criteria stated |
| Notes | Universal antibiotic prophylaxis according to review protocol. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|

**Penney 1998** *(Continued)*

| | |
|---|---|
| Random sequence generation (selection bias) | Low risk |
| Allocation concealment (selection bias) | Low risk |
| Incomplete outcome data (attrition bias) | High risk |

**Sonne-Holm 1981**

| | |
|---|---|
| Methods | - Multicentre (2 hospitals), Denmark (Copenhagen)<br>- Study period 1978-1979<br>- Follow-up visit after 4 weeks |
| Participants | - 564 women randomised, 493 analysed<br>- Women presenting for surgical abortion in first trimester<br>- Exclusion criteria: patients participating in another study; allergy to treatment; antibiotics indicated a priori;<br>Preoperative infections:<br>1) History of PID: arm 1: 47/254 , arm 2: 58/239<br>2) Chlamydia: not reported<br>3) Gonorrhoea: not reported<br>4) Bacterial vaginosis: not reported |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br>- Intervention, arm 1: penicillin G 2 million IU 2 doses, intra-muscular (perioperative, x 1 30 min before, x 1 3h after), pivampicillin 350 mg three times daily, oral, 4 days (postoperative)<br>- Control, arm 2: placebo |
| Outcomes | 1) Post-abortal infection defined as<br>a) Patient seen at follow-up visit after 4 weeks, at least 4 of the following: temperature > 38 °C for > 24h; continued pelvic pain > 5 days; vaginal bleeding more than menstrual flow > 5 days; foul discharge; infection diagnosed by general practitioner<br>b) Patient seen before scheduled follow-up, at least 2 of the following: temperature > 38 °C; moderate tenderness of the uterus; tender adnexal mass; pathologic discharge or bleeding<br>2) Adverse events of antibiotic treatment |
| Notes | Unclear if intervention was universal antibiotic prophylaxis according to protocol definition; preoperative testing for infections not mentioned. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|

**Sonne-Holm 1981** *(Continued)*

| | |
|---|---|
| Incomplete outcome data (attrition bias) | High risk |

**Sorensen 1992**

| | |
|---|---|
| Methods | - Single centre, Denmark<br>- Study period: October 1985 - March 1988<br>- Follow-up visits after 1 and 4 weeks |
| Participants | - 432 women randomised, 378 analysed<br>- Women presenting for surgical abortion in first trimester<br>- Exclusion criteria: allergic to treatment; receiving antibiotics at time of abortion; signs of infection before abortion; positive test for gonorrhoea<br>Preoperative infections:<br>1) History of PID: arm 1: 50/189, arm 2: 40/189<br>2) Chlamydia: arm 1: 13/189 , arm 2: 14/189<br>3) Gonorrhoea: all tested, 3 women with positive tests excluded<br>4) Bacterial vaginosis: not reported |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br>- Intervention, arm 1: erythromycin 500 mg twice daily, oral (pre-and postoperative, starting on the evening before abortion, total 15 doses)<br>- Control, arm 2: placebo |
| Outcomes | Postabortal PID defined as: pelvic pain plus at least 2 of the following: temperature > 38 °C; tenderness of uterus; tenderness of tubes; adnexal mass; abnormal discharge; abnormal bleeding |
| Notes | Not universal antibiotic prophylaxis according to protocol definition: study population included only women without gonorrhoea at baseline. |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | |
| Allocation concealment (selection bias) | Low risk | |
| Incomplete outcome data (attrition bias) | Low risk | |

**Westrom 1981**

| | |
|---|---|
| Methods | - Single centre, Sweden (Lund)<br>- Study period: September 1979 - March 1980<br>- Follow-up visit after 5 days |
| Participants | - 278 women randomised, 212 analysed<br>- Women presenting for surgical abortion in first trimester<br>- Exclusion criteria: positive test for gonorrhoea; ongoing antibiotic treatment at the time of abortion; abortion combined with hysterectomy<br>Preoperative infections:<br>1) History of PID: not reported<br>2) Chlamydia: not reported<br>3) Gonorrhoea: two patients testing positive excluded from analysis<br>4) Bacterial vaginosis: not reported |
| Interventions | **Antibiotic prophylaxis compared to placebo**<br>- Intervention, arm 1: tinidazole 2 g single dose, (oral preoperative, 12h before)<br>- Control, arm 2: placebo |
| Outcomes | Post-abortion endometritis defined as all of the following: temperature > 38 °C in first 5 postoperative days; lower abdominal pain; tenderness of uterus |
| Notes | Not universal antibiotic prophylaxis according to protocol definition: study population included only women without gonorrhoea at baseline. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Incomplete outcome data (attrition bias) | Low risk | |

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

| Study | Reason for exclusion |
|---|---|
| Bennett 2009 | Not a RCT (observational cohort study). |
| Blackwell 1993 | Not a RCT (observational cohort study). |
| Chen 2007 | Not a RCT (mathematical modelling study). |
| Cormier 1988 | 1. Includes participants post-partum as well as post-abortion; 2. Outcome is not PID, but isolation of micro-organisms from curettage material. |
| Faucher 2006 | Not a RCT (narrative review). |

| Study | Reason for exclusion |
|---|---|
| Gemzell-Danielsson 2008 | 1. Includes participants with mid-trimester abortion; 2. Not antibiotic prophylaxis. |
| Giertz 1987 | Includes participants after first-trimester. |
| Grossmann 2008 | 1. Includes participants with second-trimester abortion; 2. Not a RCT (narrative review). |
| Gupta 2007 | Not a RCT (narrative review). |
| Heisterberg 1985c | Outcome was post-abortal bacter aemia, not upper genital tract infection. |
| Henriques 1994 | Stratification of control group according to risk assessment post-randomisation, so not possible to analyse as randomised comparison. |
| May 2007 | Not a RCT (systematic review of antibiotics for incomplete abortion). |
| Miller 2004 | Only 51% of the participants were women undergoing first-trimester abortion and results not stratified according to gestational age. |
| Nguyen 2009 | Not a RCT (observational cohort study). |
| Prager 2009 | 1. Includes participants with second-trimester abortion; 2. Not a RCT (systematic review). |
| Spence 1982 | Participants were in second-trimester of pregnancy. |

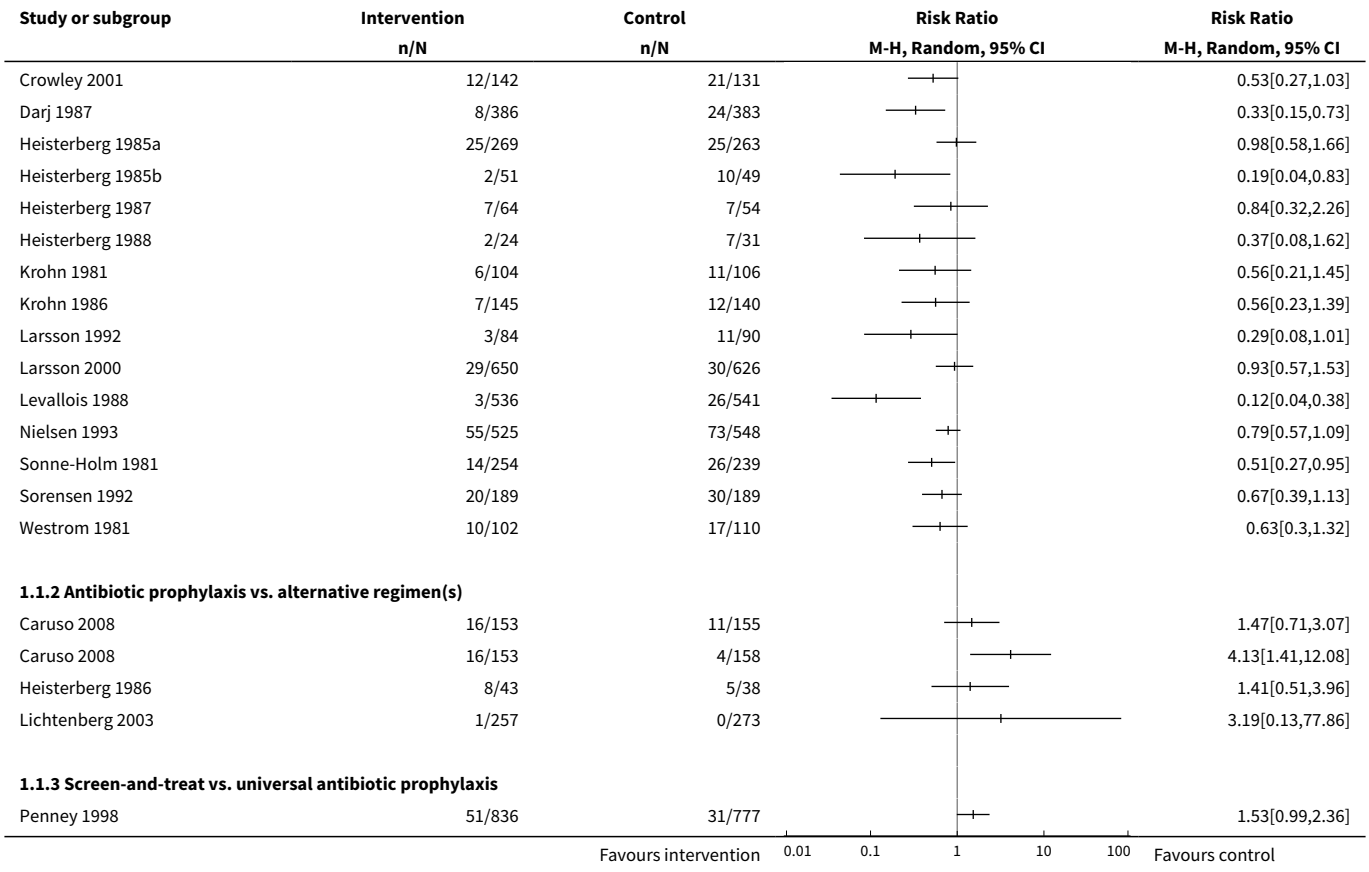
## DATA AND ANALYSES

### Comparison 1. All included studies, 19 trials: by intervention

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Control arm and strategy | 19 | | Risk Ratio (M-H, Random, 95% CI) | Totals not selected |
| 1.1 Antibiotic prophylaxis vs. placebo | 15 | | Risk Ratio (M-H, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 1.2 Antibiotic prophylaxis vs. alternative regimen(s) | 3 | | Risk Ratio (M-H, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 1.3 Screen-and-treat vs. universal antibiotic prophylaxis | 1 | | Risk Ratio (M-H, Random, 95% CI) | 0.0 [0.0, 0.0] |

### Analysis 1.1. Comparison 1 All included studies, 19 trials: by intervention, Outcome 1 Control arm and strategy.

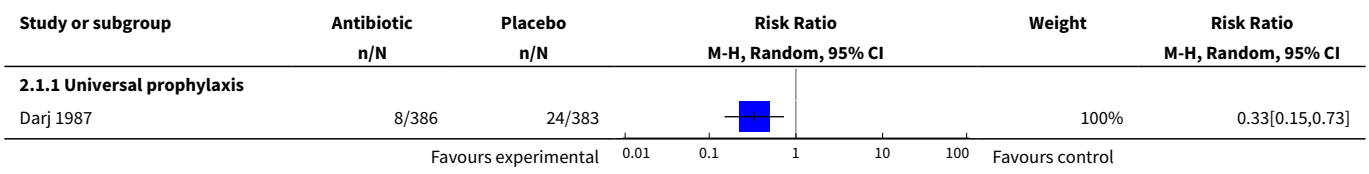
| Study or subgroup | Intervention n/N | Control n/N | Risk Ratio M-H, Random, 95% CI | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|
| 1.1.1 Antibiotic prophylaxis vs. placebo | | | | |

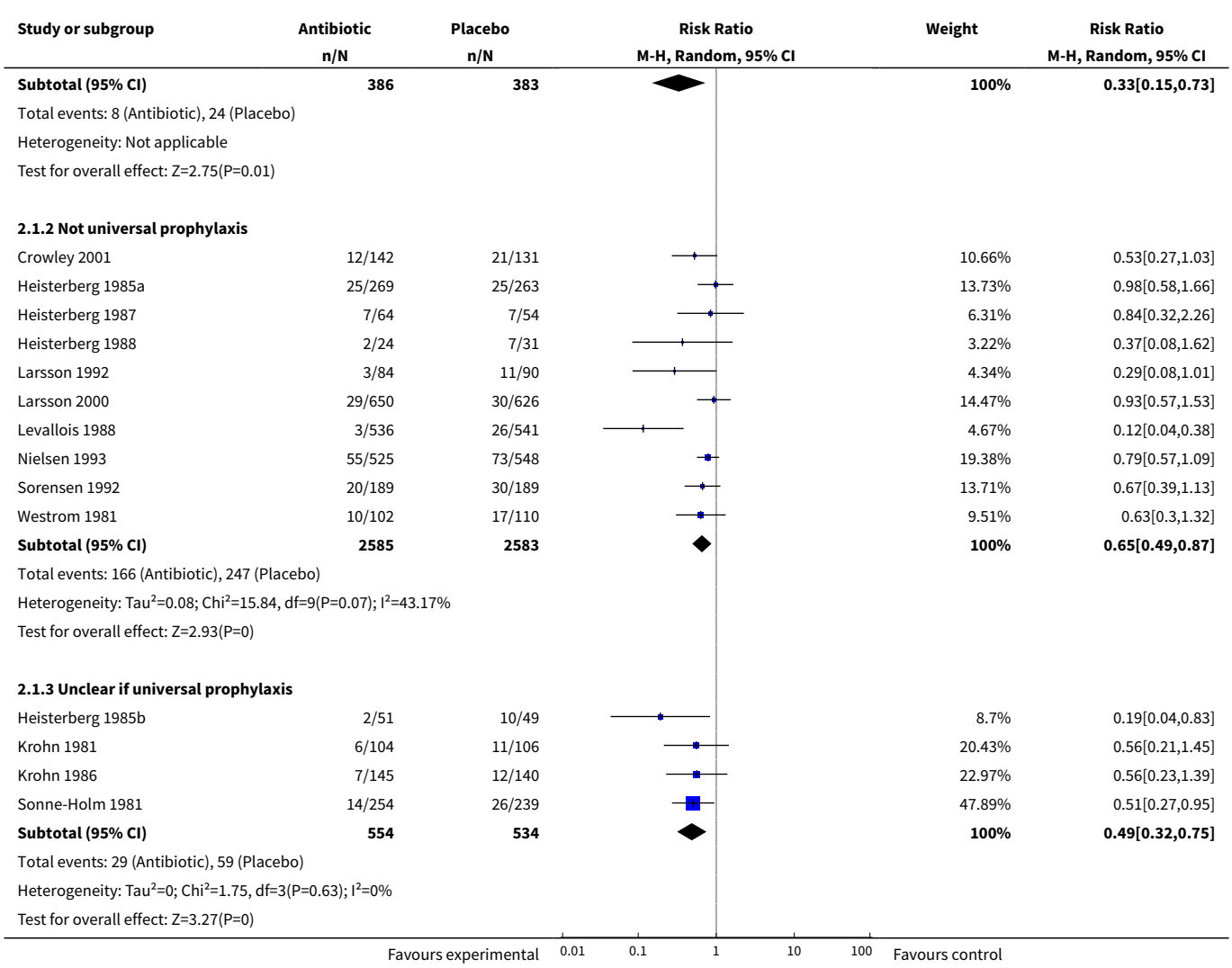



## Comparison 2. Antibiotics vs placebo, 15 trials: by universal prophylaxis

| Outcome or subgroup title | No. of studies | No. of partici-pants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Type of antibiotic prophylaxis | 15 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 Universal prophylaxis | 1 | 769 | Risk Ratio (M-H, Random, 95% CI) | 0.33 [0.15, 0.73] |
| 1.2 Not universal prophylaxis | 10 | 5168 | Risk Ratio (M-H, Random, 95% CI) | 0.65 [0.49, 0.87] |
| 1.3 Unclear if universal prophylaxis | 4 | 1088 | Risk Ratio (M-H, Random, 95% CI) | 0.49 [0.32, 0.75] |

### Analysis 2.1. Comparison 2 Antibiotics vs placebo, 15 trials: by universal prophylaxis, Outcome 1 Type of antibiotic prophylaxis.



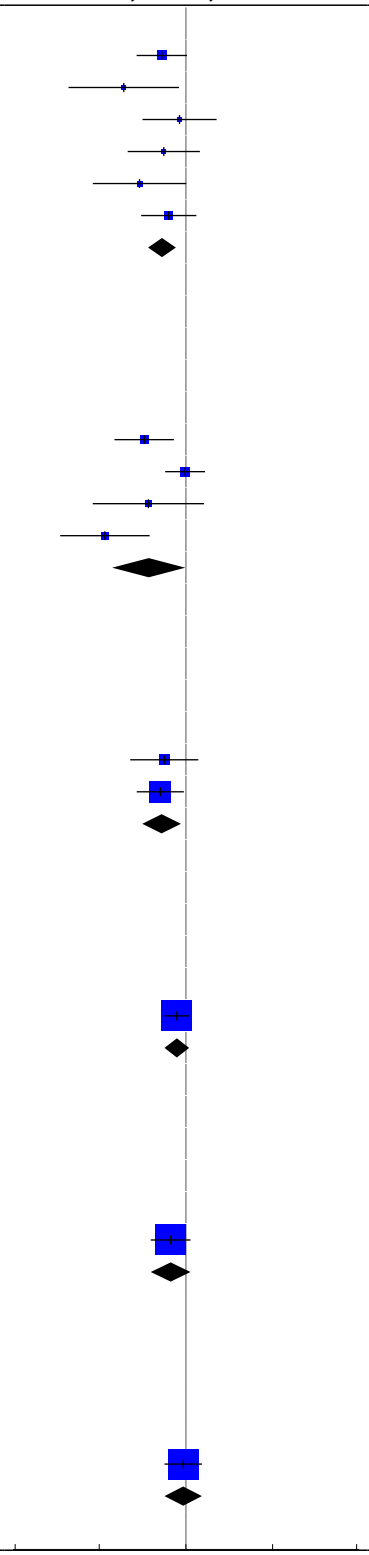



## Comparison 3. Antibiotics vs. placebo, 15 trials: by class of antibiotic

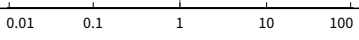
| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Antibiotic class | 15 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 Nitromidazole | 6 | 1087 | Risk Ratio (M-H, Random, 95% CI) | 0.53 [0.37, 0.77] |
| 1.2 Tetracycline | 4 | 2433 | Risk Ratio (M-H, Random, 95% CI) | 0.37 [0.14, 0.98] |
| 1.3 Beta lactam | 2 | 778 | Risk Ratio (M-H, Random, 95% CI) | 0.52 [0.31, 0.88] |
| 1.4 Fluoroquinolone | 1 | 1073 | Risk Ratio (M-H, Random, 95% CI) | 0.79 [0.57, 1.09] |
| 1.5 Macrolide | 1 | 378 | Risk Ratio (M-H, Random, 95% CI) | 0.67 [0.39, 1.13] |
| 1.6 Glycoside | 1 | 1276 | Risk Ratio (M-H, Random, 95% CI) | 0.93 [0.57, 1.53] |

## Analysis 3.1. Comparison 3 Antibiotics vs. placebo, 15 trials: by class of antibiotic, Outcome 1 Antibiotic class.

| Study or subgroup | Antibiotics n/N | Placebo n/N | Risk Ratio M-H, Random, 95% CI | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|
| **3.1.1 Nitromidazole** | | | | | |
| Crowley 2001 | 12/142 | 21/131 | | 30.51% | 0.53[0.27,1.03] |
| Heisterberg 1985b | 2/51 | 10/49 | | 6.33% | 0.19[0.04,0.83] |
| Heisterberg 1987 | 7/64 | 7/54 | | 14.1% | 0.84[0.32,2.26] |
| Krohn 1981 | 6/104 | 11/106 | | 14.87% | 0.56[0.21,1.45] |
| Larsson 1992 | 3/84 | 11/90 | | 8.84% | 0.29[0.08,1.01] |
| Westrom 1981 | 10/102 | 17/110 | | 25.35% | 0.63[0.3,1.32] |
| **Subtotal (95% CI)** | **547** | **540** | | **100%** | **0.53[0.37,0.77]** |
| Total events: 40 (Antibiotics), 77 (Placebo) | | | | | |
| Heterogeneity: $Tau^2$=0; $Chi^2$=3.87, df=5(P=0.57); $I^2$=0% | | | | | |
| Test for overall effect: Z=3.37(P=0) | | | | | |
| **3.1.2 Tetracycline** | | | | | |
| Darj 1987 | 8/386 | 24/383 | | 27.72% | 0.33[0.15,0.73] |
| Heisterberg 1985a | 25/269 | 25/263 | | 30.83% | 0.98[0.58,1.66] |
| Heisterberg 1988 | 2/24 | 7/31 | | 18.98% | 0.37[0.08,1.62] |
| Levallois 1988 | 3/536 | 26/541 | | 22.47% | 0.12[0.04,0.38] |
| **Subtotal (95% CI)** | **1215** | **1218** | | **100%** | **0.37[0.14,0.98]** |
| Total events: 38 (Antibiotics), 82 (Placebo) | | | | | |
| Heterogeneity: $Tau^2$=0.72; $Chi^2$=13.61, df=3(P=0); $I^2$=77.97% | | | | | |
| Test for overall effect: Z=1.99(P=0.05) | | | | | |
| **3.1.3 Beta lactam** | | | | | |
| Krohn 1986 | 7/145 | 12/140 | | 32.42% | 0.56[0.23,1.39] |
| Sonne-Holm 1981 | 14/254 | 26/239 | | 67.58% | 0.51[0.27,0.95] |
| **Subtotal (95% CI)** | **399** | **379** | | **100%** | **0.52[0.31,0.88]** |
| Total events: 21 (Antibiotics), 38 (Placebo) | | | | | |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.04, df=1(P=0.85); $I^2$=0% | | | | | |
| Test for overall effect: Z=2.46(P=0.01) | | | | | |
| **3.1.4 Fluoroquinolone** | | | | | |
| Nielsen 1993 | 55/525 | 73/548 | | 100% | 0.79[0.57,1.09] |
| **Subtotal (95% CI)** | **525** | **548** | | **100%** | **0.79[0.57,1.09]** |
| Total events: 55 (Antibiotics), 73 (Placebo) | | | | | |
| Heterogeneity: Not applicable | | | | | |
| Test for overall effect: Z=1.43(P=0.15) | | | | | |
| **3.1.5 Macrolide** | | | | | |
| Sorensen 1992 | 20/189 | 30/189 | | 100% | 0.67[0.39,1.13] |
| **Subtotal (95% CI)** | **189** | **189** | | **100%** | **0.67[0.39,1.13]** |
| Total events: 20 (Antibiotics), 30 (Placebo) | | | | | |
| Heterogeneity: Not applicable | | | | | |
| Test for overall effect: Z=1.5(P=0.13) | | | | | |
| **3.1.6 Glycoside** | | | | | |
| Larsson 2000 | 29/650 | 30/626 | | 100% | 0.93[0.57,1.53] |
| **Subtotal (95% CI)** | **650** | **626** | | **100%** | **0.93[0.57,1.53]** |
| Total events: 29 (Antibiotics), 30 (Placebo) | | | | | |



| Study or subgroup | Antibiotics n/N | Placebo n/N | Risk Ratio M-H, Random, 95% CI | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|
| Heterogeneity: Not applicable | | | | | |
| Test for overall effect: Z=0.28(P=0.78) | | | | | |

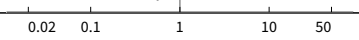


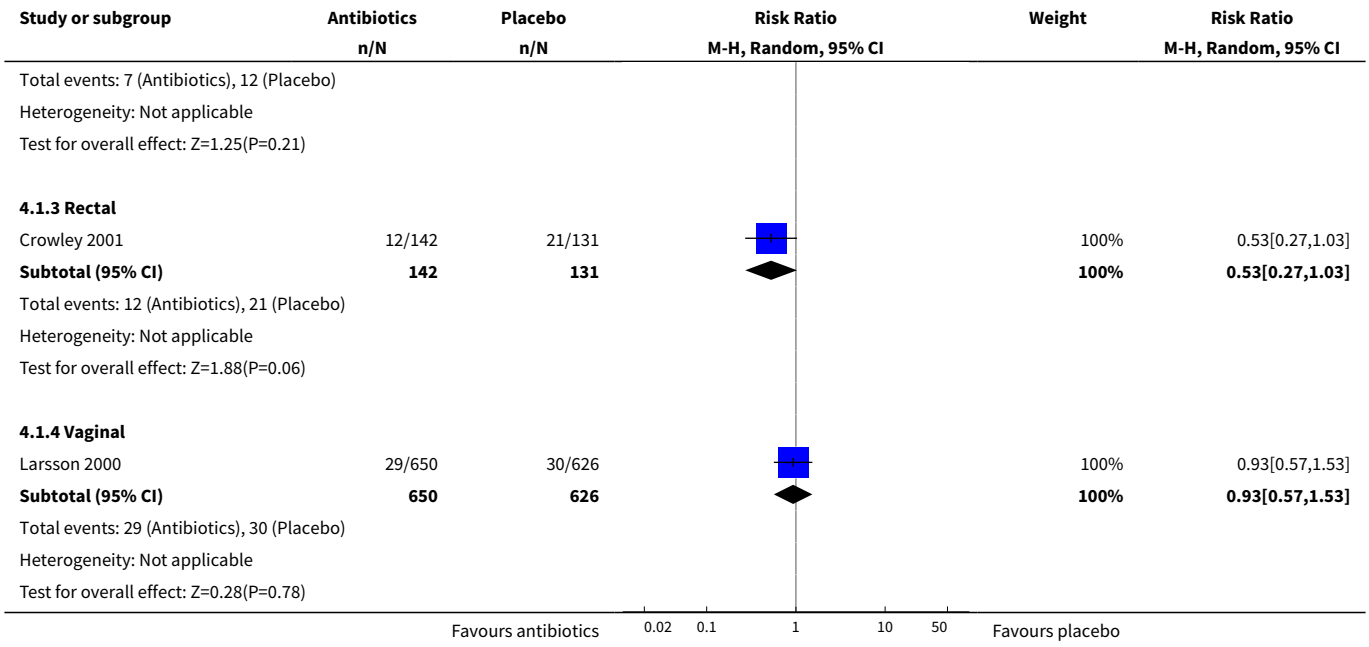

## Comparison 4. Antibiotics vs. placebo, 15 trials: by route of antibiotic administration

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Route of antibiotic administration | 15 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 Oral | 12 | 5191 | Risk Ratio (M-H, Random, 95% CI) | 0.54 [0.40, 0.74] |
| 1.2 Intravenous | 1 | 285 | Risk Ratio (M-H, Random, 95% CI) | 0.56 [0.23, 1.39] |
| 1.3 Rectal | 1 | 273 | Risk Ratio (M-H, Random, 95% CI) | 0.53 [0.27, 1.03] |
| 1.4 Vaginal | 1 | 1276 | Risk Ratio (M-H, Random, 95% CI) | 0.93 [0.57, 1.53] |

## Analysis 4.1. Comparison 4 Antibiotics vs. placebo, 15 trials: by route of antibiotic administration, Outcome 1 Route of antibiotic administration.

| Study or subgroup | Antibiotics n/N | Placebo n/N | Risk Ratio M-H, Random, 95% CI | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|
| **4.1.1 Oral** | | | | | |
| Darj 1987 | 8/386 | 24/383 | | 8.54% | 0.33[0.15,0.73] |
| Heisterberg 1985a | 25/269 | 25/263 | | 12.63% | 0.98[0.58,1.66] |
| Heisterberg 1985b | 2/51 | 10/49 | | 3.48% | 0.19[0.04,0.83] |
| Heisterberg 1987 | 7/64 | 7/54 | | 6.43% | 0.84[0.32,2.26] |
| Heisterberg 1988 | 2/24 | 7/31 | | 3.44% | 0.37[0.08,1.62] |
| Krohn 1981 | 6/104 | 11/106 | | 6.67% | 0.56[0.21,1.45] |
| Larsson 1992 | 3/84 | 11/90 | | 4.56% | 0.29[0.08,1.01] |
| Levallois 1988 | 3/536 | 26/541 | | 4.87% | 0.12[0.04,0.38] |
| Nielsen 1993 | 55/525 | 73/548 | | 16.59% | 0.79[0.57,1.09] |
| Sonne-Holm 1981 | 14/254 | 26/239 | | 10.91% | 0.51[0.27,0.95] |
| Sorensen 1992 | 20/189 | 30/189 | | 12.61% | 0.67[0.39,1.13] |
| Westrom 1981 | 10/102 | 17/110 | | 9.27% | 0.63[0.3,1.32] |
| **Subtotal (95% CI)** | **2588** | **2603** | | **100%** | **0.54[0.4,0.74]** |
| Total events: 155 (Antibiotics), 267 (Placebo) | | | | | |
| Heterogeneity: $Tau^2$=0.11; $Chi^2$=20.62, df=11(P=0.04); $I^2$=46.65% | | | | | |
| Test for overall effect: Z=3.97(P<0.0001) | | | | | |
| **4.1.2 Intravenous** | | | | | |
| Krohn 1986 | 7/145 | 12/140 | | 100% | 0.56[0.23,1.39] |
| **Subtotal (95% CI)** | **145** | **140** | | **100%** | **0.56[0.23,1.39]** |

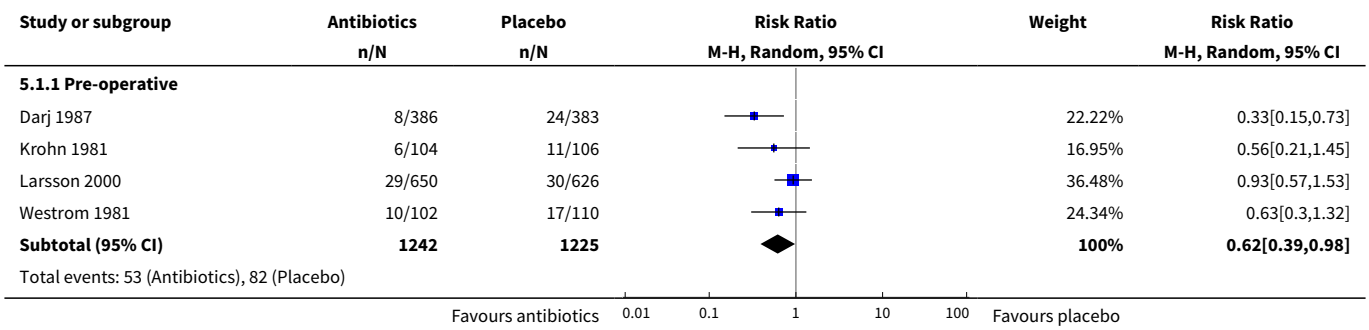


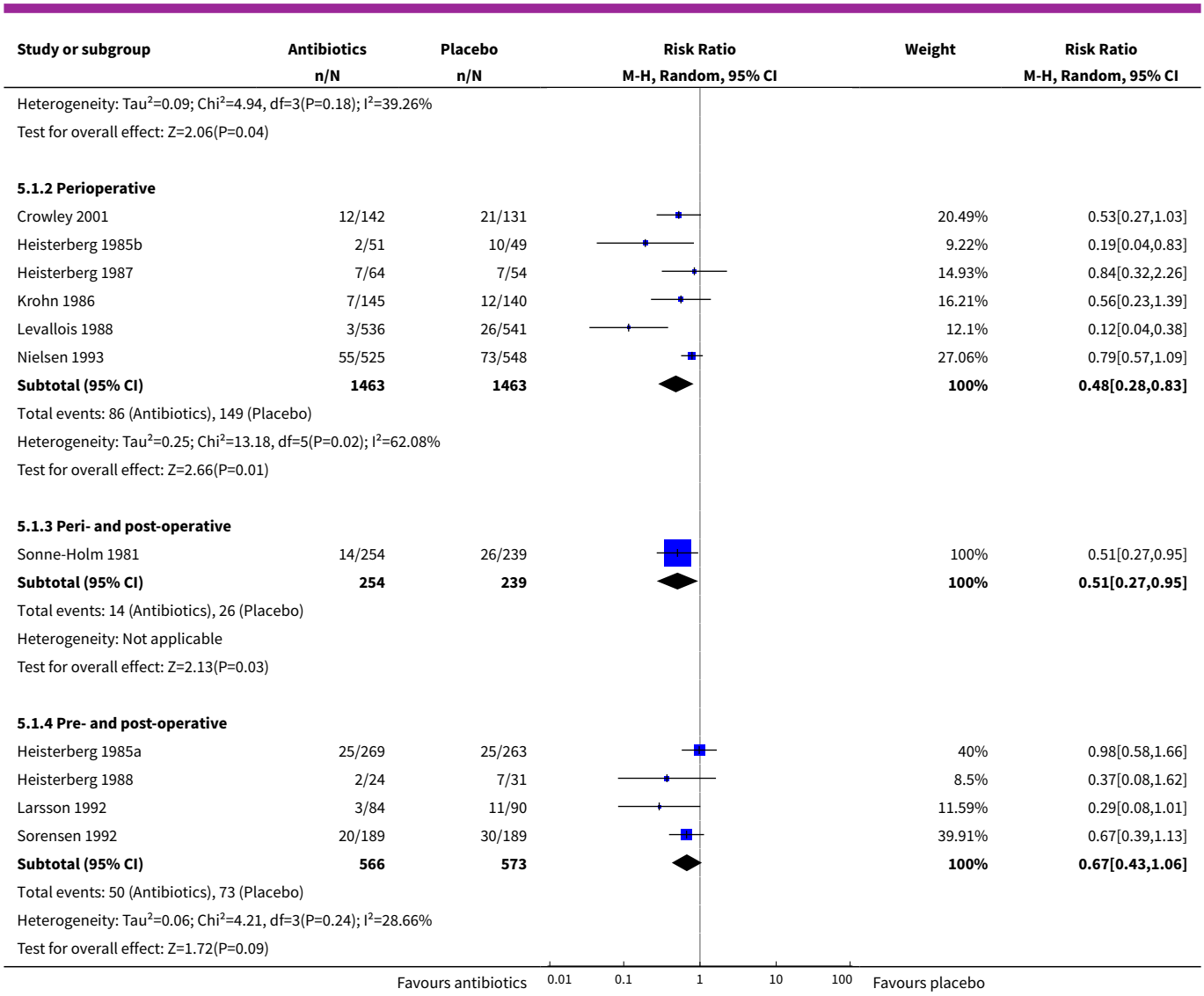



## Comparison 5. Antibiotics vs. placebo, 15 trials: by timing of antibiotic administration

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Timing of antibiotic administration | 15 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 Pre-operative | 4 | 2467 | Risk Ratio (M-H, Random, 95% CI) | 0.62 [0.39, 0.98] |
| 1.2 Perioperative | 6 | 2926 | Risk Ratio (M-H, Random, 95% CI) | 0.48 [0.28, 0.83] |
| 1.3 Peri- and post-operative | 1 | 493 | Risk Ratio (M-H, Random, 95% CI) | 0.51 [0.27, 0.95] |
| 1.4 Pre- and post-operative | 4 | 1139 | Risk Ratio (M-H, Random, 95% CI) | 0.67 [0.43, 1.06] |

### Analysis 5.1. Comparison 5 Antibiotics vs. placebo, 15 trials: by timing of antibiotic administration, Outcome 1 Timing of antibiotic administration.

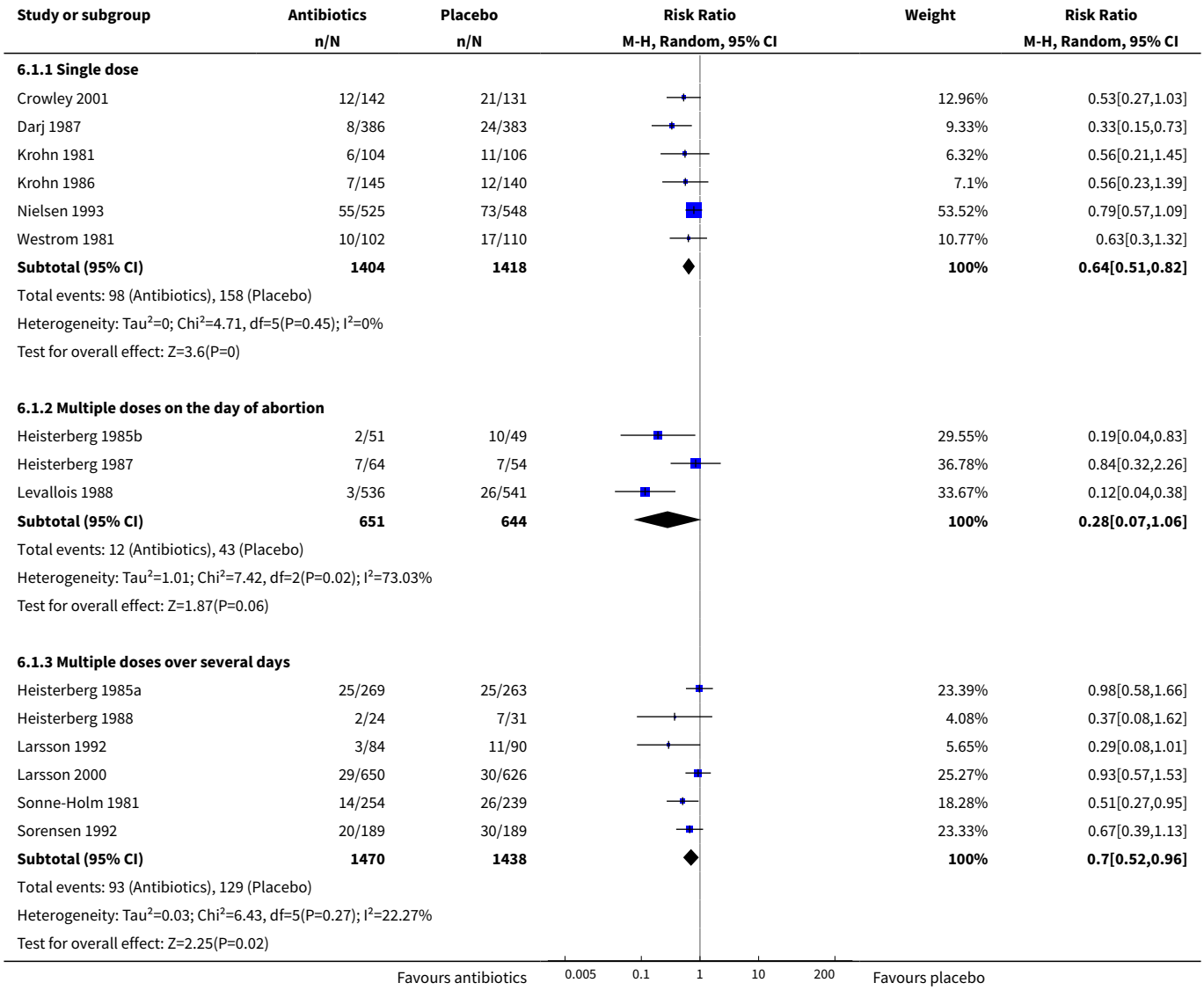





## Comparison 6. Antibiotics vs. placebo, 15 trials: by dosing schedule

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Antibiotic dosing schedule | 15 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 Single dose | 6 | 2822 | Risk Ratio (M-H, Random, 95% CI) | 0.64 [0.51, 0.82] |
| 1.2 Multiple doses on the day of abortion | 3 | 1295 | Risk Ratio (M-H, Random, 95% CI) | 0.28 [0.07, 1.06] |
| 1.3 Multiple doses over several days | 6 | 2908 | Risk Ratio (M-H, Random, 95% CI) | 0.70 [0.52, 0.96] |

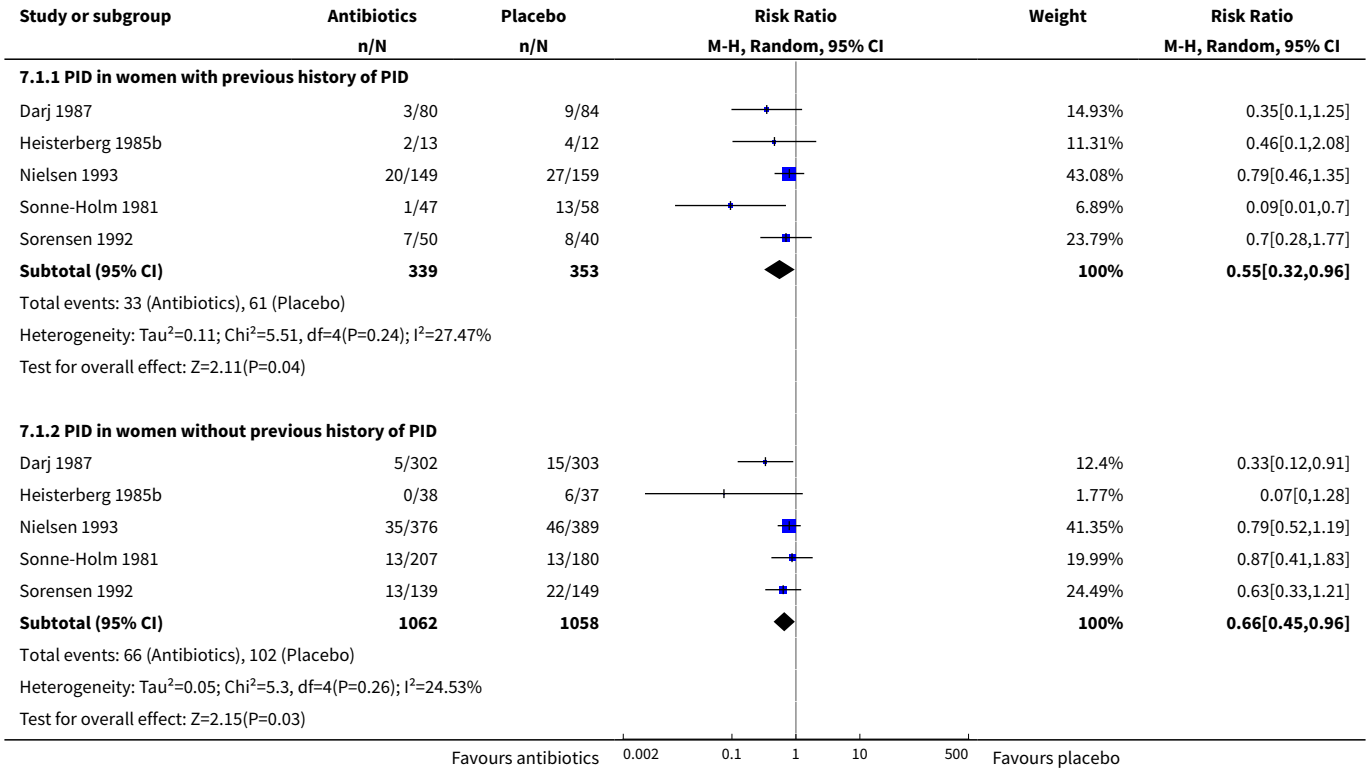
## Analysis 6.1. Comparison 6 Antibiotics vs. placebo, 15 trials: by dosing schedule, Outcome 1 Antibiotic dosing schedule.




## Comparison 7. Women with a history of pelvic inflammatory disease (PID), 5 trials

| Outcome or subgroup title | No. of studies | No. of partici-pants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 PID stratified according to previous history of PID | 5 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 PID in women with previous history of PID | 5 | 692 | Risk Ratio (M-H, Random, 95% CI) | 0.55 [0.32, 0.96] |
| 1.2 PID in women without previous history of PID | 5 | 2120 | Risk Ratio (M-H, Random, 95% CI) | 0.66 [0.45, 0.96] |

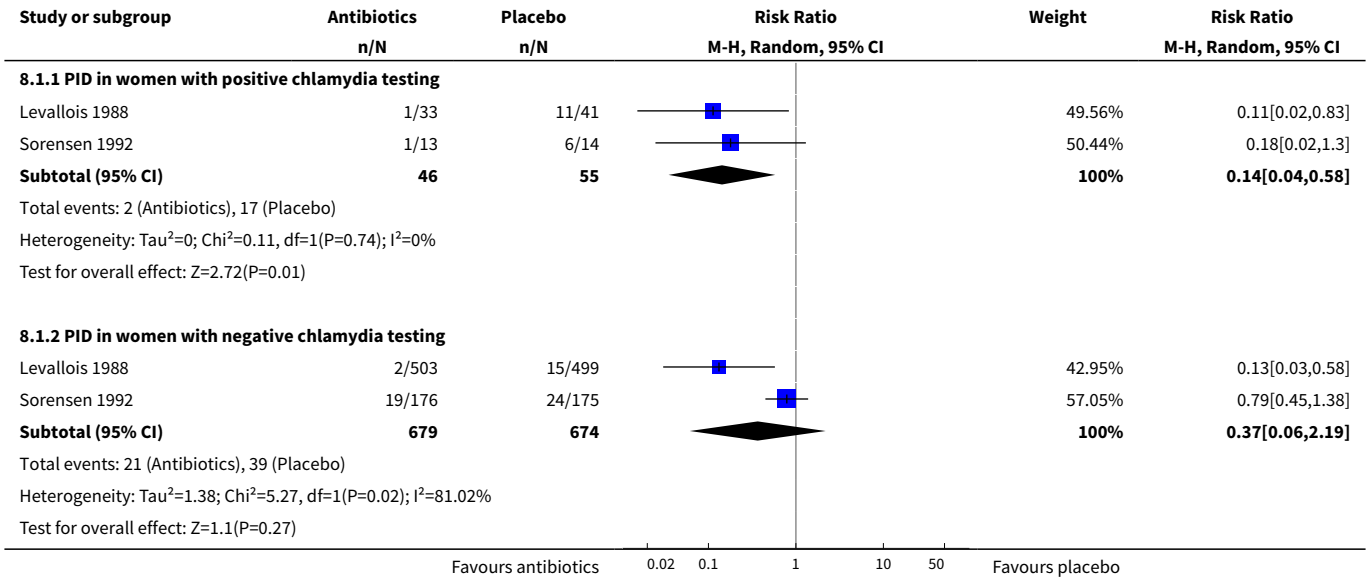
### Analysis 7.1. Comparison 7 Women with a history of pelvic inflammatory disease (PID), 5 trials, Outcome 1 PID stratified according to previous history of PID.




## Comparison 8. Women with chlamydia at baseline, 2 trials

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 PID stratified according to positive chlamydia testing | 2 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 PID in women with positive chlamydia testing | 2 | 101 | Risk Ratio (M-H, Random, 95% CI) | 0.14 [0.04, 0.58] |
| 1.2 PID in women with negative chlamydia testing | 2 | 1353 | Risk Ratio (M-H, Random, 95% CI) | 0.37 [0.06, 2.19] |

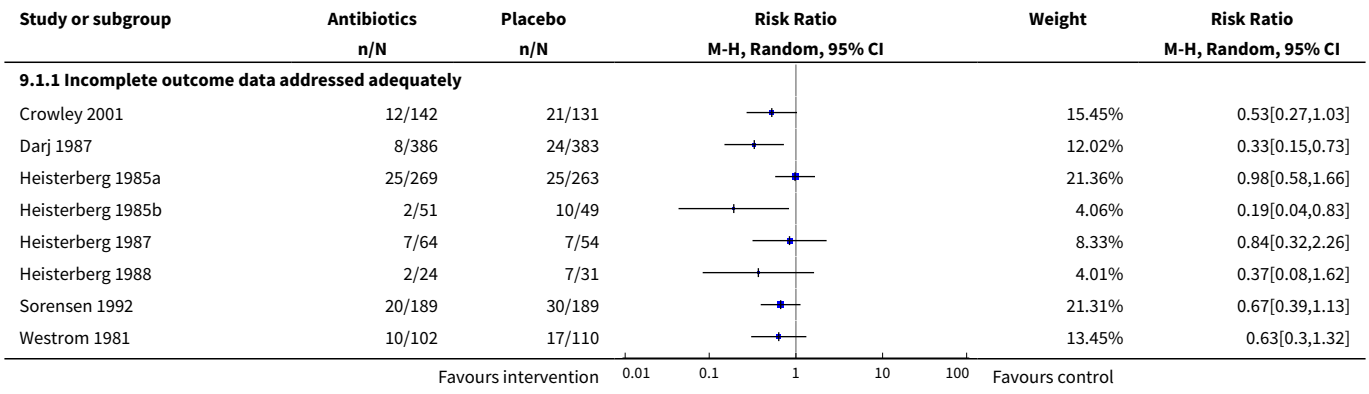
### Analysis 8.1. Comparison 8 Women with chlamydia at baseline, 2 trials, Outcome 1 PID stratified according to positive chlamydia testing.

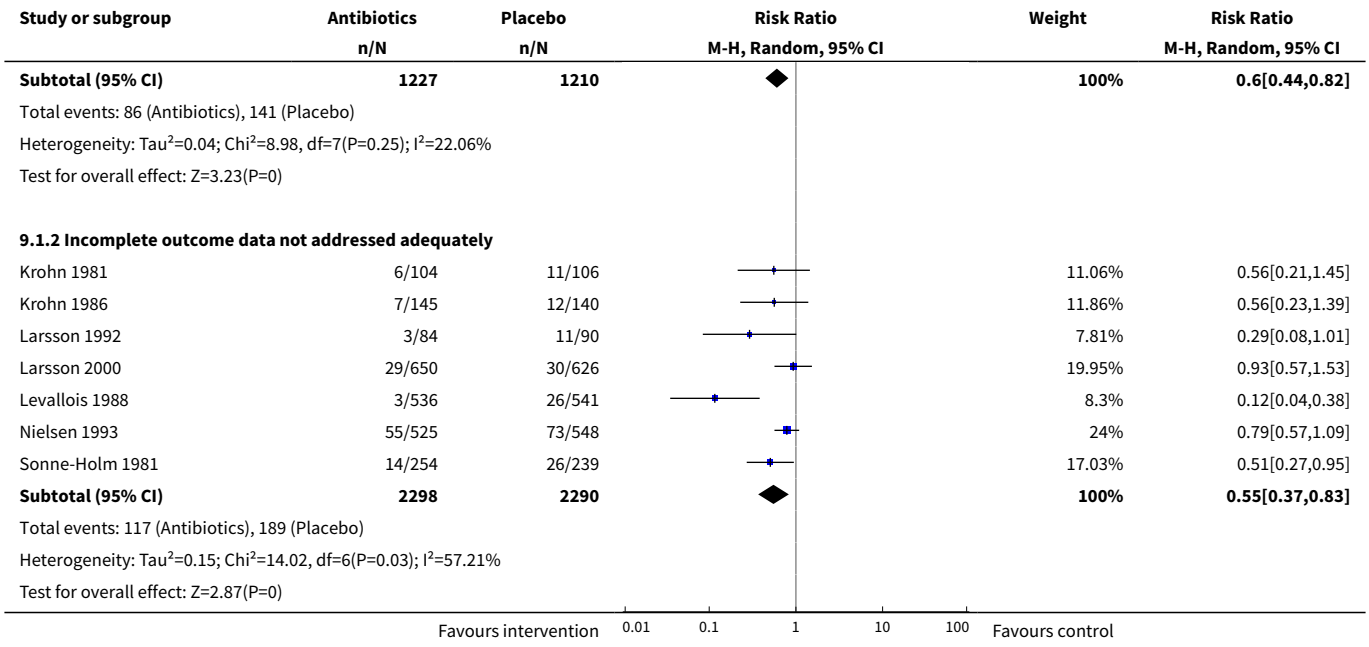



## Comparison 9. Antibiotics, vs. placebo, 15 trials: by reported analysis of outcome data

| Outcome or subgroup title | No. of studies | No. of partici-pants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Dealing with incomplete outcome data | 15 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 Incomplete outcome data addressed adequately | 8 | 2437 | Risk Ratio (M-H, Random, 95% CI) | 0.60 [0.44, 0.82] |
| 1.2 Incomplete outcome data not addressed adequately | 7 | 4588 | Risk Ratio (M-H, Random, 95% CI) | 0.55 [0.37, 0.83] |

### Analysis 9.1. Comparison 9 Antibiotics, vs. placebo, 15 trials: by reported analysis of outcome data, Outcome 1 Dealing with incomplete outcome data.

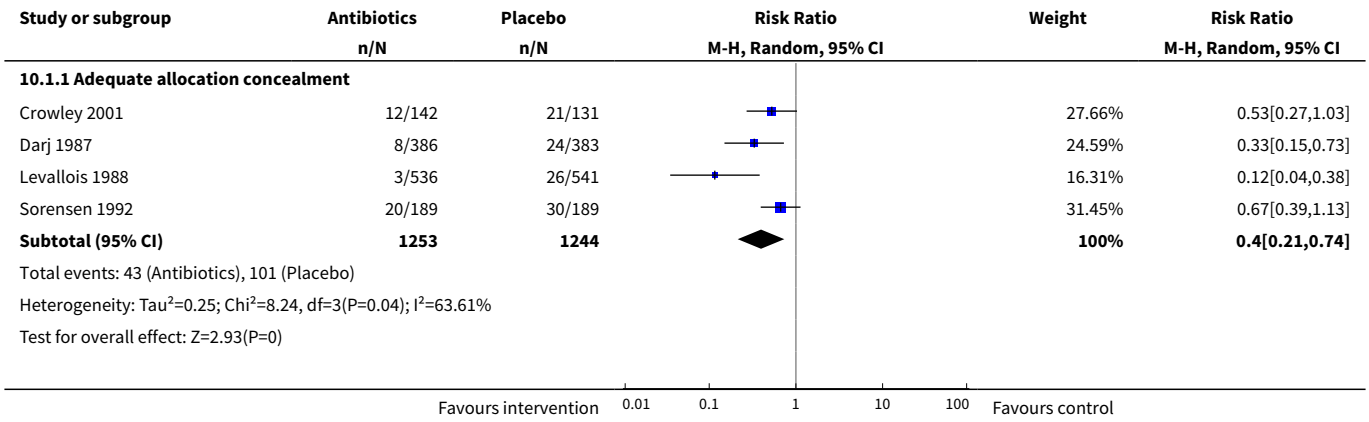




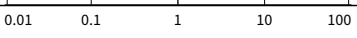

## Comparison 10. Antibiotics vs. placebo, 15 trials: by reporting of allocation concealment

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Concealment of allocation | 15 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 Adequate allocation concealment | 4 | 2497 | Risk Ratio (M-H, Random, 95% CI) | 0.40 [0.21, 0.74] |
| 1.2 Inadequate allocation concealment | 11 | 4528 | Risk Ratio (M-H, Random, 95% CI) | 0.71 [0.58, 0.87] |

### Analysis 10.1. Comparison 10 Antibiotics vs. placebo, 15 trials: by reporting of allocation concealment, Outcome 1 Concealment of allocation.



| Study or subgroup | Antibiotics n/N | Placebo n/N | Risk Ratio M-H, Random, 95% CI | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|
| **10.1.2 Inadequate allocation concealment** | | | | | |
| Heisterberg 1985a | 25/269 | 25/263 | | 14.06% | 0.98[0.58,1.66] |
| Heisterberg 1985b | 2/51 | 10/49 | | 1.97% | 0.19[0.04,0.83] |
| Heisterberg 1987 | 7/64 | 7/54 | | 4.31% | 0.84[0.32,2.26] |
| Heisterberg 1988 | 2/24 | 7/31 | | 1.94% | 0.37[0.08,1.62] |
| Krohn 1981 | 6/104 | 11/106 | | 4.54% | 0.56[0.21,1.45] |
| Krohn 1986 | 7/145 | 12/140 | | 5.09% | 0.56[0.23,1.39] |
| Larsson 1992 | 3/84 | 11/90 | | 2.73% | 0.29[0.08,1.01] |
| Larsson 2000 | 29/650 | 30/626 | | 15.6% | 0.93[0.57,1.53] |
| Nielsen 1993 | 55/525 | 73/548 | | 31.89% | 0.79[0.57,1.09] |
| Sonne-Holm 1981 | 14/254 | 26/239 | | 10.27% | 0.51[0.27,0.95] |
| Westrom 1981 | 10/102 | 17/110 | | 7.6% | 0.63[0.3,1.32] |
| **Subtotal (95% CI)** | **2272** | **2256** | | **100%** | **0.71[0.58,0.87]** |
| Total events: 160 (Antibiotics), 229 (Placebo) | | | | | |
| Heterogeneity: $Tau^2$=0.01; $Chi^2$=10.56, df=10(P=0.39); $I^2$=5.27% | | | | | |
| Test for overall effect: Z=3.26(P=0) | | | | | |



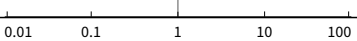

Favours intervention — Favours control

## Comparison 11. Antibiotics vs. placebo, 15 trials: by reporting of blinding

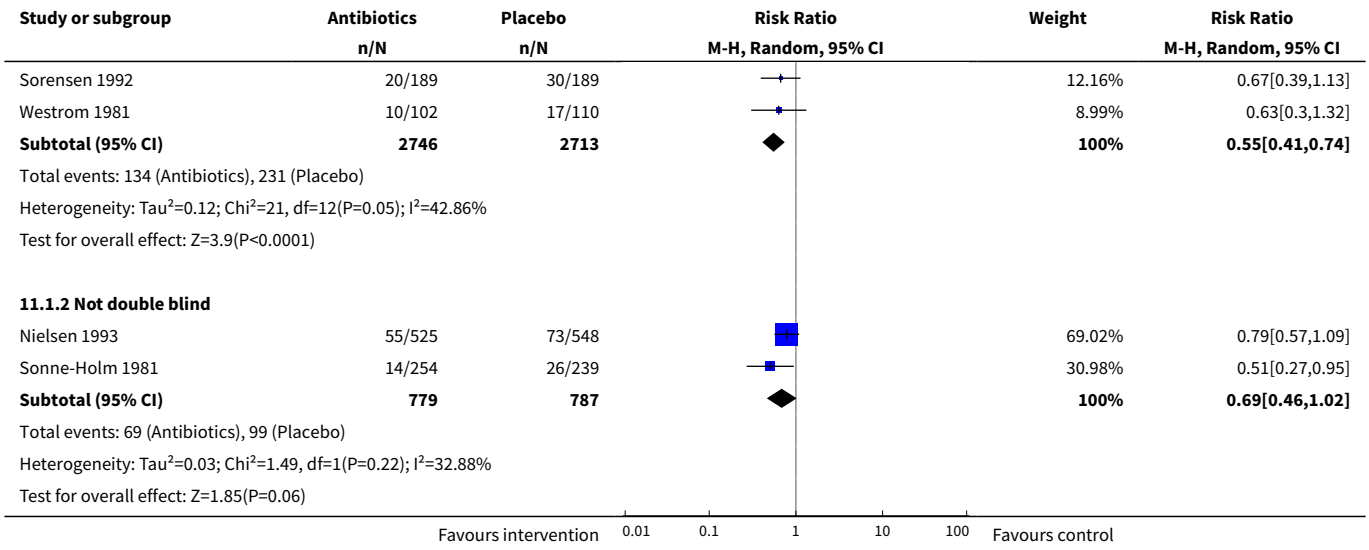
| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Reported blinding | 15 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 Double blind | 13 | 5459 | Risk Ratio (M-H, Random, 95% CI) | 0.55 [0.41, 0.74] |
| 1.2 Not double blind | 2 | 1566 | Risk Ratio (M-H, Random, 95% CI) | 0.69 [0.46, 1.02] |

## Analysis 11.1. Comparison 11 Antibiotics vs. placebo, 15 trials: by reporting of blinding, Outcome 1 Reported blinding.

| Study or subgroup | Antibiotics n/N | Placebo n/N | Risk Ratio M-H, Random, 95% CI | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|
| **11.1.1 Double blind** | | | | | |
| Crowley 2001 | 12/142 | 21/131 | | 9.9% | 0.53[0.27,1.03] |
| Darj 1987 | 8/386 | 24/383 | | 8.29% | 0.33[0.15,0.73] |
| Heisterberg 1985a | 25/269 | 25/263 | | 12.18% | 0.98[0.58,1.66] |
| Heisterberg 1985b | 2/51 | 10/49 | | 3.41% | 0.19[0.04,0.83] |
| Heisterberg 1987 | 7/64 | 7/54 | | 6.27% | 0.84[0.32,2.26] |
| Heisterberg 1988 | 2/24 | 7/31 | | 3.37% | 0.37[0.08,1.62] |
| Krohn 1981 | 6/104 | 11/106 | | 6.5% | 0.56[0.21,1.45] |
| Krohn 1986 | 7/145 | 12/140 | | 7.02% | 0.56[0.23,1.39] |
| Larsson 1992 | 3/84 | 11/90 | | 4.46% | 0.29[0.08,1.01] |
| Larsson 2000 | 29/650 | 30/626 | | 12.7% | 0.93[0.57,1.53] |
| Levallois 1988 | 3/536 | 26/541 | | 4.76% | 0.12[0.04,0.38] |



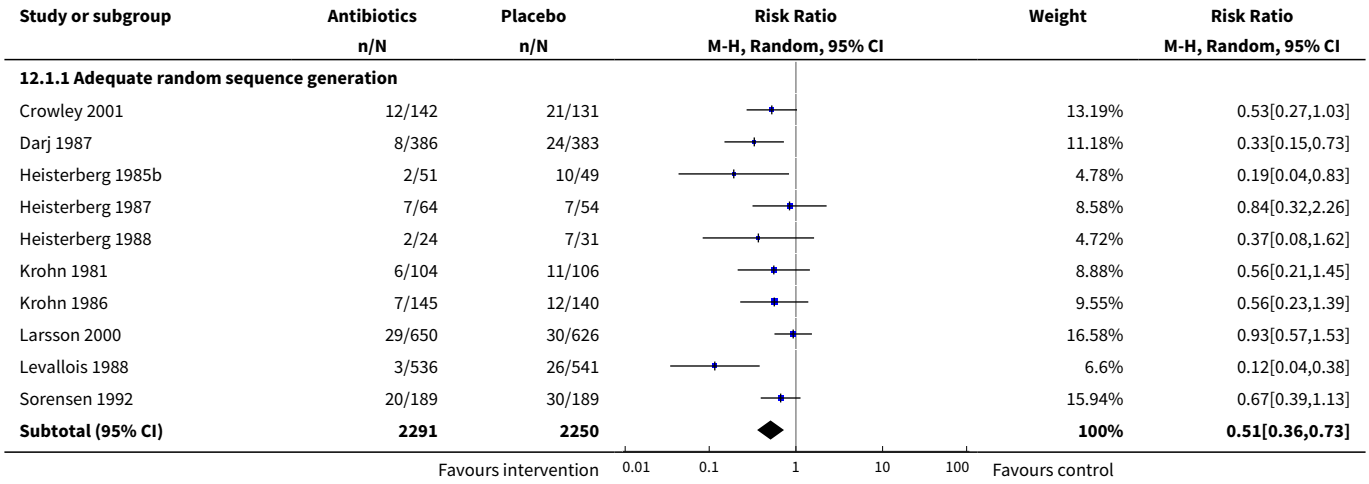

Favours intervention — Favours control

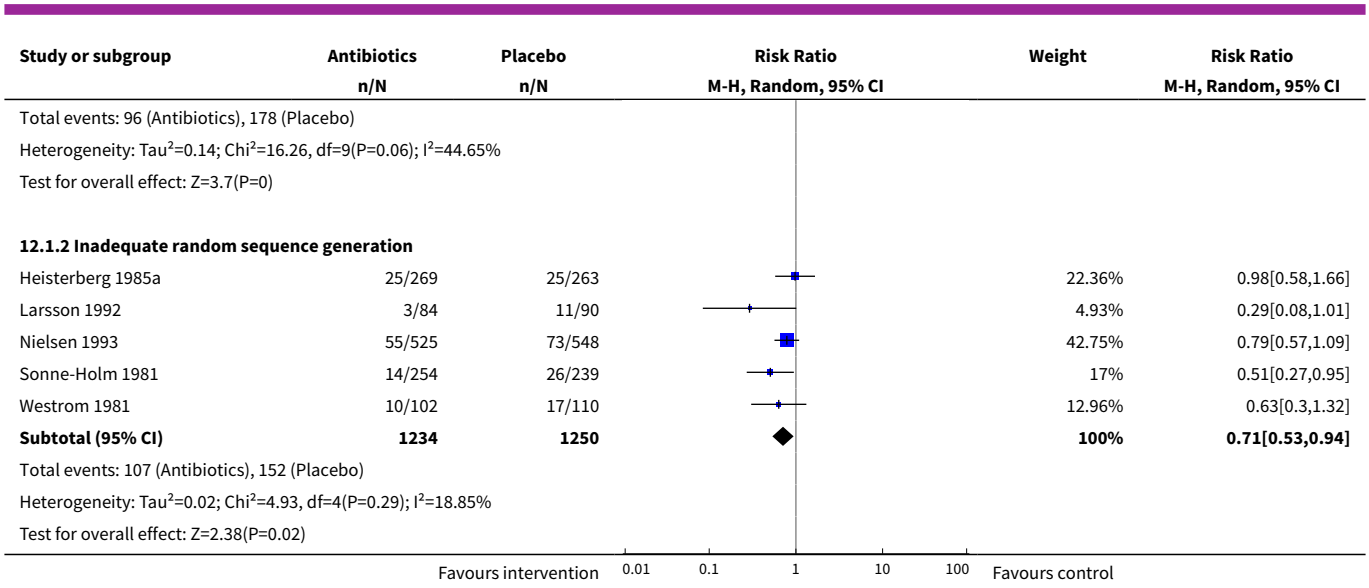



## Comparison 12. Antibiotics vs. placebo, 15 trials: by reporting of random sequence generation method

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Random sequence generation method | 15 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 1.1 Adequate random sequence generation | 10 | 4541 | Risk Ratio (M-H, Random, 95% CI) | 0.51 [0.36, 0.73] |
| 1.2 Inadequate random sequence generation | 5 | 2484 | Risk Ratio (M-H, Random, 95% CI) | 0.71 [0.53, 0.94] |

### Analysis 12.1. Comparison 12 Antibiotics vs. placebo, 15 trials: by reporting of random sequence generation method, Outcome 1 Random sequence generation method.






## ADDITIONAL TABLES

**Table 1. Testing and reporting of sexually transmitted infections and bacterial vaginosis**

| First author, year | N | PID assessment strategy | No. with history of PID | Chlamydia testing strategy (method) | No. with chlamydia | Gonorrhoea testing strategy (method) | No. with gonorrhoea | BV testing strategy (method) | No. with BV | Antibiotics used | Universal antibiotic prophylaxis |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Antibiotic prophylaxis vs. placebo* | | | | | | | | | | | |
| Crowley 2001 | 273 | Asked preop | 14 | All tested (EIA) | 21 (%) | Some tested (culture) | 1 | All tested (Gram stain) | 273 | Single dose metronidazole | No. 'All women with chlamydia were treated preoperatively.' |
| Darj 1987 | 769 | Asked preop | 164 | Not tested | Not tested | Not tested | Not tested | n.r. | n.r. | Single dose doxycycline | Yes. 'Preoperative cultures for *N. gonorrhoeae* and *C. trachomatis* were not made.' |
| Heisterberg 1985b | 532 | Asked preop | n.r. | All tested (culture) | 48 (9.0%) | All tested (culture) | 0 (all excluded) | n.r. | n.r. | Multiple doses lymecycline | No. '6 women with positive cultures for *N. gonorrhoeae* were treated and excluded.' |
| Heisterberg 1985c | 100 | Physician diagnosis | 25 | n.r. | n.r. | All tested (culture) | 0 (no positive cultures) | All tested (culture) | 19 (19.0%) | Multiple doses metronidazole | Unclear |
| Heisterberg 1987 | 118 | Physician diagnosis | 118 | n.r. | n.r. | All tested (culture) | 2 (1.7%) | All tested (culture) | 41 (34.7%) | Multiple doses metronidazole | No. '2 women had positive cultures for *N. gonorrhoeae* and received penicillin prior to abortion.' |
| Heisterberg 1988 | 55 | Asked preop | 55 | All tested (culture) | 3 (5.5%) | All tested (culture) | 0 (all excluded) | n.r. | n.r. | Multiple doses lymecycline | No. 'cultures were made for *N. gonorrhoeae* and women with positive results were treated and excluded.' |
| Krohn 1981 | 210 | n.r. | n.r. | n.r. | n.r. | All tested (culture) | n.r. | All tested (culture) | n.r. | Single dose tinidazole | Unclear |
| Krohn 1986 | 285 | n.r. | n.r. | Some tested (culture) | n.r. | All tested (culture) | 0 (no positive | All tested (culture) | n.r. | Single dose sublactam + amoxicillin | Unclear |

**Table 1. Testing and reporting of sexually transmitted infections and bacterial vaginosis** *(Continued)*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | cul-ture) | | | | |
| Larsson 1992 | 174 | n.r. | n.r. | All test-ed (cul-ture) | 0 (all ex-clud-ed) | Some tested (culture) | n.r. | All test-ed (Am-sel crite-ria) | 174 (100%) | Multiple doses metronidazole | No. '23 excluded because of *C. trachomatis* infection.' |
| Larsson 2000 | 1276 | n.r. | n.r. | All test-ed (n.r.) | 0 (all ex-clud-ed) | All tested (n.r.) | 0 (all exclud-ed) | All test-ed (Gram stain) | 220 (17.2%) | Multiple doses clin-damycin | No.'Exclusion criteria included... current infection with *Trichomonas vaginalis*, *C. trachomatis*, *N. gonorrhoeae* or vaginal candidiasis.' |
| Levallois 1988 | 1077 | n.r. | n.r. | All test-ed (n.r.) | 75 (7.0%) | All tested (n.r.) | 0 (all exclud-ed) | n.r. | n.r. | Multiple doses doxycy-cline | No. 'Patients infected by *N. gonorrhoeae* were exclud-ed before randomisation.... In phase 2 all women with positive chlamydia results were treated.' |
| Nielsen, 1993 | 1078 | Asked pre-op | 308 | Not test-ed | Not test-ed | All tested (culture) | 0 (all exclud-ed) | n.r. | n.r. | Single dose Ofloxacin | No. 'Women with positive cultures for *N. gonorrhoeae* were excluded.' |
| Sonne-Holm 1981 | 493 | Asked pre-op | 105 | n.r. | n.r. | n.r. | n.r. | n.r. | n.r. | Multiple doses peni-cillin + pivampicillin | Unclear |
| Sorensen 1992 | 378 | Asked pre-op | 90 | All test-ed (im-muno-fluores-cence or EIA) | 27 (7.1%) | All tested (culture) | 0 (all exclud-ed) | n.r. | n.r. | Multiple doses ery-thromycin | No. 'Women with a positive gonococcal culture were treated and excluded from the study.' |
| Westrom 1981 | 212 | n.r. | n.r. | n.r. | n.r. | All tested (culture) | 0 (all exclud-ed) | All test-ed (cul-ture) | n.r. | Single dose tinidazole | No.' 2 women with gonorrhoea and 3 with trichomoni-asis were excluded.' |
| *Antibiotic prophylaxis vs. alternative regimen(s)* | | | | | | | | | | | |
| Caruso 2008 | 466 | n.r. | n.r. | n.r. | n.r. | n.r. | n.r. | n.r. | n.r. | 5 days prulifloxacin vs. 3 days prulifloxacin | Unclear. STI testing not reported. |

**Table 1. Testing and reporting of sexually transmitted infections and bacterial vaginosis** *(Continued)*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Heisterberg 1986 | 81 | Antibiotics for PID | 81 | n.r. | n.r. | All tested (culture) | 0 (all excluded) | n.r. | n.r. | Multiple doses metronidazole vs. multiple doses pivampicillin | No. 'Women with positive cultures were treated before the abortion and therefore not included.' |
| Lichtenberg 2003 | 530 | Asked preop | 18 | Not tested | Not tested | Not tested | Not tested | n.r. | n.r. | 7 days doxycycline vs. 3 days doxycycline | Yes. 'We did not take cervical cultures and gave no preoperative medication'. |
| *Screen-and-treat vs. universal antibiotic prophylaxis* | | | | | | | | | | | |
| Penney 1998 | 1618 | n.r. | n.r. | All tested (EIA) | 91 (5.6%) | All tested (culture) | 3 (0.2%) | All tested (Gram stain) | 282 (17.5%) | According to strategy | Yes. Screen-and-treat vs universal prophylaxis |

EIA - enzyme-linked immunoassay; n.r. - not reported

**Table 2. Risk of bias as assessed in all 19 included trials**

| First author, year | Adequate random sequence generation | Adequate allocation concealment | Double-blind | Incomplete outcome data addressed |
|---|---|---|---|---|
| *Antibiotic prophylaxis vs. placebo* | | | | |
| Crowley 2001 | Yes | Yes | Yes | Yes |
| Darj 1987 | Yes | Yes | Yes | Yes |
| Heisterberg 1985b | Unclear | Unclear | Yes | Yes |
| Heisterberg 1985c | Yes | Unclear | Yes | Yes |
| Heisterberg 1987 | Yes | Unclear | Yes | Yes |
| Heisterberg 1988 | Yes | Unclear | Yes | Yes |
| Krohn 1981 | Yes | Unclear | Yes | Unclear |
| Krohn 1986 | Yes | Unclear | Yes | No |
| Larsson 1992 | Unclear | Unclear | Yes | No |
| Larsson 2000 | Yes | Unclear | Yes | No |
| Levallois 1988 | Yes | Yes | Yes | No |
| Nielsen, 1993 | Unclear | Unclear | Unclear | No |
| Sonne-Holm 1981 | Unclear | Unclear | Unclear | No |
| Sorensen 1992 | Yes | Yes | Yes | Yes |
| Westrom 1981 | Unclear | Unclear | Yes | Yes |
| *Antibiotic prophylaxis vs. alternative regimen(s)* | | | | |
| Caruso 2008 | Unclear | Unclear | Unclear | Unclear |
| Heisterberg 1986 | Yes | Unclear | Yes | Yes |
| Lichtenberg 2003 | Yes | Yes | Yes | Yes |
| *Screen-and-treat vs. universal antibiotic prophylaxis* | | | | |
| Penney 1998 | Yes | Yes | Yes | No |

**Table 3. Exploration of heterogeneity by study and risk of bias in 15 trials comparing antibiotic prophylaxis vs. placebo**

| Characteristic | No. of trials | Heterogeneity | Risk ratio according to statistical model |
|---|---|---|---|

**Table 3. Exploration of heterogeneity by study and risk of bias in 15 trials comparing antibiotic prophylaxis vs. placebo** *(Continued)*

| | | P value | $I^2$ (%) | Fixed (95% CI)* | Random (95% CI)† | Random (95% PI) ‡ |
|---|---|---|---|---|---|---|
| *Overall* | | | | | | |
| Overall | 15 | 0.06 | 39 | 0.61 (0.52 to 0.73) | 0.59 (0.46 to 0.75) | 0.59 (0.30 to 1.14) |
| *Universal antibiotic prophylaxis* | | | | | | |
| No | 10 | 0.07 | 43 | 0.68 (0.56 to 0.82) | 0.66 (0.49 to 0.87) | 0.65 (0.32 to 1.36) |
| Unclear | 4 | 0.63 | 0 | 0.47 (0.31 to 0.73) | 0.49 (0.32 to 0.75) | 0.49 (0.19 to 1.26) |
| *Antibiotic class* | | | | | | |
| Nitroimidazoles | 6 | 0.57 | 0 | 0.51 (0.35 to 0.73) | 0.53 (0.37 to 0.77) | 0.53 (0.31 to 0.77) |
| Tetracyclines | 4 | 0.003 | 78 | Data not pooled | | |
| Penicillins | 2 | 0.85 | 0 | 0.52 (0.31 to 0.89) | 0.52 (0.31 to 0.89) | - |
| *Antibiotic route* | | | | | | |
| Oral | 12 | 0.04 | 47 | 0.50 (0.49 to 0.71) | 0.54 (0.40 to 0.74) | 0.54 (0.24 to 1.24) |
| *Timing of antibiotics* | | | | | | |
| Preoperative | 4 | 0.18 | 39 | 0.65 (0.46 to 0.90) | 0.61 (0.39 to 0.98) | 0.61 (0.12 to 3.11) |
| Peri-operative | 6 | 0.02 | 62 | 0.58 (0.45 to 0.74) | 0.48 (0.28 to 0.82) | 0.48 (0.10 to 2.33) |
| Pre- and postoperative | 4 | 0.24 | 29 | 0.70 (0.49 to 0.98) | 0.67 (0.43 to 1.06) | 0.67 (0.16 to 2.89) |
| *Antibiotic regimen* | | | | | | |
| Single dose | 6 | 0.45 | 0 | 0.63 (0.50 to 0.80) | 0.64 (0.51 to 0.82) | 0.64 (0.46 to 0.90) |
| Multiple doses, one day | 3 | 0.02 | 73 | 0.26 (0.14 to 0.90) | 0.28 (0.07 to 1.06) | - |
| Multiple doses, several days | 6 | 0.27 | 22 | 0.71 (0.55 to 0.92) | 0.70 (0.52 to 0.96) | 0.70 (0.36 to 1.36) |
| *Control group event rate ¶* | | | | | | |
| < 12% | 7 | 0.01 | 63 | 0.58 (0.45 to 0.75) | 0.54 (0.34 to 0.85) | 0.54 (0.14 to 2.09) |
| ≥ 12% | 8 | 0.45 | 0 | 0.64 (0.51 to 0.80) | 0.66 (0.53 to 0.83) | 0.66 (0.50 to 0.87) |
| *Sequence generation* | | | | | | |
| Adequate | 10 | 0.06 | 45 | 0.53 (0.41 to 0.67) | 0.51 (0.36 to 0.73) | 0.51 (0.30 to 1.32) |
| Inadequate | 5 | 0.29 | 19 | 0.72 (0.57 to 0.91) | 0.71 (0.53 to 0.94) | 0.71 (0.37 to 1.35) |

**Table 3. Exploration of heterogeneity by study and risk of bias in 15 trials comparing antibiotic prophylaxis vs. placebo** *(Continued)*

| | | | | | | |
|---|---|---|---|---|---|---|
| *Concealment of allocation* | | | | | | |
| Adequate | 4 | 0.04 | 64 | 0.42 (0.30 to 0.59) | 0.40 (0.21 to 0.74) | 0.40 (0.03 to 4.96) |
| Inadequate | 11 | 0.39 | 5 | 0.70 (0.58 to 0.85) | 0.71 (0.58 to 0.87) | 0.71 (0.52 to 0.96) |
| *Blinding* | | | | | | |
| Adequate | 13 | 0.05 | 43 | 0.57 (0.47 to 0.70) | 0.55 (0.44 to 0.74) | 0.55 (0.24 to 1.26) |
| Inadequate | 2 | 0.22 | 33 | 0.71 (0.53 to 0.95) | 0.69 (0.46 to 1.02) | - |
| *Incomplete outcome data addressed* | | | | | | |
| Adequate | 8 | 0.25 | 22 | 0.60 (0.47 to 0.78) | 0.60 (0.44 to 0.82) | 0.60 (0.32 to 1.13) |
| Inadequate | 7 | 0.03 | 57 | 0.62 (0.50 to 0.78) | 0.55 (0.37 to 0.78) | 0.55 (0.18 to 1.72) |

* Fixed-effect model, Mantel-Haenszel method;
† Random-effects model, Der Simonian Laird model, confidence interval using Mantel-Haenszel method;
‡ PI, prediction interval is the confidence interval of the approximate predictive distribution of a future trial, bas end on the extent of heterogeneity;
¶ Variable dichotomised at median (12%)

**Table 4. Meta-regression analysis of methodological characteristics**

| Characteristic | No. of trials | Ratio of risk ratios (95% CI)* |
|---|---|---|
| *Random sequence generation* | | |
| Adequate | 10 | 1 |
| Inadequate | 5 | 1.29 (0.74 to 2.25) |
| *Allocation concealment* | | |
| Adequate | 4 | 1 |
| Inadequate | 11 | 1.53 (0.88 to 2.68) |
| *Blinding* | | |
| Adequate | 13 | 1 |
| Inadequate | 2 | 1.18 (0.59 to 2.37) |
| *Incomplete outcome data addressed* | | |
| Adequate | 8 | 1 |
| Inadequate | 7 | 0.98 (0.55 to 1.75) |

* The ratio of risk ratios compares the effect size in trials that reported the feature inadequately with those that are reported adequately. When greater than one, it means that the magnitude of effect was lower in the inadequate trials than the adequate ones.

# APPENDICES

## Appendix 1. Search strategies

We used the following search strategies to identify published studies in the following databases:

PUBMED
(abortion, induced OR pregnancy, trimester, first) AND (antibiotics OR antibiotic prophylaxis OR tetracyclines OR lactams OR macrolides OR nitroimidazoles OR tinidazole OR quinolones OR oxolinic acid OR fluroquinolones)

EMBASE
(induced abortion or first trimester pregnancy) and (antibiotics OR antibiotic prophylaxis OR tetracyclines OR lactams OR macrolides OR nitroimidazoles OR tinidazole OR quinolones OR oxolinic acid OR fluroquinolones)

CENTRAL
abortion AND antibiotics

POPLINE
(abortion induced/pregnancy trimester first) & (antibiotics/"antibiotic prophylaxis"/tetracyclines/lactams/macrolides/ nitroimidazoles/tinidazole/quinolones/"oxolinic acid"/fluroquinolones)

LILACS
abortion antibiotics prophylaxis

# WHAT'S NEW

| Date | Event | Description |
|---|---|---|
| 10 June 2011 | Amended | Review finalised, authors changed |

# HISTORY

Protocol first published: Issue 2, 2005
Review first published: Issue 3, 2012

| Date | Event | Description |
|---|---|---|
| 9 November 2009 | Amended | contact author changed |
| 19 April 2008 | Amended | Converted to new review format. |
| 3 January 2005 | New citation required and major changes | Substantive amendment |

# CONTRIBUTIONS OF AUTHORS

Huib Van Vliet developed the topic idea. Huib van Vliet and Nicola Low edited and advised on the protocol. Nicola Low contributed to designing the literature searches. Nicola Low and Monika Muller extracted and entered data. Nicola Low and Monika Muller did the statistical analysis and drafted the report. Nathalie Kapp contributed to the interpretation of the results and made substantial comments on the report. All authors approved the final version.

## DECLARATIONS OF INTEREST

Nathalie Kapp led the revision of the World Health Organization guidelines for safe abortion care. All other authors declare that they have no conflicts of interest.

## SOURCES OF SUPPORT

### Internal sources

- No financial support, Not specified.

### External sources

- No financial support, Not specified.

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- Review uses the term 'post-abortal upper genital tract infection', protocol uses 'post-abortal pelvic infection'.
- Review distinguishes between interventions that provide 'universal antibiotic prophylaxis' without excluding those with genital infections diagnosed before randomisation and 'antibiotic prophylaxis', which refers to all other interventions in trials that stated that women with specified laboratory or clinical diagnoses would be excluded. The protocol refers to universal antibiotic prophylaxis and gives a definition of the types of antibiotics or strategy, but did not specify that women with genital infections at baseline should not be excluded.

## INDEX TERMS

### Medical Subject Headings (MeSH)

Abortion, Induced [*adverse effects]; Anti-Bacterial Agents [*therapeutic use]; Antibiotic Prophylaxis [*methods]; Pregnancy Trimester, First; Preoperative Care; Randomized Controlled Trials as Topic; Reproductive Tract Infections [*drug therapy]

### MeSH check words

Female; Humans; Pregnancy