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Oduyebo OO, Anorlu RI, Ogunsola FT

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[Intervention Review]

The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

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ABSTRACT

Background

Bacterial vaginosis (BV) is a very common cause of vaginitis that has been associated with a high incidence of obstetric and gynaecologic complications and increased risk of HIV-1 transmission. This has led to renewed research interest in its treatment.

Objectives

To assess the effects of antimicrobial agents on BV in non-pregnant women.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*), MEDLINE, EMBASE, LILACS, and African Healthline (December 2007); and proceedings of relevant international conferences (from 1981 to date).

Selection criteria

Randomised controlled trials comparing any two or more antimicrobial agents, or antimicrobial agents with placebo or no treatment, in women with clinical or Gram-stain criteria of BV.

Data collection and analysis

Two authors independently assessed trial quality and extracted data from the original publications while the third author cross checked the data.

Main results

Twenty-four trials involving 4422 participants were reviewed. Most examined symptomatic women only. Only seven trials analysed results by intention to treat; we re-analysed the remainder.

Compared with placebo, clindamycin showed a lower rate of treatment failure (relative risk (RR) 0.25, 95% confidence interval (CI) 0.16 to 0.37). Clindamycin and metronidazole showed identical rates of treatment failure, irrespective of regimen type, at two and four-week follow up (RR 1.01, 95% CI 0.69 to 1.46; RR 0.91, 95% CI 0.70 to 1.18, respectively). Clindamycin tended to cause a lower rate of adverse events (RR 0.75, 95% CI 0.56 to 1.02); metallic taste, and nausea and vomiting were more common in the metronidazole

group (RR 0.08, 95% CI 0.1 to 0.59; RR 0.23, 95% CI 0.10 to 0.51, respectively). Given intravaginally as gelatin tablets, lactobacillus was more effective than oral metronidazole (RR 0.20, 95% CI 0.05 to 0.08). Similarly, oral lactobacillus combined with metronidazole was more effective than metronidazole alone (RR 0.33, 95% CI 0.14 to 0.77). Clindamycin showed a lower rate of clinical failure than triple sulfonamide cream (RR 0.46, 95% CI 0.29 to 0.72). Hydrogen peroxide douche showed a higher rate of clinical failure (RR 1.75, 95% CI 1.02 to 3.00) and adverse events (RR 2.33, 95% CI 1.21 to 4.52) than a single 2 g dose of metronidazole.

Authors' conclusions

Clindamycin preparations, oral metronidazole, and oral and intravaginal tablets of lactobacillus were effective for bacterial vaginosis. Hydrogen peroxide douche and triple sulphonamide cream were ineffective. Metronidazole caused metallic taste, nausea and vomiting. We need better-designed trials with larger sample sizes to test the effectiveness of promising drugs.

PLAIN LANGUAGE SUMMARY

The effects of antimicrobial treatment on bacterial vaginosis in non-pregnant women

Bacterial vaginosis (BV) is a very common cause of symptomatic and asymptomatic vaginal infection. It has been associated with a high incidence of obstetric and gynaecologic complications and an increased risk of transmission of HIV (human immunodeficiency virus). This review evaluated the effectiveness and adverse effects of antimicrobial agents used to treat BV in non-pregnant women. Twenty-four trials involving 4422 women were reviewed. With regard to less treatment failure, clindamycin was superior to placebo but comparable to metronidazole, irrespective of the dose regimen. Metronidazole tended to cause a higher rate of adverse events, such as metallic taste and nausea and vomiting, than did clindamycin. Oral lactobacillus combined with metronidazole was more effective than metronidazole alone. Administered in an intravaginal gelatin tablet, lactobacillus was also more effective than oral metronidazole. Triple sulfonamide cream was less effective compared with clindamycin. Hydrogen peroxide douche was not as effective as a single 2 g dose of metronidazole yet caused more harms. Only one trial involved asymptomatic women and the result was not conclusive. There was insufficient evidence to reach a conclusion on the effectiveness of other promising drugs. Drugs effective for bacterial vaginosis include clindamycin preparations, oral metronidazole, and oral and intravaginal tablets of lactobacillus. Adverse effects of metronidazole include metallic taste, and nausea and vomiting. Information on possible side effects of lactobacillus preparations is required.

BACKGROUND

Bacterial vaginosis (BV) is the name given to a vaginal disease that manifests as abnormal vaginal flora, sometimes in combination with malodorous discharge. This syndrome has been strongly associated with absence of lactobacilli and the presence of *Gardnerella vaginalis* and some anaerobes. There is still disagreement on the specific roles played by each organism and the exact sequence of events in the vagina that leads to the clinical expression we recognize as BV (Joesoef 1999a).

Lactobacillus species are the most prevalent organisms in the healthy vagina and serve to protect it from being colonised by potentially pathogenic organisms (Eschenbach 1989; Hill 1984). They are able to do this because they produce lactic acid, which maintains an acidic vaginal environment. They also produce hydrogen peroxide which is toxic to other organisms and prevents them from colonizing the vagina (Klebanoff 1991). *Gardnerella vaginalis*, anaerobes, and sometimes *Mycoplasma hominis* and *Mobiluncus* species also colonise the vagina but in small numbers. In BV, there is overgrowth of these other organisms, suppression of lactobacilli, and a rise in pH. The overgrowth of the other bacteria is associated with biochemical changes including increased concentration of diamines, polyamines, organic acids, and enzymes such as mucinases, sialidases, and collagenases in vaginal fluid. These biochemical end products cause a further increase in pH and are responsible for the unpleasant fishy smell of the vaginal discharge present in women with BV. The discharge is more noticeable after unprotected intercourse and is typically thin, greyish, and homogenous. However, the disease is not associated with an obvious inflammatory response so most women tend to be asymptomatic (Hay 1994).

In clinical practice BV is diagnosed using the Amsel criteria. These include a thin greyish homogenous discharge, pH of vaginal fluid > 4.5, release of a fishy odour on adding alkali, and clue cells (bacteria adherent to epithelial cells seen on microscopy). At least three of

the four criteria have to be present for the diagnosis to be confirmed (Amsel 1983). An alternative diagnostic method which is more relevant for asymptomatic women is the use of a Gram-stained vaginal smear with the Nugent or Spiegel score. The vaginal flora are examined and graded as normal (lactobacillus predominant), intermediate, or BV (lactobacillus-deficient mixed flora) (Spiegel 1983; Nugent 1991).

BV is a very common cause of vaginitis in women of childbearing age. It occurs more commonly in sexually active women although infection in those who are not sexually active has been documented (Priestley 1997). Although not regarded as a sexually transmitted infection (STI), BV is associated with sexual intercourse and is commonly studied along with STIs. Prevalence ranges from 17.7% in pregnant women to 40% in commercial sex workers (Dan 2003; Riedner 2003; Tosun 2003). In 2002 in Ibadan, Nigeria, BV was found to be the third most common ailment in commercial sex workers (Bakare 2002). Other studies have shown that 20% to 51% of women in sub-Saharan Africa are infected (Begum 2003; Laurent 2003).

BV is a mild disease but even when asymptomatic it has been associated with a high incidence of endometritis and pelvic inflammatory disease (PID) following abortion and gynaecologic procedures (Larsson 1992; Soper 1993). Many studies have shown a strong association between BV and obstetric complications such as late miscarriages, premature rupture of the membranes, and preterm birth (Guaschino 2003; Leitich 2003).

The emergence of the HIV pandemic and the recognition that ulcerative and non-ulcerative genital diseases interact and reinforce each other has made the control of such diseases more important than ever. Both symptomatic and asymptomatic BV have been strongly associated with an increased risk of HIV-1 transmission (Martin 1999). Since treatment could help to restore normal vaginal flora, identification and treatment of every case could reduce susceptibility of women to HIV-1 infection.

Antibiotic therapy is the mainstay of management of BV. Antimicrobials are directed at altering the abnormal flora by killing some of the organisms vital to the maintenance of BV. Treatment is then generally followed by a reversion to more typical, normal flora. This change is accompanied by the disappearance of signs and symptoms characteristic of BV.

Antibiotics traditionally used to treat BV include the 5-nitro-imidazoles like metronidazole, tinidazole, and more recently secnidazole, which are available as tablets or gel in single or multiple doses. They inhibit anaerobes that support *Gardnerella vaginalis* but do not affect lactobacilli, thereby reducing the risk of late-stage relapse (Hillier 1993; Joesoef 1995; Joesoef 1999b; Baylson 2004). They are associated with mild gastro-intestinal side effects such as nausea and vomiting. Other side effects include metallic taste and, less commonly, hypersensitivity reactions (Bhaduri 1997).

Clindamycin, which is a lincosamide, is considered to be an effective alternative drug to the 5-nitro-imidazoles. It is available as tablets, cream or gel and side effects include diarrhea and pseudomembranous colitis (Trexler 1997).

All these antibiotics have been shown to achieve cure rates of 70% to 80% after four weeks of treatment in controlled trials (Lugo-Miro 1992; Hillier 1999). Recently, there has been renewed research interest in BV and efforts to identify more effective treatment have resulted in clinical trials of other antimicrobial agents that were not previously used, such as ciprofloxaxin, erythromycin, ornidazole (a nitro-imidazole), lactic acid, and hydrogen peroxide administered alone and in combinations. It has thus become necessary to investigate their effectiveness and safety in a systematic review (Covino 1993; Saracoglu 1998; Andreeva 2002; Chaithong 2003; Milani 2003; Wilson 2005).

OBJECTIVES

To assess the effects of antimicrobial agents on bacterial vaginosis in non-pregnant women.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials.

Types of participants

Women with clinical (Amsel 1983) or Gram-stain criteria of BV (Spiegel 1983; Nugent 1991) in whom other causes of vaginal discharge have been excluded.
Excluded: pregnant women; a Cochrane review of antibiotics in pregnant women has been published (McDonald 2005).

Types of interventions

Any antimicrobial agent (antibiotics, vaginal acidifying preparations or devices, pre- and probiotics in any dosage or regimen using any route of administration) compared with placebo or no treatment.
Comparison of any two or more antimicrobial regimens.

Types of outcome measures

Primary

Treatment failure

Defined as at least three Amsel criteria, at: seven days after treatment, one to two-month follow up (relapse), or any other follow-up period in symptomatic women.

Abnormal vaginal flora consistent with BV as defined by Gram-stain scores (for example Nugent score 7 to 10) in asymptomatic women seven days after treatment or at one to two-month follow up.

Secondary

Adverse events

Known adverse effects such as metallic taste, nausea, vomiting, diarrhea, hypersensitivity, and pseudomembranous colitis.

Any unknown adverse events that the participant or clinician considered to be serious.

Any event leading to discontinuation of therapy.

Search methods for identification of studies

We attempted to identify all relevant trials regardless of language or publication status (published, unpublished, in press, and in progress). Specialised guidance on comprehensive searches was provided by the South African Cochrane Centre in Capetown.

Databases

Using search terms for "Bacterial vaginosis" and "antimicrobial agents" the following databases were searched (1981 to December 2007).

- Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2007, Issue 4)
- MEDLINE
- EMBASE
- LILACS
- Africa Healthline

The full search strategy is listed in Table 1.

Conference proceedings

We searched all the available proceedings of the following international conferences (from 1981 to date):

- International conference of AIDS and STDs in Africa;
- Biennial meeting of the International Society of Sexually Transmitted Diseases and Research;
- Microbicides conferences (2004 and 2006).

Researchers, organizations and pharmaceutical companies

We contacted organizations and individual researchers working in the field for unpublished and ongoing trials but none were reported. We contacted pharmaceutical companies producing the various antimicrobial agents for on-going trials. Only Pfizer answered and indicated they were not conducting any trials. Such companies (and the antimicrobial agent) included:

- Aventis (metronidazole);
- Trichem (clindamycin);
- Pharmacia Canada (clindamycin)
- Pfizer (tinidazole);
- Mission Pharmacal (tinidazole).

Reference lists

We also reviewed the reference lists of all studies identified by the above methods.

Data collection and analysis

Study selection

The abstracts obtained were evaluated using the selection criteria described above to identify all potentially relevant studies. This was done independently by the three authors (OO, RA, FT). Using a form based on the inclusion criteria, full articles of the studies found relevant were assessed for eligibility. Disagreements were handled by discussion to reach consensus and, when necessary, consulting the review mentor. Translations were obtained as applicable and multiple publications from the same data set were only used once.

Assessment of methodological quality

Methodological quality of the included trials was assessed according to generation of allocation sequence, allocation concealment, blinding, and loss to follow up. We used the following criteria and assessments.

1. Generation of allocation sequence: adequate (if the method used was described and the resulting sequences were unpredictable), unclear (if the method was not described), inadequate (sequences could be related to prognosis such as alternative allocation), or not done.

2. Allocation concealment: adequate (if participants and investigators enrolling participants could not foresee assignment), unclear (if method was not described), inadequate (if participants and investigators could foresee upcoming assignment), or not done.

3. Blinding of participant, caregivers, and outcome assessors: yes, no, or not stated.

4. Intention-to-treat analysis: yes (if all participants randomised were included in the final analysis), or no (if some were not).

Data extraction

We extracted data on a self-developed standardised form, which was piloted by OO. The information that was extracted included general information on the trials; details on inclusion and exclusion criteria; methods of randomisation, allocation concealment; and blinding; length of follow up; loss to follow up; treatment benefits and harms. Where possible, data were extracted to allow an intention-to-treat analysis (we sought data on every participant with each outcome by allocated treatment group irrespective of adherence to treatment or length of follow up). We had only categorical outcomes and so recorded the total number of particpants and those experiencing the event in each group. Authors were contacted for missing data, incomplete data, or unclear information. OO and RA independently extracted data from the original publications while FO cross checked the data. Differences of opinion were resolved by consensus. OO entered the extracted data into RevMan4. She used double data entry.

Data analysis

Studies were stratified in subcategories according to type of antibiotic and comparison groups (other antibiotic, placebo, or no treatment). We looked at the relative effects of treatment by calculating the risk ratios (RR) with 95% confidence intervals (CI). For statistically significant results, we determined the absolute effect of treatment by calculating absolute risk reduction (RD) and number needed to treat (NNT).

We performed meta-analyses for studies that could be combined, using Review Manager 4.2.8 software. Data were pooled using the random-effects model. Heterogeneity was assessed by Cochrane Q test (with 90% CI) and the I^2 statistic. Significant heterogeneity was indicated by $P < 0.1$ and $I^2 > 70\%$. We had intended to explore significant heterogeneity in subgroup analyses but could not because of insufficient data. Subgroups planned were clinical versus bacteriological failures, low-income versus high-income countries, oral versus topical (gel, cream, solution) regimens, and poor versus good-quality studies. We were to perform sensitivity analyses to explore the robustness of findings and quality issues, but most comparisons included only one trial.

RESULTS

Description of studies

Trial selection

Results of the search

The search identified 701 references out of which 53 were considered eligible after initial screening (Appendix 1). One ongoing study (Wilson 2005) was identified from a conference proceeding. An attempt was made to contact the author but there was no response.

Included studies

Out of the 53 studies retrieved, 24 trials involving 4422 participants were included in the review (see table 'Characteristics of included studies'). Nine of them, especially the large ones, were funded by pharmaceutical companies. One was funded by a university research fund and one by a national government fund. Sources of funding were not reported in the remaining trials. The trials were of varying size, ranging from a clinic-based study involving 22 women to large multicentre trials involving 23 countries. The trials were carried out in many parts of the world including the United States of America, Germany, Sweden, Italy, Venezuela, Thailand, Belgium, United Kingdom, Nigeria, and Austria.

Excluded studies

A total of 29 studies were excluded (see table 'Characteristics of excluded studies') for various reasons including:

- not a randomised controlled trial (10 trials);
- BV not diagnosed by Amsel's or Gram-stain criteria (14 trials);
- particpants with STDs not excluded before randomisation (two trials);
- randomisation not to drug but to sexual partner (two trials);
- duplicate publications (one trial).

Interventions

Various preparations (gel, ovule, cream, tablet, douche) of antimicrobials, acid buffer, and probiotics were studied. Six studies compared clindamycin (topical in four, oral in two) preparations with oral metronidazole (Greaves 1988; Andres 1992; Schmitt 1992; Fischbach 1993; Paavonen 2000; Beigi 2004). Different concentrations and preparations of clindamycin were compared in two studies (Livengood 1990; Sobel 2001). Clindamycin cream was also compared with: triple sulfonamide (McCormack 2001), tinidazole and metronidazole in combination with acid buffering gel (Milani 2003), and lactobacillus (Eriksson 2005; Anukam 2006a; Anukam 2006b). Various preparations and regimens of metronidazole, alone and in combination (Voorspoels 2002; Schwebke 2006); and secnidazole (Nunez 2005) were studied. Three studies looked at single-dose regimens (Voorspoels 2002; Chaithong 2003; Nunez 2005).

Participants and outcomes

Inclusion of participants was based on the study inclusion and exclusion criteria. Twenty-three of the 24 included trials looked at symptomatic women only. The women studied were between 15 and 75 years of age.

The trials measured a wide variety of well-defined outcomes. All except one (Schwebke 2000) measured treatment failure and side effects. These were measured at one follow-up visit only in eight trials (Greaves 1988; Burana 1990; Livengood 1990; Voorspoels 2002; Chaithong 2003; Gerli 2003; Eriksson 2005; Nunez 2005) and at two follow-up visits in 16 trials. Both Amsel and Gram-stain criteria were possible for BV diagnosis. Thirteen trials used Amsel criteria both at baseline and follow up (Piot 1983; Greaves 1988; Wathne 1989; Burana 1990; Schinder 1991; Paavonen 2000; Sobel 2001; Voorspoels 2002; Chaithong 2003; Gerli 2003; Milani 2003; Eriksson 2005; Nunez 2005); in 11 trials both methods were used for diagnosis at baseline; in the remainder only Amsel criteria were used to define outcomes at follow up. Only one trial (Eriksson 2005) used both Amsel and Gram-stain criteria to define treatment failure.

Risk of bias in included studies

The description of the interventions used in the studies was good and the outcomes were well described.

Randomisation

Nine trials reported adequate methods of randomisation: seven used computer-generated random numbers (Andres 1992; Fischbach 1993; Schwebke 2000; Chaithong 2003; Milani 2003; Beigi 2004; Anukam 2006a), one used a table of random numbers (Nunez 2005), and one used block randomisation (Schwebke 2006). An inadequate method, a random list, was used in one trial (Sobel 2001). The method was unclear in the remaining trials.

Allocation concealment

Out of the nine trials which used adequate randomisation methods, allocation concealment was adequate in only six. Two such studies gave sequentially numbered medication tubes and drug packets to participants (Fischbach 1993; Nunez 2005; Anukam 2006a). Two trials concealed allocation by a centralised phone-call procedure (Milani 2003; Schwebke 2006). The name of the drug was written on a paper and presented to investigators in a sealed envelope at enrollment in another study (Beigi 2004). Although the randomisation method was unclear in one study, allocation was concealed by use of numbered tubes containing 50 g of vaginal cream supplied in sequence to participants as they entered the study (Livengood 1990).

Blinding

Most of the trials were blinded. The participants, investigators, and outcome assessors were blinded in two trials (Livengood 1990; Chaithong 2003). Investigators and participants were blinded in 12 trials (Piot 1983; Greaves 1988; Andres 1992; Schmitt 1992; Fischbach 1993; Stein 1993; Schwebke 2000; McCormack 2001; Paavonen 2000; Voorspoels 2002; Eriksson 2005; Nunez 2005), while investigators only were blinded in four trials (Wathne 1989; Sobel 2001; Milani 2003; Wilson 2005a). Only outcome assessors were blinded in one trial (Gerli 2003). Four studies were not blinded (Burana 1990; Schinder 1991; Beigi 2004; Anukam 2006b).

Exclusions

Only seven of the trials analysed results by intention to treat (Wathne 1989; Fischbach 1993; Paavonen 2000; Sobel 2001; Chaithong 2003; Gerli 2003; Milani 2003). Three of the remaining trials had less than 10% exclusions from analysis, leaving 13 trials with exclusion rates between 20% and 42%. Two studies applied exclusion criteria after participants had been randomised (Andres 1992; Sanchez 2004). In four studies rates of exclusion of randomised participants from analysis, including loss to follow up, were similar in the two study arms (Greaves 1988; Fischbach 1993; McCormack 2001; Eriksson 2005). In the other studies the details were not available for comparison.

Effects of interventions

Metronidazole versus placebo

There were two trials that compared topical metronidazole with placebo gel (Schwebke 2000; Voorspoels 2002). The Schwebke trial compared 0.75% metronidazole gel applied intravaginally at bedtime for five days with placebo. The Voorspoel study had four intervention arms with various concentrations of single-dose bioadhesive tape metronidazole (100 mg, 250 mg, and 500 mg) and a placebo. In order to include the three treatment arms in the meta-analysis, the number of participants in the placebo group was divided into three (Ramsay 2003). Metronidazole showed a lower failure rate compared with placebo. The combined RR was 0.58 (95% CI 0.44 to 0.78) with no heterogeneity (Comparison 01-01). Only the Schwebke trial had results for the second follow-up visit and metronidazole showed no effect at four weeks (Comparison 01-02: RR 0.68, 95% CI 0.44 to 1.07). In terms of adverse effects, Comparison 01 03 showed a higher rate of candida infection in the metronidazole group although this was not significant (RR 13.34, 95% CI 0.78 to 228.71).

Clindamycin versus placebo

Clindamycin cream was compared with placebo in two trials (Livengood 1990; Stein 1993). The Livengood trial had four intervention arms. In the three treatment arms 0.1%, 1%, or 2% clindamycin was applied intravaginally twice daily for five days. The participants in the placebo arm were divided into three for analysis (Ramsay 2003). The clindamycin regimen used in the Stein trial was 2% cream applied intravaginally at bedtime for seven days.

Clindamycin cream showed a benefit with lower treatment failure compared to placebo. The combined RR was 0.25 (95% CI 0.16 to 0.37) with no heterogeneity (Comparison 02-01) while the combined RD was -0.46 (95% CI -0.65 to -0.28). In the Stein trial, clindamycin use was associated with a lower clinical failure rate (Comparison 02-02: RR 0.39, 95% CI 0.22 to 0.68) and a lower bacteriologic failure rate (RR 0.48, 95%CI 0.33 to 0.72) at the second follow-up visit; an NNT of 6 and 7, respectively, were calculated from the RD of -0.18 (95% CI -0.29 to -0.08) for clinical failure at first follow up, and RD of -0.14 (95% CI -0.2 to -0.03) for bacteriologic failure at the second follow-up visit.

Clindamycin versus metronidazole

Six trials (Greaves 1988; Andres 1992; Schmitt 1992; Fischbach 1993; Paavonen 2000; Beigi 2004) compared clindamycin with metronidazole. In three trials, 2% clindamycin cream 5 g at bedtime for seven days was compared with oral metronidazole 500 mg twice daily for seven days (Andres 1992; Schmitt 1992; Fischbach 1993). The Paavonen trial compared clindamycin ovule 100 mg daily for three days with oral metronidazole 500 mg twice daily for seven days. The Beigi trial compared clindamycin ovule 100 mg daily for three days with 0.75% metronidazole gel 5 g daily for five days, while the Greaves trial compared oral clindamycin 500 mg twice daily for seven days with oral metronidazole 500 mg twice daily for seven days.

Comparisons 03-01 and 03-02 for clinical failure at the first (RR 1.01, 95% CI 0.69 to 1.46) and second (RR 0.91, 95% CI 0.70 to 1.18) follow-up visit showed identical effects of clindamycin and metronidazole irrespective of regimen type, with no heterogeneity. Bacteriologic failure was an outcome measure only in the Fischbach trial. A lower rate favoured clindamycin but this effect was significant only at the second follow up (Comparison 03-03: RR 0.60, 95% CI 0.24 to1.53; Comparison 03-04: RR 0.45, 95% CI 0.23 to 0.89). Relapse rates in the Schmitt trial were comparable (Comparison 3-12: RR 1, 95% CI 0.44 to 2.27).

In four of the trials in which topical clindamycin was compared to oral metronidazole, clindamycin tended to cause a lower rate of adverse events (Comparison 03-06: RR 0.75, 95% CI 0.56 to 1.02). Analysed further the adverse effects metallic taste, and nausea and vomiting were more common in the metronidazole groups (Comparison 03-07: RR 0.08, 95% CI 0.1 to 0.59; Comparison 03-08: RR 0.23, 95% CI 0.10 to 0.51). In Comparisons 03-05, 03-06, and 03-09, rates of other reported side effects were identical (RR 1.62, CI 0.35 to 7.43; RR 1.12, 95% CI 0.79 to 1.58; RR 1.70, 95% CI 0.50 to 5.73, respectively).

Tinidazole versus metronidazole

A singe oral dose of 2 g tinidazole was compared with 500 mg metronidazole administered twice daily for seven days (Burana 1990) and one vaginal tablet of 400 mg metronidazole twice daily on five consecutive days (Schinder 1991). While tinidazole appeared to be more effective in the Schinder trial (RR 0.17, 95% CI 0.02 to 1.35) it appeared less effective in the Burana trial (Comparison 04-01: RR 1.75, 95% CI 0.55 to 5.61), although neither finding was significant. Findings were similar for overall adverse events (Comparison 04-02: RR 0.36, 95% CI 0.12 to 1.07; RR 2.05, 95% CI 0.19 to 21.70) and for nausea and vomiting, respectively (Comparison 04-03: RR 0.38, 95% CI 0.11 to1.33; RR 1.03, 95% CI 0.07 to 5.82).

Clindamycin ovule versus clindamycin cream

Clindamycin vaginal ovules 100 mg daily for three days were compared with 2% clindamycin vaginal cream 5 g at bedtime for seven days (Sobel 2001). As shown in Comparisons 05-01 and 05-02, at both follow-up visits the rates of clinical failure were identical in both groups. The rates of adverse effects in general, discontinuation, and candida infection were also identical (Comparisons 05-03, 05-04, 05-05).

Vaginal lactobacilli tampons versus placebo

Lactobacilli tampons were compared with placebo adjunctive therapy after an open treatment with clindamycin ovule 100 mg daily for three days (Eriksson 2005). There was no difference in the rates of cure at first (Comparison 06-01: RR 0.90, 95% CI 0.71 to 1.14) or second (Comparison 06-02: RR 0.85, 95% CI 0.67 to 1.08) follow up; nor in adverse effects like candidiasis (Comparison 06-03: RR 1.70, 95% CI 0.58 to1.98), and itching or burning (Comparison 06-04: RR 0.50, 95% CI 0.16 to1.63).

Lactobacilli versus metronidazole

One trial compared two gelatin capsules of lactobacillus species (spp) (containing 10^9 organisms) inserted vaginally for five nights with metronidazole 500 mg given orally twice daily for five days (Anukam 2006b). Clinical failure rates were identical at two weeks (Comparison 14-01) but lower in the lactobacillus group at four-weeks follow up (Comparison 14-02: RR 0.27, 95% CI 0.09 to 0.83; RD -0.40, 95% CI -0.67 to -0.13, NNT 3). There was a similar trend for bacteriologic failure (Comparison 14-03: RR 0.20, 95% CI 0.05 to 0.08; RD -0.40, 95% CI -0.66 to -0.14, NNT 3).

In another trial, oral metronidazole 500 mg twice daily for seven days was compared with the same regimen of metronidazole combined with oral lactobacillus (containing 10^9 organisms) given twice daily for 30 days (Anukam 2006a). Comparison 14-03 showed a lower rate of bacteriological failure in the lactobacillus plus metronidazole group (Comparison 14-03: RR 0.33, 95% CI 0.14 to 0.77). Meta-analysis of this trial with Anukam 2006b, which compared lactobacillus intravaginal gelatin capsule with oral metronidazole, showed a lower combined bacteriological failure rate for lactobacillus therapy (Comparison 14-03: RR 0.28, 95% CI 0.14 to 0.59; RD -0.27, 95% CI -0.46 to -0.07, NNT 4). There was no difference in the rates of adverse effects like headache and overeating (Comparison 14-06: RR 6.4, 95% CI 0.34 to 122.71) although the discontinuation rate from the study was higher in

the oral lactobacillus group (Comparison 14-05: RR 4.92, 95% CI 1.51 to 16.06).

Oral tinidazole combined with an acid gel versus clindamycin

In the Milani trial (Milani 2003), the effects of oral 2g single dose of tinidazole in addition to an acid buffering gel were compared with 2% clindamycin cream for seven days. One week after therapy, the women in the tinidazole group were treated with the acid gel 2 g every three days for an additional three weeks. Tinidazole was found to be comparable with clindamycin after one week of treatment (Comparison 08-01: RR 1.0, 95% CI 0.32 to 3.12). At the second follow-up visit, there appeared to be a lower failure rate in the clindamycin group although this effect was not significant (Comparison 08-02: RR 0.29, 95% CI 0.06 to 1.27). Relapse rates were also comparable (Comparison 08-05: RR 0.33, 95% CI 0.04 to 3.01).

Clindamycin cream versus triple sulfonamide cream

A 2% clindamycin cream at bedtime for seven days was compared with triple sulfonamide cream at bedtime for seven days (McCormack 2001). The comparison showed a lower clinical failure rate in the clindamycin group at first follow up, though this effect was not significant (Comparison 09-01: RR 0.61, 95% CI 0.34 to 1.09). However, a lower clinical failure rate at second follow up (Comparison 09-02: RR 0.36, 95% CI 0.23 to 0.59; RD -0.55, 95% CI -0.50 to -0.21, NNT 2) and lower bacteriologic failure rates at first (Comparison 09-03: RR 0.37, 95% CI 0.18 to 0.75; RD -0.19, 95% CI -0.32 to -0.07, NNT 5) and second (Comparison 09-04: RR 0.46, 95% CI 0.29 to 0.72; RD -0.28, 95% CI -0.42 to -0.13, NNT 4) follow ups were seen with clindamycin cream. The rate of discontinuation from the trial was comparable in both groups (Comparison 09-13: RR 3.11, 95% CI 0.13 to 75.68).

Polyhexamethylene biguanide (PHMB) douche compared with clindamycin cream

A single dose of polyhexamethylene biguanide douche was compared with 2% clindamycin cream for seven days (Gerli 2003). The rates of clinical failure were identical (Comparison 10-01: RR 1.03, 95% CI 0.37 to 2.86). The PMHB group had a higher rate of adverse effects (Comparison 01-02: RR 0.13, 95% CI 0.02 to 0.96) though the higher rates of individual adverse event like candidiasis (Comparison 10-03: RR 0.15, 95% CI 0.02 to 1.18) and discontinuation of treatment (Comparison 10-04: RR 0.15, 95% CI 0.02 to 1.18) were not significant.

Single hydrogen peroxide douche versus single-dose oral metronidazole

A 20 ml douche of 3% hydrogen peroxide as a single dose was compared with a 2 g single dose of oral metronidazole (Chaithong 2003). The rate of clinical failure was higher in the hydrogen peroxide group than the metronidazole group (Comparison 11-01: RR 1.75, 95% CI 1.02 to 3.00). The rate of reduced eating and vomiting was lower (Comparison 11-02: RR 0.29, 95% CI 0.15 to 0.8) but the rate of vaginal irritation was higher (Comparison 11-03: RR 2.33, 95% CI 1.21 to 4.52) in the hydrogen peroxide group. An NNH of 5 was calculated from an RD of 0.19 (95% CI 0.05 to 0.33).

Cefadroxil versus metronidazole

Oral cefadroxil 500 mg twice a day for seven days was compared to oral metronidazole 400 mg twice a day for seven days (Wathne 1989). Cefadroxil was comparable to metronidazole in clinical failure rates at both follow-up visits (Comparisons 12-01, 12-02). Candida infection rates were also comparable (Comparison 12-03: RR 1.00, 95% CI 0.17 to 5.89).

Secnidazole 1 g versus 2 g

A 1 g dose of secnidazole was compared with 2 g, both in a single-dose oral regimen (Nunez 2005). Both were comparable in clinical failure rate (Comparison 13 01: RR 5.13, 95% CI 0.27 to 96.0) and rate of adverse events (Comparison 13-02: RR 1.00, 95% CI 0.17 to 5.89).

Seven-day versus 14-day regimen of metronidazole with or without azithromycin

In the Schwebke trial, which had four arms, 750 mg oral metronidazole for seven days was compared with the same dose for 14 days, with or without 1g oral azithromycin on days one and three (Schwebke 2006). In order to compare the three arms with the recommended seven-day regimen (control group) in a meta-analysis, the number of participants in the control group was divided into three. The 14-day regimen of metronidazole combined with azithromycin showed a lower failure rate than the seven-day regimen without azithromycin at two weeks (Comparison 15-01: RR 0.49, CI 0.6 to 0.93), which was not sustained at four-weeks follow up. The 14-day regimen without azithromycin and the seven-day regimen with azithromycin had equivalent clinical failure and adverse effect rates with the seven-day regimen without azithromycin, at both follow-up visits (Comparisons 15-01,15-02, 15-03, 15-04, 15-05).

DISCUSSION

This review shows that clindamycin cream was more effective than placebo for eradicating symptoms of bacterial vaginosis. Meta-

analysis of six trials also showed that clindamycin and metronidazole have equivalent effectiveness for eradication of symptoms of BV, achieving clinical cure in 91% and 91.9 % of cases after two to three weeks and 84.8% and 84.3% of cases after four weeks of treatment, respectively. The six trials compared various regimens of both topical and oral preparations of the antibiotics and individually showed a tendency for equivalent effectiveness, which meta-analysis confirmed. Clindamycin tablets, ovules, cream, and oral metronidazole were effective (Greaves 1988; Livengood 1990; Andres 1992; Schmitt 1992; Fischbach 1993; Stein 1993; Paavonen 2000; Beigi 2004). Evidence for the effectiveness of metronidazole gel must be sought in future studies. The administration of metronidazole bioadhesive tape was studied in only one trial which investigated asymptomatic women and was reported to be ineffective (Voorspoels 2002).

Topical preparations are available for both clindamycin and metronidazole and would be especially useful in pregnancy and other situations in which such preparations are preferred. They are, however, more expensive than oral preparations and are not likely to be available in developing countries.

The disadvantage of oral regimens is the long duration of treatment, five to seven days, which may not be complied with especially by women who are asymptomatic. A systematic review compared single with multiple-dose regimens of metronidazole and found them to have equivalent effectiveness (Lugo-Miro 1992). None of the nine trials in the Lugo-Miro review were eligible for this review because the standardised methods of BV diagnosis, a criterion for eligibility in this review, were not used. Such trials which examine the clinical effectiveness of single-dose metronidazole are urgently needed, especially from developing countries where costs as well as compliance to long-duration regimens are a problem.

While both clindamycin and metronidazole were equivalent in resolving signs and symptoms of BV, clindamycin was shown in one trial to be more effective than metronidazole for bacteriological cure, although the evidence was not very strong (Fischbach 1993). A higher bacteriologic failure rate of metronidazole would be of concern because it is the more affordable option for developing countries.

Unfortunately only the Fischbach trial reported bacteriologic failure as an outcome. Though the trial was characterized by a large sample size, there was a high rate of exclusions from analysis. Intention-to-treat analysis in this review served to eliminate attrition bias; nevertheless we need to have good quality trials reporting bacteriologic failure so that the implication of this finding can be more meaningful. Furthermore, the higher bacteriologic failure was evident only at four weeks and not at two-weeks follow up, so it is not quite clear whether this outcome would actually mean failed therapy or relapse, especially since relapse was not reported as defined by this review. The only trial that reported relapse found high but equivalent rates with both antibiotics (Schmitt 1992).

Metronidazole is the cheaper, more available, and widely used option in developing countries but causes more adverse effects than clindamycin, in particular a metallic taste and gastro-intestinal symptoms (Greaves 1988; Schmitt 1992; Fischbach 1993). One trial showed that metronidazole did not cause more candidiasis than placebo (Schwebke 2000). Also, the occurrence of post-antibiotic candidiasis was found to be equivalent for both drugs (Schmitt 1992; Fischbach 1993; Paavonen 2000; Beigi 2004).

Oral metronidazole and topical clindamycin are not 100% effective and have high relapse rates, so it is clear that we need other agents that can increase their effectiveness or provide good alternatives. Lactobacillus probiotic given orally for 30 days to augment oral metronidazole proved to be more effective for clinical and bacteriologic eradication of BV compared with metronidazole alone (Anukam 2006a). When given intravaginally for five days as a gelatin tablet it was as effective as oral metronidazole administered for five days; but at four weeks lactobacillus gelatin tablets were more effective than oral metronidazole (Anukam 2006b). Adding lactobacillus to clindamycin ovules did not improve effectiveness but this was investigated in only one trial (Eriksson 2005).

The use of lactobacillus probiotic was not associated with adverse effects in any of the trials. In one of the two relevant trials some women reported headache and increased rate of eating, but there is no evidence that these were associated with the probiotic. However, the significantly higher rate of discontinuation from the lactobacillus group probably implies unreported but significantly higher rates of adverse effects attributable to the probiotic (Anukam 2006a). Emphasis should, therefore, be laid on identifying side effects in future studies.

Oral tinidazole appears to be an effective drug for BV and is equivalent in effectiveness to clindamycin (Milani 2003). Unfortunately only one trial with a small sample size of 32 participants provided this evidence. Moreover, the two trials that compared it with metronidazole gave opposite but insignificant results. The trials could not be combined because of significant heterogeneity (Burana 1990; Schinder 1991). More trials should investigate the effectiveness and adverse effects of tinidazole as the single-dose regimen makes it attractive for use.

While there is good clinical and bacteriologic evidence that triple sulphonamide cream (McCormack 2001) and hydrogen peroxide douche (Chaithong 2003) are not as effective as clindamycin, polyhexamethylene biguanide douche shows promise as there is good evidence of equivalent effectiveness with clindamycin, but in only one small trial which also found reduced side effects compared with clindamycin (Gerli 2003). In case of cefadroxil versus metronidazole, the small sample size did not permit a clear effect to be found (Wathne 1989).

A 1 g dose of secnidazole compared with 2 g secnidazole showed equivalent effectiveness in one trial but there is a need to compare

this drug with either metronidazole or clindamycin, which are the current gold standards in a large population.

AUTHORS' CONCLUSIONS

Implications for practice

This review found clindamycin in cream, ovules, and tablets and oral metronidazole to be effective for eradicating symptoms of bacterial vaginosis. It also found that lactobacillus probiotic given orally for 30 days augments the therapeutic effects of metronidazole, and when given intravaginally as gelatin tablet twice daily for five days is more effective than metronidazole gel.

Metronidazole causes adverse effects like nausea and metallic taste. There is no evidence that either of the two antibiotics cause vaginal candidiasis if given for seven days, or that clindamycin causes diarrhoea if given for five days.

There is no advantage in increasing the duration of metronidazole therapy beyond seven days. With the two antibiotics, attention must be paid to the possibility of relapse or clinical failure, apparent at four-weeks follow up

Hydrogen peroxide douche and triple sulphonamide therapy are not effective for treatment of bacterial vaginosis.

Implications for research

There is a need for trials in asymptomatic women as the only trial in this review revealed lack of effectiveness of metronidazole gel, suggesting either the need to determine the effectiveness of metronidazole gel for BV or possible challenges of treatment in asymptomatic BV.

Larger, better-designed trials should investigate the effectiveness of topical metronidazole therapy and other promising drugs. There is an urgent need to study single-dose regimens of metronidazole, tinidazole and secnidazole, as well as relapse rates. Studies of adverse events associated with lactobacillus probiotic therapy are also needed.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Andres 1992

Methods	Random allocation: computer-generated list Allocation concealment: not mentioned Some exclusion criteria were applied after randomisation Blinding: investigators, participants Loss to follow up: 2 Analysis: no ITT
Participants	60 women aged 18 to 60 years were randomised, 14 were excluded from analysis Inclusion criteria: Amsel criteria, Gram-stain criteria Exclusion criteria: pregnancy, breastfeeding, allergy to clindamycin or metronidazole, antimicrobials within the previous 2 weeks, antibiotic asociated colitis, diarrhea, presence of STDs, menstrual bleeding
Interventions	1. 2% Clindamycin 5g intravaginally at bedtime for 7 days 2. Oral metronidazole 500mg twice daily for 7 days
Outcomes	Primary: cure, clinically improved, and clinical failure 5-8 days and 4 weeks after treatment completion defined as follows - Clinical cure if no evidence of bacterial vaginosis on examination - Cllinically improved if the vaginal secretions were not entirely normal as regards odour - Clinical failure if bacterial vaginosis did not clear at first or second follow up Secondary: side effects Clinical cure and clinically improved are not assessed in the review
Notes	Informed consent: written Ethical approval: no statement Study location: no report Study setting Study duration: no report Funding

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Anukam 2006a

Methods	Random allocation: computer-generated list Allocation concealment: identical looking probiotic and placebo capsules prepared and distributed in numbered containers by the pharmacy Blinding: investigators, participants Loss to follow up: 19 Analysis: no ITT
Participants	125 women out of the 500 screened, aged 18 to 44 years, were randomised; 19 were excluded from analysis Inclusion criteria: symptomatic women Nugent score 7-10, positive sialidase test Exclusion criteria: pregnancy; breastfeeding; allergy to metronidazole, warfarin, lithium or disulfiram; antimicrobials within the previous 2 weeks; presence of STDs and HIV; menstrual bleeding
Interventions	1. Oral metronidazole 500mg twice daily for 7 days 2. Oral metronidazole 500mg twice daily for 7 days + oral lactobacillus GR -1 and RC -14 twice daily for 30 days
Outcomes	Primary: cure defined as normal Nugent score, absence of clue cells, negative sialidase tests, and no symptoms and treatment failure defined as BV 7-10 or positive sialidase test Secondary: side effects
Notes	Informed consent: no statement Ethical approval: obtained from the local university Study location: Benin city, Nigeria Study setting: community clinics Study duration: 6 months Funding: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Anukam 2006b

Methods	Random allocation: method unclear Blinding: no Loss to follow up: 5 Analysis: no ITT
Participants	40 out of the 350 premenopausal women screened were randomised Inclusion criteria: symptomatic women Nugent score 7-10, positive sialidase test Exclusion criteria: pregnancy, presence of STDs and HIV, menstrual bleeding, younger than 18 and older than 50 years

Anukam 2006b (*Continued*)

Interventions	1. Gelatin capsules containing (10^9 organisms) lactobacillus rhamnosus GR -1 and L reuteri RC -14: 2 capsules inserted vaginally at night for 5 days 2. 0.75% Metronidazole vaginal gel twice daily for 5 days
Outcomes	Symptoms failure Bacteriologic failure: Nugent score 7-10 or positive sialidase test
Notes	Informed consent: no statement Ethical approval: University of Benin Study location: Benin city, Nigeria Study setting: community clinics Study duration: not stated Funding: none

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Beigi 2004

Methods	Random allocattion: permuted block design with a block size of 8 Allocation concealment: name of drug printed on a piece of paper, sealed in an envelop and opened by the investigator at enrolment Blinding: no Loss to follow up: 4 Analysis: no ITT
Participants	119 women were randomised, 4 were excluded from analysis Inclusion criteria: 3 or 4 Amsel criteria and a Gram-stain score of 4 or more Exclusion criteria: pregnancy, hypersensitivity tometronidazole or clindamycin, currently menstruating, on IUCD, antibiotics in the previous 7 days, pesence of STDs
Interventions	1. Clindamycin intravaginal ovules daily for 3 days 2. Metronidazole intravaginal (metrogel) daily for 5 days
Outcomes	- Clinical failure defined as persistence of 2 or more Amsel criteria for BV - Clinical success defined as having less than 2 of Amsel criteria - Antimicrobial resistance (not assessed in this review)
Notes	Informed consent: written Ethical approval: yes Study location: USA Study setting: Study duration: 14 months Funding: 3M Pharmaceuticals, NIH/NIAD

Beigi 2004 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

Burana 1990

Methods	Random allocation: method unclear Blinding: no Loss to follow up: 71 Analysis: no ITT
Participants	171 women aged 15 to 45 years old enrolled, 71 were excluded from analysis; sexual partners also treated Inclusion criteria: at least 3 Amsel criteria. Exclusion criteria: pregnancy, lactation, prostitutes, antibiotic or vaginal suppositories in the previous 2 weeks
Interventions	1. Oral tinidazole 2g single dose* 2. Oral metronidazole 500mg twice daily for 7 days*
Outcomes	Cure: defined as absence of symptoms and presence of < 3 Amsel criteria Side effects
Notes	Informed consent: unclear Ethical approval: no statement Study location: Thailand Study setting Study duration: 12 months Funding: BJ Limited

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Chaithong 2003

Methods	Random allocation: computer-generated random numbers Allocation concealment: not mentioned Blinding: investigators, participants, outcome assessors Loss to follow up: none Analysis: ITT

Chaithong 2003 (*Continued*)

Participants	142 women enrolled Inclusion criteria: BV diagnosed by Amsel criteria Age 15-45 years Exclusion criteria: hydrogen peroxide or metronidazole allergy, pregnancy, vaginal or cervical ulceration or co-infection, current use of IUCD, immunosuppression, diabetes mellitus, antibiotic use within 2 weeks, menopause
Interventions	1. Hydrogen peroxide douching (single dose) 2. 2g Single dose oral metronidazole
Outcomes	Primary: cure defined as absence of at least 3 of Amsel criteria Secondary: adverse effects
Notes	Informed consent: written Ethical approval: yes Study location: Bangkok, Thailand Study setting: Study duration: no report Funding: university research fund

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Eriksson 2005

Methods	Random allocation: method unclear Allocation concealment: not mentioned Blinding: investigator, participants Loss to follow up: 30 Analysis: no ITT
Participants	255 women enrolled, 187 excluded from analysis Inclusion criteria: BV by Amsel's criteria Exclusion criteria: age < 18 yrs, pregnancy, breastfeeding, antibiotic in the preceding week, ongoing STDs, unwilling to use tampons
Interventions	1. Clindamycin 100mg ovule daily for 3 days + tampons impregnated with lactobacillus during the next menstruation 2. Clindamycin 100mg ovule daily for 3 days
Outcomes	Primary: cure, improved, treatment failure - Cure defined as no Amsel criteria fulfilled + Nugent score 0-3 - Improved defined as 1 or 2 Amsel criteria + Nugent score 4-6 - Treatment failure defined as 3 or 4 Amsel criteria + Nugent score 7-10

Eriksson 2005 (*Continued*)

	Secondary: adverse events
Notes	Informed consent: written Ethical approval: yes Study location: multicentre, 13 clinics in Swden Study setting Study duration: no report Funding: Ellen Ab, Stockholm Sweden

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Fischbach 1993

Methods	Random allocation: computer random number-generation program to develop a drug randomisation code Allocation concealment: sequentially-numbered medication tubes and bottles given to participants as they are enrolled Blinding: investigators, participants Loss to follow up: 64 Analysis: ITT
Participants	407 women enrolled, 173 were excluded from analysis Inclusion criteria: BV by Amsel and Gram-stain (Spiegel) criteria Exclusion criteria: pregnancy, breastfeeding, menstruation, allergy to clidamycin or metronidazole, antimicrobial therapy 2 weeks before the study, history of antibiotic associated colitis or frequent periodic diarrrhea, atrophic vaginitis, active CNS disease, blood dyscrasias
Interventions	1. 2% Clindamycin cream 5g intravaginally at bedtime for + placebo capsules twice daily for 7 days 2. Oral metronidazole 500mg twice daily for + placebo vaginal cream 5g intravaginally at bedtime for 7 days
Outcomes	Primary - Cure - Improvement - Failure - Side effect failure Secondary - Changes in Gram-stain - Patients' evaluation of efficacy
Notes	Informed consent: written Ethical approval: yes Study location: multicentre (7 sites) study - Germany, Austria, Switzerland Study setting Study duration: no report

Fischbach 1993 (*Continued*)

	Funding: Upjohn Company	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

Gerli 2003

Methods	Random allocation: randomisation table Allocation concealment: not mentioned Blinding: outcome assesors Loss to follow up: 10 Analysis: ITT	
Participants	110 symptomatic women 18-40 years old enrolled Inclusion criteria: Amsel criteria Exclusion criteria: not listed	
Interventions	1. Polyhexamethylene biguanide gel solution single dose 2. 2% Clindamycin cream 5g intravaginally for 7 days	
Outcomes	- Achievement - Improvement - Failure	
Notes	Informed consent: written Ethical approval: yes Study location: Italy Study setting Study duration: no report Funding: no infomation	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

Greaves 1988

Methods	Random allocation: method unclear (a pre-constructed random sequence) Allocation concealment: not mentioned Blinding: investigators, participants Loss to follow up: 32 Analysis: no ITT
Participants	143 symptomatic women enrolled, 44 excluded from analysis Inclusion criteria: Amsel criteria Exclusion criteria: menstruating, antibiotics or treatment for vaginitis in the preceding 2 weeks, allergy to metronidazole or clindamycin, <18 years of age, STDs
Interventions	1. Oral clindamycin, 500mg twice daily for 7 days 2. Oral metronidazole, 500mg twice daily for 7 days
Outcomes	Cure: defined as resolution of vaginal discharge, absence of complaints related to vaginitis after therapy and failure to satisfy pre-determined criteria
Notes	Informed consent: written Ethical approval: yes Study location: Washington Study setting Study duration: no report Funding: no information

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Livengood 1990

Methods	Random allocation: unclear (method by Upjohn Company) Allocation concealment: numbered tubes containing 50g of vaginal cream supplied in sequence to participants as they entered the study Blinding: investigator, participants, outcome assessors Loss to follow up: 5 Analysis: no ITT
Participants	72 women aged 18 -45 years enrolled, 10 excluded from analysis Inclusion criteria: Amsel criteria and Gram stain criteria (Spiegel) Exclusion citeria: pregnancy, breastfeeding, allergy to clindamycin, antibiotic use in the previous 2 weeks, diarrhea, STDs
Interventions	1. Clindamycin 0.1% 2. Clindamycin 1% 3. Clindamycin 2%, all 5g intravaginal cream twice daily for 5 days 4. Placebo cream 5g twice daily for 5 days

Livengood 1990 (*Continued*)

Outcomes	- Cure: defined as absence of clue cells plus the presence of at least 2 other Amsel criteria - Therapeutic failure: defined as criteria for cure not met (retreated with 1% clindamycin) - Side effect failure: side effect severe enough to require discontinuation of treatment before completion of regimen
Notes	Informed consent: written Ethical approval: no statement Study location: USA, 2 hospital clinics Study setting Study duration: no report Funding: Upjohn Company

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

Livengood 1990a

Methods	Same as for Livengood 1990
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Livengood 1990b

Methods	Same as for Livengood 1990
Participants	
Interventions	
Outcomes	
Notes	

Livengood 1990b (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

McCormack 2001

Methods	Random allocation: method unclear Blinding: investigators, participants Loss to follow up: 23 Analysis: no ITT
Participants	281 symptomatic women were enrolled, 122 excluded from analysis Inclusion criteria: all 4 Amsel criteria, Nugent score for BV, and culture for Gardnerella vaginalis in women 16 years or older Exclusion criteria: breastfeeding, allergy to clindamycin or sulphonamides, antimicrobial therapy in the previous 2 weeks, antibiotic associated diarrhoea, menstruation, presence of other vaginal or cervical infections
Interventions	1. 2% Clindamycin vaginal cream 5g at bedtime for 7 days 2. Triple sulfonamide vaginal cream 5g at bedtime for 7 days
Outcomes	Primary - Treatment failure - defined as a return to normal of one or none of the diagnostic findings - Improvement - defined as a return to normal for two of the 3 findings - Cure defined as a return to normal for all 3 diagnostic findings - Side effects Secondary: Gram-stain, patients' evaluation of efficacy (not assessed in this review)
Notes	Informed consent: written Ethical approval: yes Study location: multicentre, New York, USA Study setting Study duration: no report Funding: no information

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Milani 2003

Methods	Random allocation: computer-generated list with blocks of 8 Allocation concealment: by a centralised phone-call procedure Blinding: investigator only Loss to follow up: 6 Analysis: intent to treat
Participants	64 women were enrolled Eligibility criteria: BV by Amsel criteria, age 20-75 years Exclusion criteria: pregnancy, topical antibiotics in the previous 2 weeks
Interventions	1. 2g Tinidazole + acid buffering gel 2. Clindamycin cream alone
Outcomes	Primary: laboratory cure rate - Laboratory cure rate defined as clinical cure rate plus a negative result of the BV: clue and whiff tests Secondary: clinical cure rate, vaginal normalisation - Clinical cure defined as absence of at least 2 out of 4 sign and symptoms of BV - Vaginal nomalisation defined as the percentage of women with a vaginal pH < 4.5 - Adverse events
Notes	Informed consent: written Ethical approval: yes Study location: no report Study setting Study duration: 6 months Funding: Mipharm Spa

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

Nunez 2005

Methods	Random allocation: table of random numbers Allocation concealment: packets of drugs prepared and numbered independently Blinding: participants, investigators Loss to follow up: 4 Analysis: no ITT
Participants	80 women 18 to 60 years old were enrolled, 4 excluded from analysis Inclusion criteria: symptomatic women with at least 3 Amsel criteria Exclusion criteria: pregnancy/breastfeeding, antibiotic therapy in the previous 4 weeks and allergy to metronidazole or its derivatives
Interventions	1. 1g oral secnidazole single dose 2. 2g oral secnidazole single dose

Nunez 2005 (*Continued*)

Outcomes	Primary outcome: clinical curre, cytologic cure - Clinical cure defined as absence of characteristic symptoms + at least 2 of (vaginal pH < 5, no fishy odour, no clue cells) - Cytologic cure defined as absence of Gardnerella vaginalis on a Pap smear (not assessed in this review) Secondary outcome: adverse effects
Notes	Informed consent: written Ethical approval: yes Study location: Venezuela Study setting: clinic of an urban public hospital Study duration: 3 years Funding: no information Socio-economic status: low and middle

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Paavonen 2000

Methods	Random allocation: unclear (conducted and maintained by the sponsor) Allocation concealment: not mentioned Blinding: participants and investigators Loss to follow up: 53 Analysis: ITT
Participants	399 women were enrolled, 166 were excluded from analysis Inclusion criteria: women with BV but method of diagnosis not clear Exclusion criteria: pregnancy, breastfeeding, menstruation, antibiotics in the previous 2 weeks, STDs
Interventions	1. Clindamycin ovule 100mg vaginally for 3 days 2. Metronidazole 500mg twice daily for 7 days
Outcomes	Primary: cure, failure, non-assessable efficacy - Cure defined as resolution of amine odour and clue cells at both follow-up visits - Clinical failure -defined as no resolution of amine odour or clue cells at either follow-up visit - Non-assessable defined as inadequate data to categorise outcome as cure or failure - Adverse effects failure: did not complete study therapy because of treatment-related adverse effects Secondary: clinical status (cure, clinical failure, adverse effects, non-assessable status) at each follow-up visit - Symptoms of vaginitis or cevicitis - Patient evaluation efficacy (cure improvement, failure) at second follow-up visit - Treatment safety: medical events reported spontaneously by participants

Paavonen 2000 (*Continued*)

Notes	Informed consent: written Ethical approval: yes Study location: multicentre, multiracial (23 countries) Study setting: Study duration: no report Funding: grant from Pharmacia and Upjohn which markets clindamycin, 2 of the 3 authors are employees of Pharmacia and Upjohn and one of them owns stock and stock options in the company

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Piot 1983

Methods	Random allocation: method unclear Allocation concealment: not mentioned Blinding: Investigators, participants Loss to follow up: 17 Analysis: no ITT
Participants	85 women enrolled but 28 excluded from analysis Inclusion criteria: nonspecific vaginitis (BV) by Amsel criteria Exclusion criteria: antibiotics in the preceding 3 weeks
Interventions	1. Oral tinidazole 500mg twice daily for 5 days + triple sulfonamide cream intravaginally twice daily for7 days 2. Oral tinidazole 500mg twice daily for 5 days + placcebo cream intravaginally twice daily for7 days 3. Oral placebo twice daily for 5 days + triple sulfonamide cream intravaginally twice daily for7 days 4. Oral placebo twice daily for 5 days + placebo cream intravaginally twice daily for 7 days
Outcomes	Cure: defined as absence of at least 3 of -abnormal vaginal discharge, clue cells, vaginal pH of 5 and positive amine test
Notes	Informed consent: obtained Ethical approval: no statement Study location: Belgium Study setting Study duration: no report Funding: National fonds voor Wettenschappeljik Onderzoek Belgium and Roerig NV, Belgium

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Schinder 1991

Methods	Random allocation: method unclear Blinding: no Some exclusion criteria applied after randomisation Loss to follow up: Analysis: no ITT
Participants	100 women aged 18 -55 years were enrolled, 25 were excluded from analysis Inclusion criteria: 3 or more Amsel criteria Exclusion criteria: STDs
Interventions	1. Oral tinidazole 2g single dose 2. Oral metronidazole 400mg twice daily fo 5 days
Outcomes	Healing: defined as disappearanceof all symptoms of the infection Improvement: defined as one or two inclusion criteria in the study still exist but clearly less pronounced Failure: defined as all symptoms that existed before the treatment are still present
Notes	Informed consent: written Ethical approval: no statement Study location: multicentre study Study setting: Study duration: no report Funding: no information Not clear if ethical approval or informed consent obtained Multicentre study Simultaneous treatment of partner if partner had complaints

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Schmitt 1992

Methods	Random allocation: provided by Upjohn Pharmaceutical Company Allocation concealment: not mentioned Blinding: investigators, participants Loss to follow up: 2 Analysis: no ITT
Participants	61 women enrolled, 13 were excluded from analysis Inclusion criteria: Amsel and Gram-stain criteria for BV Exclusion criteria: age <18 or > 60 years, pregnancy, breastfeeding, allergy to clindamycin or metronidazole, antimicrobial therapy within the previous 2 weeks, presence of STDs, menses, diarrhea, antibiotic-associated colitis
Interventions	1. 2% Vaginal clindamycin cream 5g per day for 7 days 2. Oral metronidazole 500mg twice daily for 7 days

Schmitt 1992 (*Continued*)

Outcomes	Primary outcome: cure, symptomatic failure, asymptomatic failure, non-evaluable Secondary outcome: side effects
Notes	Informed consent: written Ethical approval: yes Study location: Michigan State University Clinic Study setting: clinic Study duration: no report Funding: Upjohn Company

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Schwebke 2000

Methods	Random allocation: computer-generated randomisation scheme with a block of 6 patients in a 1:1 ratio Blinding: investigators, participants Loss to follow up: 4 Analysis: no ITT
Participants	75 women enrolled but 17 excluded fom analysis Inclusion criteria: women who denied symptoms of vaginal discharge and odour but met Amsel and Nugent criteria Exclusion criteria: pregnancy, antibiotic therapy in the previous 2 weeks, current STD
Interventions	1. Metronidazole gel 5g intravaginally daily at bedtime for 5 days 2. Placebo gel 5g intravaginally daily at bedtime for 5 days
Outcomes	Normalisation of clincal parameters: defined as vaginal pH 4.5 or more, negative whiff test, and an absence of clue cells Improvement in Nugent score
Notes	Informed consent: unclear Ethical approval: yes Study location: Birmingham, UK Study setting Study duration: Funding: 3M Pharmaceuticals

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Schwebke 2006

Methods	Random allocation: block randomisation Allocation concealment: randomisation scheme used to generate a list of randomisation numbers Blinding: investigators, participants Loss to follow up: 137 Analysis: no ITT
Participants	567 women were randomised, 143 were excluded from analysis Inclusion criteria: 3 or 4 Amsel criteria and a Gram-stain score of 7 or more Exclusion criteria: pregnancy, breastfeeding, hypersensitivity to metronidazole or clindamycin, chronic disease, pesence of STDs
Interventions	1. Oral metronidazole 750mg daily for 7 days + azithromycin 1gm orally on days 1 and 3 2. Oral metronidazole 750mg daily for 14 days + azithromycin 1gm orally on days 1 and 3 3. Oral metronidazole 750mg daily for 14 days 4. Oral metronidazole 750mg daily for 7 days
Outcomes	Primary: not cured normalisation of 0 or 1 of the criteria, cured if vaginal pH and whiff tests results normalised and if clue cells were absent, improved if normalisation of or more of the criteria, and not cured normalisation of 0 or 1 of the criteria Secondary: adverse events
Notes	Informed consent: no statement Ethical approval: no statement Study location: Birmingham UK Study setting: an STD clinic Study duration: 3 years Funding: Pfizer, National institutes of Health

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Schwebke 2006a

Methods	Same as for Schwbeke 2006
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias

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

Schwebke 2006a (*Continued*)

Allocation concealment?	Unclear risk	D - Not used

Schwebke 2006b

Methods	Same as for Schwbeke 2006	
Participants		
Interventions		
Outcomes		
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Sobel 2001

Methods	Random allocation: using random list of patient numbers in a 1:1 ratio Allocation concealment: not mentioned Blinding: investigators only Analysis was by intent to treat.
Participants	662 women were enrolled Inclusion criteria: symptomatic women who fulfilled Amsel's criteria and were between 16 and 60 years of age Exclusion criteria: allergy to clindamycin or lincomycin, pregnancy or breastfeeding, systemic or vaginal antimicrobial in the previous 2 weeks, STDs, anticipation of menses
Interventions	1. Vaginal clindamycin ovule 100mg at bedtime for 3 days 2. Vaginal clindamycin cream 5g intravaginally at bedtime for 7 days
Outcomes	Primary: cure defined as resolution of 2 or 3 diagnostic criteria at first follow-up visit and 3 or more criteria at second visit Secondary: side effects, patient evaluation of efficacy and Gram-stain scores
Notes	Informed consent: written Ethical approval: yes Study location: multticentre, multiracial Study setting Study duration: no report Funding: Phamacia and Upjohn

Sobel 2001 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Stein 1993

Methods	Random allocation: (unclear) randomisation schedule by the Upjohn Company Allocation concealment: not mentioned Blinding: investigators, paticipants Loss to follow up: none Analysis: No ITT
Participants	215 symptomatic women enrolled, 81 were excluded from analysis Inclusion criteria: at least 3 Amsel and Gram-stain criteria Exclusion criteria: allergy to clindamycin, nursing, menstruating, history of antibiotic asociated diarrhea, antibiotic therapy within the previous 2 weeks, concurrent genital infection
Interventions	Arm 1: 2% clindamycin cream, 5g intravaginally at bedtime for 7days Arm 2: placebo cream 5g intravaginally at bedtime for 7days
Outcomes	First follow-up visit - Clinical cure aand microbiologic cure (not assessed in this review) - Clinical cure - Improvement - Failure Final follow-up visit - Cure - Improvement - Failure - Recurrences
Notes	Informed consent: written Ethical approval: yes Study location: Michigan Study setting: ambulatory clinic the general community Study duration: no report Funding: Upjohn Company

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Voorspoels 2002

Methods	Random allocation: unclear Allocation concealment: not mentioned Blinding: investigator, participants Loss to follow up: 6 Analysis: no ITT
Participants	116 symptomatic women were enrolled, 16 were excluded from analysis Inclusion criteria: at least 3 Amsel criteria for BV Exclusion criteria: cervicitis, vulvovaginitis caused by other organisms, recent antimicrobial therapy, pregnancy, total hysterectomy
Interventions	Arm 1: 100mg metronidazole single dose bioadhesive tablets Arm 2: 250mg metronidazloe single dose bioadhesive tablets Arm 3: 500mg metronidazole single dose bioadhesive tablets Arm 4: placebo
Outcomes	Primary: cured, not cured Secondary: side effects
Notes	Informed consent: unclear Ethical approval: yes Study location: Belgium Study setting Study duration: no report Funding: no infomation

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	B - Unclear

Voorspoels 2002a

Methods	Same as for Voorspoels 2002
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias

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

Voorspoels 2002a (*Continued*)

Allocation concealment?	Unclear risk	D - Not used

Voorspoels 2002b

Methods	Same as for Voorspoels 2002
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Wathne 1989

Methods	Random allocation: unclear Allocation concealment: unclear Blinding: investigator Loss to follow up: none Analysis: ITT
Participants	22 women enrolled Inclusion criteria: 3 or 4 Amsel criteria + absence of lactobacillus Exclusion criteria: STDs
Interventions	Arm 1: cefadroxil 500mg orally twice daily for 7 days Arm 2: metronidazole 400mg orally twice daily for 7 days
Outcomes	Cure
Notes	Informed consent: unclear Ethical approval: yes Study location: Sweden Study setting Study duration: no report Funding: no information

Risk of bias

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

Wathne 1989 (*Continued*)

Allocation concealment?	Unclear risk	B - Unclear

B = Allocation concealment unclear
ITT = intention-to-treat
IRB = Institutional review board
BV = bacterial vaginosis
STD = sexually transmittted diseases
* sexual partners also treated

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

Study	Reason for exclusion
Andreeva 2002	Not a randomised controlled trial
Blackwell 1983	BV not diagnosed by Amsel or Gram stain criteria
Eschenback 1983	BV not diagnosed by Amsel or Gram stain criteria
Facchin 1995	Not a randomised controlled trial
Ferris 1995	STDs not excluded from participants
Fredricsson 1986	BV not diagnosed by Amsel or Gram stain criteria
Hagstrom 1983	BV not diagnosed by Amsel or Gram stain criteria
Hovick 1983	BV not diagnosed by Amsel or Gram stain criteria
Improda 1993	Randomisation not to drug but tosexual partner
Jerve 1984	BV not diagnosed by Amsel or Gram stain criteria
Jones 1985	BV not confimed by Amsel or Gram stain criteria
Kira 1994	Not a randomised controlled trial
Lefevre 1985	Not a randomised controlled trial
Linhares 1995	Not a randomised controlled trial, BV not diagnosed by Amsel or Gram stain criteria
Malouf 1981	Diagnosis not by Amsel or Gram stain criteria
Martins 1985	Not a randomised controlled trial

(*Continued*)

Milankovis 2002	Not a randomised controlled trial
Mohanty 1987	Not a randomised controlled trial, trichomoniasis not excluded
Naud 2003	BV not diagnosed by Amsel or Gram stain criteria
Purdon 1984	BV not diagnosed by Amsel or Gram-stain criteria
Sanchez 2004	Candidiasis and trichomoniasis not excluded before randomisation, women without BV also randomised
Sanz 1995	Not a randomised controlled trial
Sanz Sanz 1985	Diagnosis of BV not by Amsel or Gram-stain criteria
Sanz Sanz 2001	BV not diagnosed by Amsel or Gram-stain criteria
Sobel 1993	Duplicate publication
Swedberg 1985	BV not diagnosed by Amsel or Gram-stain criteria
Van Der Meijden 1983	BV not confirmed by Amsel or Gram-stain criteria, STDs not excluded from participants
Vutyavanich 1993	Randomisation not to drug but to sexual partner
Wei 2001	Not a randomised controlled trial

BV = bacterial vaginosis

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

Wilson 2005

Trial name or title	
Methods	Random allocation: method unclear Allocation concealment: unclear Blinding: Investigator Loss to follow-up: 13 Analysis:
Participants	51 symptomatic women were randomised Inclusion criteria: Amsel criteria and Nugent score
Interventions	1: 5 % tea tree oil gel 5 g daily fo 5 days 2: 0.75% metronidazole 5g daily for 5 days

Wilson 2005 (*Continued*)

Outcomes	Pesistence Recurrence Adverse reactions
Starting date	
Contact information	
Notes	Incomplete information from conference proceedings. Author to be contacted

DATA AND ANALYSES

Comparison 1. Topical metronidazole versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure 1	4	191	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.44, 0.79]
2 Clinical failure 2	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Candida infection	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 2. 2% clindamycin cream versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure 1	4	285	Risk Ratio (M-H, Random, 95% CI)	0.19 [0.09, 0.41]
2 Clinical failure 2	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Bacteriologic failure 2	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 3. Metronidazole versus clindamycin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure 1	6	1189	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.64, 1.75]
2 Clinical failure 2	4	985	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.75, 1.27]
3 Bacteriologic failure 1	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Bcteriologic failure 2	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Discontinuation	4	927	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.17, 1.47]
6 Adverse events	4	927	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.54, 1.05]
7 Metallic taste	2	204	Risk Ratio (M-H, Random, 95% CI)	0.09 [0.01, 0.68]
8 Nausea/vomiting	3	611	Risk Ratio (M-H, Random, 95% CI)	0.27 [0.11, 0.69]
9 Candida	4	986	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.78, 1.58]
10 Diarrhea	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
11 Vaginal irritation	2	468	Risk Ratio (M-H, Random, 95% CI)	1.59 [0.31, 8.17]
12 Relapse	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 4. Tinidazole versus metronidazole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure 1	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2 Adverse events	2	175	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.13, 2.98]
3 Nausea/vomiting	2	175	Risk Ratio (M-H, Random, 95% CI)	0.45 [0.14, 1.42]

Comparison 5. Clindamycin ovule versus clindamycin cream

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure 1	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Clinical failure 2	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Adverse events	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Discontinuation	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Candida infection	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 6. Clindamycin ovule + lactobacilli versus clindamycin ovule alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical cure 1	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Clinical cure 2	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Candida infection	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Itching/burning	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 7. Clindamycin cream versus oral metronidazole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure 1	3	528	Risk Ratio (M-H, Random, 95% CI)	1.43 [0.57, 3.60]
2 Clinical failure 2	2	467	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.59, 1.84]

Comparison 8. Clindamycin cream versus oral tinidazole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 clinical failure 2	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Relapse	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 9. 2%Clindamycin cream versus triple sulfonamide cream

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure1	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Clinical failure 2	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Bacteriological failure 1	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Bacteriological failure 2	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Discontinuation	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 10. Polyhexamethylene biguanide douche versus clindamycin cream

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Discontinuation	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Adverse effects	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Candida infection	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 11. Single hydrogen peroxide douche versus single dose metronidazole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure 1	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Reduced eating/vomitting	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Vaginal irritation	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 12. Cefadroxil versus metronidazole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Clinical failure 2	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Candida infection	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 13. 1g versus 2g secnidazole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical failure 1	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Adverse effects	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 14. lactobacillus versus metronidazole

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 clinical failure	1	40	Risk Ratio (M-H, Random, 95% CI)	0.25 [0.06, 1.03]
2 clinical failure 2	1	40	Risk Ratio (M-H, Random, 95% CI)	0.27 [0.09, 0.83]
3 bacteriologic failure 2	2	165	Risk Ratio (M-H, Random, 95% CI)	0.28 [0.14, 0.59]
4 bacteriologic failure 1	1	40	Risk Ratio (M-H, Random, 95% CI)	0.25 [0.06, 1.03]
5 discontinuation	1	125	Risk Ratio (M-H, Random, 95% CI)	4.92 [1.51, 16.06]
6 Headache	1	125	Risk Ratio (M-H, Random, 95% CI)	6.47 [0.34, 122.71]

Comparison 15. metronidazole vs metronidazole + azithromycin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 clinical failure 1	3	554	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.46, 0.92]
2 clinical failure 2	3	554	Risk Ratio (M-H, Random, 95% CI)	1.22 [0.82, 1.83]
3 bacteriologic failure 1	3	554	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.44, 1.01]
4 bacteriologic failure 2	3	554	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.68, 1.81]
5 Nausea	3	554	Risk Ratio (M-H, Random, 95% CI)	1.90 [0.82, 4.42]
5.1 metro + azith vs metro	2	372	Risk Ratio (M-H, Random, 95% CI)	2.17 [0.78, 6.02]
5.2 metro 7 days vs 14 days	1	182	Risk Ratio (M-H, Random, 95% CI)	1.43 [0.32, 6.39]
6 Candida	2	372	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.34, 1.18]

Analysis 1.1. Comparison 1 Topical metronidazole versus placebo, Outcome 1 Clinical failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 1 Topical metronidazole versus placebo

Outcome: 1 Clinical failure 1

Study or subgroup	Metronidazole n/N	placebo n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Schwebke 2000	17/37	27/38		52.9 %	0.65 [0.43, 0.97]
Voorspoels 2002	9/28	6/10		15.8 %	0.54 [0.26, 1.12]
Voorspoels 2002a	10/30	6/10		16.9 %	0.56 [0.27, 1.14]
Voorspoels 2002b	8/28	6/10		14.4 %	0.48 [0.22, 1.03]
Total (95% CI)	**123**	**68**		**100.0 %**	**0.59 [0.44, 0.79]**

Total events: 44 (Metronidazole), 45 (placebo)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.58$, df = 3 (P = 0.90); $I^2 = 0.0\%$

Test for overall effect: Z = 3.57 (P = 0.00036)

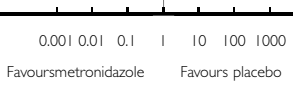
Analysis 1.2. Comparison 1 Topical metronidazole versus placebo, Outcome 2 Clinical failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 1 Topical metronidazole versus placebo

Outcome: 2 Clinical failure 2

Study or subgroup	Metronidazole n/N	placebo n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Schwebke 2000	16/37	24/38		0.68 [0.44, 1.07]

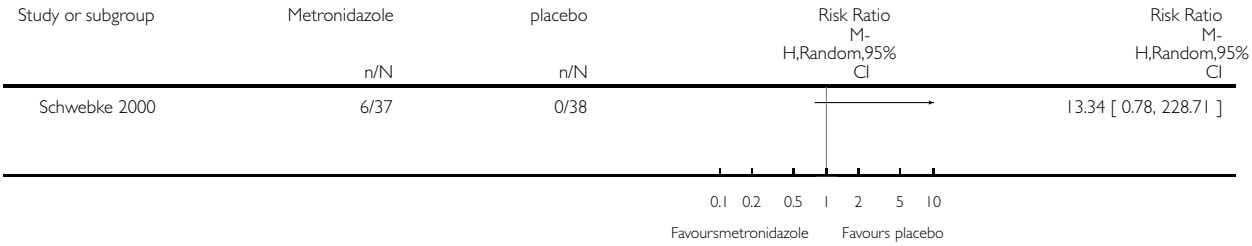


Analysis 1.3. Comparison 1 Topical metronidazole versus placebo, Outcome 3 Candida infection.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 1 Topical metronidazole versus placebo

Outcome: 3 Candida infection

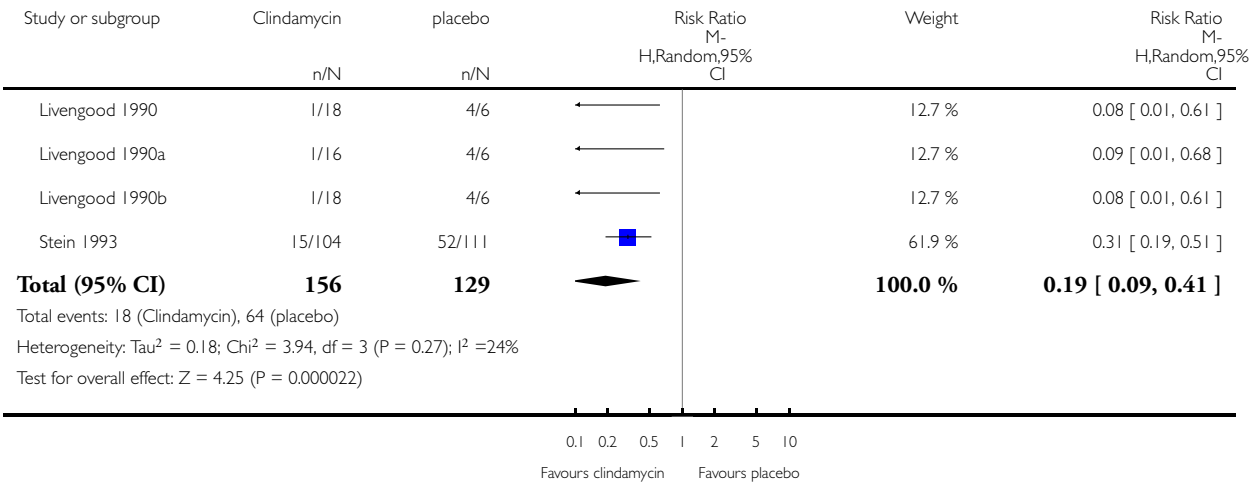


Analysis 2.1. Comparison 2 2% clindamycin cream versus placebo, Outcome 1 Clinical failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 2 2% clindamycin cream versus placebo

Outcome: 1 Clinical failure 1

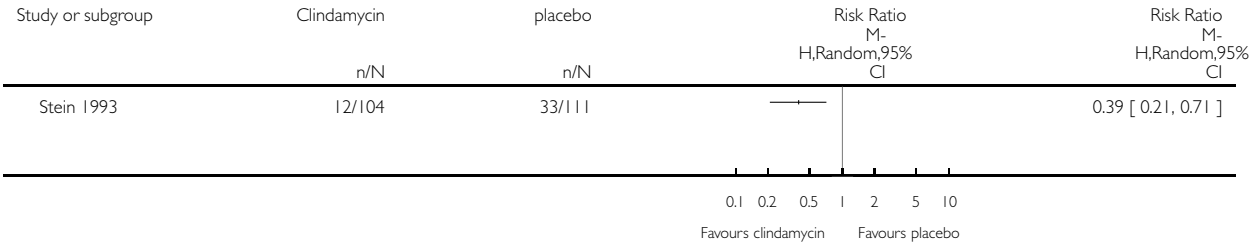


Analysis 2.2. Comparison 2 2% clindamycin cream versus placebo, Outcome 2 Clinical failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 2 2% clindamycin cream versus placebo

Outcome: 2 Clinical failure 2

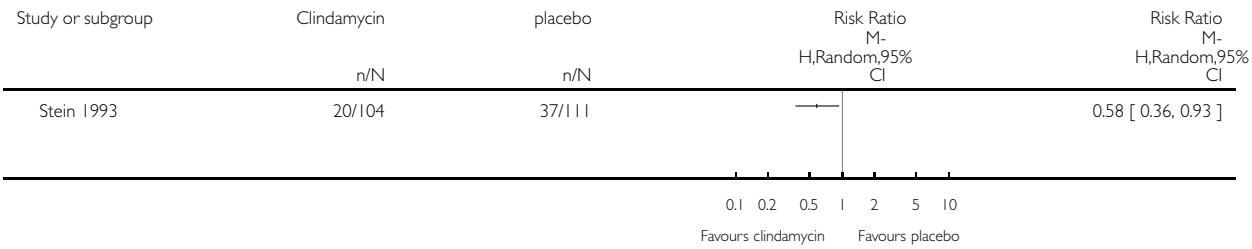


Analysis 2.3. Comparison 2 2% clindamycin cream versus placebo, Outcome 3 Bacteriologic failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 2 2% clindamycin cream versus placebo

Outcome: 3 Bacteriologic failure 2



Analysis 3.1. Comparison 3 Metronidazole versus clindamycin, Outcome 1 Clinical failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 1 Clinical failure 1

Study or subgroup	Clindamycin n/N	Metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Andres 1992	1/30	4/30		5.0 %	0.25 [0.03, 2.11]
Beigi 2004	9/60	14/59		24.5 %	0.63 [0.30, 1.35]
Fischbach 1993	18/204	10/203		24.8 %	1.79 [0.85, 3.79]
Greaves 1988	3/71	2/72		7.1 %	1.52 [0.26, 8.83]
Paavonen 2000	13/200	15/199		26.0 %	0.86 [0.42, 1.77]
Schmitt 1992	7/31	3/30		12.4 %	2.26 [0.64, 7.93]
Total (95% CI)	**596**	**593**		**100.0 %**	**1.06 [0.64, 1.75]**

Total events: 51 (Clindamycin), 48 (Metronidazole)

Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 7.32$, df = 5 (P = 0.20); $I^2 = 32\%$

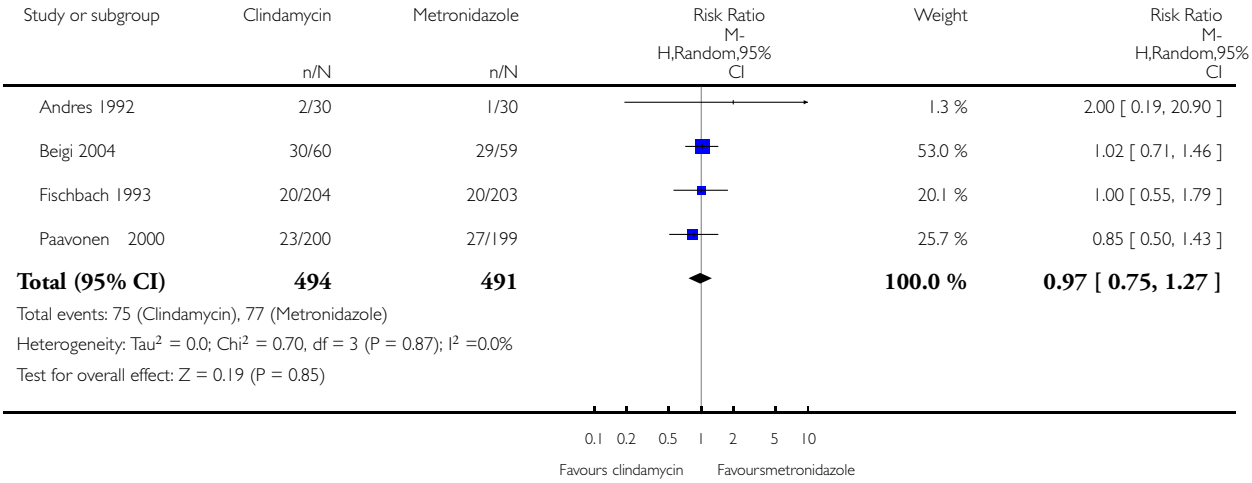
Test for overall effect: Z = 0.21 (P = 0.83)

Analysis 3.2. Comparison 3 Metronidazole versus clindamycin, Outcome 2 Clinical failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 2 Clinical failure 2

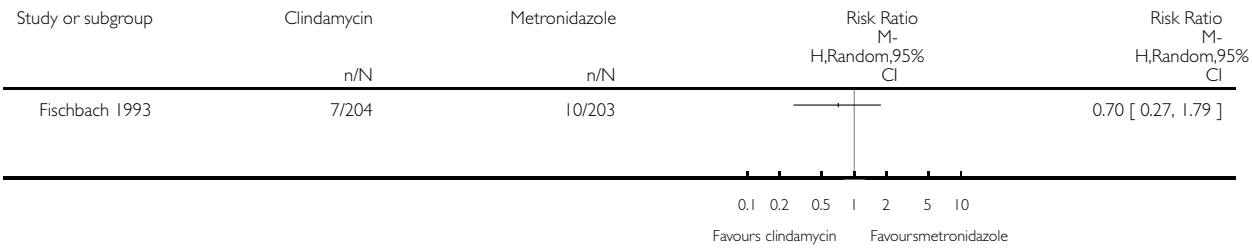


Analysis 3.3. Comparison 3 Metronidazole versus clindamycin, Outcome 3 Bacteriologic failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 3 Bacteriologic failure 1

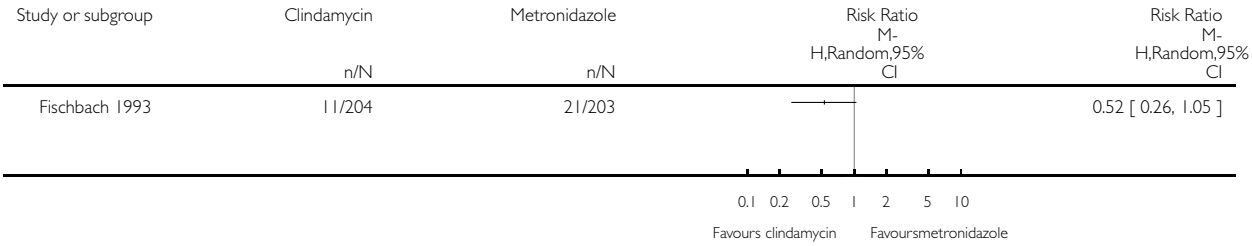


Analysis 3.4. Comparison 3 Metronidazole versus clindamycin, Outcome 4 Bcteriologic failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 4 Bcteriologic failure 2

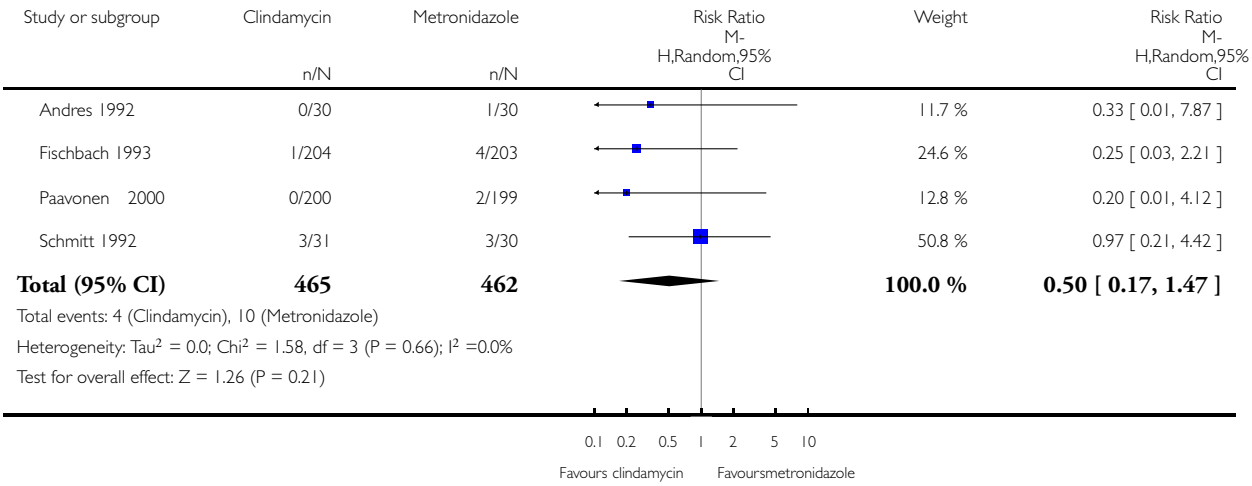


Analysis 3.5. Comparison 3 Metronidazole versus clindamycin, Outcome 5 Discontinuation.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 5 Discontinuation



Analysis 3.6. Comparison 3 Metronidazole versus clindamycin, Outcome 6 Adverse events.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 6 Adverse events

Study or subgroup	Clindamycin n/N	Metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Andres 1992	10/30	12/30		21.9 %	0.83 [0.43, 1.63]
Fischbach 1993	24/204	23/203		31.6 %	1.04 [0.61, 1.78]
Paavonen 2000	21/200	32/199		33.9 %	0.65 [0.39, 1.09]
Schmitt 1992	5/31	12/30		12.6 %	0.40 [0.16, 1.01]
Total (95% CI)	**465**	**462**		**100.0 %**	**0.75 [0.54, 1.05]**
Total events: 60 (Clindamycin), 79 (Metronidazole)					
Heterogeneity: Tau^2 = 0.02; Chi^2 = 3.55, df = 3 (P = 0.31); I^2 =15%					
Test for overall effect: Z = 1.66 (P = 0.096)					

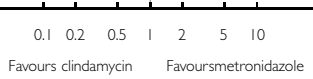
Analysis 3.7. Comparison 3 Metronidazole versus clindamycin, Outcome 7 Metallic taste.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 7 Metallic taste

Study or subgroup	Clindamycin n/N	Metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Greaves 1988	0/71	3/72		47.6 %	0.14 [0.01, 2.75]
Schmitt 1992	0/31	8/30		52.4 %	0.06 [0.00, 0.95]
Total (95% CI)	**102**	**102**		**100.0 %**	**0.09 [0.01, 0.68]**
Total events: 0 (Clindamycin), 11 (Metronidazole)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.21, df = 1 (P = 0.65); I^2 =0.0%					
Test for overall effect: Z = 2.33 (P = 0.020)					



Analysis 3.8. Comparison 3 Metronidazole versus clindamycin, Outcome 8 Nausea/vomiting.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 8 Nausea/vomiting

Study or subgroup	Clindamycin n/N	Metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Fischbach 1993	1/204	8/203		20.0 %	0.12 [0.02, 0.99]
Greaves 1988	4/71	10/72		69.4 %	0.41 [0.13, 1.23]
Schmitt 1992	0/31	5/30		10.6 %	0.09 [0.01, 1.53]
Total (95% CI)	**306**	**305**		**100.0 %**	**0.27 [0.11, 0.69]**
Total events: 5 (Clindamycin), 23 (Metronidazole)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.75$, df = 2 (P = 0.42); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.75 (P = 0.0059)					

Analysis 3.9. Comparison 3 Metronidazole versus clindamycin, Outcome 9 Candida.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 9 Candida

Study or subgroup	Clindamycin n/N	Metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Beigi 2004	21/60	22/59		53.4 %	0.94 [0.58, 1.51]
Fischbach 1993	15/204	8/203		17.4 %	1.87 [0.81, 4.30]
Paavonen 2000	7/200	6/199		10.6 %	1.16 [0.40, 3.39]
Schmitt 1992	9/31	8/30		18.6 %	1.09 [0.48, 2.45]
Total (95% CI)	**495**	**491**		**100.0 %**	**1.11 [0.78, 1.58]**

Total events: 52 (Clindamycin), 44 (Metronidazole)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.03$, df = 3 (P = 0.57); $I^2 = 0.0\%$

Test for overall effect: Z = 0.60 (P = 0.55)

Analysis 3.10. Comparison 3 Metronidazole versus clindamycin, Outcome 10 Diarrhea.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 10 Diarrhea

Study or subgroup	Clindamycin n/N	Metronidazole n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Fischbach 1993	1/204	0/203		2.99 [0.12, 72.85]

Analysis 3.11. Comparison 3 Metronidazole versus clindamycin, Outcome 11 Vaginal irritation.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

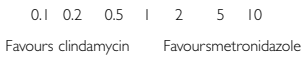
Outcome: 11 Vaginal irritation

Study or subgroup	Clindamycin n/N	Metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Fischbach 1993	2/204	2/203		70.2 %	1.00 [0.14, 7.00]
Schmitt 1992	2/31	0/30		29.8 %	4.84 [0.24, 96.89]
Total (95% CI)	**235**	**233**		**100.0 %**	**1.59 [0.31, 8.17]**

Total events: 4 (Clindamycin), 2 (Metronidazole)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.77$, df = 1 (P = 0.38); $I^2 = 0.0\%$

Test for overall effect: Z = 0.56 (P = 0.58)



Analysis 3.12. Comparison 3 Metronidazole versus clindamycin, Outcome 12 Relapse.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 3 Metronidazole versus clindamycin

Outcome: 12 Relapse

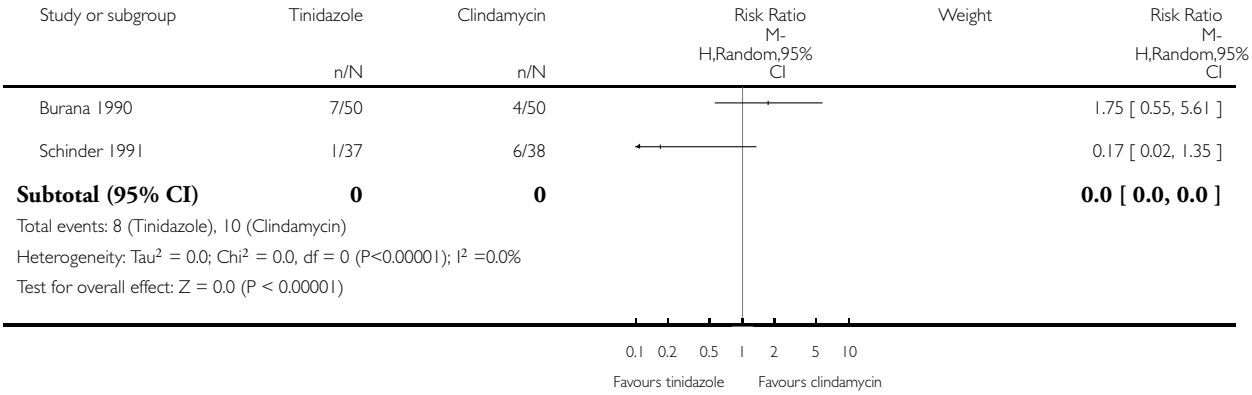
Study or subgroup	Clindamycin n/N	Metronidazole n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Schmitt 1992	7/18	7/18		1.00 [0.44, 2.27]

Analysis 4.1. Comparison 4 Tinidazole versus metronidazole, Outcome 1 Clinical failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 4 Tinidazole versus metronidazole

Outcome: 1 Clinical failure 1

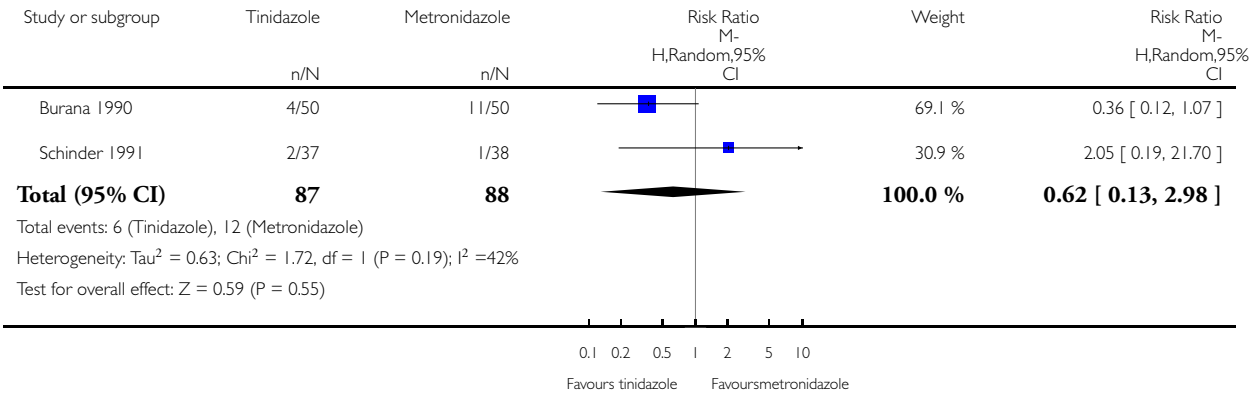


Analysis 4.2. Comparison 4 Tinidazole versus metronidazole, Outcome 2 Adverse events.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 4 Tinidazole versus metronidazole

Outcome: 2 Adverse events

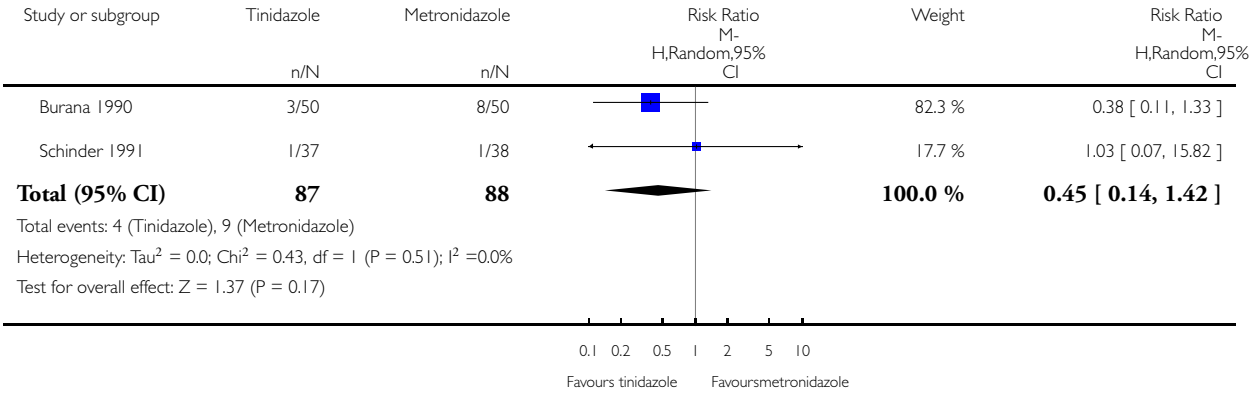


Analysis 4.3. Comparison 4 Tinidazole versus metronidazole, Outcome 3 Nausea/vomiting.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 4 Tinidazole versus metronidazole

Outcome: 3 Nausea/vomiting

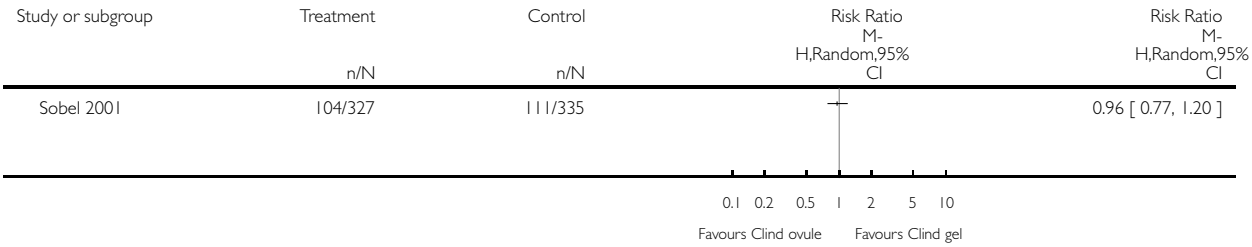


Analysis 5.1. Comparison 5 Clindamycin ovule versus clindamycin cream, Outcome 1 Clinical failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 5 Clindamycin ovule versus clindamycin cream

Outcome: 1 Clinical failure 1

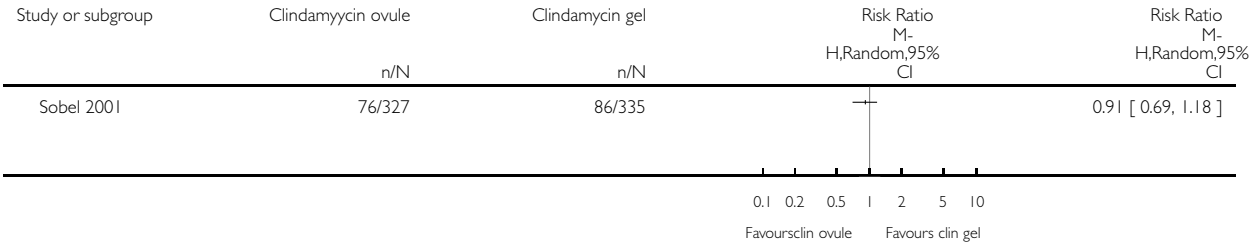


Analysis 5.2. Comparison 5 Clindamycin ovule versus clindamycin cream, Outcome 2 Clinical failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 5 Clindamycin ovule versus clindamycin cream

Outcome: 2 Clinical failure 2

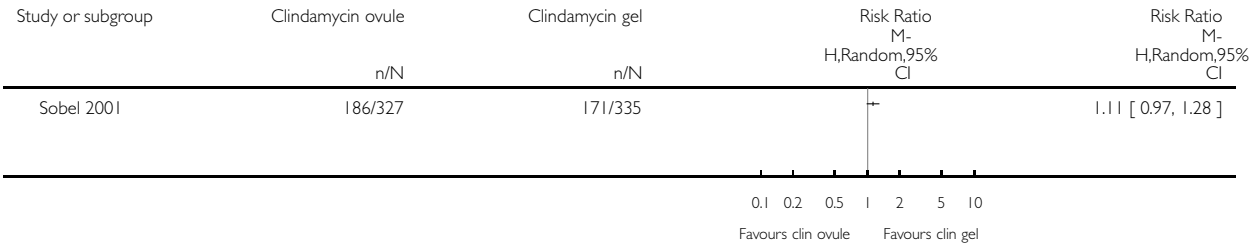


Analysis 5.3. Comparison 5 Clindamycin ovule versus clindamycin cream, Outcome 3 Adverse events.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 5 Clindamycin ovule versus clindamycin cream

Outcome: 3 Adverse events

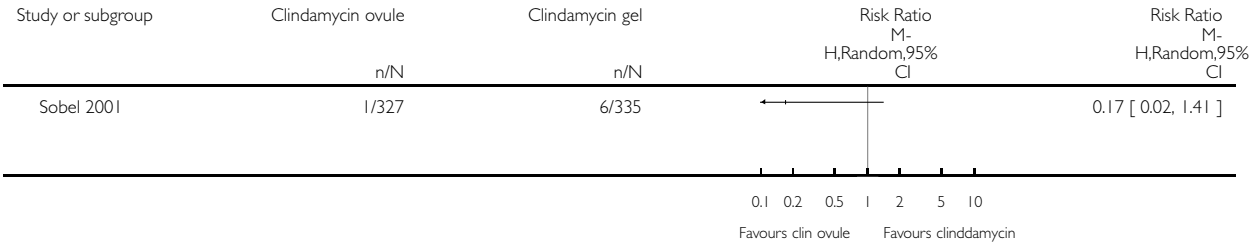


Analysis 5.4. Comparison 5 Clindamycin ovule versus clindamycin cream, Outcome 4 Discontinuation.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 5 Clindamycin ovule versus clindamycin cream

Outcome: 4 Discontinuation



Analysis 5.5. Comparison 5 Clindamycin ovule versus clindamycin cream, Outcome 5 Candida infection.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 5 Clindamycin ovule versus clindamycin cream

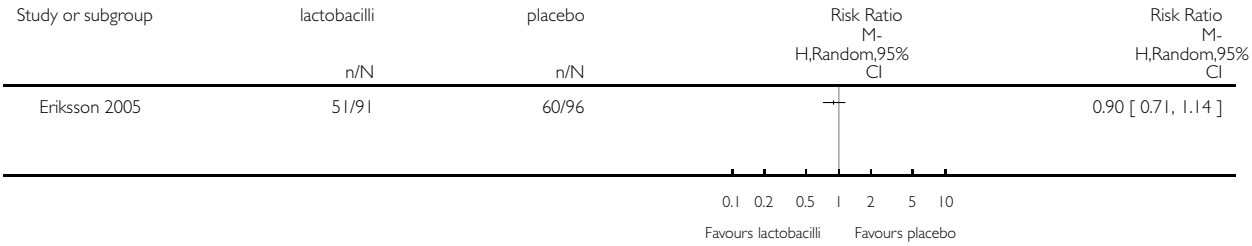
Outcome: 5 Candida infection

Analysis 6.1. Comparison 6 Clindamycin ovule + lactobacilli versus clindamycin ovule alone, Outcome 1 Clinical cure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 6 Clindamycin ovule + lactobacilli versus clindamycin ovule alone

Outcome: 1 Clinical cure 1

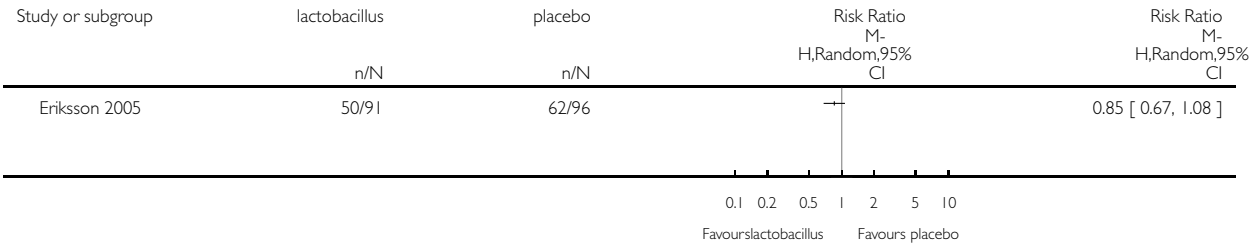


Analysis 6.2. Comparison 6 Clindamycin ovule + lactobacilli versus clindamycin ovule alone, Outcome 2 Clinical cure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 6 Clindamycin ovule + lactobacilli versus clindamycin ovule alone

Outcome: 2 Clinical cure 2

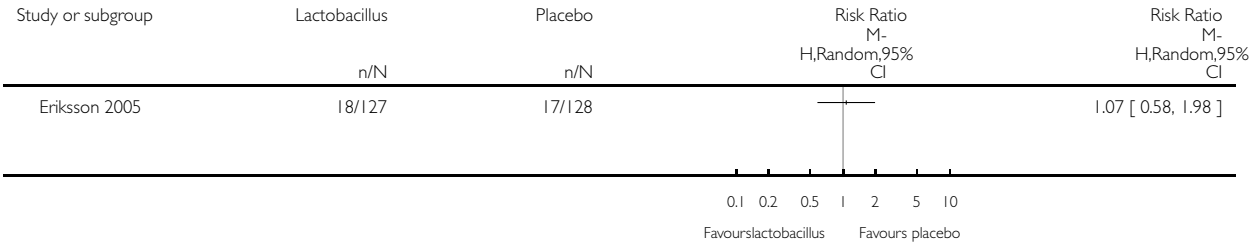


Analysis 6.3. Comparison 6 Clindamycin ovule + lactobacilli versus clindamycin ovule alone, Outcome 3 Candida infection.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 6 Clindamycin ovule + lactobacilli versus clindamycin ovule alone

Outcome: 3 Candida infection

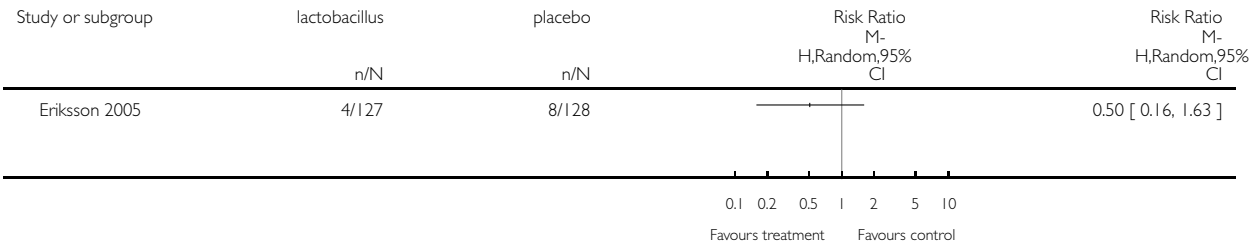


Analysis 6.4. Comparison 6 Clindamycin ovule + lactobacilli versus clindamycin ovule alone, Outcome 4 Itching/burning.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 6 Clindamycin ovule + lactobacilli versus clindamycin ovule alone

Outcome: 4 Itching/burning



Analysis 7.1. Comparison 7 Clindamycin cream versus oral metronidazole, Outcome 1 Clinical failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 7 Clindamycin cream versus oral metronidazole

Outcome: 1 Clinical failure 1

Study or subgroup	clindamycin n/N	metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Andres 1992	1/30	4/30		15.1 %	0.25 [0.03, 2.11]
Fischbach 1993	18/204	10/203		52.6 %	1.79 [0.85, 3.79]
Schmitt 1992	7/31	3/30		32.2 %	2.26 [0.64, 7.93]
Total (95% CI)	**265**	**263**		**100.0 %**	**1.43 [0.57, 3.60]**

Total events: 26 (clindamycin), 17 (metronidazole)

Heterogeneity: $Tau^2 = 0.27$; $Chi^2 = 3.32$, df = 2 (P = 0.19); $I^2 = 40\%$

Test for overall effect: Z = 0.77 (P = 0.44)

Analysis 7.2. Comparison 7 Clindamycin cream versus oral metronidazole, Outcome 2 Clinical failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 7 Clindamycin cream versus oral metronidazole

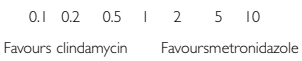
Outcome: 2 Clinical failure 2

Study or subgroup	clindamycin n/N	metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Andres 1992	2/30	1/30		5.9 %	2.00 [0.19, 20.90]
Fischbach 1993	20/204	20/203		94.1 %	1.00 [0.55, 1.79]
Total (95% CI)	**234**	**233**		**100.0 %**	**1.04 [0.59, 1.84]**

Total events: 22 (clindamycin), 21 (metronidazole)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.32$, df = 1 (P = 0.57); $I^2 = 0.0\%$

Test for overall effect: Z = 0.12 (P = 0.90)

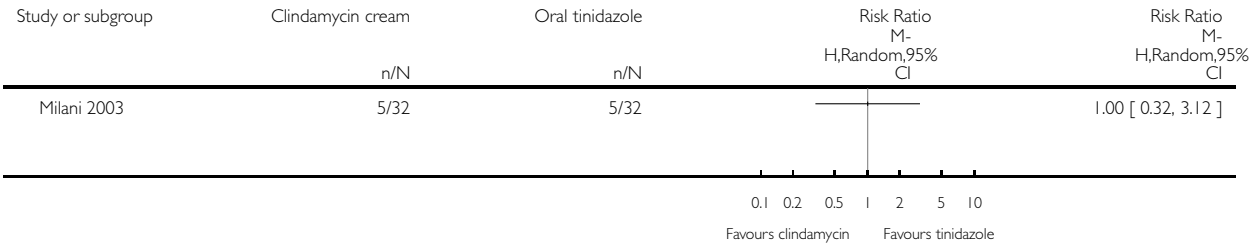


Analysis 8.1. Comparison 8 Clindamycin cream versus oral tinidazole, Outcome 1 Clinical failure.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 8 Clindamycin cream versus oral tinidazole

Outcome: 1 Clinical failure

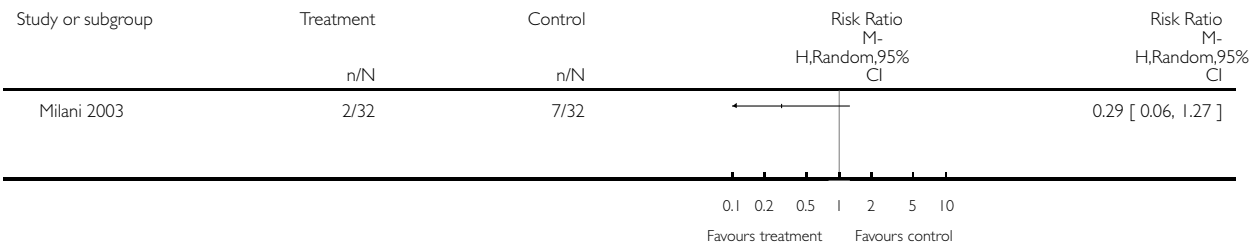


Analysis 8.2. Comparison 8 Clindamycin cream versus oral tinidazole, Outcome 2 clinical failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 8 Clindamycin cream versus oral tinidazole

Outcome: 2 clinical failure 2

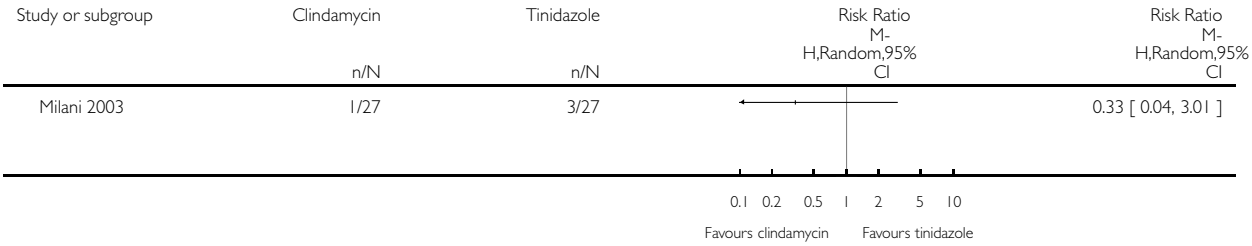


Analysis 8.3. Comparison 8 Clindamycin cream versus oral tinidazole, Outcome 3 Relapse.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 8 Clindamycin cream versus oral tinidazole

Outcome: 3 Relapse

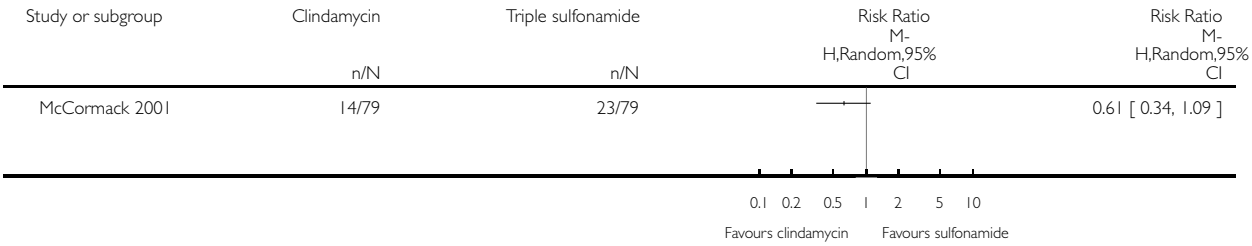


Analysis 9.1. Comparison 9 2%Clindamycin cream versus triple sulfonamide cream, Outcome 1 Clinical failure1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 9 2%Clindamycin cream versus triple sulfonamide cream

Outcome: 1 Clinical failure1



Analysis 9.2. Comparison 9 2%Clindamycin cream versus triple sulfonamide cream, Outcome 2 Clinical failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 9 2%Clindamycin cream versus triple sulfonamide cream

Outcome: 2 Clinical failure 2

Study or subgroup	Clindamycin n/N	Sulfonamide n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
McCormack 2001	16/79	44/79		0.36 [0.23, 0.59]

Analysis 9.3. Comparison 9 2%Clindamycin cream versus triple sulfonamide cream, Outcome 3 Bacteriological failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 9 2%Clindamycin cream versus triple sulfonamide cream

Outcome: 3 Bacteriological failure 1

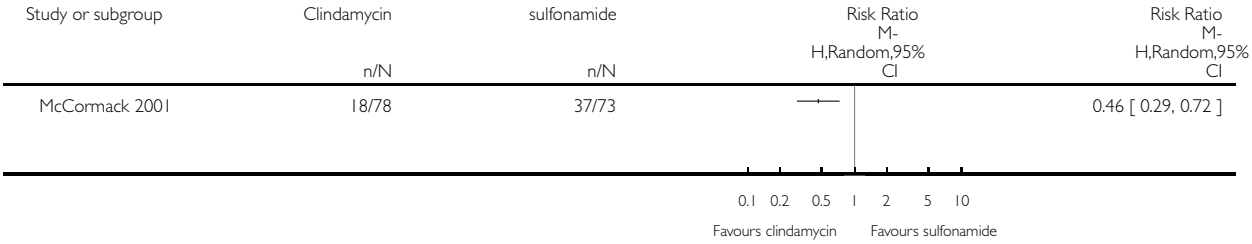
Study or subgroup	Clindamycin n/N	Metronidazole n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
McCormack 2001	9/79	24/78		0.37 [0.18, 0.75]

Analysis 9.4. Comparison 9 2%Clindamycin cream versus triple sulfonamide cream, Outcome 4 Bacteriological failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 9 2%Clindamycin cream versus triple sulfonamide cream

Outcome: 4 Bacteriological failure 2

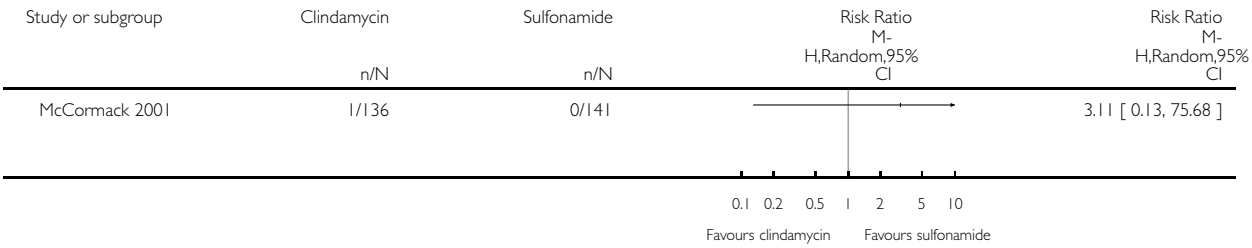


Analysis 9.5. Comparison 9 2%Clindamycin cream versus triple sulfonamide cream, Outcome 5 Discontinuation.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 9 2%Clindamycin cream versus triple sulfonamide cream

Outcome: 5 Discontinuation



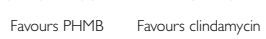
Analysis 10.1. Comparison 10 Polyhexamethylene biguanide douche versus clindamycin cream, Outcome 1 Clinical failure.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 10 Polyhexamethylene biguanide douche versus clindamycin cream

Outcome: 1 Clinical failure

Study or subgroup	PHMB n/N	Clindamycin n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Gerli 2003	7/53	6/47		1.03 [0.37, 2.86]



Analysis 10.2. Comparison 10 Polyhexamethylene biguanide douche versus clindamycin cream, Outcome 2 Discontinuation.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 10 Polyhexamethylene biguanide douche versus clindamycin cream

Outcome: 2 Discontinuation

Study or subgroup	PHMB n/N	Clindamycin n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Gerli 2003	0/53	3/47		0.13 [0.01, 2.40]

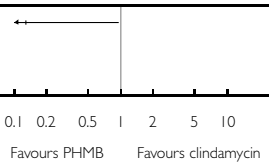
Analysis 10.3. Comparison 10 Polyhexamethylene biguanide douche versus clindamycin cream, Outcome 3 Adverse effects.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 10 Polyhexamethylene biguanide douche versus clindamycin cream

Outcome: 3 Adverse effects

Study or subgroup	PHMB n/N	Clindamycin n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Gerli 2003	1/53	8/53		0.13 [0.02, 0.96]



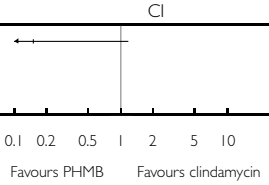
Analysis 10.4. Comparison 10 Polyhexamethylene biguanide douche versus clindamycin cream, Outcome 4 Candida infection.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 10 Polyhexamethylene biguanide douche versus clindamycin cream

Outcome: 4 Candida infection

Study or subgroup	PHMB n/N	Clindamycin n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Gerli 2003	1/53	6/47		0.15 [0.02, 1.18]

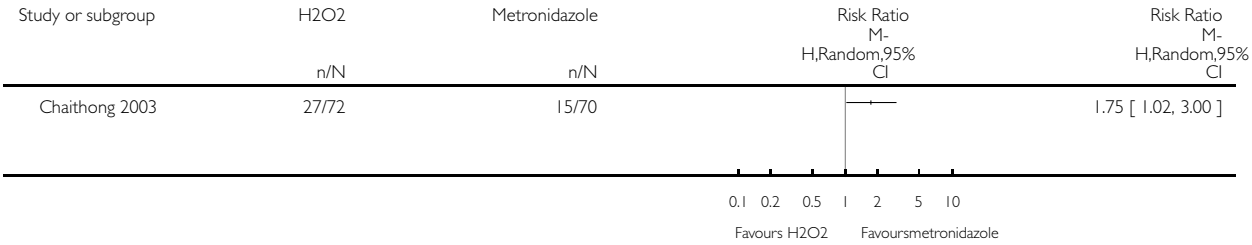


Analysis 11.1. Comparison 11 Single hydrogen peroxide douche versus single dose metronidazole, Outcome 1 Clinical failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 11 Single hydrogen peroxide douche versus single dose metronidazole

Outcome: 1 Clinical failure 1

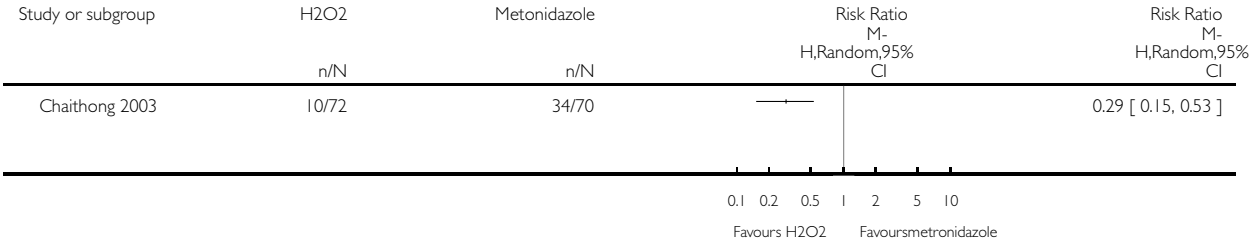


Analysis 11.2. Comparison 11 Single hydrogen peroxide douche versus single dose metronidazole, Outcome 2 Reduced eating/vomitting.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 11 Single hydrogen peroxide douche versus single dose metronidazole

Outcome: 2 Reduced eating/vomitting



Analysis 11.3. Comparison 11 Single hydrogen peroxide douche versus single dose metronidazole, Outcome 3 Vaginal irritation.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 11 Single hydrogen peroxide douche versus single dose metronidazole

Outcome: 3 Vaginal irritation

Study or subgroup	H2O2 n/N	Metronidazole n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Chaithong 2003	24/72	10/70		2.33 [1.21, 4.52]

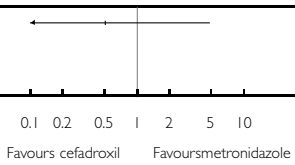
Analysis 12.1. Comparison 12 Cefadroxil versus metronidazole, Outcome 1 Clinical failure.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 12 Cefadroxil versus metronidazole

Outcome: 1 Clinical failure

Study or subgroup	Oral cefadroxil n/N	Oral metronidazole n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Wathne 1989	1/11	2/11		0.50 [0.05, 4.75]

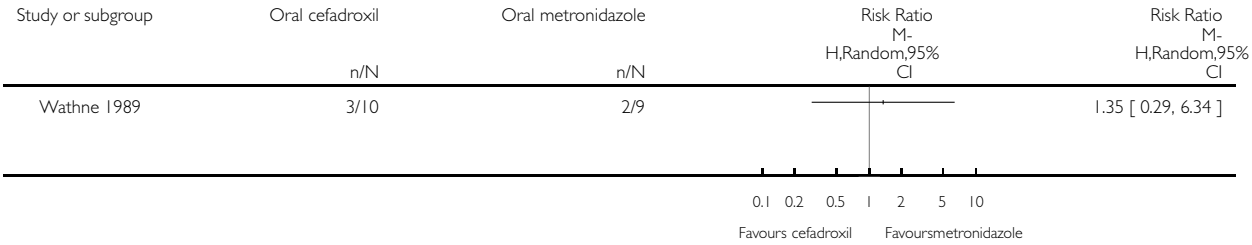


Analysis 12.2. Comparison 12 Cefadroxil versus metronidazole, Outcome 2 Clinical failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 12 Cefadroxil versus metronidazole

Outcome: 2 Clinical failure 2

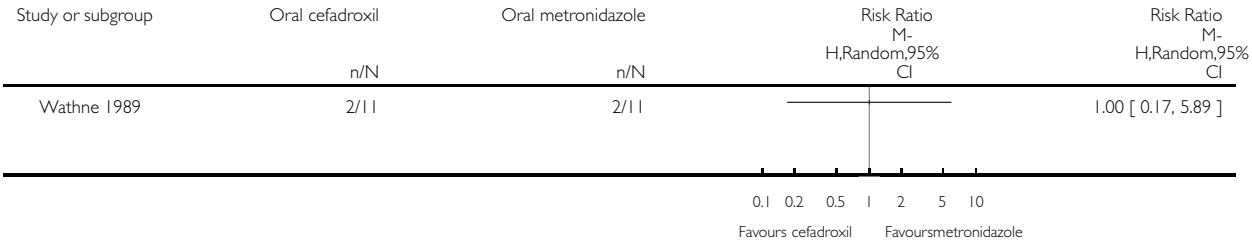


Analysis 12.3. Comparison 12 Cefadroxil versus metronidazole, Outcome 3 Candida infection.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 12 Cefadroxil versus metronidazole

Outcome: 3 Candida infection

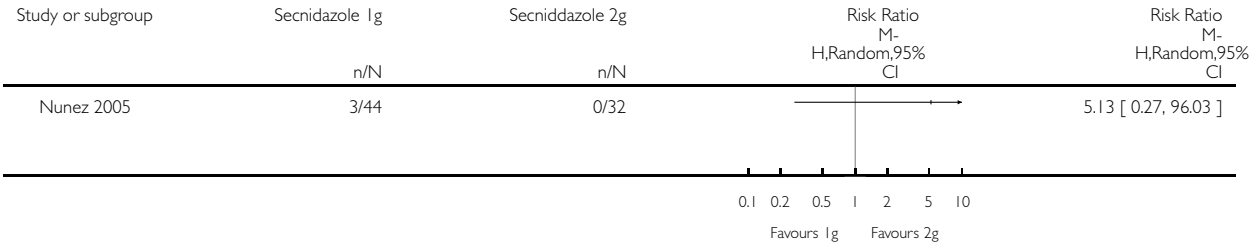


Analysis 13.1. Comparison 13 1g versus 2g secnidazole, Outcome 1 Clinical failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 13 1g versus 2g secnidazole

Outcome: 1 Clinical failure 1

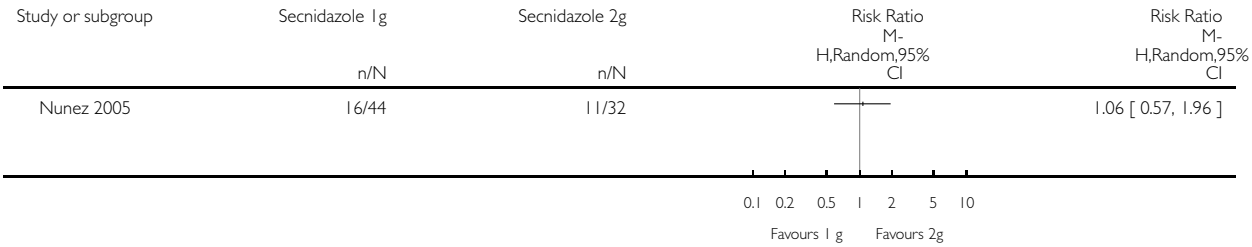


Analysis 13.2. Comparison 13 1g versus 2g secnidazole, Outcome 2 Adverse effects.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 13 1g versus 2g secnidazole

Outcome: 2 Adverse effects



Analysis 14.1. Comparison 14 lactobacillus versus metronidazole, Outcome 1 clinical failure.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 14 lactobacillus versus metronidazole

Outcome: 1 clinical failure

Study or subgroup	lactobacillu n/N	metro n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Anukam 2006b	2/20	8/20		100.0 %	0.25 [0.06, 1.03]
Total (95% CI)	**20**	**20**		**100.0 %**	**0.25 [0.06, 1.03]**
Total events: 2 (lactobacillu), 8 (metro)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.91 (P = 0.056)					

Analysis 14.2. Comparison 14 lactobacillus versus metronidazole, Outcome 2 clinical failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 14 lactobacillus versus metronidazole

Outcome: 2 clinical failure 2

Study or subgroup	lactobbacillu n/N	metro n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Anukam 2006b	3/20	11/20		100.0 %	0.27 [0.09, 0.83]
Total (95% CI)	**20**	**20**		**100.0 %**	**0.27 [0.09, 0.83]**
Total events: 3 (lactobbacillu), 11 (metro)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.28 (P = 0.023)					

Analysis 14.3. Comparison 14 lactobacillus versus metronidazole, Outcome 3 bacteriologic failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 14 lactobacillus versus metronidazole

Outcome: 3 bacteriologic failure 2

Study or subgroup	lactobacillus n/N	metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Anukam 2006a	6/65	17/60		72.1 %	0.33 [0.14, 0.77]
Anukam 2006b	2/20	10/20		27.9 %	0.20 [0.05, 0.80]
Total (95% CI)	**85**	**80**		**100.0 %**	**0.28 [0.14, 0.59]**
Total events: 8 (lactobacillus), 27 (metronidazole)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.34, df = 1 (P = 0.56); I^2 =0.0%					
Test for overall effect: Z = 3.37 (P = 0.00076)					

Analysis 14.4. Comparison 14 lactobacillus versus metronidazole, Outcome 4 bacteriologic failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 14 lactobacillus versus metronidazole

Outcome: 4 bacteriologic failure 1

Study or subgroup	lactobacillus n/N	metronidazole gel n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Anukam 2006b	2/20	8/20		100.0 %	0.25 [0.06, 1.03]
Total (95% CI)	**20**	**20**		**100.0 %**	**0.25 [0.06, 1.03]**
Total events: 2 (lactobacillus), 8 (metronidazole gel)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.91 (P = 0.056)					

Analysis 14.5. Comparison 14 lactobacillus versus metronidazole, Outcome 5 discontinuation.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 14 lactobacillus versus metronidazole

Outcome: 5 discontinuation

Study or subgroup	metro +lactobacillus n/N	metro n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Anukam 2006a	16/65	3/60		100.0 %	4.92 [1.51, 16.06]
Total (95% CI)	**65**	**60**		**100.0 %**	**4.92 [1.51, 16.06]**
Total events: 16 (metro +lactobacillus), 3 (metro)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.64 (P = 0.0082)					

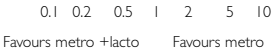
Analysis 14.6. Comparison 14 lactobacillus versus metronidazole, Outcome 6 Headache.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 14 lactobacillus versus metronidazole

Outcome: 6 Headache

Study or subgroup	metro +lactobacillus n/N	metro n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Anukam 2006a	3/65	0/60		100.0 %	6.47 [0.34, 122.71]
Total (95% CI)	**65**	**60**		**100.0 %**	**6.47 [0.34, 122.71]**
Total events: 3 (metro +lactobacillus), 0 (metro)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.24 (P = 0.21)					



Analysis 15.1. Comparison 15 metronidazole vs metronidazole + azithromycin, Outcome 1 clinical failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 15 metronidazole vs metronidazole + azithromycin

Outcome: 1 clinical failure 1

Study or subgroup	metro 7+azth n/N	metro n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Schwebke 2006	33/142	12/44		37.7 %	0.85 [0.48, 1.50]
Schwebke 2006a	19/142	12/44		29.7 %	0.49 [0.26, 0.93]
Schwebke 2006b	23/138	12/44		32.6 %	0.61 [0.33, 1.12]
Total (95% CI)	**422**	**132**		**100.0 %**	**0.65 [0.46, 0.92]**

Total events: 75 (metro 7+azth), 36 (metro)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.66$, df = 2 (P = 0.44); $I^2 = 0.0\%$

Test for overall effect: Z = 2.43 (P = 0.015)

Analysis 15.2. Comparison 15 metronidazole vs metronidazole + azithromycin, Outcome 2 clinical failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 15 metronidazole vs metronidazole + azithromycin

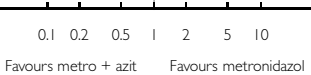
Outcome: 2 clinical failure 2

Study or subgroup	metronidazole + azth n/N	metro n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Schwebke 2006	27/142	8/44		32.1 %	1.05 [0.51, 2.13]
Schwebke 2006a	31/142	8/44		33.3 %	1.20 [0.60, 2.42]
Schwebke 2006b	36/138	8/44		34.6 %	1.43 [0.72, 2.85]
Total (95% CI)	**422**	**132**		**100.0 %**	**1.22 [0.82, 1.83]**

Total events: 94 (metronidazole + azth), 24 (metro)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.40$, df = 2 (P = 0.82); $I^2 = 0.0\%$

Test for overall effect: Z = 0.97 (P = 0.33)



Analysis 15.3. Comparison 15 metronidazole vs metronidazole + azithromycin, Outcome 3 bacteriologic failure 1.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 15 metronidazole vs metronidazole + azithromycin

Outcome: 3 bacteriologic failure 1

Study or subgroup	metronidazole+azth n/N	metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Schwebke 2006	23/142	9/44		35.8 %	0.79 [0.40, 1.58]
Schwebke 2006a	15/142	9/44		30.2 %	0.52 [0.24, 1.10]
Schwebke 2006b	20/138	9/44		34.1 %	0.71 [0.35, 1.44]
Total (95% CI)	**422**	**132**		**100.0 %**	**0.67 [0.44, 1.01]**
Total events: 58 (metronidazole+azth), 27 (metronidazole)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.71$, df = 2 (P = 0.70); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.89 (P = 0.058)					

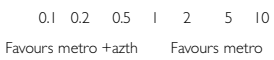
Analysis 15.4. Comparison 15 metronidazole vs metronidazole + azithromycin, Outcome 4 bacteriologic failure 2.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 15 metronidazole vs metronidazole + azithromycin

Outcome: 4 bacteriologic failure 2

Study or subgroup	metronidazole + azth n/N	metronidazole n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Schwebke 2006	14/142	6/44		29.8 %	0.72 [0.30, 1.77]
Schwebke 2006a	22/142	6/44		34.0 %	1.14 [0.49, 2.62]
Schwebke 2006b	29/138	6/44		36.2 %	1.54 [0.68, 3.47]
Total (95% CI)	**422**	**132**		**100.0 %**	**1.11 [0.68, 1.81]**
Total events: 65 (metronidazole + azth), 18 (metronidazole)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.52$, df = 2 (P = 0.47); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.42 (P = 0.68)					

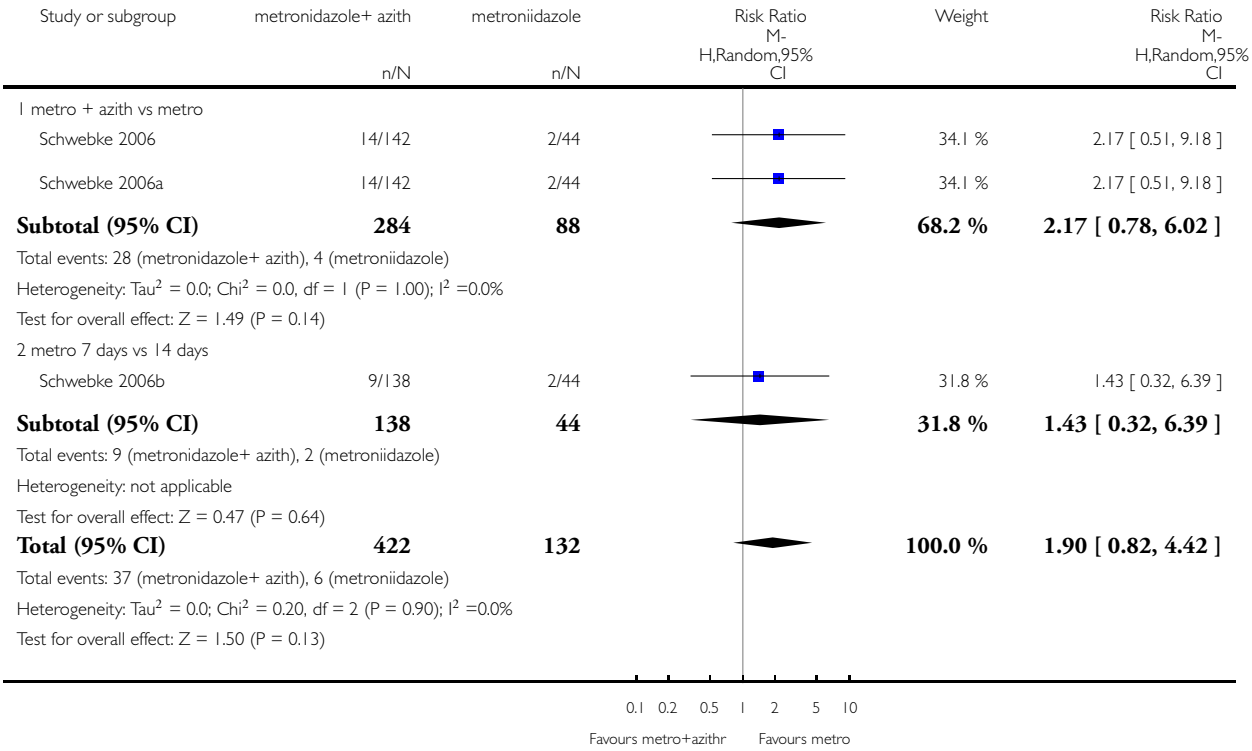


Analysis 15.5. Comparison 15 metronidazole vs metronidazole + azithromycin, Outcome 5 Nausea.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 15 metronidazole vs metronidazole + azithromycin

Outcome: 5 Nausea

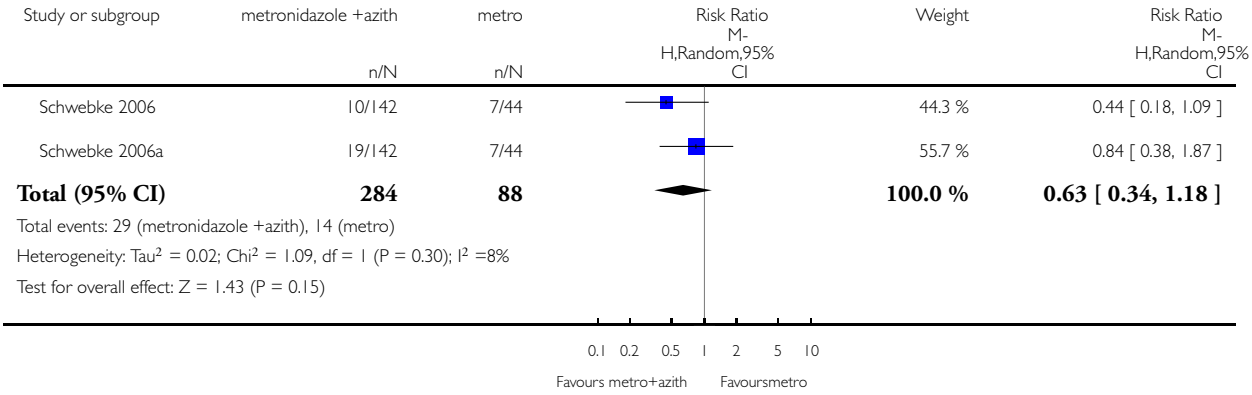


Analysis 15.6. Comparison 15 metronidazole vs metronidazole + azithromycin, Outcome 6 Candida.

Review: The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women

Comparison: 15 metronidazole vs metronidazole + azithromycin

Outcome: 6 Candida



ADDITIONAL TABLES

Table 1. Search strategy

#1	(BACTERIAL VAGINOSIS) OR (VAGINOSIS BACTERIAL) OR (BACTERIAL VAGINITIS)
#2	(BACTERIAL INFECTION) OR (BACTERIAL INFECTIONS)
#3	VAGINITIS OR VAGINOSIS
#4	#2 AND #3
#5	(NONSPECIFIC VAGINITIS) OR (NON-SPECIFIC VAGINITIS) OR (NONSPECIFIC VAGINOSIS) OR (NON-SPECIFIC VAGINOSIS)
#6	#1 OR #4 OR #5
#7	"ANTIMICROBIAL THERAPY" OR "ANTIMICROBIAL TREATMENT"
#8	"ANTIMICROBIAL AGENTS" OR ANTIMICROBIAL* OR ANTIBIOTIC OR ANTIBIOTICS
#9	TREATMENT OR THERAPY
#10	#8 AND #9

Table 1. Search strategy (*Continued*)

#11	#7 OR #10
#12	RANDOMIZED CONTROLLED TRIAL[PT] OR CONTROLLED CLINICAL TRIAL[PT] OR RANDOMIZED CONTROLLED TRIALS[MH] OR CONTROLLED CLINICAL TRIALS[MH]
#13	DOUBLE-BLIND METHOD[MH] OR SINGLE-BLIND METHOD[MH] OR CLINICAL TRIALS[MH] OR "CLINICAL TRIAL"
#14	((SINGL* OR DOUBL* OR TRIPL* OR TREBL*) AND (MASK* OR BLIND*))
#15	PLACEBO[TW] OR PLACEBOS[MH] OR RE DESIGN[MH:NOEXP]
#16	CONTROL[TW] OR PROSPECTIVE*[TW] OR RANDOM*[TW] OR VOLUNTEER*[TW]
#17	#12 OR #13 OR #14 OR #15 OR #16
#18	(ANIMALS[TW] OR ANIMAL[MH]) NOT HUMAN[MH]
#19	#17 NOT #18
#20	#6 AND #11 AND #19
#21	PREGNANCY[MH]
#22	#20 NOT #21

APPENDICES

Appendix 1. Detailed search strategies

#1	(BACTERIAL VAGINOSIS) OR (VAGINOSIS BACTERIAL) OR (BACTERIAL VAGINITIS)
#2	(BACTERIAL INFECTION) OR (BACTERIAL INFECTIONS)
#3	VAGINITIS OR VAGINOSIS
#4	#2 AND #3

(*Continued*)

#5	(NONSPECIFIC VAGINITIS) OR (NON-SPECIFIC VAGINITIS) OR (NONSPECIFIC VAGINOSIS) OR (NON-SPECIFIC VAGINOSIS)
#6	#1 OR #4 OR #5
#7	"ANTIMICROBIAL THERAPY" OR "ANTIMICROBIAL TREATMENT"
#8	"ANTIMICROBIAL AGENTS" OR ANTIMICROBIAL* OR ANTIBIOTIC OR ANTIBIOTICS
#9	TREATMENT OR THERAPY
#10	#8 AND #9
#11	#7 OR #10
#12	RANDOMIZED CONTROLLED TRIAL[PT] OR CONTROLLED CLINICAL TRIAL[PT] OR RANDOMIZED CONTROLLED TRIALS[MH] OR CONTROLLED CLINICAL TRIALS[MH]
#13	DOUBLE-BLIND METHOD[MH] OR SINGLE-BLIND METHOD[MH] OR CLINICAL TRIALS[MH] OR "CLINICAL TRIAL"
#14	((SINGL* OR DOUBL* OR TRIPL* OR TREBL*) AND (MASK* OR BLIND*))
#15	PLACEBO[TW] OR PLACEBOS[MH] OR RE DESIGN[MH:NOEXP]
#16	CONTROL[TW] OR PROSPECTIVE*[TW] OR RANDOM*[TW] OR VOLUNTEER*[TW]
#17	#12 OR #13 OR #14 OR #15 OR #16
#18	(ANIMALS[TW] OR ANIMAL[MH]) NOT HUMAN[MH]
#19	#17 NOT #18
#20	#6 AND #11 AND #19
#21	PREGNANCY[MH]
#22	#20 NOT #21
	Search set numbers CENTRAL 43 EMBASE 510 MEDLINE 148 Total 701 Number of records retrieved 53

HISTORY

Protocol first published: Issue 4, 2006

Review first published: Issue 3, 2009

Date	Event	Description
2 July 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

OO Oduyebo: wrote the body of the review, contacted experts for trials and clarification of methods, contacted drug manufacturing companies, screened trials for inclusion, assessed methodical quality, and prepared submission for Cochrane HIV/AIDS Review Group.

R Anorlu: screened trials for inclusion, edited final versions of the protocol, and contributed to the body of the review.

FT Ogunsola: screened trials for inclusion, contacted drug manufacturing companies, edited the final versions of the protocol and review.

DECLARATIONS OF INTEREST

None

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Internal sources

- College of Medicine, University of Lagos, Nigeria.

External sources

- Reviews for Africa Programme Fellowship, South Africa.

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Infective Agents [adverse effects; therapeutic use]; Clindamycin [adverse effects; therapeutic use]; Lactobacillus; Metronidazole [adverse effects; therapeutic use]; Probiotics [therapeutic use]; Randomized Controlled Trials as Topic; Vaginal Douching [adverse effects]; Vaginosis, Bacterial [*therapy]

MeSH check words

Female; Humans