Antibiotic prophylaxis for transrectal prostate biopsy (Review)

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[Intervention Review]

Antibiotic prophylaxis for transrectal prostate biopsy

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Editorial group: Cochrane Prostatic Diseases and Urologic Cancers Group.
Publication status and date: New, published in Issue 5, 2011.
Review content assessed as up-to-date: 30 August 2010.

Citation: Zani EL, Clark OAC, Rodrigues Netto Jr N. Antibiotic prophylaxis for transrectal prostate biopsy. *Cochrane Database of Systematic Reviews* 2011, Issue 5. Art. No.: CD006576. DOI: 10.1002/14651858.CD006576.pub2.

ABSTRACT

Background

Transrectal prostate biopsy (TRPB) is a well established procedure used to obtain tissue for the histological diagnosis of carcinoma of the prostate. Despite the fact that TRPB is generally considered a safe procedure, it may be accompanied by traumatic and infective complications, including asymptomatic bacteriuria (bacteria in the urine), urinary tract infection (UTI), transitory bacteremia (bacteria in the blood), fever episodes, and sepsis (pathogenic microorganisms or their toxins in the blood). Although infective complications after TRPB are well known, there is uncertainty about the necessity and effectiveness of routine prophylactic antibiotics and their adverse effects, as well as a clear lack of standardization.

Objectives

To evaluate the effectiveness and adverse effects of prophylactic antibiotic treatment in TRPB.

Search methods

The search covered the principal electronic databases: MEDLINE, EMBASE, LILACS and the Cochrane Central Register of Controlled Trials (CENTRAL). Experts were consulted and references from the relevant articles were scanned.

Selection criteria

All randomized, controlled trials (RCTs) of men who underwent TRPB and received prophylactic antibiotics or placebo/no treatment, were selected, and all RCTs looking at one type of antibiotic versus another, including comparable dosages, routes of administration, frequency of administration, and duration of antibiotic treatment.

Data collection and analysis

Two reviewers (ELZ, OACC) independently selected included trials and extracted study data. Any disagreements were resolved by a third party (NRNJ).

Main results

Overall, more than 3500 references were considered and 19 original reports with a total of 3599 patients were included.

There were 9 trials analysing antibiotics versus placebo/no treatment, with all outcomes significantly favouring antibiotic use ($P < 0.05$) ($I^2 = 0\%$), including bacteriuria (risk ratio (RR) 0.25 (95% confidence interval (CI) 0.15 to 0.42), bacteremia (RR 0.67, 95% CI

0.49 to 0.92), fever (RR 0.39, 95% CI 0.23 to 0.64), urinary tract infection (RR 0.37, 95% CI 0.22 to 0.62), and hospitalization (RR 0.13, 95% CI 0.03 to 0.55). Several classes of antibiotics were effective prophylactically for TRPB, while the quinolones, with the highest number of studies (5) and patients (1188), were the best analysed. For 'antibiotics versus enema', we analysed four studies with a limited number of patients. The differences between groups for all outcomes were not significant. For 'antibiotic versus antibiotic + enema', only the risk of bacteremia (RR 0.25, 95% CI 0.08 to 0.75) was diminished in the 'antibiotic + enema group'. Seven trials reported the effects of short-course (1 day) versus long-course (3 days) antibiotics. Long course was significantly better than short-course treatment only for bacteriuria (RR 2.09, 95% CI 1.17 to 3.73). For 'single versus multiple dose', there was significantly greater risk of bacteriuria for single-dose treatment (RR 1.98, 95% CI 1.18 to 3.33). Comparing oral versus systemic administration - intramuscular injection (IM), or intravenous (IV) - of antibiotics, there were no significant differences in the groups for bacteriuria, fever, UTI and hospitalization.

Authors' conclusions

Antibiotic prophylaxis is effective in preventing infectious complications following TRPB. There is no definitive data to confirm that antibiotics for long-course (3 days) are superior to short-course treatments (1 day), or that multiple-dose treatment is superior to single-dose.

PLAIN LANGUAGE SUMMARY

Antibiotic prophylaxis for transrectal prostate biopsy

Prostate cancer is the second most commonly diagnosed cancer in men and transrectal prostate biopsy is the procedure to obtain tissue for the histological diagnosis of carcinoma of the prostate. Despite the fact that infective complications after transrectal prostate biopsy are well known, there is uncertainty about the necessity and effectiveness of routine prophylactic antibiotics and a clear lack of standardization in antibiotic prophylaxis for transrectal prostate biopsy. In nine trials we observed that antibiotic prophylaxis is effective in preventing infectious complications (bacteriuria, bacteremia, fever, urinary tract infection, sepsis) and hospitalization following prostate biopsy. Several classes of antibiotics are effective for prophylaxis in prostate biopsy, with the quinolones the best analysed class. There are no definitive data to confirm that antibiotic for long-course is superior to short-course treatment, or that multiple-dose treatment is superior to single-dose treatment.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Antibiotic compared to placebo for patients submitted to transrectal prostate biopsy

Patient or population: patients submitted to transrectal prostate biopsy
Settings: low risk patients
Intervention: Antibiotic
Comparison: placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	placebo	Antibiotic				
Bacteriuria	Study population		RR 0.25 (0.15 to 0.42)	870 (8 studies)	⊕⊕⊕◯ **moderate**[1]	
	148 per 1000	37 per 1000 (22 to 62)				
	Medium risk population					
	261 per 1000	65 per 1000 (39 to 110)				
Bacteremia	Study population		RR 0.67 (0.49 to 0.92)	494 (6 studies)	⊕⊕⊕◯ **moderate**[1]	
	190 per 1000	127 per 1000 (93 to 175)				
	Medium risk population					
	268 per 1000	180 per 1000 (131 to 247)				
Fever	Study population		RR 0.39 (0.23 to 0.64)	820 (9 studies)	⊕⊕⊕◯ **moderate**[1]	

	108 per 1000	**42 per 1000** (25 to 69)			
	Medium risk population				
	67 per 1000	**26 per 1000** (15 to 43)			
UTI	**Study population**		**RR 0.37** (0.22 to 0.62)	1077 (5 studies)	⊕⊕⊕○ **moderate**[2]
	90 per 1000	**33 per 1000** (20 to 56)			
	Medium risk population				
	65 per 1000	**24 per 1000** (14 to 40)			
Hospitalization	**Study population**		**RR 0.13** (0.03 to 0.55)	650 (3 studies)	⊕⊕⊕○ **moderate**[1]
	33 per 1000	**4 per 1000** (1 to 18)			
	Medium risk population				
	130 per 1000	**17 per 1000** (4 to 72)			
Adverse event	**Study population**		**RR 1.62** (0.23 to 11.56)	127 (2 studies)	⊕⊕○○ **low**[2,3]
	16 per 1000	**26 per 1000** (4 to 185)			
	Medium risk population				
	74 per 1000	**120 per 1000** (17 to 855)			

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

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

[1] some studies with unclear allocation concealment and lack of blinding
[2] studies with unclear allocation concealment
[3] few patients and few events - wide confidence interval

BACKGROUND

Description of the condition

Prostate cancer (PCa) is the second most commonly diagnosed cancer in men and represents a significant health problem. Worldwide, more than 900,000 men are diagnosed with prostate cancer every year with an estimated 258,000 deaths in 2008 (Ferlay 2010). Incidence rates of prostate cancer vary by more than 25-fold worldwide and nearly three-quarters of the registered cases occur in economically developed countries (658,000 cases). The highest incidence rates are in Australia/New Zealand (104.2 per 100,000), Western and Northern Europe and North America, largely because the widespread use of prostate-specific antigen (PSA) testing in those regions (Ferlay 2010). In these countries prostate cancer is the most frequently diagnosed cancer among men (ACS 2010; Ferlay 2007).

While screening - by digital rectal examination (DRE) and PSA analysis - has increased detection of early stage prostate cancer, it is not yet known whether early detection and subsequent treatment improves disease-specific morbidity and mortality (Andriole 2009). The American Cancer Society and American Urological Association recommend annual screening (ACS 2009; AUA 2009), while in contrast, the United States Preventive Task Force believes that there is insufficient scientific evidence to recommend it (US Task Force 2008).

Two recent studies evaluated the influence of screening on the rate of death from PCa and obtained different results. The first (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial), conducted in 10 centers in the United States, recruited 76,693 men who underwent PSA tests and DRE versus usual clinical care (which could include screening for PCa) (Andriole 2009). With 7 years of follow up, more men in the screening group were diagnosed with PCa (7.4% versus 6.1%), but cancer mortality was low and equal in both groups (0.13% and 0.11%). The second study, the European Randomized Study of Screening for Prostate Cancer (ERSPC), was conducted in 7 European countries and included 162,243 men followed for a median of 9 years. The men were randomized into two groups: screening (an average of once per 4 years) versus no screening (Schröder 2009). In the screening group the rate of PCa diagnosis was higher (8.2% versus 4.8%) and mortality was 20% lower (0.29% versus 0.36%) relative to the no-screening group, but at the cost of a high rate of overdiagnosis and overtreatment.

The prostate biopsy has evolved from the digitally guided biopsy to the current standard of the transrectal ultrasound-guided systematic biopsy (TRPB) method. The TRPB is a well established out-patient procedure performed to obtain tissue for the histological diagnosis of carcinoma of the prostate in men with either an elevated, or rising, PSA, or an abnormal DRE that raises suspicions of prostate cancer (Hodge 1989a; Sruogis 2005).

Description of the intervention

Despite the fact that TRPB is generally considered a safe procedure, it may be accompanied by traumatic and infective complications, the latter including asymptomatic bacteriuria, urinary tract infection, transitory bacteremia, fever episodes, and sepsis (Crawford 1982; Isen 1999a; Aron 2000a). Although infective complications after TRPB are well known and rarely fatal (Breslin 1978; Brewster 1993; Borer 1999), there is no agreement that their treatment by antibiotic prophylaxis is really necessary.

There is significant variability in the reported infection rates after TRPB. Historically, the use of larger gauge needles (14 gauge) to perform the biopsy was associated with infection rates of 2% to 79%, but, with thinner needles, rates from 0% to 37%, irrespective of the use of antibiotics (Aron 2000a; Fong 1991; Enlud 1997; Roach 1991; Freitas 1999; Ruebush 1979; Shigemura 2005).

The need for prophylaxis has been questioned by several authors, who note the incidence of post-procedural bacteremia is relatively low, usually transient, and resolves without additional therapy (Enlud 1997; Wendel 1967; Astraldi 1937). In one prospective study (N = 415), patients who underwent TRPB with no antibiotic prophylaxis had an infection complication rate of 2.9% (Enlud 1997).

Even among those who use antibiotic prophylaxis there is much variability in the type, dose, frequency of administration, and duration of treatment. Some reviews that surveyed radiology and urology departments that regularly undertook TRPB have shown a total of 48 different regimens utilizing 13 different antibiotics (Taylor 1997; Shandera 1998), ranging from a single oral dose of ciprofloxacin before TRPB, to intravenous cefuroxime and rectal metronidazole before the procedure, followed by oral cephalexin for 5 days.

How the intervention might work

Recent studies, including randomized, controlled trials comparing the use of antibiotic versus placebo/no treatment in TRPB, have shown that antibiotic prophylaxis results in a lower incidence of post-biopsy febrile episodes, positive urine cultures, and bacteremia (Yang 2001a; Aron 2000a; Freitas 1999; Isen 1999a; Kapoor 1998).

Several prospective, randomized trials have examined the value of different types of antibiotics and different regimens of antibiotic prophylaxis in TRPB, with variable results (Cormio 2002; Petteffi 2002; Sabbagh 2004; Isen 1999a). These data confirm that there is a clear lack of standardization in antibiotic prophylaxis for transrectal prostate biopsy with widely varying costs for each of the different regimens.

Why it is important to do this review

The need for prophylaxis has been questioned by some authors (Enlud 1997; Wendel 1967) and several studies included a placebo group versus use of antibiotic (Tekdogan 2006; Wang 2004; Yang 2001a; Aron 2000a), demonstrating doubt about the effectiveness of prophylactic antibiotics. Among studies that used antibiotic prophylaxis there is much variability in the type, dose, frequency of administration, and duration of treatment of antibiotics, with conflicting results. Therefore, a systematic review is necessary to evaluate whether antibiotic prophylaxis is necessary for TRPB, and if so, what is the most effective and safest method.

This systematic review evaluated the effectiveness of antibiotic prophylaxis in reducing the risk of infective complications following TRPB, with no restriction of language. The review also evaluated what should be the antibiotic of choice for prophylaxis in TRPB.

OBJECTIVES

The objectives of this review were:

- to evaluate the effectiveness of antibiotic prophylaxis in reducing the risk of infective complications following TRPB (bacteriuria, bacteremia, fever, urinary tract infection);
- to evaluate what should be the antibiotic of choice for prophylaxis in transrectal prostate biopsy, including dosage, route of administration, frequency of administration and duration of treatment.

METHODS

Criteria for considering studies for this review

Types of studies

All randomized, controlled trials (RCT) in which patients received TRPB and prophylactic antibiotics versus placebo/no treatment, and all RCTs looking at one type of antibiotic versus another, compared dosage, route of administration, frequency of administration, or duration of treatment.

Types of participants

Inclusion criteria

Male patients who required TRPB and received prophylactic antibiotics or placebo/no treatment.

Exclusion criteria

- history of hypersensitivity to antibiotic in study
- significant gastrointestinal disease or inability to tolerate oral medication
- presence of culture-proven urinary tract infection prior to intervention
- presence of indwelling bladder catheters
- history of endoscopic manipulation of the urinary tract within 7 days prior to the study enrollment
- antibiotic(s) given during the preceding 10 days
- patients with prostheses (e.g. hip replacement, prosthetic cardiac valves) and congenital heart disease requiring prophylactic antibiotics

Subgroups

Patients with co-morbid conditions potentially immunosuppressive (and thus prone to infections), such as diabetes, renal failure, chronic corticosteroids use, and immunodeficiency conditions.

Types of interventions

- antibiotic versus placebo or no treatment
- antibiotic class A (quinolones, sulfonamides, aminoglycosides, cephalosporins, β-lactamase inhibitors, metronidazole) versus class B (quinolones, sulfonamides, aminoglycosides, cephalosporins, β-lactamase inhibitors, metronidazole)
- single-dose versus multiple-dose treatment
- short-course (one day) versus long-course treatment (three days)
- oral versus systemic administration (intravenous (IV) and intramuscular (IM))
- antibiotic versus enema

Types of outcome measures

Therapeutic response according to the definition by the authors of each study, analyzing the following variables.

1. Sepsis: SIRS caused by infection (SIRS - defined as two or more of the following: temperature $\geq 38^{o}$ C (centigrade) or less than 36^{o} C; heart rate more than 90 beats/minute; respiratory rate more than 20 breaths/minute or respiratory alkalosis; white blood cell count more than 12,000 or immature forms more than 4000 or more than 10%) (Levy 2002)
2. Fever (temperature > 37.5^{o} C)
3. Bacteremia: defined as the presence of bacteria in blood culture, accessed due to protocol blood collection, irrespective of clinical signs
4. Bacteriuria: the presence of bacteria in the urine in the post-procedure period and/or culture proven (presence of any uropathogen not present previously and/or colony forming units

(CFU) > 100,000/mL) (millilitres) in the absence of clinical signs of infection, diagnosed due to protocol urine collection

5. UTI: bacteriuria on post-procedure period associated with clinical signs of UTI (dysuria, frequency, urgency)

Primary outcomes

1. Bacteriuria
2. Bacteremia
3. Fever
4. Urinary tract infection
5. Sepsis

Secondary outcomes

1. Mortality
2. Hospitalization due to infective complications
3. Adverse effects of antibiotics (gastrointestinal, allergic)

Search methods for identification of studies

Electronic searches

Strategies of search for electronic databases: for MEDLINE we used the methodological search strategy for RCTs, previously reported (Robinson 2002); for EMBASE we used adaptations of this same strategy, previously reported (Lefebvre 1996); for LILACS we used the methodological search strategy previously reported by one of the reviewers (Castro 1999).

There was no restrictions for language.

Relevant trials were obtained from the following sources:

- the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* (Issue 1, 2008 to Issue 1, 2010);
- MEDLINE (1966 to 2010);
- EMBASE (1980 to 2010);
- LILACS (1980 to 2010).

To the methodological search strategy of each database we added the specific terms pertinent to this review as free text and MeSH terms.

1. methodological search strategy
2. PROSTATE/ all subheadings
3. prostat*
4. #2 or #3
5. BIOPSY/ all subheadings
6. biops*
7. #5 or #6
8. #4 and #7
9. ANTI-INFECTIVE AGENTS/ all subheadings
10. ANTI-INFECTIVE AGENTS, LOCAL/
11. ANTIPARASITIC AGENTS/
12. ANTIVIRAL AGENTS/
13. DISINFECTANTS/
14. ANTIFUNGAL AGENTS/
15. #10 or #11 or #12 or #13 or #14
16. #9 not #15
17. ANTIBIOTIC-PROPHYLAXIS/ all subheadings
18. antibiot*
19. antimicr*
20. prophyla*
21. prevent*
22. #16 or #17 or #18 or #19 or #20 or #21
23. #8 and #22
24. #1 and #23
25. INFECTION/ all subheadings
26. infect*
27. #25 or #26
28. #8 and #27
29. #1 and #28
30. FEVER/ all subheadings
31. pyrex*
32. #30 or #31
33. #8 and #32
34. #1 and #33

Searching other resources

- reference lists of urology textbooks, review articles and relevant trials (All references of relevant articles were scanned and all additional articles of potential interest were retrieved for further analysis.)
- reference lists of abstracts from urology scientific meetings
- letters seeking information about unpublished or incomplete trials to investigators known to be involved in previous studies

Data collection and analysis

Selection of studies

All potential trials' titles and abstracts were read by two reviewers independently, and were selected for eligibility according to the criteria specified in the protocol. Each of these articles was read by reviewers who evaluated for inclusion. If the article did not fit the inclusion criteria, the reasons for exclusion were detailed (see 'Characteristics of included studies' and 'Characteristics of excluded studies' tables). Any discrepancies were resolved by discussion, or by input of a third party.

Data extraction and management

For each included article a careful analysis and an attentive reading was done to extract data. A specific formulary for data extraction

was created and submitted to a pre-test with three studies of the same area, but not included in this review. There was no detection of any failure or ambiguity and the formulary was approved for use in the major search.

Two of the reviewers independently extracted the data from the articles (ELZ, OACC). Data were extracted on the selected clinical outcomes, methodological characteristics, and demographics of participants.

Assessment of risk of bias in included studies

The methodological quality of each selected trial was assessed by the same two reviewers (ELZ, OACC). Criteria assessed were the generation and concealment of the sequence of randomization, blinding (investigators, participants, outcome assessors and data analysis), intention-to-treat analysis, use of placebo, completeness of follow up and source of funding.

Trials were assessed for methodological quality using the standard Cochrane criteria for allocation concealment.

A - Adequate: randomization method described that does not allow investigator/participant to know or influence the intervention group before an eligible participant entered into the study.

B - Unclear: randomization stated but no information on method used is available.

C - Inadequate: method of randomization used such as alternate medical record numbers or unsealed envelopes; any information in the study which indicated that investigators or participants could influence intervention group.

Only RCTs with allocation concealment classified as score A and B were used in this review.

To assess the possibility of publication bias (Egger 2001) we performed a funnel-plot test (Egger 1997).

Measures of treatment effect

For dichotomous outcome (bacteriuria, bacteremia, fever, UTI, sepsis, hospitalization, death) results were expressed as risk ratios (RR) with 95% confidence intervals (CI). Data were pooled using the fixed-effects model. Heterogeneity was analysed using an I^2 test (Higgins 2003). When there was considerable heterogeneity among the studies ($I^2 > 50\%$), the random-effects model was utilized. When possible, the risk difference with 95% CI was calculated for each adverse effect, either compared to no treatment . If "considerable" heterogeneity was detected ($I^2 > 50\%$), a possible explanation was pursued. If a reasonable cause was found, a separate analysis was performed. If the cause was not apparent and heterogeneity was caused by divergent data in terms of direction of results (i.e. data favouring one or other treatment), we did not pool the data. The studies were included in a meta-analysis using the outcomes presented above. The meta-analysis was performed using the Review Manager 5 package. In case it was not possible to perform a meta-analysis of the data, the results were presented in a descriptive form with individual evaluation of the results of each study.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

A total of 3599 men were randomized. Weighted mean age was 66.6 (14 trials), which ranged from 40 to 94 years (12 trials). Three trials reported racial data, with 81.4% White and 11.3% Black. Nineteen trials reported trial origination (India = 1, China = 1, Turkey = 3, Greece = 1, Italy = 1, France = 1, United Kingdom = 3, United States = 4, Canada = 1, Brazil = 2, multinational = 1). Study discontinuations ranged from 0% to 25%, with an overall mean of 4.7%. Weighted mean follow up was 13.5 days, and ranged from 4 to 28 days.

Nine placebo controlled trials described the effects of antibiotics versus placebo/no treatment in preventing infectious complications following TRPB (Aron 2000a; Aron 2000b; Brown 1981; Crawford 1982; Isen 1999a; Isen 1999b; Kapoor 1998; Melekos 1990; Ruebush 1979; Tekdogan 2006; Yang 2001a; Yang 2001b). Five trials (1229 patients) compared quinolones to placebo (Aron 2000a; Aron 2000b; Isen 1999a; Kapoor 1998; Tekdogan 2006; Yang 2001a; Yang 2001b). Two studies compared quinolones to nitroimidazoles (Aron 2000a and Aron 2000b = tinidazole; Yang 2001a and Yang 2001b = metronidazole). Two trials (189 patients) compared sulfonamides to placebo (Isen 1999b; Ruebush 1979). Two trials (129 patients) compared penicillins to placebo (Melekos 1990 = piperacillin; Crawford 1982 = carbenicillin). One trial (40 patients) compared gentamicin to placebo (Brown 1981). The majority of trials (eight) utilized pre-biopsy enema, except one (Ruebush 1979). Three trials were three-armed studies (Aron 2000a; Aron 2000b; Isen 1999a; Isen 1999b; Yang 2001a; Yang 2001b). One trial (Isen 1999a; Isen 1999b) compared data of two different antibiotics versus placebo, and two trials compared antibiotic short-course and long-course versus placebo (Aron 2000a; Aron 2000b; Yang 2001a; Yang 2001b). Included patients in both groups were low risk patients; excluded patients had predisposing factors for infection (see 'Exclusion criteria').

Four trials (Brown 1981; Freitas 1999; Melekos 1990; Tekdogan 2006) described the effects of antibiotics compared to enemas in preventing infectious complications. Three trials (280 patients) were designed to compared antibiotic versus enema versus antibiotic + enema versus placebo/no treatment (Brown 1981 = gentamicin, povidone iodine enema; Melekos 1990 = piperacillin, povidone iodine enema; Tekdogan 2006 = ciprofloxacin, rifampicin enema). One trial (120 patients) (Freitas 1999) compared antibi-

otic (ciprofloxacin) for 2 days versus antibiotic for 7 days versus antibiotic (2 days) + enema versus enema (sodium biphosphate).
Six trials reported the effects of short-course versus long-course antibiotics (Aron 2000a; Aron 2000b; Briffaux 2009; Cam 2008; Petteffi 2002; Schaeffer 2007; Yang 2001a; Yang 2001b). All studies (1693 patients) compared quinolones for one day versus three days. Five trials (1588 patients) utilized ciprofloxacin (Aron 2000a; Aron 2000b; Briffaux 2009; Cam 2008; Schaeffer 2007 = ciprofloxacin extended release; Yang 2001a; Yang 2001b), and in two studies quinolones were compared to a nitroimidazole antibiotics (Aron 2000a and Aron 2000b = tinidazole; Yang 2001a and Yang 2001b = metronidazole). One trial utilized norfloxacin (Petteffi 2002).
Seven trials reported the effects of single-dose versus multiple-dose treatment (Aron 2000a; Aron 2000b; Bates 1998; Briffaux 2009; Cam 2008; Petteffi 2002; Schaeffer 2007; Yang 2001a; Yang 2001b). Five trials (1588 patients) utilized ciprofloxacin (Aron 2000a; Aron 2000b; Briffaux 2009; Cam 2008; Schaeffer 2007 = ciprofloxacin extended release; Yang 2001a; Yang 2001b), and in two studies quinolones were compared to nitroimidazole antibiotics (Aron 2000a and Aron 2000b = tinidazole; Yang 2001a and Yang 2001b = metronidazole). One trial utilized norfloxacin (Petteffi 2002) and one trial utilized co-amoxiclav (Bates 1998).
Seven trials compared different classes of antibiotics (Brewster 1995; Cam 2008; Cormio 2002; Fong 1991; Isen 1999a; Isen 1999b; Shivde 2002). We performed three subgroup analyses: quinolones versus other antibiotics, sulfonamide versus other antibiotics and piperacillin tazobactam versus other antibiotics.
Quinolones were compared to other antibiotics in three studies (648 patients) (Cam 2008 = ceftriaxone; Cormio 2002 = piperacillin tazobactam; Isen 1999a = sulfonamide). Sulfonamide were compared to other antibiotics in three studies (326 patients) (Fong 1991 = netilmicin-metronidazole; Isen 1999b = ofloxacin; Shivde 2002 = gentamicin). Piperacillin tazobactam were compared to other antibiotics in two studies (247 patients) (Brewster 1995 = cefuroxime; Cormio 2002 = ciprofloxacin).
Four trials compared oral versus systemic administration with 754 patients (Cam 2008 = ceftriaxone versus ciprofloxacin; Cormio 2002 piperacillin-tazobactam versus ciprofloxacin; Fong 1991 = netilmicin+metronidazole versus sulfonamide; Shivde 2002 = gentamicin versus sulfonamide).

Results of the search

Overall, more than 3500 references were scanned and updated to March 2010. Fifty-six were selected for full text analysis and were retrieved. Of these, 37 were excluded for various reasons (see 'Characteristics of excluded studies' table). Nineteen original reports of trials on the role of antibiotic in transrectal prostate biopsy with a total of 3599 patients were included in the final analysis (see the 'Characteristics of included studies' table).

Included studies

See 'Characteristics of included studies'.

Excluded studies

Thirty seven studies were excluded (Akay 2006; Anjum 1996; Argyropoulos 2007; Aus 1993; Aus 1996; Bjerklund 2004; Bosquet Sanz 2006; Carey 2001; Eaton 1981; Eggert 1999; Ferreira 1985; Herranz Amo 1996; Hosokawa 2005; Hotta 2001; Huang 2006; Ito 2002; Janoff 2000; Jeon 2003; Khan 1984; Lindert 2000; Lindstedt 2006; Mari 2007; Meyer 1987; Otrock 2004; Peters 2003; Puig 2006; Rees 1980; Roach 1991; Sabbagh 2004; Saleem 2001; Sharpe 1982; Shigemura 2005; Thompson 1982; Tobias-Machado 2003; Vaz 1994; Wang 2004; Yamamoto 2008). See 'Characteristics of excluded studies' table for details.
The major causes of exclusion were:

- studies not randomized - Anjum 1996; Aus 1993; Carey 2001; Eaton 1981; Eggert 1999; Hosokawa 2005; Huang 2006; Janoff 2000; Jeon 2003; Lindstedt 2006; Otrock 2004; Puig 2006; Rees 1980;
- inadequate randomization - Akay 2006; Hotta 2001; Roach 1991; Shigemura 2005; Tobias-Machado 2003;
- single studies of a determined intervention - Argyropoulos 2007; Ferreira 1985; Vaz 1994; Yamamoto 2008;
- lack of adequate exclusion criteria of patients - Bosquet Sanz 2006; Herranz Amo 1996; Ito 2002; Mari 2007; Meyer 1987; Peters 2003; Sabbagh 2004; Wang 2004 (We tried to contact the authors of these studies for more informations but to no avail.);
- different definitions of short-course and long-course treatment than considered in review protocol - Aus 1996; Ito 2002; Mari 2007.

Risk of bias in included studies

See 'Characteristics of included studies' table, 'Figure 1', 'Figure 2' and 'Summary of findings for the main comparison', 'Summary of findings 2', 'Summary of findings 3', 'Summary of findings 4' for details.

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

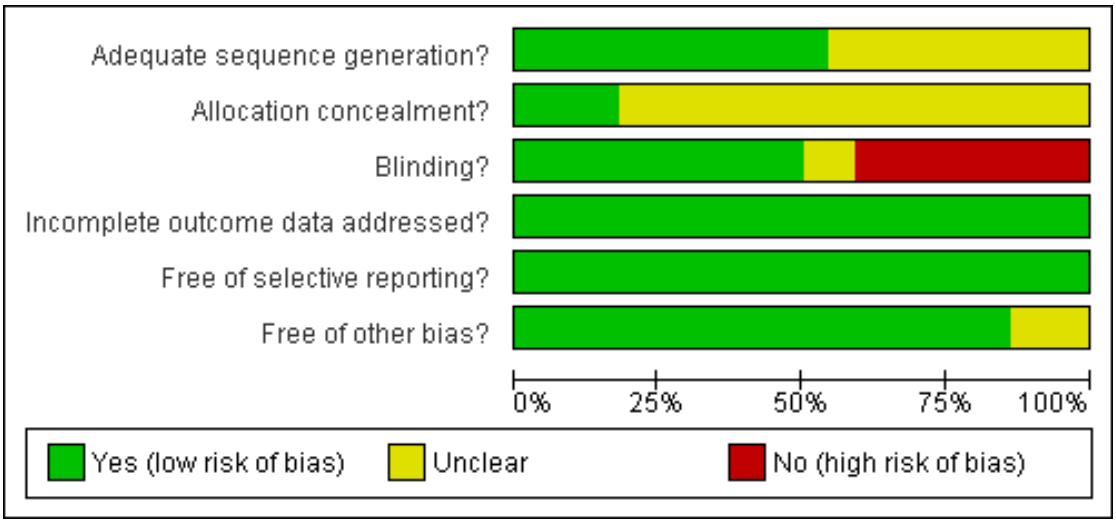
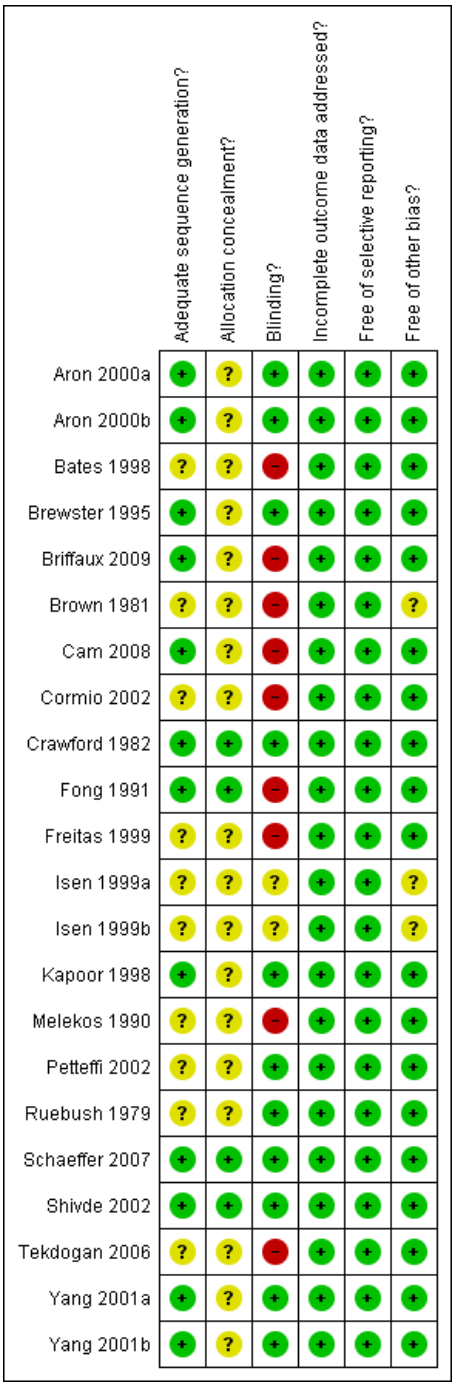


Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Allocation

Ten of the included studies described adequate randomization (Aron 2000a; Aron 2000b; Brewster 1995; Briffaux 2009; Cam 2008; Crawford 1982; Fong 1991; Kapoor 1998; Schaeffer 2007; Shivde 2002; Yang 2001a; Yang 2001b) and five reported an adequate allocation concealment (Crawford 1982; Fong 1991; Ruebush 1979; Schaeffer 2007; Shivde 2002).

Blinding

Six trials were double blinded (Aron 2000a; Aron 2000b; Crawford 1982; Kapoor 1998; Ruebush 1979; Schaeffer 2007; Yang 2001a; Yang 2001b)

Incomplete outcome data

All included studies apparently addressed incomplete outcome data.

Selective reporting

All included studies were apparently free of selective reporting.

Other potential sources of bias

The majority of included studies were apparently free of other potential sources of bias.

Ten trials were placebo controlled (Aron 2000a; Aron 2000b; Brown 1981; Cormio 2002; Crawford 1982; Isen 1999a; Isen 1999b; Kapoor 1998; Melekos 1990; Ruebush 1979; Tekdogan 2006; Yang 2001a; Yang 2001b). A sample size was pre-planned in two studies (Briffaux 2009; Freitas 1999). An intention-to-treat analysis was performed in ten trials (Aron 2000a; Aron 2000b; Briffaux 2009; Cam 2008; Cormio 2002; Crawford 1982; Freitas 1999; Kapoor 1998; Petteffi 2002; Schaeffer 2007; Yang 2001a; Yang 2001b). Four papers referred to multicentric studies (Briffaux 2009; Kapoor 1998; Ruebush 1979; Schaeffer 2007). Three studies had industry funding (Brewster 1995; Cormio 2002; Schaeffer 2007).

Publication bias was unlikely according to the funnel plots inspection.

Effects of interventions

See: **Summary of findings for the main comparison** Antibiotic compared to placebo for patients submitted to transrectal prostate biopsy; **Summary of findings 2** Short course compared to long course treatment for patients submitted to transrectal prostate biopsy; **Summary of findings 3** Single dose compared to multiple dose antibiotic for patients submitted to transrectal prostate biopsy; **Summary of findings 4** Oral compared to systemic antibiotic (IM or IV) for patients submitted to transrectal prostate biopsy

Our analysis included 19 trials with a total of 3599 patients. Not all articles allowed data extraction for all end points (See 'Table 1' for a more detailed description of the extractable end point of each article and 'Table 2' for included studies in each category of comparison). The outcomes were analysed in each subgroup of intervention.

Antibiotic versus placebo or no treatment

Nine trials compared antibiotic to placebo or no treatment (Aron 2000a; Aron 2000b; Brown 1981; Crawford 1982; Isen 1999a; Isen 1999b; Kapoor 1998; Melekos 1990; Ruebush 1979; Tekdogan 2006; Yang 2001a; Yang 2001b). The majority of trials (eight) utilized pre-biopsy enema, except one (Ruebush 1979). Three trials were three-armed studies. One trial (Isen 1999a; Isen 1999b) presented and compared data of two different antibiotics versus placebo, and two trials presented and compared data of antibiotic short-course and long-course versus placebo (Aron 2000a; Aron 2000b; Yang 2001a; Yang 2001b).

Bacteriuria

Data on bacteriuria could be extracted from 7 trials with 870 patients (1 trial subdivided) (Brown 1981; Crawford 1982; Isen 1999a; Isen 1999b; Kapoor 1998; Melekos 1990; Ruebush 1979; Tekdogan 2006). There were 61 events of bacteriuria among 412 patients randomized to receive placebo and 18 among 458 patients randomized to receive antibiotics. The meta-analysis was significant and favoured antibiotic use (RR 0.25, 95% CI 0.15 to 0.42, $P < 0.05$). No heterogeneity was detected in the analysis ($I^2 = 0\%$) ('Figure 3'). Analysing only trials with pre-biopsy enema, the results were similar (RR 0.28, 95% CI 0.17 to 0.46; $I^2 = 0\%$) ('Figure 4').

Figure 3. Forest plot of comparison: 1 Antibiotic (classes) versus placebo, outcome: 1.1 Bacteriuria.

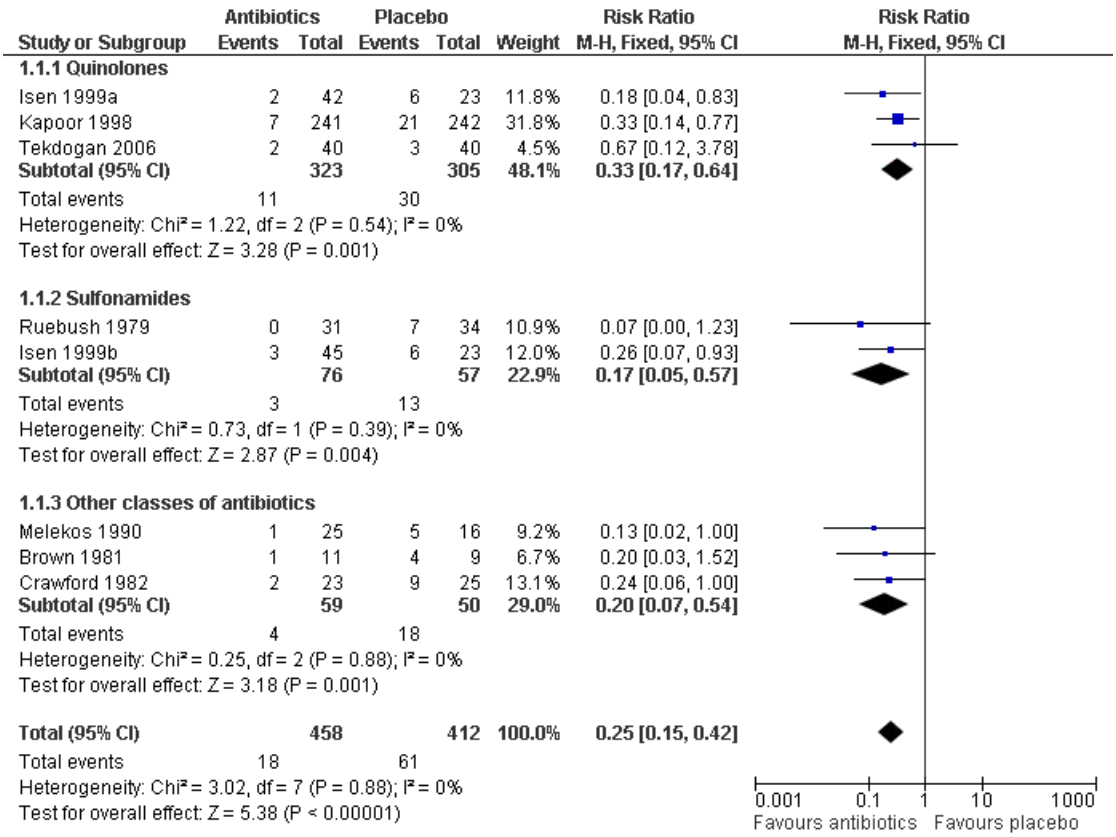
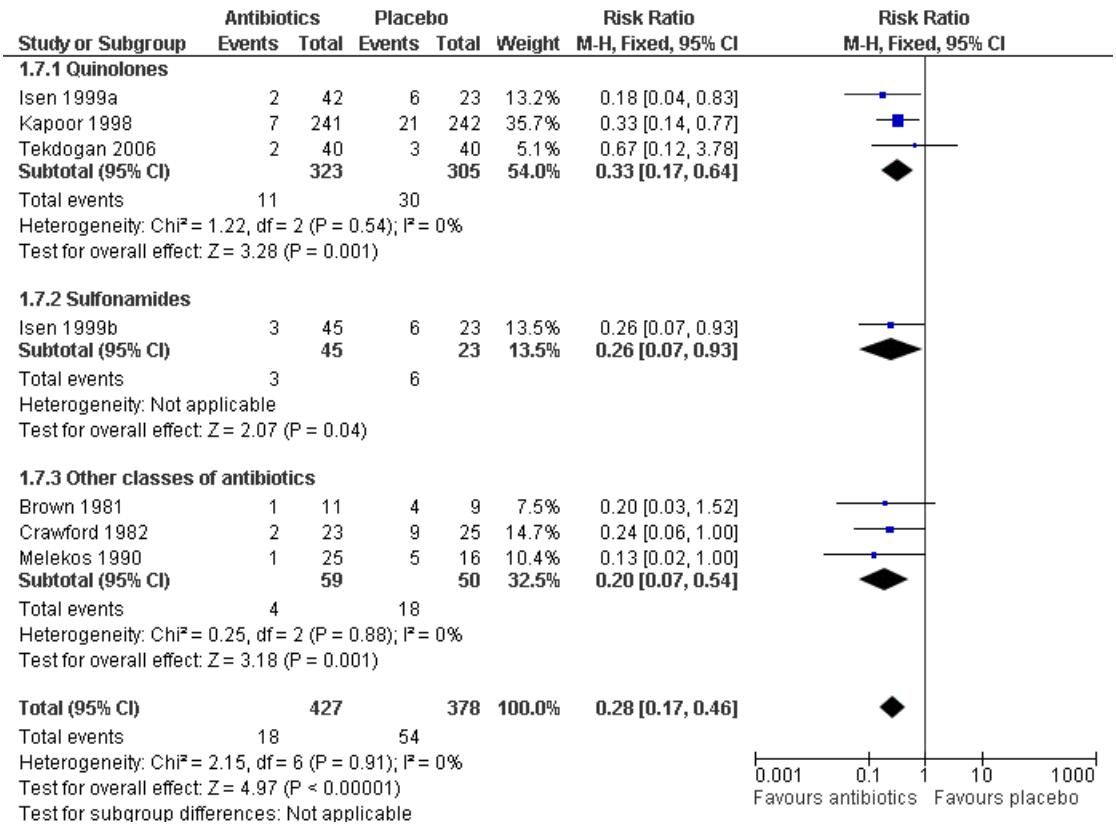


Figure 4. Forest plot of comparison: 1 Antibiotics (classes) versus placebo, outcome: 1.7 Bacteriuria (with pre-biopsy enema).



Bacteremia

We collect data on bacteremia from 5 trials with 494 patients (Aron 2000a; Aron 2000b; Brown 1981; Crawford 1982; Melekos 1990; Ruebush 1979). There were 45 events of bacteremia among 237 patients randomized to placebo and 34 events among 257 patients randomized to receive antibiotic. The comparison was significant and favoured antibiotic use (RR 0.67, 95% CI 0.49 to 0.92, P < 0.05) (I^2 = 40%) ('Figure 5'). Analysing only trials with pre-biopsy enema, the results also favoured antibiotics (RR 0.44, 95% CI 0.22 to 0.87 ;I^2 = 32%) ('Figure 6').

Figure 5. Forest plot of comparison: 1 Antibiotic (classes) versus placebo, outcome: 1.2 Bacteremia.

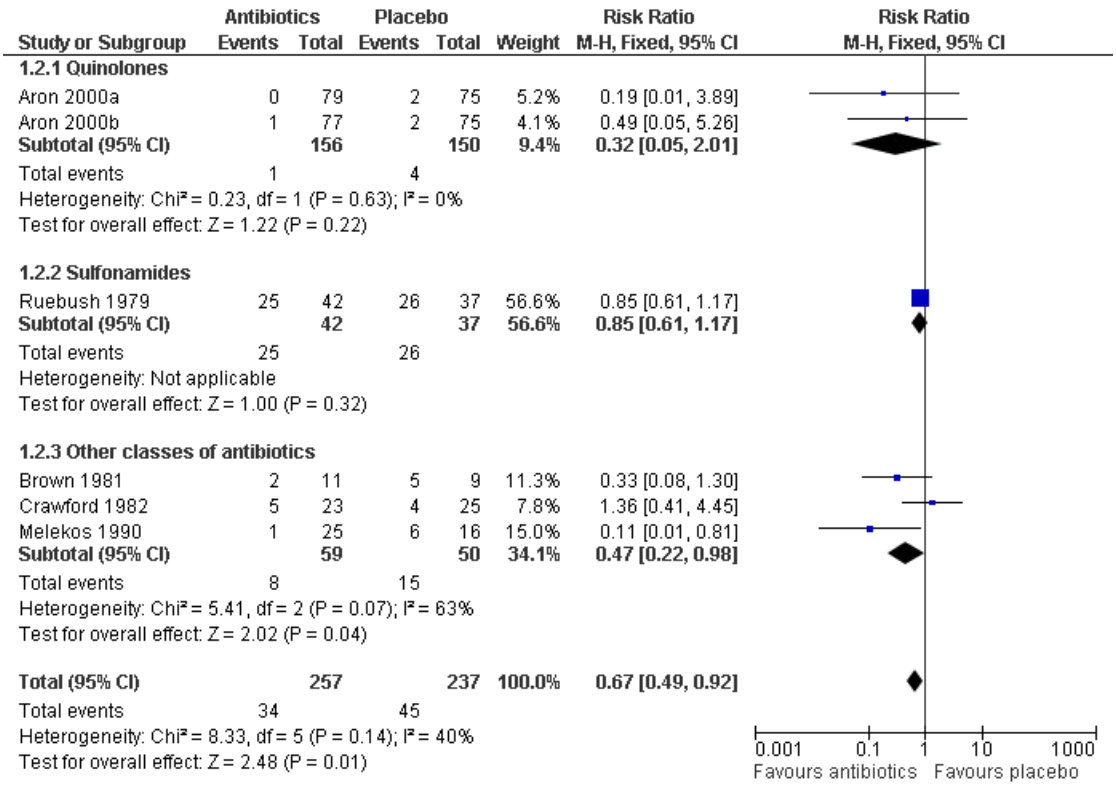
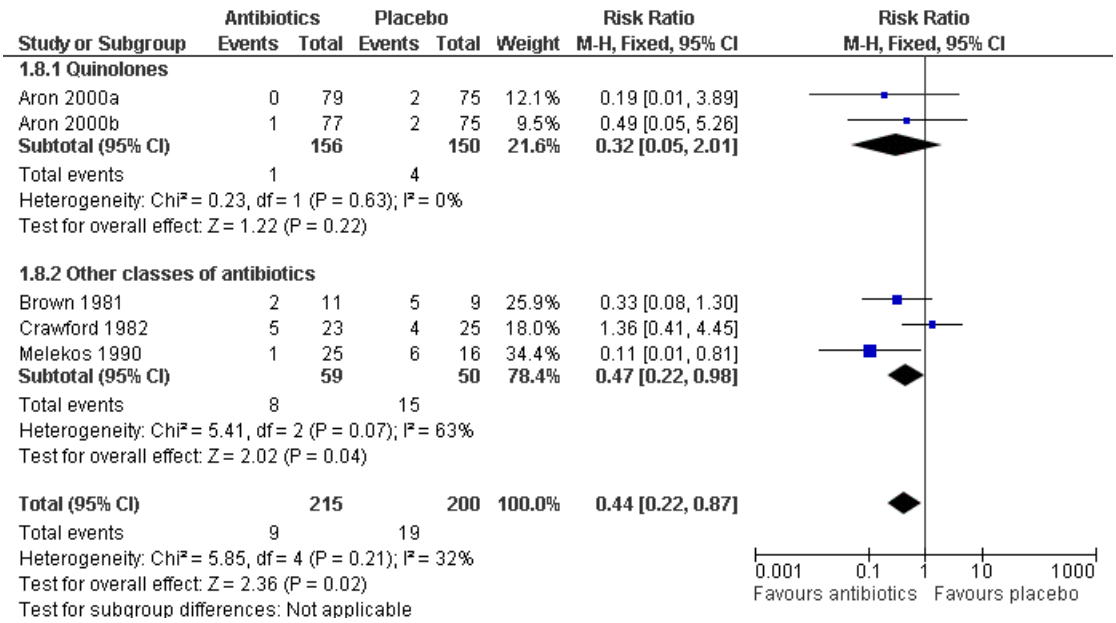


Figure 6. Forest plot of comparison: 1 Antibiotics (classes) versus placebo, outcome: 1.8 Bacteremia (with pre-biopsy enema).



Fever

Data on fever was extracted from 7 trials with 820 patients (Aron 2000a; Aron 2000b; Brown 1981; Crawford 1982; Melekos 1990; Ruebush 1979; Tekdogan 2006; Yang 2001a; Yang 2001b). There were 43 events of fever among 397 patients randomized to placebo and 17 among 423 patients randomized to receive antibiotic. The comparison was significant and favoured antibiotic use (RR 0.39, 95% CI 0.23 to 0.64). No heterogeneity was detected in the analysis (I^2 = 0%) ('Figure 7'). Analysing only trials with pre-biopsy enema, the results were similar and favoured antibiotics (RR 0.34, 95% CI 0.20 to 0.61). No heterogeneity was detected (I^2 = 0%) ('Figure 8').

Figure 7. Forest plot of comparison: 1 Antibiotic (classes) versus placebo, outcome: 1.3 Fever.

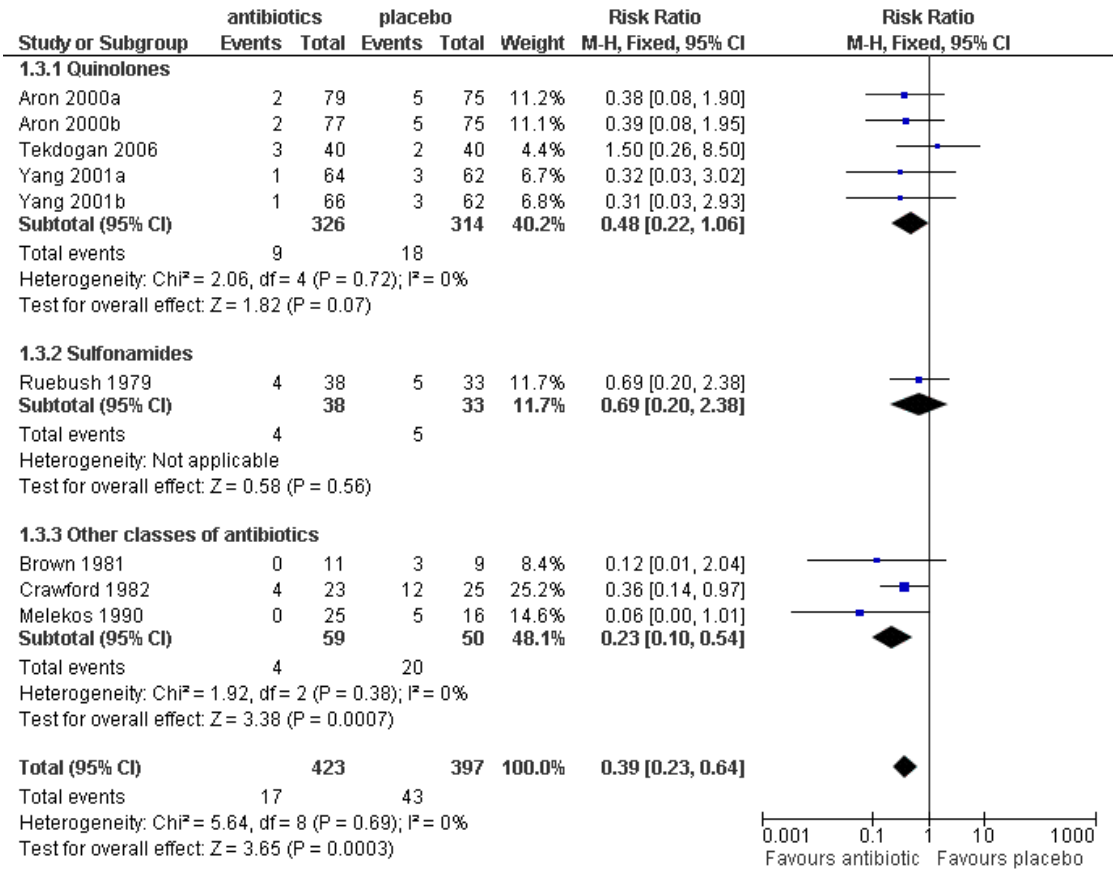
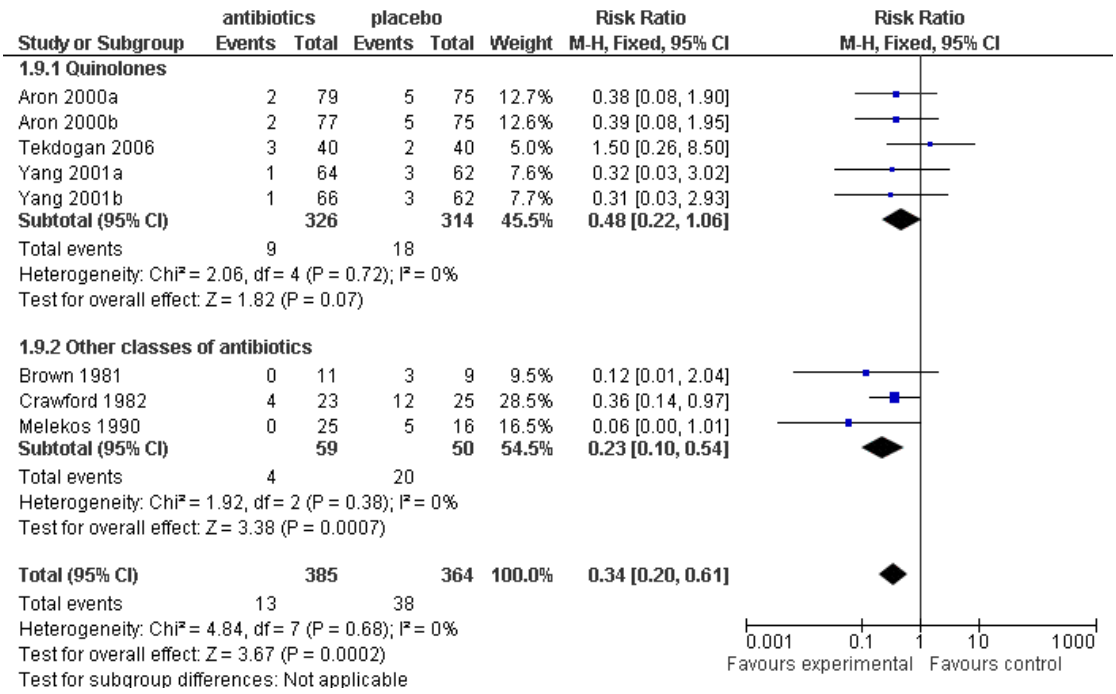


Figure 8. Forest plot of comparison: 1 Antibiotics (classes) versus placebo, outcome: 1.9 Fever (with pre-biopsy enema).

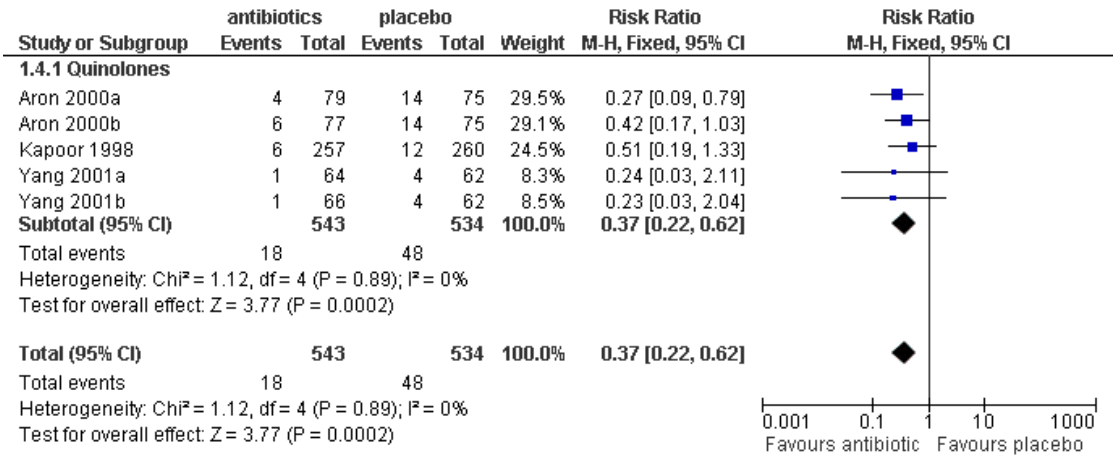


Urinary tract infection

('Figure 9')

We collected data on UTI from 3 trials with 1077 patients (Aron 2000a; Aron 2000b; Kapoor 1998; Yang 2001a; Yang 2001b). There were 48 events among 534 patients randomized to placebo, and 18 among 543 randomized to receive antibiotic. The meta-analysis was significant and favoured antibiotics (RR 0.37, 95% CI 0.22 to 0.62). No heterogeneity was detected in the analysis (I^2 = 0%). All trials used pre-biopsy enemas.

Figure 9. Forest plot of comparison: 1 Antibiotic (classes) versus placebo, outcome: 1.4 UTI.



Sepsis

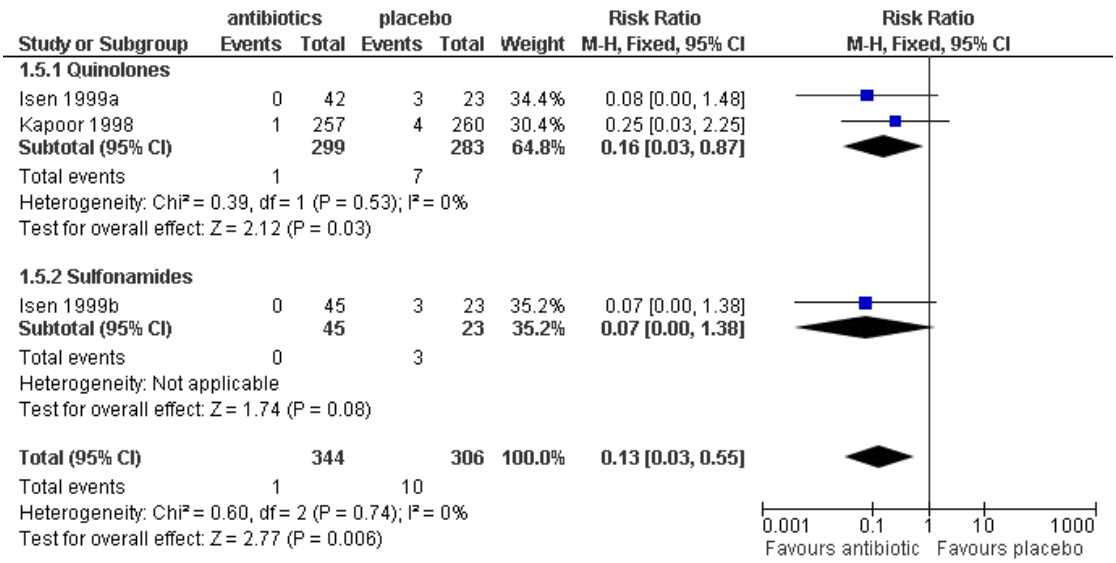
This endpoint was reported in only one study (Crawford 1982). There were 3 events of sepsis among 25 patients randomized to placebo and 1 event among 23 randomized to antibiotic use (RR 0.36, 95% CI 0.04 to 3.24).

Hospitalization

('Figure 10')

Data on hospitalization could be collect from 2 trials (1 trial subdivided) with 650 patients (Isen 1999a; Isen 1999b; Kapoor 1998). There were 10 hospitalizations among the 306 patients randomized to placebo and only 1 among the 344 patients randomized to antibiotics. The comparison was significant and favoured antibiotics (RR 0.13, 95% CI 0.03 to 0.55). No heterogeneity was detected (I^2 = 0%). All trials used pre-biopsy enemas.

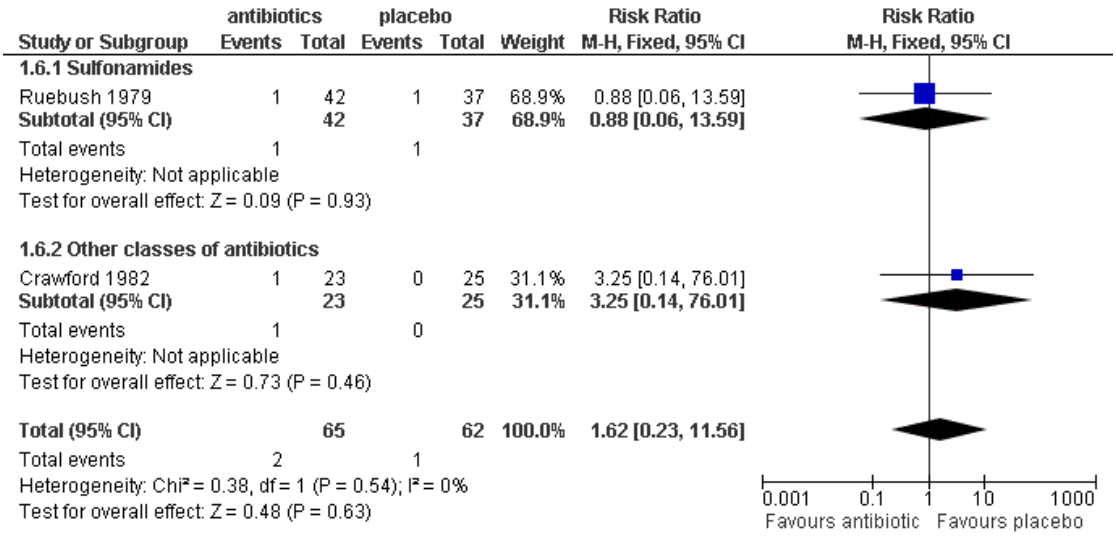
Figure 10. Forest plot of comparison: 1 Antibiotic (classes) versus placebo, outcome: 1.5 Hospitalization.



Adverse effects

('Figure 11')
This endpoint (nausea and abdominal cramps in Crawford 1982, pruritis and diarrhea in Ruebush 1979) was poorly reported among the included studies, and was extracted from only two studies with 127 patients. The comparison was not significant (RR 1.62, 95% CI 0.23 to 11.56), and no heterogeneity was detected (I^2 = 0%).

Figure 11. Forest plot of comparison: 1 Antibiotic (classes) versus placebo, outcome: 1.6 Adverse events.



Mortality

There were no cases of mortality reported in the included studies.

Quinolones versus placebo

Bacteriuria

('Figure 3')
Three trials were included with 628 patients (Isen 1999a; Kapoor 1998; Tekdogan 2006); the meta-analysis favoured quinolones (RR 0.33, 95% CI 0.17 to 0.64; I^2 = 0%).

Bacteremia

('Figure 5')
One trial was included (Aron 2000a; Aron 2000b), with two subgroups (antibiotic short-course and long-course) with 306 patients. The comparison between the groups (quinolones versus placebo) was not significant (RR 0.32, 95% CI 0.05 to 2.01; I^2 = 0%).

Fever

('Figure 7')
Three trials (Aron 2000a; Aron 2000b; Tekdogan 2006; Yang 2001a; Yang 2001b) (two with subgroups) were included with 640 patients. The comparison between the groups (quinolones x placebo) was not significant (RR 0.48, 95% CI 0.22 to 1.06; I^2 = 0%).

UTI

('Figure 9')

Three trials were included (Aron 2000a; Aron 2000b; Kapoor 1998;Yang 2001a; Yang 2001b) with 1077 patients; the comparison favoured quinolones (RR 0.37, 95% CI 0.22 to 0.62; I^2 = 0%).

Hospitalization

('Figure 10')
Two trials were included with 582 patients (Isen 1999a; Kapoor 1998) and favoured quinolones (RR 0.16, 95% CI 0.03 to 0.87; I^2 = 0%).

Sulfonamide versus placebo

Bacteriuria

('Figure 3')
Two studies were included with 133 patients (Isen 1999b; Ruebush 1979) and use of sulfonamide lowered risk relative to placebo (RR 0.17, 95% CI 0.05 to 0.57; I^2 = 0%); only one trial (Ruebush 1979) reported data for bacteremia (26 events in 37 patients in the placebo group versus 25 events in 42 antibiotic patients (RR 0.85 95% CI 0.61 to 1.17), fever (5 events in 33 in the placebo group versus 4 in 38 patients in antibiotic group (RR 0.69 CI 0.20 to 2.38) and adverse events (1 in 37 in placebo versus 1 in 42 in antibiotic group (RR 0.88 95% CI 0.06 to 13.59) and only one trial reported data for hospitalization (Isen 1999b) (3 events among 23 randomized to placebo versus 0 in 45 randomized to antibiotic (RR 0.07, 95% CI 0.00 to 1.38).

Other classes of antibiotics (except quinolones and sulfonamides)

The outcomes analysed were bacteriuria, bacteremia and fever. For adverse events only one trial reported (Crawford 1982). There was 1 event among 23 patients randomized to antibiotic use (diarrhea, nausea and abdominal cramps) versus 0 among 25 randomized to placebo.

Bacteriuria

('Figure 3')
Three studies were included with 109 patients (Brown 1981; Crawford 1982; Melekos 1990) and favoured antibiotic use (RR 0.20, 95% CI 0.07 to 0.54; I^2 = 0%).

Bacteremia

('Figure 5')
Three studies were included with 109 patients (Brown 1981; Crawford 1982; Melekos 1990). The comparison was significant and favoured "other classes" (RR 0.47, 95% CI 0.22 to 0.98, P < 0.05), but with considerable heterogeneity (I^2 = 63%). The heterogeneity is caused by one trial (Crawford 1982), but the reason was not apparent. We then re-analysed the data utilizing random effects, but heterogeneity was still 63%. By eliminating Crawford we eliminated the heterogeneity (fixed effect RR 0.20, 95% CI 0.06 to 0.62; I^2 = 0%).

Fever

('Figure 7')
Three studies were included with 109 patients (Brown 1981; Crawford 1982; Melekos 1990). Use of antibiotics lowered risk of fever (RR 0.23, 95% CI 0.10 to 0.54; I^2 = 0%).

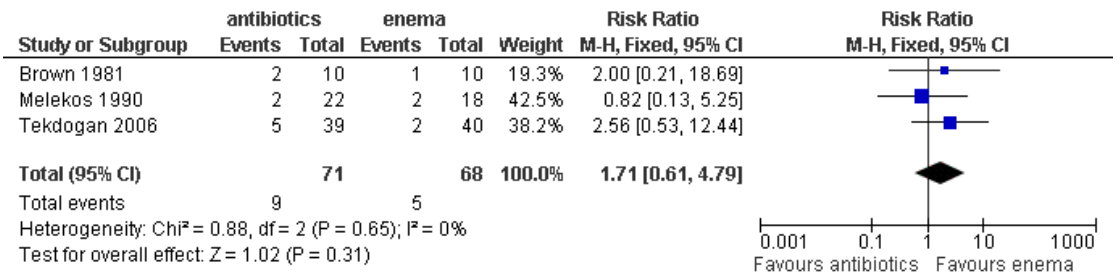
Antibiotic versus enema

Antibiotic was compared with enema in four studies (Brown 1981; Freitas 1999; Melekos 1990; Tekdogan 2006).

Bacteriuria

('Figure 12')
Data on bacteriuria were extracted from 3 trials with 139 patients (Brown 1981; Melekos 1990; Tekdogan 2006). There were 5 events of bacteriuria among 68 patients randomized to enema and 9 among 71 randomized to receive antibiotic. The comparison between the groups was not significant (RR 1.71, 95% CI 0.61 to 4.79; I^2 = 0%).

Figure 12. Forest plot of comparison: 2 Antibiotic versus Enema, outcome: 2.1 Bacteriuria.

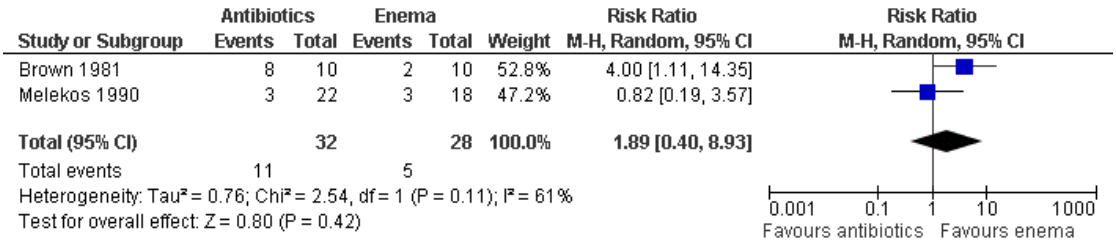


Bacteremia

('Figure 13')

Data on bacteremia were collected from 2 trials with 60 patients (Brown 1981; Melekos 1990). There were 5 events of bacteremia among 28 patients randomized to enema and 11 among 32 randomized to receive antibiotics. The comparison between the groups was not significant (RR 1.89, 95% CI 0.40 to 8.93) (I^2 = 61%) using a random-effects model. There was no explicit cause for the heterogeneity, and the limited number of studies made a sensitivity analysis unviable.

Figure 13. Forest plot of comparison: 2 Antibiotic versus Enema, outcome: 2.2 Bacteremia.

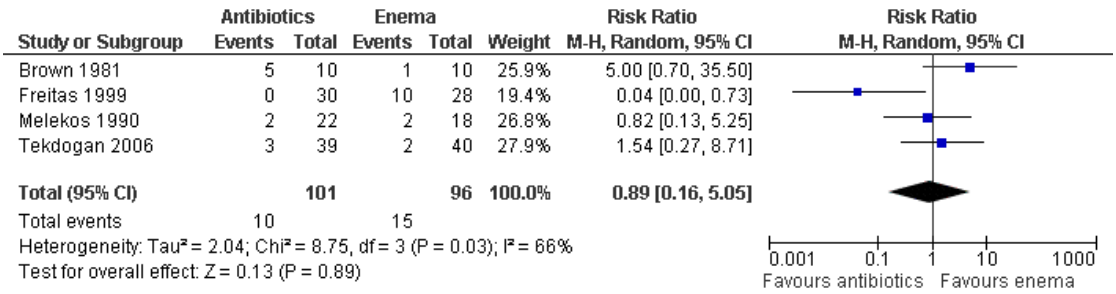


Fever

('Figure 14')

Four trials with 197 patients reported data on fever (Brown 1981; Freitas 1999; Melekos 1990; Tekdogan 2006). There were 15 events of fever among 96 patients randomized to enema and 10 among 101 randomized to receive antibiotic. The comparison between groups was not significant (RR 0.89, 95% CI 0.16 to 5.05) (I^2 = 66%) using a random-effects model. No apparent cause was identified for the heterogeneity and a sensitivity analysis was not viable due to the limited number of studies.

Figure 14. Forest plot of comparison: 2 Antibiotic versus Enema, outcome: 2.3 Fever.



UTI, sepsis and hospitalization

These endpoints were reported in only one study (Freitas 1999). There were 11 events of UTI among 28 patients randomized to enema versus 2 events among 30 randomized to antibiotic use (RR 0.17, 95% CI 0.04 to 0.70); 2 events of sepsis and 2 events of hospitalization in 28 patients in the group taking enemas versus 0 events in the antibiotic group (P > 0.05).

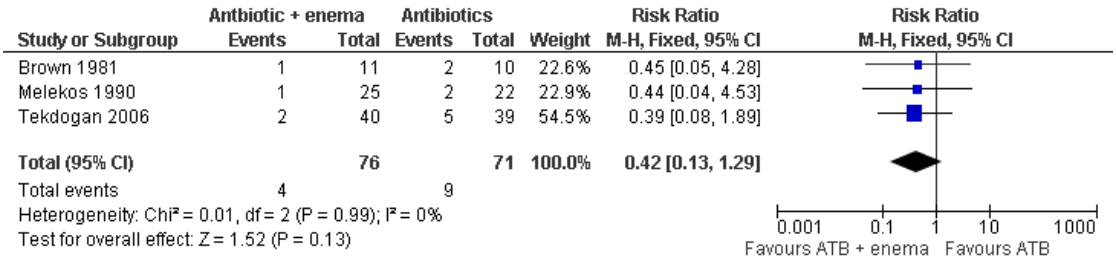
Antibiotic versus antibiotic + enema

This intervention was reported for four trials (Brown 1981; Freitas 1999; Melekos 1990; Tekdogan 2006).

Bacteriuria

('Figure 15')

Figure 15. Forest plot of comparison: 3 Antibiotic versus Antibiotic + Enema, outcome: 3.1 Bacteriuria.



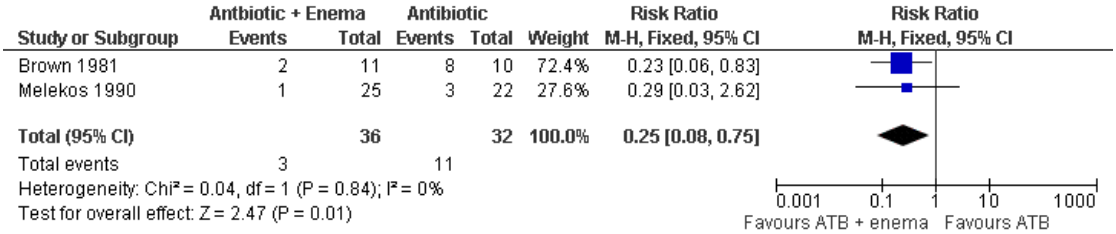
Data on bacteriuria were extracted from 3 trials with 147 patients (Brown 1981; Melekos 1990; Tekdogan 2006). There were 9 events of bacteriuria among 71 patients randomized to antibiotic and 4 among 76 randomized to receive antibiotic + enema. The comparison between the groups was not significant (RR 0.42, 95% CI 0.13 to 1.29; I^2 = 0%).

Bacteremia

('Figure 16')

Data on bacteremia were collected from 2 trials with 68 patients (Brown 1981; Melekos 1990). There were 11 events of bacteremia among 32 patients randomized to antibiotic and 3 among 36 randomized to receive antibiotic + enema. Combination therapy lowered risk relative to monotherapy (RR 0.25, 95% CI 0.08 to 0.75; I^2 = 0%).

Figure 16. Forest plot of comparison: 3 Antibiotic versus Antibiotic + Enema, outcome: 3.2 Bacteremia.

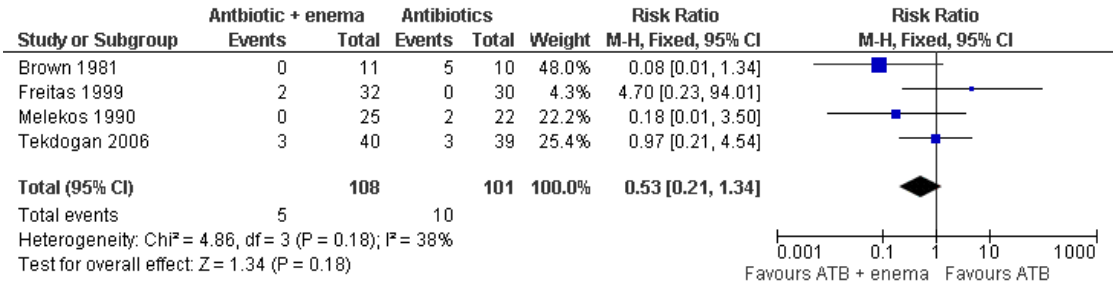


Fever

('Figure 17')

Data on fever were collected from 4 trials with 209 patients (Brown 1981; Freitas 1999; Melekos 1990; Tekdogan 2006). There were 10 events of fever among 101 patients randomized to enema and 5 among 108 randomized to receive antibiotic. The comparison between the groups was not significant (RR 0.53, 95% CI 0.21 to 1.34; I^2 = 38%).

Figure 17. Forest plot of comparison: 3 Antibiotic versus antibiotic + enema, outcome: 3.3 Fever.



Short-course (one day) versus long-course treatment (three days)

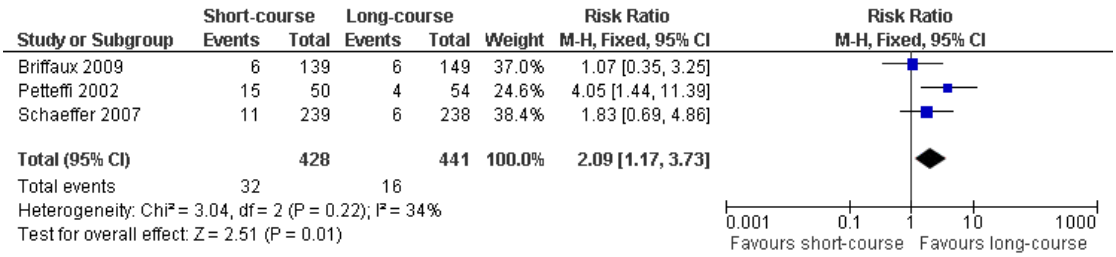
This intervention was reported in six trials (Aron 2000a; Cam 2008; Briffaux 2009; Petteffi 2002; Schaeffer 2007; Yang 2001a).

Bacteriuria

('Figure 18')

Data on bacteriuria were extracted from 3 trials with 869 patients (Briffaux 2009; Petteffi 2002; Schaeffer 2007). There were 32 events of bacteriuria among 428 patients randomized to short-course treatment and 16 among 441 randomized to long-course treatment. The comparison favoured long-course treatment (RR 2.09, 95% CI 1.17 to 3.73; I^2 = 34%).

Figure 18. Forest plot of comparison: 4 Short-course treatment versus long-course treatment, outcome: 4.1 Bacteriuria.



Bacteremia

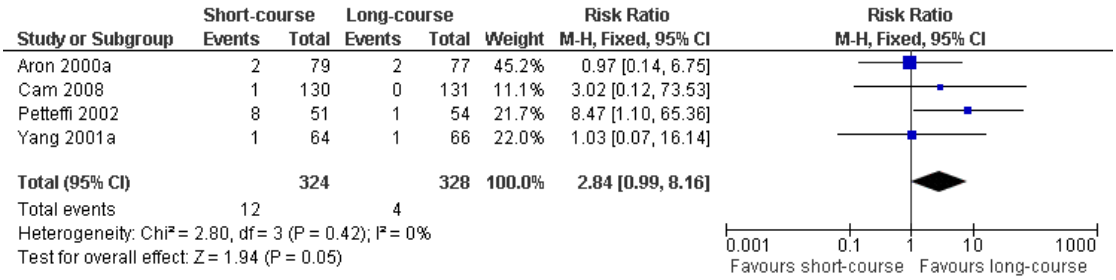
Data on bacteremia were collected from 1 trial with 156 patients (Aron 2000a). There was no events among 79 patients randomized to short-course treatment and 1 among 77 randomized to long-course treatment (RR 0.33, 95% CI 0.01 to 7.86).

Fever

('Figure 19')

Data on fever were collected from 4 trials with 652 patients (Aron 2000a; Cam 2008; Petteffi 2002; Yang 2001a). There were 12 events of fever among 324 patients randomized to short-course treatment and 4 among 328 randomized to long-course treatment. The comparison between the groups was not significant (RR 2.84, 95% CI 0.99 to 8.16), and with no heterogeneity (I^2 = 0%).

Figure 19. Forest plot of comparison: 4 Short-course treatment versus long-course treatment, outcome: 4.3 Fever.

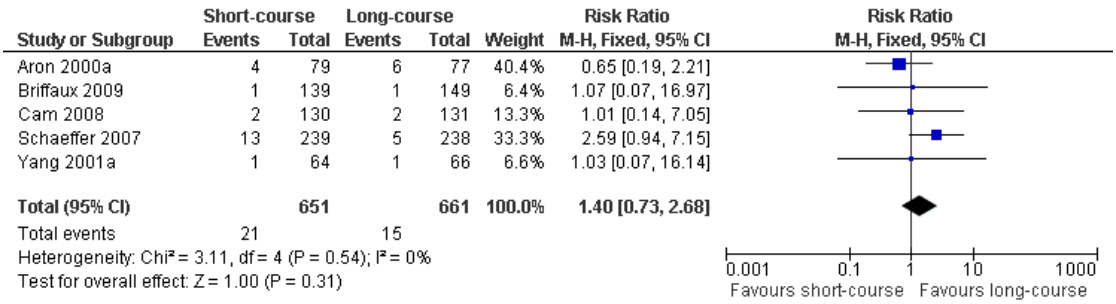


Urinary tract infection

('Figure 20')

From 5 trials that included 1312 patients were collected data on UTI (Aron 2000a; Briffaux 2009; Cam 2008; Schaeffer 2007; Yang 2001a). There were 21 events of UTI among 651 patients randomized to short-course treatment and 15 among 661 randomized to long-course treatment. The comparison between the groups was not significant (RR 1.40, 95% CI 0.73 to 2.68) and no heterogeneity was detected (I^2 = 0%).

Figure 20. Forest plot of comparison: 4 Short-course treatment versus long-course treatment, outcome: 4.4 UTI.

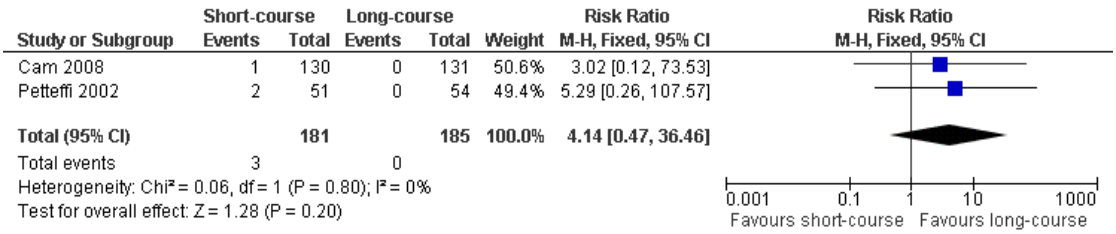


Hospitalization

('Figure 21')

Data on hospitalization was extracted from 2 trials with 366 patients (Cam 2008; Petteffi 2002). There were 3 events among 181 patients randomized to short-course treatment and 0 among 185 randomized to long-course treatment. The comparison between the groups was not significant (RR 4.14, 95% CI 0.47 to 36.46) and with no heterogeneity (I^2 = 0%).

Figure 21. Forest plot of comparison: 4 Short-course treatment versus long-course treatment, outcome: 4.5 Hospitalization.



Single dose versus multiple dose treatment

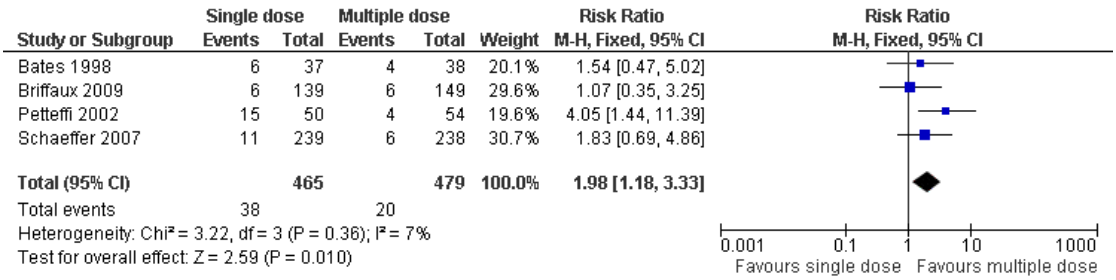
This intervention was reported in 7 trials (Aron 2000a; Bates 1998; Briffaux 2009; Cam 2008; Petteffi 2002; Schaeffer 2007; Yang 2001a).

Bacteriuria

('Figure 22')

We were able to collect data on bacteriuria from 4 trials with 944 patients (Bates 1998; Briffaux 2009; Petteffi 2002; Schaeffer 2007). There were 38 events among 465 patients randomized to single-dose treatment and 20 among 479 randomized to multiple-dose treatment. The comparison favoured multiple-dose treatment (RR 1.98; 95% CI 1.18 to 3.33) (I^2 = 7%).

Figure 22. Forest plot of comparison: 5 Multiple dose versus single dose, outcome: 5.1 Bacteriuria.



Bacteremia

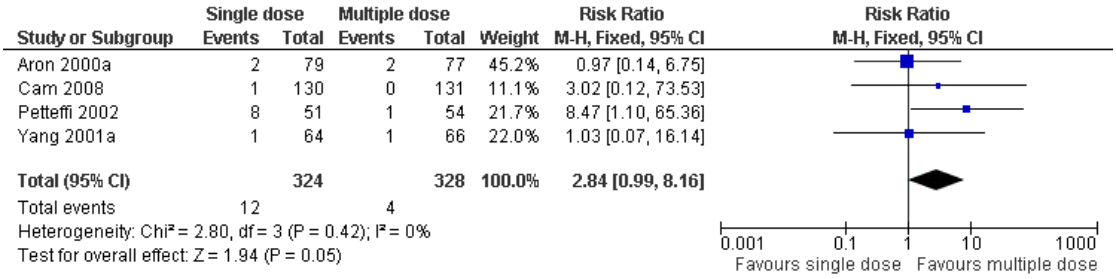
Data on bacteremia could be extracted from 1 trial with 156 patients (Aron 2000a). There were no events among 79 patients randomized to single-dose treatment and 1 among 77 of those randomized to multiple-dose treatment (RR 0.33, 95% CI 0.01 to 7.86).

Fever

('Figure 23')

We collected data on fever from 4 trials with 652 patients (Aron 2000a; Cam 2008; Petteffi 2002; Yang 2001a). There were 12 events among 324 patients randomized to single-dose treatment and 4 among 328 of those randomized to multiple-dose treatment. The comparison between the groups was not significant (RR 2.84, 95% CI 0.0.99 to 8.16) and with no heterogeneity (I^2 = 0%).

Figure 23. Forest plot of comparison: 5 Multiple dose versus single dose, outcome: 5.3 Fever.

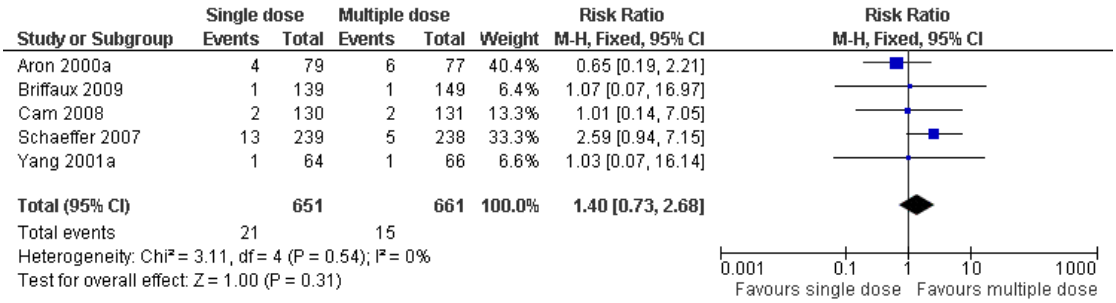


Urinary tract infection

('Figure 24')

Data on UTI was extracted from 5 trials with 1312 patients (Aron 2000a; Briffaux 2009; Cam 2008; Schaeffer 2007; Yang 2001a). There were 21 events among 651 patients randomized to single-dose treatment and 15 among 661 of those randomized to multiple-dose treatment. The comparison between the groups was not significant (RR 1.40, 95% CI 0.73 to 2.68), and no heterogeneity (I^2 = 0%).

Figure 24. Forest plot of comparison: 5 Multiple dose versus single dose, outcome: 5.4 UTI.



Sepsis

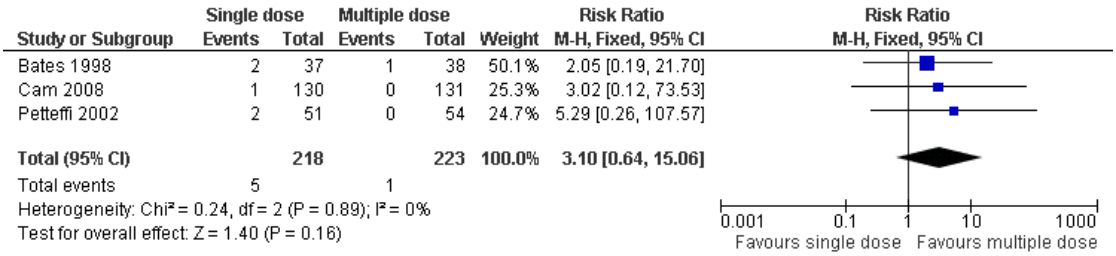
This endpoint was reported in only one study (Bates 1998). There were 2 events of sepsis among 37 patients in single dose group versus 1 event of sepsis among 38 in group multiple dose treatment (P > 0.05).

Hospitalization

('Figure 25')

Data on hospitalization was collected from 3 trials with 441 patients (Bates 1998; Cam 2008; Petteffi 2002). There were 5 hospitalizations among 218 patients randomized to single-dose treatment and 1 among those 223 patients randomized to multiple-dose treatment. The comparison between the groups was not significant (RR 3.10, 95% CI 0.64 to 15.06), and no heterogeneity was detected (I^2 = 0%).

Figure 25. Forest plot of comparison: 5 Multiple dose versus single dose, outcome: 5.5 Hospitalization.



Antibiotic class A versus B

Included in this section were studies that compared different types of antibiotics, subdivided into classes of antibiotics. We performed three subgroup analyses: quinolone versus other antibiotics; sulfonamide versus other antibiotics; and piperacillin tazobactam versus other antibiotics.

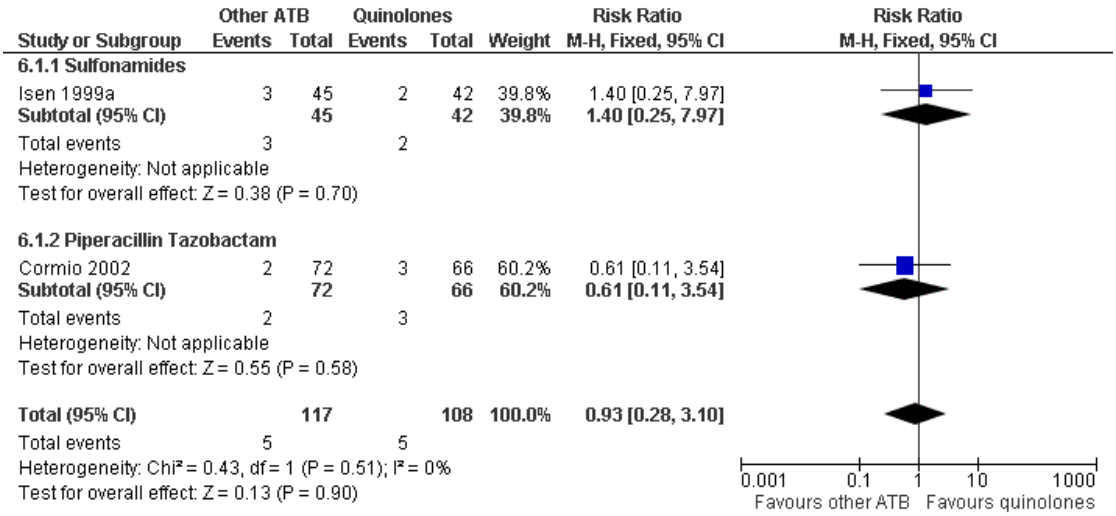
Quinolones versus other antibiotics

The outcomes analysed were bacteriuria, fever, UTI, sepsis and hospitalization. The comparisons between the groups (quinolone and other antibiotics) were not significant for all outcomes.

Bacteriuria

('Figure 26')

Figure 26. Forest plot of comparison: 6 Quinolones versus other classes of antibiotics, outcome: 6.1 Bacteriuria.

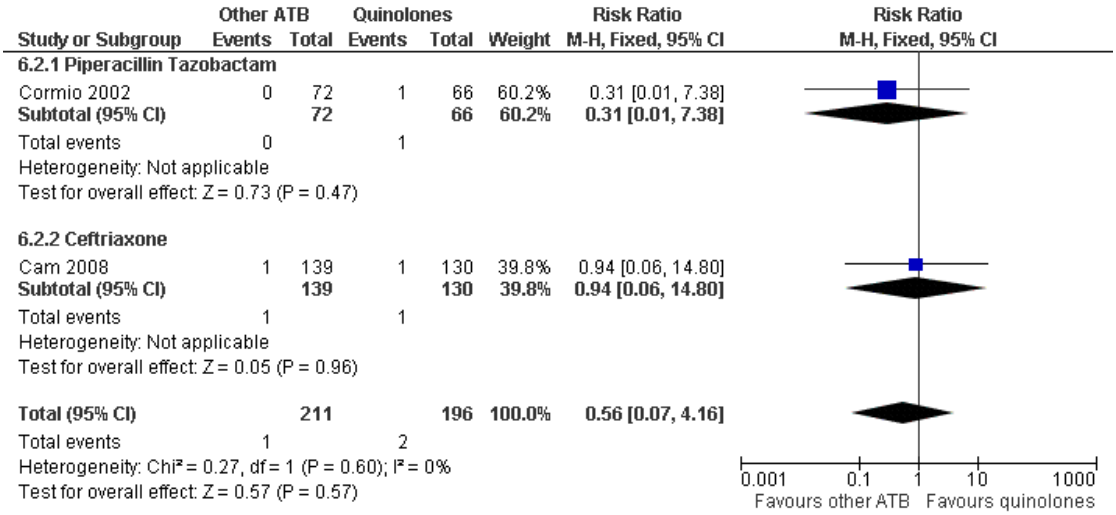


Two trials with 225 patients (Cormio 2002; Isen 1999a) compared quinolone versus sulfonamide and quinolone versus piperacillin tazobactam (RR 0.93, 95% CI 0.28 to 3.10); no heterogeneity was detected (I^2 = 0%).

Fever

('Figure 27')

Figure 27. Forest plot of comparison: 6 Quinolones versus other classes of antibiotics, outcome: 6.3 Fever.

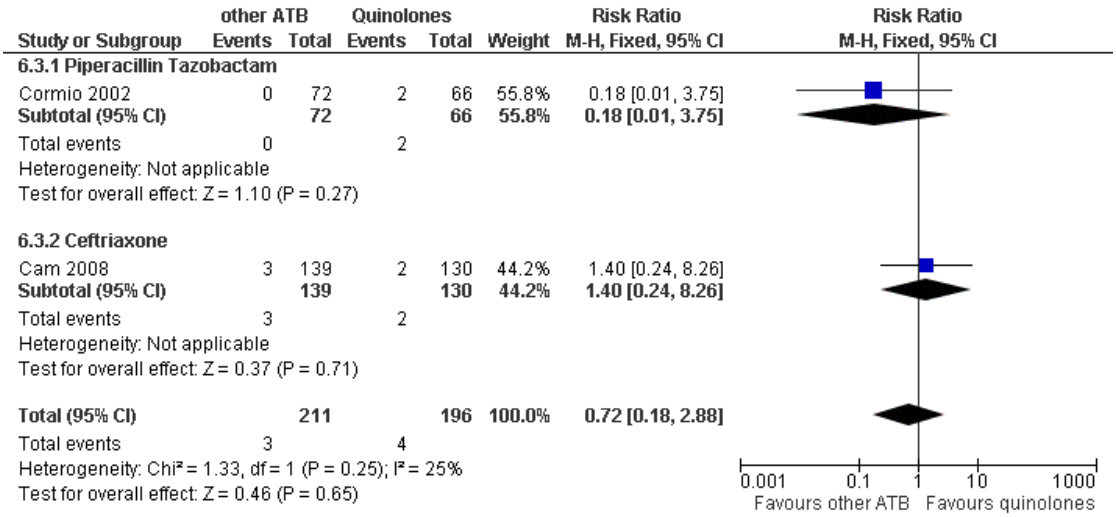


Two trials (Cormio 2002; Cam 2008) with 561 patients compared quinolone versus piperacillin tazobactam and ceftriaxone (RR 0.56, 95% CI 0.07 to 4.16). There was no heterogeneity (I^2 = 0%).

UTI

('Figure 28')

Figure 28. Forest plot of comparison: 6 Quinolones versus other classes of antibiotics, outcome: 6.4 UTI.



Two trials with 407 patients compared quinolone versus piperacillin-tazobactam and ceftriaxone (Cormio 2002; Cam 2008) (RR 0.72, 95% CI 0.18 to 2.88). Moderate heterogeneity was detected (I^2 = 25%).

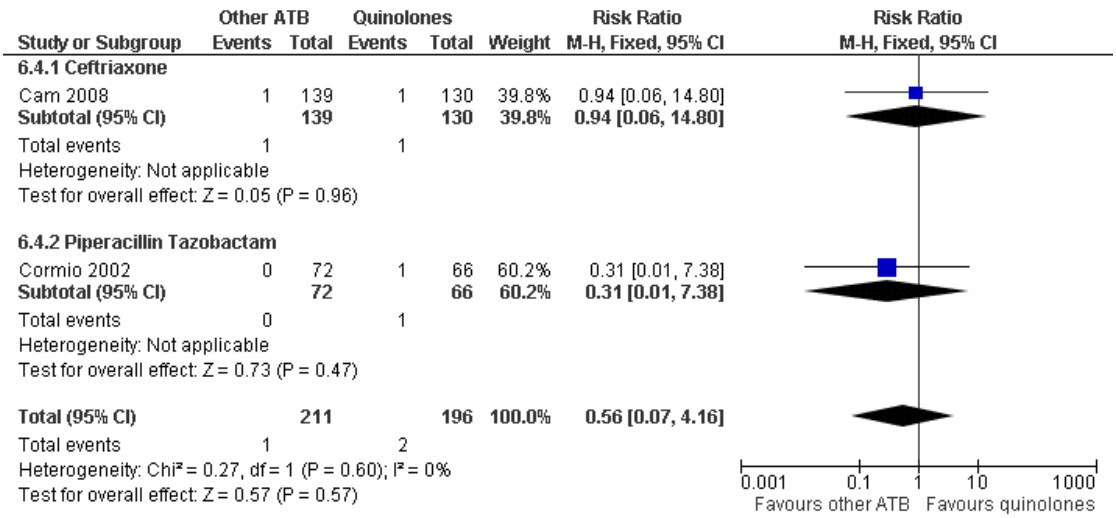
Sepsis

This endpoint was reported in only one study (Cormio 2002). There was one event among 66 randomized to quinolone and 0 events in group piperacillin/tazobactam (P > 0.05)

Hospitalization

('Figure 29')

Figure 29. Forest plot of comparison: 6 Quinolones versus other classes of antibiotics, outcome: 6.5 Hospitalization.

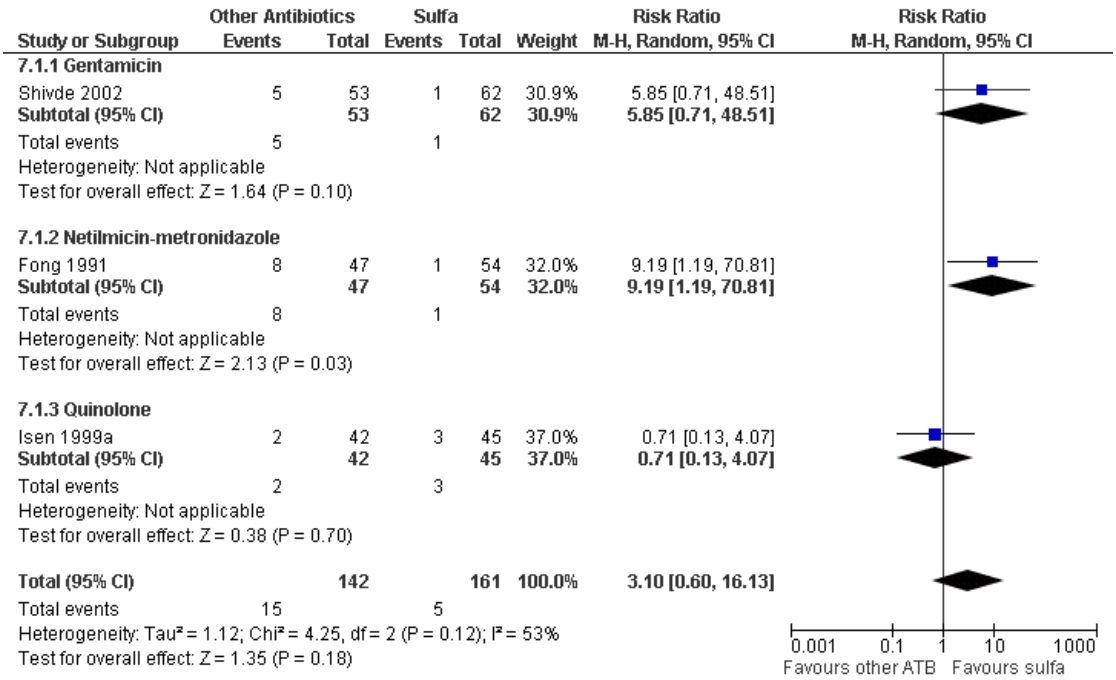


Two trials with 407 patients (Cam 2008; Cormio 2002) compared quinolone versus piperacillin-tazobactam and ceftriaxone (RR 0.56, 95% CI 0.07 to 4.16); no heterogeneity was detected (I^2 = 0%).

Sulfonamide versus other antibiotics

The outcomes analysed were bacteriuria, bacteremia and UTI. For bacteriuria ('Figure 30'), three trials were included (Fong 1991; Isen 1999a; Shivde 2002) with 303 patients comparing sulfonamide to gentamicin, netilmicin-metronidazole and quinolone. There were 5 events among 161 patients using sulfonamide and 15 events among 142 randomized to other antibiotics. The comparison between these groups was not significant (RR 3.10, 95% CI 0.60 to 16.13; I^2 = 53%), using a random-effects model. There was no apparent reason for heterogeneity. Bacteremia and UTI were reported in only one study (Fong 1991). There were 13 events of bacteremia and 2 events of UTI among 47 patients randomized to the netilmicin-metronidazole group and 20 events of bacteremia and 0 events of UTI among 54 randomized to sulfonamide (P > 0.05).

Figure 30. Forest plot of comparison: 7 Sulfonamides versus other antibiotics, outcome: 7.1 Bacteriuria.



Piperacillin tazobactam versus other antibiotics

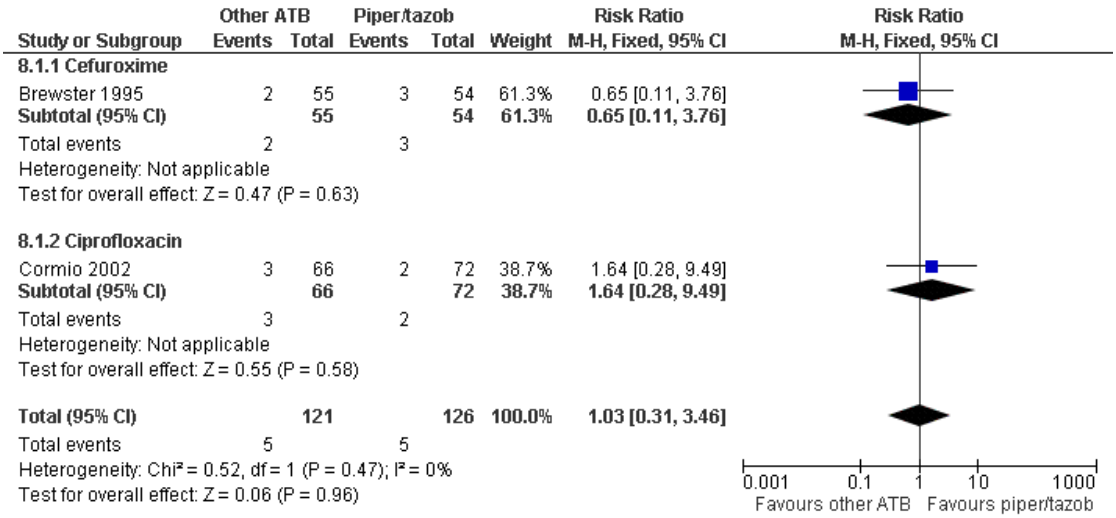
The outcomes analysed were bacteriuria, bacteremia, fever, UTI, sepsis, hospitalization and adverse events.

For bacteriuria, UTI, sepsis and hospitalization, two trials were included (Brewster 1995; Cormio 2002) with 247 patients. The comparisons between the groups were not significant for all outcomes.

Bacteriuria

('Figure 31')

Figure 31. Forest plot of comparison: 8 Piperacillin tazobactam versus other antibiotics, outcome: 8.1 Bacteriuria.

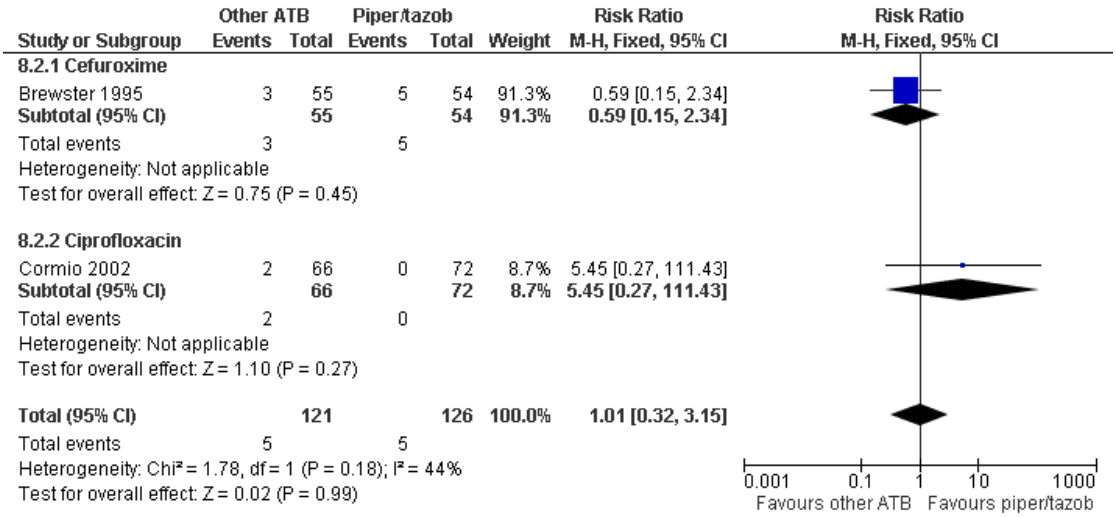


The RR was 1.03, 95% CI 0.31 to 3.46 and no heterogeneity (I^2 = 0%).

UTI

('Figure 32')

Figure 32. Forest plot of comparison: 8 Piperacillin tazobactam versus other antibiotics, outcome: 8.2 UTI.

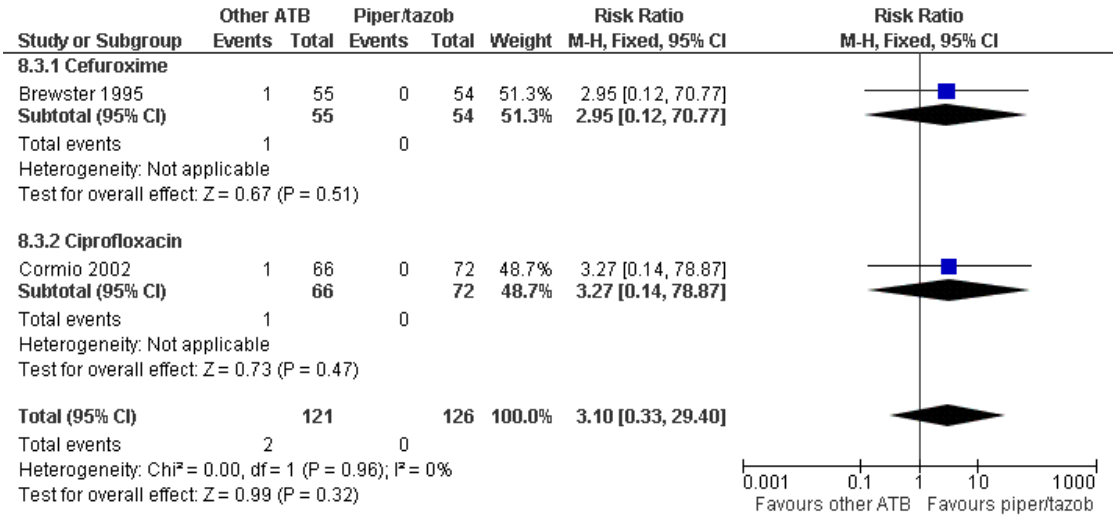


The risk ratio was 1.01, 95% CI 0.32 to 3.15, but with heterogeneity (I^2 = 44%).

Sepsis

('Figure 33')

Figure 33. Forest plot of comparison: 8 Piperacillin tazobactam versus other antibiotics, outcome: 8.3 Sepsis.

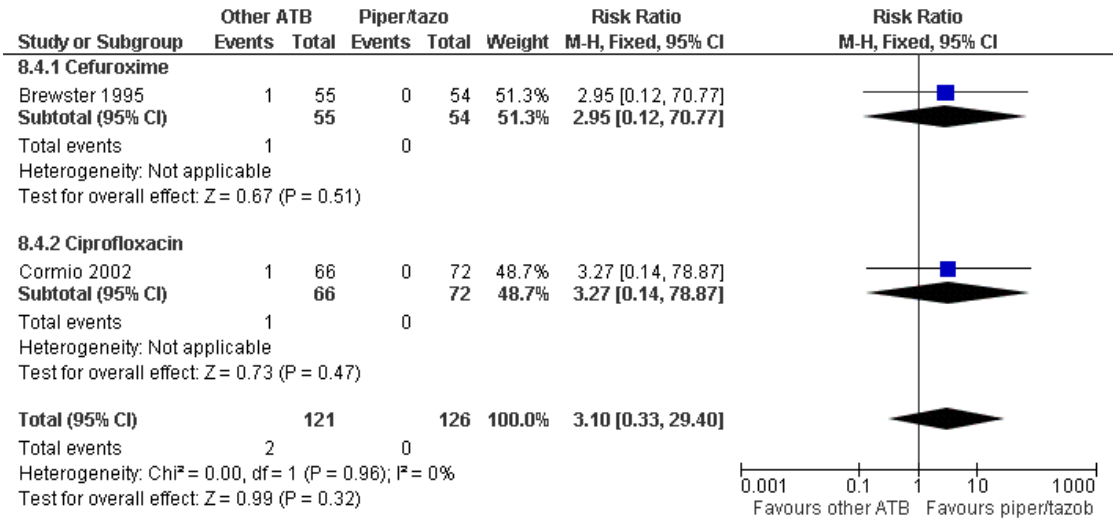


The risk ratio was 3.10, 95% CI 0.33 to 29.40, and no heterogeneity (I^2 = 0%).

Hospitalization

('Figure 34')

Figure 34. Forest plot of comparison: 8 Piperacillin tazobactam versus other antibiotics, outcome: 8.4 Hospitalization.



The RR was 3.10, 95% CI 0.33 to 29.40, P > 0.05, and no heterogeneity was detected (I^2 = 0%).

For bacteremia and adverse events only one trial reported (Brewster 1995). There were 0 events of bacteremia and 16 adverse events (diarrhea) among 54 patients randomized to piperacillin-tazobactam (P < 0.05) and 1 event of bacteremia (P > 0.05) and 2 of adverse events (diarrhea) among 55 randomized to cefuroxime (P < 0.05); fever was reported in one trial (Cormio 2002). There was 1 event of fever among 66 patients randomized to quinolone and 0 events in 72 patients randomized to piperacillin-tazobactam (P > 0.05)

Oral versus systemic administration

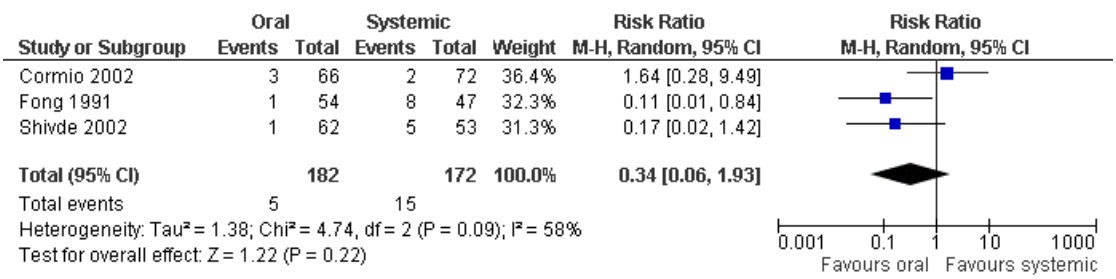
The outcomes analysed were bacteriuria, fever, UTI and hospitalization. Bacteremia and sepsis were reported in only one study and meta-analysis was not realized. There were 13 events of bacteremia among 47 patients randomized to systemic antibiotic versus 20 events of bacteremia among 54 randomized to oral antibiotic (P > 0.05) (Fong 1991). There was 1 event of sepsis among 66 patients randomized to oral antibiotic versus 0 events among 72 randomized to systemic antibiotic (P > 0.05) (Cormio 2002).

Bacteriuria

('Figure 35')

Data on bacteriuria was extracted from 3 trials with 354 patients (Cormio 2002; Fong 1991; Shivde 2002). There were 5 events of bacteriuria among 182 patients randomized to oral treatment and 15 among 172 randomized to systemic treatment. The comparison between groups was not significant (RR 0.34, 95% CI 0.06 to 1.93; I^2 = 58%, using the random-effects model). There was no explicit cause to justify heterogeneity.

Figure 35. Forest plot of comparison: 9 Oral versus systemic antibiotic administration, outcome: 9.1 Bacteriuria.

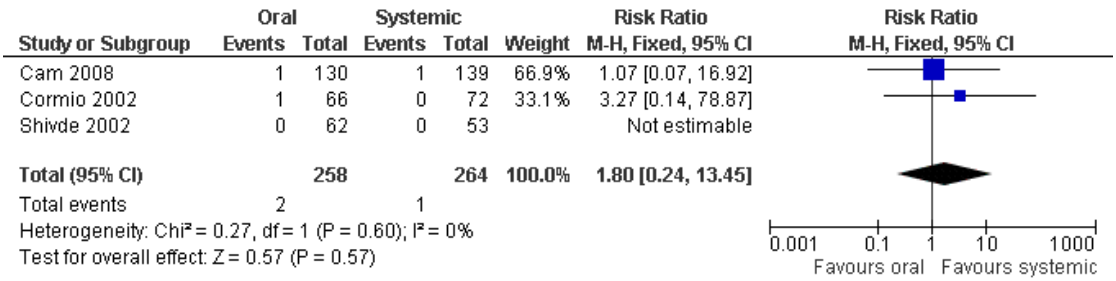


Fever

('Figure 36')

Data on fever was collected from 3 trials with 522 patients (Cam 2008; Cormio 2002; Shivde 2002). There were 2 events of bacteriuria among 258 patients randomized to oral treatment and 1 among 264 randomized to systemic treatment. The comparison between the groups was not significant (RR 1.80, 95% CI 0.24 to 13.45). No heterogeneity was detected (I^2 = 0%).

Figure 36. Forest plot of comparison: 9 Oral versus systemic antibiotic administration, outcome: 9.2 Fever.

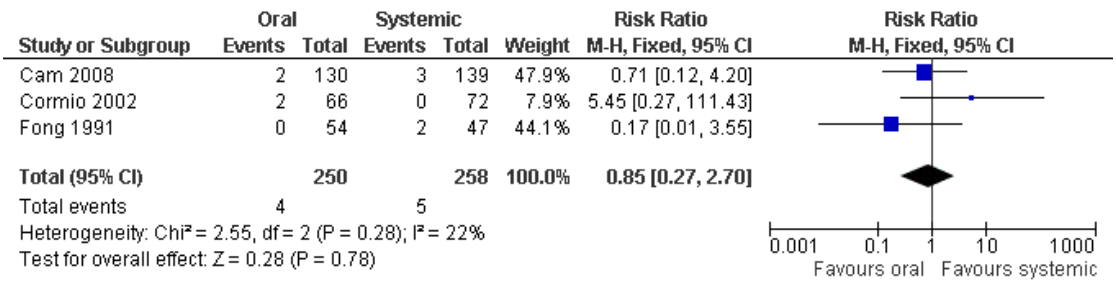


UTI

('Figure 37')

We collected data on UTI from 3 trials with 508 patients (Cam 2008; Cormio 2002; Fong 1991). There were 4 events of UTI among 250 patients randomized to oral treatment and 5 among 258 randomized to systemic treatment. The comparison between the groups was not significant (RR 0.85, 95% CI 0.27 to 2.70). Heterogeneity was detected (I^2 = 22%).

Figure 37. Forest plot of comparison: 9 Oral versus systemic antibiotic administration, outcome: 9.3 UTI.

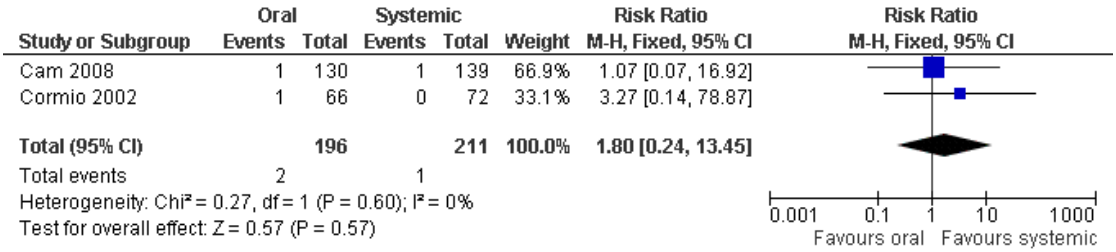


Hospitalization

('Figure 38')

Data on hospitalization was extracted from 2 trials with 407 patients (Cam 2008; Cormio 2002). There were 2 events of hospitalization among 196 patients randomized to oral treatment and 1 among 211 randomized to systemic treatment. The comparison between the groups was not significant (RR 1.80, 95% CI 0.24 to 13.45). No heterogeneity was detected (I^2 = 0%).

Figure 38. Forest plot of comparison: 9 Oral versus Systemic antibiotic administration, outcome: 9.4 Hospitalization.



ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Short course compared to long course treatment for patients submitted to transrectal prostate biopsy

Patient or population: patients submitted to transrectal prostate biopsy
Settings: low risk patients
Intervention: Short course
Comparison: long course treatment

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	long course treatment	Short course				
Bacteriuria	Study population		RR 2.09 (1.17 to 3.73)	869 (3 studies)	⊕⊕⊕◯ **moderate**[1]	
	36 per 1000	75 per 1000 (42 to 134)				
	Medium risk population					
	40 per 1000	84 per 1000 (47 to 149)				
Fever	Study population		RR 2.84 (0.99 to 8.16)	652 (4 studies)	⊕⊕⊕◯ **moderate**[1]	
	12 per 1000	34 per 1000 (12 to 98)				
	Medium risk population					
	19 per 1000	54 per 1000 (19 to 155)				
UTI	Study population		RR 1.4 (0.73 to 2.68)	1312 (5 studies)	⊕⊕⊕◯ **moderate**[1]	

	23 per 1000	**32 per 1000** (17 to 62)			
	Medium risk population				
	15 per 1000	**21 per 1000** (11 to 40)			
Hospitalization	**Study population**		**RR 4.14** (0.47 to 36.46)	366 (2 studies)	⊕⊕◯◯ **low**[1,2]
	0 per 1000	**0 per 1000** (0 to 0)			
	Medium risk population				
	0 per 1000	**0 per 1000** (0 to 0)			

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

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

[1] most of the studies with unclear allocation concealment
[2] few events - wide confidence interval

Single dose compared to multiple dose antibiotic for patients submitted to transrectal prostate biopsy

Patient or population: patients submitted to transrectal prostate biopsy
Settings: low risk patients
Intervention: Single dose
Comparison: multiple dose antibiotic

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	multiple dose antibiotic	Single dose				
Bacteriuria	Study population		RR 1.98 (1.18 to 3.33)	944 (4 studies)	⊕⊕⊕○ **moderate**[1]	
	42 per 1000	83 per 1000 (50 to 140)				
	Medium risk population					
	57 per 1000	113 per 1000 (67 to 190)				
Fever	Study population		RR 2.84 (0.99 to 8.16)	652 (4 studies)	⊕⊕○○ **low**[1,2]	
	12 per 1000	34 per 1000 (12 to 98)				
	Medium risk population					
	19 per 1000	54 per 1000 (19 to 155)				
UTI	Study population		RR 1.4 (0.73 to 2.68)	1312 (5 studies)	⊕⊕⊕○ **moderate**[1]	

	23 per 1000	**32 per 1000** (17 to 62)			
	Medium risk population				
	15 per 1000	**21 per 1000** (11 to 40)			
Hospitalization	**Study population**		**RR 3.1** (0.64 to 15.06)	441 (3 studies)	⊕⊕◯◯ **low**[1,2]
	4 per 1000	**12 per 1000** (3 to 60)			
	Medium risk population				
	0 per 1000	**0 per 1000** (0 to 0)			

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

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

[1] most of the studies with unclear allocation concealment
[2] studies with large confidence interval

Oral compared to systemic antibiotic (IM or IV) for patients submitted to transrectal prostate biopsy

Patient or population: patients submitted to transrectal prostate biopsy
Settings: low risk patients
Intervention: Oral
Comparison: systemic antibiotic (IM or IV)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	systemic antibiotic (IM or IV)	Oral				
Bacteriuria	Study population		RR 0.34 (0.06 to 1.93)	354 (3 studies)	⊕⊕⊕○ **moderate**[1]	
	87 per 1000	30 per 1000 (5 to 168)				
	Medium risk population					
	94 per 1000	32 per 1000 (6 to 181)				
Fever	Study population		RR 1.8 (0.24 to 13.45)	522 (3 studies)	⊕⊕⊕○ **moderate**[2]	
	4 per 1000	7 per 1000 (1 to 54)				
	Medium risk population					
	0 per 1000	0 per 1000 (0 to 0)				
UTI	Study population		RR 0.85 (0.27 to 2.7)	508 (3 studies)	⊕⊕⊕○ **moderate**[2]	

	19 per 1000	**16 per 1000** (5 to 51)			
	Medium risk population				
	22 per 1000	**19 per 1000** (6 to 59)			
Hospitalization	**Study population**		**RR 1.8** (0.24 to 13.45)	407 (2 studies)	⊕⊕◯◯ **low**[3,4]
	5 per 1000	**9 per 1000** (1 to 67)			
	Medium risk population				
	4 per 1000	**7 per 1000** (1 to 54)			

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

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

[1] large heterogeneity
[2] most of studies with unclear allocation concealment
[3] studies with unclear allocation concealment and unclear blinding
[4] studies with wide confidence interval

DISCUSSION

Summary of main results

This systematic review addressed the totality of the evidence for antibiotic prophylaxis for transrectal prostate biopsy. The results favoured the use of antibiotics in transrectal prostate biopsy to prevent infectious complications. In the analysis antibiotic versus placebo/no treatment, all outcomes significantly favored antibiotics versus placebo. Nine trials compared antibiotic to placebo or no treatment, and eight trialsutilized pre-biopsy enemas. These results confirm the necessity of antibiotic prophylaxis for transrectal prostate biopsy and emphasize substantial infection and hospitalization rates without antibiotic prophylaxis (bacteriuria 14.8% without antibiotics versus 3.9% with antibiotics; bacteremia 8.6% versus 2.1%; fever 10.8% versus 4.0%; UTI 9.0% versus 3.3%; hospitalization 3.3% versus 0.3%) (see 'Summary of findings for the main comparison').

Analysing the different classes of antibiotics versus placebo/no treatment, in the quinolones group the results favoured the use of antibiotics to prevent bacteriuria, UTI and hospitalization, and there was a tendency toward fever reduction as well; in 'other antibiotics', the use of antibiotics prevented bacteriuria and fever. In analysing studies that directly compared different classes of antibiotics, there was no difference between quinolones and 'other classes of antibiotics' (sulfonamides, piperacillin tazobactam and ceftriaxone). Comparing sulfonamide to 'other classes of antibiotics' and comparing piperacillin tazobactam with 'other antibiotics', there were no differences for any outcome. The quinolones were the most analysed, with the largest number of patients and trials included, and therefore indicate the best evidence for the use of antibiotic prophylaxis for prostate biopsy.

For 'antibiotic versus enema and antibiotic versus antibiotic + enema', only four trials were analysed, with a limited number of patients. The difference between the groups was not significant for any outcome, and all had some heterogeneity. In the analysis 'antibiotic versus antibiotic + enema', only the risk of bacteremia was diminished for the group antibiotic + enema, and with no differences in the outcomes for bacteriuria and fever.

Comparing 'antibiotic short-course versus long-course', there was a significant difference favouring long-course treatment only for bacteriuria. For bacteremia, fever, UTI and hospitalization, the differences between the groups were not significant. (see 'Summary of findings 2').

For the analysis 'multiple-dose versus single-dose treatment' there was a significant reduction only in the risk of bacteriuria with the multiple-dose treatment arm; for the outcome fever, the comparison favoured the multiple-dose treatment arm, but it was not significant (P = 0.06). (see 'Summary of findings 3').

Comparing the different ways of administering antibiotics (oral versus systemic), the comparisons were not significant for bacteriuria, fever, UTI and hospitalization (see 'Summary of findings 4').

Overall completeness and applicability of evidence

The information provided by this review are relevant and fairly robust, especially regarding effectiveness of antibiotic prophylaxis in reducing the risk of infective complications following TRPB in low risk patients (see 'Exclusion criteria'). Regarding what should be the antibiotic of choice for prophylaxis in TRPB, the data are insufficient to confirm that antibiotic use for long course is superior to short course or that multiple-dose is superior to single-dose treatment.

Quality of the evidence

For the analysis antibiotic versus placebo/no treatment, the quality of the evidence was moderate, especially due to unclear allocation concealment and lack of blinding in several studies. Nine studies were included (see 'Summary of findings for the main comparison').

For the analysis antibiotic short-course versus long-course six trials were included. The quality of the evidence was moderate, especially due to unclear allocation concealment in several studies, with good numbers of patients and no heterogeneity (see 'Summary of findings 2').

For the analysis 'multiple-dose versus single-dose treatment' the quality of the evidence is moderate to low, specially due unclear allocation concealment and wide confidence interval in several studies, with good numbers of patients and no heterogeneity. Seven trials were included (see 'Summary of findings 3').

For 'antibiotic versus enema' and 'antibiotic versus antibiotic + enema', the quality of the evidence is poor because of a limited number of studies (4), patients and events.

Potential biases in the review process

This systematic review probably identified all relevant studies and all relevant data about interventions and outcomes could be obtained. The methods used for review process were rigorous and probably free of bias.

Agreements and disagreements with other studies or reviews

A systematic review of literature (Bootsma 2008) was conducted to address antibiotic prophylaxis in urologic procedures, and included articles searched in the electronic databases MEDLINE, EMBASE and *The Cochrane Library*, and with some language restrictions (English, French, Spanish, German). Only the transurethral resection of the prostate and prostate biopsy sections were well researched and had a high and moderate-to-high level of evidence, respectively, in favour of using antibiotic prophylaxis. The authors presented a narrative review, without meta-analysis, and the results were presented in a descriptive form. They showed a significant decrease of bacteriuria after prostate biopsy with the

use of antibiotic prophylaxis compared to no use of antibiotics (moderate to high evidence); nevertheless, no conclusive evidence was found regarding the effect of antibiotic prophylaxis on symptomatic UTIs and other infectious complications.

A meta-analysis of antibiotic prophylaxis use in transrectal prostatic biopsy was published recently (Yang 2009), but examined only English and Chinese medical literature. Twelve trials with 1987 patients were included (Melekos 1990; Fong 1991; Brewster 1995; Aus 1996; Kapoor 1998; Isen 1999a; Aron 2000a; Yang 2001a; Cormio 2002; Petteffi 2002; Tobias-Machado 2003; Akay 2006). The authors proposed to compare an antibiotic-treated group versus a control group with the outcomes bacteriuria, bacteremia and fever. In the methodology section the control group was defined as "receiving placebo or no agent"; however, included in this group were studies comparing two different types of antibiotics (Fong 1991; Cormio 2002; Tobias-Machado 2003), studies comparing antibiotic short course versus long course (Aus 1996; Petteffi 2002; Tobias-Machado 2003), and all without placebo comparators. Therefore, the authors "created" a control group that was not completely a no treatment or placebo group. There were also two studies with inadequate randomization (Akay 2006; Tobias-Machado 2003). Yang's use of poor methodology resulted in limited validity, and should be consulted with caution.

Compared to the two reviews presented above, our systematic review is wider ranging, by comparing not only antibiotics to placebo, but also comparing different classes of antibiotics, doses, and duration of treatment.

The sextant biopsy scheme significantly improved cancer detection over digitally directed biopsy of palpable nodules and ultrasound-guided biopsy of specific hypoechoic lesions (Hodge 1989a; Hodge 1989b) and remained the gold standard for several years. Numerous groups have published series showing improved cancer detection rates by incorporating additional laterally directed cores into the standard systematic sextant technique, ultimately taking anywhere from 8 to 13 cores (Eskew 1997; Naughton 2000a; Babaian 2000; Presti 2000). At present, the six-cores scheme is considered inadequate for routine prostate biopsy for cancer detection because it may miss over 20% of cancers. Extended biopsy protocols do not result in increased complications compared to sextant biopsy (Mariappan 2004; Naughton 2000b; Naughton 2001; Paul 2004; Paul 2005).

Many of the studies included in this analysis are from when 6-core biopsies were standard. Currently, 12 to 16 core biopsies are being performed. Nevertheless, as discussed above, extended biopsy protocols do not result in increased complications compared to sextant biopsy technique. There was no randomized controlled study comparing different antibiotics regimens for different number of cores on biopsy.

The rule of saturation biopsy is most often applied to patients with previous negative biopsies and patients who have been diagnosed with prostate cancer and remain on active surveillance protocols or are considering focal therapy (Jones 2006). The safety and efficacy of saturation biopsy has been well established, but further studies are needed to validate these strategies over extended biopsy schemes (Patel 2009). Complications with saturation biopsy were similar to extended biopsy technique.

AUTHORS' CONCLUSIONS

Implications for practice

Antibiotic prophylaxis is effective in preventing infectious complications following prostate biopsy. Several classes of antibiotics are effective for prophylaxis in prostate biopsy and the quinolones was the best analysed class, with higher numbers of studies and patients. There is no definitive data to confirm that antibiotic use for long course (3 days) is superior to antibiotic for short course (1 day), or that multiple-dose is superior to single-dose treatment. There is no significant difference between different ways of administering antibiotics (oral versus IM or IV) to prevent infectious complications.

Implications for research

Following these results, it is unlikely that future trials will feature a no-treatment control group for antibiotic prophylaxis in prostate biopsy. Trials comparing different classes of antibiotics, short-course versus long-course treatment and multiple-dose versus single-dose treatment are necessary to confirm or deny our findings.

ACKNOWLEDGEMENTS

Thanks to the Prostatic Diseases and Urologic Cancers Group for the opportunity to conduct a systematic review and by their support of the review, especially James Tacklind, Timothy J. Wilt and Roderick MacDonald. Thanks also to the Brazilian Cochrane Centre for their technical support, and to Tony Burson for his dedication in helping to write an English-language review. Thanks to authors who kindly sent information of their studies, contributing to the improvement of data on this review: Anthony J. Schaeffer, E. David Crawford, Haydar Kamil Cam, Marcos Tobias Machado, Simon Brewster, Subodh Shivde.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Aron 2000a

Methods	randomized, double-blinded, placebo-controlled trial
Participants	231 male adults submitted to TRPB
Interventions	antibiotic for 1 day (Ciprofloxacin 500 mg orally + tinidazole 600 mg orally single dose) or antibiotic for 3 days (ciprofloxacin 500 mg orally 12/12h 3d + Tinidazole 600 mg orally 12/12h 3d) (with enema) or placebo
Outcomes	bacteremia, fever, UTI, infectious complications
Notes	exclusion criteria: bleeding diathesis, UTI, immunosuppressed patients, heart disease, indwelling catheter TCI: urine cultures (48 hours), blood cultures (if fever) Fever: 38^{o} C digitally directed TRPB; 18 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	"Patients were randomized into three groups, using computer-generated random numbers."
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	Low risk	Double-blinded study. "Patients in group 1 . . . received a placebo tablet twice a day for 3 days, . . . In group 2, 79 patients . . were given a single dose of ciprofloxacin (500 mg) and tinidazole (600 mg) orally at the same time, followed by placebo tablet twice a day for five more doses. In group 3, 77 patients . . were given the same combination and dose but for 3 days."
Incomplete outcome data addressed? All outcomes	Low risk	"No patient was excluded from the study after randomization"
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Aron 2000b

Methods	randomized, double-blinded, placebo-controlled trial
Participants	231 male adults submitted to TRPB
Interventions	antibiotic for 1 day (ciprofloxacin 500 mg orally + tinidazole 600 mg orally single dose) or antibiotic for 3 days (ciprofloxacin 500 mg orally 12/12h 3d + tinidazole 600 mg orally 12/12h 3d) (with enema) or placebo
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Adequate sequence generation?	Low risk	"patients were randomized into three groups, using computer-generated random numbers."
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	Low risk	Double-blinded study. "Patients in group 1 . . received a placebo tablet twice a day for 3 days, . . . In group 2, 79 patients . . . were given a single dose of ciprofloxacin (500 mg) and tinidazole (600 mg) orally at the same time, followed by placebo tablet twice a day for five more doses. In group 3, 77 patients . . were given the same combination and dose but for 3 days."
Incomplete outcome data addressed? All outcomes	Low risk	"No patient was excluded from the study after randomization"
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Bates 1998

Methods	randomized controlled trial
Participants	75 male adults submitted to TRPB
Interventions	antibiotic single dose (co-amoxiclav 1.2 g IV) or antibiotic multiple dose (co-amoxiclav 1.2g IV + co-amoxiclav 250/125 mg orally 8/8h 1 day) (with enema)
Outcomes	bacteriuria, sepsis, hospitalization
Notes	exclusion criteria: UTI, prostatitis, indwelling catheter, DM, steroid therapy, heart valves, penicillin hypersensibility, immunosuppression TCI: urine sample 72 h after biopsy Fever: >37.5º C UTI: 100.000 UFC/mL mean of four biopsy cores (2 to 6); 18 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	"Patients were then randomized to receive"
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	High risk	Not blinded
Incomplete outcome data addressed? All outcomes	Low risk	"Eight patients (four from each group) were found to have asymptomatic UTIs . . . ; these patients were excluded from the study"
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Brewster 1995

Methods	randomized controlled trial
Participants	111 male adults submitted to TRPB
Interventions	antibiotic (cefuroxime 1.5g IV single dose) or another antibiotic (piperacillin/tazobactam 4.5g IV single dose) (with enema)
Outcomes	bacteriuria, bacteremia, UTI, sepsis, hospitalization, adverse events

Brewster 1995 (*Continued*)

Notes	exclusion: penicillin hypersensibility, heart valve, heart murmur, rectal stenosis, concurrent ATB therapy, bleeding diathesis, anticoagulant therapy TCI: urine and blood cultures (after 48h) Fever: > ou = 37.5º C UTI: 100.000 UFC/mL four biopsy cores; 18 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	"One-hundred and eleven eligible consecutive patients were randomized to receive ...." Information provided by author: "utilized randomising card system"
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	Low risk	Patients were not told which drug they were given
Incomplete outcome data addressed? All outcomes	Low risk	"Of the 111 men in the study, 109 men were evaluable: one patient receiving cefuroxime failed to complete all the temperature assessments in his diary card and one patient receiving PT did not provide the 48h MSU and blood culture sample"
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Comment: Apparently free

Briffaux 2009

Methods	randomized controlled trial
Participants	288 male adult submitted to TRPB
Interventions	antibiotic for 1 day (2 Ciprofloxacin 500 mg tablets orally single dose) or antibiotic for 3 days (2 Ciprofloxacin 500 mg tablets orally + ciprofloxacin 500 mg orally 12/12h 3d)
Outcomes	bacteriuria, UTI
Notes	exclusion: allergy, risk factors for infection (diabetes, immunosuppression, urinary stent) , ATB use in the previous week, active UTI, valvular heart disease TCI: urine culture, blood cell count UTI: 10.000 UFC/mL at least 10 biopsy cores; 18 gauge needle

Briffaux 2009 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	"patients were randomized by a permutation block"
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	High risk	Not blinded
Incomplete outcome data addressed? All outcomes	Low risk	"Analysis was planned in an intention-to-treat basis"
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Comment: Apparently free

Brown 1981

Methods	randomized, placebo-controlled trial
Participants	40 male adults submitted to TRPB
Interventions	antibiotic (Gentamicin 80mg IM single dose) or enema (povidone-iodine) or ATB + enema or placebo (saline clean enema)
Outcomes	bacteriuria, bacteremia, fever
Notes	exclusion: use of ATB or urologic manipulation 24h before, positive urine or blood culture, marked general debility, valvular heart disease, valvular prostheses TCI: urine and blood cultures Fever: > 101 F (38.3^{o} C) UTI: > 100.000 UFC/mL 2 to 4 biopsy cores (mean 2.7); 18 gauge needle

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	"Patients were randomized into one of four groups"
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	High risk	Not blinded

Brown 1981 (*Continued*)

Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Unclear risk	Imprecision - few patients and few events

Cam 2008

Methods	randomized controlled trial
Participants	400 male adults submitted to TRPB
Interventions	antibiotic short course (ceftriaxone 1g IM single dose) or antibiotic short course (ciprofloxacin 500 mg orally single dose) or antibiotic long course (ciprofloxacin 500 mg orally 12/12h 3d) (without enema)
Outcomes	fever, UTI, hospitalization
Notes	exclusion: UTI, use of ATB TCI: urine culture fever: > 38.0º C 12 biopsy cores; 18 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	"The patients were prospectively randomized in three groups" Information provided by author: "utilized a computer program that assigned each subsequent patient into a group"
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	High risk	Not blinded
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Cormio 2002

Methods	randomized controlled trial
Participants	138 male adults submitted to TRPB
Interventions	antibiotic (piperacillin/tazobactam 2250 mg IM 12/12h 2d) or another antibiotic (ciprofloxacin 500 mg orally 12/12h 7d) (with enema)
Outcomes	bacteriuria, fever, ITU, sepsis, hospitalization
Notes	exclusion: indwelling catheters, ATB, immunosuppressive drugs, UTI TCI: urine culture Fever: 37.5º C UTI: 100.000 UFC/mL 6-12 biopsy cores; 18 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	"Patients scheduled for TPB at our unit were randomized to receive"
Allocation concealment?	Unclear risk	"Patients scheduled for TPB at our unit were randomized to receive"
Blinding? All outcomes	High risk	Not blinded
Incomplete outcome data addressed? All outcomes	Low risk	"Six patients (two in Group 1 and four in Group 2) were excluded because of positive urine cultures before TPB"
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Crawford 1982

Methods	randomized, double-blinded, placebo-controlled trial
Participants	48 male adults submitted to TRPB
Interventions	Antibiotic (carbenicillin 2 tablets orally 6/6h 1d) or placebo (with enema)
Outcomes	bacteriuria, bacteremia, fever, sepsis
Notes	exclusion: UTI, prosthetic devices, rheumatic valvular heart disease, allergy to penicillin, use of ATB (14 day before) TCI: urine culture (24h before, 48h and 2 weeks after biopsy) and blood cultures (15

Crawford 1982 (*Continued*)

	min after biopsy) Fever: 38.5^{o} C UTI: 100.000 UFC/mL 1 to 6 biopsy cores

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	"Patients were assigned randomly to receive the treatment drug . . or a placebo" Information provided by author: used a random generator for sequence generation
Allocation concealment?	Low risk	Information provided by author: "Used a random generator"; "the study nurse let informed the pharmacy know and they delivered the drug"
Blinding? All outcomes	Low risk	"Patients were assigned randomly to receive the treatment drug (carbenicillin indanyl sodium) or a placebo that was indistinguishable from the study drug" Information provided by author: investigators and patients were blinded
Incomplete outcome data addressed? All outcomes	Low risk	"Of 63 patients entered into the study 15 were considered nonevaluable"
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Fong 1991

Methods	randomized controlled trial
Participants	101 male adults submitted to TRPB
Interventions	ATB (netilmicin 1.5mg/Kg IV + metronidazole 500 mg orally - single dose) or another ATB (trimethoprim/sulfo methoxazole 320mg/1600mg orally - single dose) (with enema)
Outcomes	bacteriuria, symptomatic UTI, bacteremia
Notes	exclusion: allergy to drug treatment, severe constipation, indwelling catheter, antibiotic change, vomiting, failure to take the medication TCI: blood and urine culture

Fong 1991 (*Continued*)

	Fever: 38º C UTI: 100.000 UFC/mL 2-3 biopsy cores; 14 gauge needle	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	"Randomization was done by pre-selection from a table of number for regimens A and B"
Allocation concealment?	Low risk	"pre-selection from a table of number for regimens A and B. Numbered and coded envelopes contained the specific regimens"
Blinding? All outcomes	High risk	Not blinded
Incomplete outcome data addressed? All outcomes	Low risk	"Of these patients 16 (14%) were excluded from the study: 11 in group 1 and 5 in group 2"
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Freitas 1999

Methods	randomized controlled trial	
Participants	120 male adults submitted to TRPB	
Interventions	enema (sodium biphosphate) or ATB (Ciprofloxacin 500mg 12/12h 2d) or ATB long course (ciprofloxacin 500 mg 12/12h 7d) or ATB + enema	
Outcomes	bacteriuria, fever, sepsis, mortality, hospitalization	
Notes	exclusion: UTI, urologic instrumentation (72h), valvular heart disease or prostheses, use of ATB TCI: urine culture Fever: 37.5º C UTI: 100.000 UFC/mL 6 biopsy cores; 18 gauge needle	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Freitas 1999 (*Continued*)

Adequate sequence generation?	Unclear risk	The patients were divided, randomly, into four groups
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	High risk	Not blinded
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Isen 1999a

Methods	randomized, placebo-controlled trial
Participants	110 male patients submitted to TRPB
Interventions	ATB (Ofloxacin 400 mg orally single dose) or ATB (trimethoprim/sulfonamide methoxazole 160 mg/800 mg orally single dose) or placebo (with enema)
Outcomes	bacteriuria, hospitalization
Notes	exclusion: artificial heart valve, indwelling catheter, diabetes, steroid use, prostatitis, ATB use 72h before TCI: urine culture 6 biopsy cores; 18 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	"Patients were randomly divided into 3 groups"
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	Unclear risk	No information provided
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed
Free of selective reporting?	Low risk	Apparently free

Isen 1999a (*Continued*)

Free of other bias?	Unclear risk	Randomization resulted in 23, 42 and 45 patients in the three groups

Isen 1999b

Methods	randomized, placebo-controlled trial
Participants	110 male patients submitted to TRPB
Interventions	ATB (ofloxacin 400 mg orally single dose) or ATB (trimethoprim/sulfonamide methoxazole 160 mg/800 mg orally single dose) or placebo (with enema)
Outcomes	bacteriuria, hospitalization
Notes	exclusion: artificial heart valve, indwelling catheter, diabetes, steroid use, prostatitis, ATB use 72h before TCI: urine culture 6 biopsy cores; 18 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	"Patients were randomly divided into 3 groups"
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	Unclear risk	No information provided
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed analysed
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Unclear risk	The randomization result in 23, 42 and 45 patients in the three groups

Kapoor 1998

Methods	randomized, double-blinded, placebo-controlled trial
Participants	537 male adult submitted to TRPB
Interventions	Antibiotic (ciprofloxacin 500 mg orally single dose) or placebo (with enema)

Kapoor 1998 (*Continued*)

Outcomes	bacteriuria, bacteremia, fever, UTI, sepsis, hospitalization, adverse events
Notes	exclusion: hypersensibility to ciprofloxacin, valvular heart disease, significant gastrointestinal disease, epilepsy, bacteriuria, urologic manipulation, indwelling catheter, ATB use (7d), granulocyte count < 1000/mm^3 TCI: urine culture, urinalysis Fever: 37.5^o C UTI: 10.000 UFC/mL 4 biopsy cores; 18 or 20 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	"This was a prospective, randomized, double-blind, placebo controlled trial . . . ; Those patients who met enrollment criteria were assigned in a 1:1 ratio to one of the two treatment groups in accordance with a computer-generated randomization schedule."
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	Low risk	"a prospective, randomized, double-blinded, placebo-controlled trial"
Incomplete outcome data addressed? All outcomes	Low risk	"Five hundred thirty-seven patients . . . comprised the safety (intent-to-treat) population"
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Melekos 1990

Methods	randomized, placebo-controlled trial
Participants	81 male adults submitted to TRPB
Interventions	antibiotic (piperacillin 2 g IV single dose) or enema (PVPI) or ATB + enema
Outcomes	bacteriuria, bacteremia, fever
Notes	exclusion: general debility, heart disease, UTI, use of ATB 24 prior, urologic manipulation

Melekos 1990 (*Continued*)

	TCI: MSU culture, blood culture Fever: 38.5^{o} C

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	"Patients were randomized into one of the following four groups"
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	High risk	Not blinded
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed analysed
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Petteffi 2002

Methods	randomized controlled trial
Participants	105 male adults submitted to TRPB
Interventions	Antibiotic short-course (norfloxacin 400mg orally single dose) or antibiotic long-course (norfloxacin 400 mg orally 12/12h for 3 days) (with enema)
Outcomes	bacteriuria, fever, hospitalization
Notes	exclusion criteria: allergy to norfloxacin, indwelling catheter, chronic or within less than 30 days of ATB use, leucopenia, valvular cardiac conditions or valvular prosthesis, factors that could potentially interfere in the analysis results: diabetes, neoplasty, AIDS, corticosteroids use TCI: blood count, urine culture UTI: 100.000 UFC/mL 12 biopsy cores; 18 gauge needle

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	"patients randomly separated in two groups"
Allocation concealment?	Unclear risk	No information provided

Petteffi 2002 (*Continued*)

Blinding? All outcomes	Low risk	"A clinical trial, simple-blind, controlled"
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Ruebush 1979

Methods	randomized, double-blind, placebo-controlled trial
Participants	79 male patients submitted to TRPB
Interventions	ATB (trimethoprim/sulfonamide metoxazole 40/200 mg orally 12/12h 7d) or placebo (no enema)
Outcomes	bacteriuria, bacteremia, fever
Notes	exclusion criteria: valvular heart disease, intravascular prosthesis, fever, use of ATB during the week before TCI: urine culture (1d before, 2-4 hours after biopsy, 7-14 days later); blood cultures (before, during and 15 to 25 minutes after final) Fever: 37.6º C UTI: 10.000 UFC/mL 1 to 7 biopsy cores

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	"Each patient was assigned randomly to a coded bottle containing 16 tablets of a combination"
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	Low risk	"Each patient was assigned randomly to a coded bottle containing 16 tablets of a combination of 40 mg. trimethoprim and 200 mg. sulfamethoxazole or a placebo that was identical in appearance"
Incomplete outcome data addressed? All outcomes	Low risk	"Nine patients were excluded from analysis for the following reasons"

Ruebush 1979 (*Continued*)

Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Schaeffer 2007

Methods	randomized, double-blind, controlled trial
Participants	497 male adults submitted to TRPB
Interventions	Antibiotic 1day or 3 days (ciprofloxacin extended-release 1000 mg 1x/d) (with enema)
Outcomes	bacteriuria, UTI
Notes	exclusion criteria: MSU positive (>10000 UFC), hypersensitivity to quinolone, valvular heart disease, renal or hepatic insufficiency, CNS disorder that might predispose do seizures, endoscopic manipulation of urinary tract in last 7 days, indwelling catheter within 48 hours, ATB within 7 days TCI: urine culture, blood culture (if fever) UTI: 10.000 UFC/mL mean of 9.3 and 9.5 biopsy cores; 18 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	"patients were randomized to receive oral ciprofloxacin" Information provided by author: "The randomization was 1:1, with a block size of 4"
Allocation concealment?	Low risk	Information provided by author: "sealed code break envelopes will be provided to the investigator with each shipment of study medication"; "Study personnel directly involved in the conduct of the study will not be allowed to access the randomization list"
Blinding? All outcomes	Low risk	"For patients in the 1-day arm the first and third doses of ciprofloxacin XR were replaced with placebo."
Incomplete outcome data addressed? All outcomes	Low risk	intention-to-treat analysis. "The 'enrolled' population consisted of all patients enrolled in the study, including those who received no study medication"

Schaeffer 2007 (*Continued*)

Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Shivde 2002

Methods	randomized controlled trial
Participants	115 male adults submitted to TRPB
Interventions	antibiotic (trimethoprim 200 mg orally 2 doses) or another antibiotic (gentamicin 120 mg IV single dose) (without enema)
Outcomes	bacteriuria, fever
Notes	exclusion criteria: valvular heart diseases and protheses, symptomatic UTI, drug sensitivities, diabetes TCI: urine sample, urine culture UTI: 100.000 UFC/mL 4 to 6 biopsy cores; 18 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Low risk	"The patients recruited in this study were randomised to receive" Contact with author: "we employed the 'Blocked randomisation' process"
Allocation concealment?	Low risk	Contact with author: "employed central randomisation"; "The procedure was carried out by specialist registrars working with the respective consultants and hence the Senior Registrar, the other main investigators were blinded to the process of antibiotic prophylaxis received by the enrolled patients"
Blinding? All outcomes	Low risk	blinded evaluators, but not patients
Incomplete outcome data addressed? All outcomes	Low risk	"a total of 128 patients were enrolled in the trial but only 115 were available for the final analysis"
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Tekdogan 2006

Methods	randomized, placebo-controlled trial
Participants	159 male adults submitted to TRPB
Interventions	Antibiotic (ciprofloxacin 1000 mg/d 4d) or enema (rifampicin) or enema + ATB or none treatment
Outcomes	bacteriuria, fever
Notes	exclusion criteria: previous prostatic biopsy or prostatic surgery, diabetes, abnormal blood leukocyte counts, neurogenic disease with voiding dysfunction, valvular heart disease, UTI, catheterization in last 15 days, any antibiotic - anticoagulant - immunosuppressive treatment TCI: MSU culture 2 days after biopsy, blood culture (if fever) Fever: 38º C UTI: 100.000 UFC/mL 6 biopsy cores; 18 gauge needle

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	"Patients were randomized into four groups."
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	High risk	No blinded
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

Yang 2001a

Methods	randomized, blinded, placebo-controlled trial
Participants	192 male adults submitted to TRPB
Interventions	ATB short course (ciprofloxacin 500 mg orally + metronidazole 400 mg orally single dose) or ATB long course (ciprofloxacin 500 mg orally 12/12h + metronidazole 400 mg orally 12/12h 3d) or placebo (with enema)
Outcomes	fever, UTI

Yang 2001a (*Continued*)

Notes	exclusion criteria: coagulation disturbance, acute infectious disease, severe cardiac disease TCI: urine culture, blood culture (if fever) Fever: 38º C UTI: 100.000 UFC/mL 13 biopsy cores; 18 gauge needle

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Patients were randomly divided into three groups by computer generated sequence
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	Low risk	Group A received placebo orally 2/day for 3 days; group B received ciprofloxacin and metronidazole 1x and other 5x were given oral placebo; group C received ciprofloxacin and metronidazole 2x/day for 3 days
Incomplete outcome data addressed? All outcomes	Low risk	all patients analysed analysed
Free of selective reporting?	Low risk	apparently free
Free of other bias?	Low risk	apparently free

Yang 2001b

Methods	a randomized, blinded, placebo-controlled trial
Participants	192 male adults submitted to TRPB
Interventions	ATB short course (Ciprofloxaxin 500 mg orally + Metronidazole 400 mg orally single dose) or ATB long course (ciprofloxacin 500 mg orally 12/12 hours + metronidazole 400 mg orally 12/12 hours/3 days) or placebo (with enema)
Outcomes	fever, UTI
Notes	exclusion criteria: coagulation disturbance, acute infectious disease, severe cardiac disease TCI: urine culture, blood culture (if fever) Fever: 38º C UTI: 100.000 UFC/mL 13 biopsy cores; 18 gauge needle

Risk of bias

Yang 2001b (*Continued*)

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Patients were randomly divided into three groups by computer-generated sequence
Allocation concealment?	Unclear risk	No information provided
Blinding? All outcomes	Low risk	Group A received placebo orally 2x/day for 3 days; group B received ciprofloxacin and metronidazole 1x and other 5x were given oral placebo; group C received ciprofloxacin and metronidazole 2x/day for 3 days
Incomplete outcome data addressed? All outcomes	Low risk	All patients analysed
Free of selective reporting?	Low risk	Apparently free
Free of other bias?	Low risk	Apparently free

TCI: tests of control of infection. TRPB: transrectal prostate biopsy. ATB: antibiotic. UTI: urine tract infection. DM: diabetes. CNS: central nervous system.

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

Study	Reason for exclusion
Akay 2006	inadequate randomization - the patients were divided into two groups according to their order of arrival
Anjum 1996	not randomized
Argyropoulos 2007	single study comparing time of administration of antibiotic making impossible the realization of meta-analysis
Aus 1993	not randomized
Aus 1996	short-course antibiotic versus long-course antibiotic, but long-course so long (7 days) - the review protocol considered long-course as 3 days
Bjerklund 2004	doesn't have patients and interventions of interest
Bosquet Sanz 2006	without exclusion criteria of patients - we tried to contact the authors but to no avail

(*Continued*)

Carey 2001	not randomized - retrospective study
Eaton 1981	case report
Eggert 1999	not randomized
Ferreira 1985	single study comparing local and systemic administration of antibiotic making impossible realization of meta-analysis
Herranz Amo 1996	without adequate exclusion criteria of patients (included patients with co-morbidities and with urinary catheter)
Hosokawa 2005	not randomized
Hotta 2001	inadequate randomization determined by preference of the urologist
Huang 2006	retrospective study
Ito 2002	without exclusion criteria of patients; short-course antibiotic versus long-course antibiotic, but short-course so long (3 days), that was considered long-course in the protocol review
Janoff 2000	retrospective study
Jeon 2003	retrospective study
Khan 1984	doesn't have patients and interventions of interest
Lindert 2000	not randomized
Lindstedt 2006	not randomized
Mari 2007	without exclusion criteria of patients (except UTI); short-course antibiotic versus long-course antibiotic, but long-course so long (5 days)
Meyer 1987	without exclusion criteria of patients - we tried to contact the authors but to no avail
Otrock 2004	retrospective study
Peters 2003	without exclusion criteria of patients - we tried to contact the authors but to no avail
Puig 2006	retrospective study
Rees 1980	not randomized
Roach 1991	inadequate randomization - by alternation

(*Continued)*

Sabbagh 2004	without adequate exclusion criteria of patients (no urinalysis taken prior to the procedure) - we tried to contact the authors but to no avail
Saleem 2001	doesn't have intervention of interest
Sharpe 1982	doesn't have patients and interventions of interest
Shigemura 2005	inadequate randomization by alternation
Thompson 1982	not randomized- don't have patients and interventions of interest
Tobias-Machado 2003	inadequate randomization - only the groups of interventions were randomized, but patients were not randomized
Vaz 1994	single study comparing lomefloxacin versus lomefloxacin plus metronidazole
Wang 2004	without exclusion criteria of patients - we tried to contact the authors but to no avail
Yamamoto 2008	single study comparing trovafloxacin versus levofloxacin

DATA AND ANALYSES

Comparison 1. Antibiotics (classes) versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Bacteriuria	8	870	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.15, 0.42]
1.1 Quinolones	3	628	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.17, 0.64]
1.2 Sulfonamides	2	133	Risk Ratio (M-H, Fixed, 95% CI)	0.17 [0.05, 0.57]
1.3 Other classes of antibiotics	3	109	Risk Ratio (M-H, Fixed, 95% CI)	0.20 [0.07, 0.54]
2 Bacteremia	6	494	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.49, 0.92]
2.1 Quinolones	2	306	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.05, 2.01]
2.2 Sulfonamides	1	79	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.61, 1.17]
2.3 Other classes of antibiotics	3	109	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.22, 0.98]
3 Fever	9	820	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.23, 0.64]
3.1 Quinolones	5	640	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.22, 1.06]
3.2 Sulfonamides	1	71	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.20, 2.38]
3.3 Other classes of antibiotics	3	109	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.10, 0.54]
4 UTI	5	1077	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.22, 0.62]
4.1 Quinolones	5	1077	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.22, 0.62]
5 Hospitalization	3	650	Risk Ratio (M-H, Fixed, 95% CI)	0.13 [0.03, 0.55]
5.1 Quinolones	2	582	Risk Ratio (M-H, Fixed, 95% CI)	0.16 [0.03, 0.87]
5.2 Sulfonamides	1	68	Risk Ratio (M-H, Fixed, 95% CI)	0.07 [0.00, 1.38]
6 Adverse events	2	127	Risk Ratio (M-H, Fixed, 95% CI)	1.62 [0.23, 11.56]
6.1 Sulfonamides	1	79	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.06, 13.59]
6.2 Other classes of antibiotics	1	48	Risk Ratio (M-H, Fixed, 95% CI)	3.25 [0.14, 76.01]
7 Bacteriuria (with pre-biopsy enema)	7	805	Risk Ratio (M-H, Fixed, 95% CI)	0.28 [0.17, 0.46]
7.1 Quinolones	3	628	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.17, 0.64]
7.2 Sulfonamides	1	68	Risk Ratio (M-H, Fixed, 95% CI)	0.26 [0.07, 0.93]
7.3 Other classes of antibiotics	3	109	Risk Ratio (M-H, Fixed, 95% CI)	0.20 [0.07, 0.54]
8 Bacteremia (with pre-biopsy enema)	5	415	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.22, 0.87]
8.1 Quinolones	2	306	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.05, 2.01]
8.2 Other classes of antibiotics	3	109	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.22, 0.98]
9 Fever (with pre-biopsy enema)	8	749	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.20, 0.61]
9.1 Quinolones	5	640	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.22, 1.06]
9.2 Other classes of antibiotics	3	109	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.10, 0.54]

Comparison 2. Antibiotics versus enema

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Bacteriuria	3	139	Risk Ratio (M-H, Fixed, 95% CI)	1.71 [0.61, 4.79]
2 Bacteremia	2	60	Risk Ratio (M-H, Random, 95% CI)	1.89 [0.40, 8.93]
3 Fever	4	197	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.16, 5.05]

Comparison 3. Antibiotics versus antibiotics + enema

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Bacteriuria	3	147	Risk Ratio (M-H, Fixed, 95% CI)	0.42 [0.13, 1.29]
2 Bacteremia	2	68	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.08, 0.75]
3 Fever	4	209	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.21, 1.34]

Comparison 4. Short-course versus long-course treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Bacteriuria	3	869	Risk Ratio (M-H, Fixed, 95% CI)	2.09 [1.17, 3.73]
2 Fever	4	652	Risk Ratio (M-H, Fixed, 95% CI)	2.84 [0.99, 8.16]
3 UTI	5	1312	Risk Ratio (M-H, Fixed, 95% CI)	1.40 [0.73, 2.68]
4 Hospitalization	2	366	Risk Ratio (M-H, Fixed, 95% CI)	4.14 [0.47, 36.46]

Comparison 5. Single versus multiple dose

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Bacteriuria	4	944	Risk Ratio (M-H, Fixed, 95% CI)	1.98 [1.18, 3.33]
2 Fever	4	652	Risk Ratio (M-H, Fixed, 95% CI)	2.84 [0.99, 8.16]
3 UTI	5	1312	Risk Ratio (M-H, Fixed, 95% CI)	1.40 [0.73, 2.68]
4 Hospitalization	3	441	Risk Ratio (M-H, Fixed, 95% CI)	3.10 [0.64, 15.06]

Comparison 6. Quinolones versus other classes of antibiotics

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Bacteriuria	2	225	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.28, 3.10]
1.1 Sulfonamides	1	87	Risk Ratio (M-H, Fixed, 95% CI)	1.4 [0.25, 7.97]
1.2 Piperacillin Tazobactam	1	138	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.11, 3.54]
2 Fever	2	407	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.07, 4.16]
2.1 Piperacillin Tazobactam	1	138	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.01, 7.38]
2.2 Ceftriaxone	1	269	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.06, 14.80]
3 UTI	2	407	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.18, 2.88]
3.1 Piperacillin Tazobactam	1	138	Risk Ratio (M-H, Fixed, 95% CI)	0.18 [0.01, 3.75]
3.2 Ceftriaxone	1	269	Risk Ratio (M-H, Fixed, 95% CI)	1.40 [0.24, 8.26]
4 Hospitalization	2	407	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.07, 4.16]
4.1 Ceftriaxone	1	269	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.06, 14.80]
4.2 Piperacillin Tazobactam	1	138	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.01, 7.38]

Comparison 7. Sulfonamides versus other antibiotics

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Bacteriuria	3	303	Risk Ratio (M-H, Random, 95% CI)	3.10 [0.60, 16.13]
1.1 Gentamicin	1	115	Risk Ratio (M-H, Random, 95% CI)	5.85 [0.71, 48.51]
1.2 Netilmicin-metronidazole	1	101	Risk Ratio (M-H, Random, 95% CI)	9.19 [1.19, 70.81]
1.3 Quinolone	1	87	Risk Ratio (M-H, Random, 95% CI)	0.71 [0.13, 4.07]

Comparison 8. Piperacillin tazobactam versus other antibiotics

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Bacteriuria	2	247	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.31, 3.46]
1.1 Cefuroxime	1	109	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.11, 3.76]
1.2 Ciprofloxacin	1	138	Risk Ratio (M-H, Fixed, 95% CI)	1.64 [0.28, 9.49]
2 UTI	2	247	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.32, 3.15]
2.1 Cefuroxime	1	109	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.15, 2.34]
2.2 Ciprofloxacin	1	138	Risk Ratio (M-H, Fixed, 95% CI)	5.45 [0.27, 111.43]
3 Sepsis	2	247	Risk Ratio (M-H, Fixed, 95% CI)	3.10 [0.33, 29.40]
3.1 Cefuroxime	1	109	Risk Ratio (M-H, Fixed, 95% CI)	2.95 [0.12, 70.77]
3.2 Ciprofloxacin	1	138	Risk Ratio (M-H, Fixed, 95% CI)	3.27 [0.14, 78.87]
4 Hospitalization	2	247	Risk Ratio (M-H, Fixed, 95% CI)	3.10 [0.33, 29.40]
4.1 Cefuroxime	1	109	Risk Ratio (M-H, Fixed, 95% CI)	2.95 [0.12, 70.77]
4.2 Ciprofloxacin	1	138	Risk Ratio (M-H, Fixed, 95% CI)	3.27 [0.14, 78.87]

Comparison 9. Oral versus systemic antibiotic administration (IM or IV)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Bacteriuria	3	354	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.06, 1.93]
2 Fever	3	522	Risk Ratio (M-H, Fixed, 95% CI)	1.80 [0.24, 13.45]
3 UTI	3	508	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.27, 2.70]
4 Hospitalization	2	407	Risk Ratio (M-H, Fixed, 95% CI)	1.80 [0.24, 13.45]

Analysis 1.1. Comparison 1 Antibiotics (classes) versus placebo, Outcome 1 Bacteriuria.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 1 Antibiotics (classes) versus placebo

Outcome: 1 Bacteriuria

Study or subgroup	Antibiotics n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Quinolones					
Isen 1999a	2/42	6/23		11.8 %	0.18 [0.04, 0.83]
Kapoor 1998	7/241	21/242		31.8 %	0.33 [0.14, 0.77]
Tekdogan 2006	2/40	3/40		4.5 %	0.67 [0.12, 3.78]
Subtotal (95% CI)	**323**	**305**		**48.1 %**	**0.33 [0.17, 0.64]**
Total events: 11 (Antibiotics), 30 (Placebo)					
Heterogeneity: Chi^2 = 1.22, df = 2 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 3.28 (P = 0.0010)					
2 Sulfonamides					
Ruebush 1979	0/31	7/34		10.9 %	0.07 [0.00, 1.23]
Isen 1999b	3/45	6/23		12.0 %	0.26 [0.07, 0.93]
Subtotal (95% CI)	**76**	**57**		**22.9 %**	**0.17 [0.05, 0.57]**
Total events: 3 (Antibiotics), 13 (Placebo)					
Heterogeneity: Chi^2 = 0.73, df = 1 (P = 0.39); I^2 =0.0%					
Test for overall effect: Z = 2.87 (P = 0.0041)					
3 Other classes of antibiotics					
Melekos 1990	1/25	5/16		9.2 %	0.13 [0.02, 1.00]
Brown 1981	1/11	4/9		6.7 %	0.20 [0.03, 1.52]
Crawford 1982	2/23	9/25		13.1 %	0.24 [0.06, 1.00]
Subtotal (95% CI)	**59**	**50**		**29.0 %**	**0.20 [0.07, 0.54]**

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Study or subgroup	Antibiotics n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Total events: 4 (Antibiotics), 18 (Placebo)					
Heterogeneity: Chi^2 = 0.25, df = 2 (P = 0.88); I^2 =0.0%					
Test for overall effect: Z = 3.18 (P = 0.0015)					
Total (95% CI)	**458**	**412**	◆	**100.0 %**	**0.25 [0.15, 0.42]**
Total events: 18 (Antibiotics), 61 (Placebo)					
Heterogeneity: Chi^2 = 3.02, df = 7 (P = 0.88); I^2 =0.0%					
Test for overall effect: Z = 5.38 (P < 0.00001)					

0.001 0.01 0.1 1 10 100 1000

Favours antibiotics Favours placebo

Analysis 1.2. Comparison 1 Antibiotics (classes) versus placebo, Outcome 2 Bacteremia.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 1 Antibiotics (classes) versus placebo

Outcome: 2 Bacteremia

Study or subgroup	Antibiotics n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Quinolones					
Aron 2000a	0/79	2/75		5.2 %	0.19 [0.01, 3.89]
Aron 2000b	1/77	2/75		4.1 %	0.49 [0.05, 5.26]
Subtotal (95% CI)	**156**	**150**	◆	**9.4 %**	**0.32 [0.05, 2.01]**
Total events: 1 (Antibiotics), 4 (Placebo)					
Heterogeneity: Chi^2 = 0.23, df = 1 (P = 0.63); I^2 =0.0%					
Test for overall effect: Z = 1.22 (P = 0.22)					
2 Sulfonamides					
Ruebush 1979	25/42	26/37		56.6 %	0.85 [0.61, 1.17]
Subtotal (95% CI)	**42**	**37**	◆	**56.6 %**	**0.85 [0.61, 1.17]**
Total events: 25 (Antibiotics), 26 (Placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.00 (P = 0.32)					
3 Other classes of antibiotics					
Brown 1981	2/11	5/9		11.3 %	0.33 [0.08, 1.30]

0.001 0.01 0.1 1 10 100 1000

Favours antibiotics Favours placebo

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Study or subgroup	Antibiotics n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crawford 1982	5/23	4/25		7.8 %	1.36 [0.41, 4.45]
Melekos 1990	1/25	6/16		15.0 %	0.11 [0.01, 0.81]
Subtotal (95% CI)	**59**	**50**		**34.1 %**	**0.47 [0.22, 0.98]**
Total events: 8 (Antibiotics), 15 (Placebo)					
Heterogeneity: Chi^2 = 5.41, df = 2 (P = 0.07); I^2 =63%					
Test for overall effect: Z = 2.02 (P = 0.043)					
Total (95% CI)	**257**	**237**		**100.0 %**	**0.67 [0.49, 0.92]**
Total events: 34 (Antibiotics), 45 (Placebo)					
Heterogeneity: Chi^2 = 8.33, df = 5 (P = 0.14); I^2 =40%					
Test for overall effect: Z = 2.48 (P = 0.013)					

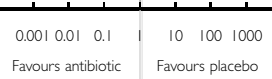
Analysis 1.3. Comparison 1 Antibiotics (classes) versus placebo, Outcome 3 Fever.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 1 Antibiotics (classes) versus placebo

Outcome: 3 Fever

Study or subgroup	antibiotics n/N	placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Quinolones					
Aron 2000a	2/79	5/75		11.2 %	0.38 [0.08, 1.90]
Aron 2000b	2/77	5/75		11.1 %	0.39 [0.08, 1.95]
Tekdogan 2006	3/40	2/40		4.4 %	1.50 [0.26, 8.50]
Yang 2001a	1/64	3/62		6.7 %	0.32 [0.03, 3.02]
Yang 2001b	1/66	3/62		6.8 %	0.31 [0.03, 2.93]
Subtotal (95% CI)	**326**	**314**		**40.2 %**	**0.48 [0.22, 1.06]**
Total events: 9 (antibiotics), 18 (placebo)					
Heterogeneity: Chi^2 = 2.06, df = 4 (P = 0.72); I^2 =0.0%					
Test for overall effect: Z = 1.82 (P = 0.069)					



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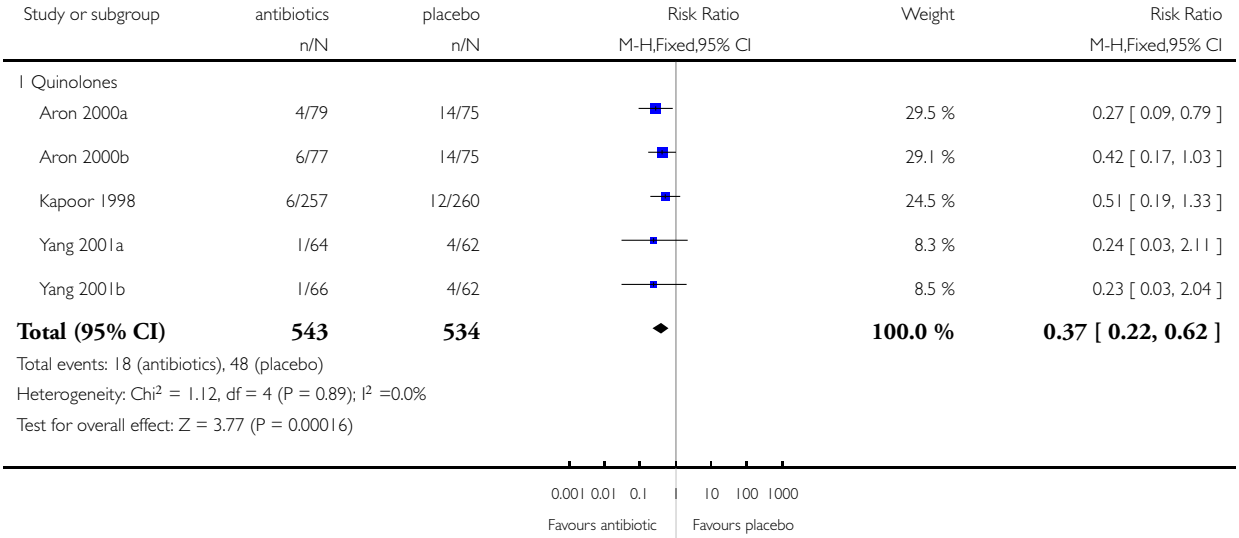
Study or subgroup	antibiotics n/N	placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
2 Sulfonamides					
Ruebush 1979	4/38	5/33		11.7 %	0.69 [0.20, 2.38]
Subtotal (95% CI)	**38**	**33**		**11.7 %**	**0.69 [0.20, 2.38]**
Total events: 4 (antibiotics), 5 (placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.58 (P = 0.56)					
3 Other classes of antibiotics					
Brown 1981	0/11	3/9		8.4 %	0.12 [0.01, 2.04]
Crawford 1982	4/23	12/25		25.2 %	0.36 [0.14, 0.97]
Melekos 1990	0/25	5/16		14.6 %	0.06 [0.00, 1.01]
Subtotal (95% CI)	**59**	**50**		**48.1 %**	**0.23 [0.10, 0.54]**
Total events: 4 (antibiotics), 20 (placebo)					
Heterogeneity: Chi^2 = 1.92, df = 2 (P = 0.38); I^2 =0.0%					
Test for overall effect: Z = 3.38 (P = 0.00074)					
Total (95% CI)	**423**	**397**		**100.0 %**	**0.39 [0.23, 0.64]**
Total events: 17 (antibiotics), 43 (placebo)					
Heterogeneity: Chi^2 = 5.64, df = 8 (P = 0.69); I^2 =0.0%					
Test for overall effect: Z = 3.65 (P = 0.00027)					

Analysis 1.4. Comparison 1 Antibiotics (classes) versus placebo, Outcome 4 UTI.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 1 Antibiotics (classes) versus placebo

Outcome: 4 UTI



Analysis 1.5. Comparison 1 Antibiotics (classes) versus placebo, Outcome 5 Hospitalization.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 1 Antibiotics (classes) versus placebo

Outcome: 5 Hospitalization

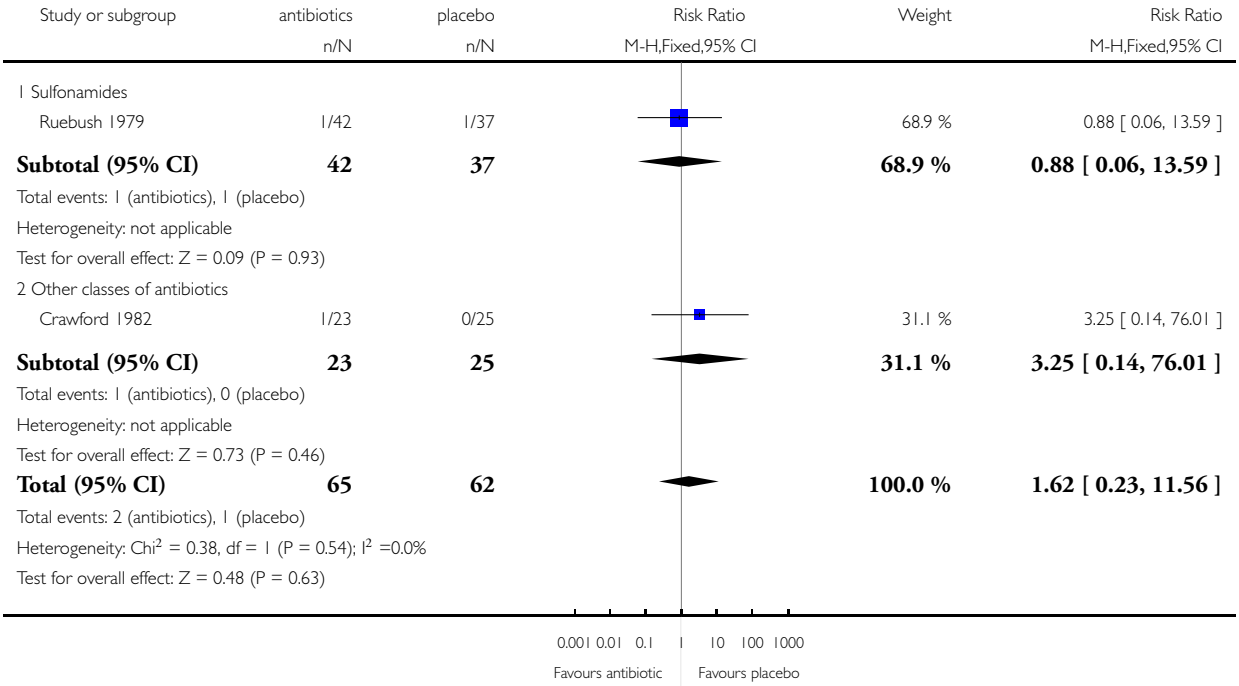
Study or subgroup	antibiotics n/N	placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Quinolones					
Isen 1999a	0/42	3/23		34.4 %	0.08 [0.00, 1.48]
Kapoor 1998	1/257	4/260		30.4 %	0.25 [0.03, 2.25]
Subtotal (95% CI)	**299**	**283**		**64.8 %**	**0.16 [0.03, 0.87]**
Total events: 1 (antibiotics), 7 (placebo)					
Heterogeneity: Chi^2 = 0.39, df = 1 (P = 0.53); I^2 =0.0%					
Test for overall effect: Z = 2.12 (P = 0.034)					
2 Sulfonamides					
Isen 1999b	0/45	3/23		35.2 %	0.07 [0.00, 1.38]
Subtotal (95% CI)	**45**	**23**		**35.2 %**	**0.07 [0.00, 1.38]**
Total events: 0 (antibiotics), 3 (placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.74 (P = 0.082)					
Total (95% CI)	**344**	**306**		**100.0 %**	**0.13 [0.03, 0.55]**
Total events: 1 (antibiotics), 10 (placebo)					
Heterogeneity: Chi^2 = 0.60, df = 2 (P = 0.74); I^2 =0.0%					
Test for overall effect: Z = 2.77 (P = 0.0056)					

Analysis 1.6. Comparison 1 Antibiotics (classes) versus placebo, Outcome 6 Adverse events.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 1 Antibiotics (classes) versus placebo

Outcome: 6 Adverse events



Analysis 1.7. Comparison 1 Antibiotics (classes) versus placebo, Outcome 7 Bacteriuria (with pre-biopsy enema).

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 1 Antibiotics (classes) versus placebo

Outcome: 7 Bacteriuria (with pre-biopsy enema)

Study or subgroup	Antibiotics n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Quinolones					
Isen 1999a	2/42	6/23		13.2 %	0.18 [0.04, 0.83]
Kapoor 1998	7/241	21/242		35.7 %	0.33 [0.14, 0.77]
Tekdogan 2006	2/40	3/40		5.1 %	0.67 [0.12, 3.78]
Subtotal (95% CI)	**323**	**305**		**54.0 %**	**0.33 [0.17, 0.64]**
Total events: 11 (Antibiotics), 30 (Placebo)					
Heterogeneity: Chi^2 = 1.22, df = 2 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 3.28 (P = 0.0010)					
2 Sulfonamides					
Isen 1999b	3/45	6/23		13.5 %	0.26 [0.07, 0.93]
Subtotal (95% CI)	**45**	**23**		**13.5 %**	**0.26 [0.07, 0.93]**
Total events: 3 (Antibiotics), 6 (Placebo)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.07 (P = 0.038)					
3 Other classes of antibiotics					
Brown 1981	1/11	4/9		7.5 %	0.20 [0.03, 1.52]
Crawford 1982	2/23	9/25		14.7 %	0.24 [0.06, 1.00]
Melekos 1990	1/25	5/16		10.4 %	0.13 [0.02, 1.00]
Subtotal (95% CI)	**59**	**50**		**32.5 %**	**0.20 [0.07, 0.54]**
Total events: 4 (Antibiotics), 18 (Placebo)					
Heterogeneity: Chi^2 = 0.25, df = 2 (P = 0.88); I^2 =0.0%					
Test for overall effect: Z = 3.18 (P = 0.0015)					
Total (95% CI)	**427**	**378**		**100.0 %**	**0.28 [0.17, 0.46]**
Total events: 18 (Antibiotics), 54 (Placebo)					
Heterogeneity: Chi^2 = 2.15, df = 6 (P = 0.91); I^2 =0.0%					
Test for overall effect: Z = 4.97 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 0.0, df = 2 (P = 0.0), I^2 =0.0%					

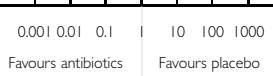
Analysis 1.8. Comparison 1 Antibiotics (classes) versus placebo, Outcome 8 Bacteremia (with pre-biopsy enema).

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 1 Antibiotics (classes) versus placebo

Outcome: 8 Bacteremia (with pre-biopsy enema)

Study or subgroup	Antibiotics n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Quinolones					
Aron 2000a	0/79	2/75		12.1 %	0.19 [0.01, 3.89]
Aron 2000b	1/77	2/75		9.5 %	0.49 [0.05, 5.26]
Subtotal (95% CI)	**156**	**150**		**21.6 %**	**0.32 [0.05, 2.01]**
Total events: 1 (Antibiotics), 4 (Placebo)					
Heterogeneity: Chi^2 = 0.23, df = 1 (P = 0.63); I^2 =0.0%					
Test for overall effect: Z = 1.22 (P = 0.22)					
2 Other classes of antibiotics					
Brown 1981	2/11	5/9		25.9 %	0.33 [0.08, 1.30]
Crawford 1982	5/23	4/25		18.0 %	1.36 [0.41, 4.45]
Melekos 1990	1/25	6/16		34.4 %	0.11 [0.01, 0.81]
Subtotal (95% CI)	**59**	**50**		**78.4 %**	**0.47 [0.22, 0.98]**
Total events: 8 (Antibiotics), 15 (Placebo)					
Heterogeneity: Chi^2 = 5.41, df = 2 (P = 0.07); I^2 =63%					
Test for overall effect: Z = 2.02 (P = 0.043)					
Total (95% CI)	**215**	**200**		**100.0 %**	**0.44 [0.22, 0.87]**
Total events: 9 (Antibiotics), 19 (Placebo)					
Heterogeneity: Chi^2 = 5.85, df = 4 (P = 0.21); I^2 =32%					
Test for overall effect: Z = 2.36 (P = 0.018)					
Test for subgroup differences: Chi^2 = 0.0, df = 1 (P = 0.0), I^2 =0.0%					



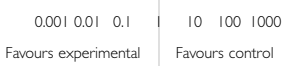
Analysis 1.9. Comparison 1 Antibiotics (classes) versus placebo, Outcome 9 Fever (with pre-biopsy enema).

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 1 Antibiotics (classes) versus placebo

Outcome: 9 Fever (with pre-biopsy enema)

Study or subgroup	antibiotics n/N	placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Quinolones					
Aron 2000a	2/79	5/75		12.7 %	0.38 [0.08, 1.90]
Aron 2000b	2/77	5/75		12.6 %	0.39 [0.08, 1.95]
Tekdogan 2006	3/40	2/40		5.0 %	1.50 [0.26, 8.50]
Yang 2001a	1/64	3/62		7.6 %	0.32 [0.03, 3.02]
Yang 2001b	1/66	3/62		7.7 %	0.31 [0.03, 2.93]
Subtotal (95% CI)	**326**	**314**		**45.5 %**	**0.48 [0.22, 1.06]**
Total events: 9 (antibiotics), 18 (placebo)					
Heterogeneity: Chi^2 = 2.06, df = 4 (P = 0.72); I^2 =0.0%					
Test for overall effect: Z = 1.82 (P = 0.069)					
2 Other classes of antibiotics					
Brown 1981	0/11	3/9		9.5 %	0.12 [0.01, 2.04]
Crawford 1982	4/23	12/25		28.5 %	0.36 [0.14, 0.97]
Melekos 1990	0/25	5/16		16.5 %	0.06 [0.00, 1.01]
Subtotal (95% CI)	**59**	**50**		**54.5 %**	**0.23 [0.10, 0.54]**
Total events: 4 (antibiotics), 20 (placebo)					
Heterogeneity: Chi^2 = 1.92, df = 2 (P = 0.38); I^2 =0.0%					
Test for overall effect: Z = 3.38 (P = 0.00074)					
Total (95% CI)	**385**	**364**		**100.0 %**	**0.34 [0.20, 0.61]**
Total events: 13 (antibiotics), 38 (placebo)					
Heterogeneity: Chi^2 = 4.84, df = 7 (P = 0.68); I^2 =0.0%					
Test for overall effect: Z = 3.67 (P = 0.00024)					
Test for subgroup differences: Chi^2 = 0.0, df = 1 (P = 0.0), I^2 =0.0%					



Analysis 2.1. Comparison 2 Antibiotics versus enema, Outcome 1 Bacteriuria.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 2 Antibiotics versus enema

Outcome: 1 Bacteriuria

Study or subgroup	antibiotics n/N	enema n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Brown 1981	2/10	1/10		19.3 %	2.00 [0.21, 18.69]
Melekos 1990	2/22	2/18		42.5 %	0.82 [0.13, 5.25]
Tekdogan 2006	5/39	2/40		38.2 %	2.56 [0.53, 12.44]
Total (95% CI)	**71**	**68**		**100.0 %**	**1.71 [0.61, 4.79]**

Total events: 9 (antibiotics), 5 (enema)

Heterogeneity: Chi^2 = 0.88, df = 2 (P = 0.65); I^2 =0.0%

Test for overall effect: Z = 1.02 (P = 0.31)

Analysis 2.2. Comparison 2 Antibiotics versus enema, Outcome 2 Bacteremia.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 2 Antibiotics versus enema

Outcome: 2 Bacteremia

Study or subgroup	Antibiotics n/N	Enema n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Brown 1981	8/10	2/10		52.8 %	4.00 [1.11, 14.35]
Melekos 1990	3/22	3/18		47.2 %	0.82 [0.19, 3.57]
Total (95% CI)	**32**	**28**		**100.0 %**	**1.89 [0.40, 8.93]**

Total events: 11 (Antibiotics), 5 (Enema)

Heterogeneity: Tau^2 = 0.76; Chi^2 = 2.54, df = 1 (P = 0.11); I^2 =61%

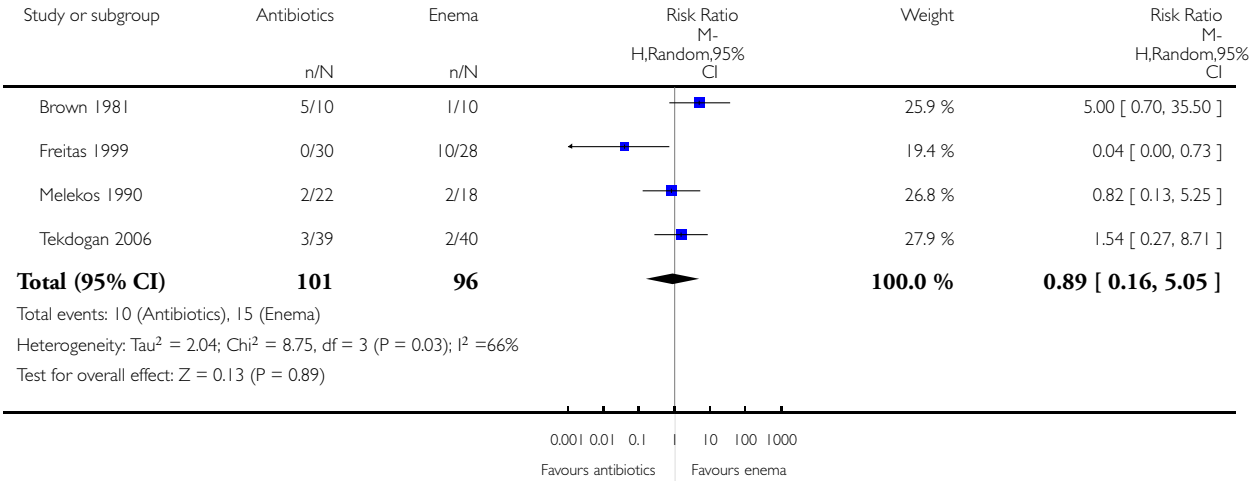
Test for overall effect: Z = 0.80 (P = 0.42)

Analysis 2.3. Comparison 2 Antibiotics versus enema, Outcome 3 Fever.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 2 Antibiotics versus enema

Outcome: 3 Fever

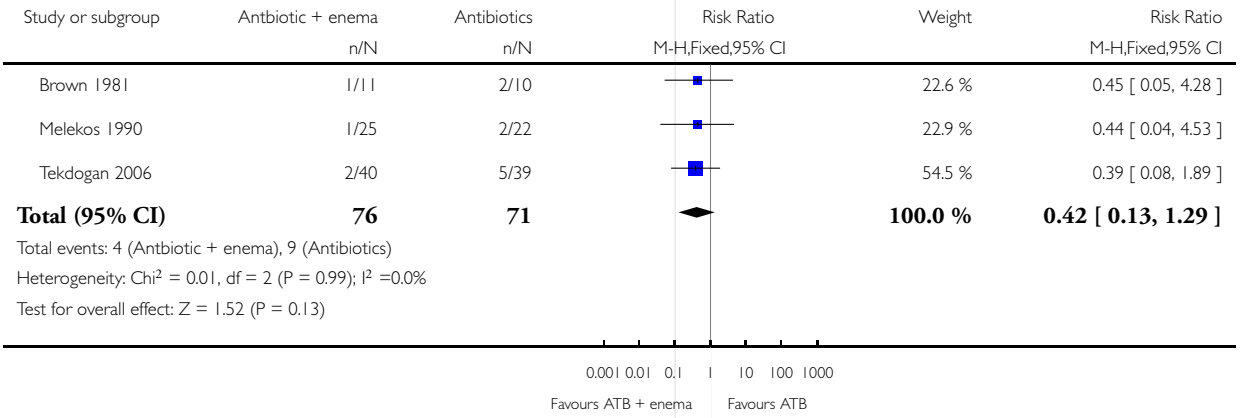


Analysis 3.1. Comparison 3 Antibiotics versus antibiotics + enema, Outcome 1 Bacteriuria.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 3 Antibiotics versus antibiotics + enema

Outcome: 1 Bacteriuria



Analysis 3.2. Comparison 3 Antibiotics versus antibiotics + enema, Outcome 2 Bacteremia.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 3 Antibiotics versus antibiotics + enema

Outcome: 2 Bacteremia

Study or subgroup	Antbiotic + Enema n/N	Antibiotic n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Brown 1981	2/11	8/10		72.4 %	0.23 [0.06, 0.83]
Melekos 1990	1/25	3/22		27.6 %	0.29 [0.03, 2.62]
Total (95% CI)	**36**	**32**		**100.0 %**	**0.25 [0.08, 0.75]**

Total events: 3 (Antbiotic + Enema), 11 (Antibiotic)

Heterogeneity: $Chi^2 = 0.04$, df = 1 (P = 0.84); $I^2 = 0.0\%$

Test for overall effect: Z = 2.47 (P = 0.014)

Analysis 3.3. Comparison 3 Antibiotics versus antibiotics + enema, Outcome 3 Fever.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 3 Antibiotics versus antibiotics + enema

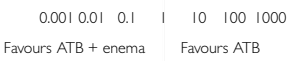
Outcome: 3 Fever

Study or subgroup	Antbiotic + enema n/N	Antibiotics n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Brown 1981	0/11	5/10		48.0 %	0.08 [0.01, 1.34]
Freitas 1999	2/32	0/30		4.3 %	4.70 [0.23, 94.01]
Melekos 1990	0/25	2/22		22.2 %	0.18 [0.01, 3.50]
Tekdogan 2006	3/40	3/39		25.4 %	0.98 [0.21, 4.54]
Total (95% CI)	**108**	**101**		**100.0 %**	**0.53 [0.21, 1.34]**

Total events: 5 (Antbiotic + enema), 10 (Antibiotics)

Heterogeneity: Chi^2 = 4.86, df = 3 (P = 0.18); I^2 =38%

Test for overall effect: Z = 1.34 (P = 0.18)



Analysis 4.1. Comparison 4 Short-course versus long-course treatment, Outcome 1 Bacteriuria.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 4 Short-course versus long-course treatment

Outcome: 1 Bacteriuria

Study or subgroup	Short-course n/N	Long-course n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Briffaux 2009	6/139	6/149		37.0 %	1.07 [0.35, 3.25]
Petteffi 2002	15/50	4/54		24.6 %	4.05 [1.44, 11.39]
Schaeffer 2007	11/239	6/238		38.4 %	1.83 [0.69, 4.86]
Total (95% CI)	**428**	**441**		**100.0 %**	**2.09 [1.17, 3.73]**

Total events: 32 (Short-course), 16 (Long-course)

Heterogeneity: Chi^2 = 3.04, df = 2 (P = 0.22); I^2 =34%

Test for overall effect: Z = 2.51 (P = 0.012)

Analysis 4.2. Comparison 4 Short-course versus long-course treatment, Outcome 2 Fever.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 4 Short-course versus long-course treatment

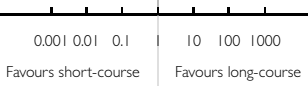
Outcome: 2 Fever

Study or subgroup	Short-course n/N	Long-course n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Aron 2000a	2/79	2/77		45.2 %	0.97 [0.14, 6.75]
Cam 2008	1/130	0/131		11.1 %	3.02 [0.12, 73.53]
Petteffi 2002	8/51	1/54		21.7 %	8.47 [1.10, 65.36]
Yang 2001a	1/64	1/66		22.0 %	1.03 [0.07, 16.14]
Total (95% CI)	**324**	**328**		**100.0 %**	**2.84 [0.99, 8.16]**

Total events: 12 (Short-course), 4 (Long-course)

Heterogeneity: $Chi^2 = 2.80$, df = 3 (P = 0.42); $I^2 = 0.0\%$

Test for overall effect: Z = 1.94 (P = 0.053)

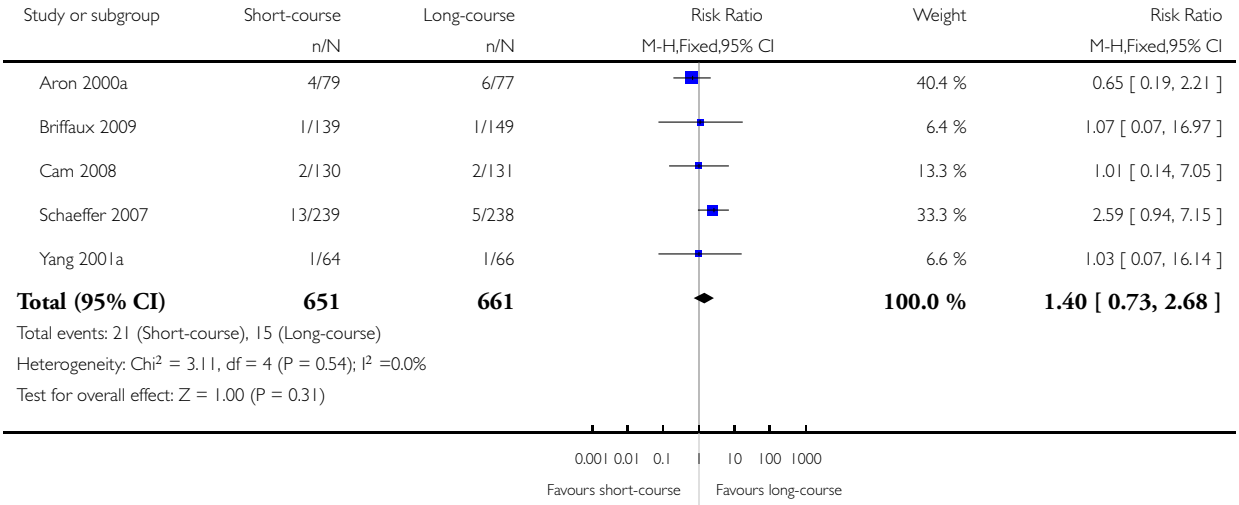


Analysis 4.3. Comparison 4 Short-course versus long-course treatment, Outcome 3 UTI.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 4 Short-course versus long-course treatment

Outcome: 3 UTI

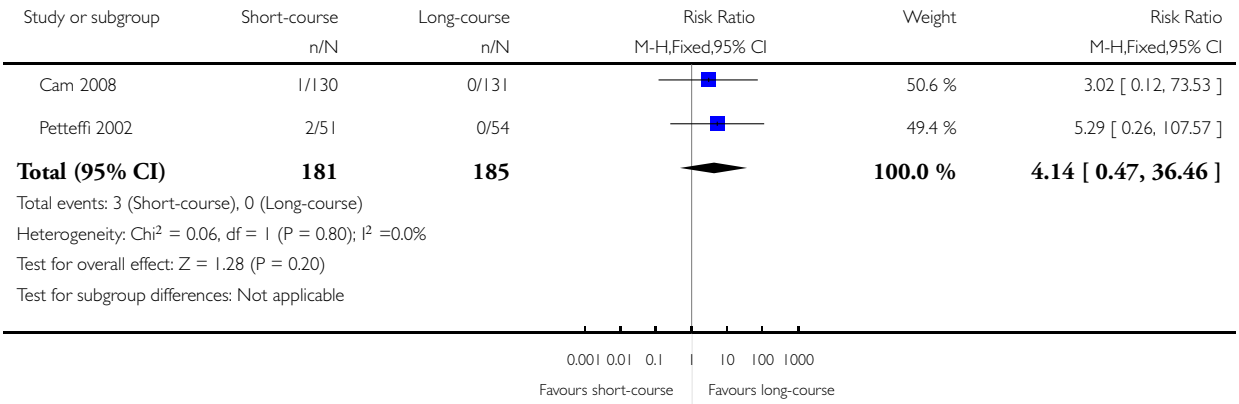


Analysis 4.4. Comparison 4 Short-course versus long-course treatment, Outcome 4 Hospitalization.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 4 Short-course versus long-course treatment

Outcome: 4 Hospitalization

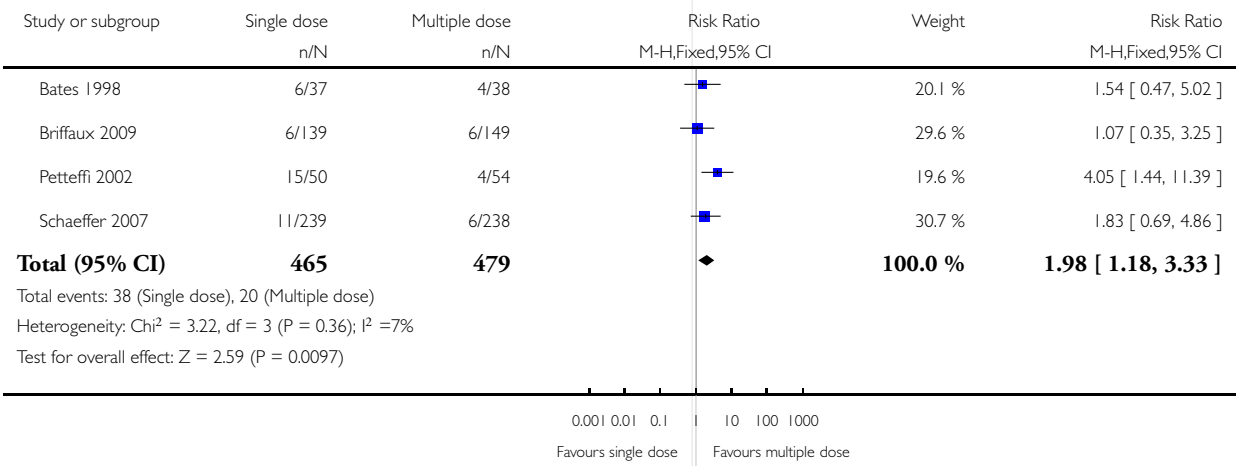


Analysis 5.1. Comparison 5 Single versus multiple dose, Outcome 1 Bacteriuria.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 5 Single versus multiple dose

Outcome: 1 Bacteriuria



Analysis 5.2. Comparison 5 Single versus multiple dose, Outcome 2 Fever.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 5 Single versus multiple dose

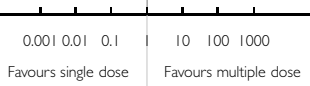
Outcome: 2 Fever

Study or subgroup	Single dose n/N	Multiple dose n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Aron 2000a	2/79	2/77		45.2 %	0.97 [0.14, 6.75]
Cam 2008	1/130	0/131		11.1 %	3.02 [0.12, 73.53]
Petteffi 2002	8/51	1/54		21.7 %	8.47 [1.10, 65.36]
Yang 2001a	1/64	1/66		22.0 %	1.03 [0.07, 16.14]
Total (95% CI)	**324**	**328**		**100.0 %**	**2.84 [0.99, 8.16]**

Total events: 12 (Single dose), 4 (Multiple dose)

Heterogeneity: $Chi^2 = 2.80$, df = 3 (P = 0.42); $I^2 = 0.0\%$

Test for overall effect: Z = 1.94 (P = 0.053)



Analysis 5.3. Comparison 5 Single versus multiple dose, Outcome 3 UTI.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 5 Single versus multiple dose

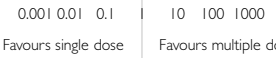
Outcome: 3 UTI

Study or subgroup	Single dose n/N	Multiple dose n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Aron 2000a	4/79	6/77		40.4 %	0.65 [0.19, 2.21]
Briffaux 2009	1/139	1/149		6.4 %	1.07 [0.07, 16.97]
Cam 2008	2/130	2/131		13.3 %	1.01 [0.14, 7.05]
Schaeffer 2007	13/239	5/238		33.3 %	2.59 [0.94, 7.15]
Yang 2001a	1/64	1/66		6.6 %	1.03 [0.07, 16.14]
Total (95% CI)	**651**	**661**		**100.0 %**	**1.40 [0.73, 2.68]**

Total events: 21 (Single dose), 15 (Multiple dose)

Heterogeneity: $Chi^2 = 3.11$, df = 4 (P = 0.54); $I^2 = 0.0\%$

Test for overall effect: Z = 1.00 (P = 0.31)



Analysis 5.4. Comparison 5 Single versus multiple dose, Outcome 4 Hospitalization.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 5 Single versus multiple dose

Outcome: 4 Hospitalization

Study or subgroup	Single dose n/N	Multiple dose n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Bates 1998	2/37	1/38		50.1 %	2.05 [0.19, 21.70]
Cam 2008	1/130	0/131		25.3 %	3.02 [0.12, 73.53]
Petteffi 2002	2/51	0/54		24.7 %	5.29 [0.26, 107.57]
Total (95% CI)	**218**	**223**		**100.0 %**	**3.10 [0.64, 15.06]**

Total events: 5 (Single dose), 1 (Multiple dose)

Heterogeneity: $Chi^2 = 0.24$, df = 2 (P = 0.89); $I^2 = 0.0\%$

Test for overall effect: Z = 1.40 (P = 0.16)

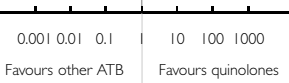
Analysis 6.1. Comparison 6 Quinolones versus other classes of antibiotics, Outcome 1 Bacteriuria.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 6 Quinolones versus other classes of antibiotics

Outcome: 1 Bacteriuria

Study or subgroup	Other ATB n/N	Quinolones n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Sulfonamides					
Isen 1999a	3/45	2/42		39.8 %	1.40 [0.25, 7.97]
Subtotal (95% CI)	**45**	**42**		**39.8 %**	**1.40 [0.25, 7.97]**
Total events: 3 (Other ATB), 2 (Quinolones)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.38 (P = 0.70)					
2 Piperacillin Tazobactam					
Cormio 2002	2/72	3/66		60.2 %	0.61 [0.11, 3.54]
Subtotal (95% CI)	**72**	**66**		**60.2 %**	**0.61 [0.11, 3.54]**
Total events: 2 (Other ATB), 3 (Quinolones)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.55 (P = 0.58)					
Total (95% CI)	**117**	**108**		**100.0 %**	**0.93 [0.28, 3.10]**
Total events: 5 (Other ATB), 5 (Quinolones)					
Heterogeneity: Chi^2 = 0.43, df = 1 (P = 0.51); I^2 =0.0%					
Test for overall effect: Z = 0.13 (P = 0.90)					

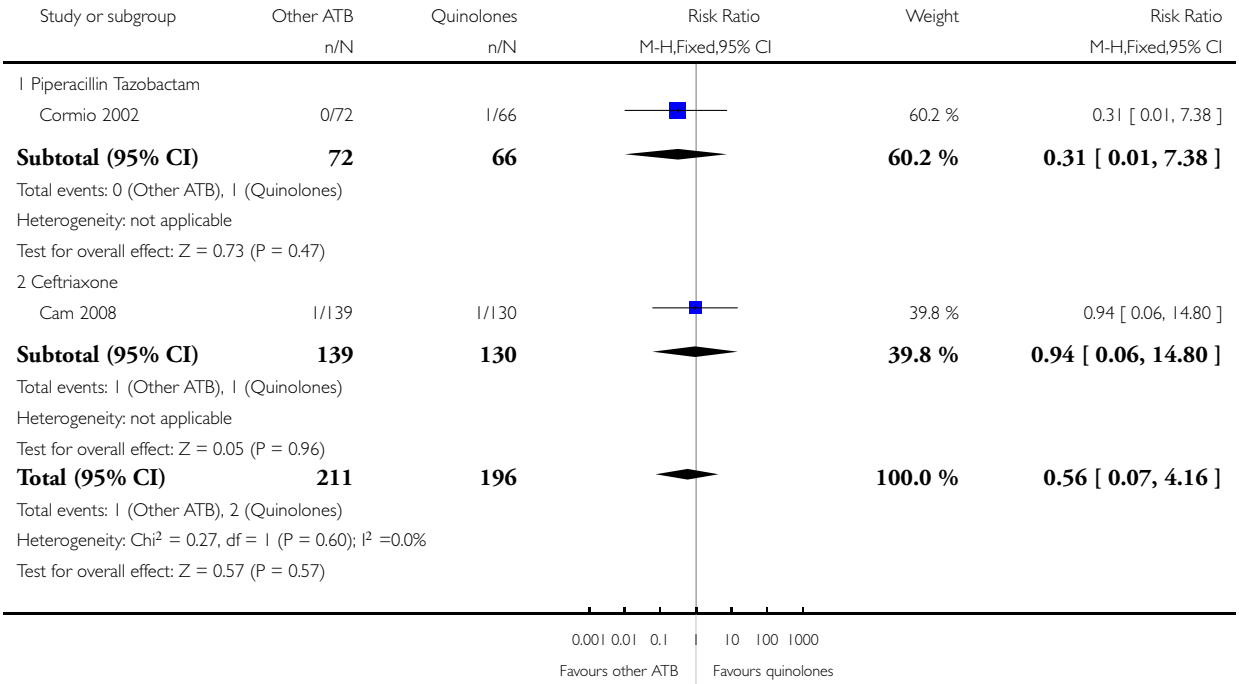


Analysis 6.2. Comparison 6 Quinolones versus other classes of antibiotics, Outcome 2 Fever.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 6 Quinolones versus other classes of antibiotics

Outcome: 2 Fever

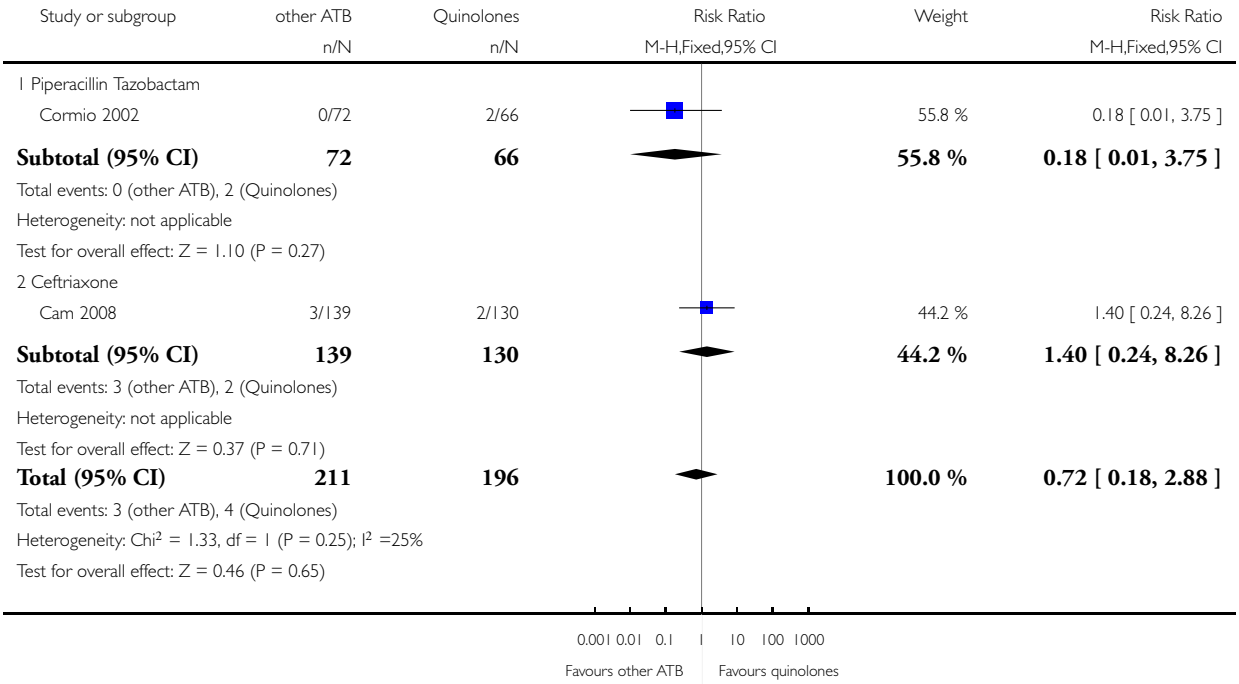


Analysis 6.3. Comparison 6 Quinolones versus other classes of antibiotics, Outcome 3 UTI.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 6 Quinolones versus other classes of antibiotics

Outcome: 3 UTI

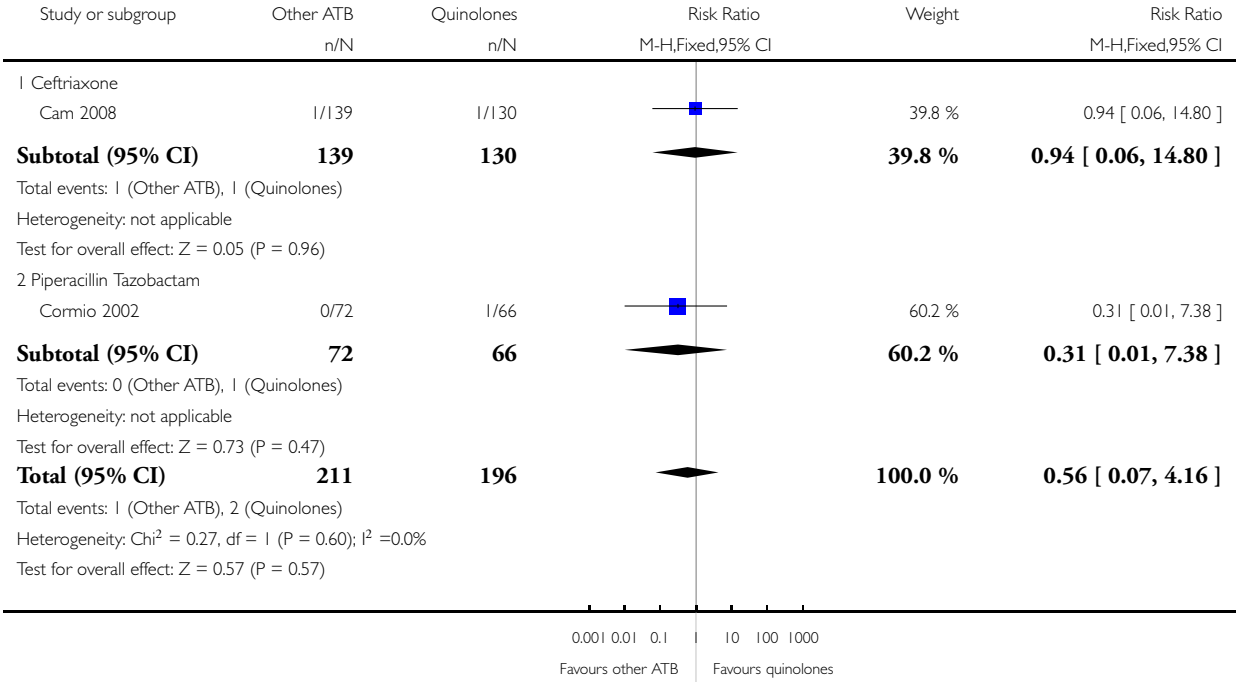


Analysis 6.4. Comparison 6 Quinolones versus other classes of antibiotics, Outcome 4 Hospitalization.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 6 Quinolones versus other classes of antibiotics

Outcome: 4 Hospitalization

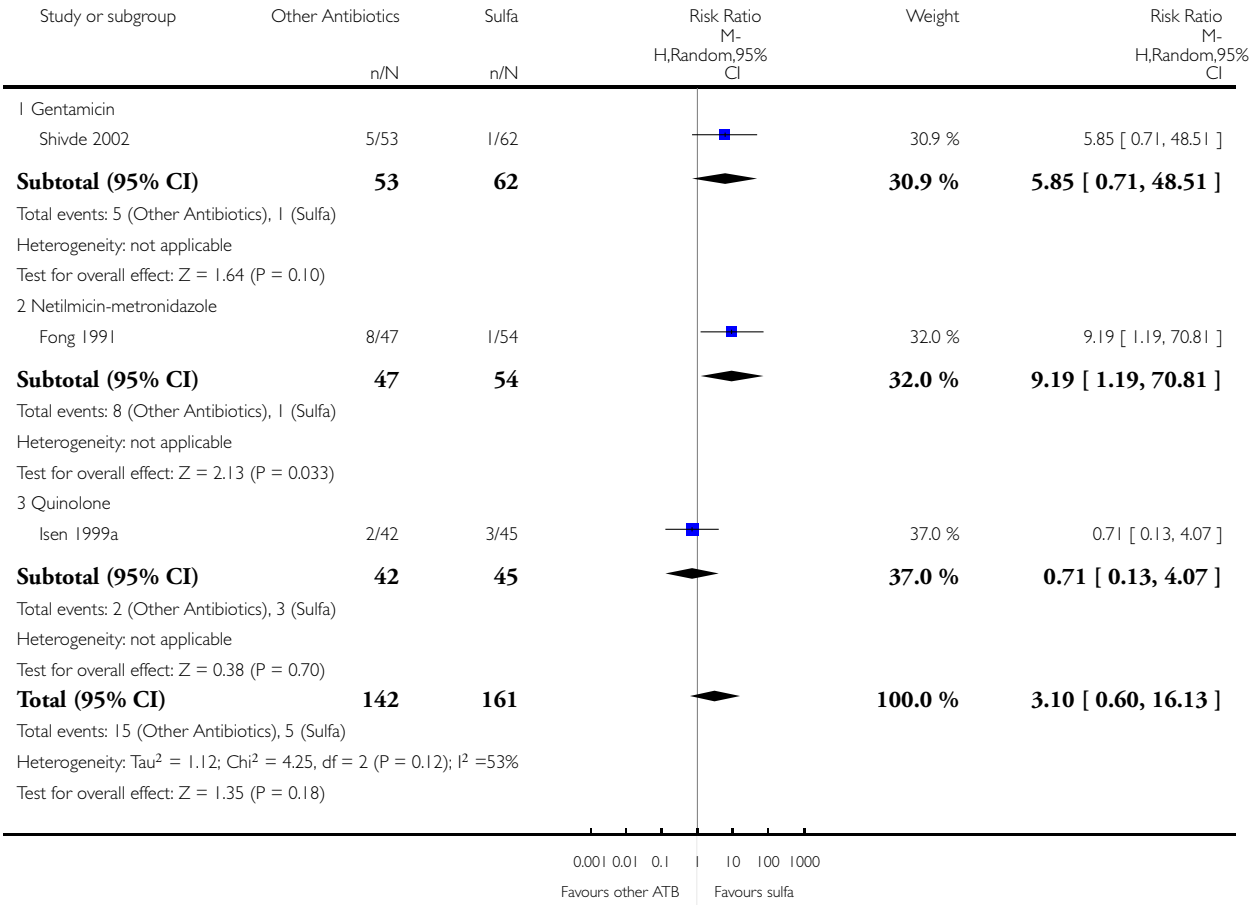


Analysis 7.1. Comparison 7 Sulfonamides versus other antibiotics, Outcome 1 Bacteriuria.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 7 Sulfonamides versus other antibiotics

Outcome: 1 Bacteriuria

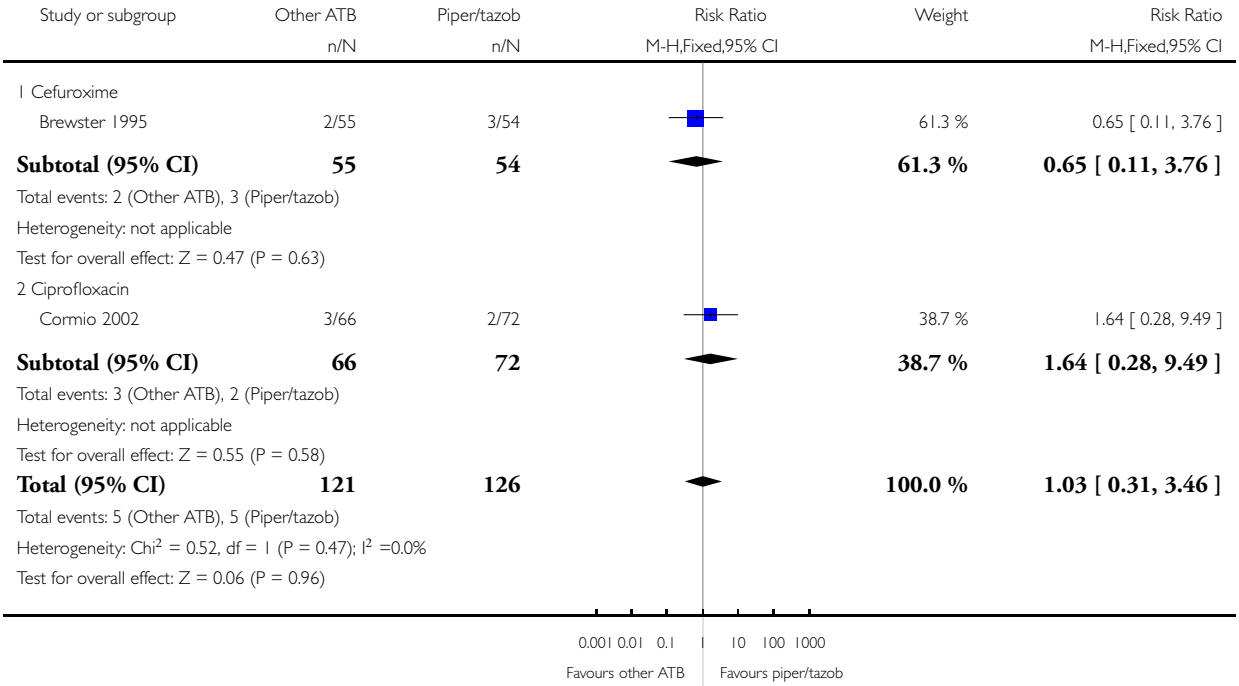


Analysis 8.1. Comparison 8 Piperacillin tazobactam versus other antibiotics, Outcome 1 Bacteriuria.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 8 Piperacillin tazobactam versus other antibiotics

Outcome: 1 Bacteriuria

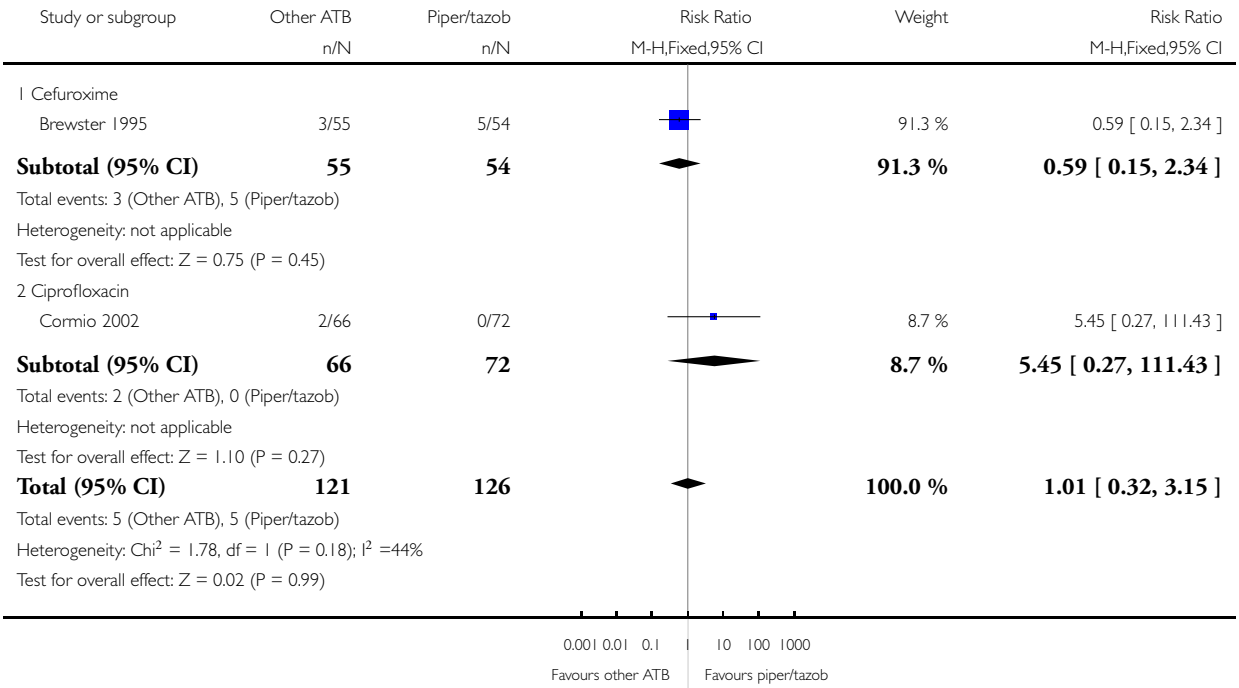


Analysis 8.2. Comparison 8 Piperacillin tazobactam versus other antibiotics, Outcome 2 UTI.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 8 Piperacillin tazobactam versus other antibiotics

Outcome: 2 UTI

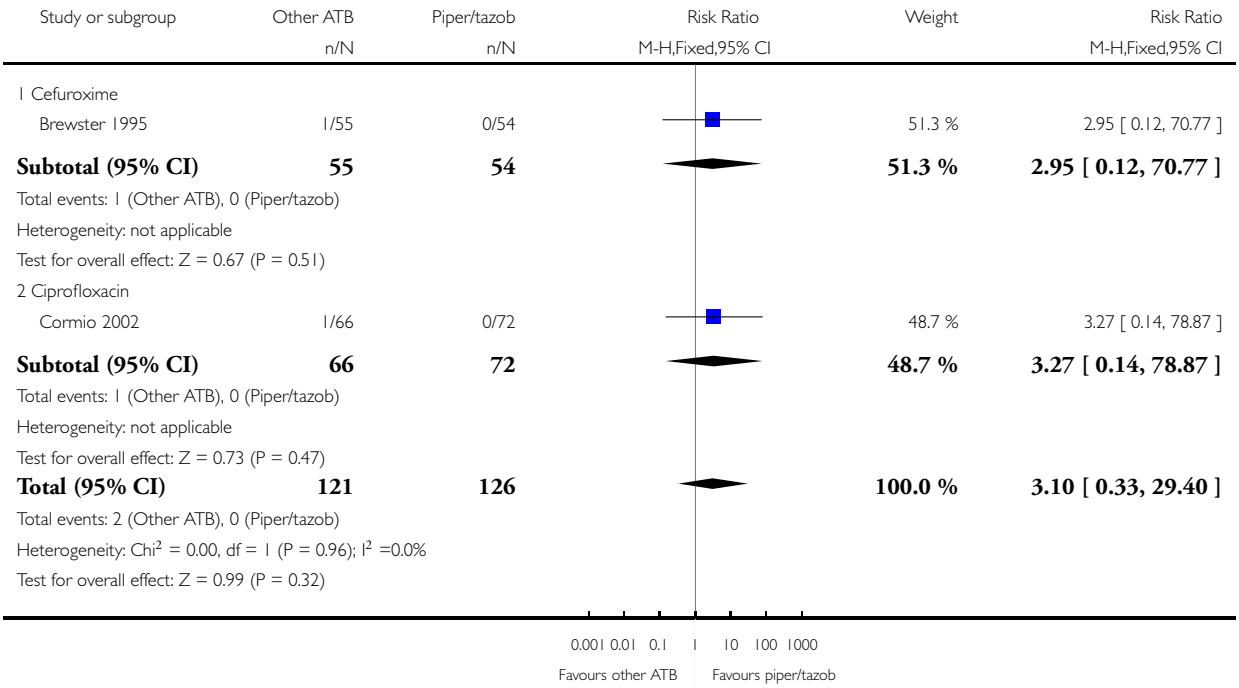


Analysis 8.3. Comparison 8 Piperacillin tazobactam versus other antibiotics, Outcome 3 Sepsis.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 8 Piperacillin tazobactam versus other antibiotics

Outcome: 3 Sepsis

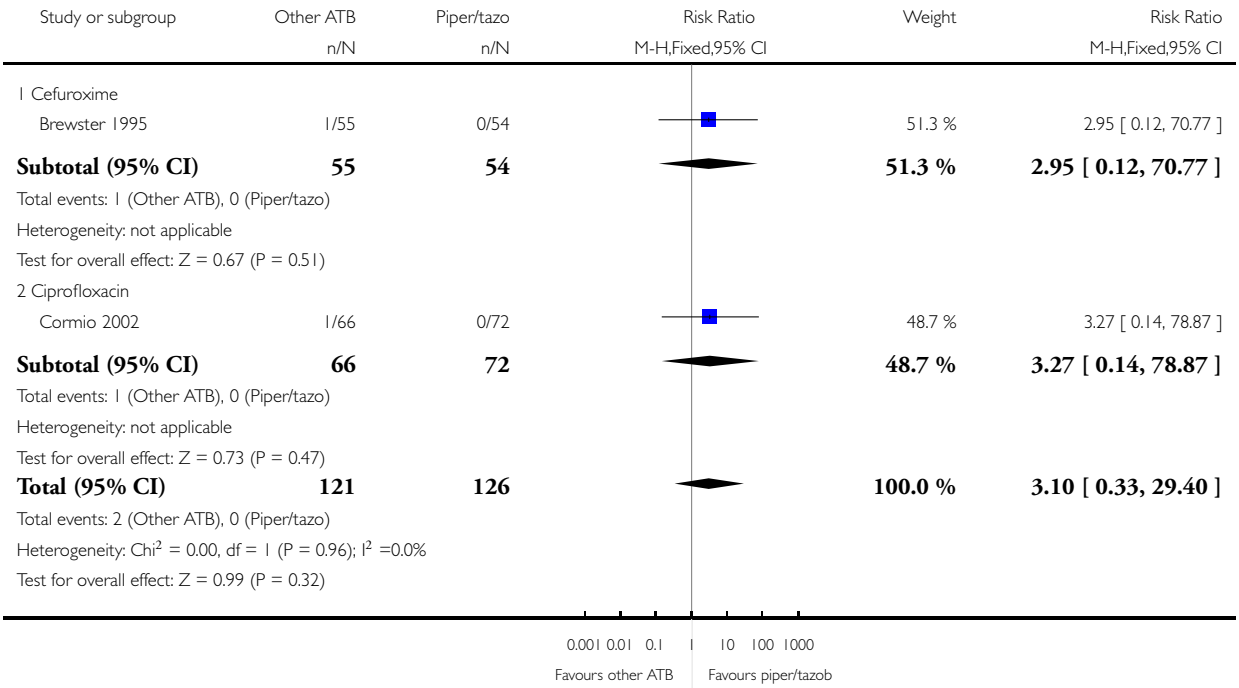


Analysis 8.4. Comparison 8 Piperacillin tazobactam versus other antibiotics, Outcome 4 Hospitalization.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 8 Piperacillin tazobactam versus other antibiotics

Outcome: 4 Hospitalization



Analysis 9.1. Comparison 9 Oral versus systemic antibiotic administration (IM or IV), Outcome 1 Bacteriuria.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 9 Oral versus systemic antibiotic administration (IM or IV)

Outcome: 1 Bacteriuria

Study or subgroup	Oral n/N	Systemic n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Cormio 2002	3/66	2/72		36.4 %	1.64 [0.28, 9.49]
Fong 1991	1/54	8/47		32.3 %	0.11 [0.01, 0.84]
Shivde 2002	1/62	5/53		31.3 %	0.17 [0.02, 1.42]
Total (95% CI)	**182**	**172**		**100.0 %**	**0.34 [0.06, 1.93]**

Total events: 5 (Oral), 15 (Systemic)

Heterogeneity: $Tau^2 = 1.38$; $Chi^2 = 4.74$, df = 2 (P = 0.09); $I^2 = 58\%$

Test for overall effect: Z = 1.22 (P = 0.22)

Analysis 9.2. Comparison 9 Oral versus systemic antibiotic administration (IM or IV), Outcome 2 Fever.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 9 Oral versus systemic antibiotic administration (IM or IV)

Outcome: 2 Fever

Study or subgroup	Oral n/N	Systemic n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Cam 2008	1/130	1/139		1.07 [0.07, 16.92]
Cormio 2002	1/66	0/72		3.27 [0.14, 78.87]
Shivde 2002	0/62	0/53		0.0 [0.0, 0.0]
Total (95% CI)	**258**	**264**		**1.80 [0.24, 13.45]**

Total events: 2 (Oral), 1 (Systemic)

Heterogeneity: Chi^2 = 0.27, df = 1 (P = 0.60); I^2 =0.0%

Test for overall effect: Z = 0.57 (P = 0.57)

Test for subgroup differences: Not applicable

Analysis 9.3. Comparison 9 Oral versus systemic antibiotic administration (IM or IV), Outcome 3 UTI.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 9 Oral versus systemic antibiotic administration (IM or IV)

Outcome: 3 UTI

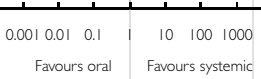
Study or subgroup	Oral n/N	Systemic n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Cam 2008	2/130	3/139		47.9 %	0.71 [0.12, 4.20]
Cormio 2002	2/66	0/72		7.9 %	5.45 [0.27, 111.43]
Fong 1991	0/54	2/47		44.1 %	0.17 [0.01, 3.55]
Total (95% CI)	**250**	**258**		**100.0 %**	**0.85 [0.27, 2.70]**

Total events: 4 (Oral), 5 (Systemic)

Heterogeneity: Chi^2 = 2.55, df = 2 (P = 0.28); I^2 =22%

Test for overall effect: Z = 0.28 (P = 0.78)

Test for subgroup differences: Not applicable

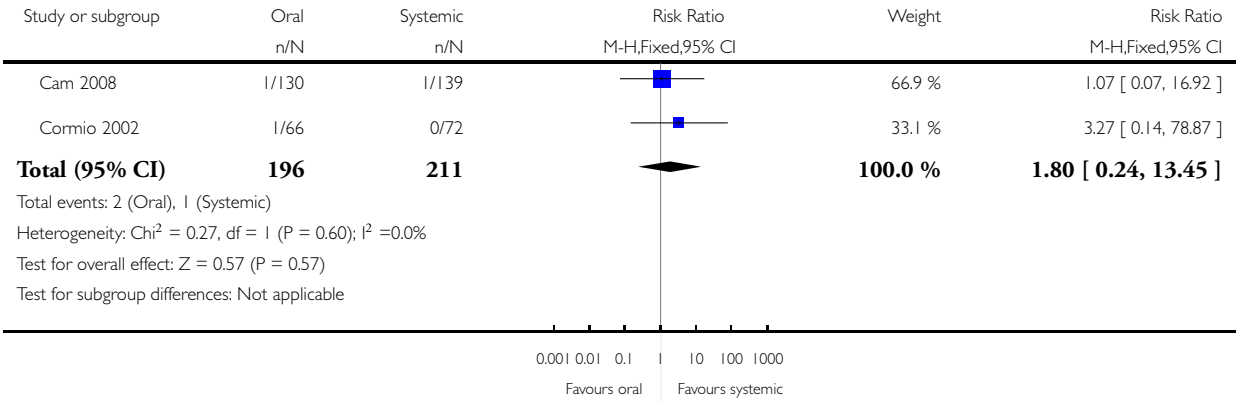


Analysis 9.4. Comparison 9 Oral versus systemic antibiotic administration (IM or IV), Outcome 4 Hospitalization.

Review: Antibiotic prophylaxis for transrectal prostate biopsy

Comparison: 9 Oral versus systemic antibiotic administration (IM or IV)

Outcome: 4 Hospitalization



ADDITIONAL TABLES

Table 1. Outcomes analysed in each included study

Study	Bacteriuria	Bacteremia	Fever	UTI	Sepsis	Mortality	Hospitalization	Adverse events
Aron 2000		X	X	X				
Bates 1998	X				X		X	
Brewster 1995	X	X		X	X		X	X
Briffaux 2008	X			X				
Brown 1981	X	X	X					

Table 1. Outcomes analysed in each included study (*Continued*)

Cam 2008			X	X			X	
Cormio 2002	X		X	X	X		X	
Crawford 1982	X	X	X		X			X
Fong 1991	X	X		X				
Freitas 1999			X	X	X	X	X	
Isen 1999	X						X	X
Kapoor 1998	X	X	X	X	X		X	X
Melekos 1990	X	X	X					
Petteffi 2002	X		X				X	
Ruebush 1979	X	X	X					X
Schaeffer 2007	X			X				
Shivde 2002	X		X					
Tekdogan 2006	X		X					
Yang 2001			X	X				

Table 2. Included studies in each category of comparison

ATB X Placebo	**ATB X Enema and ATB X ATB + enema**	**Short X Long-course**	**Multiple X Single-dose**	**Quinolones X another**	**Sulfonamide X another**	**Piperacilin Tazobactan X another**	**Oral versus systemic administration**
Ruebush 1979	Brown 1981	Aron 2000	Bates 1998	Isen 1999	Fong 1991	Brewster 1995	Fong 1991
Brown 1981	Melekos 1990	Yang 2001	Aron 2000	Cormio 2002	Isen 1999	Cormio 2002	Cormio 2002

Table 2. Included studies in each category of comparison (*Continued*)

Crawford 1982	Freitas 1999	Petteffi 2002	Yang 2001	Cam 2008	Shivde 2002		Shivde 2002
Melekos 1990	Tekdogan 2006	Schaeffer 2007	Petteffi 2002				Cam 2008
Kapoor 1998		Briffaux 2008	Schaeffer 2007				
Isen 1999		Cam 2008	Briffaux 2008				
Aron 2000			Cam 2008				
Yang 2001							
Tekdogan 2006							

WHAT'S NEW

Last assessed as up-to-date: 30 August 2010.

Date	Event	Description
30 September 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 3, 2007

Review first published: Issue 5, 2011

Date	Event	Description
3 April 2007	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

ELZ: trial selection, quality assessment, data extraction, data entry, data analysis, writing of protocol and review

OACC: trial selection, quality assessment, data extraction, data entry, data analysis, writing of protocol, revision of protocol and review

NRN Jr: data analysis, writing of protocol, resolution of disagreements, revision of protocol and review

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- None, Not specified.

External sources

- None, Not specified.

INDEX TERMS

Medical Subject Headings (MeSH)

Antibiotic Prophylaxis [*methods]; Bacteremia [prevention & control]; Bacterial Infections [*prevention & control]; Bacteriuria [prevention & control]; Biopsy, Needle [*adverse effects; methods]; Hospitalization [statistics & numerical data]; Prostate [*pathology]; Prostatic Neoplasms [pathology]; Urinary Tract Infections [prevention & control]

MeSH check words

Humans; Male