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Review Article

Antibiotic prophylaxis for transurethral urological surgeries: Systematic review

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Abstract

The use of antibiotic prophylaxis to prevent urinary tract infection and bacteremia (sepsis) following endoscopic urologic procedures is a controversial topic. Evidence in the literature revealed that urological instrumentation is associated with increased incidence of urinary tract infection and bacteremia. The aim of this review is to evaluate the effectiveness of antibiotic prophylaxis in reducing the risk of urinary tract infection in patients who had transurethral urological surgeries. We have selected all RCTs of adult population who underwent all different types of transurethral urological surgery, including cystoscopy, transurethral resection of prostate and transurethral resection of bladder tumor, and received prophylactic antibiotics or placebo/no treatment. At first, more than 3000 references were identified and reviewed; of which 42 studies with a total of 7496 patients were included in the final analysis. All those trials were analyzing antibiotic prophylaxis versus placebo/no treatment, and they were significantly favoring antibiotic use in reducing all outcomes, including bacteriuria (RR 0.36, 95% CI 0.29 to 0.46, $P < 0.0001$) with moderate heterogeneity detected ($I^2 = 48\%$), symptomatic UTI (RR 0.38, 95% CI 0.28 to 0.51, $P < 0.0001$) with no significant heterogeneity was detected ($I^2 = 17\%$), bacteremia (RR 0.43, 95% CI 0.23 to 0.82, $P < 0.0001$) with no noted heterogeneity ($I^2 = 0\%$), and fever ≥38.5 Celsius (RR 0.41, 95% CI 0.23 to 0.73, $P = 0.003$); also, there was no noted heterogeneity ($I^2 = 0\%$). However, using antibiotic prophylaxis did not reduce the incidence of low grade temperature (RR 0.82, 95% CI 0.61 to 1.11, $P = 0.20$) or in moderate grade temperature (RR 1.03, 95% CI 0.71 to 1.48, $P = 0.89$). Antibiotic prophylaxis appears to be an effective intervention in preventing urinary tract infections and its sequels following transurethral urological surgeries in patients with preoperative sterile urine.

Key Words: Antibiotic prophylaxis, urinary tract infection, endourology, bacteremia

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INTRODUCTION

The trend in all surgical disciplines has been shifting toward non-operative or minimally invasive treatment, which has multiple applications with varied outcomes comparable to open surgery. The goal is to decrease the morbidity of surgical procedures, minimize hospital stays, better cosmesis, and improve patients' quality of life. Endourology, which began

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with the development of cystoscopy, initially defined as "the closed and controlled manipulation within the urinary tract," is one of the most challenging and rapidly evolving areas in urology practice. The goal of endoscopy is to access and treat organs, through natural or artificial orifices in the body, with a telescope. The gradual evolution toward the modern endoscopes started with Philipp Bozzinis construction of the lichtleiter in 1806 for direct inspection and treatment of the uterus and bladder.[1] Since then, significant development and advancements have been made in the field of endo-urology. With continued refinements, a wide range of rigid, semi-rigid, and flexible endoscopes made available, and at the present time, they made up the bulk of our urologic surgical practice.

The risk of urinary tract infection following endoscopic urologic procedures and the use of antibiotic prophylaxis are highly controversial topics. Traditionally, endo-urological surgeries were considered clean contaminated procedures and did not require antibiotic coverage.[2] However, evidence in the literature revealed that urological instrumentation is associated with increased incidence of urinary tract infection and bacteremia.[3] Potential sources of bacteria leading to infection include the prostatic adenoma, urethral flora, bladder colonization, or perioperative contamination.[4] Urinary catheters represent an essential part of our medical care as an investigative and management tool. Catheter-related UTIs account for roughly 40% of all nosocomial infections that increase the mean hospital stay, morbidity, and cost.[5] In a sterile urine preoperatively, the incidence of symptomatic UTI following cystoscopy is 5%, and the incidence of asymptomatic bacteriuria has been reported ranging between 10% and 35% in most of the series.[6-8] Following ureteroscopy, the reported incidence of UTI ranges between 3.9% and 25%.[9-11]

Sepsis following UTI (urosepsis) is a syndrome resulting from complicated UTI in a patient with one or more of the following signs: Tachypnea, tachycardia, hyperthermia or hypothermia, or evidence of inadequate end-organ perfusion. Septic shock, defined as sepsis syndrome that is accompanied by hypotension, is a rare event after urological procedures with a favorable prognosis.[12] The reported rates of urosepsis following the transurethral resection of prostate (TURP) range from 1% to 4%, with an associated mortality rate of 13%, which raises up to 20% in men over 64 years old.[13-15] Compared to TURP, Fewer data are available on the infectious complications of transurethral resection of bladder tumor (TURBT). However, it has been documented before that the infection rates following TURBT range from 18% to 75%, which was correlated to patient gender and the preoperative urine culture results.[12]

Administration of antibiotic prophylaxis in high risk cases is accepted and even recommended practice, but their use in low risk population remains controversial, and question persist, particularly on the appropriate class and duration of treatment.[16,17] After an earlier critical review of 75 studies,[18] which did not recommend the use of antibiotic prophylaxis due to methodology and design flaws, later studies supported the routine use of perioperative antibiotics for low risk patients undergoing all different types of endo-urological procedures with variable degrees of certainty.[16,19-26]

OBJECTIVES

The aim of this review is to assess the effectiveness of antibiotic prophylaxis given at the perioperative period, in comparison to placebo/no treatment, in reducing the incidence of urinary tract infections following transurethral urological surgeries in adult patients.

MATERIALS AND METHODS

Criteria for considering studies for this review

Types of studies

All randomized, controlled trials (RCT) and quasi-RCTs, (RCTs in which allocation to treatment was obtained in predictable methods or uncertain) looking at adult patients who had transurethral urological surgery and received antibiotic prophylaxis versus placebo/no treatment during the perioperative period. The first period of randomized crossover studies shall also be included. All studies, which have been included in previous meta-analyses and which comply with our inclusion criteria, were included.

Type of participants

Inclusion criteria

Patients with sterile preoperative urine, who had an elective transurethral urological surgeries, which includes: Cystoscopy, transurethral resection of prostate (TURP), transurethral resection of bladder tumor (TURBT), optical urethrotomy (VIU), urethral dilation, and bladder neck incision (BNI), were included.

Exclusion criteria

All patients with culture-proven UTIs prior to intervention, patients with neurogenic bladder, patients with indwelling catheters, and patients who have received antibiotics during the preceding 10 days were excluded. Also, patients with co-morbid conditions such as diabetes, renal failure (serum creatinine levels higher than 2 mg/dl), and immunocompromised individuals who are prone to infections were excluded. Studies evaluated two active arms with no control group were also excluded. Studies assessed the risk of infection after one week from surgery was excluded, unless data are available for the first week. And finally, patients with prostheses (e.g., hip replacement, knee replacement, and prosthetic cardiac valves) and congenital heart disease requiring prophylactic antibiotics were also excluded.

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Subgroups

Transurethral urological surgeries broadly were divided into two main groups: Urological procedure without mucosa penetration, like cystoscopies which carries a lower risk of infection, or urological procedure with mucosa penetration, like TURP, TURBT, BNI, and VIU which carries a slightly higher risk of infection. Therefore, subgroup analysis was performed for those two groups, and a third group was created if the study included all different type of urological procedure, and they did not report the results separately. Another subgroup analysis was performed for the different grades of fever.

Types of interventions

Use of any antibacterial agents, alone or in combination, single dose or multiple doses, for one day or several days versus placebo or no treatment.

Type of outcome measures

Primary outcomes

- Asymptomatic bacteriuria: Defined as the presence of bacteria in the urine in a patient who has no symptoms or signs. Bacteriuria defined as a single bacterial growth of 10^5 colony forming units per ml in urine culture on a clean catch urine or >10^3 per ml on an in-out catheter specimen or suprapubic puncture specimen and between postoperative days 2 and 10.
- Symptomatic UTI: Defined as bacteriuria (as defined above) in patient with symptoms including pain (flank, lower abdominal), lower urinary tract symptoms (dysurea, frequency, urgency, or incontinence), hematuria, or fever.

Secondary outcomes

- Bacteremia: Defined as the presence of bacteria in blood culture irrespective of clinical signs.
- Fever: Which was graded into the following
  1. Low grade fever: Any temperature ≥37.3 Celsius and less than 38 Celsius.
  2. Moderate grade fever: Any temperature ≥38 Celsius and less than 38.5 Celsius.
  3. High grade fever: Any temperature ≥38.5 Celsius.

Search methods for identification of studies

Electronic searches

A comprehensive and exhaustive search strategy was formulated in an attempt to identify all relevant studies regardless of language or publication status, initially. All relevant studies were obtained from the following electronic databases:

- MEDLINE from 1966 to 21st April 2011
- EMBASE from 1980 to 31st Dec 2010
- LILACS from 1980 to 2010
- Cochrane Central Register of Controlled Trials (CENTRAL).
- Reference lists of relevant articles, reviews, studies, and book chapters.
- All major urological conference proceedings were searched accordingly: American Urological Association (AUA) meetings from 1996 up to May 2011, European Urology Association meeting from 2004 and up to date, and Canadian Urology Association meetings from 2006 up to date.

Along with MeSH terms and relevant keywords, I used the Cochrane Highly Sensitive Search Strategy for identifying reports of randomized controlled trials in MEDLINE.[27] See Appendix 1 for examples of the search strategies across different databases.

Limits

The initial search strategy was performed without limits to language, and after reviewing the titles and then the abstracts of the search results, 10 trials could possibly be included but were not, due to language barrier, 4 in French, 4 in Spanish, and 2 in Italian languages.

Data collection and analysis

The methodology for data collection and analysis was based on the guidance of Cochrane Handbook of Systematic Reviews of Intervention.[27] Abstracts of all trials identified by electronic or bibliographic search were examined by two authors. When necessary, the full text was obtained to determine the eligibility of studies for inclusion.

Selection of studies

All potential trials' titles and abstracts were read by two reviewers and were selected for eligibility according to the criteria specified in the protocol. Where suitability was uncertain or no abstract available, the full article was obtained. The articles were excluded if it did not fit the inclusion criteria; the reasons for exclusion were detailed in the section Appendix 2: Characteristics of Excluded Studies.

Data extraction and management

For each included article, an attentive reading followed by data extraction using a standardized data extraction form. Extracted information included: Study details, participants details, intervention details, and outcome details.

Assessment of risk of bias in included studies

The Methodological quality of each selected trial was assessed comprehensively. We used the Cochrane Collaboration tool for assessing the risk of bias for each individual study and presented results in a summery [Table 1]. To assess the possibility of publication bias, a funnel-plot test was performed. Attempts were made to minimize the potential for publication bias by performing a very sensitive, broad, and comprehensive search strategy.

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Measures of treatment effect

For dichotomous outcomes, which include bacteriuria, symptomatic urinary tract infection, bacteremia, and fever, results were expressed as risk ratios (RR) with 95% confidence intervals (CI). Data were pooled using the fixed-effects model. 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.

Assessment of heterogeneity

Heterogeneity was analyzed, initially by eye-balling and then, by using the X^2 statistic with a significant level of 0.10, and the I^2 test. When there was considerable heterogeneity among the studies ($I^2 > 50\%$), the random-effects model was utilized. If considerable heterogeneity was still detected ($I^2 > 50\%$), a possible explanation was pursued, and sensitivity analysis was performed. If heterogeneity persisted and 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 did not pool the data. The studies were included in a meta-analysis using the outcomes presented above.

RESULTS

Results of the search

Search was conducted on 21st April 2011, and produced 2291 titles after 726 duplicates were removed [Figure 1]. After initial screening of titles, 844 abstract were reviewed by two authors. A further irrelevant 671 references were excluded at that stage. Full articles were obtained for 173 references; however, 10 references were discarded due to language barrier despite its relevance to the topic (review the excluded trials), and a further 89 references were discarded because it was either irrelevant reports or reviews articles. The remaining of the studies were reviewed initially for fulfilling my inclusion and exclusion criteria, and then for its relevance, based on study design, type of participants, exposures, and outcomes measures. Finally, 42 original reports of trials were identified as meeting inclusion criteria for data extraction and were included in the final meta-analysis.[3,14,28-67]

Risk of bias in included trials

Adequate randomization was identified in 15 trials (36%), and 12 trials reported an adequate allocation concealment (29%). Thirteen trials were double-blinded, and a further 5 trials reported an adequate blinding process. Most of the included trials, 34 trials which represent 81% of all included trials, addressed an incomplete outcome data. Selective reporting section was very confusing where 27 trials (64%) were unclear and 14 trials were adequate. The majority of included trials were apparently free of other potential source of bias. Most, if not all, of the trials included did not mention that they performed intention to treat analysis. Additionally, most of the time, the methodology section of the included trials were insufficiently detailed and underreported. Publication bias was unlikely according to the funnel plots inspection [Figure 2].

Effects of intervention

Summary of findings for the main comparison: Antibiotic prophylaxis versus placebo/no treatment, outcome: 1.1 Bacteriuria, 1.2, Bacteriuria according to the urological procedure performed, and 1.3 Bacteriuria according Antibiotic course (single dose, ≤3 days course, or >3 days course) are illustrated on Figures 3-5, respectively. Summary of findings for outcome: 2 Symptomatic urinary tract infection, outcome: 3 Bacteremia and outcome: 4 Fever, divided according to temperature grades, are illustrated in Figures 6-8, respectively.

The analysis included 42 trials with a total of 7496 patients. All studies reported the incidence of bacteriuria within 1 week postoperatively. However, not all trials allowed data extraction for all other end points, especially for bacteremia.

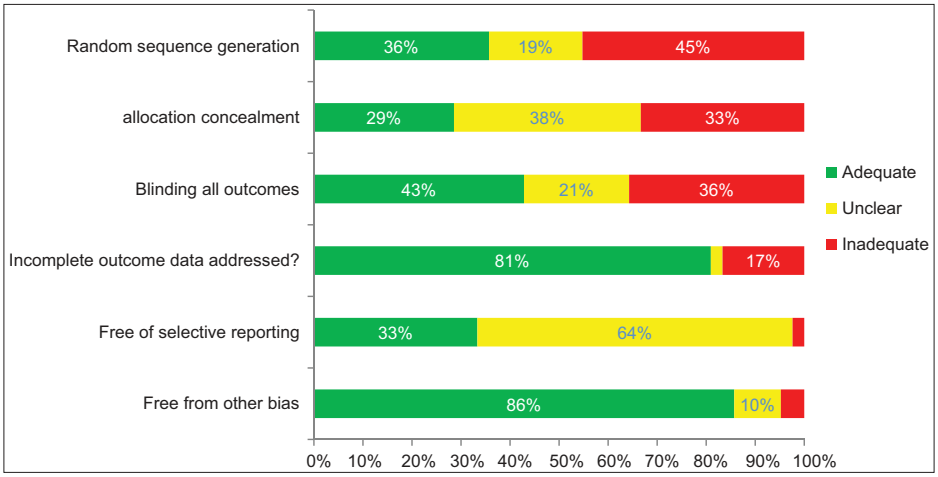

Table 1: Risk of bias graph: Author's judgment about each risk of bias item presented as percentages across all included studies

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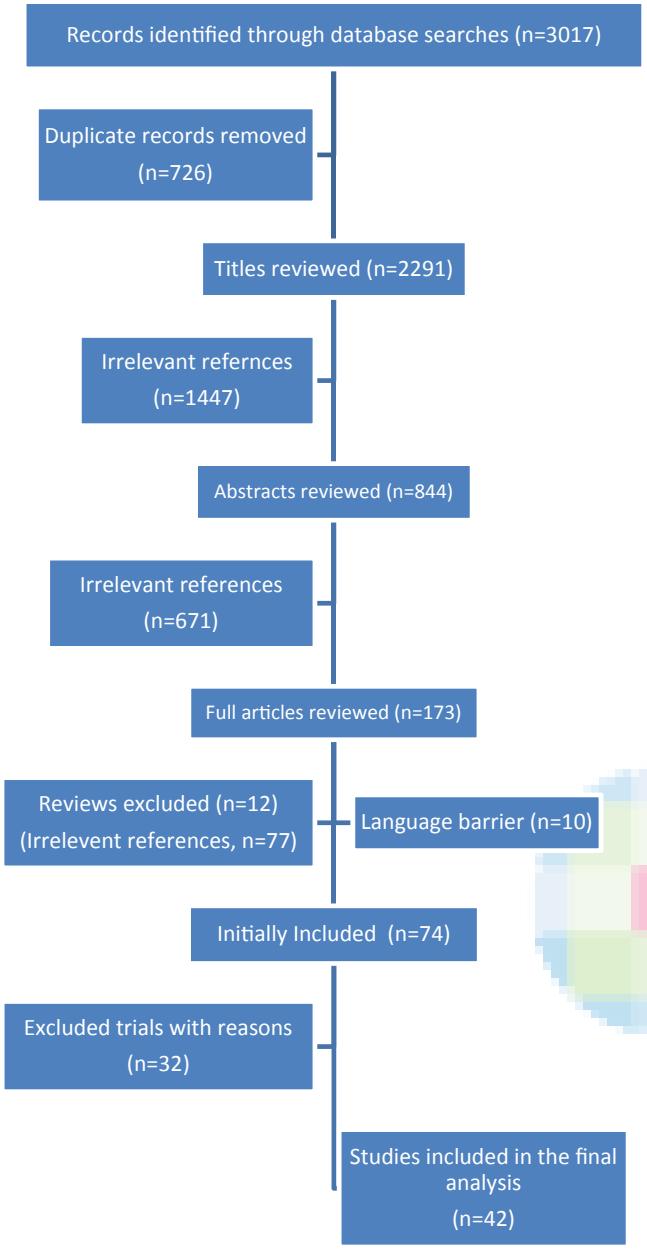

Figure 1: Flow-chart of screening process

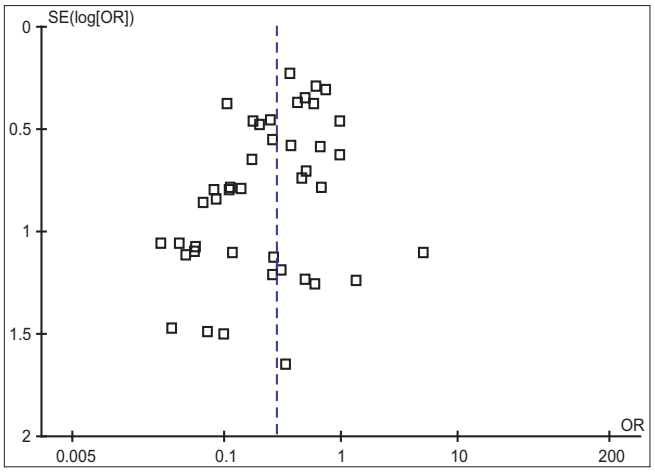

Figure 2: Funnel plots for included trials

Results of the main outcome number 1: Bacteriuria

Data on bacteriuria could be extracted from all included trials, 42 trials, with 7496 patients. There were 555 events of bacteriuria among 3147 patients randomized to receive placebo or no treatment, and 294 events among 4349 patients randomized to receive antibiotics. The meta-analysis was significant and favored antibiotic use (RR 0.36, 95% CI 0.29 to 0.46, $P < 0.0001$). A moderate heterogeneity was detected in the analysis ($I^2 = 48\%$) [Figure 3]. This heterogeneity was expected before hand, and the decision to perform subgroup analysis according to the invasiveness of the surgical procedure was preplanned, and the results of this section are shown in Figure 4. The results for the minimal invasive surgeries, mainly cystoscopies, were reported in 5 trials, "Cam 2009," "Higgins 1966," "Johnson 2007," "Mendoza 1971," and "Wilson 2005." There were 55 bacteriuria events among 1002 patients randomized to control, and 43 events among 1681 patients randomized to receive antibiotic prophylaxis. The results did not reach to a statistical significance (RR 0.5, 95 CI 0.22-1.15, $P < 0.1$), which implies that antibiotic prophylaxis may have no role in preventing urinary tract infections in patients undergoing diagnostic cystoscopy. A mild heterogeneity was detected in the analysis ($I^2 = 29\%$). Furthermore, there was a significant reduction of bacteriuria events in endoscopic urologic surgeries with variable degrees of mucosal penetration, Figure 4. For combined surgeries, bacteriuria events were significantly reduced in the antibiotic arm (RR 0.15, 95% CI: 0.07-0.32, $P < 0.0001$), with no heterogeneity detected in the analysis ($I^2 = 0\%$). As well, bacteriuria events were significantly reduced in patient received antibiotic prophylaxis and undergone transurethral surgeries with mucosa perforation (RR 0.38, 95% CI: 0.29-0.49, $P < 0.0001$). However, the heterogeneity for this subgroup was still significant with an I^2 of 51%. Sensitivity analysis was performed, and after excluding "Stricker 1988," "Qvist 1984," "Ibrahim 2002," and "Conn 1988," the I^2 dropped to insignificant level. Those articles were re-reviewed, and the most significant methodological difference were: Using different courses of antibiotic prophylaxis (single dose, up to 3 days course, or more than 3 days course), and using different classes of antibiotics agents. The first part was only checked in this review, and the results are summarized in Figure 5 while the second part will be assessed in a different review. This step did not include trials with more than two active arms because they were using two different antibiotic courses on the same control. This analysis was significant and favored antibiotic use (RR 0.38, 95% CI 0.30 to 0.47, $P < 0.0001$), which was also evidenced across the three different antibiotic courses, and a mild heterogeneity was detected in the analysis ($I^2 = 36\%$).

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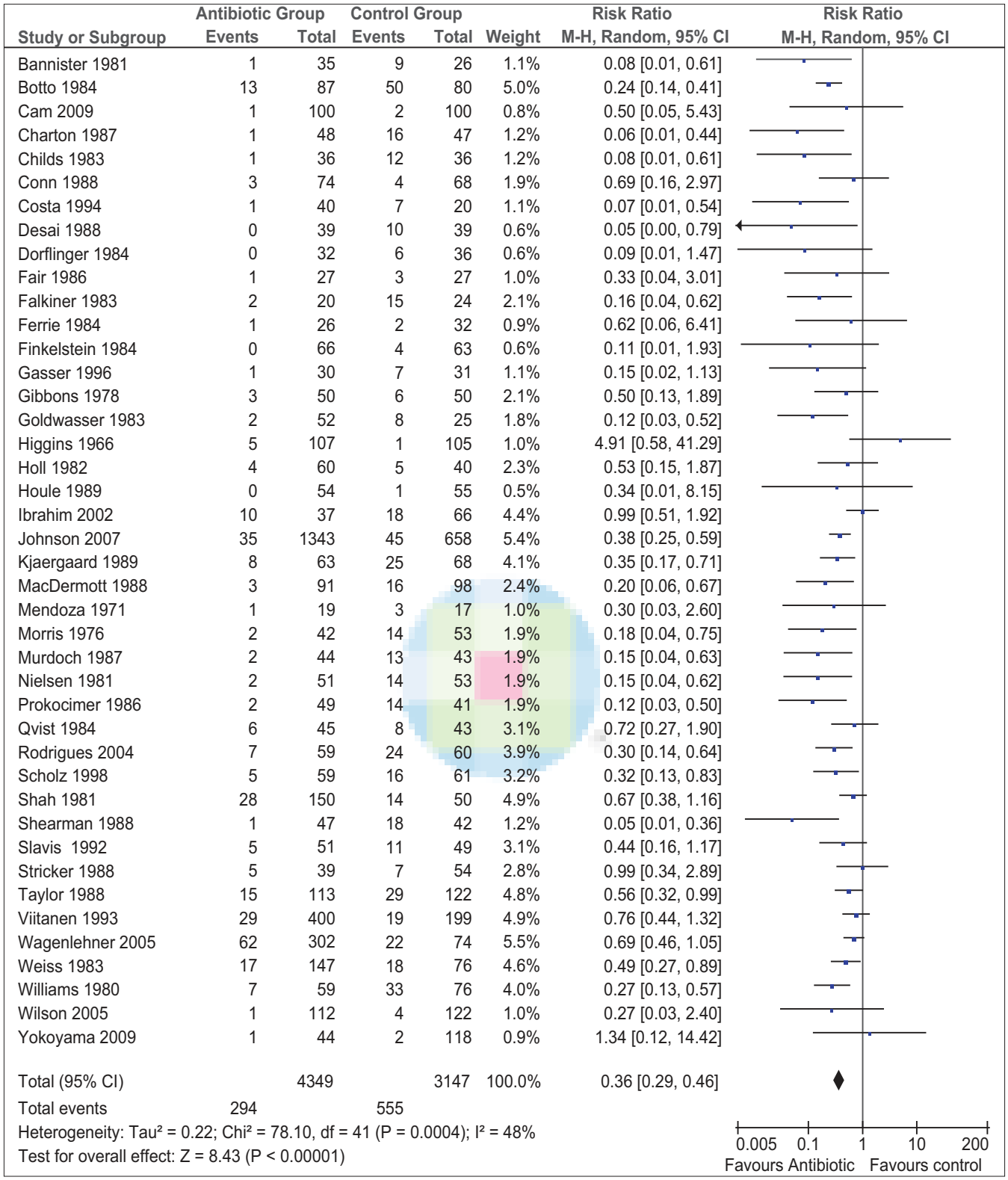

Figure 3: Forest plot of comparison: Antibiotic prophylaxis versus placebo/no treatment, outcome: 1.1 bacteriuria

Results of the main outcome number 2: Symptomatic urinary tract infection

Data on symptomatic UTI could be extracted from 22 trials, with 5211 patients. There were 223 events (10.1%) of symptomatic UTI among 2204 patients randomized to receive placebo or no treatment, and 87 events (3%) among 3007 patients randomized to receive antibiotics. The meta-analysis was significant and favored antibiotic use (RR 0.38, 95% CI 0.28

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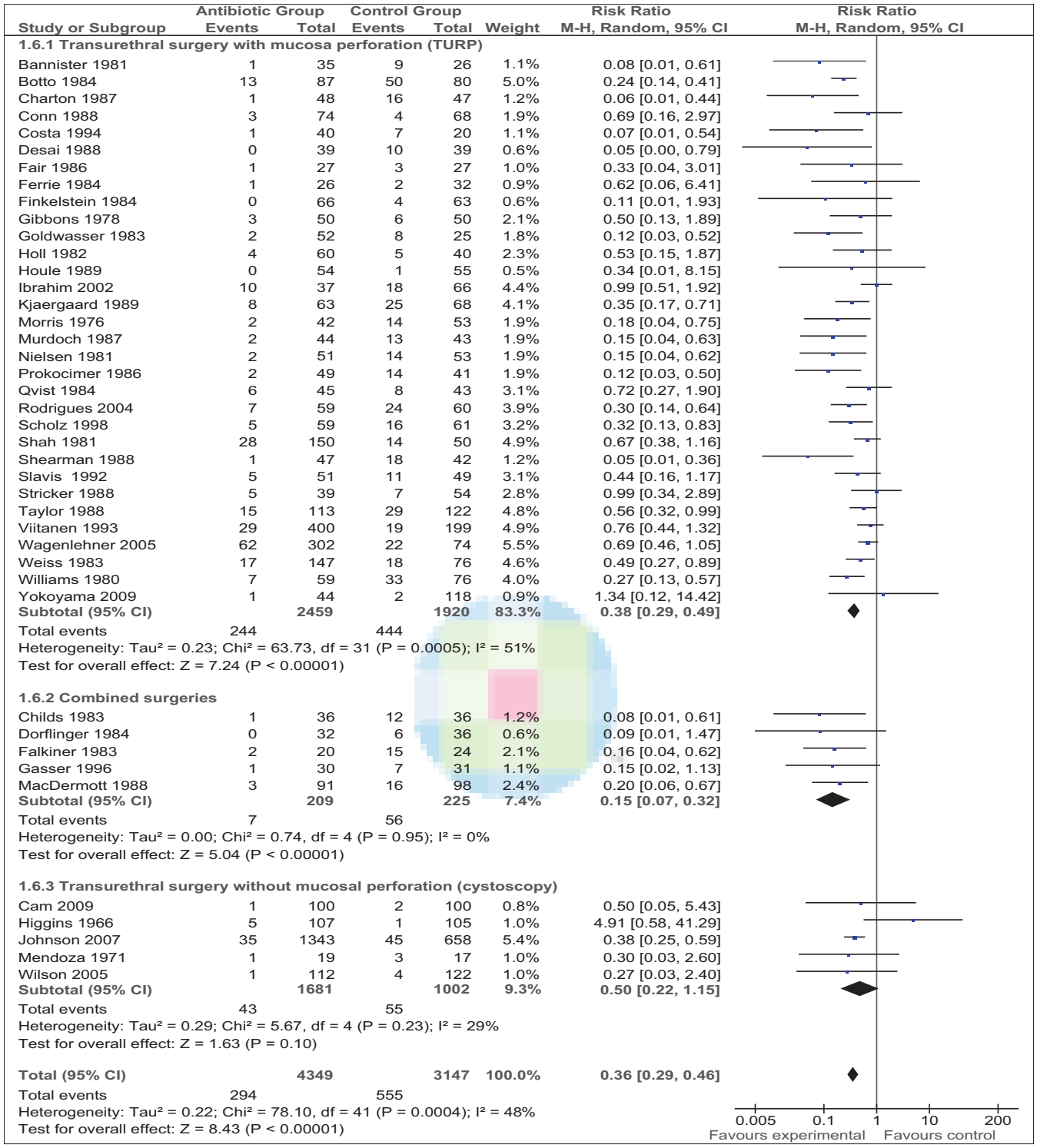

Figure 4: Forest plot of comparison: Antibiotic prophylaxis versus control/placebo, outcome: 1.2 bacteriuria according to the urological procedure performed

to 0.51, $P < 0.0001$). No significant heterogeneity was detected in the analysis ($I^2 = 17\%$), [Figure 6].

Results of the outcome number 3: Bacteremia

Data on bacteremia could be extracted from 8 trials only, with 1044 patients assessed. There were 30 events (6.1%) of bacteremia among 490 patients randomized to receive placebo or no treatment, and 12 events (2.1%) among 554 patients randomized to receive antibiotics. The meta-analysis was significant and favored antibiotic use (RR 0.43, 95% CI 0.23 to 0.82, $P < 0.0001$). There was no heterogeneity detected in the analysis ($I^2 = 0\%$), [Figure 7].

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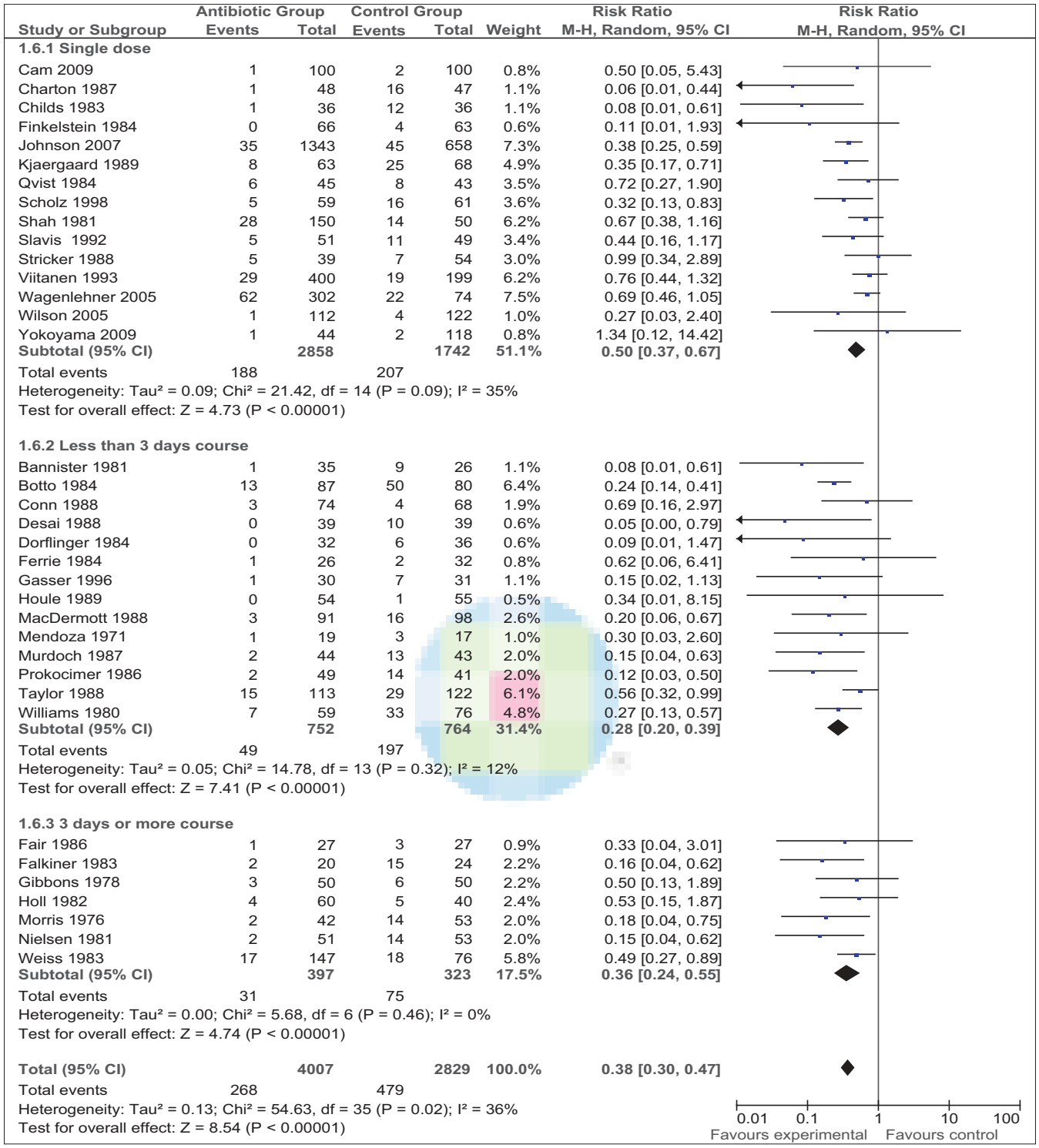

Figure 5: Forest plot of comparison: Antibiotic prophylaxis versus control/placebo, outcome: 1.3 bacteriuria according antibiotic course (single dose, ≤3 days course, or >3 days course)

Results of the outcome number 4: Fever

The incidence of fever following endoscopic urologic intervention was reported in 15 trials, including 1650 patients, and summary of the results are shown in Figure 8." Overall, there were 150 events (23%) of fever among 651 patients randomized to receive placebo or no treatment, and 136 events (15%) among 909 patients randomized to receive antibiotics. However, the overall meta-analysis was not quite significant (RR 0.79, 95% CI 0.61 to 1.03, $P = 0.08$). There was no significant heterogeneity detected in the analysis ($I^2 = 32\%$), especially after performing the subgroup analysis according to the temperature grade, [Figure 8]. The subgroup analysis was performed based

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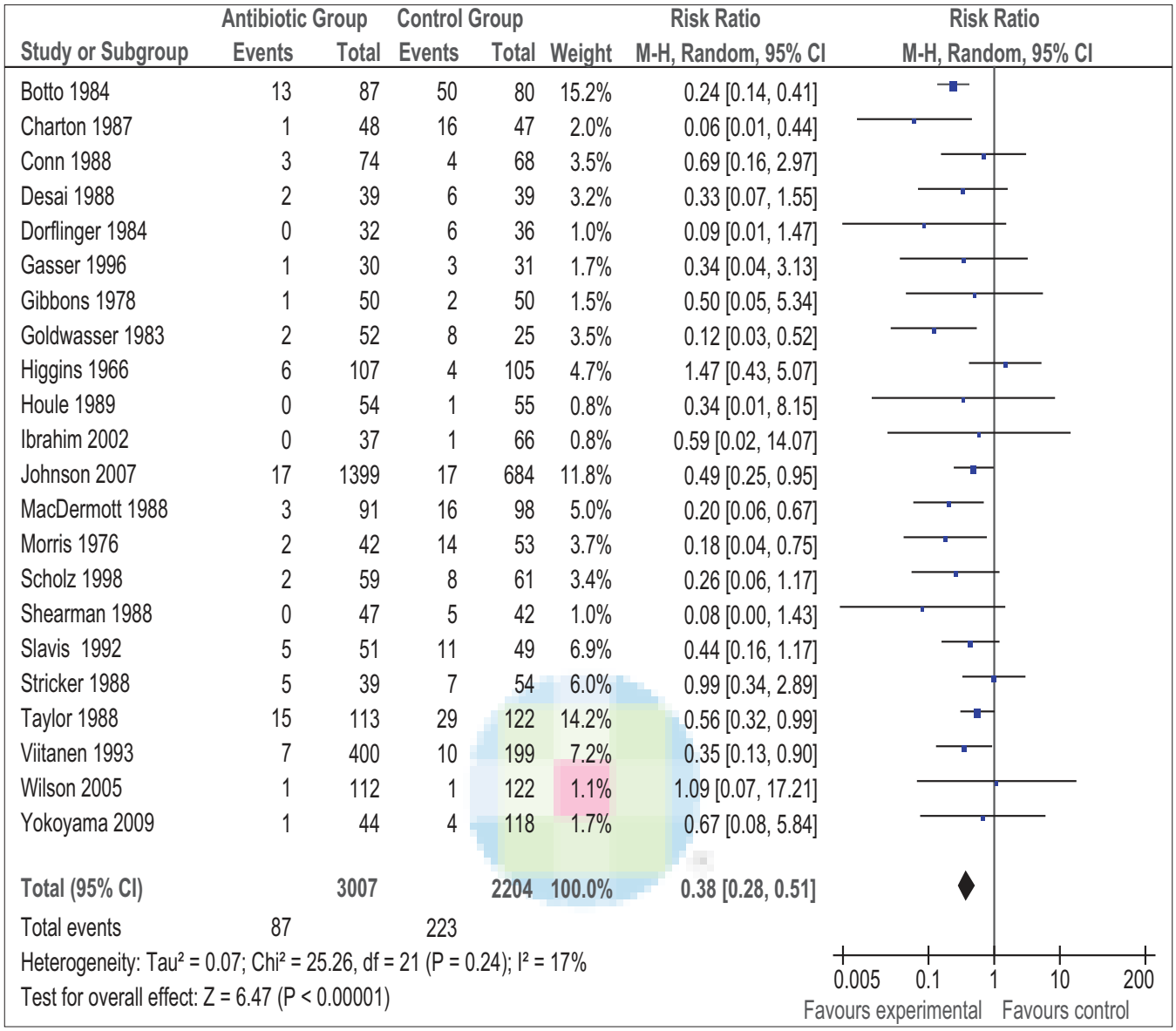

Figure 6: Forest plot of comparison: Antibiotic prophylaxis versus control/placebo, outcome: 2 symptomatic urinary tract infection

on the different levels of temperature's grades as defined in the methodology section. In high grade temperature, ≥38.5 C, 6 trials documented that antibiotic prophylaxis significantly reduced the risk of having a high temperature, with 30 events (11.7%) of high fever among 255 patients randomized to receive placebo or no treatment, and 23 events (4.6%) among 503 patients randomized to receive antibiotics (RR 0.41, 95% CI 0.23 to 0.73, $P = 0.003$). There was no heterogeneity detected in the analysis ($I^2 = 0\%$). However, in 10 trials, using antibiotic prophylaxis did not reduce the incidence of low grade temperature (29.5% in the antibiotic group versus 38.5% in the control group) (RR 0.82, 95% CI 0.61 to 1.11, $P = 0.20$) or in moderate grade temperature (26.5% in the antibiotic group versus 25.7% in the control group) (RR 1.03, 95% CI 0.71 to 1.48, $P = 0.89$).

DISCUSSION

This systematic review evaluated all currently available trials addressing the use of antibiotic prophylaxis in endourological surgeries. It offers a comprehensive assessment supported by high level of evidence, which will help in improving the current practice. This review was designed to answer only one vital question: Do we need to use antibiotic prophylaxis in all endourological surgeries, even the low risk one, like cystoscopy? Apart from transurethral resection of prostate, the decision of using antibiotic prophylaxis in most endourological intervention is not well addressed, and our decision most of the time is driven by the personal experience of our senior staff rather than evidenced-based. The risk of urinary tract infection (UTI) following endoscopic urologic procedures is a highly controversial topic. As we have seen from all included

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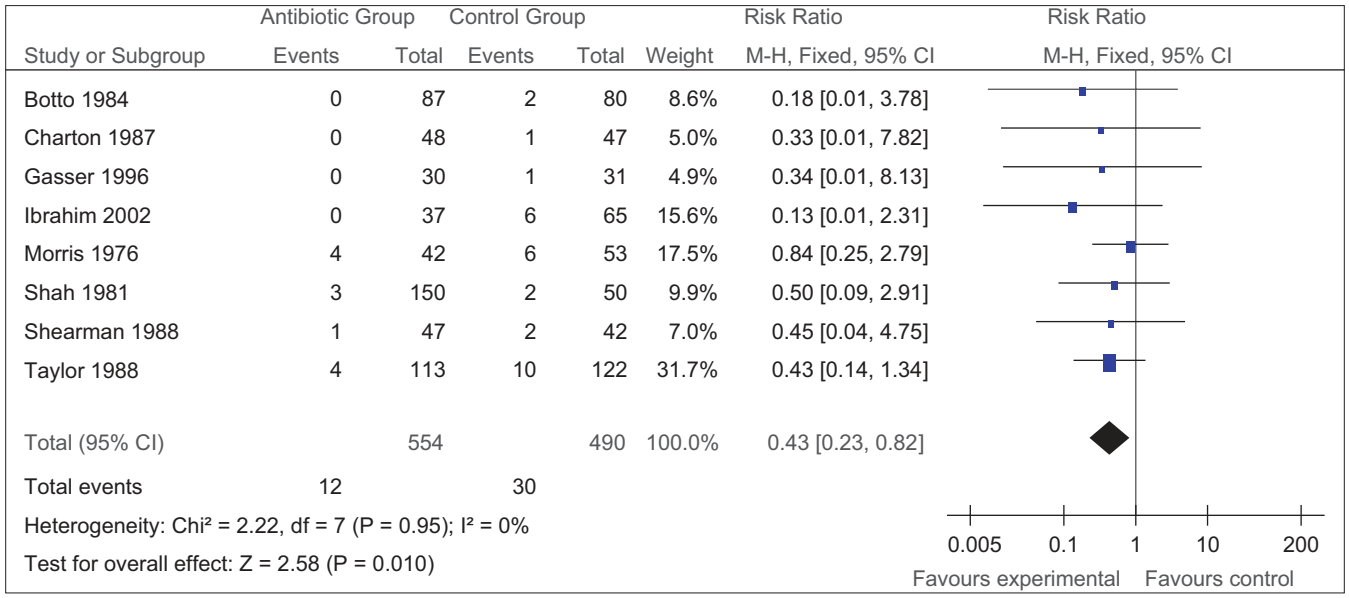

Figure 7: Forest plot comparison: Antibiotic prophylaxis versus control/placebo, outcome: 3 bacteremia

trials, part of the controversy reflects the difficulties of even defining and classifying UTI, and in distinguishing among the varied urologic procedures.

The results of this review indicate that prophylactic antibiotics significantly reduce postoperative bacteriuria, bacteremia, symptomatic urinary tract infection, and high grade temperature in patient undergoing endourological intervention, even in low risk group, which includes patients without catheters, patients with negative urine cultures, and patients performing diagnostic cystoscopy. The reduction is clinically significant, and it was constant across most of the included studies, regardless of the weaknesses in the methodological designs, which were more appreciated in the older studies. But, we have to keep in mind that most of the trials were evaluating patients who had TURP or TURBT, rather than cystoscopy or other diagnostic transurethral surgeries where the mucosa will be violated and penetrated, which carries a high risk of infection. Studies assessing the effectiveness of antibiotic for cystoscopies were lacking, and the evidence is weak for this group.

This review provided strong evidence that any antibiotic prophylaxis, in patient going for TURP and TURBT, will reduce the postoperative bacteriuria from 17.6% to 6.8%, will reduce symptomatic UTI from 10.1% to 2.9%, and furthermore, a reduction in the postoperative bacteremia episodes from 6.1% to 2.1%. However, there are significant variations in duration, antibiotic choice, or even dose given across all included article, which definitely played a role in the moderate heterogeneity in the analysis performed. Trials assessing a standard antibiotic regimen, antibiotic safety profiles and side effects, and cost-analysis are vital.

Traditionally, cystoscopy is the most commonly performed procedure in urology practices all over the world, and it is considered a "clean" procedure that does not merit routine prophylactic antimicrobial therapy. Most reports indicate that symptomatic infections occur following fewer than 5% of procedures, provided the urine is sterile preoperatively. However, the prevalence of asymptomatic bacteriuria has been reported after as many as 35% of cystoscopy procedures in some series, with most series in the 10% range. The significances of bacteriuria at the time of the surgery are not well appreciated, but patients with positive preoperative bacteriuria have a high incidence of bacteremia and sepsis. Because of the current lack of evidence, in this procedure, clinician needs to weigh the benefits of adding antibiotics prophylaxis to prevent UTI against adverse events, costs, and development of bacterial resistance. Also, the urologist should always keep in mind that antibiotic prophylaxis is not the only means to prevent infection following surgery.

Systematic reviews are limited by the quality of the available evidence and the way it is reported. For example, the literature contains considerable debate about the concentration of bacteria in urine that is considered "significant." The traditional threshold was >100,000 colony-forming units (CFU) per mL of a single species. This definition was based on older population surveys where patients were required to have repeated samples showing $>10^5$ CFU/mL. More recent literature suggests that $>10^2$ CFU/mL represents significant bacteriuria in a patient with urinary tract symptoms, but the precise definition of significant debate. This variation in defining significant bacteriuria may underestimate or overestimate the incidence of bacteriuria, according to the cut limit used.

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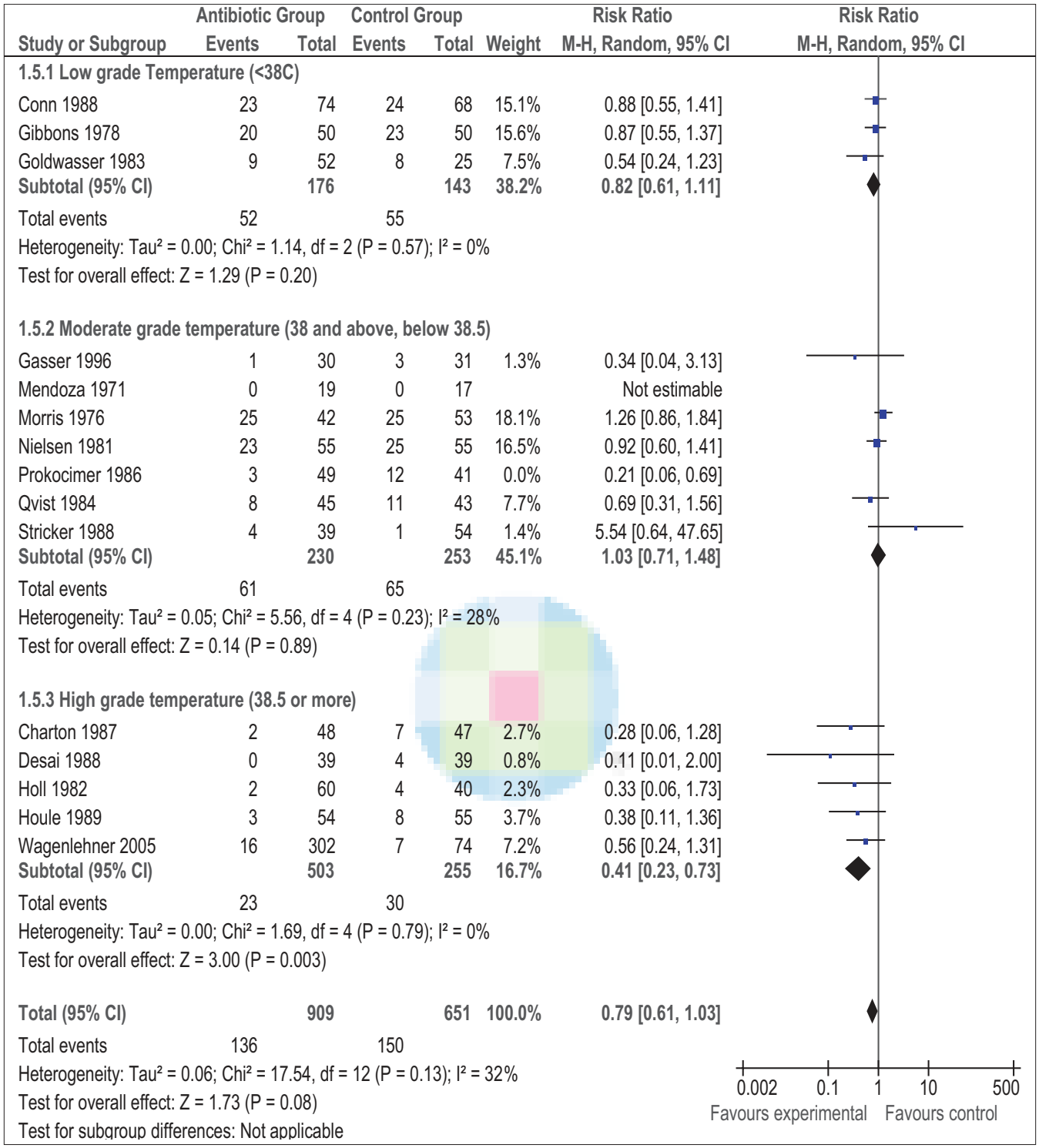

Figure 8: Forest plot of comparison: Antibiotic prophylaxis versus control/placebo, outcome: 4 fever, divided according to temperature grades

Future RCTs are required to assess the effectiveness of antibiotic prophylaxis in patients undergoing minor transurethral urological procedures, which represent the bulk of our everyday practice. Also, standardization of the definition of significant bacteriuria would lead to a proficient reporting. Finally, there is no doubt that antibiotic prophylaxis is required for surgeries like TURP or TURBT, but the optimal antibiotic regimens (antibiotic class, dose, and course) are still to be determined in a properly designed RCT.

CONCLUSION

Prophylactic antibiotics, regardless to the type of antibiotic used, decrease the incidence of bacteriuria, bacteremia,

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symptomatic urinary tract infection, and high grade fever, especially in patients undergoing transurethral resection of prostate and transurethral resection of bladder tumor. Evidence for usage in less invasive endo-urological procedure is lacking. Therefore, further well-designed double-blinded placebo controlled studies are required for minor urological surgeries (urethroscopy, cystoscopy, and ureteroscopy).

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Appendix 1: Search strategies

Databases	Search terms
CENTRAL	1. MeSH descriptor Urologic Surgical Procedures, this term only 2. MeSH descriptor Cystoscopy, this term only 3. MeSH descriptor Ureteroscopy, this term only 4. MeSH descriptor Nephroscopy, this term only 5. MeSH descriptor Transurethral Resection of Prostate, this term only 6. MeSH descriptor Dilatation, this term only 7. MeSH descriptor Urethral Obstruction explode all trees 8. (Urologic surgical*):ti, ab, kw or (urologic surger*):ti, ab, kw in Clinical Trials 9. (Urological surgical*):ti, ab, kw or (urological surger*):ti, ab, kw in Clinical Trials 10. (Cytoscop*):ti, ab, kw in clinical trials 11. (Ureteroscop*):ti, ab, kw in clinical trials 12. (Optical urethrotom*):ti, ab, kw in clinical trials 13. "Transurethral resection of bladder":ti, ab, kw in Clinical Trials 14. (TURBT):ti, ab, kw in clinical trials 15. "Bladder neck incision":ti, ab, kw in clinical trials 16. "Double-J stents":ti, ab, kw in clinical trials 17. "Double-J stent":ti, ab, kw in clinical trials 18. "Dj stent" or "dj stents":ti, ab, kw in clinical trials 19. (Nephroscop*):ti, ab, kw in clinical trials 20. (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19) 21. MeSH descriptor Anti-Bacterial Agents explode all trees 22. MeSH descriptor Antibiotic Prophylaxis, this term only 23. (prophylaxis):ti, ab, kw in clinical trials 24. (#21 OR #22 OR #23) 25. (#20 AND #24)
MEDLINE	1. Urologic Surgical Procedures/ 2. Cystoscopy/ 3. Ureteroscopy/ 4. Nephroscopy/ 5. "Transurethral Resection of Prostate"/ 6. Dilatation/ 7. Exp Urethral Obstruction/ 8. (Urologic$ surgical$ or urologic$ surger$).tw. 9. Cytoscop$.tw. 10. Ureteroscop$.tw. 11. Optical urethrotom$.tw. 12. Transurethral resection of bladder$.tw. 13.TURBT.tw. 14. Bladder neck incision$.tw. 15. "Bouble-J stent$".tw. 16. "Dj stent$".tw. 17. OR/1-16 18. Exp Anti-Bacterial Agents/ 19. Antibiotic Prophylaxis/ 20. Prophylaxis.tw. 21. OR/18-20 22. AND/17,21

Cont...

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Appendix 1: Continued

Databases	Search terms
EMBASE	1. Urological procedures/ 2. Urologic surgery/ 3. Cystoscopy/ 4. Ureteroscopy/ 5. Nephrostcopy/ 6. Transurethral resection/ 7. Ureter dilatation/ 8. Urethra obstruction/ 9. Urogenital endoscopy/ 10. Urogenital endoscopy/or urethroscopy/ 11. (Urologic$ surgical$ or urologic$ surger$).tw. 12. Cytoscop$.tw. 13. Ureteroscop$.tw. 14. Optical urethrotom$.tw. 15. Transurethral resection of bladder$.tw. 16. TURBT.tw. 17. Bladder neck incision$.tw. 18."Double-J stent$".tw. 19. "Dj stent$".tw. 20. OR/1-19 21. Exp antiinfective agent/ 22. Antibiotic prophylaxis/ 23. Prophylaxis.tw. 24. OR/21-23 25. AND/20,24

Appendix 2: Characteristics of excluded studies

Asuero Mantero 1989	Excluded because Language barrier (Spanish)
Childs 1985	Excluded because two active interventions, Piperacillin versus cefotaxime, no control group
Christiano 2000	Excluded because two active interventions, oral versus IV, no control group involved
Cirillo Marucco 1985	Excluded because language barrier (Italian)
Claude 1972	Excluded because language barrier (French)
Cundiff 1999	Excluded because all patients included for urodynamic studies
Cutajar 1992	Excluded because they included patients with active urinary tract infection proven by culture
Dalet 1988	Excluded because language barrier (Spanish)
Da Silva 1992	Excluded because two active interventions and no control group
Delavierre 1993	Excluded because language barrier (French)
Derluyn 1974	Excluded because two active interventions and no control group
Goldwasser 1983	Excluded because two arms each has different surgery (TURP v TURBT) and no antibiotic used
Grabe 1984	Excluded because they enrolled patient with positive urine cultures and analysis could not seperat
Hall 1996	Excluded because two active interventions and no control group
Harvey 1986	Excluded because the initial urine samples were obtained 4 weeks after surgery
Ishizaka 2007	Excluded because two active interventions, Fosfomycin versus cefotiam, and no control group
Jimenez-Cruz 1993	Excluded because two active interventions, Pefloxacin versus ceftriaxone, and no control group
Jimenez-Cruz 1993	Excluded because language barrier (Spanish), (Actas Urologica Espanolas journal)
Karmouni 2001	Excluded because language barrier (French)
Lepage 1990	Excluded because two active interventions, cefazolin versus cefotiam, and no control group
Luzuriaga 1990	Excluded because language barrier (Spanish)
Manson 1988	Excluded because the initial urine samples were obtained 2 weeks after surgery
Marchini 1984	Excluded because they included patients with active urinary tract infection proven by culture
Mazzitelli 1984	Excluded because did not fulfill my inclusion and exclusion criteria
Mclin 1968	Excluded because they included patients with active urinary tract infection proven by culture
Murdoch 1987	Excluded because they included patients with active urinary tract infection proven by culture
Osca Garcia 1993	Excluded because two active interventions, pefloxacin versus ceftriaxone, and no control group
Ozturk 2007	Excluded because there was a significant difference between two active arms apart from control
Periti 1984	Excluded because two active interventions, single versus multiple doses, and no control group
Rafal'skii 2005	Excluded because 3 active interventions, oral cipro versus IV cipro versus routine antibiotics only
Ragnaud 1983	Excluded because language barrier (French)
Rizzo 1987	Excluded because two active interventions, cefotetan versus cefoxitin, and no control group
Ronconi 1983	Excluded because language barrier (Italian)
Savoca 2000	Excluded because two active interventions, rufloxacin versus ciprofloxacin, and no control group
Schulman 1970	Excluded because did not fulfill my inclusion and exclusion criteria
Tigano 1983	Excluded because did not fulfill my inclusion and exclusion criteria
Tsugawa 1998	Excluded because all cultures obtained more than 1 week after surgery
Turano 1992	Types of urology surgery perform are no specified, including endoscopy with open surgery
Valdevenito 2004	Excluded because two active interventions, cefazolin versus ciprofloxacin, and no control group
Wagenlehner 2006	Excluded because the outcome measure was antibiotic tissue penetration
Wooster 1990	Excluded because the included patients with vascular graft
Yamamoto 2004	Excluded because did not fulfill my inclusion and exclusion criteria