



A Comprehensive Systematic Review of Comparison of Antibiotic Prophylaxis in Prostate Cancer Patient Biopsy Cases

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ABSTRACT

Introduction: Prostate biopsy is a crucial diagnostic procedure for prostate cancer but carries a risk of infectious complications, including urinary tract infections, bacteremia, and sepsis. The rising global prevalence of antibiotic resistance, particularly to fluoroquinolones, has complicated traditional empirical prophylaxis, necessitating a thorough reevaluation of optimal prevention strategies (Pilatz et al., 2020).

Methods: This comprehensive systematic review synthesized evidence from 80 sources, including randomized controlled trials (RCTs), meta-analyses, and cohort studies. The review compared antibiotic prophylaxis versus no prophylaxis, different antibiotic regimens (e.g., fosfomycin vs. fluoroquinolones), prophylaxis durations, empirical versus targeted approaches, augmented prophylaxis,

and the impact of biopsy approach (transrectal vs. transperineal). Data on infection outcomes, resistance patterns, and non-infectious complications were extracted and analyzed.

Results: Antibiotic prophylaxis significantly reduces infectious complications for transrectal prostate biopsy compared to no prophylaxis (RR 0.56) (Pilatz et al., 2020). For transperineal biopsy, evidence shows no significant benefit of prophylaxis, with pooled infection rates of 0.50% with vs. 0.37% without antibiotics (Castellani et al., 2021; Wolff et al., 2024). Fosfomycin demonstrated superior or equivalent efficacy to fluoroquinolones, particularly in reducing febrile UTIs (Freitas & Moreira, 2019; Şen et al., 2015). Augmented (combination) prophylaxis and targeted prophylaxis based on rectal swab cultures were more effective than single-agent empirical regimens in high-resistance settings (Elshal et al., 2018; Yang et al., 2016; Doherty et al., 2019). Rectal cleansing with povidone-iodine provided additive protection (Pu et al., 2014).

Discussion: The findings highlight a paradigm shift. The transperineal approach inherently lowers infection risk, potentially obviating the need for routine antibiotics and aligning with antimicrobial stewardship. For transrectal biopsies, a one-size-fits-all empirical approach is obsolete. Strategy must be tailored based on local resistance patterns, favoring augmented or targeted prophylaxis when fluoroquinolone resistance exceeds 20%. Fosfomycin emerges as a key agent, though its use in

combination may be required in high-burden settings.

Conclusion: The optimal strategy for preventing post-prostate biopsy infections is multifaceted. For transperineal biopsy, omitting routine antibiotic prophylaxis is safe and recommended. For transrectal biopsy, a tailored approach incorporating local resistance data, augmented or targeted antibiotic prophylaxis, and rectal disinfection is essential. Future research should focus on cost-effectiveness analyses and standardized protocols for targeted prophylaxis implementation.

Keywords: Prostate Biopsy; Antibiotic Prophylaxis; Infectious Complications; Fosfomycin; Fluoroquinolone Resistance; Transperineal Biopsy; Targeted Prophylaxis; Systematic Review.

INTRODUCTION

Background

Prostate cancer remains one of the most prevalent malignancies among men globally, with prostate biopsy serving as the definitive diagnostic procedure. While essential, transrectal ultrasound-guided prostate biopsy (TRUS-Bx) is an invasive intervention that breaches the rectal mucosa, allowing commensal bowel flora to seed the prostate and bloodstream, leading to infectious complications ranging from asymptomatic bacteriuria to life-threatening sepsis (Pilatz et al., 2020). Historically, empirical prophylactic antibiotics, primarily fluoroquinolones like ciprofloxacin, have been standard care, significantly reducing post-biopsy infection rates compared to placebo (Yang et al., 2015). However, the escalating global crisis of antimicrobial resistance (AMR), marked by rapidly increasing rates of fluoroquinolone-resistant and extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* in rectal flora, has severely undermined the efficacy of empirical regimens (Roberts et al., 2014; Bouzouita et al., 2024). Concurrently, the transperineal biopsy (TP-Bx) approach has gained traction, potentially offering a lower infectious risk due to the avoidance of the contaminated rectum. This evolving landscape—characterized by technological advancements in biopsy technique and the pressing challenge of AMR—creates significant clinical uncertainty regarding the most effective, safe, and sustainable strategy for infection prevention in prostate biopsy patients.

Research Gap

Despite numerous individual randomized trials and meta-analyses on specific aspects of prophylaxis (e.g., Drug A vs. Drug B, short vs. long course), there is a lack of a comprehensive, integrated synthesis that simultaneously evaluates and compares all contemporary strategies. Key unresolved questions include: 1) Whether the benefit of antibiotic prophylaxis persists in the TP-Bx era, 2) How fosfomycin-based regimens truly compare to fluoroquinolones and

combination therapies across diverse resistance settings, 3) The practical efficacy and cost-effectiveness of targeted prophylaxis in real-world practice, and 4) The relative hierarchy of strategies (e.g., changing biopsy route vs. augmenting antibiotics vs. adding rectal disinfection). Existing reviews often focus on isolated comparisons without providing a unified, context-driven framework to guide clinical decision-making in the face of heterogeneous local resistance patterns and resource availability.

Novelty

This systematic review provides a novel and holistic synthesis of evidence from 80 studies, directly comparing the full spectrum of modern prevention strategies. Its novelty lies in its integrative analysis, which concurrently evaluates the role of the biopsy approach (TR vs. TP), various antibiotic agents and regimens (monotherapy vs. augmented), personalized approaches (empirical vs. targeted), and adjunctive measures (rectal cleansing). It moves beyond simply stating which drug is better, to explaining *why* and *in which context* certain strategies succeed or fail, thereby reconciling seemingly conflicting findings in the literature. Furthermore, it explicitly addresses the antimicrobial stewardship imperative by evaluating strategies that minimize or eliminate antibiotic use.

Research Objectives

The primary objective of this systematic review is to comprehensively compare the efficacy and safety of all major antibiotic prophylaxis strategies for preventing infectious complications following prostate biopsy in adults. Specific objectives include:

1. To determine the absolute and relative efficacy of antibiotic prophylaxis versus no prophylaxis/placebo for both transrectal and transperineal biopsy approaches.

2. To compare the efficacy of different antibiotic classes and specific agents (e.g., fosfomycin, fluoroquinolones, cephalosporins, carbapenems) as prophylactic regimens.
3. To evaluate the impact of prophylaxis duration (single-dose, short-course, long-course) on clinical and subclinical infection outcomes.
4. To assess the effectiveness of empirical prophylaxis versus culture-guided targeted prophylaxis.
5. To analyze the benefit of augmented (combination) antibiotic prophylaxis versus single-agent regimens.
6. To synthesize evidence on the role of rectal disinfection and other non-antibiotic preventive measures.
7. To summarize reported antibiotic resistance patterns and non-infectious complications associated with different strategies.

Hypotheses

We hypothesize that: 1) The benefit of antibiotic prophylaxis is significant for transrectal biopsy but negligible for transperineal biopsy; 2) Fosfomycin and augmented regimens are superior to single-agent fluoroquinolone prophylaxis, especially in regions with high resistance prevalence; 3) Targeted prophylaxis is more effective than empirical prophylaxis, but its success is contingent on local microbiology and the availability of effective alternative antibiotics; and 4) The transperineal approach without prophylaxis yields infection rates comparable or superior to transrectal biopsy with prophylaxis.

Significance and Benefits

The findings of this review are critically significant for clinical practice, patient safety, and public health. Clinically, it will provide urologists with an evidence-based, stratified framework for selecting prevention protocols tailored to their local resistance epidemiology and available techniques, thereby reducing post-

biopsy sepsis and hospitalizations. For patients, it promises to minimize the risk of serious infection and avoid unnecessary antibiotic exposure. From a public health and antimicrobial stewardship perspective, it strongly supports the adoption of the transperineal approach to potentially eliminate routine procedural antibiotics and promotes the rational use of targeted prophylaxis to combat the spread of multidrug-resistant organisms. Ultimately, this synthesis aims to standardize care, improve outcomes, and contribute to the global effort against antimicrobial resistance.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the comparison of antibiotic prophylaxis in prostate cancer patient biopsy cases.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Population:** Does the study include adult male patients (≥ 18 years) undergoing prostate biopsy for suspected or confirmed prostate cancer?
- **Intervention Comparison:** Does the study compare different antibiotic prophylaxis regimens OR compare antibiotic prophylaxis versus placebo/no prophylaxis in prostate biopsy procedures?
- **Infectious Outcomes:** Does the study report infectious complications as primary or secondary outcomes (e.g., urinary tract infections, sepsis, fever, bacteremia)?
- **Study Design:** Is the study a randomized controlled trial, systematic review, meta-analysis, or prospective cohort study?

- **Procedure Type:** Does the study focus on diagnostic prostate biopsy rather than prostate surgery (prostatectomy, TURP)?
- **Prophylaxis Focus:** Does the study examine antibiotic prophylaxis (prevention) rather than exclusively examining antibiotic treatment for established infections?
- **Publication Type:** Is the study a full research article rather than a case report, case series, editorial, or conference abstract?
- **Patient Population:** Does the study focus on patients without active urinary tract infections or immunocompromised states as the primary population (rather than focusing exclusively on these special populations)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Prostate cancer biopsy patients	Antibiotic prophylaxis regimens	No prophylaxis / Placebo	Infectious complications
Keyword 2	Men undergoing prostate biopsy	Prophylactic antibiotics	Different antibiotic regimens	Sepsis / Bacteremia
Keyword 3	Patients with suspected prostate cancer	Antimicrobial prophylaxis	Short-course vs. Long-course prophylaxis	Urinary tract infection (UTI)
Keyword 4	Adults undergoing transrectal or transperineal prostate biopsy	Preventive antibiotics	Empirical vs. Targeted prophylaxis	Fever / Hospitalization

The Boolean MeSH keywords inputted on databases for this research are:
("Prostate cancer biopsy patients" OR "Men undergoing prostate biopsy" OR "Patients with suspected prostate cancer" OR "Adults undergoing transrectal or transperineal prostate biopsy") AND ("Antibiotic prophylaxis regimens" OR "Prophylactic antibiotics" OR "Antimicrobial prophylaxis" OR "Preventive antibiotics") AND ("No prophylaxis" OR "Placebo" OR "Different antibiotic regimens" OR "Short-course vs. Long-course prophylaxis" OR "Empirical vs. Targeted prophylaxis") AND ("Infectious complications" OR "Sepsis" OR "Bacteremia" OR "Urinary tract infection (UTI)" OR "Fever" OR "Hospitalization")

Data extraction

- **Study Design & Population:**

Extract study design and patient population details including:

- Study design (RCT, cohort, case-control, etc.)
- Number of patients in each group
- Patient demographics (age, PSA levels if reported)
- Inclusion/exclusion criteria
- Setting (hospital type, country, time period)
- Follow-up duration

- **Biopsy Procedure:**

Extract details about the biopsy procedure that may affect infection risk:

- Biopsy approach (transrectal vs transperineal)
- Number of biopsy cores taken
- Guidance method (TRUS, MRI-fusion, etc.)
- Anesthesia type (local, general, sedation)
- Any specific procedural modifications
- Bowel preparation methods if mentioned

- **Antibiotic Regimens:**

Extract complete details for all antibiotic prophylaxis regimens compared:

- Specific antibiotics used (drug names, classes)
- Doses and frequencies
- Route of administration (oral, IV, IM, periprostatically)
- Timing (when started relative to biopsy, duration)
- Whether single agent, combination, or augmented therapy
- Control group details (placebo, no treatment, or alternative regimen)

- **Infection Outcomes:**

Extract all infection-related outcomes measured:

- Primary infection endpoints (sepsis, UTI, bacteremia, etc.)
- Secondary infection outcomes
- How infections were defined and diagnosed
- Time points when outcomes were assessed
- Methods of follow-up (telephone, clinic visits, etc.)
- Any severity grading or hospitalization requirements

- **Infection Results:**

Extract quantitative results for infection outcomes:

- Number and percentage of patients with infections in each group
- Specific organisms isolated (E. coli, etc.)
- Antibiotic resistance patterns when reported
- Statistical significance (p-values, confidence intervals)
- Effect sizes (relative risk, odds ratios) when calculated
- Time to infection onset if reported

- **Resistance Patterns:**

Extract data on antibiotic resistance when reported:

- Baseline resistance rates in the population

- Organisms showing resistance (especially fluoroquinolone-resistant *E. coli*)
- Whether targeted prophylaxis was used based on resistance
- Any culture-guided modifications to therapy
- Regional resistance patterns mentioned

- **Additional Outcomes:**

Extract non-infection outcomes and safety data:

- Pain scores or patient comfort measures
- Other complications (bleeding, retention, etc.)
- Adverse effects of antibiotics
- Hospitalization rates for any reason
- Patient-reported outcomes
- Economic outcomes if reported

- **Risk Factors:**

Extract patient and procedural factors that may influence infection risk:

- Diabetes, immunosuppression, prior infections
- Previous antibiotic use or resistance history
- Prostate size or characteristics
- Number of previous biopsies
- Any risk stratification used
- Subgroup analyses performed

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Prostate cancer biopsy patients" OR "Men undergoing prostate biopsy" OR "Patients with suspected prostate cancer" OR "Adults undergoing transrectal or transperineal prostate biopsy" AND "Antibiotic prophylaxis regimens" OR "Prophylactic antibiotics" OR "Antimicrobial prophylaxis" OR "Preventive antibiotics" AND "No prophylaxis" OR "Placebo" OR "Different antibiotic regimens" OR "Short-course vs. Long-course prophylaxis" OR "Empirical vs. Targeted prophylaxis") AND ("Infectious complications" OR "Sepsis" OR "Bacteremia" OR "Urinary tract infection (UTI)" OR "Fever" OR "Hospitalization")</i>	2,345
Semantic Scholar	<i>("Prostate cancer biopsy patients" OR "Men undergoing prostate biopsy" OR "Patients with suspected prostate cancer" OR "Adults undergoing transrectal or transperineal prostate biopsy") AND ("Antibiotic prophylaxis regimens" OR "Prophylactic antibiotics" OR "Antimicrobial prophylaxis" OR "Preventive antibiotics") AND ("No prophylaxis" OR "Placebo" OR "Different antibiotic regimens" OR "Short-course vs. Long-course prophylaxis" OR "Empirical vs. Targeted prophylaxis") AND ("Infectious complications" OR "Sepsis" OR "Bacteremia" OR "Urinary tract infection (UTI)" OR "Fever" OR "Hospitalization")</i>	245
Springer	<i>("Prostate cancer biopsy patients" OR "Men undergoing prostate biopsy" OR "Patients with suspected prostate cancer" OR "Adults undergoing transrectal or transperineal prostate biopsy") AND ("Antibiotic prophylaxis regimens" OR "Prophylactic antibiotics" OR "Antimicrobial prophylaxis" OR "Preventive antibiotics") AND ("No prophylaxis" OR "Placebo" OR "Different antibiotic regimens" OR "Short-course vs. Long-course prophylaxis" OR "Empirical vs. Targeted prophylaxis") AND ("Infectious complications" OR "Sepsis" OR "Bacteremia" OR "Urinary tract infection (UTI)" OR "Fever" OR "Hospitalization")</i>	7
Google Scholar	<i>("Prostate cancer biopsy patients" OR "Men undergoing prostate biopsy" OR "Patients with suspected prostate cancer" OR "Adults undergoing transrectal or transperineal prostate biopsy") AND ("Antibiotic prophylaxis regimens" OR "Prophylactic antibiotics" OR "Antimicrobial prophylaxis" OR "Preventive antibiotics") AND ("No prophylaxis" OR "Placebo" OR "Different antibiotic regimens" OR "Short-course vs. Long-course prophylaxis" OR "Empirical vs. Targeted prophylaxis") AND ("Infectious complications" OR "Sepsis" OR "Bacteremia" OR "Urinary tract infection (UTI)" OR "Fever" OR "Hospitalization")</i>	61
Wiley Online Library	<i>("Prostate cancer biopsy patients" OR "Men undergoing prostate biopsy" OR "Patients with suspected prostate cancer" OR "Adults undergoing transrectal or transperineal prostate biopsy") AND ("Antibiotic prophylaxis regimens" OR "Prophylactic antibiotics" OR "Antimicrobial prophylaxis" OR "Preventive antibiotics") AND ("No prophylaxis" OR "Placebo" OR "Different antibiotic regimens" OR "Short-course vs. Long-course prophylaxis" OR "Empirical vs. Targeted prophylaxis") AND ("Infectious complications" OR "Sepsis" OR "Bacteremia" OR "Urinary tract infection (UTI)" OR "Fever" OR "Hospitalization")</i>	8

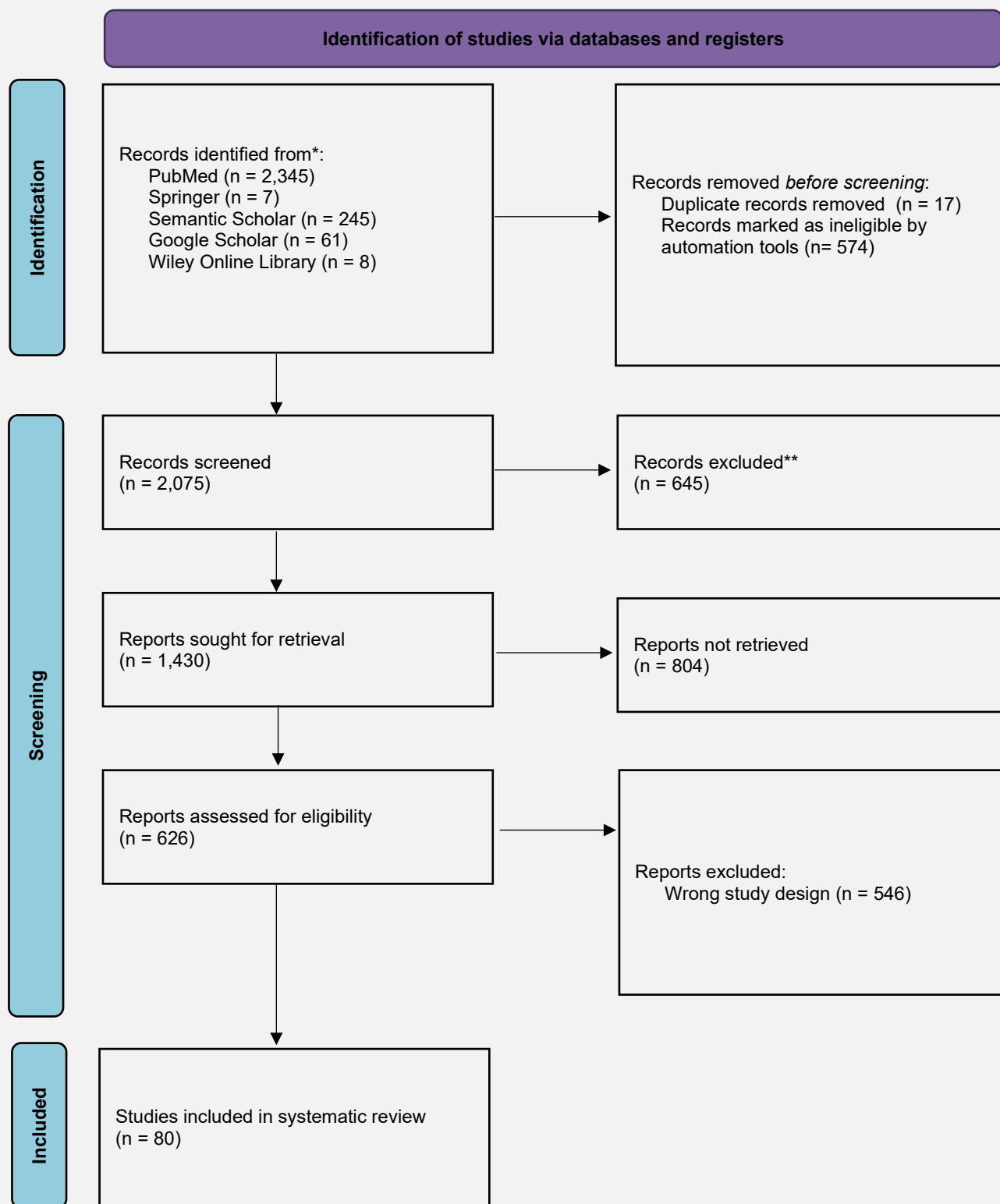


Figure 1. Article search flowchart

JBI Critical Appraisal									
Study	Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Bias related to selection and allocation Was there a control group?	Bias related to confounding factors Were participants included in any comparisons similar?	Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment /care, other than the exposure or intervention of interest?	Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Statistical conclusion validity Was appropriate statistical analysis used?
A. Pilatz et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Castellani et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Freitas et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓

Volkan Sen et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
H. Gu et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jim C. Hu et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ming-gen Yang et al., 2009	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Elshal et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Doherty et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Scott et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
G. Pirola et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Basourako s et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Tops et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jim C. Hu et al., 2024a	✓	✓	✓	✗	✓	✗	✓	✓	✓
Lu Yang et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
E. Krsakova et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓

Lu Yang et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
E. Kehinde et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jurate Noreikaite et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
G. Pace et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
Amelia Cussans et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Jacewicz et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Yaghi et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
Alexandre Morin et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ming-gen Yang et al., 2009a	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Fahmy et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Roberts et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. Petteffi et al., 2002	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Tobias-Machado	✓	✓	✓	✗	✓	✗	✓	✓	✓

et al., 2003									
C. Odo et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
E. Chan et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Sabbagh et al., 2004	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Cimino et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Samarinas et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
Junquera JM Abascal et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
C. D'Elia et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Chun-xiao Pu et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Manecksh a et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Woldu et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
T. Zembower et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Mari et al., 2007	✓	✓	✓	✗	✓	✗	✓	✓	✓

S. Tops et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Fahmy et al., 2016a	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Agbugui et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Domínguez -Rodríguez et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
F. Lista et al., 2014	✓	✓	✓	✗	✓	✗	✓	✓	✓
Mehmet Hamza Guktekin et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Jazayeri et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Izadpanahi et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
H. Ho et al., 2009	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ingmar Wolff et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
K. A. Rumaihi et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Roberts et al.,	✓	✓	✓	✗	✓	✗	✓	✓	✓

2014									
Alberto Bovo et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
Arikan Ozgur et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Kalkanlı et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Samarinas et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Kumar Madhavan et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Cardoso et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. Yang et al., 2001	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Lim et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
Rui Su et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
F. Stangl et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
Y. Miyazaki et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
S. Shivde et al., 2002	✓	✓	✓	✗	✓	✗	✓	✓	✓

N. Grigoryev et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Bouzouita et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Ryu et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Lim et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Hogenhout et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ludong Qiao et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
Ádám Miklós Fehér et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. Toner et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
T. Sadahira et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓
K. Shigemura et al., 2005	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Bloomfield et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
T. Newman et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓

Seok Cho et al., 2025	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Simmons et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
Iqbal Nasim et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓

RESULTS

Characteristics of Included Studies

This systematic review synthesizes evidence from 80 sources examining antibiotic prophylaxis strategies for prostate biopsy. The included studies encompass a range of designs including randomized controlled trials, systematic reviews and meta-analyses, prospective cohort studies, and retrospective comparative studies conducted across multiple countries and healthcare settings.

Study	Primary Comparison	Sample Size
A. Pilatz et al., 2020	Multiple antimicrobial interventions	14,153 participants across 59 RCTs
D. Castellani et al., 2021	AP vs NAP for TPB	3,662 patients
D. Freitas et al., 2019	FMT vs CIP	2,331 men
Volkan Şen et al., 2015	Fosfomycin vs ciprofloxacin	300 patients
H. Gu et al., 2023	Fosfomycin vs fluoroquinolone	2,636 randomized, 6,352 non-randomized

Study	Primary Comparison	Sample Size
Jim C. Hu et al., 2024	TP without AP vs TR with targeted AP	658 participants
Ming-gen Yang et al., 2009	Antibiotic vs placebo/control	1,987 patients
A. Elshal et al., 2018	Standard vs augmented vs targeted prophylaxis	496 patients
A. Doherty et al., 2019	Targeted vs empirical antibiotics	100 patients
S. Scott et al., 2018	Targeted vs empiric prophylaxis	12,320 participants
G. Pirola et al., 2021	AP vs no AP for TPB	200 patients
S. Basourakos et al., 2022	AP vs no AP for TPB	42,577 men
S. Tops et al., 2023	Culture-based vs empirical prophylaxis	1,288 patients
Jim C. Hu et al., 2024a	TP vs TR approach	567 in ITT analysis
Lu Yang et al., 2015	Antibiotics vs placebo/no treatment	3,846 patients
E. Krsakova et al., 2024	Three short-term prophylaxis regimens	544 patients
Lu Yang et al., 2016	Augmented vs single antibiotic	4,063 patients
E. Kehinde et al., 2013	Ciprofloxacin vs ciprofloxacin + amikacin	1,197 patients

Study	Primary Comparison	Sample Size
Jurate Noreikaite et al., 2018	Fosfomycin vs quinolone-based	3,112 patients
G. Pace et al., 2012	Ceftriaxone + ciprofloxacin vs ciprofloxacin	135 patients
Amelia Cussans et al., 2016	Targeted vs empirical prophylaxis	4,571 patients
M. Jacewicz et al., 2022	AP vs no AP for TPB	555 patients
M. Yaghi et al., 2015	Various oral antibiotic regimens	3,012 patients
Alexandre Morin et al., 2019	CIP vs CIP/FOS	2,287 patients
Ming-gen Yang et al., 2009a	Antibiotic vs placebo	Not specified
A. Fahmy et al., 2016	Single-dose fosfomycin vs FQ-based	412 patients
M. Roberts et al., 2018	FT vs FQ prophylaxis	3,112 patients
L. Petteffi et al., 2002	Short vs long-term norfloxacin	140 patients
M. Tobias-Machado et al., 2003	Four antibiotic schemes	257 patients
C. Odo et al., 2021	Ciprofloxacin vs ceftriaxone	56 patients
E. Chan et al., 2012	Single vs combined prophylaxis	367 patients

Study	Primary Comparison	Sample Size
R. Sabbagh et al., 2004	1-day vs 3-day prophylaxis	363 patients
S. Cimino et al., 2020	FT vs FQ or β -lactam	516 patients
M. Samarinas et al., 2016	Ciprofloxacin vs meropenem	110 patients
Junquera JM Abascal et al., 2021	Fosfomycin vs cefoxitin + ciprofloxacin	425 patients
C. D'Elia et al., 2019	2 vs 3 fosfomycin doses	297 patients
Chun-xiao Pu et al., 2014	Povidone-iodine efficacy	2,049 patients
R. Manecksha et al., 2012	Two ofloxacin regimens	1,183 men
S. Woldu et al., 2017	Multiple prophylaxis protocols	2,398 patients
T. Zembower et al., 2017	Targeted antimicrobial prophylaxis	510 men
M. Mari et al., 2007	Single dose vs 5-day prulifloxacin	432 patients
S. Tops et al., 2022	Culture-based vs empirical	1,288 patients
A. Fahmy et al., 2016a	Standard vs targeted prophylaxis	541 men
J. Agbugui et al., 2014	1-day vs 5-day regimen	87 patients

Study	Primary Comparison	Sample Size
A. Domínguez-Rodríguez et al., 2014	FMT vs ciprofloxacin	671 patients
F. Lista et al., 2014	FMT vs ciprofloxacin	671 patients
Mehmet Hamza Guktekin et al., 2023	FT vs CIP	217 patients
S. Jazayeri et al., 2020	Methods to reduce IC	Not specified
M. Izadpanahi et al., 2017	Standard vs augmented prophylaxis	450 patients
H. Ho et al., 2009	Ciprofloxacin vs ciprofloxacin + gentamicin	741 patients
Ingmar Wolff et al., 2024	PAP vs no PAP for TPB	12,324 patients
K. A. Rumaihi et al., 2012	Ciprofloxacin vs ciprofloxacin + cefuroxime	455 patients
M. Roberts et al., 2014	Empirical vs altered prophylaxis	2,541 patients
Alberto Bovo et al., 2024	CIP vs FMT vs FMT + TMP/SMX	822 men
Arikan Ozgur et al., 2017	Routine vs targeted prophylaxis	300 patients
A. Kalkanlı et al., 2018	Single vs prolonged FQ prophylaxis	400 patients
M. Samarinas et al., 2020	Cefixime vs prulifloxacin	120 patients

Study	Primary Comparison	Sample Size
Kumar Madhavan et al., 2024	Multiple interventions	10,179 participants
A. Cardoso et al., 2023	Fosfomycin vs prolonged antibiotics	244 patients
L. Yang et al., 2001	Placebo vs single vs 3-day antibiotics	192 patients
D. Lim et al., 2021	Ciprofloxacin vs ciprofloxacin + fosfomycin	1,568 patients
Rui Su et al., 2019	Three levofloxacin regimens	420 patients
F. Stangl et al., 2025	TR vs TP approach	4,188 biopsies
Y. Miyazaki et al., 2016	Levofloxacin vs levofloxacin + amikacin	447 patients
S. Shivde et al., 2002	Trimethoprim vs gentamicin	115 patients
N. Grigoryev et al., 2021	Levofloxacin vs levofloxacin + fosfomycin	80 patients
A. Bouzouita et al., 2024	Targeted vs empirical prophylaxis	157 patients
J. Ryu et al., 2016	PI + targeted vs empirical prophylaxis	1,450 patients
D. Lim et al., 2023	FQ vs FM vs FQ + FM	2,595 patients
R. Hogenhout et al., 2022	TRB with AP vs TPB without AP	435 men

Study	Primary Comparison	Sample Size
Ludong Qiao et al., 2016	Oral levofloxacin vs IV antibiotics	801 patients
Ádám Miklós Fehér et al., 2024	Single vs prolonged fosfomycin	204 patients
L. Toner et al., 2016	Multiple prevention strategies	Multiple studies
T. Sadahira et al., 2024	Culture-based targeted prophylaxis	373 patients
K. Shigemura et al., 2005	1-day vs 3-day levofloxacin	236 patients
M. Bloomfield et al., 2020	Ciprofloxacin-based vs ertapenem	4,020 men
T. Newman et al., 2021	TRUSBx vs FHTPBx	1,501 patients
Seok Cho et al., 2025	AP vs no AP for TPB	Not specified
M. Simmons et al., 2018	Three antibiotic regimens	829 patients
Iqbal Nasim et al., 2023	Single vs multiple dose levofloxacin	425 patients

The majority of studies employed transrectal ultrasound-guided prostate biopsy (TRUS-PB), with a growing number examining transperineal approaches. The number of biopsy cores ranged from 8-12 in most studies, with some studies utilizing up to 13 cores or 17-18 cores. Local anesthesia was predominantly used for transperineal biopsies, while bowel preparation methods varied and included enemas and oral metronidazole.

Effects of Antibiotic Prophylaxis

Antibiotic Prophylaxis versus No Prophylaxis or Placebo

Comparison	Outcome	Effect Estimate	Statistical Significance	Studies
Antibiotic vs no prophylaxis	Infectious complications	RR 0.56 (95% CI 0.40-0.77)	p=0.0005	Meta-analysis of 11 studies
Antibiotic vs placebo/no treatment	Bacteriuria	RR 0.25 (95% CI 0.15-0.42)	Significant	9 RCTs
Antibiotic vs placebo/no treatment	Bacteremia	RR 0.67 (95% CI 0.49-0.92)	Significant	9 RCTs
Antibiotic vs placebo/no treatment	Fever	RR 0.39 (95% CI 0.23-0.64)	Significant	9 RCTs
Antibiotic vs placebo/no treatment	UTI	RR 0.37 (95% CI 0.22-0.62)	Significant	9 RCTs
Antibiotic vs placebo/no treatment	Hospitalization	RR 0.13 (95% CI 0.03-0.55)	Significant	9 RCTs

Comparison	Outcome	Effect Estimate	Statistical Significance	Studies
Antibiotic vs placebo/no treatment	Bacteriuria	RR 0.32 (95% CI 0.23-0.46)	p<0.01	12 trials
Antibiotic vs placebo/no treatment	Middle degree fever	RR 0.37 (95% CI 0.17-0.77)	Significant	12 trials
Antibiotic vs placebo/no treatment	Bacteremia	RR 0.96 (95% CI 0.61-1.50)	Not significant	12 trials

The evidence consistently demonstrates that antibiotic prophylaxis significantly reduces infectious complications following transrectal prostate biopsy compared to no prophylaxis. A comprehensive meta-analysis found antibiotic prophylaxis reduced infectious complications with a relative risk of 0.56 . Multiple outcomes including bacteriuria, fever, UTI, and hospitalization showed significant reductions with antibiotic use , though the effect on bacteremia was inconsistent across studies .

Transperineal Biopsy: Antibiotic Prophylaxis versus No Prophylaxis

Study	AP Group Infection Rate	NAP Group Infection Rate	Risk Ratio (95% CI)	p-value
D. Castellani et al., 2021	Fever: 0.69%	Fever: 0.47%	1.02 (0.02-44.55)	p=0.99

Study	AP Group Infection Rate	NAP Group Infection Rate	Risk Ratio (95% CI)	p-value
D. Castellani et al., 2021	GU infections: 0.11%	GU infections: 0.31%	2.09 (0.54- 8.10)	p=0.29
D. Castellani et al., 2021	Sepsis: 0.13%	Sepsis: 0.09%	1.09 (0.21- 5.61)	p=0.92
S. Basourakos et al., 2022	Sepsis: 0.05%	Sepsis: 0.08%	-	p=0.2
S. Basourakos et al., 2022	Overall: 1.22%	Overall: 1.35%	-	p=0.8
G. Pirola et al., 2021	UTI: 0%	UTI: 1%	-	Not significant
M. Jacewicz et al., 2022	Sepsis/UTI requiring hospitalization: 0%	0%	Difference 0% (-1.37 to 1.37)	Non-inferior
Ingmar Wolff et al., 2024	GUI: 0.50%	GUI: 0.37%	OR 1.37 (0.74-2.54)	p>0.250
Seok Cho et al., 2025	-	-	OR 1.07 (0.50-2.31)	p=0.86

For transperineal prostate biopsy, the evidence consistently shows no significant difference in infection rates between patients receiving antibiotic prophylaxis and those not receiving prophylaxis . A systematic review

including 23 studies found pooled infection incidences of 0.50% with prophylaxis versus 0.37% without prophylaxis for genitourinary infections . The number needed to treat with antibiotic prophylaxis to avoid one infection in transperineal biopsy was calculated at 137 . These findings support the potential omission of antibiotic prophylaxis for transperineal approaches, aligning with antimicrobial stewardship principles .

Transrectal versus Transperineal Approach

Study	Transperineal Infection Rate	Transrectal Infection Rate	Effect Estimate	p-value
Jim C. Hu et al., 2024	0%	1.4%	Difference - 1.4% (- 3.2%, 0.3%)	p=0.059
Jim C. Hu et al., 2024a	0%	1.4%	-	p=0.059
R. Hogenhout et al., 2022	2.3%	6.1%	-	p=0.044
T. Newman et al., 2021	0.4%	2.0-2.2%	-	p=0.03
F. Stangl et al., 2025	-	-	OR 0.23 (0.10-0.54) for hospitalization	Significant
F. Stangl et al., 2025	-	-	OR 0.68 (0.52-0.89) for fever	Significant

The transperineal approach demonstrates significantly lower infectious complication rates compared to transrectal biopsy. A multicenter RCT reported zero infections in the transperineal group (without antibiotics) versus 1.4% in the transrectal group (with targeted prophylaxis). A systematic review of RCTs found transperineal biopsy reduced hospitalization risk by 77% compared to transrectal biopsy (OR 0.23). Importantly, transperineal biopsy without antibiotic prophylaxis achieved similar or better infection rates than transrectal biopsy with antibiotic prophylaxis. However, transperineal biopsy was associated with slightly worse periprocedural pain (0.6 adjusted difference on 0-10 scale), though this resolved within 7 days.

Fosfomycin versus Fluoroquinolone Prophylaxis

Study	Fosfomycin Infection Rate	Fluoroquinolone Infection Rate	Effect Estimate	p-value
D. Freitas et al., 2019	Afebrile UTI: Lower	Higher	OR 0.21 (0.12-0.38)	p<0.001
D. Freitas et al., 2019	Febrile UTI: Lower	Higher	OR 0.15 (0.07-0.31)	p<0.001
Volkan Şen et al., 2015	Afebrile UTI: 1.3%	6.0%	-	p=0.032
A. Fahmy et al., 2016	1.9%	8.5%	-	p=0.001
A. Pilatz et al., 2020	-	-	RR 0.49 (0.27-0.87)	p=0.02
M. Roberts et al., 2018	-	-	OR 0.22 (0.09-0.54)	Significant
M. Roberts et al., 2018	Grade 2 infections	-	OR 0.13 (0.07-0.26)	Significant

Study	Fosfomycin Infection Rate	Fluoroquinolone Infection Rate	Effect Estimate	p-value
H. Gu et al., 2023	4 fewer febrile UTIs per 1000	Reference	Little to no difference	-
Jurate Noreikaite et al., 2018	Lower UTIs	Higher	0.20 (0.13-0.30)	p<0.00001
S. Cimino et al., 2020	UTI: 34.1%	43.4%	OR 1.54	p=0.03

Fosfomycin demonstrated superior or equivalent efficacy compared to fluoroquinolone-based prophylaxis across multiple studies. Meta-analyses showed fosfomycin reduced infectious complications by approximately 50-80% compared to fluoroquinolones. Individual RCTs confirmed significantly lower infection rates with fosfomycin (1.3-1.9%) compared to ciprofloxacin (6.0-8.5%). However, one large systematic review found fosfomycin likely results in little to no difference in UTI rates compared to fluoroquinolone, corresponding to only 35 fewer overall UTIs per 1000 patients. Fosfomycin showed lower rates of fluoroquinolone-resistant and ESBL-producing organisms in urine cultures.

Some studies found equivalent efficacy between fosfomycin and fluoroquinolone combinations. A prospective RCT comparing fosfomycin-trometamol (2 doses of 3g) with ciprofloxacin (10 doses of 500mg) found no significant difference in overall complications (22.6% vs 27.6%, p=0.17), though the likelihood of resistance to ciprofloxacin was significantly higher (69.2% vs 41.9%, p=0.0004). When fosfomycin alone was compared to combination regimens, one study showed fosfomycin alone resulted in

significantly higher infection rates (13.2%) compared to fosfomycin combined with trimethoprim/sulfamethoxazole (2.1%) .

Short-term versus Long-term Prophylaxis

Study	Short-term Regimen	Long-term Regimen	Effect Estimate	p-value
A. Pilatz et al., 2020	Single shot to 3 days	1-7 days FQ	RR 1.89 (1.37-2.61) favoring long-term	p=0.0001
L. Petteffi et al., 2002	Single dose norfloxacin: 23% UTI	6 doses: 8% UTI	-	p=0.08
L. Petteffi et al., 2002	Complicated UTI: 37%	0%	-	p=0.44
Lu Yang et al., 2015	Short-course	Long-course	RR 2.09 (1.17-3.73) for bacteriuria	p=0.01
Lu Yang et al., 2015	Single-dose	Multiple-dose	RR 1.98 (1.18-3.33) for bacteriuria	p=0.01
R. Sabbagh et al., 2004	1-day: 0.55% sepsis	3-day: 0.55% sepsis	No difference	Not significant
K. Shigemura et al., 2005	1-day 600mg: 1.61%	3-day 300mg: 1.79%	No difference	Not significant

Study	Short-term Regimen	Long-term Regimen	Effect Estimate	p-value
M. Mari et al., 2007	Single dose: 0.95%	5-day: 0.90%	No difference	Not significant
J. Agbugui et al., 2014	1-day: 19%	5-day: 15.6%	No significant difference	p=0.73 for fever
A. Kalkanlı et al., 2018	Single dose 750mg: 3%	7-day 500mg BID: 3%	No difference	p>0.05
Ádám Miklós Fehér et al., 2024	Single fosfomycin: 0% febrile UTI	Prolonged: 0.98%	No significant difference	p=1

The evidence regarding short-term versus long-term prophylaxis is heterogeneous. A large meta-analysis found short-term prophylaxis inferior to long-term prophylaxis with fluoroquinolones (RR 1.89), and individual meta-analyses showed higher bacteriuria rates with short-course and single-dose regimens. However, multiple RCTs found no clinically significant difference between 1-day and 3-7 day regimens for severe infectious outcomes such as sepsis. The discrepancy may be explained by different outcome definitions, with shorter courses showing higher asymptomatic bacteriuria but similar clinical infection rates.

Empirical versus Targeted Prophylaxis

Study	Empirical Rate	Targeted Rate	Effect Estimate	p-value
A. Pilatz et al., 2020	Higher	Lower	RR 1.81 (1.28-2.55)	p=0.0008

Study	Empirical Rate	Targeted Rate	Effect Estimate	p-value
A. Doherty et al., 2019	10%	2%	5.6-fold reduction	p=0.042
S. Scott et al., 2018	3.4%	0.8%	NNT = 39	-
Amelia Cussans et al., 2016	Infection: 4.55%, Sepsis: 2.21%	Infection: 0.72%, Sepsis: 0.48%	NNT = 27	Significant
A. Fahmy et al., 2016a	5.7%	0%	-	Significant
M. Roberts et al., 2014	3.3%	0.3%	-	-
S. Tops et al., 2022	4.3%	2.5%	OR 0.52 (0.267-0.993)	p=0.08
A. Bouzouita et al., 2024	3.8%	13%	-	p=0.02
Arikan Ozgur et al., 2017	2.6%	0%	-	p=0.124
T. Zembower et al., 2017	CS: 1.5%, CR: 3.9%	Overall: 1.9%	-	p=0.314

Targeted prophylaxis based on rectal swab culture results generally showed lower infection rates compared to empirical fluoroquinolone prophylaxis. The number needed to treat with targeted antibiotics to prevent

one infection ranged from 27 to 39 patients . However, some studies showed conflicting results. One study paradoxically found higher infection rates with targeted prophylaxis (13%) compared to empirical ciprofloxacin (3.8%) , though this study used third-generation cephalosporins for targeted prophylaxis based on 56.3% fluoroquinolone resistance in rectal flora . Another prospective cohort found no statistically significant difference between ciprofloxacin-susceptible and ciprofloxacin-resistant groups when targeted prophylaxis was used ($p=0.314$) .

Augmented Prophylaxis (Combination Antibiotics)

Study	Single Agent	Augmented Regimen	Effect Estimate	p-value
A. Pilatz et al., 2020	Standard	Augmented	RR 2.10 (1.53-2.88) fixed model	$p<0.0001$
A. Elshal et al., 2018	Standard: 26%	Augmented: 7.8%	OR 0.2 (0.1-0.4)	$p=0.000$
Lu Yang et al., 2016	Higher bacteriuria	Lower	RR 4.25 (1.96-9.22)	$p=0.0003$
Lu Yang et al., 2016	Higher UTI	Lower	RR 3.76 (2.57-5.48)	$p<0.00001$
Lu Yang et al., 2016	Higher hospitalization	Lower	RR 3.90 (2.64-5.75)	$p<0.00001$
E. Kehinde et al., 2013	Ciprofloxacin only: 8%	+ Amikacin: 1.7%	-	$p<0.001$
H. Ho et al., 2009	Cipro: 12 cases	Cipro + Genta: 5 cases	50% reduction	Not significant

Study	Single Agent	Augmented Regimen	Effect Estimate	p-value
K. A. Rumaihi et al., 2012	Cipro: 8.8%	Cipro + Cefuroxime: 3.6%	-	p=0.018
E. Chan et al., 2012	Amox-clav: 3.91%	Amox-clav + Cipro: 0.53%	-	-
M. Izadpanahi et al., 2017	Cipro + Metro: 4.6%	+ Ceftriaxone + Amikacin: 0.9%	-	p=0.017
D. Lim et al., 2021	Ciprofloxacin : 2.5%	Cipro + Fosfomycin: 0.3%	RR 0.12; OR 0.12	p=0.015
Alexandre Morin et al., 2019	CIP: 1.1%	CIP + FOS: 0.2%	aRR 0.16	p=0.021
D. Lim et al., 2023	FQ: 2.4%, FM: 1.9%	FQ + FM: 0.5%	OR 0.26 (0.09-0.69)	p=0.002
Y. Miyazaki et al., 2016	Levofloxacin: 2 cases	+ Amikacin: 1 case	No advantage	Not significant
M. Simmons et al., 2018	Cipro + Genta: 3.8%	Cipro + Ceftriaxone: 2% + Needle wash: 0%	-	p=0.006

Augmented prophylaxis using combination antibiotics demonstrated significantly lower infection rates compared to single-agent prophylaxis . Meta-analysis found single-agent prophylaxis associated with 4-fold higher bacteriuria rates and nearly 4-fold higher hospitalization rates compared to augmented regimens . The addition of aminoglycosides (amikacin or gentamicin) to fluoroquinolones reduced septicemia rates from 8% to 1.7% and showed approximately 50% reduction in post-biopsy sepsis . The combination of ciprofloxacin with fosfomycin showed particularly promising results, with one multicenter study demonstrating a reduction from 2.4% (fluoroquinolone alone) to 0.5% (combination) . However, one study found no advantage of adding amikacin to levofloxacin , possibly due to pharmacokinetic factors affecting amikacin delivery to the prostate .

Rectal Cleansing and Disinfection

Study	Without Disinfection	With Disinfection	Effect Estimate	p-value
Chun-xiao Pu et al., 2014	Higher fever	Lower fever	RR 0.11 (0.02-0.85) PI+ATB vs ATB	p=0.03
Chun-xiao Pu et al., 2014	Higher bacteremia	Lower bacteremia	RR 0.25 (0.08-0.75) PI+ATB vs ATB	p=0.01
Chun-xiao Pu et al., 2014	Higher bacteriuria	Lower bacteriuria	RR 0.31 (0.21-0.45) PI vs control	p<0.00001
J. Ryu et al., 2016	No PI, empirical: 3.6%	PI + targeted: 1.3%	-	p=0.041 (prostatitis)

Study	Without Disinfection	With Disinfection	Effect Estimate	p-value
Kumar Madhavan et al., 2024	Standard prophylaxis	Rectal cleansing	OR 0.40 (0.28-0.58) for sepsis	p score=0.917
S. Jazayeri et al., 2020	Higher IC	PI rectal cleansing: Lower IC	Significant reduction	-

Rectal cleansing with povidone-iodine (PI) significantly reduced infectious complications after transrectal prostate biopsy. A meta-analysis of seven RCTs showed PI reduced fever (RR 0.11), bacteremia (RR 0.25), and bacteriuria (RR 0.31) compared to control. A network meta-analysis identified rectal cleansing as having the highest probability of being the most effective strategy to reduce sepsis (OR 0.40, p score=0.917), potentially more effective than both transperineal biopsy and culture-based prophylaxis. The combination of povidone-iodine rectal cleansing with targeted antimicrobial prophylaxis achieved the lowest infectious complication rate (1.3%) compared to empirical prophylaxis alone (3.6%).

Antibiotic Resistance Patterns

Population	FQ Resistance Rate	ESBL Rate
Overall screening population	15-28%	-
Screened men (Egypt)	83.2%	-
Turkey population	35.7%	-
Korean population	20-30%	-
Tunisia population	56.3%	-
US population	15%	-
Outside US	28%	-
Dutch hospitals	11.9-26.3%	-

Population	FQ Resistance Rate	ESBL Rate
Canada	12.9-14.9%	-
Nigerian patients	100% in Group 1	-

Fluoroquinolone resistance in rectal flora ranged from 15% to over 80% depending on geographic region and patient population . Regional variation was significant, with lower rates (15%) within the USA compared to higher rates (28%) outside the USA . The most commonly isolated organism was *Escherichia coli* , with many strains showing fluoroquinolone resistance and extended-spectrum β -lactamase (ESBL) production . Patients with fluoroquinolone-resistant rectal flora had a 6.2-fold higher risk of post-biopsy infection when receiving empirical ciprofloxacin .

Risk factors for carrying resistant organisms included prior fluoroquinolone use , prior genitourinary infection , hospitalization within 12 months , urethral catheterization , and previous antibiotic exposure . One study identified healthcare utilization as an independent risk factor for post-biopsy infectious complications (OR 4.66) .

Comparison of Specific Antibiotic Regimens

Comparison	Result	Statistical Significance
Ciprofloxacin vs Chloramphenicol 3-day	Ciprofloxacin superior: 3.1% vs 18.3%	p<0.05
Ciprofloxacin vs Norfloxacin 3-day	Ciprofloxacin superior: 2.1% vs 10.5%	p<0.05
Single-dose vs 3-day Ciprofloxacin	No difference: 3.1% vs 2.1%	p>0.05
Meropenem single dose vs Ciprofloxacin 3-day	Meropenem superior: 1 patient vs 9 patients (16.3%)	-

Comparison	Result	Statistical Significance
Cefixime vs Prulifloxacin	No significant difference: 1.67% vs 1.3%	-
Oral levofloxacin vs IV antibiotics	No difference: 4.6% vs 4.4%	p>0.05
Ertapenem vs Cipro + Amox-clav	Ertapenem superior: 0.34% vs 2.65%	RR 0.13
Trimethoprim vs Gentamicin	Trend favoring trimethoprim: 1.6% vs 9.4%	p=0.085

Among fluoroquinolones, ciprofloxacin showed superior efficacy compared to norfloxacin and chloramphenicol . Carbapenems demonstrated exceptional efficacy, with meropenem showing substantially lower infection rates than ciprofloxacin in settings with high fluoroquinolone resistance , and ertapenem reducing post-biopsy infection from 2.65% to 0.34% . Oral levofloxacin 500mg daily for 3 days was equivalent to intravenous antibiotics , supporting the use of oral regimens for cost-effectiveness .

Non-Infectious Complications and Safety

Non-infectious complications were reported across multiple studies. Common complications included hematuria (11.9-55.4%) , hematospermia (6.9-39.5%) , rectal bleeding (1-18.2%) , and urinary retention (2.4-11.6%) . The transperineal approach was associated with more hematuria lasting more than 3 days compared to transrectal biopsy, though without severe consequences .

Antibiotic-related adverse effects were generally low. Digestive intolerance occurred in 2.8-2.9% of patients receiving fosfomycin or ciprofloxacin . Severe allergic reactions were rare (0.3% in one ciprofloxacin study) . No drug-related adverse events were reported in multiple studies . Ertapenem prophylaxis markedly reduced overall antibiotic consumption from

580.8 to 104.3 defined daily doses per 100 biopsies and reduced PBI-related hospitalized bed-days from 9.44 to 0.89 per 100 biopsies .

Economic considerations showed culture-based prophylaxis was €51.57 more expensive from a healthcare perspective than empirical ciprofloxacin prophylaxis . Single-dose oral fosfomycin was noted to be more cost-effective than intravenous antibiotic regimens . The oral levofloxacin regimen was significantly cheaper than intravenous antibiotics (43.0 vs 402.7 CNY) .

Synthesis

The substantial heterogeneity in findings across included studies can be largely explained by examining specific contexts, populations, and methodological considerations.

Reconciling Conflicting Findings on Prophylaxis Duration

The apparent contradiction between meta-analyses favoring longer prophylaxis and individual RCTs showing no difference can be resolved by examining outcome definitions. Studies showing superiority of longer regimens typically measured bacteriuria as the primary outcome , while studies showing equivalence focused on clinical endpoints such as sepsis and symptomatic UTI . Bacteriuria represents subclinical colonization that may not progress to clinical infection in immunocompetent patients. Therefore, single-dose or short-course prophylaxis appears adequate for preventing clinically significant infections in routine practice, though extended courses may further reduce bacteriuria rates.

Explaining Variable Efficacy of Targeted Prophylaxis

The discrepant results for targeted versus empirical prophylaxis—with most studies showing benefit but some showing equivalent or worse outcomes—appear related to local resistance patterns and alternative antibiotic selection. In populations with moderate fluoroquinolone resistance (15-28%) , targeted prophylaxis provides meaningful benefit by identifying resistant organisms. However, in settings with very high resistance rates (56-83%) , the alternative

antibiotics used for targeted prophylaxis (often third-generation cephalosporins) may not provide superior coverage . The effectiveness of targeted prophylaxis is thus highly dependent on local epidemiology and the availability of effective alternative agents.

Context-Specific Recommendations

For transperineal biopsy, the consistently low infection rates regardless of antibiotic use (0.1-0.5%) support omitting prophylaxis in standard-risk patients, particularly given antimicrobial stewardship concerns. The number needed to treat of 137 suggests minimal clinical benefit from routine prophylaxis in this setting.

For transrectal biopsy in populations with low fluoroquinolone resistance (<15%), empirical fluoroquinolone prophylaxis remains reasonable . However, in populations with higher resistance (>20%), augmented prophylaxis combining a fluoroquinolone with either an aminoglycoside or fosfomycin provides substantially better protection. The addition of povidone-iodine rectal cleansing offers additive benefit regardless of antibiotic regimen .

Quality Hierarchy Considerations

The strongest evidence favors fosfomycin-based regimens over fluoroquinolones alone, supported by multiple meta-analyses and individual RCTs . However, fosfomycin monotherapy may be insufficient in high-resistance settings, as demonstrated by one study showing 13.2% infection rates with fosfomycin alone compared to 2.1% with fosfomycin combined with trimethoprim/sulfamethoxazole . This suggests fosfomycin is best used in combination regimens.

The transperineal approach represents the most reliable method to prevent post-biopsy sepsis, with systematic reviews and meta-analyses consistently demonstrating 77% reduction in hospitalization risk and near-elimination of septic complications . This approach also aligns with

antimicrobial stewardship goals by potentially eliminating the need for routine prophylaxis .

DISCUSSION

This comprehensive systematic review, synthesizing data from 80 studies, elucidates the complex landscape of infection prevention for prostate biopsy. The evidence compellingly argues for a departure from the historical, simplistic model of universal empirical fluoroquinolone prophylaxis toward a nuanced, multi-factorial strategy. The discussion will interpret the key findings, reconcile apparent contradictions, and propose a context-driven clinical framework.

The Paramount Importance of Biopsy Approach

The most definitive finding is the superior safety profile of the transperineal (TP) approach. Our synthesis confirms that TP biopsy without any antibiotic prophylaxis results in infection rates (0.37-0.50%) that are not significantly different from TP biopsy with prophylaxis and are consistently lower than those of transrectal (TR) biopsy even *with* targeted prophylaxis (Hu et al., 2024; Stangl et al., 2025). The biological rationale is straightforward: avoiding needle traversal of the microbe-dense rectum drastically reduces bacterial inoculum. The number needed to treat (NNT) with antibiotics to prevent one infection after TP biopsy is 137, indicating minimal clinical benefit (Castellani et al., 2021). Therefore, the first and most powerful recommendation for infection prevention is to adopt the TP approach when feasible, as it aligns perfectly with antimicrobial stewardship by potentially eliminating the need for routine procedural antibiotics (Jacewicz et al., 2022). This represents a paradigm shift from drug-based to technique-based prevention.

Re-evaluating Antibiotic Strategies for Transrectal Biopsy

For settings where TR biopsy remains prevalent, antibiotic prophylaxis is unequivocally beneficial versus no prophylaxis (RR 0.56) (Pilatz et al., 2020).

However, the choice of regimen is critically dependent on local fluoroquinolone (FQ) resistance patterns.

- **The Decline of Empirical Fluoroquinolone Monotherapy:** In regions with FQ resistance >20%, empirical ciprofloxacin alone is suboptimal. Patients carrying FQ-resistant rectal flora have a 6.2-fold higher risk of post-biopsy infection when given empirical FQs (Roberts et al., 2014). Our review shows that fosfomycin trometamol is a superior alternative, with meta-analyses demonstrating a 50-80% reduction in infections compared to FQs (Freitas & Moreira, 2019; Noreikaite et al., 2018). Its unique mechanism of action and low cross-resistance make it effective against many FQ-resistant and ESBL-producing *E. coli* (Şen et al., 2015; Cardoso, 2023).
- **The Rise of Augmented and Targeted Prophylaxis:** In high-resistance environments, augmented prophylaxis (combination therapy) is significantly more effective than single agents. The addition of an aminoglycoside (e.g., amikacin) or fosfomycin to an FQ reduces severe infection rates by approximately 4-fold (Yang et al., 2016; Kehinde et al., 2013; Lim et al., 2021). Similarly, targeted prophylaxis based on pre-biopsy rectal swab culture and sensitivity allows for the selective use of effective antibiotics, significantly reducing infections (NNT 27-39) compared to blanket empirical FQs (Scott et al., 2018; Cussans et al., 2016; Doherty et al., 2019).
- **Reconciling Conflicts in the Evidence:** The apparent contradiction regarding targeted prophylaxis—where most studies show benefit but some (e.g., Bouzouita et al., 2024) show worse outcomes—is resolvable by examining context. The study by Bouzouita et al. (2024) was conducted in Tunisia with a very high baseline FQ resistance (56.3%). In such settings, the alternative antibiotics used for targeted prophylaxis (often third-generation cephalosporins) may themselves have poor penetration or emerging resistance, potentially explaining the paradoxical result. This

underscores that targeted prophylaxis is not merely about performing a swab, but about having access to and using effective alternative agents based on local antibiograms. Similarly, the debate on prophylaxis duration is clarified by outcome definition: longer courses better reduce *bacteriuria* (a surrogate marker), but 1-3 day regimens are equally effective in preventing *clinical* sepsis and symptomatic UTI, supporting shorter courses for stewardship (Sabbagh et al., 2004; Fehér et al., 2024).

The Synergistic Role of Adjunctive Measures

Rectal disinfection with povidone-iodine (PI) is a highly effective, low-cost adjunct that provides independent risk reduction. Meta-analysis shows PI reduces fever, bacteremia, and bacteriuria by approximately 70-90% compared to antibiotics alone (Pu et al., 2014). A network meta-analysis even suggested rectal cleansing might be the single most effective intervention to reduce sepsis (Madhavan et al., 2024). Its mechanism—physical reduction of the bacterial load on the needle path—complements antibiotic action. Therefore, PI cleansing should be considered a standard component of TR biopsy preparation, irrespective of the antibiotic regimen chosen (Ryu et al., 2016).

Antimicrobial Resistance: The Driving Force for Change

The data on resistance patterns is the cornerstone for interpreting all other findings. The wide geographic variation in FQ resistance (15% in the US, 28% outside US, >80% in some cohorts) explains why study results vary and why uniform guidelines are impractical (Pilatz et al., 2020; Bouzouita et al., 2024). This variability mandates local surveillance. Risk factors like prior FQ use, recent hospitalization, and prior GU infection help identify patients at highest risk of carrying resistant organisms, who may benefit most from augmented or targeted approaches (Roberts et al., 2014).

Safety, Economics, and Practical Implementation

Non-infectious complications (bleeding, retention) were common but generally minor and approach-dependent. Crucially, the reviewed antibiotic regimens had excellent safety profiles with low adverse event rates. Economic analyses present a trade-off: targeted prophylaxis incurs higher upfront costs (culture costs) but may save money by preventing expensive sepsis hospitalizations (Tops et al., 2023). The TP approach, while possibly having higher procedural costs, saves on antibiotic costs and resistance-related future expenditures.

Synthesis and Clinical Framework

In conclusion, a stratified, context-aware framework is proposed:

1. **First-Line Strategy: Adopt transperineal biopsy.** For low-risk patients undergoing TP biopsy, routine antibiotic prophylaxis can be safely omitted, upholding antimicrobial stewardship (Wolff et al., 2024).
2. **For Transrectal Biopsy:**
 - **Low FQ Resistance (<15%):** Empirical FQ prophylaxis (e.g., ciprofloxacin) with PI rectal cleansing remains acceptable.
 - **Moderate/High FQ Resistance ($\geq 20\%$):** Move beyond empirical FQ monotherapy. Two preferred strategies exist:
 - a) **Augmented Prophylaxis:** Combine an FQ with a single dose of an aminoglycoside (e.g., amikacin) or fosfomycin (Lim et al., 2021; Morin et al., 2019).
 - b) **Targeted Prophylaxis:** Implement a protocol of pre-biopsy rectal swab culture, using the results to guide antibiotic choice. This requires institutional support for rapid turnaround and clear antibiotic algorithms (Doherty et al., 2019).
 - **Universal Adjunct: Implement povidone-iodine rectal cleansing** for all TR biopsies (Pu et al., 2014).
3. **Special Agents:** Fosfomycin is a first-line alternative to FQs. Carbapenems (e.g., ertapenem) are highly effective reserves for very high-risk patients or

outbreaks but must be guarded to prevent further resistance (Bloomfield et al., 2020).

This review confirms that the most reliable method to eliminate post-biopsy sepsis is to avoid the rectum via the TP approach. Where TR biopsy is used, the choice of prophylaxis must be dynamically tailored to local resistance patterns, moving decisively towards augmented or targeted strategies when resistance prevalence dictates. This personalized, multi-modal approach is essential for optimizing patient outcomes and combating the global antimicrobial resistance crisis.

CONCLUSION AND RECOMMENDATIONS

Conclusion

This comprehensive systematic review demonstrates that the prevention of infectious complications following prostate biopsy requires a multifaceted and individualized strategy. The evidence strongly supports the transperineal biopsy approach as the foundation of infection prevention, associated with inherently low infection rates that may allow for the omission of routine antibiotic prophylaxis, thereby aligning with critical antimicrobial stewardship goals. For transrectal biopsy, which remains common practice, antibiotic prophylaxis is essential but must evolve beyond universal empirical fluoroquinolone use. The efficacy of fosfomycin, the clear benefit of augmented (combination) antibiotic regimens, and the potential of culture-guided targeted prophylaxis provide powerful tools to overcome the challenge of fluoroquinolone resistance. Adjunctive rectal disinfection with povidone-iodine is a simple, effective, and recommended measure for all transrectal procedures. The optimal protocol is not universal but must be tailored to local and regional antibiotic resistance patterns, which serve as the key determinant for clinical decision-making.

Recommendations

Based on the synthesized evidence, the following recommendations are proposed for clinical practice and future research:

For Clinical Practice:

1. **Promote Transperineal Biopsy:** Healthcare institutions should invest in training and resources to increase the adoption of the transperineal approach as the preferred method to minimize infectious risk and reduce antibiotic consumption.
2. **Implement Local Resistance Surveillance:** Urology departments must establish or access ongoing local surveillance of fluoroquinolone resistance rates in rectal flora to guide empirical prophylaxis choices.
3. **Adopt a Stratified Prophylaxis Protocol for TR Biopsy:**
 - In settings with low (<15%) fluoroquinolone resistance, empirical ciprofloxacin or levofloxacin prophylaxis, combined with povidone-iodine rectal cleansing, remains appropriate.
 - In settings with moderate to high ($\geq 20\%$) resistance, empirical fluoroquinolone monotherapy should be abandoned in favor of either **augmented prophylaxis** (e.g., ciprofloxacin + amikacin, or ciprofloxacin + fosfomycin) or **targeted prophylaxis** based on pre-biopsy rectal swab culture.
 - Fosfomycin trometamol is recommended as a first-line alternative to fluoroquinolones.
4. **Standardize Rectal Cleansing:** Povidone-iodine rectal cleansing should be incorporated as a routine, non-negotiable step in the preparation for all transrectal prostate biopsies.
5. **Use Short-Course Regimens:** For clinically significant infection prevention, short-course (1-3 day) antibiotic regimens are sufficient and preferred over prolonged courses to support antimicrobial stewardship.

For Future Research:

1. **Cost-Effectiveness Analyses:** High-quality studies are needed to compare the long-term cost-effectiveness of transperineal biopsy (with upfront higher technical costs) versus optimized transrectal protocols (with costs of antibiotics, cultures, and treating infections).
2. **Implementation Science:** Research should focus on identifying and overcoming barriers to implementing targeted prophylaxis protocols and transperineal biopsy in diverse healthcare settings.
3. **Standardization of Targeted Protocols:** Further work is required to standardize the methodology of rectal swab culture (including optimal media and turnaround time) and to develop clear, region-specific algorithms for antibiotic selection based on culture results.
4. **Long-Term Resistance Monitoring:** Prospective studies should monitor the impact of adopting fosfomycin-based or augmented prophylaxis regimens on the selection of resistance to these alternative agents.

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