Species-Level Attribution of Bacterial Uropathogens in Adult Men: A Critical Narrative Review of Distribution, Mechanisms, Antimicrobial Resistance and Diagnostic Uncertainty

Amit Bag
Kolkata, India.
Email: amit18.sdi@gmail.com

Abstract

Urinary tract infection in adult men has long been treated as a minor variant of a predominantly female disease, and the microbiological literature reflects that assumption. Most large aetiological surveys pool the sexes, report proportions dominated by female specimens, and offer little that clarifies which organisms genuinely cause disease in the male urinary tract and which merely occupy it. This critical narrative review examines the evidence for species-level attribution of bacterial uropathogens in men, covering relative frequency, pathogenic mechanism, syndrome specificity, resistance behaviour and the diagnostic assumptions that determine what is counted as a pathogen. Literature was identified through open scholarly web searching, retrieval of indexed biomedical records, bibliographic verification through a metadata registry, citation tracking from recent reviews, and consultation of professional guidance, with a search period extending to 1 June 2026. Evidence was appraised for design adequacy, representativeness, sex-stratification and the transparency of case definitions rather than scored with a formal instrument. *Escherichia coli* remains the leading isolate in men, but its reported share varies far more widely than in women, and the residual fraction is occupied by organisms whose pathogenic status is genuinely contested. *Enterococcus faecalis* is recovered from male urine at frequencies that culture-based attribution cannot easily distinguish from colonisation. Urease-producing and device-associated species dominate the catheterised male tract through mechanisms that are mechanistically well characterised but clinically difficult to separate from asymptomatic carriage. Fastidious Gram-positive organisms are recovered disproportionately from older men, and their apparent rarity partly reflects laboratory method. Prostatic involvement introduces a compartment with no analogue in women, altering persistence, recurrence and antibiotic selection. Confidence is highest for mechanistic descriptions of individual species and lowest for the sex-specific epidemiological claims that clinical guidance depends upon. Progress requires male-stratified, syndrome-anchored studies that pair standardised sampling with methods capable of detecting organisms that routine culture systematically discards.

Keywords: Urinary tract infection; men; uropathogens; Escherichia coli; Enterococcus faecalis; catheter-associated infection; antimicrobial resistance; urinary microbiota.

1. Introduction

Urinary tract infection is among the most frequently diagnosed bacterial conditions in clinical medicine, and its aetiological description has been remarkably stable for four decades. A short list of organisms, headed by

Escherichia coli and followed by *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus faecalis* and *Staphylococcus saprophyticus*, appears in review after review as the causative repertoire (Flores-Mireles et al., 2015). That list was assembled largely from studies of young, otherwise healthy, non-pregnant women with acute cystitis, because that population supplied the cleanest natural experiment: a short urethra, a defined symptom complex, a high pre-test probability of infection, and a specimen in which a single organism at high density is the norm. The resulting picture has been transposed onto men with comparatively little scrutiny.

The transposition is not obviously safe. The male urinary tract differs from the female tract in ways that plausibly alter which organisms reach the bladder, which persist there, and which cause disease once established. The urethra is several times longer, the distance from the perineal reservoir is greater, and prostatic secretions contribute antibacterial zinc-containing peptides to the distal tract. Against those protective features, men accumulate obstructive and instrumental risks with age that women largely do not: benign prostatic enlargement, prostatic inflammation, urethral stricture, and a high lifetime probability of transurethral instrumentation. Lipsky (1989) argued on the basis of the then-available evidence that most men with bacteriuria harbour a functional or anatomical abnormality, that Gram-negative and Gram-positive organisms other than *E. coli* account for a substantial share of episodes, and that the diagnostic threshold used for women is inappropriate in men. Much subsequent clinical guidance has been built on that framing, yet the underlying microbiological claims have rarely been re-examined with contemporary methods.

Two developments have made re-examination urgent. The first is the recognition that the urinary tract of healthy adults is not sterile. Culture-independent sequencing and expanded culture protocols have demonstrated resident microbial communities in the bladder of asymptomatic individuals, and the male urobiome appears to differ from the female urobiome in composition and, by several accounts, in diversity (Reasoner et al., 2025). Once a resident community is accepted, every positive urine culture becomes an act of interpretation rather than a simple detection, and the interpretation is harder in men because the reference range for a normal male urinary community is poorly defined and because the sampling methods used to characterise it are not equivalent. Voided specimens from men incorporate urethral and preputial organisms that are not present in the bladder, and paired comparisons show that voided and catheterised samples from the same individual frequently disagree (Hrbacek et al., 2021; Yu & Jung, 2022). A recent systematic review of the male urinary and prostatic microbiome also identified substantial heterogeneity in sampling and reporting, reinforcing the limited definition of a normal male ecological baseline (Pina-Vaz et al., 2024).

The second development is the reclassification of male urinary tract infection within clinical taxonomy. Acute cystitis in men without systemic features was historically classified as complicated infection by virtue of sex alone, a convention that justified prolonged therapy and broad-spectrum agents. Contemporary guidance has moved away from that position, treating anatomical or functional abnormality rather than male sex as the criterion for complexity (Bonkat et al., 2024; Kranz et al., 2024). The reclassification has direct microbiological consequences. If afebrile male cystitis is to be managed as an uncomplicated infection with narrow-spectrum agents and short courses, then the assumption that its causative organisms resemble those of female cystitis must be tested rather than assumed, and the frequency of organisms poorly covered by narrow-spectrum agents must be quantified in men specifically. The randomised evidence that seven days of therapy is non-inferior to fourteen in afebrile men (Drekonja et al., 2021) makes the question practical rather than academic, because shorter courses tolerate less diagnostic error.

The available aetiological evidence for men is thinner than the confidence of clinical guidance implies. A systematic review restricted to acute cystitis or afebrile urinary tract infection in adult men without systemic features identified only six eligible studies across more than a decade of publication, conducted in six different settings, with sample sizes spanning two orders of magnitude and with *E. coli* reported in anywhere between roughly a third and almost all episodes (Georgiou et al., 2026). A range of that width is not a measurement; it is a statement that the underlying studies are not measuring the same thing. Large male-specific laboratory series exist and provide better resolution, but they are concentrated in a small number of high-income settings and rely on routine specimens submitted for clinical reasons, so they describe the organisms that reach a laboratory rather than the organisms that cause disease (Salm et al., 2022, 2023). Recent multicentre data from France confirm the persistence of a broad male-specific species distribution, while the reliance on routine midstream cultures submitted for suspected infection continues to limit separation of symptomatic disease from bacteriuria (Reissier et al., 2025).

Attribution is further complicated by the fact that the organisms recovered from men differ from those recovered from women in a direction that maximises interpretive difficulty. Gram-positive organisms, particularly *E. faecalis*, are recovered from male urine considerably more often than from female urine, and they are also the organisms whose presence is most easily explained by colonisation, contamination or device carriage (Salm et al., 2023). The species that are most over-represented in men are therefore the species about which culture alone is least informative. Similar reasoning applies to the fastidious Gram-positive organisms that are recovered disproportionately from older men and that standard aerobic culture protocols are poorly configured to detect (Kakodkar & Hamula, 2022; Lainhart & Gonzalez, 2018). Contemporary analysis of polymicrobial urine cultures likewise emphasises that conventional contamination rules may obscure clinically relevant mixed communities, further weakening single-isolate attribution (Moreland et al., 2025).

Existing reviews address adjacent questions without resolving this one. Comprehensive mechanistic reviews describe uropathogen biology in detail but treat the host as sex-neutral (Flores-Mireles et al., 2015; Nielubowicz & Mobley, 2010). Species-focused reviews of *E. faecalis*, *P. mirabilis* and *K. pneumoniae* are thorough within their subject but do not compare species against one another in a male-specific frame (Armbruster & Mobley, 2012; Codelia-Anjum et al., 2023; Mim et al., 2026). Reviews of complicated infection and of catheter-associated infection cover populations in which men predominate, yet they organise the evidence by clinical category rather than by organism (Nicolle, 2014; Wagenlehner et al., 2020). Reviews of the urobiome describe sex differences in resident communities but concentrate on non-infectious urological conditions (Reasoner et al., 2025). The specific question of which bacterial species cause urinary tract infection in men, with what confidence, by what mechanism, and with what diagnostic caveats, falls between these literatures. A recent male-specific clinical review similarly concluded that causative microbiology is less predictable in men and that evidence from clinical trials focused specifically on male patients remains limited (Drekonja, 2024).

1.1 Scope, Research Gap and Objectives

This review addresses bacterial species attribution in urinary tract infection among adult men, defined as males aged eighteen years and over. It covers the relative frequency of individual species in male urine, the mechanisms by which those species colonise and injure the male urinary tract, the distribution of species across clinically distinct male syndromes, the interaction between antimicrobial resistance and apparent species distribution, and the diagnostic assumptions that determine which organisms are counted as pathogens. Prostatic infection is treated as an integral part of the male urinary tract rather than as a separate disease, because the prostate constitutes an anatomical compartment with no female analogue and materially alters persistence and recurrence.

Several areas are excluded. Paediatric and adolescent populations are outside the scope, since the determinants of infection in boys differ substantially and the relevant literature is organised around distinct questions. Fungal, mycobacterial, parasitic and viral urinary infections are excluded, as are sexually transmitted urethritis syndromes, which overlap symptomatically with lower urinary tract infection but constitute a separate aetiological and diagnostic problem. Renal transplantation and profound immunosuppression are considered only where they illuminate general mechanisms of species selection. Detailed antimicrobial dosing, surgical management and non-antibiotic prophylaxis are outside the scope except where they bear on species attribution.
The knowledge gap addressed is specific. Species-level aetiological data for men exist, but they are dominated by routine laboratory series from a narrow range of settings, they rarely separate symptomatic infection from bacteriuria, they seldom stratify by the clinical syndrome or by the presence of a device, and they almost never apply methods capable of detecting organisms that routine culture discards. As a consequence, the confidence attaching to statements about which organisms cause urinary tract infection in men is substantially lower than the confidence with which such statements are made. No existing review evaluates that mismatch directly.

The objectives are, first, to determine what can defensibly be concluded about the relative frequency of individual bacterial species in male urinary tract infection and how far that frequency varies with setting, syndrome and method; second, to compare the mechanistic evidence for pathogenicity across the principal species implicated in men, distinguishing demonstrated causation from mechanistic plausibility; third, to assess how far the male-specific evidence supports current diagnostic thresholds and clinical categories; fourth, to examine the reciprocal relationship between antimicrobial resistance and apparent species distribution; and fifth, to identify the study designs that would materially reduce the present uncertainty. The intended contribution is

an integrated, sex-specific critical synthesis that separates well-supported species attributions from those resting on extrapolation from female cohorts or on the limitations of routine culture.

2. Methods for Literature Selection

2.1 Review Design and Rationale

A critical narrative review was selected in preference to a systematic review, scoping review or meta-analysis because the primary difficulty in this field is conceptual rather than arithmetical. The constituent studies use incompatible case definitions, apply different quantitative culture thresholds, sample different anatomical compartments, and vary in whether they separate symptomatic infection from bacteriuria. Pooling proportions across such studies would generate a summary estimate with high apparent precision and low interpretive validity, and the systematic review that has been attempted in the most tightly defined male subgroup concluded that heterogeneity in design and definition prevented meaningful synthesis even after formal screening (Georgiou et al., 2026). A critical narrative approach permits explicit comparison of the assumptions embedded in different study designs, which is the analytical task this evidence base requires.

Narrative synthesis does not license selective citation or the omission of appraisal. The review therefore adopts a transparent and reportable search process, states the sources actually consulted, applies explicit eligibility criteria, and appraises each body of evidence against criteria appropriate to its design. Where evidence is inconsistent, the inconsistency is presented rather than resolved by preference. Where a conclusion rests on a single study or a single setting, that dependence is stated. Formal risk-of-bias instruments were not applied, since the majority of the included evidence consists of routine laboratory surveillance series and mechanistic laboratory work for which validated appraisal tools are either unavailable or would generate uninformative scores.

2.2 Information Sources

Literature was identified through open scholarly web searching conducted during the preparation of this review; through retrieval of indexed biomedical bibliographic records and open-access full texts located by that searching; through Crossref Metadata Search, accessed programmatically, which was used both for discovery and for verification of bibliographic detail; and through resolution of Digital Object Identifiers to their registered records. Backward citation searching was applied to recent reviews and to the reference lists of retrieved primary studies. Professional guidance from recognised infectious diseases and urological bodies was consulted directly.

Subscription-based bibliographic databases were not accessible during the preparation of this review. No search of Web of Science, Scopus, Embase or comparable subscription indexes was performed, and no claim is made that such a search was undertaken. Complete database export records were not supplied. The consequences of this restriction for coverage are addressed in the Limitations.

2.3 Search Strategy and Search Period

Search concepts were constructed from four elements: the population, expressed through terms for men, male, and male-specific anatomical structures; the condition, expressed through terms for urinary tract infection, cystitis, bacteriuria, pyelonephritis, prostatitis and catheter-associated infection; the organisms, expressed through named genera and species together with generic terms for uropathogen and bacterial aetiology; and the analytical dimension, expressed through terms for virulence, biofilm, urease, phylogroup, sequence type, antimicrobial resistance, microbiota, diagnostic threshold and epidemiology.

Representative combinations included the male population and condition terms crossed with organism terms, as in the structure (men OR male) AND ("urinary tract infection" OR bacteriuria OR cystitis) AND ("*Escherichia coli*" OR "*Enterococcus faecalis*" OR "*Proteus mirabilis*" OR "*Klebsiella pneumoniae*" OR "*Aerococcus*" OR "Actinotignum"); the same population and condition terms crossed with mechanistic terms, as in (male) AND ("urinary tract infection") AND (virulence OR biofilm OR urease OR phylogroup OR "sequence type"); the population and condition terms crossed with the prostatic compartment, as in (men OR male) AND (prostatitis OR "prostate biopsy") AND (bacteria OR infection OR "*Escherichia coli*"); and the population and condition

terms crossed with diagnostic and ecological terms, as in (male) AND (urine OR urinary) AND (microbiome OR microbiota OR "expanded quantitative urine culture" OR "16S"). Resistance-focused searching combined the population and condition terms with resistance vocabulary, as in (men OR male) AND ("urinary tract infection") AND ("antimicrobial resistance" OR "extended-spectrum beta-lactamase" OR carbapenem OR fluoroquinolone).

The search period was set to begin in 1989, the year in which the first substantial synthesis of male-specific urinary tract infection was published and the year from which the modern framing of the problem can be traced. Foundational work published before that date was admitted where it was necessary to explain the origin of a diagnostic convention or a mechanistic model. The final search date was 1 June 2026.

2.4 Eligibility Criteria

Publications were eligible if they were peer-reviewed journal articles or formal guidance from recognised professional or governmental bodies; if they addressed bacterial urinary tract infection, bacteriuria, prostatic infection or urinary microbial ecology; and if they reported data on adult men specifically, reported sex-stratified data from which male-specific findings could be extracted, or addressed mechanisms or methods directly relevant to the male urinary tract. Mechanistic laboratory studies and animal studies were eligible where they addressed a mechanism of specific relevance to the male tract, such as prostatic invasion or catheter biofilm formation. English-language publications were eligible.

Publications were excluded if they were confined to paediatric populations; if they addressed fungal, mycobacterial, parasitic or viral urinary infection; if they addressed sexually transmitted urethritis without reference to urinary tract infection; if they were case reports, conference abstracts, editorials or commentaries used as primary evidence; if they were preprints for which peer-reviewed equivalents existed; if they were promotional, non-scholarly or of unverifiable provenance; or if their bibliographic identity could not be confirmed against an authoritative record. Studies reporting only pooled male and female data without any means of separating the sexes were excluded from aetiological frequency claims but were admitted where they contributed mechanistic or methodological evidence.

2.5 Screening, Duplicate Handling and Study Selection

Records identified through searching were screened on title and abstract for relevance to the review scope, and candidates retained at that stage were assessed on full text where the full text was accessible. Duplicates arising from the retrieval of the same article through different routes, including separate records for repository copies, publisher records and metadata entries, were identified by matching Digital Object Identifier, title and author list, and were consolidated to a single record. Records lacking a resolvable identifier or complete bibliographic metadata were not retained. No formal screening counts are reported, because the search was iterative and topic-directed rather than a single enumerated systematic process, and reporting counts would misrepresent the method. Sources that could not be verified against an authoritative bibliographic record were discarded regardless of apparent relevance.

2.6 Critical Appraisal and Evidence Synthesis

Each retained study was appraised against criteria appropriate to its design. For laboratory surveillance series, the criteria were the size and representativeness of the sampled population, whether specimens were consecutive or selected, whether symptomatic infection was distinguished from bacteriuria, whether sex stratification was reported, whether the quantitative threshold and the specimen type were stated, and whether the identification method was capable of resolving fastidious organisms. For clinical trials, the criteria were the adequacy of randomisation and blinding, the appropriateness of the non-inferiority margin, the completeness of follow-up, and the generalisability of the enrolled population. For mechanistic studies, the criteria were the physiological relevance of the model system, the use of appropriate genetic controls, independent replication, and the distance between the demonstrated mechanism and the clinical endpoint it is invoked to explain. For guidance documents, the criteria were the transparency of the evidence grading and the extent to which male-specific recommendations rested on male-specific data.

Themes were developed inductively from the appraised evidence and organised around the determinants of species attribution rather than around individual organisms or individual studies. Where studies disagreed, the disagreement was examined for its most probable source, distinguishing genuine biological or geographical variation from differences in case definition, specimen type, threshold or laboratory method. Claims were graded informally through the language used in the text, with stronger formulations reserved for findings replicated across independent settings and designs, and conditional formulations used where evidence rested on a single study, a single setting or a mechanism not yet demonstrated in men.

3. Determinants of Species Selection in the Male Urinary Tract

3.1 Anatomical and Physiological Filters

The organisms recovered from male urine are not a random sample of the perineal and intestinal flora. They are the survivors of a sequence of filters, and the composition of each filter differs between the sexes. The length of the male urethra imposes a longer ascent, and the volume and velocity of male voiding impose a greater washout burden on organisms that fail to adhere. Prostatic secretions contribute zinc and antimicrobial peptides to the distal urethra. The combined effect is a lower baseline incidence of infection in men across most of adult life and, by implication, a requirement that organisms reaching the male bladder possess adhesive or persistence traits that are dispensable in the shorter female tract. That inference is mechanistically reasonable but has not been demonstrated directly, since no study has compared the virulence gene content of paired male and female isolates from the same setting with sufficient power to establish which traits are conditionally required.

The filters change with age and with intervention. Bladder outlet obstruction from prostatic enlargement reduces washout, increases post-void residual volume, and converts a hydrodynamically hostile compartment into a stagnant one. Instrumentation bypasses the urethral filter entirely and introduces an abiotic surface on which organisms that adhere poorly to urothelium can nonetheless establish. The prostate provides a compartment in which organisms can persist beyond the reach of agents that concentrate in urine but penetrate glandular tissue poorly. Each of these changes alters not only the probability of infection but the identity of the organisms likely to be recovered, and the direction of the alteration is consistent across the literature: obstruction and instrumentation shift the recovered flora away from *Escherichia coli* and towards enterococci, urease-producing Gram-negative organisms and non-fermenting Gram-negative bacilli (Jacobsen et al., 2008; Nicolle, 2014; Salm et al., 2023).

3.2 The Male Urobiome as Ecological Baseline

The demonstration that the bladder of asymptomatic adults harbours resident microbial communities has changed the interpretive framework for every urine culture. Expanded quantitative urine culture, which uses larger specimen volumes, additional media and extended incubation under varied atmospheric conditions, recovers organisms from a substantial proportion of specimens reported as no growth by standard protocols (Deen et al., 2023). Culture-independent sequencing extends detection further, at the cost of losing the distinction between viable and non-viable organisms. Neither method resolves the central problem, which is that the presence of an organism carries no intrinsic information about its causal role.

The male urobiome has been characterised less thoroughly than the female urobiome, and the characterisation that exists is methodologically fragile. Comparative work indicates that the male urinary community differs from the female community in composition and has been reported to display greater alpha diversity, with the difference most pronounced in men below sixty years of age (Reasoner et al., 2025). Interpretation is complicated by specimen type. Voided urine from men traverses a urethra colonised by organisms that are not resident in the bladder, and paired sampling shows that first-catch, midstream and catheterised specimens from the same man yield different community structures, with alpha diversity depending systematically on the collection method (Hrbacek et al., 2021). Studies of the male urinary community based on voided specimens therefore describe the urogenital tract rather than the bladder, whereas catheterised or suprapubic specimens describe the bladder at the cost of invasiveness and, in the case of transurethral catheterisation, a small risk of introducing organisms (Elsayed et al., 2024).

The practical consequence for species attribution is substantial and under-acknowledged. If organisms such as *Aerococcus*, *Actinotignum*, *Corynebacterium*, *Gardnerella* and various anaerobes are ordinary residents of the male urogenital tract, then their recovery from a voided specimen is uninformative in isolation, and their

recovery from a catheterised specimen in a symptomatic man is considerably more meaningful than routine reporting conventions allow. The literature on the male urobiome has developed largely in the context of benign prostatic enlargement and lower urinary tract symptoms rather than infection (Yu & Jung, 2022), so the ecological baseline against which infection should be judged has been established in a population that overlaps with, but is not identical to, the population in which the judgement must be made.

3.3 Diagnostic Thresholds and the Manufacture of Aetiology

Quantitative culture thresholds determine which organisms enter aetiological statistics, and the thresholds applied to men have a weak evidential foundation. The convention that a lower threshold, in the region of a thousand colony-forming units per millilitre, is appropriate for symptomatic men derives from early observations that contamination is less likely in male voided specimens and that clinically significant male infection frequently presents with lower bacterial densities (Lipsky, 1989). The convention is plausible and is embedded in guidance, but it has not been re-derived using contemporary methods, and it interacts awkwardly with the recognition of a resident urinary community. A threshold low enough to capture genuine low-density infection is also low enough to capture resident organisms, and the two cannot be distinguished by density alone.

Table 1. Conceptual distinctions governing the attribution of pathogenic status to bacteria recovered from male urine.

Distinction	Practical significance in men	Basis of the distinction	Supporting references
Symptomatic infection versus asymptomatic bacteriuria	Determines whether an isolate warrants treatment; routine laboratory series cannot separate the two, so reported male species distributions mix both populations	Strong outcome evidence supports withholding treatment for ASB in men; the diagnostic separation itself relies on clinical assessment rather than microbiology	Nicolle et al. (2019); Salm et al. (2023)
Bladder organism versus urethral or preputial organism	Voided male specimens traverse a colonised urethra; paired sampling shows voided and catheterised specimens from the same man frequently disagree	Demonstrated empirically by paired-specimen studies using sequencing and expanded culture	Hrbacek et al. (2021); Yu and Jung (2022)
Resident urobiome member versus invading pathogen	Organisms present in asymptomatic men cannot be assumed pathogenic when recovered during symptoms; the male ecological baseline remains poorly defined	Established in principle by culture-independent and expanded culture work; male-specific reference ranges not established	Deen et al. (2023); Elsayed et al. (2024); Reasoner et al. (2025)
Monomicrobial versus polymicrobial growth	Polymicrobial growth is conventionally read as contamination, yet interspecies interactions on devices are causally relevant; nearly half of polymicrobial male specimens contain *E. faecalis*	Convention for voided specimens; contradicted by mechanistic evidence from catheter biofilm models	Gaston et al. (2020); Salm et al. (2023)
Recoverable by routine culture versus recoverable only by expanded methods	Fastidious and slow-growing organisms recovered disproportionately from older men are systematically excluded by standard aerobic protocols	Demonstrated by expanded culture and mass spectrometric identification; magnitude of the deficit in symptomatic men not quantified	Cattoir et al. (2010); Kakodkar and Hamula (2022); Deen et al. (2023)
Quantitative threshold applied to	A lower threshold is conventionally accepted for	Derived from early observational work; not re-	Lipsky (1989); Nicolle et al.

Distinction	Practical significance in men	Basis of the distinction	Supporting references
male specimens	symptomatic men, but a threshold low enough to detect low-density infection also captures resident organisms	derived using contemporary methods or in light of the urobiome	(2019)

Note. ASB = asymptomatic bacteriuria

The definition of asymptomatic bacteriuria compounds the difficulty. Professional guidance defines asymptomatic bacteriuria in men by a single voided specimen yielding a single organism at a density of at least a hundred thousand colony-forming units per millilitre, and recommends against screening or treating it in men without planned urological intervention (Nicolle et al., 2019). The recommendation is well supported by trial evidence on outcomes, but it creates an asymmetry in the aetiological literature: laboratory series that report the organisms isolated from male urine cannot distinguish specimens submitted for symptomatic infection from specimens submitted for other reasons, so the reported species distribution is a mixture of two distinct biological populations. Series that report high proportions of Gram-positive organisms in men may be describing genuine infection, resident flora, or the consequences of submitting specimens from catheterised or asymptomatic individuals, and the reports themselves rarely permit the distinction.

Table 1 sets out the principal conceptual distinctions that determine whether an organism recovered from male urine is counted as a pathogen. The distinctions matter because they are frequently collapsed in primary studies, and because the direction of the resulting error is not random: collapsing them systematically inflates the apparent contribution of organisms associated with colonisation and devices, and systematically deflates the apparent contribution of organisms that routine culture cannot recover. The table also indicates where the evidential basis for each distinction is strong and where it rests on convention.

4. *Escherichia coli* in Men: Dominance, Population Structure and Tissue Tropism

4.1 Relative Frequency and the Width of its Variation

Escherichia coli is the most frequently isolated organism from male urine in essentially every series that has examined the question, and the finding is robust across settings, decades and laboratory methods. The informative observation is not the dominance itself but the width of its variation. In female cystitis, the proportion attributable to *E. coli* clusters tightly in the region of three quarters to nine tenths of episodes. In men, the systematic review of afebrile lower urinary tract infection found reported proportions ranging from approximately one third to almost all episodes across six studies (Georgiou et al., 2026). Large routine laboratory series from male outpatients report *E. coli* as the leading organism but with a share materially below that seen in female cystitis, with Gram-positive organisms occupying much of the remainder (Salm et al., 2022, 2023). Hospital-based series that include catheterised and instrumented men report lower proportions still, with *E. coli* accounting for roughly a third of confirmed infections in a large Chinese laboratory series that pooled both sexes and all clinical contexts (Wu et al., 2026).

Three explanations for the variation compete, and the available data do not separate them cleanly. The first is genuine case-mix variation: series drawn from primary care in men without devices will differ from series drawn from urology wards. The second is definitional: studies that require symptoms and a high threshold will report a higher *E. coli* share than studies that count any positive culture, because the organisms that displace *E. coli* in the tail of the distribution are disproportionately those associated with colonisation. The third is methodological: laboratories differ in whether they report mixed growth, in whether they identify Gram-positive isolates to species level, and in whether their culture conditions can recover fastidious organisms at all. The third explanation is the least discussed and probably the most consequential, because it operates in the same direction in every study that uses conventional aerobic culture.

A defensible summary is that *E. coli* is the leading uropathogen in men in all settings examined, that its share is lower and more variable than in women, and that the magnitude of the difference cannot be estimated with useful precision from the present evidence. Claims that assign a specific proportion to *E. coli* in male urinary tract infection should be read as descriptions of particular laboratory populations rather than as estimates of a general parameter.

4.2 Population Structure and Virulence Gene Content

Uropathogenic *E. coli* is not a taxonomic entity but an operational one, defined by isolation from urine rather than by a definable genetic boundary. The population is structured into phylogroups, of which B2 and, to a lesser extent, Dare enriched among extraintestinal isolates, and phylogroup membership correlates with virulence gene content. A large characterisation of urinary isolates found phylogroup B2 dominant, at approximately two thirds of isolates, followed by D, B1, F, C and A, and reported that B2 isolates carried the highest average number of virulence genes at approximately ten per isolate, while multidrug resistance was most prevalent in phylogroups C, E, F and D rather than in B2 (Wang et al., 2023). The inverse relationship between virulence gene burden and multidrug resistance is a recurring observation and has direct clinical implications, since it implies that the most resistant isolates are not necessarily the most virulent and that resistance and virulence may follow partially independent evolutionary trajectories.

Whether the male urinary tract selects a distinguishable subpopulation of *E. coli* remains unresolved. The mechanistic argument is straightforward: a longer urethra, greater washout and prostatic secretions should impose stronger selection for adhesion and iron acquisition. The empirical evidence is limited to small comparative studies of male and female isolates, generally single-centre, generally using multiplex detection of a handful of virulence genes, and generally underpowered for the comparisons attempted. Such studies have reported differences in phylogroup distribution and in the prevalence of individual adhesin and siderophore genes between male and female isolates, but the reported differences are inconsistent across studies and are of uncertain significance given the number of comparisons performed. No adequately powered comparative genomic study of paired male and female urinary isolates from a common source population has been published, and until one is, the proposition that male urinary tract infection selects a distinct *E. coli* population should be regarded as plausible but unproven.

The virulence mechanisms themselves are well characterised, largely from work that did not distinguish the sexes. Type 1 fimbriae mediate FimH-dependent attachment to mannosylated uroplakin receptors on the urothelium and are required for bladder colonisation. P fimbriae, encoded by the *pap* operon, mediate attachment to globoseries glycolipids and are associated with pyelonephritis. Secreted toxins including alpha-haemolysin and cytotoxic necrotising factor 1 damage host cells and liberate nutrients. Multiple siderophore systems, including aerobactin, yersiniabactin and salmochelin, permit iron acquisition in the iron-restricted urinary environment. Capsular polysaccharides and lipopolysaccharide modifications mediate resistance to complement and phagocytosis (Nielubowicz & Mobley, 2010; Terlizzi et al., 2017). The relative importance of these systems in men has not been established, and the assumption that it is identical to that in women is an assumption rather than a finding.

4.3 Intracellular Persistence and the Prostatic Compartment

Two persistence mechanisms are of particular relevance to men. The first is the formation of intracellular bacterial communities within superficial urothelial cells, demonstrated in murine models as biofilm-like aggregates that resist both antibiotic exposure and innate immune clearance and that can seed subsequent episodes (Anderson et al., 2003). The evidence for this mechanism in human disease is indirect, resting on morphological observations in exfoliated urothelial cells and on the epidemiological pattern of recurrence with the same strain. Its relevance to men has not been examined separately, and no reason has been advanced for expecting it to differ.

The second is prostatic invasion, which has no female analogue and which is mechanistically better supported than it was a decade ago. Work using a stem cell-derived prostate epithelial organoid model has shown that uropathogenic *E. coli* preferentially attaches to, invades and replicates within luminal rather than basal prostate epithelial cells, and has identified FimH-dependent binding to prostatic acid phosphatase as the receptor interaction mediating that tropism (Guedes et al., 2026). The finding is important because it provides a molecular explanation for a long-observed clinical pattern: that infection in men frequently involves the prostate, that prostatic involvement is often clinically silent, and that recurrence with the same organism is common despite apparently adequate therapy of the bladder. The organoid model is a considerable methodological advance over previous cell line work, but it remains a model, the receptor interaction has been demonstrated in a defined system rather than in human tissue during natural infection, and the extent to which

prostatic invasion occurs in men with uncomplicated cystitis rather than in those with clinical prostatitis is unknown.

The therapeutic implications are nonetheless real and are already visible in clinical data. Agents that achieve high urinary concentrations but poor prostatic penetration might be expected to fail more often in men if occult prostatic involvement were common. Observational evidence provides partial support: a retrospective evaluation of nitrofurantoin and pivmecillinam for lower urinary tract infection in men reported acceptable clinical outcomes overall, but identified urinary catheterisation as associated with new antibiotic prescription, with an odds ratio of 2.34 and a confidence interval from 1.14 to 4.80, and prostate cancer as associated with relapse, with an odds ratio of 3.01 and a confidence interval from 1.09 to 8.29 (Montelin et al., 2019). The study was retrospective, single-region and modest in size, and the associations identified are consistent with prostatic involvement but do not demonstrate it. The randomised evidence that seven days of ciprofloxacin or trimethoprim–sulfamethoxazole is non-inferior to fourteen days in afebrile men, with symptom resolution in 93.1 per cent and 90.2 per cent respectively (Drekonja et al., 2021), suggests that occult prostatic involvement is either less common or less consequential than the traditional emphasis on prolonged therapy implied, at least among men treated with agents that penetrate prostatic tissue reasonably well. The trial enrolled predominantly older men from two veterans' medical centres and used agents with good tissue penetration, so its findings do not extend automatically to narrow-spectrum agents with poor prostatic distribution.

4.4 Sequence type 131 and the Entanglement of Resistance with Recurrence

The global expansion of *E. coli* sequence type 131, and particularly of its fluoroquinolone-resistant, CTX-M-producing clade C2 subpopulation, has altered the resistance landscape of urinary infection worldwide. Its significance for men is twofold. First, ST131 is disproportionately represented among extended-spectrum beta-lactamase-producing urinary isolates, which are more prevalent in men than in women in most sex-stratified series. Second, ST131 appears to be associated with recurrence. A prospective cohort of 297 patients followed for one year after a first episode of infection caused by an extended-spectrum beta-lactamase-producing *E. coli* found that 68 developed recurrent infection, that half of those with recurrence were infected with ST131 isolates, and that clade C2 predominated among ST131 isolates; no association was found between recurrence and phylogroup, *bla*CTX-M gene type or resistance profile as such (Lindblom et al., 2022). Comparative genomic analysis of paired isolates from patients with recurrence showed that sequential isolates were essentially identical, differing by between two and eighteen single nucleotide polymorphisms, indicating persistence of the same strain rather than reinfection with a new one (Jaén-Luchoro et al., 2023).

The persistence finding is important for men specifically, because the plausible reservoirs for a persisting strain include the intestinal tract, which is shared with women, and the prostate, which is not. Neither cohort was designed to identify the reservoir, and neither was sex-stratified in a way that permits male-specific inference. The proposition that prostatic persistence contributes to the recurrence of ST131 infection in men is mechanistically coherent given the organoid evidence for prostatic tropism, but it is at present an inference joining two separate literatures rather than a demonstrated relationship.

The interaction between resistance and apparent aetiology deserves emphasis. Where fluoroquinolone resistance is common, empirical therapy shifts towards agents with different spectra, and organisms intrinsically resistant to those agents become relatively more prominent in subsequent cultures. Resistance therefore alters not only treatment success but the observed species distribution, and cross-sectional aetiological surveys conducted in high-resistance settings are not directly comparable with those conducted in low-resistance settings even when the underlying populations are similar.

5. Gram-Positive Uropathogens and the Attribution Problem

5.1 *Enterococcus faecalis*: Frequency without Certainty

The most striking sex difference in the aetiological literature concerns *Enterococcus faecalis*. A retrospective multicentre analysis of urine specimens from 99,415 adult male outpatients submitted from 6,749 practices reported *E. faecalis* as the second most frequently detected organism, present in approximately sixteen per cent of specimens from men with suspected infection, with the highest proportion, approximately seventeen per cent,

in young men, and with *E. faecalis* isolated in approximately forty-seven per cent of polymicrobial specimens (Salm et al., 2023). The companion analysis of antimicrobial resistance in a comparably sized male outpatient population from the same laboratory network confirmed the prominence of Gram-positive organisms in male specimens (Salm et al., 2022). Hospital-based series report similar patterns, with *E. faecalis* second only to *E. coli* in a large Chinese series at approximately eleven per cent of confirmed infections across both sexes (Wu et al., 2026), and sex-stratified analyses from a European urological centre report a higher Gram-negative to Gram-positive ratio in men than the enterococcal literature alone would suggest, with Gram-negative organisms accounting for approximately seventy-seven per cent of male isolates (Popescu et al., 2026).

The frequency is therefore reasonably well established. The interpretation is not. Enterococci are gastrointestinal commensals with a well-documented capacity for asymptomatic colonisation of the urinary tract, particularly in the presence of devices or obstruction. The high proportion of polymicrobial specimens containing *E. faecalis* is consistent with colonisation, since polymicrobial growth in a voided specimen is conventionally read as contamination. The concentration of enterococcal isolation among younger men, reported in the German series, is counterintuitive if devices and obstruction are the principal drivers, and has not been explained. None of the large series distinguishes symptomatic infection from bacteriuria with sufficient reliability to determine what proportion of enterococcal isolates represent disease.

Mechanistic evidence establishes that *E. faecalis* is capable of causing urinary infection rather than merely accompanying it. Enterococci possess adhesins that mediate attachment to fibrinogen deposited on catheter surfaces, form robust biofilms, exhibit intrinsic resistance to cephalosporins and to clinically achievable concentrations of aminoglycosides used alone, and acquire resistance readily (Codelia-Anjum et al., 2023). Experimental work in a murine catheter-associated infection model has shown that *E. faecalis* and *Proteus mirabilis* are the most prevalent and persistent co-colonisers of catheterised urine, that they co-localise on catheter biofilms, that *P. mirabilis* preferentially adheres to *E. faecalis* during biofilm development, and that contact-dependent interactions between the two species produce a biofilm architecture that increases antimicrobial recalcitrance for both (Gaston et al., 2020). The proposal arising from that work, that *E. faecalis* functions as a pioneer species establishing a surface suitable for colonisation by more conventionally pathogenic organisms, reframes the attribution question: an organism may be causally important without being the proximate cause of symptoms.

The gap between the mechanistic and the clinical literature is wide. Mechanistic work establishes capability in device-associated models; clinical series establish frequency without establishing causation; and no study has combined male-specific clinical phenotyping with the microbiological detail necessary to determine when enterococcal isolation from male urine warrants treatment. This is the single largest unresolved attribution problem in the male-specific literature.

5.2 Staphylococci, Streptococci and the Residual Gram-positive Flora

Staphylococcus saprophyticus occupies a prominent place in the general uropathogen list on the strength of its association with acute cystitis in young sexually active women. Its contribution in men is small in every series that reports species-level Gram-positive identification, and its inclusion in male-oriented clinical guidance is an inheritance from the female literature rather than a male-specific finding. *Staphylococcus aureus* in urine occupies a different position. Its recovery from urine is uncommon in the absence of a device but carries disproportionate clinical weight, because it may reflect haematogenous seeding from a distant focus rather than ascending infection, and because it is associated with structural abnormality and instrumentation. The literature supporting this interpretation is largely observational and of considerable age, and the proportion of *S. aureus* bacteriuria in men that reflects ascending infection rather than seeding has not been quantified in a contemporary cohort.

Coagulase-negative staphylococci other than *S. saprophyticus*, viridans streptococci and *Streptococcus agalactiae* are recovered from male urine with modest frequency and are generally interpreted as contaminants or colonisers unless recovered from a catheterised specimen in a symptomatic patient. That interpretation is conventional rather than evidentially established, and the emergence of the urobiome literature has begun to complicate it. The broader point is that the Gram-positive fraction of male urinary isolates is heterogeneous, includes organisms of genuinely different clinical significance, and is frequently reported at genus level or as a single aggregated category in the very studies that establish its size (Kline & Lewis, 2016).

Table 2 summarises the principal evidence on species distribution in male urine from the studies that report male-specific or sex-stratified data. The comparison illustrates both the consistency of *E. coli* dominance and the substantial variation in every other component of the distribution, and it makes visible the dependence of the reported distribution on setting and on whether symptomatic infection was distinguished from bacteriuria. The table is not exhaustive of the available evidence; it presents the series that report male-specific data with sufficient methodological detail to permit interpretation.

Table 2. Reported bacterial species distribution in male urinary specimens across studies providing male-specific or sex-stratified data

Study, setting and design	Male population sampled	Reported distribution and principal limitation for attribution	Supporting references
Retrospective multicentre laboratory analysis, outpatient practices, Germany, 2015-2020	99,415 adult male outpatients; midstream specimens submitted for suspected infection	*E. faecalis* second most frequent organism at approximately 16% of specimens, highest in young men at approximately 17%, and present in approximately 47% of polymicrobial specimens. Indication for specimen submission not recorded, so symptomatic infection and bacteriuria are not separable	Salm et al. (2023)
Retrospective observational laboratory analysis, outpatient practices, Germany, 2015-2020	102,736 adult male outpatients; midstream specimens	*E. coli* leading organism with a share materially below that reported in female cystitis; resistance in male *E. coli* sufficient to challenge standard empirical recommendations. Same limitation regarding specimen indication	Salm et al. (2022)
Systematic literature review of afebrile lower urinary tract infection in men, 2011-2023	Six eligible studies from six settings; sample sizes 18 to 4,876; median age 44-71 years	*E. coli* reported in approximately 32.9% to 94% of patients. The width of the range reflects irreconcilable differences in case definition, inclusion criteria and setting rather than a measurable parameter	Georgiou et al. (2026)
Retrospective laboratory analysis, two general hospitals, Shanghai, 2023; both sexes pooled	5,671 confirmed infections from 61,450 patients investigated	*E. coli* approximately 36.1%, *E. faecalis* approximately 11.2%, *K. pneumoniae* approximately 8.2%. Sexes pooled, so male-specific inference is indirect; hospital case mix	Wu et al. (2026)
Retrospective descriptive analysis, tertiary urological centre, Romania, 2023-2025	2,270 male patients with at least one positive urine culture above the standard threshold	Gram-negative organisms approximately 77.2% of male isolates, with a higher Gram-negative to Gram-positive ratio than enterococcal frequency data alone would predict; resistance higher in male than female isolates. Tertiary urological case mix limits generalisability	Popescu et al. (2026)

Note. Percentages are those reported by the cited studies and are not directly comparable because case definitions, specimen types, quantitative thresholds and identification methods differ across studies

6. Urease-Producing and Device-Associated Gram-Negative Species

6.1 *Proteus mirabilis* and the Crystalline Biofilm

Proteus mirabilis occupies a distinctive position in male urinary infection because its principal pathogenic mechanism is chemical rather than immunological. The organism expresses a potent urease that hydrolyses urea

to ammonia and carbon dioxide, raising urinary pH and precipitating calcium and magnesium phosphates as struvite and hydroxyapatite. Those crystals become embedded in the developing biofilm, producing the crystalline biofilms that encrust and obstruct indwelling catheters and that seed infection stones within the urinary tract (Jacobsen et al., 2008). The mechanism is unusually well documented, having been characterised through in vitro bladder models, electron microscopy of explanted catheters, and genetic studies demonstrating that urease-negative mutants fail to maintain colonisation. The organism additionally expresses a repertoire of at least fourteen distinct fimbriae, exhibits swarming differentiation on surfaces, and displays reciprocal regulation between adhesion and motility that appears tuned to the transition between ascent and colonisation (Armbruster & Mobley, 2012).

The male relevance is indirect but strong. *P. mirabilis* is disproportionately associated with long-term catheterisation, with neurogenic bladder and with obstructive uropathy, all of which are more common in men. The organism therefore appears in male series at frequencies exceeding those in unselected female series, but the excess is attributable to case mix rather than to any male-specific tropism, and no study has demonstrated a sex-specific determinant of *P. mirabilis* colonisation independent of device use and obstruction. Two clinical consequences follow. Crystalline encrustation is a mechanical problem that antimicrobial therapy does not resolve, so the isolation of *P. mirabilis* from a catheterised man carries an implication for device management that isolation of *E. coli* does not. And the organism's capacity to alkalinise urine and generate infection stones creates a self-sustaining cycle in which the stone protects the organism from both host defences and antimicrobial exposure, making eradication without stone clearance improbable.

6.2 *Klebsiella pneumoniae* and the Convergence of Resistance with Virulence

Klebsiella pneumoniae is consistently the second or third most frequent Gram-negative organism in male urine and is the organism whose resistance behaviour has changed most rapidly. Its virulence apparatus comprises capsular polysaccharide, which mediates resistance to phagocytosis and complement; type 1 and type 3 fimbriae, which mediate attachment to urothelium and to abiotic surfaces respectively; siderophore systems for iron acquisition in the iron-restricted urinary environment; and a biofilm capacity that is particularly consequential on devices (Mim et al., 2026). The type 3 fimbrial system is of specific relevance to catheterised men, since it mediates adhesion to catheter surfaces in a manner that type 1 fimbriae do not.

The resistance trajectory is the more urgent concern. Carbapenem-resistant *K. pneumoniae* has become established in urinary isolates in many settings, and male sex has been reported among the factors associated with carbapenem-resistant infection in urological populations. A case-control study in a urology clinic compared 62 patients with carbapenem-resistant *K. pneumoniae* urinary infection against 136 with multidrug-resistant but carbapenem-susceptible infection, and identified differences in residence, in the proportion with upper tract involvement, and in prior healthcare exposure (Radu et al., 2024). Longitudinal microbiological work has shown that recurrent infection with carbapenem-resistant *K. pneumoniae* frequently reflects persistence of the same strain rather than reinfection: among 41 patients with recurrent klebsiella urinary infection identified from 589 urinary isolates over four years, 56.1 per cent involved carbapenem-resistant strains, and genomic analysis established strain identity across episodes in a substantial proportion (Cao et al., 2025). Both studies are single-centre and retrospective, both were conducted in settings with high baseline carbapenem resistance, and neither is sex-stratified in a way that permits male-specific inference, so the association between male sex and carbapenem-resistant klebsiella infection remains an observation requiring confirmation rather than an established relationship.

The convergence of hypervirulence and carbapenem resistance in *K. pneumoniae* is a development whose urinary implications remain poorly defined. Hypervirulent lineages, historically associated with community-acquired invasive disease in the absence of comorbidity, have acquired carbapenemase-encoding plasmids, and the resulting organisms have been recovered from urinary sources. Whether such lineages behave differently in the male urinary tract, and whether they contribute disproportionately to urosepsis in men with obstruction, has not been examined.

6.3 *Pseudomonas aeruginosa* and Other Non-fermenting Bacilli

Pseudomonas aeruginosa is uncommon in community-acquired male urinary infection and common in men with long-term catheters, recent instrumentation or repeated antimicrobial exposure. Its position in male series is

therefore almost entirely a function of case mix. Its clinical importance is disproportionate to its frequency, owing to intrinsic resistance to many agents, a strong biofilm phenotype on catheter surfaces, and the limited oral therapeutic options available. The organism's recovery from male urine after transurethral manipulation has been noted in the prostatitis literature, and its presence should raise the probability of a device, a structural abnormality or prior instrumentation rather than being interpreted as primary ascending infection.

Other non-fermenting Gram-negative bacilli, including *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*, appear in male urinary series from high-dependency and long-term care settings. The evidence supporting their pathogenic role in the urinary tract specifically is weak, consisting largely of case series in which they were recovered alongside other organisms from catheterised patients. Their appearance in aetiological tables should be read as evidence about the population sampled rather than about urinary pathogenicity.

Table 3 compares the principal pathogenic mechanisms of the species implicated in male urinary tract infection and indicates, for each, the strength of the evidence linking the mechanism to disease in men rather than to disease in general or to laboratory models. The comparison shows a consistent pattern: mechanisms are best characterised for the organisms whose pathogenicity is least contested, and least characterised for the organisms about which attribution is most uncertain. That inversion is a structural weakness of the field rather than an accident of individual studies.

Table 3. Comparison of principal pathogenic mechanisms across bacterial species implicated in male urinary tract infection

Species	Principal mechanisms	Male-specific relevance and strength of evidence	Supporting references
Escherichia coli	Type 1 fimbrial FimH-mediated adhesion to uroplakin; P fimbrial adhesion in upper tract disease; alpha-haemolysin and cytotoxic necrotising factor 1; multiple siderophore systems; capsule and lipopolysaccharide-mediated immune evasion; intracellular bacterial communities	Mechanisms characterised largely in sex-neutral models. FimH-dependent invasion of luminal prostate epithelial cells via prostatic acid phosphatase provides a male-specific mechanism, demonstrated in an organoid model but not yet in human tissue during natural infection	Anderson et al. (2003); Nielubowicz and Mobley (2010); Terlizzi et al. (2017); Guedes et al. (2026)
Enterococcus faecalis	Adhesion to fibrinogen deposited on catheter surfaces; robust biofilm formation; intrinsic cephalosporin resistance; readily acquired resistance; pioneer colonisation facilitating subsequent adhesion by other species	Frequency in male urine well documented; mechanistic capability established in device-associated models. Clinical significance of isolation from male urine remains the largest unresolved attribution problem	Gaston et al. (2020); Codelia-Anjum et al. (2023); Salm et al. (2023)
Proteus mirabilis	Potent urease raising urinary pH and precipitating struvite and hydroxyapatite; crystalline biofilm formation causing catheter encrustation and blockage; at least fourteen fimbrial systems; swarming differentiation with reciprocal regulation of adhesion and motility	Excess frequency in men attributable to catheterisation, neurogenic bladder and obstruction rather than to any demonstrated male-specific tropism. Mechanistic evidence strong; isolation implies a device or stone management problem more reliably than a treatable cause of symptoms	Jacobsen et al. (2008); Armbruster and Mobley (2012); Gaston et al. (2020)
Klebsiella pneumoniae	Capsular polysaccharide mediating phagocytosis and complement resistance; type 1 and type 3 fimbriae, the latter	Type 3 fimbrial adhesion is directly relevant to catheterised men. Reported association between male sex and	Radu et al. (2024); Cao et al. (2025); Mim et al. (2026)

Species	Principal mechanisms	Male-specific relevance and strength of evidence	Supporting references
	mediating adhesion to abiotic surfaces; siderophore systems; biofilm formation on devices	carbapenem-resistant infection derives from single-centre retrospective studies in high-resistance settings and is not established	
Pseudomonas aeruginosa and other non-fermenting bacilli	Intrinsic resistance to multiple agent classes; strong biofilm phenotype on catheter surfaces; limited oral therapeutic options	Presence in male series is almost entirely a function of case mix, reflecting devices, instrumentation and prior antimicrobial exposure. Evidence for primary urinary pathogenicity of *Acinetobacter* and *Stenotrophomonas* is weak	Jacobsen et al. (2008); Nicolle (2014); Wagenlehner et al. (2020)
Fastidious Gram-positive organisms including *Aerococcus urinae*, *Actinotignum schaalii* and *Corynebacterium urealyticum*	Slow growth requiring enriched media and increased carbon dioxide; urease production in *C. urealyticum* with alkaline encrustation; frequent overgrowth by conventional uropathogens in mixed culture	Recovered disproportionately from older men with obstructive uropathy. Capability established by case-based and mechanistic evidence; true population contribution unquantified because detection is method-dependent. Only *A. urinae* has established susceptibility breakpoints	Cattoir et al. (2010); Kline and Lewis (2016); Lainhart and Gonzalez (2018); Kakodkar and Hamula (2022)

Note. Species names are italicised at first mention within each cell in accordance with binomial nomenclature conventions

7. Fastidious and Under-Recognised Organisms

The organisms most likely to be missed by routine urine culture are also those recovered disproportionately from older men. *Aerococcus urinae* and *Aerococcus sanguinicola* grow as small alpha-haemolytic colonies that are readily dismissed as contaminants and were routinely misidentified by conventional biochemical methods before mass spectrometric identification became widespread (Cattoir et al., 2010). *Actinotignum schaalii*, formerly classified within *Actinobaculum*, is a slow-growing facultatively anaerobic Gram-positive rod that requires enriched medium and increased carbon dioxide for reliable recovery and that is frequently overgrown by conventional uropathogens in mixed cultures. A review of reported cases found urinary tract infection to be the commonest manifestation, accounting for approximately seventy per cent of documented infections, followed by bacteraemia and abscess formation, and identified obstructive uropathy and advanced age as the dominant predisposing factors (Kakodkar & Hamula, 2022). *Alloscardovia omnicolens* presents comparable identification difficulties. Of these organisms, only *A. urinae* has established antimicrobial susceptibility testing criteria and interpretive breakpoints, so even correct identification does not yield actionable susceptibility data for the others (Lainhart & Gonzalez, 2018).

Corynebacterium urealyticum deserves separate consideration because its pathogenic mechanism parallels that of *P. mirabilis*. The organism is urease-producing, multiresistant, slow-growing, and associated with alkaline-encrusted cystitis and pyelitis in men with prior urological surgery or catheterisation. It is frequently dismissed as skin flora, and its recovery requires prolonged incubation that routine protocols do not provide (Kline & Lewis, 2016). *Gardnerella vaginalis* and various anaerobes have been detected in the male urinary tract by sequencing and expanded culture, and their pathogenic status in men is entirely unresolved.

The evidence base for all of these organisms shares a characteristic structure: mechanistic and case-based evidence establishes that they can cause disease, laboratory method determines whether they are detected, and no population-based study has estimated their true contribution to male urinary tract infection under conditions of adequate detection. The consequence is a systematic and unquantified underestimate. Where laboratories have adopted mass spectrometric identification and extended culture conditions, recovery of these organisms has increased substantially, but such changes alter case ascertainment over time and therefore confound

comparisons of aetiological distributions across eras. Reported increases in the frequency of fastidious organisms cannot be distinguished from improvements in their detection, and no study has attempted to separate the two.

The clinical significance of the underestimate is greatest in exactly the population where male urinary infection is most common and most consequential: older men with obstruction, devices or prior urological intervention. In that group, a negative or non-significant routine culture in the presence of pyuria and symptoms should not be interpreted as excluding bacterial infection, and the interpretation of culture-negative symptomatic disease as non-infectious is an inference that current laboratory methods do not support.

8. Syndrome-Specific Attribution in Men

Aggregating all male urinary tract infection into a single aetiological category obscures more than it reveals, because the male tract supports several clinically distinct syndromes with different pathogen distributions.

Afebrile lower urinary tract infection in men without devices or structural abnormality most closely resembles female cystitis in its aetiology, with *E. coli* predominant, and it is the syndrome for which the reclassification away from automatic complexity is best justified. The randomised evidence supporting seven days of therapy applies to this group, with the qualifications that the trial population was predominantly older, that the agents used penetrate prostatic tissue, and that the primary outcome was symptom resolution rather than microbiological eradication (Drekonja et al., 2021). Aetiological data for this syndrome specifically remain the weakest part of the evidence base, resting on six heterogeneous studies (Georgiou et al., 2026).

Febrile urinary tract infection in men frequently involves the prostate, whether or not clinical prostatitis is diagnosed. Acute bacterial prostatitis is caused predominantly by organisms that also cause other genitourinary infections, headed by *E. coli* and with enterococci contributing a minority of episodes, and it arises usually by ascending infection but also through instrumentation (Brede & Shoskes, 2011). The National Institutes of Health classification, which separates acute bacterial prostatitis, chronic bacterial prostatitis, chronic prostatitis and chronic pelvic pain syndrome, and asymptomatic inflammatory prostatitis, remains the framework within which this literature is organised (Krieger et al., 1999). Its principal analytical limitation for present purposes is that the boundary between categories two and three is defined by the recovery of an organism using localisation cultures, so any improvement in microbiological detection reclassifies patients from the non-bacterial to the bacterial category without any change in their underlying disease. The proportion of chronic pelvic pain syndrome that is microbiologically driven is therefore method-dependent and unknown.

Post-procedural infection constitutes a distinct syndrome with a distinct aetiology. Transrectal prostate biopsy inoculates rectal flora directly, and the organisms recovered are correspondingly enriched for fluoroquinolone-resistant and extended-spectrum beta-lactamase-producing *E. coli*, with a marked contribution from resistant clonal lineages (Acosta et al., 2022). The evidence supporting a change in practice is now randomised: the PREVENT trial assigned 658 biopsy-naive participants to transperineal biopsy without antibiotic prophylaxis or transrectal biopsy with prophylaxis targeted to rectal culture results, and recorded zero infections in the transperineal arm against four, or 1.4 per cent, in the transrectal arm, a difference of 1.4 percentage points with a confidence interval from minus 3.2 to 0.3 and a p value of 0.059, with equivalent cancer detection (Hu et al., 2024). The trial did not reach conventional statistical significance for its primary endpoint, a point frequently overlooked in secondary reporting, and its transrectal arm used targeted rather than empirical prophylaxis, which is not standard practice in many settings. Its most defensible interpretation is that transperineal biopsy achieves very low infection rates without any antibiotic exposure, which is an antimicrobial stewardship argument of considerable force independent of the significance of the between-arm comparison. Meta-analytic evidence comparing fosfomycin with fluoroquinolone prophylaxis for transrectal biopsy provides a further option where the transrectal route is retained, though the underlying trials are small and heterogeneous (Gu et al., 2023).

Catheter-associated infection is the syndrome in which male-specific attribution is hardest and most consequential. Bacteriuria accumulates at a daily rate of several per cent during indwelling catheterisation and becomes effectively universal with prolonged catheterisation; catheter-acquired infection accounts for approximately a fifth of healthcare-associated bacteraemia in acute care and more than half in long-term care (Nicolle, 2014). The flora is polymicrobial, is dominated by organisms adapted to abiotic surfaces, and includes

species whose recovery in a non-catheterised patient would be dismissed. Because bacteriuria is expected, the isolation of an organism carries almost no diagnostic information; the diagnosis rests on clinical features that are themselves unreliable in the populations most often catheterised. Species attribution in this syndrome is therefore best understood as a description of catheter ecology rather than as an identification of a causative agent, and the mechanistic work on interspecies interactions in catheter biofilms supports that reading (Gaston et al., 2020).

Table 4 sets out the syndrome-specific distribution of organisms in men together with the diagnostic caveats attaching to each. The purpose of the comparison is to make explicit that the same organism carries different evidential weight in different male syndromes, and that a single aggregated aetiological table for male urinary tract infection cannot be interpreted without knowing the syndrome mix of the underlying population.

Table 4. Syndrome-specific species attribution in men and the diagnostic caveats attaching to each syndrome

Male syndrome	Predominant organisms	Principal diagnostic caveat	Supporting references
Afebrile lower urinary tract infection without device or structural abnormality	*E. coli* predominant; Gram-positive organisms occupying a larger share than in female cystitis	The aetiological evidence for this syndrome specifically is the weakest in the field, resting on six heterogeneous studies with irreconcilable definitions. Reclassification away from automatic complexity is justified on outcome grounds rather than on male-specific aetiological data	Drekonja et al. (2021); Bonkat et al. (2024); Georgiou et al. (2026)
Febrile urinary tract infection and acute bacterial prostatitis	*E. coli* predominant, with enterococci contributing a minority of episodes; *Pseudomonas* more probable after transurethral manipulation	Prostatic involvement is frequent and often clinically silent, so the distinction between cystitis and prostatitis is unreliable. The boundary between bacterial prostatitis and chronic pelvic pain syndrome is defined by organism recovery and therefore shifts with laboratory method	Krieger et al. (1999); Brede and Shoskes (2011)
Post-procedural infection following transrectal prostate biopsy	Rectal flora inoculated directly, enriched for fluoroquinolone-resistant and extended-spectrum beta-lactamase-producing *E. coli* including resistant clonal lineages	Aetiology reflects the patient's rectal flora rather than urinary tract ecology. In the PREVENT trial the between-arm difference did not reach conventional significance ($p = 0.059$), and the transrectal comparator used targeted rather than empirical prophylaxis	Acosta et al. (2022); Gu et al. (2023); Hu et al. (2024)
Catheter-associated infection and long-term catheterisation	Polymicrobial flora dominated by organisms adapted to abiotic surfaces, notably *E. faecalis*, *P. mirabilis*, *K. pneumoniae* and *P. aeruginosa*	Bacteriuria is expected and becomes effectively universal with prolonged catheterisation, so isolation of an organism carries almost no diagnostic information. Attribution here describes catheter ecology rather than identifying a causative agent	Jacobsen et al. (2008); Nicolle (2014); Gaston et al. (2020)
Recurrent infection with resistant lineages	*E. coli* sequence type 131, particularly clade C2; carbapenem-resistant *K. pneumoniae* in high-resistance settings	Genomic comparison of sequential isolates indicates persistence of the same strain rather than reinfection, but the reservoir is unidentified. The	Lindblom et al. (2022); Jaen-Luchoro et al. (2023); Cao et al. (2025)

Male syndrome	Predominant organisms	Principal diagnostic caveat	Supporting references
		intestinal reservoir is shared with women; the prostatic reservoir is not, and its contribution is inferred rather than demonstrated	

Note. PREVENT = PReclude infection EVEnts with No prophylaxis Transperineal trial.

9. Antimicrobial Resistance and its Feedback on Apparent Aetiology

Resistance in male urinary isolates is consistently higher than in female isolates within the same setting, a finding reported across independent laboratory networks and health systems. The German male outpatient series, drawn from more than a hundred thousand specimens across a national laboratory network, documented resistance levels in male *E. coli* isolates sufficient to challenge standard empirical recommendations and identified predictors of trimethoprim and ciprofloxacin resistance (Salm et al., 2022). Sex-stratified analysis from a European urological centre reported higher resistance among male isolates across multiple agent classes (Popescu et al., 2026). A large laboratory series reported *E. coli* resistance to ampicillin of approximately seventy-six per cent, to levofloxacin of approximately fifty-nine per cent and to cefazolin of approximately forty-nine per cent, with carbapenem resistance at approximately one per cent, and reported substantially higher resistance in *K. pneumoniae* (Wu et al., 2026). The pattern is consistent even though the absolute values are setting-specific.

The explanations for the male excess are partly confounded. Men who present with urinary infection are older, have more comorbidity, are more likely to have devices and structural abnormality, are more likely to have had recent antimicrobial exposure, and are more likely to have been hospitalised. Whether any male-specific biological factor contributes beyond this confounding has not been established, and the available studies rarely adjust adequately for the relevant covariates.

Resistance interacts with aetiology in both directions. Higher resistance prevalence drives empirical therapy towards broader agents, which alters the selective environment and shifts the recovered flora. Organisms with intrinsic resistance to the agents in current use become relatively more prominent, so the aetiological distribution observed in a high-resistance setting partly reflects the antibiotics used in that setting rather than the underlying propensity of organisms to cause disease. This feedback is rarely acknowledged in aetiological surveys, and it constitutes a substantial obstacle to comparing distributions across settings or across time.

The global burden estimates provide the scale of the problem without resolving its male-specific dimension. Bacterial antimicrobial resistance was estimated to be associated with approximately 4.95 million deaths and attributable to approximately 1.27 million deaths in 2019 (Antimicrobial Resistance Collaborators, 2022), with forecasts projecting substantial increases through to 2050 (GBD 2021 Antimicrobial Resistance Collaborators, 2024). Urinary tract infection specifically was estimated to account for approximately 64,890 deaths attributable to and approximately 0.26 million deaths associated with resistance in 2019, with *E. coli* and *K. pneumoniae* together responsible for more than half of that burden and with third-generation cephalosporin-resistant and fluoroquinolone-resistant *E. coli* each exceeding six thousand attributable deaths (Li et al., 2022). Global burden analyses of urinary tract infection as a disease entity have likewise documented substantial and unevenly distributed burden (He et al., 2025). None of these analyses reports sex-stratified, pathogen-specific urinary estimates in a form that permits male-specific inference, and their reliance on modelled inputs from settings with variable surveillance quality limits the precision of any subgroup interpretation.

The stewardship implication for men is nonetheless clear and is partly independent of the uncertainty. Shorter courses in afebrile men have randomised support (Drekonja et al., 2021), narrow-spectrum agents have observational support in appropriately selected men (Montelin et al., 2019), avoidance of treatment for asymptomatic bacteriuria has strong guideline support (Nicolle et al., 2019), and elimination of antibiotic prophylaxis through a change of biopsy route has trial support (Hu et al., 2024). Each of these reduces selection pressure without requiring the aetiological uncertainty to be resolved first.

10. Methodological Weaknesses of the Male-Specific Evidence Base

The recurring weaknesses in this literature are structural rather than incidental, and they interact in ways that make the aggregate uncertainty greater than the sum of the individual limitations.

The first is the scarcity of sex-stratified reporting. Most large aetiological studies pool the sexes, and because female specimens predominate in almost every laboratory population, pooled distributions approximate the female distribution. Male-specific findings must therefore be extracted from a small number of dedicated studies, most of which are laboratory surveillance series from a narrow range of high-income settings.

The second is the conflation of infection with bacteriuria. Routine laboratory series report the organisms isolated from submitted specimens and cannot distinguish specimens submitted for symptomatic infection from those submitted for surveillance, pre-procedural assessment or investigation of non-specific symptoms. Because the organisms over-represented in men are also those most associated with colonisation, this conflation systematically distorts male-specific distributions in a predictable direction.

The third is the dependence on specimen type. Voided specimens from men include urethral organisms; catheterised specimens do not, but are collected in a population selected by the indication for catheterisation. The two specimen types therefore sample different biological compartments and different clinical populations, and studies rarely report which was used.

The fourth is the limitation of routine culture. Conventional aerobic protocols with short incubation and standard media systematically fail to recover fastidious, slow-growing and anaerobic organisms, and the organisms so excluded are disproportionately those associated with older men and obstructive uropathy. The magnitude of this exclusion has been demonstrated by expanded culture in other populations (Deen et al., 2023) but has not been quantified in male infection specifically.

The fifth is geographical and healthcare-setting concentration. The most methodologically informative male-specific series originate from a small number of European laboratory networks and North American veterans' health systems, and the trial evidence on treatment duration derives from a single national health system. Extrapolation to settings with different resistance ecologies, different catheterisation practices and different access to microbiological diagnosis is not warranted.

The sixth is the disconnection between mechanistic and clinical evidence. Mechanistic work is generally performed in models that do not distinguish sex, or in male-specific models such as prostate organoids that have no clinical counterpart, while clinical series lack the microbiological detail to test mechanistic predictions. Assertions that a mechanism explains a clinical observation in men therefore generally join two literatures rather than reporting a demonstrated relationship.

Table 5 summarises these weaknesses, the direction of the bias each is expected to introduce, and the study design that would address it. Presenting the expected direction of bias is analytically important, because several of the weaknesses act in the same direction and their combined effect is therefore additive rather than self-cancelling.

Table 5. Structural weaknesses of the male-specific evidence base, the expected direction of the resulting bias, and the study design required to address each

Weakness	Expected direction of bias	Design that would address it	Supporting references
Scarcity of sex-stratified reporting	Pooled distributions approximate the female distribution because female specimens predominate in laboratory populations, understating male-specific differences	Mandatory sex-stratified species-level reporting in aetiological studies; extraction of male data in existing datasets	Georgiou et al. (2026); Popescu et al. (2026)
Conflation of	Inflates the apparent	Prospective cohort recruiting	Nicolle et al.

symptomatic infection with bacteriuria	contribution of organisms associated with colonisation and devices, which are precisely those over-represented in men	symptomatic men with a uniform symptom instrument, recording device status and indication for each specimen	(2019); Salm et al. (2023)
Dependence on unreported specimen type	Voided specimens overstate urethral and preputial organisms; catheterised specimens sample a population selected by the indication for catheterisation	Standardised single-method collection within a defined protocol, with paired-specimen substudies to quantify the difference	Hrbacek et al. (2021); Elsayed et al. (2024)
Limitations of routine aerobic culture	Systematically understates fastidious, slow-growing and anaerobic organisms, and the exclusion is concentrated in older men with obstructive uropathy	Paired standard, expanded quantitative and molecular detection on the same specimens, with prespecified analysis against symptoms and treatment response	Cattoir et al. (2010); Deen et al. (2023); Kakodkar and Hamula (2022)
Geographical and healthcare-setting concentration	Overstates the generalisability of resistance patterns and species distributions derived from a small number of high-income systems	Multicentre studies in settings with differing resistance ecologies and catheter practices, using common definitions	Drekonja et al. (2021); Salm et al. (2022); Wu et al. (2026)
Disconnection between mechanistic and clinical evidence	Encourages the inference that a demonstrated mechanism explains a clinical observation when the two derive from separate literatures	Comparative whole-genome sequencing of male and female isolates from a common catchment; strain-level comparison of index and recurrent isolates	Wang et al. (2023); Jaen-Luchoro et al. (2023); Guedes et al. (2026)

Note. The listed biases act predominantly in the same direction and are therefore additive rather than mutually cancelling.

11. Future Directions

The research priorities that follow are ordered by the extent to which they would reduce the uncertainty identified in this review, and are distinguished between those achievable with existing methods and those requiring longer-term investment.

The most immediate priority is a multicentre, male-specific, syndrome-stratified aetiological study using standardised specimen collection. The unresolved problem is that no current dataset permits separation of symptomatic male infection from male bacteriuria at species level. Existing evidence is inadequate because it consists of routine laboratory series in which the indication for the specimen is unrecorded, and because the single systematic attempt to synthesise the tightly defined male subgroup found only six eligible studies with irreconcilable definitions (Georgiou et al., 2026). The appropriate design is a prospective cohort recruiting men presenting with lower urinary tract symptoms across primary, secondary and long-term care, applying a uniform symptom instrument, recording device status, obstruction and prior instrumentation, and collecting specimens by a single specified method with paired expanded and standard culture. Outcome measures should include species-level identification, quantitative counts, symptom resolution and recurrence at defined intervals. Such a study is achievable with existing methods and would establish, for the first time, the proportion of male urinary isolates of each species that are associated with symptomatic disease.

A closely related priority is the quantification of the detection deficit created by routine culture in men. Current evidence establishes that expanded culture recovers organisms missed by standard protocols but has not quantified the deficit in symptomatic men, nor determined whether the additionally recovered organisms are associated with symptoms. The appropriate design is a paired-specimen study within the cohort described above, applying standard culture, expanded quantitative culture and targeted molecular detection to the same specimens, with prespecified analysis of the association between additionally recovered organisms and symptom

severity, pyuria and treatment response. Older men with obstructive uropathy should be sampled preferentially, since that is the group in which the deficit is expected to be greatest. The implementation consequence is direct: if organisms recovered only by expanded methods are associated with symptoms and with response to therapy, then routine protocols for symptomatic men require revision.

The third priority concerns *Enterococcus faecalis*, which represents the largest single attribution uncertainty in male urinary infection. The unresolved question is what proportion of enterococcal isolates from male urine represent disease requiring treatment. Existing evidence establishes frequency and mechanistic capability but not clinical significance. The appropriate design is a prospective observational study of men with enterococcal isolation stratified by device status, symptom profile and polymicrobial versus monomicrobial growth, with follow-up of untreated and treated patients and prespecified endpoints of symptom persistence, progression to febrile infection and recurrence. A subsequent randomised comparison of treatment against observation in the subgroup with monomicrobial enterococcal isolation and lower tract symptoms would be feasible and would directly inform practice. The unexplained concentration of enterococcal isolation among younger men reported in the largest male-specific series warrants specific investigation, since it is inconsistent with a purely device-driven explanation.

The fourth priority is the determination of whether the male urinary tract selects a distinguishable bacterial population. The unresolved question is whether *E. coli* isolates causing infection in men differ systematically in phylogroup, virulence gene content or accessory genome from those causing infection in women drawn from the same source population. Existing evidence consists of small single-centre studies with inconsistent findings and insufficient power. The appropriate design is comparative whole-genome sequencing of consecutive urinary isolates from men and women within a defined catchment, with sample sizes calculated for the detection of modest differences in gene prevalence, adjustment for age and clinical context, and analysis of accessory genome content rather than a predetermined gene panel. A positive finding would support sex-specific risk stratification; a negative finding would justify treating the male and female uropathogen populations as a single entity and would simplify empirical guidance.

The fifth priority addresses the prostatic compartment. The unresolved question is how frequently prostatic invasion occurs in men with apparently uncomplicated lower urinary tract infection, and whether it predicts recurrence. Existing evidence establishes a receptor-mediated mechanism for prostatic epithelial invasion in an organoid model (Guedes et al., 2026) but provides no estimate of its clinical frequency. Appropriate approaches include prospective follow-up of men treated with agents of contrasting prostatic penetration, with recurrence and strain identity as endpoints, and the development of non-invasive markers of prostatic bacterial involvement. Strain-level genomic comparison of index and recurrent isolates would distinguish persistence from reinfection, an approach already validated in the resistance literature (Jaén-Luchoro et al., 2023). This priority requires methodological development and belongs to a longer time horizon than the preceding three.

The sixth priority is geographical extension of the male-specific evidence base. Almost all methodologically adequate male-specific data derive from Western Europe and North America. Studies conducted in settings with different resistance ecologies, different catheter practices and different access to microbiological diagnosis are needed before any male-specific empirical recommendation can be regarded as generalisable. Such studies should adopt the same standardised definitions as the priority cohort described above, since the principal obstacle to synthesis at present is definitional rather than volumetric.

A cross-cutting requirement applies to all of these priorities. Reporting standards for aetiological studies of urinary infection should mandate sex-stratified species-level data, explicit statement of specimen type and quantitative threshold, separation of symptomatic infection from bacteriuria, and description of culture conditions sufficient to determine which organisms could have been detected. The absence of these elements, rather than any shortage of published studies, is the principal reason that the aetiology of urinary tract infection in men remains less well established than the confidence of clinical guidance implies.

12. Conclusions

The species-level attribution of bacterial uropathogens in men rests on a narrower and more fragile evidence base than the stability of the conventional uropathogen list suggests. *Escherichia coli* is the leading cause of urinary tract infection in men in every setting examined, and this conclusion is secure. The proportion of male

infection it causes is lower and considerably more variable than in women, and no defensible general estimate of that proportion can be derived from present evidence, because the reported range across male-specific studies is wide enough to indicate that the underlying studies are measuring different phenomena rather than sampling a common parameter.

The organisms occupying the remainder of the distribution present a genuine and unresolved attribution problem. Enterococci are recovered from male urine at frequencies that no current dataset can partition between disease and colonisation, and the mechanistic evidence establishes capability without establishing clinical significance. Urease-producing and device-associated species dominate the catheterised and obstructed male tract through mechanisms that are well characterised in the laboratory, but their isolation carries an implication for device and stone management more reliably than it identifies a treatable cause of symptoms. Fastidious Gram-positive organisms are recovered disproportionately from older men, and their apparent rarity is substantially a product of laboratory method rather than of biology; the resulting underestimate is systematic, is concentrated in the population where male urinary infection is most common, and remains unquantified.

Confidence should be graded rather than uniform. It is highest for the mechanistic characterisation of individual species, where genetic and model-based evidence is strong and independently replicated. It is intermediate for the demonstration that resistance is higher in male than in female urinary isolates, a finding replicated across independent health systems though incompletely adjusted for confounding by age, comorbidity and device exposure. It is lowest for precisely the claims that clinical guidance most depends upon: the species distribution of symptomatic male urinary infection, the threshold at which an organism in male urine warrants treatment, and the frequency with which infection involves the prostate.

Two structural features explain this pattern. The first is that male urinary infection is investigated predominantly through routine laboratory specimens, which record which organisms reached a laboratory rather than which caused disease, and which cannot separate symptomatic infection from bacteriuria. The second is that the diagnostic method itself determines the aetiology observed: conventional aerobic culture reliably recovers the organisms whose pathogenicity is least contested and systematically fails to recover those about which attribution is most uncertain, so the evidence base is thinnest where the questions are hardest.

The clinical consequence is not paralysis. Several management positions are well supported and do not require the aetiological uncertainty to be resolved: shorter antibiotic courses are non-inferior in afebrile men, asymptomatic bacteriuria in men should not be screened for or treated outside defined circumstances, and the transperineal biopsy route achieves very low infection rates without antibiotic prophylaxis. What the uncertainty does preclude is confident empirical narrowing of therapy on the assumption that the male aetiological distribution resembles the female one, and confident dismissal of symptomatic culture-negative disease in older men as non-infectious. Reducing that uncertainty requires male-stratified, syndrome-anchored studies that pair standardised sampling with detection methods capable of recovering the organisms that routine culture discards, rather than further accumulation of pooled laboratory surveillance.

13. Limitations

This review is subject to the limitations intrinsic to narrative synthesis. Study identification, selection and interpretation involved judgement at every stage, and despite a documented search process, explicit eligibility criteria and structured appraisal, the possibility of selection bias and interpretive bias cannot be excluded. A different reviewer applying the same criteria might reasonably have emphasised different studies or drawn different inferences from the same evidence, particularly in relation to organisms whose pathogenic status is contested.

Access to subscription bibliographic databases was not available during preparation, and no search of such databases was performed. Literature identification relied on open scholarly searching, retrieval of indexed and open-access records, bibliographic metadata searching and citation tracking. This restriction is likely to have reduced the completeness of retrieval, and the reduction will not have been uniform: older material, material in journals with limited open availability, and material indexed principally in subscription systems will have been retrieved less reliably than recent open-access material. The resulting evidence base is therefore likely to be weighted towards recent and openly available publications.

Language restriction to English excluded literature that may be relevant, particularly given that some of the most informative male-specific laboratory series originate from European settings where substantial local publication occurs in other languages. Retrieval was also constrained by full-text accessibility, and appraisal of some studies relied on abstracts and structured summaries rather than complete methodological detail, which limits the depth of appraisal that could be applied to those sources.

The evidence base itself imposes further constraints. Study designs were heterogeneous, encompassing routine laboratory surveillance, prospective cohorts, randomised trials, mechanistic laboratory work and guidance documents, and comparability across these designs is limited. Case definitions, quantitative thresholds, specimen types and identification methods varied across studies in ways that were frequently unreported, preventing quantitative synthesis and requiring that many comparisons be made qualitatively. Geographical representation was uneven, with the most methodologically informative male-specific data concentrated in a small number of high-income health systems, so the geographical generalisability of several conclusions is uncertain. Reliance on observational evidence was substantial, and only a small number of randomised trials addressed questions within the review scope. Publication bias is likely to have affected the reporting of unusual organisms, since positive identifications are more likely to be published than negative surveys.

The field is developing rapidly in two respects that further qualify these conclusions. Laboratory identification methods have changed substantially over the period covered, so aetiological distributions reported in different eras are not directly comparable, and apparent temporal trends in the frequency of fastidious organisms cannot be separated from improvements in their detection. Understanding of the resident urinary microbial community is evolving quickly, and conclusions drawn about the significance of individual organisms may require revision as the ecological baseline for the male urinary tract becomes better defined. Long-term evidence is scarce throughout: few studies followed men beyond a single episode, and the natural history of recurrent male urinary infection at strain level remains largely undescribed.

No formal quantitative synthesis was undertaken, and no formal risk-of-bias instrument was applied, so the appraisal reported here is structured but not standardised, and the relative weight assigned to individual studies reflects reasoned judgement rather than a scored assessment.

Declaration of AI Use

This manuscript was prepared through the combined contributions of all author(s), including contributions to the study design, data, content development, results, interpretation, and related scholarly work. The author(s) acknowledge the use of Grammarly and ChatGPT to assist with grammar checking, language refinement, reference formatting. These AI-assisted tools were not used as authors and did not replace the intellectual contributions or scholarly judgment of the author(s). All AI-assisted outputs, including content, references, and interpretations, were carefully reviewed, revised, verified, and approved by the author(s). The author(s) accept full responsibility for the accuracy, integrity, and final content of the manuscript.

Competing Interests

Author has declared that no competing interests exist.

References

Acosta, H., Sadahira, T., Sekito, T., Maruyama, Y., Iwata, T., Araki, M., Ogawa, K., Tsuboi, I., & Wada, K. (2022). Post-prostate biopsy acute bacterial prostatitis and screening cultures using selective media: An overview. *International Journal of Urology, 29*(6), 486–493. https://doi.org/10.1111/iju.14824

Anderson, G. G., Palermo, J. J., Schilling, J. D., Roth, R., Heuser, J., & Hultgren, S. J. (2003). Intracellular bacterial biofilm-like pods in urinary tract infections. *Science, 301*(5629), 105–107. https://doi.org/10.1126/science.1084550

Antimicrobial Resistance Collaborators. (2022). Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *The Lancet, 399*(10325), 629–655. https://doi.org/10.1016/S0140-6736(21)02724-0

Armbruster, C. E., & Mobley, H. L. T. (2012). Merging mythology and morphology: The multifaceted lifestyle of *Proteus mirabilis*. *Nature Reviews Microbiology, 10*(11), 743–754. https://doi.org/10.1038/nrmicro2890

Bonkat, G., Wagenlehner, F., & Kranz, J. (2024). Keep it simple: A proposal for a new definition of uncomplicated and complicated urinary tract infections from the EAU Urological Infections Guidelines Panel. *European Urology, 86*(3), 195–197. https://doi.org/10.1016/j.eururo.2024.05.007

Brede, C. M., & Shoskes, D. A. (2011). The etiology and management of acute prostatitis. *Nature Reviews Urology, 8*(4), 207–212. https://doi.org/10.1038/nrurol.2011.22

Cao, H., Cheng, H., Zhou, J., Zhao, J., Xu, M., & Fei, Y. (2025). Clinical and microbiological characteristics of carbapenem-resistant *Klebsiella pneumoniae* associated recurrent urinary tract infections. *Infection and Drug Resistance, 18*, 2049–2063. https://doi.org/10.2147/IDR.S515177

Cattoir, V., Kobal, A., & Legrand, P. (2010). *Aerococcus urinae* and *Aerococcus sanguinicola*, two frequently misidentified uropathogens. *Scandinavian Journal of Infectious Diseases, 42*(10), 775–780. https://doi.org/10.3109/00365548.2010.485576

Codelia-Anjum, A., Lerner, L. B., Elterman, D., Zorn, K. C., Bhojani, N., & Chughtai, B. (2023). Enterococcal urinary tract infections: A review of the pathogenicity, epidemiology, and treatment. *Antibiotics, 12*(4), 778. https://doi.org/10.3390/antibiotics12040778

Deen, N. S., Ahmed, A., Tasnim, N. T., & Khan, N. (2023). Clinical relevance of expanded quantitative urine culture in health and disease. *Frontiers in Cellular and Infection Microbiology, 13*, 1210161. https://doi.org/10.3389/fcimb.2023.1210161

Drekonja, D. M. (2024). Urinary tract infection in male patients: Challenges in management. *Infectious Disease Clinics of North America, 38*(2), 311–323. https://doi.org/10.1016/j.idc.2024.03.009

Drekonja, D. M., Trautner, B., Amundson, C., Kuskowski, M., & Johnson, J. R. (2021). Effect of 7 vs 14 days of antibiotic therapy on resolution of symptoms among afebrile men with urinary tract infection: A randomized clinical trial. *JAMA, 326*(4), 324–331. https://doi.org/10.1001/jama.2021.9899

Elsayed, N. S., Wolfe, A. J., & Burk, R. D. (2024). Urine microbiome in individuals with an impaired immune system. *Frontiers in Cellular and Infection Microbiology, 13*, 1308665. https://doi.org/10.3389/fcimb.2023.1308665

Flores-Mireles, A. L., Walker, J. N., Caparon, M., & Hultgren, S. J. (2015). Urinary tract infections: Epidemiology, mechanisms of infection and treatment options. *Nature Reviews Microbiology, 13*(5), 269–284. https://doi.org/10.1038/nrmicro3432

Gaston, J. R., Andersen, M. J., Johnson, A. O., Bair, K. L., Sullivan, C. M., Guterman, L. B., White, A. N., Brauer, A. L., Learman, B. S., Flores-Mireles, A. L., & Armbruster, C. E. (2020). *Enterococcus faecalis* polymicrobial interactions facilitate biofilm formation, antibiotic recalcitrance, and persistent colonization of the catheterized urinary tract. *Pathogens, 9*(10), 835. https://doi.org/10.3390/pathogens9100835

GBD 2021 Antimicrobial Resistance Collaborators. (2024). Global burden of bacterial antimicrobial resistance 1990–2021: A systematic analysis with forecasts to 2050. *The Lancet, 404*(10459), 1199–1226. https://doi.org/10.1016/S0140-6736(24)01867-1

Georgiou, M. E., Wittkopf, P., Martin, A. L., Kamar, J., Preib, M. T., Joshi, A. V., Mulgirigama, A., & Mitrani-Gold, F. S. (2026). Epidemiology of acute cystitis or afebrile urinary tract infection in adult men: A systematic literature review. *Infectious Diseases and Therapy, 15*(6), 1589–1606. https://doi.org/10.1007/s40121-026-01346-z

Gu, H. M., Gu, J. S., Chung, H. S., Jung, S. I., Kwon, D., Kim, M. H., Jung, J. H., Han, M. A., Kang, S. J., Hwang, E. C., & Dahm, P. (2023). Fosfomycin for antibiotic prophylaxis in men undergoing a transrectal prostate biopsy: A systematic review and meta-analysis. *Medicina, 59*(5), 911. https://doi.org/10.3390/medicina59050911

Guedes, M., Peters, S., Joshi, A., Dorn, S., Rieger, J., Klapproth, K., Beste, T., Leipold, A. M., Rosenfeldt, M., Saliba, A. E., Dobrindt, U., Kalogirou, C., & Aguilar, C. (2026). Uropathogenic *Escherichia coli* invade luminal prostate cells via FimH–PPAP receptor binding. *Nature Microbiology, 11*(2), 535–550. https://doi.org/10.1038/s41564-025-02231-0

He, Y., Zhao, J., Wang, L., Han, C., Yan, R., Zhu, P., Qian, T., Yu, S., Zhu, X., & He, W. (2025). Epidemiological trends and predictions of urinary tract infections in the Global Burden of Disease Study 2021. *Scientific Reports, 15*(1), 4702. https://doi.org/10.1038/s41598-025-89240-5

Hrbacek, J., Morais, D., Cermak, P., Hanacek, V., & Zachoval, R. (2021). Alpha-diversity and microbial community structure of the male urinary microbiota depend on urine sampling method. *Scientific Reports, 11*(1), 23758. https://doi.org/10.1038/s41598-021-03292-x

Hu, J. C., Assel, M., Allaf, M. E., Ehdaie, B., Vickers, A. J., Cohen, A. J., Ristau, B. T., Green, D. A., Han, M., Rezaee, M. E., Pavlovich, C. P., Montgomery, J. S., Kowalczyk, K. J., Ross, A. E., Kundu, S. D., Patel, H. D., Wang, G. J., Graham, J. N., Schaeffer, A. J., & Schaeffer, E. M. (2024). Transperineal versus transrectal magnetic resonance imaging-targeted and systematic prostate biopsy to prevent infectious complications: The PREVENT randomized trial. *European Urology, 86*(1), 61–68. https://doi.org/10.1016/j.eururo.2023.12.015

Jacobsen, S. M., Stickler, D. J., Mobley, H. L. T., & Shirtliff, M. E. (2008). Complicated catheter-associated urinary tract infections due to *Escherichia coli* and *Proteus mirabilis*. *Clinical Microbiology Reviews, 21*(1), 26–59. https://doi.org/10.1128/CMR.00019-07

Jaen-Luchoro, D., Kahnamouei, A., Yazdanshenas, S., Lindblom, A., Samuelsson, E., Ahren, C., & Karami, N. (2023). Comparative genomic analysis of ST131 subclade C2 of ESBL-producing *E. coli* isolates from patients with recurrent and sporadic urinary tract infections. *Microorganisms, 11*(7), 1622. https://doi.org/10.3390/microorganisms11071622

Kakodkar, P., & Hamula, C. (2022). A 2-year retrospective case series on isolates of the emerging pathogen *Actinotignum schaalii* from a Canadian tertiary care hospital. *Microorganisms, 10*(8), 1608. https://doi.org/10.3390/microorganisms10081608

Kline, K. A., & Lewis, A. L. (2016). Gram-positive uropathogens, polymicrobial urinary tract infection, and the emerging microbiota of the urinary tract. *Microbiology Spectrum, 4*(2), UTI-0012-2012. https://doi.org/10.1128/microbiolspec.UTI-0012-2012

Kranz, J., Bartoletti, R., Bruyere, F., Cai, T., Geerlings, S., Koves, B., Schubert, S., Pilatz, A., Veeratterapillay, R., Wagenlehner, F. M. E., Bausch, K., Devlies, W., Horvath, J., Leitner, L., Mantica, G., Mezei, T., Smith, E. J., & Bonkat, G. (2024). European Association of Urology guidelines on urological infections: Summary of the 2024 guidelines. *European Urology, 86*(1), 27–41. https://doi.org/10.1016/j.eururo.2024.03.035

Krieger, J. N., Nyberg, L., Jr., & Nickel, J. C. (1999). NIH consensus definition and classification of prostatitis. *JAMA, 282*(3), 236–237. https://doi.org/10.1001/jama.282.3.236

Lainhart, W., & Gonzalez, M. D. (2018). *Aerococcus urinae*, *Alloscardovia omnicolens*, and *Actinotignum schaalii*: The AAA minor league team of urinary tract infection pathogens. *Clinical Microbiology Newsletter, 40*(10), 77–82. https://doi.org/10.1016/j.clinmicnews.2018.05.001

Li, X., Fan, H., Zi, H., Hu, H., Li, B., Huang, J., Luo, P., & Zeng, X. (2022). Global and regional burden of bacterial antimicrobial resistance in urinary tract infections in 2019. *Journal of Clinical Medicine, 11*(10), 2817. https://doi.org/10.3390/jcm11102817

Lindblom, A., Kiszakiewicz, C., Kristiansson, E., Yazdanshenas, S., Kamenska, N., Karami, N., & Ahren, C. (2022). The impact of the ST131 clone on recurrent ESBL-producing *E. coli* urinary tract infection: A prospective comparative study. *Scientific Reports, 12*(1), 10048. https://doi.org/10.1038/s41598-022-14177-y

Lipsky, B. A. (1989). Urinary tract infections in men: Epidemiology, pathophysiology, diagnosis, and treatment. *Annals of Internal Medicine, 110*(2), 138–150. https://doi.org/10.7326/0003-4819-110-2-138

Mim, T. J., Ahmad, I., Hrach, V. L., Amoateng, K. K., Shihab, M. P. R., Abdulsalam, H. A., Kumar, D., Choudhary, N., & Kondaveeti, S. B. (2026). *Klebsiella pneumoniae* and urinary tract infections: Pathogenesis, resistance, and advances in management. *European Journal of Medical Research, 31*(1), 1004. https://doi.org/10.1186/s40001-026-04589-1

Montelin, H., Forsman, K. J., & Tangden, T. (2019). Retrospective evaluation of nitrofurantoin and pivmecillinam for the treatment of lower urinary tract infections in men. *PLOS ONE, 14*(1), e0211098. https://doi.org/10.1371/journal.pone.0211098

Moreland, R. B., Brubaker, L., & Wolfe, A. J. (2025). Polymicrobial urine cultures: Reconciling contamination with the urobiome while recognizing the pathogens. *Frontiers in Cellular and Infection Microbiology, 15*, 1562687. https://doi.org/10.3389/fcimb.2025.1562687

Nicolle, L. E. (2014). Catheter-associated urinary tract infections. *Antimicrobial Resistance & Infection Control, 3*(1), 23. https://doi.org/10.1186/2047-2994-3-23

Nicolle, L. E., Gupta, K., Bradley, S. F., Colgan, R., DeMuri, G. P., Drekonja, D., Eckert, L. O., Geerlings, S. E., Koves, B., Hooton, T. M., Juthani-Mehta, M., Knight, S. L., Saint, S., Schaeffer, A. J., Trautner, B., Wullt, B., & Siemieniuk, R. (2019). Clinical practice guideline for the management of asymptomatic bacteriuria: 2019 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases, 68*(10), e83–e110. https://doi.org/10.1093/cid/ciy1121

Nielubowicz, G. R., & Mobley, H. L. T. (2010). Host–pathogen interactions in urinary tract infection. *Nature Reviews Urology, 7*(8), 430–441. https://doi.org/10.1038/nrurol.2010.101

Pina-Vaz, T., Silva, A. C., Silva, C., Miranda, I., Cruz, F., & Silva, J. A. (2024). The urinary and prostatic microbiome in non-neurogenic male LUTS/BPH: A systematic review. *Neurourology and Urodynamics, 43*(8), 1938–1947. https://doi.org/10.1002/nau.25530

Popescu, R. I., Toma, C., Petca, R. C., Mareș, C., Ostafi, L., Petca, A., & Jinga, V. (2026). Comprehensive evaluation of uropathogens' AMR in a Romanian tertiary center: Male vs. female comparison. *Microorganisms, 14*(6), 1236. https://doi.org/10.3390/microorganisms14061236

Radu, V. D., Costache, R. C., Onofrei, P., Miron, A., Bandac, C. A., Arseni, D., Mironescu, M., Miftode, R. S., Boiculese, L. V., & Miftode, I. L. (2024). Urinary tract infections with carbapenem-resistant *Klebsiella pneumoniae* in a urology clinic: A case-control study. *Antibiotics, 13*(7), 583. https://doi.org/10.3390/antibiotics13070583

Reasoner, S. A., Francis, J., & Hadjifrangiskou, M. (2025). The urinary microbiome: The next frontier of bacterial ecology. *Journal of Bacteriology, 207*(8), e00105-25. https://doi.org/10.1128/jb.00105-25

Reissier, S., Penven, M., Amara, M., Dortet, L., Riverain, E., Caspar, Y., Degand, N., Farfour, E., Corvec, S., Barraud, O., Le Brun, C., Isnard, C., Jacquier, H., Mizrahi, A., Potron, A., Larréché, S., Mérens, A., Cattoir, V., & GMC Study Group. (2025). Bacterial epidemiology and antibiotic resistance rates in male urinary tract infections in France, 2019–2023. *Infectious Diseases Now, 55*(7), 105123. https://doi.org/10.1016/j.idnow.2025.105123

Salm, J., Salm, F., Arendarski, P., & Kramer, T. S. (2022). High antimicrobial resistance in urinary tract infections in male outpatients in routine laboratory data, Germany, 2015 to 2020. *Eurosurveillance, 27*(30), 2101012. https://doi.org/10.2807/1560-7917.ES.2022.27.30.2101012

Salm, J., Salm, F., Arendarski, P., & Kramer, T. S. (2023). High frequency of *Enterococcus faecalis* detected in urinary tract infections in male outpatients: A retrospective, multicenter analysis, Germany 2015 to 2020. *BMC Infectious Diseases, 23*(1), 812. https://doi.org/10.1186/s12879-023-08824-6

Terlizzi, M. E., Gribaudo, G., & Maffei, M. E. (2017). Uropathogenic *Escherichia coli* (UPEC) infections: Virulence factors, bladder responses, antibiotic, and non-antibiotic antimicrobial strategies. *Frontiers in Microbiology, 8*, 1566. https://doi.org/10.3389/fmicb.2017.01566

Wagenlehner, F. M. E., Bjerklund Johansen, T. E., Cai, T., Koves, B., Kranz, J., Pilatz, A., & Tandogdu, Z. (2020). Epidemiology, definition and treatment of complicated urinary tract infections. *Nature Reviews Urology, 17*(10), 586–600. https://doi.org/10.1038/s41585-020-0362-4

Wang, M. C., Fan, Y. H., Zhang, Y. Z., Bregente, C. J. B., Lin, W. H., Chen, C. A., Lin, T. P., & Kao, C. Y. (2023). Characterization of uropathogenic *Escherichia coli* phylogroups associated with antimicrobial resistance, virulence factor distribution, and virulence-related phenotypes. *Infection, Genetics and Evolution, 114*, 105493. https://doi.org/10.1016/j.meegid.2023.105493

Wu, W., Wu, Q., Zhong, W., & Han, L. (2026). Distribution and drug-resistance analysis of uropathogens in urinary tract infections. *Canadian Journal of Infectious Diseases and Medical Microbiology, 2026*, 1700474. https://doi.org/10.1155/cjid/1700474

Yu, S. H., & Jung, S. I. (2022). The potential role of urinary microbiome in benign prostate hyperplasia/lower urinary tract symptoms. *Diagnostics, 12*(8), 1862. https://doi.org/10.3390/diagnostics12081862