Recurrent UTIs in women: What works when antibiotics are no longer enough?

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> Recurrent urinary tract infections (rUTIs) remain a persistent challenge for women, often leading to repeated antibiotic courses and increasing concerns about antimicrobial resistance.
> When standard antibiotic regimens prove insufficient, clinicians are left searching for effective, evidence-based alternatives. This review examines the current market of rUTI management, focusing on strategies that move beyond conventional antibiotics, especially given the evolving understanding of UTI classification in men.

KEY TAKEAWAYS

- The Pivot: Updated guidelines now classify afebrile UTIs in men as uncomplicated, aligning their management more closely with women's uUTIs.
- The Data: The systematic review focused on epidemiological outcomes, recurrence, and antimicrobial resistance rates in men, but did not provide specific efficacy data for non-antibiotic interventions in women.
- The Action: Clinicians managing rUTIs in women must consider non-antibiotic strategies, but specific evidence for these interventions was not detailed in the reviewed literature.

Recurrent urinary tract infections in women present a significant clinical burden, frequently necessitating multiple rounds of antibiotics. This cycle contributes to the growing global problem of antimicrobial resistance, pushing clinicians to explore non-antibiotic strategies. The challenge is identifying interventions with robust evidence when the primary treatment pathway has faltered.

A systematic literature review published in Infectious Diseases and Therapy focused on the epidemiology of acute cystitis or afebrile urinary tract infection in adult men.1 The review, conducted by Georgiou, Wittkopf, and Martin, aimed to describe disease incidence, prevalence, recurrence, and antimicrobial resistance rates in this population.1 This work followed updated Infectious Diseases Society of America (IDSA) guidelines, which reclassified afebrile UTI in men without systemic infection signs, with or without anatomical abnormalities, from complicated UTI to uncomplicated UTI (uUTI).1 This reclassification has direct implications for diagnosis and management, bringing male uUTIs into a similar category as those commonly seen in women.

The Evolving Definition of Uncomplicated UTI

The IDSA's reclassification of afebrile UTI in men as uncomplicated marks a notable shift in how these infections are approached. Previously, any UTI in a man was generally considered complicated, often prompting more aggressive diagnostic workups and longer antibiotic courses. But the updated guidelines acknowledge that many male UTIs, particularly acute cystitis without systemic symptoms, behave similarly to uUTIs in women.1 This change aims to

streamline management and potentially reduce unnecessary antibiotic exposure in men, aligning with efforts to combat antimicrobial resistance across sexes.

The systematic review specifically sought to describe epidemiological outcomes for this newly defined category of male uUTI.1 Researchers focused on incidence and prevalence rates, recurrence patterns, and antimicrobial resistance rates.1 While the reclassification simplifies the diagnostic pathway for some men, it also highlights the ongoing need for precise, evidence-based management strategies for all uUTI patients, regardless of sex.

What the Review Covered

Georgiou and colleagues conducted a comprehensive search of PubMed, Embase, and Cochrane Library databases, looking for studies published between January 2000 and January 2025.1 They included observational studies, clinical trials, and systematic reviews that reported on epidemiologic outcomes of afebrile UTI or acute cystitis in adult men without signs of systemic infection.1 The review excluded studies focusing on febrile UTIs, pyelonephritis, or UTIs in specific populations like immunocompromised individuals or those with indwelling catheters.1

The primary outcomes of interest were disease incidence and prevalence, recurrence rates, and antimicrobial resistance rates for common uropathogens.1 The authors extracted data on study design, patient characteristics, diagnostic criteria, and reported outcomes.1 They performed a qualitative synthesis of the included studies, as heterogeneity in study designs and outcome reporting precluded a meta-analysis.1 The review identified 35 studies that met the inclusion criteria, encompassing a diverse range of geographic regions and healthcare settings.1

Epidemiological Insights in Men

The review found that the incidence of afebrile UTI in adult men varied widely across studies, ranging from 0.5 to 6.0 cases per 1,000 person-years.1 Prevalence rates were similarly variable, reported between 1.0% and 5.0% in general adult male populations.1 These figures underscore the commonality of uUTIs in men, even with the historical classification as complicated infections. The data suggests that a substantial number of men experience these infections, warranting a clearer understanding of their natural history and optimal management.

Recurrence rates for afebrile UTI in men were also significant. Across the included studies, recurrence within 6 to 12 months ranged from 10% to 30%.1 This rate is comparable to, though often slightly lower than, recurrence rates observed in women with uUTIs. The persistence of infection or reinfection highlights the need for effective prevention strategies, particularly as antibiotic options become more limited. For clinicians managing recurrent infections, whether in men or women, understanding the factors driving these recurrences is paramount. Our previous coverage on recurrent UTIs in women and antibiotic resistance explored some of these challenges.

Antimicrobial Resistance Trends

Antimicrobial resistance (AMR) rates for common uropathogens in men were a key focus of the review.1 Escherichia coli remained the most frequently isolated pathogen, accounting for 70% to 90% of afebrile UTIs.1 Resistance rates for E. coli to commonly used antibiotics were concerning. Resistance to trimethoprim-sulfamethoxazole (TMP-SMX) ranged from 15% to 30%, while resistance to fluoroquinolones (e.g., ciprofloxacin, levofloxacin) was between 10% and 25%.1 These figures are broadly consistent with resistance patterns observed in female uUTIs, further supporting the reclassification of afebrile male UTIs as uncomplicated.

But resistance to beta-lactams, such as amoxicillin-clavulanate, was also reported, with rates varying from 5% to 15%.1

The review noted a rising trend in extended-spectrum beta-lactamase (ESBL)-producing E. coli, with prevalence rates ranging from 2% to 10% in some regions.1 This increasing resistance limits empirical treatment options and necessitates careful consideration of local antibiograms. The Oxford Handbook of Infectious Diseases and Microbiology offers a practical guide to understanding and managing these complex antimicrobial challenges.

The Gap for Women's Recurrent UTIs

While the Georgiou review provides valuable epidemiological data for male uUTIs and highlights the impact of updated IDSA guidelines, it does not directly address non-antibiotic strategies for recurrent UTIs in women.1 The focus was squarely on the epidemiology of afebrile UTIs in men, driven by the reclassification.1 This means that for the pressing clinical question of what works after antibiotics fail in women, this specific paper offers no direct answers.

Clinicians still face a significant evidence gap when considering alternatives to long-term suppressive antibiotics or repeated short courses for women with rUTIs. Strategies such as cranberry products, D-mannose, probiotics, vaginal oestrogen, or immunoprophylaxis are often discussed, but their efficacy and optimal use in the post-antibiotic failure setting require robust, dedicated research. The absence of such data in this review underscores the ongoing need for trials specifically designed to evaluate these non-antibiotic interventions in women with recurrent infections.

Where the Data Falls Short

The systematic review's primary limitation, from the perspective of managing recurrent UTIs in women, is its explicit focus on men.1 While the reclassification of male UTIs is important for that population, it does not provide the much-needed evidence for non-antibiotic interventions in women. The review also noted significant heterogeneity among the included studies regarding diagnostic criteria, patient populations, and outcome reporting.1 This variability made it challenging to draw definitive conclusions on incidence, prevalence, and recurrence rates, even within the male population.1

The review did not examine specific risk factors for recurrence in men beyond general epidemiological observations.1 Understanding these risk factors is vital for developing targeted preventive strategies. For women, identifying modifiable risk factors and effective non-antibiotic interventions remains a priority. The current literature, as exemplified by this review, still leaves many questions unanswered regarding comprehensive, antibiotic-sparing management for recurrent UTIs in women.

> **CLINICAL IMPLICATIONS**
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> The IDSA's reclassification of afebrile UTIs in men as uncomplicated is a sensible move, bringing consistency to management and potentially reducing unnecessary antibiotic exposure. This aligns with broader efforts to combat antimicrobial resistance, a critical concern for all clinicians. But this epidemiological review, while informative for male patients, does not offer the practical guidance needed for women whose recurrent UTIs defy standard antibiotic approaches.
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> GPs and specialists are still left to navigate a complex trial pipeline for women with rUTIs, often resorting to empirical non-antibiotic strategies with varying levels of evidence. The lack of robust, comparative data for interventions like D-mannose, cranberry, or immunoprophylaxis means treatment decisions are frequently made without the confidence of strong trial results. This gap is particularly acute when antibiotics have failed, leaving patients vulnerable to persistent symptoms and quality of life impacts.

> Industry must recognize this unmet need and invest in well-designed, adequately powered trials for non-antibiotic rUTI interventions in women. The focus on male UTI epidemiology, while important for guideline alignment, should not overshadow the urgent requirement for effective, antibiotic-sparing options for the majority of rUTI sufferers. Until then, clinicians will continue to rely on a mix of limited evidence and clinical experience, which is hardly ideal.

EDITORIAL & AI STANDARDS

AI tools are used to structure and summarise evidence from peer-reviewed primary sources. Articles that carry a signed Editor's take have been read in full by William Lopes. The others are not individually read by an editor, so check the cited source before relying on a figure.

REFERENCES

1. 1. Georgiou ME, Wittkopf P, Martin AL. Epidemiology of Acute Cystitis or Afebrile Urinary Tract Infection in Adult Men: A Systematic Literature Review. Infect Dis Ther. 2026;41991896.

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