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Updates to Recurrent Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Guideline (2025)

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Purpose: Our perceptions of recurrent UTI (rUTI) have evolved due to additional insights into rUTI pathophysiology, an appreciation for the adverse effects of repetitive antimicrobials ("collateral damage"), rising rates of bacterial antimicrobial resistance, and better reporting of the natural history of localized cystitis and rUTI. This document seeks to guide the evaluation and management of patients with rUTIs to prevent inappropriate antibiotic use, decrease the risk of antibiotic resistance, reduce adverse effects of antibiotics, provide guidance on strategies for rUTI prevention, and improve outcomes and quality of life for women with rUTIs.

Materials and Methods: In 2024, this Guideline was reviewed via the AUA Update Literature Review process, which identified 87 studies for full-text review published between June 1, 2021 and November 1, 2024. Of those 87 studies, 14 met inclusion criteria for review. The subsequent amendment is based on data released since the last review of this Guideline in 2021.

Results: The Panel developed evidence- and consensus-based statements based on an updated review to provide guidance on evaluation and management of rUTI in women. These updates are detailed herein.

Conclusions: This update provides several new insights, including expansion of non-antibiotic options for UTI prophylaxis, greater understanding of the value of a negative urinalysis in ruling out UTI, and a paradigm shift away from microbial detection to reliance on clinician judgement when weighing the individual risks and benefits of antibiosis. This Guideline will require further review as the diagnostic and treatment options in this space continue to evolve.

Key Words: rUTI, UTI, women, localized UTI, uncomplicated UTI, acute cystitis, bacterial cystitis

Abbreviations and Acronyms

ASB = asymptomatic bacteriuria
AUA = American Urological Association
BID = twice daily
CFU = colony-forming unit
CUA = Canadian Urological Association
DNA = deoxyribonucleic acid
ESBL = extended spectrum beta-lactamase
FDA = U.S. Food and Drug Administration
FMT = fecal microbiome transplant
GNR = Gram-negative rods
hpf = high power field
IDSA = Infectious Diseases Society of America
LUTS = lower urinary tract symptoms
OAB = overactive bladder
PAC = proanthocyanidin
PPV = positive predictive value
RCT = randomized controlled trial
rUTI = recurrent urinary tract infection
SUFU = Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction
TMP-SMX = trimethoprim-sulfamethoxazole
UTI = urinary tract infection
VRE = vancomycin-resistant enterococci
WBC = white blood cells

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BACKGROUND

Terminology and Definitions

For the purposes of this Guideline, the Panel considers only recurrent episodes in women of localized cystitis (restricted to the lower urinary tract); infections with suspected upper urinary tract or systemic involvement should be managed differently. The index patient for this Guideline is an otherwise healthy adult female with localized rUTI in the absence of complicating factors. This Guideline does not specifically consider patients with complicating factors that place them at higher risk for decreased treatment efficacy or progression to systemic infection. Such complicating factors include an anatomic or functional abnormality of the urinary tract (eg, stone disease, diverticulum, neurogenic bladder), an immunocompromised host, or urinary foreign bodies (eg, indwelling urethral catheters, ureteral stents). In this Guideline, the term UTI will refer to acute, localized bacterial cystitis. While there are multiple definitions for rUTI,[1] this Guideline supports the definition of 2 episodes of acute bacterial cystitis within a 6-month period sometime within the preceding year. The definitions used in this Guideline can be found in Table 1 and the visual summary of the Guideline recommendations can be found in Figure.

Diagnosis

Strong evidence suggests that the diagnosis of acute bacterial cystitis should include the combination of acute-onset symptoms referable to the urinary tract, urinary inflammation on microscopic urinalysis (pyuria), and laboratory confirmation of significant bacteriuria.[4,5] Without symptoms, bacteriuria of any magnitude is considered asymptomatic bacteriuria (ASB). In UTI, acute-onset symptoms attributable to the urinary tract typically include dysuria in conjunction with variable degrees of increased urinary urgency and frequency, hematuria, and new or worsening incontinence. Acute-onset dysuria is a specific symptom, with more than 90% accuracy for UTI in young women in the absence of concomitant vaginal irritation or increased vaginal discharge.[6,7] Dysuria, however, can have other causes (eg, atrophic vaginitis, pelvic floor myofascial pain, vulvar lichen sclerosus), and the specificity of this symptom outside of this narrow population has not been defined.

Typically, for a diagnosis of cystitis, acute-onset symptoms should occur in conjunction with urinary inflammation (pyuria >5 white blood cells [WBC]/high power field [hpf] on microscopic urinalysis) and laboratory detection of a uropathogen from the urine, typically *Escherichia coli* (*E. coli*; 75%-95%), but occasionally other pathogens such as other Enterobacteriaceae (eg, *Proteus mirabilis* [*P. mirabilis*], *Klebsiella pneumoniae* [*K. pneumoniae*]) and *Staphylococcus saprophyticus* (*S. saprophyticus*), among other rare species.[8]

While historically standard urine culture has been the mainstay of diagnosis of an episode of acute cystitis,[9] variations in specimen processing, the colony count thresholds designating positivity, and the infectious organism detected will result in wide variations in the accuracy of diagnosis.[10] There is no laboratory test, including standard urine culture, that can provide reasonable diagnostic accuracy alone. Evolving understanding of the complex, generally beneficial microbiome of the genitourinary tract requires clinicians to take into consideration the totality of the patient presentation. The

Table 1. *Guideline Definitions*

Term	Definition
Acute bacterial cystitis	An infection of the urinary tract with: 1. Acute-onset symptoms such as dysuria in conjunction with variable degrees of increased urinary urgency and frequency, hematuria, and new or worsening incontinence 2. Urinary tract inflammation (pyuria ≥5 WBC/high power field [hpf] on microscopic urinalysis) 3. Detection of a bacterial uropathogen
Localized UTI (previously uncomplicated UTI)	An infection of the urinary tract in a healthy patient with an anatomically and functionally normal urinary tract, no signs or symptoms of upper urinary involvement or bacteremia, and no known complicating factors that would make the patient susceptible to progression to a systemic infection
Complicating factors	Patient factors that place an individual at higher risk for development of a UTI and potentially decrease efficacy of therapy. Such factors include the following: • Anatomic or functional abnormality of the urinary tract (eg, stone disease, diverticulum, neurogenic bladder) • Immunocompromised host • Indwelling urinary tract foreign body (eg, indwelling urethral catheters, ureteral stents)
Systemic UTI	An infection of the urinary tract with signs and symptoms of systemic infection, with or without localized symptoms originating from any site in the urinary tract
rUTI	Two separate episodes of acute bacterial cystitis and associated symptoms over a 6-mo period within the preceding year
Asymptomatic bacteriuria	Presence of bacteria in the urine that causes no illness or symptoms
Pyuria	Presence of increased numbers of polymorphonuclear leukocytes (WBC) in the urine as evidence of an inflammatory response in the urinary tract[2,3]

Abbreviations: WBC, white blood cells.

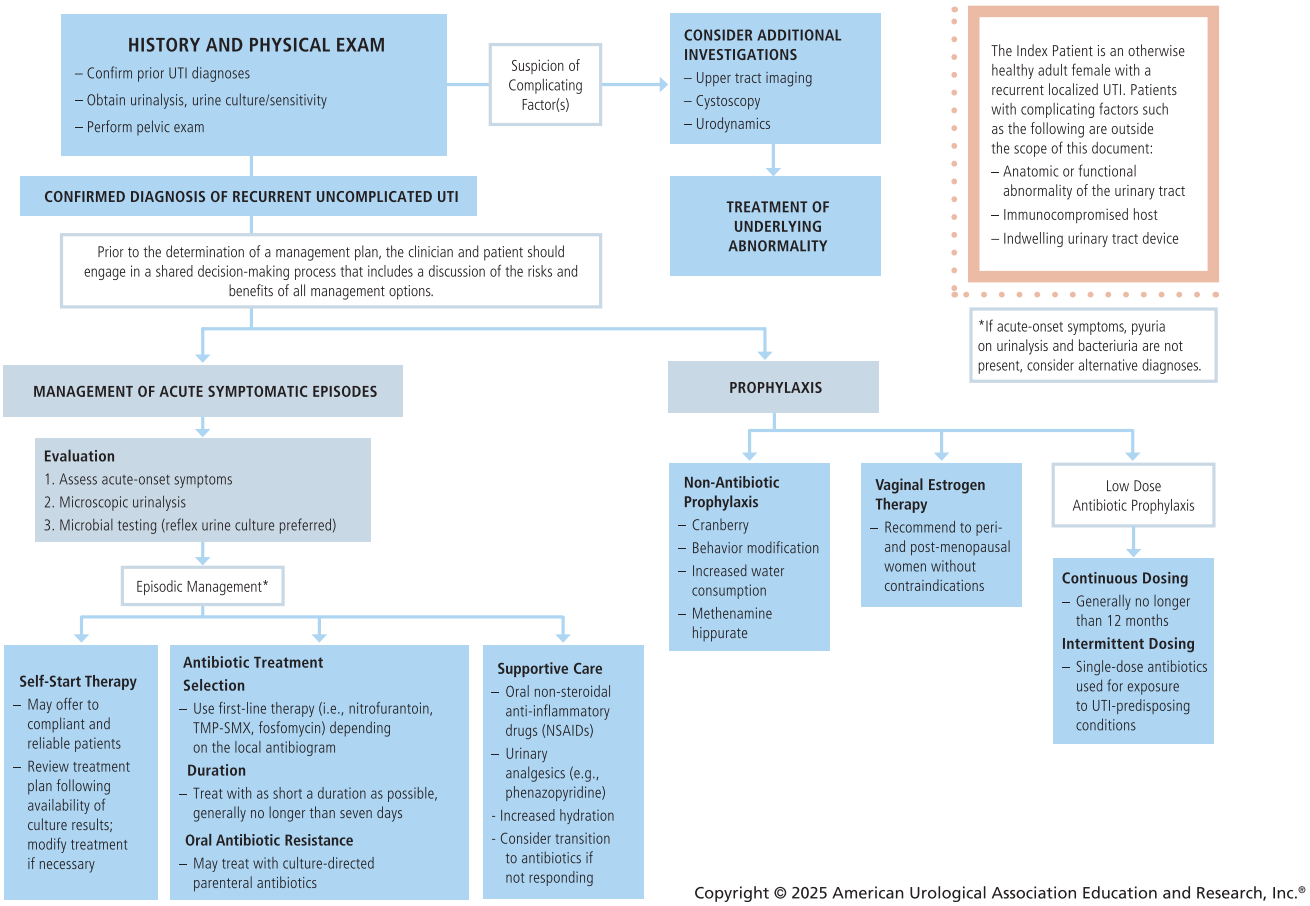

Figure. Recurrent uncomplicated UTI in women: AUA/CUA/SUFU diagnosis and treatment algorithm.

findings of standard urine culture or any other bacterial detection method are not a substitute for clinical judgement. Whenever possible, patients should be evaluated at each symptomatic presentation, with at least documentation of specific signs and symptoms and laboratory assessment. Only with this data can clinicians decide whether the summation of information (ie, the patient's clinical presentation, urinalysis findings, bacterial profiles, and current scientific evidence) suggests that antibiotic treatment is likely to be of benefit.

Education and Informed Decision Making

Substantial effort should be made to avoid unnecessary treatment unless there is a high suspicion of UTI. Antibiotic treatment of suspected UTI remains common practice, but evidence suggests that supportive care with hydration and analgesics can be reasonably attempted while awaiting urine cultures. The incidence of pyelonephritis in patients with localized UTI is low and is not substantially different in individuals receiving antibiotics vs those treated with supportive care of analgesics and hydration.[11] In weighing the rarity of pyelonephritis against the risks of empiric antibiotics, patients may choose supportive care if they perceive the treatment risks outweigh the personal benefits.

GUIDELINE STATEMENTS

Evaluation

*Clinicians should obtain a complete patient history and perform a pelvic examination in women presenting with rUTIs. (*Clinical Principle*)*

At the initial presentation for rUTI evaluation, physical examination including an abdominal and detailed pelvic examination should be performed to look for any structural or functional abnormalities. Pelvic support for the bladder, urethra, vagina, and rectum should be documented, noting the compartment and stage of any significant prolapse. The bladder and urethra should be palpated for evidence of urethritis, urethral diverticulum, Skene's gland cyst, or other enlarged vulvar or vaginal cysts, and a focused examination should document other infectious and inflammatory conditions, such as vaginitis, vulvar dermatitis, and vaginal atrophy (genitourinary syndrome of menopause). The pelvic floor musculature should be examined for tone, tenderness, banding, and trigger/tender points, as

pelvic floor myofascial pain is associated with dysuria, urinary frequency, urgency, and pelvic pain.[2] Given the number of conditions that share symptomatology with UTI and frequent misdiagnosis of acute cystitis, patients with rUTI warrant evaluation with an examination at least at initial presentation to rule out alternative explanations for the patient's relapsing symptoms and identify any structural or functional abnormalities that may be contributing to infection recurrence.

*Clinicians should obtain urinalysis, urine culture and sensitivity with each symptomatic acute cystitis episode prior to initiating treatment in patients with rUTIs. (*Moderate Recommendation; Evidence Level: Grade C*)*

Although no randomized, prospective studies were identified that were specifically designed to document direct effects of procuring urinalysis and urine culture with antibiotic sensitivities prior to initiating treatment, the bulk of observational data supports the comprehensive laboratory diagnostic evaluation of each episode (eg, urinalysis and standard urine culture) to confirm diagnosis and follow clinical responses to management. The routine prescription of antibiotics based on patient symptoms without microbiological evaluation should be discouraged as it is a common cause of rUTI overdiagnosis.

Urinalysis can provide substantial evidence informing the diagnosis of each symptomatic episode. While a positive urinalysis provides little increase in diagnostic accuracy,[9] a negative urinalysis (ie, negative nitrites and <5 WBC/hpf) is useful in ruling out acute cystitis[3] and is associated with a very low risk of progression to bacteremia.[12] A negative urinalysis exhibited high predictive accuracy for the absence of clinically relevant UTI (specificity: 92.2%; positive predictive value [PPV]: 97.4%).[3] Implementation of stewardship programs in which initial urinalysis findings prompt reflex urine culture only in the presence of a positive urinalysis can reduce 5-fold the number of patients inappropriately treated with antibiotics.[13] A positive urinalysis has a low PPV for UTI; positive leukocyte esterase (≥1+), pyuria (≥10 WBC/hpf), nitrite (≥1+), and bacteriuria (≥50 cells/field) all have PPVs for UTI lower than 50%.[12]

Urinalysis findings may combine with urine culture results to prompt a need for retesting. Discordance between urinalysis and culture results suggests test inaccuracy. For example, high levels (>100,000 colony-forming units [CFU]/mL) of urinary *E. coli*, a nitrite producer, on urine culture where the corresponding urinalysis lacks urine nitrites suggests poor collection technique leading to false positives. The presence of epithelial cells or mucus on urinalysis may suggest skin or vaginal contamination. Such information may indicate that obtaining a catheterized specimen is reasonable to evaluate the patient's culture results accurately.[14]

Standard urine culture has historically been the standard for microbial identification but has significant limitations. While highly predictive in select cases (eg, acute dysuria in premenopausal women with *E. coli*), it performs poorly outside these criteria, with contamination, mishandling, and false negatives affecting up to 40% of clinically apparent UTIs.[15-17] Molecular diagnostics are more sensitive and faster but often detect bacteria in asymptomatic individuals, limiting their utility as a replacement diagnostic. As no test reliably distinguishes infection from colonization across all patients, microbial identification should guide care but must be interpreted in context—considering symptoms, urinalysis, test type, and specific findings. Rather than endorse a specific test, organism list, or threshold, this Guideline emphasizes individualized interpretation and serial evaluation to improve outcomes, recognizing that all testing methods, including culture, are imperfect.

*To make a diagnosis of rUTI, clinicians should document evidence of inflammation (pyuria) and the presence of uropathogenic bacteria in association with symptomatic episodes. (*Clinical Principle*)*

While there are multiple definitions for rUTI, this Guideline stresses at least 2 acute, symptomatic episodes in 6 months associated with bacterial infection. The symptoms and signs associated with UTI include dysuria, urinary frequency and urgency, and new or worsening incontinence with or without gross hematuria in the absence of vaginal symptoms. Evidence of bacterial infection includes detection of significant urinary bacteria (eg, standard urine culture) and urinary inflammation (ie, pyuria with >5 WBC/hpf on microscopic urinalysis). While the episodes do not need to be in the immediate 6 months preceding the presentation, the duration and frequency of these recurrences should influence the suggested prophylactic intervention.

The absence of pyuria rules out UTI in symptomatic women with bacteriuria, making pyuria during symptomatic episodes necessary but not sufficient to consider a rUTI diagnosis.[18] Documentation of bacterial uropathogens during each episode is also critical; if bacteriuria does not consistently accompany symptomatic periods or the organisms detected are inconsistent with UTI, it may be reasonable to consider alternative diagnoses. Disorders such as interstitial cystitis/bladder pain syndrome, overactive bladder, genitourinary syndrome of menopause, urinary calculi, bacterial or fungal vaginitis, vulvar dermatitis, noninfectious vulvovestibulitis, vulvo/vestibulodynia,

pelvic floor myofascial pain, and carcinoma in situ of the bladder overlap symptomatically with acute bacterial cystitis and may co-exist with rUTIs. Given the large number of confounding diagnoses that present similarly to UTI and the high rates of bacteriuria, even in asymptomatic women, it is important to consider all clinical and laboratory data when deciding if antibiotic treatment is needed.

ASB

*Clinicians should omit surveillance urine testing, including urine culture, in asymptomatic patients with rUTIs. (*Moderate Recommendation; Evidence Level: Grade C*)*

Without appropriate symptoms, bacteriuria of any magnitude is considered ASB. Urinary odor, cloudy urine, or other chronic lower urinary tract symptoms (LUTS; eg, urgency and frequency) are generally not indicative of infection.[19] While no single, definitive symptom clearly distinguishes between ASB and UTI, an acute change in symptoms is more predictive of UTI. While pregnant women and patients scheduled to undergo invasive urinary tract procedures with anticipated mucosal injury may benefit from treatment for ASB, other populations, including women with diabetes mellitus and long-term care facility residents, do not require or benefit from additional evaluation or antimicrobial treatment.[19] Therefore, clinicians should, in general, omit testing for malodorous and/or cloudy urine when not accompanied by an acute change in other LUTS.

*Clinicians should not treat ASB in patients. (*Strong Recommendation; Evidence Level: Grade B*)*

Evaluation and treatment of rUTIs should be performed only when acute cystitis symptoms are present. There is no evidence that treatment of ASB results in improved clinical outcomes, and there is clear evidence that these practices can cause harm (eg, antibiotic side effects, development of opportunistic infections [eg, Clostridium *difficile*], antibiotic resistance). In women with a history of rUTIs and ASB, antibiotic treatment of ASB was associated with increased risk of symptomatic recurrence (47% vs 13%; RR: 3.17; 95% CI: 2.55-3.90) and development of antibiotic-resistant organisms,[20] suggesting ASB may prevent the development of symptomatic UTIs. A recent systematic review concluded that antimicrobial treatment of ASB does not appear to improve microbiologic outcomes, morbidity, or mortality,[21] even in patients with complicating factors (ie, elderly, immunosuppressed, renal transplant patients, diabetics).[22,23]

*Clinicians should use first-line therapy (i.e., nitrofurantoin, trimethoprim-sulfamethoxazole [TMP-SMX], fosfomycin) dependent on the local antibiogram for the treatment of symptomatic UTIs in women. (*Strong Recommendation; Evidence Level: Grade B*)*

When antimicrobial therapies for UTI are compared based upon efficacy in achieving clinical and/or bacteriological cure, there is relatively little to distinguish these agents. However, the Infectious Diseases Society of America (IDSA) Guideline introduced the concepts of in vitro resistance prevalence and ecological adverse effects of antimicrobial therapy (collateral damage) as key considerations in choosing UTI treatments.[24] The 3 first-line agents available in the United States (ie, nitrofurantoin, TMP-SMX, fosfomycin) are effective in treating UTI and not associated with significant risk of treatment-associated toxicity or complications.[24] Nitrofurantoin specifically shows exceptional durability against emergence of resistance.[25] TMP-SMX is not recommended for empiric use in areas where local resistance rates exceed 20%.[24] Table 2 shows first-line agents recommended by the IDSA Guideline.[24] Second-line or alternate therapies include β-lactam agents or fluoroquinolones, which are generally chosen because of resistance patterns and/or allergy considerations. Although numerous studies suggest the efficacy of fluoroquinolones, they are not first-line agents in the United States due to increasing resistance and potential adverse events, including QTc prolongation, tendon rupture, and increased risk of aortic rupture. With the exception of fosfomycin, single-dose antibiotics should not be used in the treatment of patients with rUTI.[24] Although these recommendations are from the uncomplicated UTI literature, the Panel supports management of each UTI episode per the IDSA Guidelines for cystitis, even among those with rUTI.[24]

The recent U.S. Food and Drug Administration (FDA) approval of several new antibiotics for uncomplicated UTI represents much needed progress toward new UTI therapeutics and more data will be needed to determine appropriate use in treatment of symptomatic UTIs in women. Pivmecillinam, an oral prodrug of the amidinopenicillin antibiotic mecillinam, demonstrates good efficacy, a benign safety profile, and minimal community resistance, filling a need for treatment of multi-drug resistant UTI.[26] The FDA approved sulopenem etzadroxil and probenecid oral tablets for the treatment of uncomplicated UTI caused by certain bacteria (ie, *E. coli*, *K. pneumoniae*, or *P. mirabilis*) in adult women who have limited or no alternative oral antibacterial treatment options.[27] Finally, gepotidacin (FDA-

Table 2. *First-Line Therapy for the Treatment of Localized Symptomatic UTI*

Treatment effects	Nitrofurantoin (monohydrate/macrocrystals)	TMP-SMX	Fosfomycin
Cure rate	88%-93%	90%-100%	83%-91%
Antimicrobial spectrum	Narrow: *E. coli*, *S. saprophyticus*	Typical uropathogens	Covers VRE, ESBL GNRs
Collateral damage[a]	No	Minimal	No
Resistance	Low, stable × 50 y	Increasing	Currently low
Dose and duration	100 mg BID × 5 d	One DS BID × 3 d	3 g single dose

Abbreviations: BID, twice daily; ESBL, extended spectrum beta-lactamase; GNR, Gram-negative rods; TMP-SMX, trimethoprim-sulfamethoxazole; VRE, vancomycin-resistant enterococci.
[a]Collateral damage describes ecological adverse effects of antimicrobial therapy, such as the selection of drug-resistant organisms, disruption of host microbiota, and increased risk of Clostridium *difficile* infections at both the individual and broader public health levels.

approved in March 2025) is the first of a new class of oral triazaacenaphthylene antibiotics that inhibits bacterial DNA replication by blocking 2 different type II topoisomerase enzymes. This provides activity against most target uropathogens and demonstrates similar therapeutic success as nitrofurantoin (nitrofurantoin: 47% therapeutic success; gepotidacin: 51% therapeutic success).[28]

Non-Antibiotic Prophylaxis

*Clinicians should offer cranberry as an option for prophylaxis for women with rUTIs. (*Moderate Recommendation; Evidence Level: Grade B*)*

Cranberries have been studied as a preventative measure for UTI for decades in a variety of formulations, including juice, cocktail, and tablets. The proposed mechanism of action is thought to be related to proanthocyanidins (PACs) present in cranberries and their ability to prevent the adhesion of bacteria to the urothelium. Meta-analysis supports the use of cranberry supplements standardized to at least 36 mg PACs, as these are more effective in reducing UTI recurrence than those containing less than 36 mg.[29] Many commercial cranberry products, however, do not document validation of PAC dosage.

Two recent randomized controlled trials (RCTs; N = 218) investigated use of cranberry prophylaxis[30,31] in comparison to placebo, demonstrating reduced UTI rates in the intervention group. A 2024 systematic review and network meta-analysis compared cranberry juice, cranberry tablets, and increased fluid intake for preventing and managing UTIs in over 3000 participants across 20 trials.[32] Cranberry juice consumption led to a 54% lower rate of UTIs, reduced antibiotic use by up to 50% and significantly lessened UTI symptoms compared to no treatment, supporting its use as an effective non-antimicrobial intervention. Clinical studies have also not routinely reported side effects, but the available evidence suggests the potential harms from cranberry use are minimal.

*Clinicians should inform patients with rUTIs that D-mannose alone for prophylaxis may not be effective in UTI prevention. (*Moderate Recommendation; Evidence Level: Grade B*)*

At the time of the last rUTI Guideline update (2022), evidence was insufficient to recommend or refute the use of D-mannose for the prevention of rUTI. Contemporary evidence from a high-quality, large RCT[33] (N = 598) showed no difference in UTI recurrence rate (RR: 0.92; 95% CI: 0.80-1.05), microbiological recurrence (RR: 0.90; 95% CI: 0.60-1.33), number of prescribed antibiotics (adjusted IRR: 0.88; 95% CI: 0.69-1.12), UTI-related symptoms (adjusted IRR: 0.88; 95% CI: 0.72-1.08) or hospital admissions (RR: 1.47; 95% CI: 0.47-4.61) between use of D-mannose (2 g/d) and placebo. In addition, very low-quality evidence from one RCT[34] (N = 44) showed no difference in UTI recurrence rate in participants using topical vaginal estrogen and D-mannose (2 g/d) compared to participants using vaginal estrogen alone. Treatment-related adverse events were mild and mostly gastrointestinal-related (flatulence). Thus, while D-mannose administration is unlikely to do harm, there is little evidence to support its clinical benefit in preventing UTI.

*Clinicians may offer methenamine hippurate for prophylaxis for women with rUTIs. (*Conditional Recommendation; Evidence Level: Grade C*)*

Previous studies suggested that methenamine salts provide comparable protection against UTI recurrence compared to antibiotics.[35] While the strength of this evidence was previously insufficient to recommend methenamine, a recent non-inferiority RCT[36] provides sufficient cumulative evidence to support methenamine as an effective alternative to antibiotics in the prevention of UTI. Treatment with either methenamine hippurate 1 g twice daily or a daily antibiotic (nitrofurantoin 50/100 mg, cephalexin 250 mg, or trimethotrim 100 mg) substantially decreased the incidence rate of symptomatic, antibiotic-treated UTIs. The absolute difference in UTI episodes per person-year of 0.49 (90% CI: 0.15-0.84) between the treatment arms did not exceed the predefined non-inferiority limit of one UTI per person-year. There was no difference in

microbiologically confirmed UTIs or harms during the study period.

Urine acidifiers, such as ascorbic acid (vitamin C), have been previously recommended to promote the conversion of methenamine into its bacteriostatic components, formaldehyde, and ammonia. However, urinary acidifiers have not been found to significantly lower urinary pH[37] and, in RCTs, do not enhance the effects of methenamine,[35] making concomitant use of vitamin C and methenamine unnecessary.

*When women with rUTIs have a water intake below 1.5 L/day (50 oz), clinicians may offer increased water intake for prophylaxis. (*Conditional Recommendation; Evidence Level: Grade C*)*

One medium risk of bias trial of women with rUTIs who reported < 1.5 L/d of fluid intake at baseline found increased water intake above 1.5 L was associated with fewer UTI recurrences compared with no additional fluids (mean: 1.7 vs 3.2 UTI episodes over 12 months; $P < .001$).[38] Increased water intake was also associated with lower likelihood of having at least 3 UTI episodes over 12 months (<10% vs 88%) and greater interval between UTI episodes (143 vs 84.4 days; $P < .001$). Particularly in patients with lower fluid consumption, increasing water intake may be a low-risk, effective method to reduce the risk of rUTI.

Other Preventive Methods. Several trials were identified evaluating various other prophylactic agents, including *Lactobacillus*, herbs/supplements, intravesical hyaluronic acid/chondroitin, biofeedback, and immunoactive therapy, for prevention of rUTI. However, the Panel cannot recommend these agents as it was not possible to draw reliable conclusions regarding their effectiveness due to the small number of trials for each treatment, imprecise estimates, and methodological shortcomings.

Lactobacillus

While *Lactobacillus* probiotics have been studied with greater interest in recent years given growing concerns for antibiotic resistance, the Panel is unable to recommend the use of *Lactobacillus* as a prophylactic agent for rUTI given the current lack of data indicating benefit in comparison to other available agents. While oral probiotics have yet to demonstrate improvements in clinical outcomes for adult women with rUTI, vaginal *Lactobacillus* probiotics decreased rUTI recurrence in phase 1/2 clinical trials.[39,40] No serious adverse events were reported. Data from those trials, however, suggest the specific probiotic strain is important for UTI prevention. While currently there is insufficient quality data to recommend a probiotic that is commercially available in the U.S., active research continues to strengthen the case demonstrating the utility of this approach. Lack of access to the specific *Lactobacillus* strains used in the clinical studies, however, remains a significant barrier for most healthcare providers.

Intravesical Hyaluronic Acid/Chondroitin

Two small, medium risk of bias trials[41,42] found that intravesical hyaluronic acid plus chondroitin was associated with decreased risk of experiencing ≥1 UTI at 12 months and a longer time to UTI recurrence than intravesical saline,[41] as well as better quality of life.[42] While these studies show promise, further studies are needed to assess generalizability, long-term outcomes, and overall feasibility.

Biofeedback

In a high risk of bias trial (N = 86), 12 months of uroflowmetry biofeedback reduced the prevalence of UTI to 25% while biofeedback training of the pelvic floor muscles reduced the UTI prevalence to 24%. Administration of both concurrently decreased the prevalence of UTI to only 20%. In contrast, 90% of participants who received no treatment continued to experience UTI.[43]

Follow-up Evaluation

*Clinicians should not perform a post-treatment test of cure urinalysis or urine culture in asymptomatic patients. (*Expert Opinion*)*

Where possible, documentation of symptom resolution after antibiotic treatment, particularly in cases where initial symptoms and lab diagnostics are atypical, may facilitate future decision-making. If the symptoms do not resolve, re-evaluation may be indicated. Should the initial infectious organism persist, the patient may warrant additional work up (eg, imaging or cystoscopy), while the persistence of symptoms despite bacterial clearance may warrant consideration of alternative diagnoses.

*For patients with persistent UTI symptoms after microbiological cure, clinicians should evaluate for alternative causes to patient symptoms. (*Expert Opinion*)*

Clinicians should explore alternative diagnoses for patients who continue to experience persistent LUTS after achieving microbiological cure of a UTI. While it is common to attribute ongoing symptoms to residual inflammatory effects of infection, prolonged symptoms may stem from other underlying conditions such as overactive bladder, bladder pain syndrome, pelvic floor disorders or even undiagnosed genitourinary malignancy. Comprehensive evaluation, including detailed history, physical examination including pelvic exam, and further diagnostic testing (such as cystoscopy and/or urodynamics), can help identify alternative causes.

By broadening a diagnostic perspective, clinicians can ensure patients receive appropriate treatment addressing the underlying etiology, improving symptoms and health-related quality of life.

FUTURE DIRECTIONS

Currently, there are no symptoms that are definitively predictive of acute cystitis, and no quality evidence supporting differentiation of pathogenic from non-pathogenic bacteria. In this context, defining initiatives for algorithms to predict the need for treatment and partnering with primary care colleagues and patients to provide education regarding rUTI definitions, evaluation, and treatment will provide an impactful narrative for the future.

Neither urine culture nor other methods of bacterial detection reflect any aspect of the host response, a criteria for infection vs bacteriuria. Investigations of more defined host biomarkers, such as cytokines or serum inflammatory markers, may allow more precise analysis of the host response reflecting true UTI. Further refinements of bacterial molecular genetic technologies may help point-of-care testing with faster identification of potential uropathogens. By extension, the types and content of bacteria which inhabit the urinary tract as part of the native microbiome will change our understanding of how host-bacterial interactions contribute to development of rUTI. Combinations of standard phenotypic determinations of antimicrobial susceptibilities with newer genetic antibiotic susceptibility testing is being explored as a more rapid and accurate method of determining optimal antibiotic treatment.[44]

Promising new antimicrobials such as the first oral carbapenem, sulopenem, may provide oral outpatient therapies for patients with high multidrug resistance. The growing worldwide crisis in multidrug resistance has also renewed the pursuit of non-antibiotic approaches to UTI treatment and prevention. One such promising option for treatment is the development of bacteriophage therapies, which shows promising efficacy similar to antibiotics with few side effects.[45] For prevention, the reconstitution of our native immune system, potentially by changing the microbiome of the gut or genitourinary tract may be a pathway to resolution of rUTI for select patients.[46] Prebiotics and probiotics also have been suggested as alternative approaches. Fecal Microbiome Transplant also has promise for refractory rUTI; in several studies, Fecal Microbiome Transplant performed for management of *C. difficile* colitis had the secondary effect of reducing the UTI recurrence in women with comorbid rUTI.[47,48] The accumulating data suggest that manipulation and preservation of the microbiome may provide effective alternative approaches to UTI treatment and prevention without the side effects of antibiotics.

Modulation of the host response to bacterial infection is a key dynamic for which limited information currently exists but may represent a future direction for prevention strategies. While these are not yet available in the U.S., vaccines for rUTI have demonstrated efficacy in reducing the UTI recurrence and are already in use in many nations.[49,50] Use of mannosides as therapeutic entities to prevent bacterial adhesion to the urothelium may represent a narrow-spectrum treatment strategy associated with few systemic manifestations, although clinical outcomes using such approaches have been equivocal.[51]

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