American Urogynecologic Society Best-Practice Statement: Recurrent Urinary Tract Infection in Adult Women

Linda Brubaker, MD, Cassandra Carberry, MD,*† Rahel Nardos, MD,‡ Charelle Carter-Brooks, MD,§ and Jerry L. Lowder, MD||*

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Female pelvic medicine and reconstructive surgery (FPMRS) specialists provide care for women with recurrent urinary tract infection (rUTI). In a study of more than 1100 urogynecologic patients, investigators reported a patient-reported rUTI prevalence of 19%.[1] However, clinical care varies because of a lack of evidence and best practices. In addition, variable rUTI definitions exacerbate the gap in our understanding of this common clinical problem. In the context of evolving evidence and reviews on rUTI, this document summarizes current best practice for rUTI diagnosis and management in women. These best practices do not apply to women who are pregnant, are immunosuppressed, have surgically altered urinary tracts (not including typical surgery for stress urinary incontinence or pelvic organ prolapse), or regularly use urinary catheters except where specified. In addition, this document does not cover diagnosis or treatment of asymptomatic bacteriuria.

From the *Division of Female Pelvic Medicine and Reconstructive Surgery, Department of Reproductive Medicine, University of California San Diego, San Diego, CA; †Division of Urogynecology and Reconstructive Pelvic Surgery, Department of Obstetrics and Gynecology, Alpert Medical School of Brown University, Providence, RI; ‡Division of Female Pelvic Medicine and Reconstructive Surgery, Department of Obstetrics and Gynecology, Oregon Health & Sciences University, Portland, OR; §Division of Urogynecology and Reconstructive Surgery, Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh, Pittsburgh, PA; and ||Division of Female Pelvic Medicine and Reconstructive Surgery, Department of Obstetrics and Gynecology, Washington University in St Louis, St Louis, MO.

Reprints: Linda Brubaker, MD, University of California San Diego, 9500 Gilman Drive, MC 0971, La Jolla, CA 92093.
E-mail: librubaker@ucsd.edu.

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Executive Summary—Best practices in the care of women with rUTI:
Make the rUTI Diagnosis:
UTI, culture-documented episodes (≥2 in 6 months or ≥3 in 12 months).
Urine Testing:
Avoid dipstick as sole test
Use UA if knowledge of pyuria alters your care
Avoid reflex urine culture
Interpret pretreatment urine culture and sensitivities with knowledge of local resistance patterns; consider posttreatment urine culture
Code Correctly: See Table 1.
Treat Optimally: Use nitrofurantoin, TMP-SMX or fosfomycin as first-line agents whenever possible.
Reduce Recurrence Risk: Based on specific clinical factors for affected woman.
Nonantibiotic strategies:
Vaginal estrogen in hypoestrogenic women without contraindication. Consider methenamine.
Prophylactic antibiotic regimens (ensure negative urine culture before initiating prophylaxis):
Postcoital low-dose antibiotic, if coitally associated episodes.
Judicious use of daily, low-dose oral antibiotic.

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Terminology and Definitions

A commonly used definition describes urinary tract infection (UTI) as an infection of the lower and/or upper genitourinary tract which is diagnosed based on the presence of a pathogen in the urinary tract and associated symptoms.[2] This definition assumes that the symptoms are caused by the detected uropathogens. However, neither the uropathogen detection method nor any specific symptoms are inherent in this UTI definition. Although the umbrella term UTI formally includes both upper and lower urinary tracts, the term UTI is often used interchangeably with cystitis (more accurately bacterial cystitis). There is limited evidence to support any "gold standard" UTI definition for epidemiologic or clinical research.

There are multiple definitions for rUTI. This best-practice statement endorses a clinically useful, culture-based definition: at least 2 culture-proven episodes in 6 months, or at least 3 in 1 year.[3] It is assumed that these episodes are separate events; however, there is no consensus as to diagnostic requirements to document resolution of any episode, such as a posttreatment culture. Diagnosis and care of rUTI patients does not require use of the various terms proposed to further subtype frequent UTI, although the presence of persistent organisms may alter the diagnostic and/or treatment approach (eg, earlier search for foreign body or urinary stone). Relapse indicates that the same uropathogen causes UTI symptoms within 2 weeks of completing appropriate antibiotic therapy. Recurrence specifically applies to situations in which there is evidence that the subsequent UTI occurred beyond the initial 2 weeks or with a different uropathogen.[4]

Epidemiology

Estimates of UTI incidence vary based on the research definition of UTI being used and the likely overuse of UTI codes before a completed diagnostic evaluation. Commonly cited references suggest that more than 8 million ambulatory visits (84% women) in the United States in 2007 were due to UTI; 21% were emergency department visits.[5,6] Using a woman's report of a physician diagnosis of UTI, the National Health and Nutrition Examination Survey data reported a 12.6% annual incidence of UTI in women 18 years or older.[7] In a mixed-sex population of more than 30,000 patients whose UTI diagnosis had urine culture confirmation, Canadian investigators reported the annual UTI incidence in women aged 20 to 79 years as 3% to 5% and those aged 80 to 89 years as 12%. Two percent of these women had at least 6 UTIs in 2 years.[8]

After a single UTI, 30% to 44% of women will have a recurrent UTI; 50% will have a third episode if they have had 2 UTIs in 6 months.[3] In a study of college women with a UTI,

19% experienced recurrence within 6 months.[9] In a recent study, Suskind et al,[10] using a database of health care claims, studied women aged 18 to 64 years who had an evaluation and management visit associated with an *International Classification of Disease, Ninth Revision* code for UTI and an antibiotic prescription within 14 days of that visit. They reported an overall rate of incident rUTI cases of 102 per 100,000 women per year, with the highest rates in women 18 to 34 years old and 55 to 66 years old.

Pathophysiology

Adjacent pelvic microbial niches serve as reservoirs for uropathogens that can lead to UTI/rUTI.[11] Currently, the majority of evidence for uropathogens in the urine comes from standard urine culture techniques, which have been refined to detect *Escherichia coli*. Standard cultures also detect other common pathogens including *Klebsiella* species, *Staphylococcus saprophyticus*, *Enterococcus faecalis*, and *Streptococcus agalactiae.* Culture-independent techniques, such as polymerase chain reaction testing and sequencing, confirm that standard urine cultures do not detect all uropathogens or other resident microbes of the urinary microbiota.[11] Enhanced culture techniques complement culture-independent methods to advance our understanding of UTI and rUTI prevention, pathogenesis, treatment, and recovery but are not yet widely available for clinical use.

Current evidence, based on standard cultures, indicates that *E. coli* causes most (70%–95%) community-acquired UTIs. Studies in older women suggest that *E. coli* accounts for more than half of UTIs, whereas other common organisms are *Klebsiella pneumoniae*, *Proteus mirabilis*, and *E. faecalis*. *E. coli* is also the most common cause of rUTI (66%). The uropathogens associated with rUTI are the same microbes associated with episodic (non-rUTI) UTI episodes. However, non–*E. coli* pathogens and resistant organisms are more likely to be associated with UTI episodes in women with rUTI.[3,7,12]

E. coli has multiple strains and virulence factors.[13] Uropathogenic *E. coli* (UPEC) has been widely studied in murine models, and some findings have been verified in human studies.[14,15] Uropathogenic *E. coli* have special features that facilitate urothelial attachment, allowing the microbe to take up residence within the bladder.[14,15] Uropathogenic *E. coli* can form intracellular bacterial communities that act like a biofilm, allowing bacteria to persist in quiescent intracellular reservoirs, acting as a source of recurrent infection.[16,17] Episodes of rUTIs are often associated with the same bacterial strain; this has important implications for treatment, highlighting the need for careful antimicrobial sensitivity testing and treatment selection.

In addition to bacterial factors, host factors, including hormonal status, anatomy, functional, and behavioral variables, and genetic factors likely modulate UTI and rUTI susceptibility.[3,14,18] For example, *E. coli* has an increased ability to adhere to the urothelium in women who are nonsecretors of certain blood group antigens.[3,19] Individual factors, such as pre-UTI microbiota/microbiome health, degree of inflammation, and urothelial exfoliation from an infection, may affect response to UTI, recovery from UTI, and susceptibility to future UTI.[13,14]

Risk Factors

Many commonly recommended behaviors have not been established as reducing risk for rUTI (wiping away from the urethra; voiding before and after intercourse; increasing frequency of voiding; wearing certain types of underwear; avoiding douching; or avoiding hot tubs, bubble bath, or tampons).[3] Physicians should consider the contribution of gross fecal soilage, as in women with fecal incontinence.

A personal history of UTI before age 15 years and maternal UTI history are rUTI risk factors.[3,20] A case-control study of more than 400 women reported an increased risk of rUTIs in women having a first-degree female relatives with a history of at least 5 UTIs.[21] Sexual risk factors, such as a new sexual partner, intercourse frequency, and spermicide use, are more common in premenopausal women.[21]

Women with pelvic floor disorders are at increased risk for rUTIs, especially postmenopausal women with urinary incontinence. Some investigators suggest an association between postvoid residual of at leasy 50 mL and rUTI.[19] The association with prolapse is unclear.[22]

There is a risk of rUTI after surgery for stress urinary incontinence. The early postoperative period is associated with a transient increased rUTI risk (11%) after retropubic tension-free vaginal tape with or without concomitant prolapse repair.[23] Beyond the first 6 postoperative weeks, investigators reported rUTI in 2.3% to 2.4% of participants in 2 randomized surgical trials (Stress Incontinence Surgical Treatment Efficacy trial and Trial of Mid-Urethral Slings).[24] Between 2 and 12 months, women who had a midurethral sling had a postoperative rUTI rate of 2.3%.[25] No cases of rUTI were reported during a recent 10-year follow-up of 71 women who had transobturator midurethral slings.[26]

DIAGNOSIS

Women with frequent UTI may experience diagnostic delay if clinicians do not review the UTI history; clinicians should order pretreatment urine cultures to document rUTI (culture-proven UTI ≥2 in 6 months or ≥3 in 12 months).[3] Although infrequent UTI can be assessed with less rigor and treated empirically, women with frequent UTI who are being formally assessed for rUTI should have detailed symptom assessment and pretreatment urine culture and sensitivity.[4]

Symptoms

Dysuria is a key symptom of bacterial cystitis. Frequency, urgency, hematuria, and suprapubic pain are variably present. Symptoms of flank pain, fever and chills, and nausea and vomiting should prompt consideration of pyelonephritis. In young women, there is a 90% probability of a UTI when she reports dysuria and frequency in the absence of vaginal discharge or irritation.[6] The accuracy of history and physical examination for UTI diagnosis in women suggests an increased UTI probability with dysuria (likelihood ratio [LR], 1.5; 95% confidence interval [CI], 1.2–2), frequency (LR, 1.8; 95% CI, 1.3–3), hematuria (LR, 2.0; 95% CI, 1.3–2.9), back pain (LR, 1.6; 95% CI, 1.2–2.1), and costovertebral angle tenderness (LR, 1.7; 95% CI, 1.1–2.5). The probability of UTI diagnosis is reduced with a history of vaginal discharge (LR, 0.3; 95% CI, 0.1–0.9) or vaginal irritation (LR, 0.2; 95% CI, 0.1–0.9).[27]

With aging, symptoms potentially associated with a UTI may be less clear. Acute dysuria remains a reliable symptom, new-onset frequency or urgency has been found to correlate with UTI, and new-onset urinary incontinence should prompt evaluation for UTI.[28,29] Nontraditional symptoms, such as urinary odor or urinary appearance, may be triggers for urogynecologic patients to seek care for presumed UTI.[2,3,30] Women with cognitive limitations may have difficulty reporting symptoms; family/caregivers may alert health care providers to changes in mentation or energy levels, which may indicate UTI, although this is a diagnostic challenge.[2] Despite the common clinical observation, worsening of chronic incontinence or other urinary symptoms are not reliably associated with UTI.[2,31]

There is significant symptom overlap between UTI and many urogynecologic conditions, including urgency urinary incontinence, overactive bladder, and bladder pain syndrome. Currently, our understanding of appropriate symptom attribution in this patient population is lacking.

Urine Dipstick

The urine dipstick has value to rule out, rather than rule in, UTI in patients with lower pretest probably of UTI. Because women with rUTI do not have a low pretest probability of UTI, dipstick testing is not advised and pretreatment urine culture is necessary.

Urinalysis

Beyond the standard indications for testing (hematuria, proteinuria, etc), urinalysis in women with rUTI can confirm pyuria (at least 10 white blood cells per high-power field). The interpretation of pyuria for women with rUTI remains debatable because of a lack of relevant studies in urogynecologic populations. When the finding of pyuria would alter the treatment plan, the clinician should obtain a urinalysis.

Urine Culture

The criteria for UTI diagnosis by urine culture varies and has not been validated in any urogynecologic population. The standard urine culture along with microscopic urinalysis has been used as a criterion standard for confirming suspected UTI. A positive culture is typically characterized by bacteriuria of at least 10^5 colony-forming unit s (CFU)/mL,[32] although according to the European Association of Urology guidelines, a count of 10^3 CFU/mL in symptomatic patients is sufficient for diagnosis.[33] The Society of Obstetricians and Gynaecologists of Canada clinical practice guidelines state that even 10^2 CFU is sufficient in the setting of UTI symptoms.[32] Clinicians should have a clear understanding of their clinical laboratory protocols as certain laboratories may report 10^4 or less as "no growth."

Best practices for posttreatment test of cure (test-treatment-test) urine culture vary and are based on expert opinion. Reliance on symptomatic resolution alone forgoes the ability to detect patterns of uropathogen persistence or recurrence.[20] The Canadian Urological Association guidelines suggest repeating a urine culture 1 to 2 weeks after treatment to test for persistence.[4] A repeat urine culture may allow for detection of patterns of uropathogen persistence or recurrence that may provide insight into the etiology or optimal treatment.[20] A negative posttreatment urine culture provides evidence of effective treatment. In the absence of a negative posttreatment urine culture, it is possible that 2 or 3 UTI episodes are related to a single persistent uropathogen.

However, clinicians face a dilemma when the posttreatment culture is positive and the patient's UTI symptoms have resolved. Some experts who believe that women with an active diagnosis of rUTI can also carry a diagnosis of asymptomatic bacteriuria recommend against posttreatment testing to reduce the risk of treating asymptomatic bacteriuria and lessen antibiotic exposure.[2,3,34] Young women with asymptomatic bacteriuria participating in a randomized trial who were treated were (1) more likely to develop subsequent infections at a higher rate than those who were not treated and (2) more likely to develop antibiotic-resistant organisms.[34,35]

Physical Examination

Although a physical examination may not be necessary before treatment for a woman with infrequent UTI, an examination should always occur as part of the rUTI evaluation to detect an underlying etiology, potential contributors (hypoestrogenism), and findings suggestive of upper tract involvement. In addition to an assessment of the patient's general status, focused examination should include palpation for costovertebral angle and suprapubic tenderness. The pelvic examination, including bimanual, can check for vulvar skin and/or architecture changes, urethral diverticulum, tenderness in pelvic floor muscles, urethra or bladder, vaginal discharge, and pelvic masses. In addition, detection of pelvic organ prolapse, presence of a foreign body such as a retained pessary, or eroded mesh or sutures will inform the treatment plan. These assessments should be performed with initial evaluation of a patient with rUTI and repeated as needed depending on status changes, including new signs, symptoms, or risk factors.

Additional Testing

Postvoid Residual

A postvoid residual should be measured to ensure that there is no significant urinary retention. This can be done at the time of the physical examination.

Imaging and Endoscopy

There are currently no specific guidelines for imaging studies for women with rUTI. Indications for imaging in women with UTI include persistent symptoms (persistent fever after 72 hours of appropriate antibiotic therapy), rapid recurrence after appropriate treatment, suspected stone or obstruction, and women with diabetes who are at higher risk for complications such as abscess, emphysematous pyelonephritis, and so on.[35,36] Cystourethroscopy should be considered if a woman is at risk for suspected foreign body within the bladder or urethra, although the utility of cystoscopy in evaluation of rUTI has not been well studied. One retrospective study reported that 3.8% of the 163 participants had specific findings on cystoscopy that imaging would not detect.[37] Cystoscopy with cytology should be performed when there is clinical suspicion for premalignancy or malignancy. Assessment for urinary tract stones can be initiated with plain abdominal radiographs. When the clinical situation warrants more complete assessment of the upper tracts, renal ultrasound, or computed tomographic urography should be used. In general, a computed tomographic urogram, which is with and without intravenous contrast, is the imaging modality of choice in patients suspected of having pyelonephritis, and renal and perirenal abscess. This modality can also identify a possible source of infection such as renal or ureteric stones.[38]

Coding and Documentation

Women who meet the criteria for rUTI should have this diagnosis added to their problem list to help alert other providers to the recurrent nature of the UTIs and to help ensure that best practices are followed for evaluation and treatment. In addition, methods to track UTIs (date, pathogen, antibiotic prescribed) can be developed in summary or flowsheets in the medical record.

Accurate use of *International Classification of Disease, 10th Revision, Clinical Modification* (*ICD-10-CM*) is important for correct classification of patients for clinical diagnosis and population studies of rUTI. Table 1 describes many of the *ICD-10* codes associated with lower UTI. The *ICD-10* code of "positive urine culture" can be used instead of UTI or asymptomatic bacteriuria when a urine culture is positive but the clinical criteria are not met for a UTI: for example, if a patient is asymptomatic and a culture is inadvertently obtained before treatment completion or

TABLE 1. *ICD-10-CM* UTI Terminology

ICD-10-CM Terminology	Code	Clinical Scenario for Suggested Use
Active infection		
• Bladder infection, acute • Acute cystitis without hematuria • Acute on chronic cystitis	N30.00	Acute/active infection of the bladder without hematuria
• Acute cystitis with hematuria	N30.01	Acute/active infection of the bladder with hematuria
• Bladder infection, chronic • Chronic cystitis	N30.20	Chronic infection of the bladder
• Chronic cystitis with hematuria	N30.21	Chronic infection of the bladder with hematuria
• Cystitis, unspecified without hematuria • Bacterial cystitis • Recurrent bacterial cystitis	N30.90	Recurrent bacterial infection of the bladder
• UTI	N39.0	Acute/active infection of the urinary tract, site not specified (should not be used if site known)
• Frequent UTI	N39.0	Frequent infection of the urinary tract, site not specified; clinician should become alert for possible recurrent UTI diagnosis
• Recurrent UTI	N39.0	Recurrent infection of the urinary tract, site not specified (should not be used if site known)
History of infection		
• History of cystitis • History of acute cystitis	Z87.440	History of infection of the bladder
• History of recurrent cystitis	Z87.440	History of recurrent infections of the bladder
• History of UTI	Z87.440	History of infection of the urinary tract, site not specified
• History of frequent UTI	Z87.440	History of frequent infections of the urinary tract, site not specified
• History of recurrent UTI	Z87.440	History of recurrent infections of the urinary tract, site not specified
Other		
• Asymptomatic bacteriuria	R82.71	+Urine culture, no UTI symptoms, patient not currently taking UTI antibiotics
• Positive urine culture	R82.79	+Urine culture without information regarding patient symptom status
Additional codes to specify infectious agent (active infection)		
Enterococcus		B95.2
K. pneumoniae		B96.1
E. coli		B96.2
Proteus		B96.4
Pseudomonas		B96.5

N denotes "Genitourinary System," Z, "Factors Influencing Health Status and Contact with Health Services (similar to "V-codes" in past coding terminology); R, "Symptoms, Signs and Abnormal Clinical and Lab Findings."

while the patient is on suppression but asymptomatic. We propose providers replace the active rUTI diagnosis with history of rUTI after 1 year of the affected woman no longer being treated for rUTI and not meeting the criteria for the diagnosis of rUTI.

TREATMENT

Treatment options for rUTIs can be stratified by whether complicating features, such as abnormal genitourinary anatomy, immunosuppression, and chronic catheterization, are present. Most studies have focused on oral or parenteral antibiotic therapy, whereas data on intravesical and nonantibiotic treatments are limited.

Antibiotic therapy is typically used to treat active infections and prevent future infections; the treatment regimen, route, and duration will vary based on the clinical situation and should be individualized for each patient. Various antibiotic treatment strategies have been described for symptomatic patients with recurrent infections. These can be divided into treatment of an acute episode (provider prescribed or self-treatment) or prophylaxis (to prevent further episodes). Whenever possible, rUTI patients should have a culture sent before treatment. Empiric therapy can be initiated before urine culture results if clinically indicated (such as history of UTI-related sepsis or pyelonephritis). Antibiotic choice should be tailored to the individual patient and pathogens, community and patient resistance patterns, costs, drug availability, patient allergies, and patient tolerance/ability to comply.[39] Providers should be familiar with the antibiotic-resistant patterns in their communities which is generally available via antibiograms through any clinical laboratory. Empiric regimens should be altered if necessary based on the urine culture results.

Treatment of UTI in Women With Recurrent UTI Without Complicating Features

Treatment recommendations for acute UTI in women with rUTI have been extrapolated from acute UTI treatment in women without rUTI. Conditional treatment and antibiotic therapy are the 2 treatment approaches with evidence of efficacy in uncomplicated, bacterial cystitis.[40–44]

With conditional treatment, either a nonsteroidal anti-inflammatory drug is used for symptomatic relief or patients are followed up without any form of treatment. Antibiotic therapy is only initiated if symptoms progress or do not resolve in a clinically reasonable time frame. Conditional treatment has not been studied in women older than 65 years or with rUTI. Several trials in women younger than 65 years have showed resolution rates of 20% to 47% without antibiotic treatment.[40,41,45] However, one study documented a higher rate of pyelonephritis in the placebo group at 2% to 2.6%.[45]

Antibiotics are traditional first-line treatment of bacterial cystitis in women with rUTI.[3] In women with rUTI, acute treatment can be initiated by a clinician or patient (self-treatment regimen) at the time of symptom onset.[6] Most studies of acute UTI treatment were not performed in women with rUTI or other pelvic floor disorders.

Patient Considerations for Selection of Antimicrobial Agent

Allergies

Before prescribing antibiotics for a UTI, the clinician should review drug allergies and intolerances. Patients may have reported adverse drug reactions, side effects, and/or allergies to recommended first-line UTI antibiotics. Such patients can be further evaluated to determine whether they have drug side effect/adverse reaction vs a true allergic reaction (Table 2). Clinicians should not readminister an antibiotic in patients with previously severe reactions such as Stevens-Johnson syndrome unless essential for survival of the patient.[48] Allergy desensitization may be considered for patients with challenging microbial resistance patterns.

Renal Function

Normal aging is associated with a decline in the estimated glomerular filtration rate and creatinine clearance (CrCl); this impacts the efficacy and toxicity of medications that are renally cleared, such as nitrofurantoin (recommended as first-line UTI therapy). Patients with decreased glomerular filtration rate are more likely to experience treatment failure due to reduced renal elimination.[49] Nitrofurantoin is ineffective because of inadequate urine concentrations in patients with a CrCl of less than 30 mL/min. Prescribers should be familiar with antibiotic route of clearance and specific recommendations for renal dosing if indicated. Although more than 25% of individuals at least 65 years old have an estimated glomerular filtration rate of less than 60 mL/min, changes in microbial agent or dose based on age alone are not recommended.[49,50]

Nitrofurantoin has been underused based on decreased renal clearance, although updated guidelines support its use in previously restricted populations (CrCl <60 mL/min but >30 mL/min).[49] The American Geriatrics Society 2015 Beers Criteria Update Expert Panel has updated its recommendation to decrease the CrCl threshold for using nitrofurantoin from 60 to 30 mL/min based on 2 retrospective studies.[51]

First-line Antimicrobial Agents

Few studies explore the optimal antibiotic choice in older women and women with rUTI. In the Infectious Disease Society of America guidelines for premenopausal women, 3 first-line antibiotics for UTI treatment are recommended: nitrofurantoin, trimethoprim-sulfamethoxazole (TMP-SMX) and fosfomycin[39] (Table 3). Recommendations are extrapolated from these guidelines for use in rUTI, older women, and women with urogynecologic disorders.

Nitrofurantoin is bacteriostatic and therapeutically active only in the lower urinary tract. It is effective against *E. coli* and many gram-negative species with low levels of resistance.[20,67] However, it is ineffective against other uropathogens including some *Proteus* species and some strains of *Enterobacter* and *Klebsiella.*[20] The duration of treatment is typically 7 to 10 days. A recent meta-analysis of studies of women ranging from 12 to 70 years old with variable eligibility criteria concluded that 5-day regimens are as effective,[67] although this meta-analysis is not necessarily generalizable to women with rUTI. The 2010 "International clinical practice guidelines for the treatment of acute uncomplicated cystitis in women" recommends a 5-day regimen of 100 mg orally twice daily.[39]

Trimethoprim-sulfamethoxazole is a broad-spectrum antibiotic that covers gram-positive bacteria including methicillin-resistant *Staphylococcus aureus* and most gram-negative bacteria,

TABLE 2. Evaluating Adverse Events vs Allergies[46,47]

	Definitions	Examples
Side effect	Undesirable pharmacological effect at recommended doses	Dry mouth, drowsiness
Adverse drug reaction	Any noxious or unintended reaction to a drug administered in appropriate doses by the proper route	Common: nausea, diarrhea, urticarial, rash, neurotoxicity, superinfection
	Infrequent: fever, vomiting, erythema, dermatitis, angioedema, seizures, pseudomembranous colitis	
Allergy	Immunologically mediated, demonstrates immunologic specificity and recurrence on reexposure	
	Type I: immediate hypersensitivity, IgE mediated	Anaphylaxis
	Type II: cytotoxic reactions, IgG and IgM mediated	Drug-induced hemolytic anemia
	Type III: immune complex reactions, IgG and IGM mediated	Post–streptococcal glomerulonephritis
	Type IV: T cell–mediated reactions	Contact dermatitis

• Educate patients on the difference between a side effect, adverse drug reaction, and an allergic reaction.

○ Patients may have been told they had an allergic reaction as a child, but in some cases, they may have had a viral skin rash occurring coincident with antibiotic treatment.

• Patients reporting a history consistent with an allergic reaction (eg, anaphylaxis, urticaria, angioedema, and bronchospasm) to an antibiotic can be referred to an allergist for drug allergy testing (skin prick test, radioimmunoassays, test dose challenge) to help document true allergic reactions.

○ Recurrence risk of type I hypersensitivity reactions to a drug are substantial and those reactions are often more severe than the initial reaction.

TABLE 3. Antibiotic Recommendations for Acute UTI Treatment in Women With rUTI[39,52–66]

Antibiotic Regimens for Acute Cystitis Treatment			Estimated Clinical Efficacy
First-line antibiotics			
Nitrofurantoin monohydrate/ macrocrystals	100 mg BID × 5 d	• Avoid if early pyelonephritis suspected • Minimal resistance • Minimal risk of collateral damage	93% (84–95)
Trimethoprim/sulfamethoxazole	160/800 mg BID × 3 d	• Efficacy shown in numerous clinical trials • Avoid if resistance prevalence known to be >20%	93% (90–100)
Fosfomycin trometamol	3 g single dose	• Minimal resistance • Minimal risk of collateral damage • Avoid if early pyelonephritis suspected • Lower efficacy than other agents • In vitro activity against VRE, MRSA, and ESBL gram-negative rods supported with clinical studies	91%
Second-line antibiotics			
Fluoroquinolones	Dose varies by regimen; typically 3-d regimen	• Resistance prevalence high in some areas • High risk for collateral damage	90% (85–98)
β-Lactams	Dose varies by regimen; typically for 3–7 d	• Do not use ampicillin or amoxicillin for empirical treatment • Lower efficacy than other available agents due to high resistance and decreased concentrationin the bladder • Requires close follow-up	89% (74–98)
Self-initiated regimens			
Nitrofurantoin monohydrate/ macrocrystals	100 mg BID × 5 d	See above	
Trimethoprim/sulfamethoxazole	160 mg/800 mg BID × 3 d	See above	
Fosfomycin trometamol	3 g	See above	

BID, twice a day; MRSA, methicillin-resistant *S. aureus*; VRE, vancomycin-resistant enterococci.

excluding *Pseudomonas*. When there is greater than 20% local *E. coli* resistance to TMP-SMX, an alternative treatment should be given. Reported duration of TMP-SMX treatment has ranged from 3 to 14 days, with the 3-day course being found to have similar efficacy to 5- to 10-day regimens (see duration of therapy hereinafter).[39]

Fosfomycin tromethamine, the stable salt form of fosfomycin, is taken in a single dose which is highly concentrated in the urine resulting in urine levels that persist for 30 to 40 hours. Fosfomycin has activity against both gram-positive and gram-negative bacteria, including *S. aureus*, *Enterococcus*, *Pseudomonas aeruginosa*, and *K. pneumoniae*.[68–70] Fosfomycin has maintained relatively low levels of resistance, making it a drug of choice in infections with multidrug-resistant organisms.[2,69,71–73] In addition, fosfomycin is an important therapeutic agent for treatment of extended-spectrum beta-lactamase (ESBL) *E. coli* UTI.

Second-line Antimicrobial Agents

When first-line medications are not available or cannot be prescribed because of patient allergies or intolerances or bacterial resistance, second-line antimicrobials, β-lactams, and fluoroquinolones can be used. β-Lactams (such as cefixime and cefpodoxime) have in vitro activity against most gram-negative uropathogens except *Pseudomonas*. Randomized trial evidence suggests that the effectiveness of 3-day cefpodoxime or TMP-SMX is comparable at 98.4% vs 100%.[52] Generally, cephalosporins have a lower cure rate than did TMP-SMX and fluoroquinolones.[20] Less well-studied β-lactams, like cephalexin, can also be used if first-line antibiotics are inappropriate for any reason.[39]

Although 3-day fluoroquinolones regimens (eg, ciprofloxacin and levofloxacin) are highly efficacious, they are not first-line agents because of increasing resistance, higher expense, and serious adverse events as described in a 2016 Food and Drug Administration warning.[20,39,53,74]

Not Recommended

Unless there is clear evidence of sensitivity to certain β-lactams, including amoxicillin and ampicillin, these antibiotics should rarely be used because of poor efficacy thought to be due in part to the lack of concentration in the urine.[32,39]

Duration of Short-course Therapy

The recommendation for the duration of acute bacterial cystitis treatment in women with rUTI is not evidence based and is extrapolated from women without rUTI; some experts use longer duration therapy in rUTI women. Although it did not specifically address women with rUTI, in a Cohrane systematic review and meta-analysis of 15 randomized controlled trials of 1644 elderly women comparing antibiotic duration for treatment of acute UTI, the authors found that the standard duration for short-course therapy (3–6 days), compared with 7 to 14 days, was sufficient treatment.[75] The review also reported that single-dose therapy was associated with a higher rate of persistent UTI compared with short-course therapy (risk ratio [RR], 2.01;95% CI, 1.05–3.84). Of the 15 studies included in this review, only 2 studied fosfomycin.

TABLE 4. Adverse Events of Antibiotics Used Frequently to Treat UTI[39,49,58–65,67,74,82–86]

Antibiotic	Rate of AEs	Type of AEs	Considerations
Nitrofurantoin	5%–34%	• Common side effects: nausea, headache	• Avoid use if CrCl <30 mL/min • Decreased efficacy • Increased risk of toxicity • Pulmonary fibrosis, hepatotoxicity risk with long-term use*
TMP-SMX	1.4%–38%	• Common side effects: rash, urticaria, nausea, vomiting, hematologic	• Hyperkalemia and AKI more likely if TMP-SMX use, elevated baseline Cr, taking ACE inhibitors and potassium supplements* • Hemolysis rare, can occur in patients with G6PD deficiency*
Fosfomycin	5.3%–8%	• Common side effects: diarrhea, vaginitis, nausea, headache	• Half-life of single dose 30–40 h • Serious adverse events rare
Ciprofloxacin	4%–28%	• Common side effects: nausea, vomiting, diarrhea, headache, drowsiness, insomnia • Tendinopathy, tendon rupture • Myasthenia gravis exacerbation • Peripheral neuropathy • QT interval prolongation	• Risk of use outweighs benefit if alternative available • Tendinopathy risk increased if age >60 y, taking corticosteroids, and prior heart, kidney, and lung transplant
β-Lactams	10%–27%	• Common side effects: nausea, diarrhea, headache, lightheadedness, rash, urticaria	• Compared with other UTI antimicrobials, typically have inferior efficacy and more adverse effects • Associated with a higher risk of collateral damage (selection for ESBL-producing strains, multidrug-resistance *S. aureus*, and *Clostridium difficile* colitis)

ACE, angiotensin-converting enzyme; AEs, adverse events; AKI, acute kidney injury; G6PD, glucose-6-phosphate dehydrogenase.

This document supports the practice of using standard duration therapy and tailoring treatment as clinically necessary. The efficacy of 3-day regimens of TMP-SMX and fluoroquinolones has comparable effectiveness (79%–100% and 85%–98% cure rates) and is widely accepted for UTI treatment in the absence of complicating factors.[52–57,76,77] These regimens are as effective for symptomatic relief as longer (5- to 10-day) regimens and have improved compliance, decreased costs, and lower rates of adverse reactions.[20,39,78] The efficacy of 5 days of nitrofurantoin is comparable to 3 days of TMP-SMX.[53,67,79] Five days of nitrofurantoin has better efficacy than a 3-day regimen.[40,67,80,81] Table 4 displays drug-related adverse events.

Self-treatment With Antibiotics (Patient-initiated Therapy/Self-start Therapy)

Self-treatment can be associated with standing physician orders for urine culture before and, possibly, after treatment, to help maintain diagnostic clarity. For women who are traveling or otherwise unable to submit a urine specimen, rare episodes of self-treatment without culture are permissible. Compared with continuous prophylaxis, self-treatment is associated with a higher rate of infection (2.2 UTI per year vs 0.2 UTI per year).[87] Self-treatment is an option for women (1) with the ability to reliably recognize UTI symptoms and start antibiotics, (2) who are not suitable for long-term prophylaxis, or (3) who do not wish to take long-term therapy.[4,87–90]

For self-treatment, clinicians prescribe the appropriate dose and duration of an antibiotic that will cover the most likely uropathogen based on the patient's history so that she can initiate treatment based on her symptoms. Women who use the self-treatment regimen should be capable of contacting their clinician if symptoms progress or fail to resolve within 48 hours. Table 3 displays the recommended self-treatment regimens. Antibiotic agents with minimal side effects are recommended to improve patient compliance and minimize adverse events and overtreatment.[91,92]

Fluorquinolones are not preferred agents for self-treatment regimens despite historical success, because of high cost, risk of resistance, and adverse event profile. We recommend use of other agents whenever possible.[90]

Recurrent UTI With Complicating Factors

Women with rUTI who have complicating factors, such as abnormal genitourinary anatomy, immunosuppression, and chronic catheterization, require additional vigilance in diagnosis and

TABLE 5. Recommended Regimens for Initial, Empiric Therapy of Acute UTI in Women with Complicating Factors[33,95,103,104]

Initial treatment until culture results are available to guide therapy (consider only if local resistance <20%)
Fluoroquinolone (eg, ciprofloxacin and levofloxacin)
Aminopenicillin (eg, ampicillin) plus a β-lactam inhibitor (eg, clavulanic acid)
Cephalosporin group 3a (parenteral; ie, cefotaxime, ceftriaxone, ceftizoxime, cefmenoxime, cefodizime)
Aminoglycoside
Empirical treatment in severe cases or initial failure
Fluoroquinolone (if not used for initial therapy)
Piperacillin plus a β-lactam inhibitor
Cephalosporin group 3b (parenteral; ie, cefoperazone, ceftazidime)
Carbanem
Not recommended for empirical treatment
Aminopenicillins (ie, ampicillin, amoxicillin, bacampicillin)
TMP-SMX
Fosfomycin trometamol

Adapted from Grabe.[33]

treatment because their bacterial isolates are more likely to be resistant to various antibiotics.[19,33,93,94] When empiric therapy of an acute UTI with complicating factors is initiated, treatment should be reevaluated once urine culture and sensitivity results are available.[95] The initial selection of empiric therapy should reflect the patient's individual uropathogen history, current treatment (eg, if currently on UTI suppression antibiotics), and response to prior therapy.[33,94–104] If clinically reasonable, antimicrobial therapy should be delayed pending culture results and organism susceptibility so antimicrobial treatment can be targeted based on the uropathogen profile.[95] Table 5 displays the recommended regimens for empiric therapy of UTI with complicating factors.

Pyelonephritis

Several otherwise useful UTI antibiotics are not recommended for acute pyelonephritis treatment, including nitrofurantoin and fosfomycin; TMP-SMX is not recommended for empiric treatment because of high rates of TMP-SMX resistance. Table 6 displays the recommended acute pyelonephritis treatment regimens. Empirically initiated antibiotics should be refined when the urine culture results are available.

Nonantibiotic Treatments and Nonoral/Nonparenteral Antibiotic Treatment

Ibuprofen—Initial Symptomatic Treatment

Ibuprofen may be used as an adjunct for symptoms of acute bacterial cystis. However, in women with rUTI, there is no evidence that ibuprofen should be used in lieu of an antibiotic (see previous discussion on conditional treatment).

Chinese Herbal Medicine

There is insufficient evidence to recommend Chinese herbal medicine (CHM) as rUTI treatment. The herbal products used in CHM (up to 10–15 herbs) have undergone in vitro studies showing biologic plausibility for rUTI treatment and clinical efficacy in studies. A 2015 Cochrane systematic review compared studies of CHM vs placebo, CHM vs antibiotics, and CHM plus antibiotics vs antibiotics alone.[113] The systematic review was limited by a small number (7) of studies, small sample sizes, study design problems, and an overall high bias risk. Despite these limitations, the authors of the Cochrane review concluded that CHM may be beneficial for rUTI treatment during an acute episode (either as an independent or as an adjunct therapy) and may reduce rUTI for up to 6 months after treatment.

TABLE 6. Recommended Acute Pyelonephritis Treatment Regimens[33,39,57,60,104–112]

Antibiotics	Daily Dose	Duration of Therapy
Oral regimens in patients not requiring hospitalization		
Ciprofloxacin	500–750 mg BID	7–10 d
Levofloxacin	500 mg QD	7–10 d
Levofloxacin	750 mg QD	5 d
Alternatives		
Cefpodoxime	200 mg BID	10 d
Ceftibuten	400 mg QD	10 d
Limited to pathogens with known susceptibility (not for initial empiric therapy)		
TMP-SMX	160/800 mg BID	14 d
Amoxicillin-clavulanic acid*†	0.5/0.125 g TID	14 d
Antibiotics	**Daily Dose**	
Empirical parenteral regimen for patients requiring hospitalization		
Ciprofloxacin	400 mg BID	
Levofloxacin	250–500 mg QD	
Levofloxacin	750 mg QD	
Alternatives		
Cefotaxime*	2 g TID	
Ceftriaxone	1–2 g QD	
Ceftazidime*	1–2 g TID	
Cefepime	1–2 g BID	
Amoxicillin-clavulanic acid*†	1.5 g TID	
Piperacillin/tazobactam	2.5–4.5 g TID	
Gentamicin*	5 mg/kg QD	
Ertapenem	1 g QD	
Imipenem/cilastin	0.5/0.5 g TID	
Meropenem	1 g TID	
Doripenem	0.5 g TID	

Adapted from Grabe.[33]

*Not studied as monotherapy for acute uncomplicated pyelonephritis.

†Mainly for gram-positive pathogens.

BID, twice a day; QD, 4 times a day; TID, 3 times a day.

Intravesical Instillations

Antibiotic Bladder Irrigation

Antibiotic irrigation of the bladder for prophylaxis and/or treatment provides some potential advantages over oral and parenteral routes. These include direct drug delivery to the site of infection and bypass of gastrointestinal tract which avoids collateral consequences and side effects such as gastrointestinal upset.

Gentamicin has been the antibiotic most studied for bladder irrigation.[114–116] There have been no randomized controlled trials performed to date, and all reports have been case series in individuals with complicated UTIs. Reports have included findings from in vitro, animal, and human studies. Bladder instillation regimens have included gentamicin solutions with concentrations ranging from 40–80 mg gentamicin with 50 mL normal saline; instillation volumes of 30 to 60 mL with at least a 1-hour or overnight dwell have been recommended. No elevated serum gentamicin levels were recorded, and all studies reported a meaningful reduction in UTIs while instillations were performed. Specialists may use this therapy in select patients, despite the lack of evidence from robust comparison studies. Limited current evidence supports the safety of gentamicin bladder instillations.

Colistin

Colistin is a polymyxin molecule that damages the lipopolysaccharide component of gram-negative bacteria, leading to increased membrane permeability and eventual cell death.[117,118] Giua et al[118] reported intravesical colistin use in 3 different critically ill patients with multidrug-resistant *Acinetobacter*. The intravesical treatment regimen was 100,000 UI colistin in 50 mL normal saline 3 times daily for 90 minutes for 7 days (2 patients) and 2 days (1 patient). All 3 patients were successfully treated. Although there are not sufficient data to recommend this treatment, it may be considered in a patient who has very limited treatment options.

PREVENTION

The goal of prophylaxis is to prevent or suppress subsequent infections. Although this is most commonly accomplished with antibiotics, alternative nonantibiotic options exist as well.

Antibiotic Prophylaxis

Both the European Association of Urology and the Society of Obstetricians and Gynaecologists of Canada recommend ensuring a negative urine culture before starting prophylactic antibiotics.[32] Table 7 displays recommended postcoital and continuous antibiotic regimens. Postcoital prophylaxis should be offered to women who have UTIs temporally related to sexual intercourse. These women will take a single dose of an antimicrobial agent immediately after intercourse.[6] Postcoital therapy decreased recurrence rates compared with placebo (0.3 vs 3.6 patient-years, $P = 0.001$) and was equally as efficacious as continuous daily therapy.[44,119] This strategy has decreased costs, likely fewer medication side effects, and decreased risk of antibiotic resistance.[4,119]

With continuous prophylaxis, a patient takes a single, daily antibiotic dose.[6] Compared with placebo, continuous prophylaxis decreases recurrences by up to 95%.[20] The duration of these regimens ranges from 6 months (based on observations that UTIs tend to cluster and recur within 3 months) to at least 2 years; regimens have been extended to 5 years in some reports.[96,102,113,131] A Cochrane systematic review of antibiotics for prevention of rUTI in nonpregnant women found that antibiotics given continuously for 6 to 12 months were considerably more effective than placebo in preventing rUTI (RR, 0.15; 95% CI, 0.08–0.28).[44] Although low-dose prophylaxis with antibiotics may inhibit emergence of bacteria while on therapy, this inhibition may not extend when the antibiotic is discontinued.[44,132] Several studies have found that 50% to 60% of women become reinfected within 3 months of discontinuing prophylaxis,[102,113,133] perhaps due in part to intravesical bacterial persistence.[134–136] Antibiotic prophylaxis may increase the risk of bacterial resistance. This document supports reevaluation of continuous antibiotic prophylaxis at 3 months to determine the efficacy and side effects. Antibiotic prophylaxis is rarely continued beyond 6 months, although it may have to be restarted if UTIs recur.

Estrogen

Vaginal estrogen should be used whenever possible in hypoestrogenic women with rUTI because it clearly decreases UTI recurrence. In a randomized, double-blind, placebo-controlled trial of 93 postmenopausal women assigned to topically applied

TABLE 7. Recommended Antibiotic Prophylaxis Regimens[20,44,119–130]

Antibiotic Regimens for Prevention

	Dose	UTIs Per Year
Continuous		
Trimethoprim daily	100 mg	0–1.5
Trimethoprim/sulfamethoxazole daily	40 mg/200 mg	0–0.2
Trimethoprim/sulfamethoxazole every 3 d	40 mg/200 mg	0.1
Nitrofurantoin monohydrate/macrocrystals daily	50 mg	0–0.6
Nitrofurantoin monohydrate/macrocrystals daily	100 mg	0–0.7
Cephalexin daily	125 mg	0.1
Cephalexin daily	250 mg	0.2
Fosfomycin every 10 d	3 g	0.14
Postcoital		
Trimethoprim/sulfamethoxazole	40 mg/200 mg	0.3
Trimethoprim/sulfamethoxazole	80 mg/400 mg	0
Nitrofurantoin monohydrate/macrocrystals	50–100 mg	0.1
Cephalexin	250 mg	0.03

Adapted from Hooton.[20]

intravaginal estriol cream (0.5 mg estriol in vaginal cream daily for 2 weeks, followed by twice weekly for 8 months) vs placebo, UTI incidence in the treatment group decreased significantly (0.5 vs 5.9 episodes per patient-year). In addition, after 1 month of treatment, lactobacillus appeared in 60% of the estrogen-treated group and none of the placebo group.[137] In another multicenter randomized noncontrolled trial of 108 postmenopausal women with rUTI randomized to vaginal estrogen ring (2 mg estradiol, 1 ring for 12 weeks, for a total of 36 weeks), the vaginal estrogen ring significantly decreased UTI occurrences and prolonged the time to next occurrence.[138] A Cochrane review of these studies indicated that vaginal cream may be more effective than the vaginal ring,[88] although significant heterogeneity in these studies prohibited pooling of findings. A systematic review of vaginal estrogen treatment of vulvovaginal atrophy found moderate-quality evidence of decreased UTI risk in women with vaginal atrophy using vaginal estrogen.[139] Studies comparing vaginal estrogen and antibiotics are inconclusive.[88,140–142] Oral estrogen has not been shown to be effective and should not be used for rUTI prevention.

Methenamine Salts

A 2012 Cochrane review reported evidence that methenamine hippurate may be effective for preventing UTI, specifically when used for short-term prophylaxis. Methenamine salts are converted in the urine to ammonia and formaldehyde; formaldehyde is bacteriostatic and does not induce resistance. In addition, methenamine hippurate has an acceptable side-effect profile with low reported adverse events.[143,144]

Probiotics

There is no strong evidence supporting the role of probiotics in rUTI prevention. The main organisms used in probiotics come from lactobacilli strains, which produce antimicrobial compounds that inhibit pathogenic bacteria.[145] A systematic review of 5 studies (n = 294) focusing only on premenopausal women with current UTI or history of UTI showed that using selected lactobacillus strains that achieve vaginal colonization could prevent rUTI.[146] A larger Cochrane review that included 9 probiotic intervention studies (n = 735) with variable controls in healthy premenopausal and postmenopausal women found no significant reduction in rUTI in the probiotic group.[147] However, findings from this study were inconclusive because the data were derived from small studies and inconsistent type and dose of probiotics. Robust, placebo-controlled studies are needed in patients with rUTI using optimal probiotic agents.

Cranberry

The preponderance of evidence does not support routine use of cranberry products in the care of women with rUTI. Proanthocynidins present in cranberries inhibit binding of type 1P-fimbriae of *E. coli* to uroepithelial cells. The studies included in systematic reviews of cranberry are limited by moderate heterogeneity, lack of consistency in dosing, and lack of information about proanthocynidin content. High dropout rates in cranberry juice groups suggest an adherence challenge. One systematic review of 10 trials (n = 1494) comparing cranberry products (juice, capsules, or tablets) to placebo or nonplacebo control in susceptible populations concluded that cranberry products reduced risk of UTI in various subpopulations including women with rUTI.[148] A larger Cochrane review (n = 4473) of placebo and nonplacebo controlled trials using various cranberry products in men, women, and children with a history of at least 2 UTIs in the previous 12 months did not show a reduction in symptomatic UTI except in children.[149] A more recent clinical trial of 185 elderly women randomized to cranberry capsules (72 mg, equivalent to 20 oz of cranberry juice) vs placebo showed no significant difference in bacteriuria plus pyuria; the study was not powered to detect differences in symptomatic UTI.[28]

D-Mannose and M4284

There is limited evidence supporting routine use of the simple sugar D-mannose in women with rUTI. D-Mannose, available over the counter, competitively inhibits adhesion of UPEC type 1 fimbria. D-Mannose decreases bacteria levels in animal UTI models.[150] In a recent randomized clinical trial of 308 women with acute UTIs and history of rUTI in which women were first treated for their acute UTI and then randomized to 2 g of D-Mannose daily for 6 months, 50 mg of nitrofurantoin daily, or no prophylaxis, the rate of rUTI was 15%, 20%, and 60%, respectively. The D-mannose group had significantly fewer side effects and equal adherence.[151]

Ascorbic Acid (Vitamin C)

Although vitamin C has a theoretical effect based on acidification of urine, there is insufficient evidence to support its use for UTI prevention in women with rUTI. The 2 studies that have evaluated the effect of vitamin C had contradictory results.[152,153]

Nonantibiotic Intravesical Instillations

Nonantibiotic intravesical instillations, including hyaluronic acid and chondroitin sulfate, are promising; however, they do not yet have sufficient clinical evidence for use.[154–157] The theory behind the use of hyaluronic acid and chondroitin sulfate is that damage to the glycosoaminoglycan layer of the urothelium is thought to play a key role in uncomplicated UTI.[158]

Immunoactive Prophylaxis

Immunostimulants and vaccinations are likely to play a future role in rUTI prevention, although there is insufficient evidence to recommend clinical use at this time. OM-89 is an oral immunostimulant extracted from 18 different heat-killed UPEC serotypes. In a systematic review of 4 studies (n = 891), there was a reduction in the mean number of UTI by approximately half in the treatment groups compared with placebo with a similar rate of adverse events. Urovac is a vaginal vaccination that contains 6 serotypes of UPEC, 1 strain of *Proteus vulgaris*, *K. pneumoniae*, *Morganella morganii*, and *E. faecalis*. Pooled results from 3 small studies suggest a slight reduction in rUTI (RR, 0.81; 95% CI, 0.68–0.96) but only in the groups that received booster therapy after the primary immunization.[159]

RECOMMENDATIONS

Specialists in FPMRS have a key role in the care of women with rUTI. As research on pathophysiology and best practices continues to inform our understanding of rUTI, these best practices will be updated. Key principles for current care are accuracy in diagnosis with thoughtful use of cystoscopy and imaging when needed, judicious use of appropriate antibiotics, and effective prevention strategies.

Readers are encouraged to read the entire best-practice document. The following lists highlight several key recommendations of these best practices:

Diagnosis

- Thresholds for rUTI diagnosis are at least 2 in 6 months or at least 3 in 12 months.
- Urine culture before initiating antibiotic therapy is recommended to document rUTI episodes and guide treatment.
- Urine culture after appropriate therapy may help define distinct episodes.

Antibiotic Choice

Antibiotic choice should take into account specific patient factors (allergies, renal function), complicating factors, and uropathogen sensitivity.

For acute cystitis in women with rUTI,

- nitrofurantoin is a key first-line agent;
- fosfomycin is effective; clinician may need to request sensitivity testing;
- TMP-SMX can also be used if resistance is less than 20% in the community; and
- fluoroquinolones are not first-line treatment of acute cystitis without complicating factors.

Prevention

- Postcoital antibiotic suppression is effective in women with coitally related rUTI.
- Low-dose, daily antibiotic suppression (3–6 months) is effective in women with noncoitally related rUTI.
- Effective nonantibiotic measures are

cessation of spermicides,
vaginal estrogen in hypoestrogenic women, and
methenamine.

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