



## Consensus Statement | Infectious Diseases

# Guidelines for the Prevention, Diagnosis, and Management of Urinary Tract Infections in Pediatrics and Adults

## A WikiGuidelines Group Consensus Statement

Zachary Nelson, PharmD, MPH; Abdullah Tarik Aslan, MD; Nathan P. Beahm, PharmD; Michelle Blyth, MD, MSPH; Matthew Cappiello, MD; Danielle Casaus, PharmD; Fernando Dominguez, MD; Susan Egbert, PharmD; Alexandra Hanretty, PharmD; Tina Khadem, PharmD; Katie Olney, PharmD; Ahmed Abdul-Azim, MD; Gloria Aggrey, MD; Daniel T. Anderson, PharmD; Mariana Barosa, MD, MSc; Michael Bosco, PharmD; Elias B. Chahine, PharmD; Souradeep Chowdhury, MBBS; Alyssa Christensen, PharmD; Daniela de Lima Corvino, MD; Margaret Fitzpatrick, MD, MS; Molly Fleece, MD; Brent Footer, PharmD; Emily Fox, PharmD; Bassam Ghanem, PharmD, MS; Fergus Hamilton, MRCP, PhD; Justin Hayes, MD, MPH; Boris Jegorovic, MD, PhD; Philipp Jent, MD; Rodolfo Norberto Jimenez-Juarez, MD; Annie Joseph, MBBS; Minji Kang, MD; Geena Kludjian, PharmD; Sarah Kurz, MD; Rachael A. Lee, MD, MSPH; Todd C. Lee, MD, MPH; Timothy Li, MBChB; Alberto Enrico Maraolo, MD, MSc; Mira Maximos, PharmD, MSc, ACPR; Emily G. McDonald, MD, MSc; Dhara Mehta, PharmD; Justin William Moore, PharmD, MS; Cynthia T. Nguyen, PharmD; Cihan Papan, MD; Akshatha Ravindra, MD; Brad Spellberg, MD; Robert Taylor, PhD; Alexis Thumann, PharmD; Steven Y. C. Tong, MBBS (Hons), PhD; Michael Veve, PharmD, MPH; James Wilson, DO; Arsheena Yassin, PharmD; Veronica Zafonte, PharmD; Alfredo J. Mena Lora, MD

### Abstract

**IMPORTANCE** Traditional approaches to practice guidelines frequently result in dissociation between strength of recommendation and quality of evidence.

**OBJECTIVE** To create a clinical guideline for the diagnosis and management of urinary tract infections that addresses the gap between the evidence and recommendation strength.

**EVIDENCE REVIEW** This consensus statement and systematic review applied an approach previously established by the WikiGuidelines Group to construct collaborative clinical guidelines. In May 2023, new and existing members were solicited for questions on urinary tract infection prevention, diagnosis, and management. For each topic, literature searches were conducted up until early 2024 in any language. Evidence was reported according to the WikiGuidelines charter: clear recommendations were established only when reproducible, prospective, controlled studies provided hypothesis-confirming evidence. In the absence of such data, clinical reviews were developed discussing the available literature and associated risks and benefits of various approaches.

**FINDINGS** A total of 54 members representing 12 countries reviewed 914 articles and submitted information relevant to 5 sections: prophylaxis and prevention (7 questions), diagnosis and diagnostic stewardship (7 questions), empirical treatment (3 questions), definitive treatment and antimicrobial stewardship (10 questions), and special populations and genitourinary syndromes (10 questions). Of 37 unique questions, a clear recommendation could be provided for 6 questions. In 3 of the remaining questions, a clear recommendation could only be provided for certain aspects of the question. Clinical reviews were generated for the remaining questions and aspects of questions not meeting criteria for a clear recommendation.

**CONCLUSIONS AND RELEVANCE** In this consensus statement that applied the WikiGuidelines method for clinical guideline development, the majority of topics relating to prevention, diagnosis, and treatment of urinary tract infections lack high-quality prospective data and clear recommendations could not be made. Randomized clinical trials are underway to address some of these gaps; however further research is of utmost importance to inform true evidence-based, rather than eminence-based practice.

JAMA Network Open. 2024;7(11):e2444495. doi:10.1001/jamanetworkopen.2024.44495

**Open Access.** This is an open access article distributed under the terms of the CC-BY License.

JAMA Network Open. 2024;7(11):e2444495. doi:10.1001/jamanetworkopen.2024.44495

### + Supplemental content

Author affiliations and article information are listed at the end of this article.

## Introduction

Urinary tract infections (UTIs) are among the most common infections globally, notably impacting patient quality of life and posing substantial clinical and economic challenges. UTIs exhibit diverse etiologies and clinical severities, from simple cystitis to pyelonephritis and life-threatening sepsis. Diagnosis can be a challenge, due to the lack of validated, highly accurate testing. Management is further complicated by evolving multidrug resistance. Despite advancements in diagnosis and treatment, UTIs can cause high morbidity and mortality, with profound implications in both community and health care settings.

In this third WikiGuidelines consensus statement, we provide an evidence-based approach to UTI management developed by a global network of experts for practical use across diverse clinical settings. This guideline fills a critical gap by providing pragmatic, broadly applicable recommendations tailored for generalist care and systems-based practice. Our guidance is rooted in the best available evidence and is designed for clinicians from various backgrounds and health care environments. It emphasizes a patient-centered approach to the diagnosis, prevention and treatment of UTIs and related genitourinary infections.

## Methods

Our multinational team includes 54 experts from 12 countries, including 31 physicians and 23 pharmacists or PhDs with expertise in internal medicine, pediatrics, infectious diseases, and/or microbiology (eTable 1 and 2 in the [Supplement](#)). This study followed the Standards for Quality Improvement Reporting Excellence (SQUIRE) reporting guideline and followed the WikiGuidelines charter, which requires issuing clear recommendations only when supported by sufficient hypothesis-confirming evidence, including 2 well-conducted concordant randomized clinical trials (RCTs) or 1 well-conducted RCT and a well-conducted concordant prospective observational study. When evidence does not meet these criteria, a review of the literature and discussion is presented in lieu of a recommendation with the goal of proposing reasonable management strategies that maximize benefits, minimize harms, and avoid definitive recommendations for unsubstantiated practices.

On March 15, 2023, crowdsourcing efforts began via social media to identify experts interested in contributing to the guideline development. Authors were selected based on their active professional licenses and relevant clinical expertise, with additional participants chosen for their technical expertise, such as medical librarianship, epidemiology, and biostatistics. The steering committee, elected by the board of directors, selected the chair and cochair to oversee the development of the guideline. On May 1, 2023, we solicited questions from authors about UTI prevention, diagnosis, and management, and organized by theme. Specialized groups were formed, and section leads were appointed by the cochairs to address the 5 distinct themes. Volunteer authors and section leads produced each section through performing extensive literature reviews in PubMed, Medline, and other databases without date or language restrictions. Initial drafts created by the groups were reviewed and refined by the primary and senior authors, followed by collaborative review and feedback from the entire group. Consensus was achieved through a structured process involving a series of meetings, literature reviews, and iterative revisions, with the final approval requiring either a consensus or, if necessary, a majority vote among the committee members. After multiple rounds of revisions and feedback, a finalized version for each section was realized and compiled into a cohesive manuscript by the primary and senior authors.

Results

Section 1: Prophylaxis and Prevention

An overview of findings relating to empirical treatment can be found in **Table 1**. Additional information can be found in eAppendix 1 in the [Supplement](#).

Question 1: What Is the Role of Pharmacotherapy for the Prevention of UTIs?

The clinical review found insufficient quality of evidence to enable a clear recommendation. Pharmacotherapy can be considered for the prevention of UTIs in women with recurrent UTIs (Table 1). Postcoital administration of trimethoprim/sulfamethoxazole (TMP/SMX) or ciprofloxacin appears to reduce the incidence of UTIs in women compared with placebo.<sup>1</sup> No significant difference in effectiveness between intermittent, defined as the use of antibiotics after a trigger such as coitus, and continuous strategies has been demonstrated in high quality studies.<sup>2</sup> Benefits of antibiotic prophylaxis appear confined to their usage period and the optimal duration that balances individual and ecological risks with effectiveness are unclear. Observational data indicate that nitrofurantoin, norfloxacin, and TMP/SMX are comparatively effective; however, conclusions are limited based on the study design.<sup>3</sup> There is limited and conflicting data on antibiotic prophylaxis for children.<sup>4-6</sup>

Question 2: Is There a Role for Cranberry Juice or Supplements in the Prevention of UTIs?

A sufficient quality and quantity of evidence was found to provide a clear recommendation for the role of cranberry juice or supplements in the prevention of UTIs. Most prospective studies have indicated that cranberry products can reduce the risk of symptomatic, culture-verified UTIs in women with recurrent UTIs, children, and individuals susceptible to UTIs after interventions (Table 1).<sup>7-23</sup> Evidence for their use in older adults, those with bladder emptying problems, or pregnant women is insufficient to make a clear recommendation for or against use.

Question 3: Can Water Intake Play a Role in the Prevention of UTIs?

The clinical review found insufficient quality of evidence to enable a clear recommendation. One RCT<sup>24</sup> that explored the effect of hydration on UTIs found that increased water intake significantly reduced cystitis frequency in healthy women. This RCT included 140 healthy women with recurrent cystitis, defined as 3 or more episodes in the past year, who drank less than 1.5 L of fluid per day.

Table 1. Strategies to Prevent UTIs

| Strategy                                           | Level of evidence    | Intervention                                                                                                                                                                                                                          | Comments                                                                                                                                                                                                                             |
|----------------------------------------------------|----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Continuous or postcoital antimicrobial prophylaxis | Clinical review      | TMP/SMX: continuous, 40 mg/200 mg once daily or 40 mg/200 mg 3 times weekly; postcoital, 40 mg/200 mg or 80 mg/200 mg once postcoitus; Nitrofurantoin: continuous, 50 mg or 100 mg daily; postcoital, 50 mg or 100 mg once postcoitus | The decision to use antibiotic prophylaxis must balance the need for prevention against the risk of adverse drug events, antimicrobial resistance, and microbiome disruption. <sup>a</sup>                                           |
| Cranberry products                                 | Clear recommendation | Cranberry products containing proanthocyanidin levels of 36 mg                                                                                                                                                                        | Cranberry products can reduce the recurrent UTIs in women, children, and individuals susceptible to UTIs. Data for older people, those with bladder emptying problems, or pregnant women is insufficient.                            |
| Probiotics                                         | Clinical review      | No recommendation                                                                                                                                                                                                                     | Studies were heterogenous with regard to patient populations, specific probiotics, route of administration, and study design.                                                                                                        |
| Vaginal estrogen                                   | Clear recommendation | Vaginal estrogen, such as vaginal rings, vaginal insert or vaginal cream                                                                                                                                                              | There is a wide variety of formulations and local delivery methods. Availability may vary in different countries or geographic regions.                                                                                              |
| Increased water intake                             | Clinical review      | Additional 1.5L of water                                                                                                                                                                                                              | Water intake was shown to decrease UTIs in 1 RCT among healthy women. Given the low-risk nature of the intervention, pending a confirmatory study, it is reasonable to offer this intervention to healthy women with recurrent UTIs. |
| Methenamine hippurate                              | Clear recommendation | Methenamine hippurate: 1 g twice daily; methenamine mandelate: 1 g every 6 hours                                                                                                                                                      | Methenamine is an appealing antimicrobial-sparing intervention to reduce UTIs in patients without incontinence and a fully functional bladder.                                                                                       |

Abbreviations: RCT, randomized clinical trial; TMP/SMX, trimethoprim sulfamethoxazole; UTI, urinary tract infection.

<sup>a</sup> Consider use of other options reviewed in eAppendix 1 of the [Supplement](#) in more detail prior to continuous or postcoital antimicrobials.

Participants were randomly assigned to either drink an additional 1.5 L of water daily or no additional fluids for 12 months. An observational nursing home study<sup>25</sup> was unable to demonstrate a benefit; however, it was underpowered. Beyond this single RCT,<sup>24</sup> studies are limited and further research is needed to confirm these findings and explore this intervention in broader populations (Table 1).

#### Question 4: Is There a Role for Topical Estrogen in the Prevention of UTIs?

A sufficient quality and quantity of evidence was found to provide a clear recommendation for the use of topical estrogen to prevent UTIs. Based on available evidence from 30 RCTs and 1 large retrospective observational study, topical estrogen is effective at reducing recurrent UTIs in postmenopausal women (Table 1).<sup>26</sup> The loss of estrogen during perimenopause causes changes within the vaginal microbiome, which can lead to a loss of *Lactobacillus* species, an increase in vaginal pH, and an increased risk of UTIs.<sup>27</sup> The use of topical estrogen may help to reduce vaginal atrophy, restore the vaginal microbiome, and reduce the frequency of UTIs.<sup>28</sup> Recent evidence supports using vaginal estrogen therapy for breast cancer patients with genitourinary symptoms when nonhormonal treatments fail.<sup>29</sup> Topical estrogen is thought to have minimal systemic absorption and no concerning safety signals with regard to the risk of stroke, venous thromboembolism, invasive breast cancer, colorectal cancer, or endometrial cancer were identified in a large prospective cohort study of more than 45 000 women.<sup>30</sup> It remains reasonable for biological females with a history of estrogen-related malignant neoplasms to discuss the risk and benefit of this treatment with their health care team prior to initiation.

#### Question 5: Is There a Role for Methenamine Hippurate in the Prevention of UTIs?

A sufficient quality and quantity of evidence was found to provide a clear recommendation for the use of methenamine hippurate to prevent UTIs. Methenamine, which was approved in 1967 for recurrent UTI prophylaxis in those aged 12 years and older, works by releasing formaldehyde in acidic urine, thus resulting in bacteriostasis. A systematic review,<sup>31</sup> which included a multicenter, open-label, randomized noninferiority trial conducted in the UK from June 2016 to June 2018, compared the efficacy of methenamine with daily low-dose antibiotics in preventing recurrent UTIs in women aged 18 years and older and found that methenamine was noninferior to antibiotics for the prevention of UTIs. Similarly, a nonblinded RCT compared methenamine with trimethoprim for preventing recurrent UTIs over 12 months in women aged 18 years and older found noninferiority for methenamine, with no significant difference in UTI recurrence rates between the 2 groups and similar adverse effects.<sup>32</sup> Therefore, we recommend the use of methenamine as an alternative to prophylactic antibiotics in patients with intact bladder anatomy (Table 1).

#### Question 6: Are Probiotics Effective in the Prevention of UTIs?

The clinical review found insufficient quality of evidence to enable a clear recommendation. There is inconclusive evidence to recommend for or against the use of oral or vaginal probiotics to prevent UTIs (Table 1). Studies were heterogeneous as it pertains to the patient populations (children, premenopausal women, postmenopausal women, complicated UTI in patients with comorbidities), specific probiotics, route of administration, and study design.<sup>33-36</sup>

#### Question 7: Is There a Role for D-Mannose in the Prevention of UTIs?

The clinical review found insufficient quality of evidence to enable a clear recommendation. Despite biological plausibility for effectiveness,<sup>37</sup> there is currently insufficient evidence to support or refute the use of D-mannose for the prevention of UTIs. Only 3 RCTs,<sup>38-40</sup> 1 small open-label prospective cohort study,<sup>41</sup> and a subgroup of another prospective cohort study<sup>42</sup> evaluated D-mannose alone for only prevention (not treatment) of UTIs. Discordant or uncertain results among the prospective studies along with small sample sizes and heterogeneity of specific D-mannose regimens, study populations, comparators, UTI definitions, potential for reporting bias, and follow-up periods preclude a clear recommendation for or against its use. Although poorly reported, adverse effects

were seemingly infrequent, and most included gastrointestinal symptoms and vaginal burning.<sup>40,43,44</sup>

Section 2: Diagnosis and Diagnostic Stewardship

An overview of findings relating to diagnosis and diagnostic stewardship can be found in **Table 2**. Additional information can be found in eAppendix 2 in the [Supplement](#).

Question 8: What Are the Clinical Definitions of Cystitis, Complicated UTIs, and Pyelonephritis?

The clinical review found insufficient quality of evidence to enable a clear recommendation. Cystitis and pyelonephritis are typically diagnosed clinically through signs and symptoms with evidence of inflammation (pyuria) and the presence of pathogenic bacteria in the urine (Table 2). Typical nomenclature includes the use of terms, such as cystitis, uncomplicated UTI, complicated UTI, and pyelonephritis. Cystitis, an inflammation of the bladder often indicated by dysuria, urgency, and suprapubic pain, is typically described not to show systemic infection signs like fever. Unfortunately, complicated UTI lacks a standard clinical definition due to diverse criteria in literature and guidelines. Complicated UTIs may involve catheters or other foreign bodies, complicating factors like structural anomalies or immunosuppression, or systemic symptoms. Pyelonephritis, kidney inflammation due to infection, includes cystitis symptoms plus systemic signs like fever and flank pain. More precise clinical definitions, based on clinical studies linked to outcomes, are needed. Most WikiGuidelines authors strongly encourage the use of more precise descriptions of UTI in clinical practice rather than continuing to use vague terms, such as complicated or uncomplicated.

Question 9: What Is the Role and the Sensitivity and Specificity of a Urinalysis (UA) for the Diagnosis of UTIs and When Should Clinicians Order Urine Cultures?

The clinical review found insufficient quality of evidence to enable a clear recommendation. A UA encompasses physical, chemical, and microscopic evaluations designed to aid in diagnosing kidney, metabolic, oncologic, and infectious disorders. Unfortunately, the diagnostic value of UA for UTI is limited.<sup>45,46</sup> While the absence of pyuria can help rule out infection in most patient populations, the positive predictive value of pyuria for diagnosing infection is exceedingly low as it often indicates the presence of genitourinary inflammation due to many other possible noninfectious reasons (Table 3). For these reasons, WikiGuidelines authors believe that evidence-based diagnosis of UTI should be primarily based on clinical symptoms. Clinical symptoms may be integrated with UA findings, but authors caution clinicians to not rely solely on the UA alone. Urine cultures are reasonable for complicated cases and/or recurrent UTIs, particularly in suspected pyelonephritis, to

Table 2. Clinical Practice Guideline Definitions of UTI Syndromes in Adults<sup>a</sup>

| Defining term(s)                         | Proposed IDSA                                                                                    | Current IDSA                                                                                                                                  | EAU                                                                                                                                                                                                                                                                                        | AUA, CUA, and SUFU                                                                                                                                                                                                    |
|------------------------------------------|--------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Complicated UTI and acute pyelonephritis | Any infection beyond the bladder, includes pyelonephritis, CAUTI, febrile or bacteremic patients | Urinary symptoms plus functional or structural abnormalities of the urinary tract. CVA pain and tenderness, often with fever (pyelonephritis) | Dysuria, urgency, frequency, flank pain, CVA tenderness, suprapubic pain, fever, chills, nausea, vomiting; anatomical or functional abnormalities of the urinary tract (eg, obstruction, incomplete voiding due to detrusor muscle dysfunction; presence of diabetes or immunosuppression) | Anatomical or functional abnormality of the urinary tract (eg, stone disease, diverticulum, neurogenic bladder); immunocompromised host; multidrug resistant bacteria                                                 |
| Uncomplicated UTI                        | All other infections not defined as complicated                                                  | Frequency, urgency, dysuria, or suprapubic pain in a woman with a normal genitourinary tract                                                  | Dysuria, frequency and urgency and the absence of vaginal discharge; limited to nonpregnant women with no known relevant anatomical and functional abnormalities or comorbidities                                                                                                          | Dysuria in conjunction with variable degrees of increased urinary urgency and frequency, hematuria, or new or worsening incontinence; female host; no known factors that would increase susceptibility to develop UTI |

Abbreviations: AUA, American Urological Association; CAUTI, catheter-associated urinary tract infection; CUA, Canadian Urological Association; CVA, costovertebral angle; EAU, European Association of Urology; IDSA, Infectious Disease Society of America; SUFU, Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction; UTI, urinary tract infection.

<sup>a</sup> See eAppendix 2 of the [Supplement](#) for detailed supporting information.

guide targeted therapy. In simple uncomplicated cystitis in healthy nonpregnant patients, routine cultures are not necessary.<sup>47,48</sup>

**Question 10: What Is the Role of UA and Urine Culture Testing for the Workup of Fever?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. Routine use of UA and urine cultures for the workup of fever in hospitalized patients leads to unnecessary testing and antimicrobial use.<sup>46,49,50</sup> Studies show that UTIs, including catheter-associated UTIs (CAUTI), are infrequently the source of fever, particularly in the absence of urinary tract obstruction, recent urological procedures, or immunocompromise.<sup>51</sup> Consequently, urine testing should not be automatic in febrile patients, especially geriatric patients, or those with known nonurinary sources of fever and should be reserved for cases with specific urinary or related symptoms. Further research is needed to establish clear criteria for urine testing in febrile patients.

**Question 11: How Can Diagnostic Stewardship Strategies Be Effectively Implemented in the Management of UTIs to Prevent Unnecessary Treatment of Asymptomatic Bacteriuria?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. Effective management of UTI hinges on appropriate diagnostic testing and antimicrobial stewardship, aiming to prevent the misuse of antibiotics for ASB. Symptom-based testing is key to ensure appropriate urine culture testing and proper diagnosis of UTI.<sup>52,53</sup> A 2017 systematic review<sup>54</sup> showed 45% of included patients experienced inappropriate initiation of antimicrobial treatment for ASB; various interventions, such as education on diagnostic protocols, provided a significant absolute risk reduction of 33%. Avoiding overtesting and resulting overtreatment of ASB is essential to preserving antimicrobial effectiveness.

**Question 12: What Is the Role of Novel Molecular Tests in the Diagnosis of UTI?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. The role of molecular techniques for UTI diagnosis is currently limited. Molecular diagnostics cannot distinguish true infection from ASB. Urine culture is the current reference standard for confirming the etiologic pathogen in patients with suspected infection. Although 100 000 colony forming unit (CFU)/mL has been considered the historical standard threshold for bacteriuria and diagnosing UTIs, lower CFU counts can still indicate significant infections in symptomatic patients.<sup>55-58</sup> In contrast, molecular techniques are generally unable to determine bacterial viability or quantitation in urine

Table 3. Diagnostic Testing Performance for Urinary Tract Infections<sup>a</sup>

| Test results                           | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|----------------------------------------|-----------------|-----------------|---------|---------|
| Dipstick                               |                 |                 |         |         |
| Positive leukocyte esterase            | 72-97           | 41-86           | 43-56   | 82-91   |
| Positive nitrite                       | 19-48           | 92-100          | 50-83   | 70-88   |
| Positive leukocyte esterase or nitrite | 46-100          | 42-98           | 52-68   | 78-98   |
| Microscopy, WBC/μL                     |                 |                 |         |         |
| >5 <sup>b</sup>                        | 90-96           | 47-50           | 56-59   | 83-95   |
| 10                                     | 100             | 36              | NA      | NA      |
| 50                                     | 98              | 66              | NA      | NA      |
| 100                                    | 93              | 71              | NA      | NA      |
| 200                                    | 89              | 86              | NA      | NA      |
| 300                                    | 84              | 88              | NA      | NA      |
| 400                                    | 77              | 92              | NA      | NA      |
| Imaging                                |                 |                 |         |         |
| Ultrasonography                        | 74.3            | 56.7            | NA      | NA      |
| Computerized tomography                | 81-84           | 87.5            | NA      | NA      |
| Magnetic resonance imaging             | 100             | 81.8            | NA      | NA      |

Abbreviations: HPF, high power field; NA, not applicable; NPV, negative predictive value; PPV, positive predictive value; WBC, white blood cell.

<sup>a</sup> See Section 2 of the Supplement for detailed supporting information.

<sup>b</sup> WBC/HPF.



specimens.<sup>59</sup> These factors are crucial to differentiate colonization vs infection and to delineate pathogenic organisms vs commensal flora. The increased sensitivity of these molecular tests may lead to overtreatment by detecting clinically insignificant bacteria, especially now that metagenomics has identified endogenous genitourinary microflora,<sup>60-64</sup> underscoring the need for clear guidelines to avoid unnecessary therapy. More research is required to determine the ideal role of molecular testing in UTI diagnosis.

### **Question 13: What Is the Role of Different Imaging Modalities, Such as Ultrasonography and Computed Tomography, for the Diagnosis of UTIs, and What Is the Sensitivity and Specificity These Imaging Modalities?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. Computed tomography (CT) scans do not appear to be useful in the routine initial diagnostic workup of cystitis or pyelonephritis and may not routinely alter treatment<sup>65,66</sup> CT imaging may be useful if symptoms persist or worsen beyond 72 hours or if there are concerns for kidney calculi, kidney abscess, or an alternative focus of infection.<sup>67-69</sup> Contrast CT imaging is best discussed with the radiologist but may have advantages in terms of detecting kidney abscesses. Ultrasonography, while safer and more accessible, has limited accuracy but may be a preferable first imaging modality in younger patients, pregnancy, and/or kidney transplant recipients because there is no associated ionizing radiation, and may be able to more directly visualize the transplanted organ(s) (**Table 4**). Magnetic resonance with or without contrast and/or diffusion-weighted imaging is less effective for early disease detection and stone visualization but may also have an advantage in identifying graft infection (**Table 4**).<sup>70,71</sup> We caution clinicians to only obtain radiographic studies if they are likely to alter management for a patient with known or suspected UTI.

### **Question 14: What Are the Limitations of Usual Diagnostics in Patients With Indwelling Urinary Catheters or Ileal Conduits?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. UA has a very low specificity in diagnosing UTIs in patients with indwelling urinary catheters or ileal conduits but has excellent negative predictive value.<sup>72</sup> This suggests that a negative UA can rule out CAUTI for patients with functioning bone marrow, but given the low specificity of UA in patients with urinary catheters or ileal conduits, a positive UA does not mean the patient has a CAUTI. In addition, urine cultures are not reliable tests for patients with chronic urinary catheters or ileal conduits.<sup>73-75</sup> In these cases, bacteriuria is almost always present regardless of symptoms and are a likely source of appropriate initiation of antimicrobial treatment.

## **Section 3: Empirical Treatment**

An overview of findings relating to empirical treatment can be found in **Table 3**. Additional information can be found in **eAppendix 3** in the [Supplement](#).

### **Question 15: What Are Reasonable Empirical Treatment Regimen(s) for Pediatric or Adult Patients Diagnosed With a UTI?**

A sufficient quality and quantity of evidence was found to provide a clear recommendation for empirical treatment regimens for pediatric and adult patients diagnosed with UTIs. Empirical treatment regimens for pediatric and adult patients should contain antimicrobials that have historically demonstrated efficacy and safety in the treatment of UTIs, achieve adequate urinary concentrations, and provide reliable activity against the most common pathogens based on local resistance rates. A proposed framework for selecting empirical treatment regimens is presented in **eFigure 1** and **eFigure 2** in the [Supplement](#). Presence of risk factors for antimicrobial resistance along with clinical severity also play an important role in the selection of empirical choices.<sup>76,77,182</sup> For patients with uncomplicated cystitis, nitrofurantoin is a reasonable drug of choice, based on robust evidence of efficacy and its ability to spare use of more systemically active agents for treating other

Table 4. Duration of Treatment Based on Syndrome and Antimicrobial Class Used

| Syndrome and antimicrobial class                              | Duration of therapy (level of evidence)                                                                                 | Comments                                                                                                                                                                                                                                                                                      |
|---------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Adult cystitis<sup>a</sup></b>                             |                                                                                                                         |                                                                                                                                                                                                                                                                                               |
| Aminoglycosides                                               | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment                        | Multiple observational studies suggest a single dose of an aminoglycoside achieve high clinical and/or microbiological cure rates; no comparative literature exists                                                                                                                           |
| β-lactams                                                     | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment                        | Optimal duration may depend on the specific agent and dosing used. Heterogeneity in study design and β-lactam agent and dose used in studies precludes a clear recommendation                                                                                                                 |
| Fluoroquinolones                                              | 3 d (clear recommendation)                                                                                              | Due to risk of individual and ecological collateral damage, should not be used if other treatment options exist.                                                                                                                                                                              |
| Fosfomycin (oral)                                             | Single dose (clear recommendation)                                                                                      | Alternative dosing strategies have only been studied in RCTs and observational studies of febrile UTI, bacteremic UTI, and pyelonephritis                                                                                                                                                     |
| Nitrofurantoin                                                | 5 d (clear recommendation)                                                                                              | 5-d and 7-d Courses result in comparable clinical outcomes; may use with CrCl as low as 30 mL/min                                                                                                                                                                                             |
| Pivmecillinam                                                 | 3 d (clear recommendation)                                                                                              | 3 d Regimens appear to have comparable efficacy as longer regimens and various regimens of comparators commonly used in contemporary practice.                                                                                                                                                |
| TMP/SMX                                                       | 3 d (clear recommendation)                                                                                              | Contemporary <i>Escherichia coli</i> resistance rates in most geographical regions limit utility as first-line treatment.                                                                                                                                                                     |
| <b>Adult pyelonephritis<sup>b</sup></b>                       |                                                                                                                         |                                                                                                                                                                                                                                                                                               |
| Aminoglycosides                                               | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment                        | Multiple observational studies suggest monotherapy may be effective, however the optimal duration is unknown.                                                                                                                                                                                 |
| β-lactams                                                     | 7 d (clear recommendation)                                                                                              | Dose optimization is critical based on analogous data supporting β-lactam use in the treatment of gram-negative bloodstream infection and outcomes of RCTs using IV β-lactams. 3 RCTs demonstrate comparable outcomes with 7 d of treatment vs 2-, 3-, and 6- wk regimens.                    |
| Fluoroquinolones                                              | 5 to 7 d (clear recommendation)                                                                                         | RCTs supporting 5 d of treatment used ofloxacin or levofloxacin; RCTs supporting 7 d of treatment used ciprofloxacin or fleroxacin. Ofloxacin is a second generation fluoroquinolone similar to ciprofloxacin, so may be reasonable to use 5 d of treatment when using ciprofloxacin as well. |
| Fosfomycin                                                    | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment                        | IV fosfomycin available in some countries may be reasonable empirical treatment for pyelonephritis, but there is a lack of strong data supporting the use of oral fosfomycin for the treatment of pyelonephritis.                                                                             |
| TMP/SMX                                                       | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment                        | Historical durations of 14 d were used based on a series of very small RCTs in the 1970s to 1990s; outcomes of patients who received TMP/SMX in more recent RCTs suggest 7 d may be adequate, but further prospective investigation is needed.                                                |
| <b>Adult febrile UTI<sup>b</sup></b>                          |                                                                                                                         |                                                                                                                                                                                                                                                                                               |
| Catheter-associated UTI <sup>c</sup>                          | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment                        | Data are limited to observational studies and small subgroups of RCTs, precluding a clear recommendation. Observational data suggest 5 to 7 d may be as effective as longer durations.                                                                                                        |
| Gram-negative bacteremia from a urinary source <sup>d,e</sup> | 7 d (clear recommendation)                                                                                              | Heterogeneity in trial design and selection and dosing of antimicrobials used limits ability to recommend specific antimicrobial classes. Fluoroquinolones, TMP/SMX, and β-lactams were included in published RCTs demonstrating noninferiority of 7 d to 14 d.                               |
| Prostatitis <sup>f</sup>                                      | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment for either ABP or CBP. | There is a dearth of data for both acute and chronic bacterial prostatitis that precludes a clear recommendation for duration of treatment in either scenario. Historical durations range from 14 d for ABP to 6 weeks or longer for CBP.                                                     |

(continued)



Table 4. Duration of Treatment Based on Syndrome and Antimicrobial Class Used (continued)

| Syndrome and antimicrobial class                       | Duration of therapy (level of evidence)                                                                                                      | Comments                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|--------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Pediatric cystitis (>2 mos of age) <sup>a</sup>        | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment                                             | Heterogeneity in trial design, inclusion of clinically relevant outcomes precludes a clear recommendation. Numerous RCTs suggest shorter durations are likely effective (3 to 5 d).                                                                                                                                                                                                                                                             |
| Pediatric pyelonephritis (age >2 y) <sup>b</sup>       | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment                                             | Quantity and heterogeneity of existing data preclude a clear recommendation. Observational data suggest comparably high rates of clinical success when patients are treated for 5 to 9 d compared with longer (10 to 14 d) durations.                                                                                                                                                                                                           |
| Kidney and perinephric abscess <sup>c</sup>            | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment                                             | Source control is of utmost importance. Expert opinion does not distinguish between 14 and 21 d of treatment.                                                                                                                                                                                                                                                                                                                                   |
| Emphysematous cystitis and pyelonephritis <sup>d</sup> | Clinical review, not enough evidence to provide a clear recommendation for duration of treatment or emphysematous cystitis or pyelonephritis | May vary widely depending on clinical response and whether percutaneous drainage was performed. When considering the available data for pyelonephritis and Gram-negative bacteremia from a urinary source, it may be reasonable for emphysematous cystitis and pyelonephritis to be treated in a similar fashion to other more clinically severe UTIs, such as febrile UTI, pyelonephritis, and gram negative bacteremia from a urinary source. |

Abbreviations: ABP, acute prostatitis; CBP, chronic prostatitis; CrCl, creatinine clearance; IV, intravenous; RCT, randomized clinical trials; TMP/SMX, trimethoprim sulfamethoxazole; UTI, urinary tract infection.

<sup>a</sup> See question 21 in eAppendix 4 in the [Supplement](#).

<sup>b</sup> See question 22 in eAppendix 4 in the [Supplement](#).

<sup>c</sup> See question 23 in eAppendix 4 in the [Supplement](#).

<sup>d</sup> See question 24 in eAppendix 4 in the [Supplement](#).

<sup>e</sup> No specific class of antimicrobial can be clearly recommended.

<sup>f</sup> See question 35 in eAppendix 5 in the [Supplement](#).

<sup>g</sup> See question 19 in eAppendix 4 in the [Supplement](#).

<sup>h</sup> See question 20 in eAppendix 4 in the [Supplement](#).

<sup>i</sup> See question 34 in eAppendix 5 in the [Supplement](#).

<sup>j</sup> See question 33 in eAppendix 5 in the [Supplement](#).

infections.<sup>78</sup> For patients with pyelonephritis, TMP/SMX or a first-generation cephalosporin represent reasonable first-line agents but should be dependent upon local resistance rates. Due to low resistance rates and clinical effectiveness, ceftriaxone is the recommended empirical choice for patients who require intravenous therapy, barring any risk factors for multidrug resistance.<sup>79,80</sup> In general, agents with antipseudomonal activity should only be used in patients with risk factors for nosocomial pathogens. However, it may be reasonable to use carbapenem therapy empirically in hemodynamically unstable patients for whom there is a specific concern regarding extended-spectrum  $\beta$ -lactamase-producing bacteria. Overall, selection should be guided by local susceptibilities and patient-specific risk factors.

Question 16: What Are Reasonable Empirical Treatment Regimens for Treatment of a CAUTI?

The clinical review found insufficient quality of evidence to enable a clear recommendation. There is an absence of high-quality data to inform empirical treatment in patients with CAUTI. Observational data suggest that, where possible, it may be preferable to replace or discontinue existing catheters prior to the collection of cultures and initiation of antimicrobial treatment.<sup>81</sup> UTIs diagnosed after catheter exchange are likely to respond similarly to noncatheterized patients. Empirical treatment decisions can be made based on review of the individual patient’s urinary tract anatomy or dysfunction, allergies medication list for interactions, microbiological and prior treatment history, the type of UTI (eg, cystitis vs pyelonephritis), and the clinical severity of presentation.

Question 17: What Are the Established Risk Factors for UTI Due to Multidrug Resistant Organisms and When Should Empirical Treatment Account for These Pathogens?

The clinical review found insufficient quality of evidence to enable a clear recommendation. Although no validated models exist, prior health care exposure, previous antibiotic use, and a history of UTI or known colonization seem to be the most consistent and important estimators of development of a UTI due to a multidrug resistant organism (MDRO).<sup>82-84</sup> Due to heterogeneity in the populations and methods of available studies, the timing and/or combination of the exposure(s) and the subsequent effects on the outcome are unclear. There is insufficient data available to clearly guide decisions on when empirical treatment should include the possibility of an MDRO. In the absence of such data, it may be reasonable to suggest that the severity of an infection may be an important driver of empirical antibiotic choice when combined with local resistance patterns, proposed epidemiologic risk factors, and an individualized microbiologic history.

## Section 4: Definitive Treatment and Antimicrobial Stewardship

An overview of findings relating to definitive treatment can be found in Table 4. Additional information can be found in eAppendix 4 in the [Supplement](#).

### Question 18: What Is Considered Treatment Failure of a UTI and Are There Host-Related Risk Factors That May Influence the Risk of Treatment Failure?

The clinical review found insufficient quality of evidence to enable a clear recommendation. There is no agreed upon universal definition of treatment failure. In general, treatment failure may result from clinical failure, microbiological failure, or a combination thereof. Current US Food and Drug Administration guidance suggests a composite endpoint that includes both clinical and microbiological responses. The true implications of the combination of clinical cure with microbiologic failure at follow-up remains uncertain. An analysis of individual participant data from several phase 3 studies found an increased risk of late clinical failure in patients with clinical cure but microbiological persistence,<sup>85</sup> but this phenomenon is often difficult to distinguish from a new infection. Notably, in 2 recent large RCTs, positive urine cultures at follow-up in patients who had resolved clinical signs and symptoms of infection did not appear to predict a higher risk of relapse of infection within the follow-up period.<sup>86,87</sup> Commonly identified epidemiologic risk factors for treatment failure identified in observational studies include older age, diagnosis of diabetes, presentation with septic shock, pregnancy, and immunosuppression.<sup>88-99</sup> No compelling data exist to support adjusting UTI treatment based on the potential risk factors for treatment failure that have been identified in these retrospective studies.

### Question 19: What Is the Appropriate Duration of Treatment of Acute Cystitis in Pediatric Patients Older Than 2 Months of Age?

The clinical review found insufficient quality of evidence to enable a clear recommendation. Based on several randomized trials, shorter courses (3 to 5 days, depending on the antimicrobial used) result in comparable outcomes to longer courses (7 to 14 days) and are reasonable for the treatment of cystitis in children older than 2 months of age when the likelihood of pyelonephritis is deemed to be low.<sup>100-102</sup> Small study size, heterogeneity in trial design (various durations, various antibiotics), end point definitions (with frequent use of positive culture at follow-up defining treatment failure), and outcomes, preclude a clear recommendation for duration of treatment. Several observational studies suggest that a single parenteral dose of an aminoglycoside may be a reasonable alternative treatment option.<sup>103</sup> No data exists to suggest that initial (or any) parenteral treatment for cystitis is necessary in patients who can tolerate oral treatment.

### Question 20: What Is the Appropriate Duration of Treatment of Acute Pyelonephritis in Pediatric Patients Older Than 2 Months of Age?

The clinical review found insufficient quality of evidence to enable a clear recommendation. Available randomized trial data are inadequate to provide a clear recommendation on the optimal duration of treatment for acute pyelonephritis in children older than 2 months of age.<sup>86,104,105</sup> Most existing data suggest similarly high rates of clinical success when patients receive 5 to 9 days (depending on the antimicrobial used) when compared with 10 to 14 days total.<sup>106,107</sup>

### Question 21: What Is the Appropriate Duration of Treatment for Acute Cystitis in Adults?

Based on the totality of the evidence available, we can provide clear recommendations on the optimal durations of treatment for cystitis (regardless of biological sex) for the antimicrobial classes listed below:

- Nitrofurantoin: 5 days<sup>108-110</sup>
- TMP/SMX: 3 days<sup>109,111,112</sup>
- Fluoroquinolones: 3 days<sup>109,113-118</sup>
- Oral fosfomycin: single dose<sup>78,119-127</sup>
- Pivmecillinam: 3 days<sup>109,128-132</sup>
- Gepotidacin: 5 days<sup>133</sup>

Data are insufficient to enable clear recommendations for duration of treatment for other potential treatment options, including  $\beta$ -lactams and parenteral aminoglycosides. Some pediatric data support a 5-day treatment duration when oral  $\beta$ -lactams are used to treat cystitis.<sup>105</sup>

**Question 22: What Is the Appropriate Duration of Treatment for Acute Pyelonephritis and/or Febrile UTI in Adults?**

Based on several randomized clinical trials, we can provide a clear recommendation on the duration of therapy for the following antimicrobial classes (regardless of biological sex) for the treatment of acute pyelonephritis:

- Fluoroquinolones: 5 to 7 days<sup>134-139</sup>
- Dose-optimized  $\beta$ -lactams: 7 days<sup>140-143</sup>

The clinical review found insufficient quality of evidence to enable a clear recommendation for fosfomycin, TMP/SMX, and aminoglycoside monotherapy. We cannot provide clear recommendations for pyelonephritis treatment duration with TMP/SMX, fosfomycin, or aminoglycoside monotherapy due to the lack of reproducible high-quality data or heterogeneity across small studies. We are unable to provide a clear recommendation for the treatment duration for febrile UTI. When considering the available data for pyelonephritis and gram-negative bacteremia from a urinary source, it may be reasonable for febrile UTI to be treated in a similar fashion to pyelonephritis.

**Question 23: What Is the Appropriate Duration of Treatment for CAUTIs?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. The optimal duration of antimicrobial therapy for CAUTIs has not been rigorously evaluated in large RCTs.<sup>81</sup> Data are limited to observational studies or small subgroups of RCTs evaluating complicated UTIs, so a clear recommendation cannot be made. Based on available observational data, 5 to 7 days appears as effective as longer treatment courses and represents a reasonable duration of treatment for most cases of CAUTI in conjunction with catheter exchange and/or removal, if possible.<sup>144</sup> No existing data demonstrate an association between longer courses and improved patient outcomes.

**Question 24: What Are Optimal Oral Agents and an Appropriate Duration of Treatment for Gram-Negative Bacteremia From a Urinary Source?**

A sufficient quality and quantity of evidence was found to provide a clear recommendation. Multiple RCTs comprised patients with gram negative bacteremia from predominantly urinary sources demonstrate noninferiority of 7 days compared with 14 total days of treatment for a variety of patient-oriented outcomes, such as clinical cure, clinical failure, relapse, and all-cause mortality.<sup>145-148</sup> Thus, we can provide a clear recommendation for 7 days of treatment for gram negative bacteremia from a urinary source when source control has been addressed (if applicable). Whether shorter durations might also be effective is unknown as they have not been studied. These trials tested duration as a strategy and not specific drugs; thus, while no specific class of medications can be recommended, it is also reasonable to ensure that the choice of drug and the doses used are optimized for the patient and a urinary focus of infection.

**Question 25: What Are Potential Treatment Option(s) and Appropriate Durations of Treatment for Asymptomatic Bacteriuria in Populations in Which Treatment Is Indicated?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. Unnecessary treatment of asymptomatic bacteriuria (ASB) risks side effects without benefit represents low value care and poses a threat to antimicrobial sustainability.<sup>53,149-152</sup> There is no conclusive evidence that there is any population in which treatment of ASB is required and randomized clinical trials are welcomed. There are theoretical reasons and limited evidence which support treatment of ASB in pregnant patients<sup>153,154</sup> and in those undergoing invasive urologic procedures associated with expected mucosal bleeding.<sup>155-158</sup> When treating ASB, the ideal duration of treatment is unknown. In pregnancy, it may be reasonable not to exceed the duration used for symptomatic cystitis (eg, 3 to 5 days, depending on the antimicrobial used). For patients undergoing invasive urologic procedures, most authors believe that many patients could receive a single dose of preoperative prophylaxis prior to the scheduled procedure.

**Question 26: What Are Potential Treatment Option(s) and Duration of Treatment for UTIs Caused by Multidrug Resistant Organisms?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. The potential treatment option(s) depend on the organism identified and specific resistance mechanisms. To our knowledge, no data exist to suggest that the duration of treatment for UTIs caused by multidrug resistant organisms (MDROs) needs to be modified compared with those caused by nonresistant organisms. We feel it is reasonable to determine a treatment duration based on the anatomical location and clinical severity (eg, cystitis or pyelonephritis) as well as the clinical response to treatment provided that (1) the antimicrobial being used has demonstrated activity against the organism, (2) the antimicrobial has proven or a high likelihood of efficacy for treatment of UTIs, and (3) any applicable source control has been obtained.

**Question 27: What Are Effective Antimicrobial Stewardship Strategies That Can Optimize the Rational and Sustainable Use of Antimicrobials in the Setting of Treatment of UTIs?**

A sufficient quality and quantity of evidence was found to provide a clear recommendation for deescalation and mostly or all oral treatment. Randomized clinical trials have demonstrated the individual and ecological benefits to antibiotic deescalation and all authors encourage its use when able during the treatment of UTIs.<sup>159,160</sup> Additionally, multiple RCTs demonstrate treatment of a variety of UTIs with all or mostly oral regimens result in comparable outcomes with intravenous-only treatment and may reduce hospital length of stay and adverse events associated with antibiotics and/or central venous catheters.<sup>161-174</sup>

The clinical review found insufficient quality of evidence to enable a clear recommendation for allergy assessment and cascade reporting. Our review did not yield any RCTs evaluating antibiotic allergy assessment specifically for the management of UTIs; however all authors of this consensus statement agree that thorough allergy assessment (and challenge, if indicated) can likely prevent a variety of harms based on existing data and recommendations from specialists in allergy or immunology.<sup>175-177</sup> Although we cannot provide a clear recommendation due to the observational nature of the data, we agree that optimizing the reporting of antimicrobial susceptibility results through selective or cascade reporting is a reasonable strategy to optimize treatment selection.<sup>178-180</sup>

**Section 5: Special Populations and Genitourinary Syndromes**

An overview of findings relating to special populations can be found in Table 5. Additional information can be found in eAppendix 5 in the [Supplement](#).

**Question 28: What Are Special Considerations for the Diagnosis and Treatment of UTI in Older Adults?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. Asymptomatic bacteriuria is prevalent in the older adults, particularly in institutionalized individuals, with treatment showing no benefit over placebo.<sup>181,182</sup> Overtesting and overtreatment with antibiotics for these nonsymptomatic cases remains high.<sup>183,184</sup> UTIs are more frequent in the institutionalized older adult populations and clinical tools for assessing symptoms exist to help discourage tests for nondelirium behavioral changes or falls.<sup>183</sup> Using clinical scores alongside microbiological tests is crucial due to the high rates of bacteriuria with pyuria, and the potential misinterpretation of UA results, which often leads to unnecessary antibiotic use.<sup>185,186</sup> Further research comparing clinical prediction scores for UTIs is needed.

**Question 29: What Is the Role and Utility of UA and Urine Culture Testing in Pediatric Populations?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. In pediatric care, the workup for febrile illness often includes UA and urine culture, particularly in

younger populations where symptoms cannot be elicited.<sup>187</sup> These practices can lead to the overtreatment and overdiagnosis of UTI. Major societies recommend using proper microbiological methods for diagnosis, yet clinical practices deviate, depending on less reliable methods like bagged urine samples.<sup>188-190</sup> The interpretation of UA and colony forming unit counts in urine cultures in the pediatric population are not clearly defined, leading to variability in the diagnosis and treatment of pediatric UTI.

### **Question 30: For Pediatric Patients, How Do We Delineate Cystitis vs Pyelonephritis When the Child Is Unable to Verbalize Symptoms Characteristic of UTI?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. Pediatric cystitis and pyelonephritis are common yet complex conditions in children, impacting quality of life and requiring comprehensive management.<sup>191,192</sup> In pediatric patients, distinguishing cystitis from pyelonephritis can be challenging, particularly in young children who are unable to verbalize symptoms. Clinical evaluation, including assessment for systemic signs such as fever and poor feeding, along with UA and imaging studies, are essential in making this differentiation.<sup>47,193</sup> While infections are mainly caused by gram-negative bacteria, noninfectious causes also contribute to the diagnostic challenge. Prevention of long-term kidney damage from pyelonephritis necessitates prompt recognition and treatment, considering genetic, urinary, and environmental factors.

### **Question 31: What Is the Optimal Follow-Up Timeframe for Pediatric Patients With UTI?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. Observational data suggests that clinical improvement, including fever resolution, typically occurs after 48 to 72 hours of treatment in children.<sup>194,195</sup> Authors believe it to be reasonable to conduct additional work-up (eg, kidney and bladder ultrasonography) and/or reassess the current treatment plan if patients do not experience clinical improvement within that timeframe.<sup>194,196-200</sup> Assuming the patient improves as expected, previously described treatment durations of 3 to 5 days for cystitis and 7 to 10 days for pyelonephritis are reasonable (more detail in questions 19 and 20). Routine follow-up is not necessary unless the patient is younger than age 2 years and experiences a febrile UTI or a child of any age experiences a recurrence of febrile UTI. It is reasonable to deescalate and/or target treatment as soon as culture and susceptibility results are available based on the discussion in question 27 and other studies of children who are hospitalized.<sup>201,202</sup>

### **Question 32: For Kidney Transplant Recipients, What Is the Significance of a Positive Urine Culture?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. UTIs are an important postkidney transplant complication.<sup>203,204</sup> The spectrum of causative microorganisms is broad and includes typical uropathogens, atypical pathogens, and MDROs.<sup>205</sup> This complexity demands a nuanced understanding of microbial behavior in the context of immunosuppressed individuals. Cultures need to be interpreted within their clinical context, including specific timing posttransplantation and symptoms. Routine treatment of ASB in kidney transplant recipients increases colonization with resistant organisms without providing clear benefit and should be avoided after the first 2 months from transplantation.<sup>206</sup>

### **Question 33: What Is the Empirical and Definitive Treatment of Emphysematous Cystitis and Pyelonephritis?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. The treatment of emphysematous cystitis and pyelonephritis (caused by gas producing pathogens) lacks robust data, with recommendations mostly relying on clinical judgment and case studies.<sup>207</sup> Early appropriate antibiotics targeting common pathogens like *Escherichia coli* and *Klebsiella* species is reasonable, with a general treatment approach mirroring that for nonemphysematous UTIs.<sup>208</sup> While most cases respond to medical therapy, severe instances may need surgical intervention.

Percutaneous catheter drainage, along with antibiotics, shows lower mortality for emphysematous pyelonephritis and is advisable in severe cases to include broader coverage until culture results are available.<sup>209</sup> Most authors believe a treatment duration of 7 to 14 days (adjusted per clinical response) is reasonable.<sup>210</sup>

#### **Question 34: What Is the Clinical Presentation and Diagnostic Approach for Kidney or Perinephric Abscess? What Is the Empirical and Definitive Treatment of Kidney Abscess and Perinephric Abscess?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. Perinephric abscesses are serious conditions with varied presentations.<sup>211</sup> Typical symptoms include lumbar pain and fever, with many patients presenting with costovertebral angle tenderness. CT imaging is crucial for diagnosis and management, which may include medical therapy, percutaneous drainage, or surgery for refractory cases.<sup>211</sup> These abscesses are commonly caused by gram-negative bacteria or hematogenous seeding from organisms like *Staphylococcus aureus*. Decision to opt for drainage of the abscess is often influenced by the size,<sup>212,213</sup> however, some form of drainage is often necessary for definitive treatment. Further research is needed on optimal source control intervention strategies and when medical management alone may be used.<sup>214-216</sup>

#### **Question 35: What Is the Clinical Presentation, Diagnostic Approach, and Treatment for Acute and Chronic Prostatitis?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. Acute bacterial prostatitis (ABP) and chronic bacterial prostatitis (CBP) are inflammatory prostate syndromes with ABP often presenting abruptly with febrile UTI symptoms and CBP involving more persistent symptoms or recurrent UTIs.<sup>217,218</sup> Diagnosis for ABP relies on clinical presentation and laboratory tests. CBP diagnosis involves comparing bacteria levels in prostatic fluid and urinary cultures, yet definitive testing is debated. Testing for prostate specific antigen (PSA) appears of limited utility.<sup>219</sup> Maneuvers to express prostatic fluid, such as prostate massage, are of limited clinical utility and urology consultation may be needed.<sup>219,220</sup> The optimal durations of treatment for ABP or CBP are unknown and have not been established by high-quality studies. Additional prospective studies are needed to determine the appropriate duration of treatment for ABP and CBP.

#### **Question 37: What Are Nonbacterial Causes of UTI to Consider in Certain Special Populations?**

The clinical review found insufficient quality of evidence to enable a clear recommendation. Most nonbacterial UTIs are due to *Candida* species<sup>230</sup> While 25% of intensive care unit UTIs in the US are attributed to *Candida* species, most cases of candiduria are asymptomatic and benign. If symptomatic, fluconazole and amphotericin B are preferred due to favorable urinary pharmacokinetics and pharmacodynamics, but no RCTs are available to determine the best treatment choice or duration.<sup>230,231</sup> Viral UTIs (especially BK polyomavirus and adenovirus) are less common but a noteworthy risk in immunocompromised patients.<sup>232-234</sup> A reduction in the intensity of existing immunosuppression is the primary treatment. Small case reports detail individual experiences with antivirals with in vitro activity against these viruses exist, but their retrospective nature and small size limit generalizability.<sup>235-237</sup>

#### **Question 36: What Is the Optimal Clinical Approach for Patients With Nephrolithiasis, Foreign Objects, Nephrostomy Tubes, and/or Ureteral Stents?**

A sufficient quality and quantity of evidence was found to provide a clear recommendation for the optimal clinical approach for patients with nephrolithiasis, foreign objects, nephrostomy tubes, and/or ureteral stents. Routine cystoscopy and urodynamic studies do not require antimicrobial prophylaxis in asymptomatic patients. Preoperative antibiotics do not appear to reduce infectious complications from routine cystoscopic stent removal nor nephrostomy tube placement.<sup>221,222</sup> The majority of patients with uncomplicated urologic cases undergoing percutaneous nephrolithotomy, a



single dose of antimicrobial prophylaxis appears to reduce the risk of infection.<sup>158,223-225</sup> However, in a recent meta-analysis,<sup>226</sup> single dose was found to be associated with higher rates of systemic inflammatory response syndrome (SIRS) postnephrolithotomy compared with extended perioperative dosing in patients considered high risk; however, the use of a nonspecific measure, such as SIRS, to detect complications may overidentify complications.<sup>227</sup> If there are particularly vulnerable patients, such as in pregnancy or kidney transplant, extended preoperative dosing schedules are reasonable to consider. Published RCTs use a 7-day duration preoperatively, however, it is unclear if that long of a course is routinely necessary.<sup>228,229</sup>

---

## Discussion

Despite decades of research and nearly 1000 studies reviewed, we remain unable to provide a clear recommendation on many, even some essential, aspects of the prevention, diagnosis, and treatment of urinary tract infections. This consensus statement highlights the dramatic impact of historical practice patterns on certain aspects of UTI treatment, such as duration of therapy, while also highlighting critical gaps in knowledge that impact our understanding of how effective our treatments are, such as the impact of clinical improvement without resolution of bacteriuria. Additionally, there is an obvious need to use more precise terminology to describe site(s) and extent of infections rather than the vague terms that have become commonplace in clinical practice. This will ensure that there are more clearly defined study populations, reduced heterogeneity in generalizability of those studies, and ensure that individual patients receive the highest value, most appropriate care for their specific infection.

## Limitations

This consensus statement has limitations. The main limitation of this guideline is the overall dearth of hypothesis-confirming evidence. Using the WikiGuidelines method of guideline development, only 6 clear recommendations were able to be established out of 37 questions, highlighting the need for additional high-quality prospective studies in all aspects of the management of urinary tract infections. Additionally, certain sections of the article may be less generalizable than others, such as in the empiric treatment section, which is heavily influenced by local epidemiology. Despite these limitations, we attempted to equip readers with the foundational principles that they may apply to their individual practice settings. We made an effort within this guideline to include experts internationally; however, most of the guideline authors are from high-income countries and in the future, we hope to incorporate the essential perspective of and thus provide guidance for clinicians practicing in low and middle-income countries and other resource-constrained settings.

---

## Conclusions

This consensus statement presents evidence-based strategies for managing UTIs and clinical reviews in areas where strong evidence is lacking. The guidance is based on information available up to early 2024. Pressing research gaps remain, including the need for high-quality studies to validate novel diagnostic methods, optimize treatment durations, establish standard definitions, and refine antimicrobial stewardship strategies for asymptomatic bacteriuria and MDROs. Suggestions for alternative evidence or recommendations are welcome for consideration by the authors, with updates to the guideline made as needed. No single guideline can encompass all clinical scenarios; therefore, this document is not intended to set legal medical standards or replace professional judgment for individual patient cases.

## ARTICLE INFORMATION

**Accepted for Publication:** September 17, 2024.

**Published:** November 4, 2024. doi:10.1001/jamanetworkopen.2024.44495

**Open Access:** This is an open access article distributed under the terms of the [CC-BY License](#). © 2024 Nelson Z et al. JAMA Network Open.

**Corresponding Author:** Zachary Nelson, PharmD, MPH, Park Nicollet Health Services, 6500 Excelsior Blvd, St Louis Park, MN 55426 ([Zachary.nelson2@parknicollet.com](mailto:Zachary.nelson2@parknicollet.com)).

**Author Affiliations:** HealthPartners and Park Nicollet Health Services, St Louis Park, Minnesota (Nelson, Christensen); The University of Queensland, Faculty of Medicine, UQ Centre for Clinical Research, Brisbane, Queensland, Australia (Tarik Aslan); Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta, Canada (Beahm); Louisiana State University, New Orleans (Blyth); Loma Linda University Medical Center, Loma Linda, California (Cappiello); University of Kentucky Healthcare, Lexington (Casaus, Olney); Family Health Centers of San Diego, San Diego, California (Dominguez); University of Manitoba, Winnipeg, Manitoba, Canada (Egbert); Cooper University Health Care, Camden, New Jersey (Hanretty, Kludjian); University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania (Khadem); Rutgers Health Robert Wood Johnson Medical School, New Brunswick, New Jersey (Abdul-Azim); Montgomery Medical Associates, Rockville, Maryland (Aggrey); Wellstar MCG Health, Augusta, Georgia (Anderson); NOVA Medical School, Universidade Nova de Lisboa, Lisboa, Portugal (Barosa); NYU Langone Hospital—Long Island, Mineola, New York (Bosco); Palm Beach Atlantic University, West Palm Beach, Florida (Chahine); All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India (Chowdhury); University of Alabama at Birmingham (de Lima Corvino, Fleece, R. A. Lee); University of Colorado School of Medicine and Anschutz Medical Center, Aurora (Fitzpatrick); UNC Health, Chapel Hill, North Carolina (Footer); UT Southwestern MD Anderson Cancer Center, Houston, Texas (Fox); King Abdulaziz Medical City, Jeddah, Saudi Arabia (Ghanem); University of Bristol, Bristol, United Kingdom (Hamilton); University of Arizona, Tucson (Hayes); Clinic for Infectious and Tropical Diseases “Prof. Dr. Kosta Todorovic”, Belgrade, Serbia (Jegorovic); Bern University Hospital and University of Bern, Bern, Switzerland (Jent); Hospital Infantil de Mexico Federico Gomez, Mexico City, Mexico (Jimenez-Juarez); Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom (Joseph); UT Southwestern Medical Center, Dallas, Texas (Kang); University of Michigan Medical School, Ann Arbor (Kurz); McGill University, Montreal, Quebec, Canada (T. C. Lee, McDonald); The Chinese University of Hong Kong, Hong Kong, China (Li); Department of Clinical Medicine and Surgery, Section of Infectious Diseases, University of Naples Federico II, Italy. (Maraolo); University of Toronto and Women’s College Hospital, Toronto, Ontario, Canada (Maximos); Bellevue Hospital Center, Manhattan, New York, New York (Mehta); Northwestern Medicine, Chicago, Illinois (Moore); University of Chicago Medicine, Chicago, Illinois (Nguyen); Institute for Hygiene and Public Health, University Hospital Bonn, Bonn, Germany (Papan); All India Institute of Medical Sciences, Jodhpur, Rajasthan, India (Ravindra); Los Angeles General Medical Center, Los Angeles, California (Spellberg); Newfoundland and Labrador Health Services, St John’s, Newfoundland & Labrador, Canada (Taylor); Memorial University, St. John’s, Newfoundland & Labrador, Canada (Taylor); Mercy Medical Center, Cedar Rapids, Iowa (Thumann); Department of Infectious Diseases, The University of Melbourne at the Peter Doherty Institute for Infection and Immunity, Melbourne, Australia (Tong); Victorian Infectious Diseases Service, The Royal Melbourne Hospital at the Peter Doherty Institute for Infection and Immunity, Melbourne, Australia (Tong); Henry Ford Hospital and Wayne State University, Detroit, Michigan (Veve); Rush University Medical Center, Chicago, Illinois (Wilson); Rutgers Health Robert Wood Johnson University Hospital, New Brunswick, New Jersey (Yassin); Jamaica Hospital Medical Center, Queens, New York, New York (Zafonte); University of Illinois, Chicago (Mena Lora).

**Author Contributions:** Dr Nelson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Concept and design:** Nelson, Tarik Aslan, Beahm, Casaus, Anderson, Chahine, Christensen, Fitzpatrick, Fleece, Ghanem, Hamilton, Joseph, Kludjian, R. Lee, McDonald, Ravindra, Spellberg, Veve, Mena Lora.

**Acquisition, analysis, or interpretation of data:** Nelson, Tarik Aslan, Beahm, Blyth, Cappiello, Casaus, Dominguez, Egbert, Hanretty, Khadem, Olney, Abdul Azim, Aggrey, Anderson, Barosa, Bosco, Chahine, Chowdhury, Christensen, de Lima Corvino, Fitzpatrick, Footer, Fox, Hayes, Jegorovic, Jent, Jimenez-Juarez, Kang, Kludjian, Kurz, T. Lee, Li, Maraolo, Maximos, Mehta, Moore, Nguyen, Papan, Taylor, Thumann, Tong, Veve, Wilson, Yassin, Zafonte, Mena Lora.

**Drafting of the manuscript:** Nelson, Tarik Aslan, Beahm, Cappiello, Casaus, Dominguez, Egbert, Hanretty, Khadem, Olney, Abdul Azim, Aggrey, Anderson, Barosa, Bosco, Chahine, Chowdhury, Christensen, de Lima Corvino, Fitzpatrick, Fleece, Fox, Jimenez-Juarez, Joseph, Kang, Kludjian, Kurz, R. Lee, T. Lee, Li, Maraolo, Maximos, Mehta, Moore, Nguyen, Papan, Ravindra, Spellberg, Taylor, Thumann, Veve, Wilson, Yassin, Zafonte, Mena Lora.

**Critical review of the manuscript for important intellectual content:** Nelson, Tarik Aslan, Beahm, Blyth, Cappiello, Hanretty, Khadem, Olney, Aggrey, Anderson, Chahine, Christensen, Fitzpatrick, Footer, Ghanem, Hamilton, Hayes,

Jegorovic, Jent, Jimenez-Juarez, Kang, Kurz, R. Lee, T. Lee, Maximos, McDonald, Moore, Nguyen, Papan, Spellberg, Taylor, Tong, Veve, Mena Lora.

*Statistical analysis:* T. Lee, Papan, Taylor.

*Obtained funding:* Christensen, Mehta, Spellberg, Taylor.

*Administrative, technical, or material support:* Tarik Aslan, Beahm, Cappiello, Dominguez, Hanretty, Olney, Christensen, Fleece, Footer, Kang, Kurz, McDonald, Moore, Nelson, Ravindra, Spellberg, Tong, Mena Lora.

*Supervision:* Nelson, Blyth, Cappiello, Dominguez, Egbert, Khadem, Olney, Fitzpatrick, Ghanem, Moore, Papan, Spellberg, Veve, Mena Lora.

**Conflict of Interest Disclosures:** Dr Hanretty reported receiving personal fees from Abbvie outside the submitted work. Dr Olney reported receiving grants from the Society of Infectious Diseases Pharmacists outside the submitted work. Dr Chahine reported receiving personal fees from Seqirus, Gilead, and Shionogi outside the submitted work. Dr Joseph reported receiving grants from Pfizer, nonfinancial support from Eumedica, and personal fees from Glaxo-Smith-Kline, Advanz Pharma, Pfizer, Biomerieux, and Global Access Diagnostics outside the submitted work. Dr T. Lee reported receiving salary support from Fonds de Recherche du Quebec—Santé Research and grants from Canadian Institutes of Health Research Operating Funds for clinical trials outside the submitted work. Dr McDonald reported being a member of the WikiGuidelines board and receiving governmental research salary support from Fonds de Recherche du Quebec—Santé outside the submitted work. No other disclosures were reported.

**Group Information:** The WikiGuidelines Group that established this guideline is entirely voluntary and unpaid; the group intends to establish a nonprofit organization to support development of other guidelines using this novel methodology, and eventually intends to trademark the name WikiGuidelines. All authors are members of the WikiGuidelines Group.

**Additional Contributions:** We thank Gurmeet Sehgal MS, MLS (University Libraries, Loma Linda University, Loma Linda, CA), for literature compilation for Section 5.

## REFERENCES

1. Stapleton A, Latham RH, Johnson C, Stamm WE. Postcoital antimicrobial prophylaxis for recurrent urinary tract infection: a randomized, double-blind, placebo-controlled trial. *JAMA*. 1990;264(6):703-706. doi:10.1001/jama.1990.03450060049027
2. Melekos MD, Asbach HW, Gerharz E, Zarakovitis IE, Weingaertner K, Naber KG. Post-intercourse versus daily ciprofloxacin prophylaxis for recurrent urinary tract infections in premenopausal women. *J Urol*. 1997;157(3):935-939. doi:10.1016/S0022-5347(01)65087-0
3. Jent P, Berger J, Kuhn A, Trautner BW, Atkinson A, Marschall J. Antibiotics for preventing recurrent urinary tract infection: systematic review and meta-analysis. *Open Forum Infect Dis*. 2022;9(7):ofac327. doi:10.1093/ofid/ofac327
4. Buettcher M, Trueck J, Niederer-Loher A, et al. Swiss consensus recommendations on urinary tract infections in children. *Eur J Pediatr*. 2021;180(3):663-674. doi:10.1007/s00431-020-03714-4
5. Autore G, Bernardi L, Ghidini F, et al; The Uti-Ped-Er Study Group. Antibiotic prophylaxis for the prevention of urinary tract infections in children: guideline and recommendations from the Emilia-Romagna Pediatric Urinary Tract Infections (UTI-Ped-ER) study group. *Antibiotics (Basel)*. 2023;12(6):1040. doi:10.3390/antibiotics12061040
6. Mattoo TK, Shaikh N, Nelson CP. Contemporary management of urinary tract infection in children. *Pediatrics*. 2021;147(2):e2020012138. doi:10.1542/peds.2020-012138
7. McGuinness SD, Krone R, Metz LMA. Double-blind, randomized, placebo-controlled trial of cranberry supplements in multiple sclerosis. *J Neurosci Nurs*. 2002;34(1):4. doi:10.1097/01376517-200202000-00002
8. Cowan CC, Hutchison C, Cole T, et al. A randomised double-blind placebo-controlled trial to determine the effect of cranberry juice on decreasing the incidence of urinary symptoms and urinary tract infections in patients undergoing radiotherapy for cancer of the bladder or cervix. *Clin Oncol (R Coll Radiol)*. 2012;24(2):e31-e38. doi:10.1016/j.clon.2011.05.009
9. Stothers L. A randomized trial to evaluate effectiveness and cost effectiveness of naturopathic cranberry products as prophylaxis against urinary tract infection in women. *Can J Urol*. 2002;9(3):1558-1562.
10. Maki KC, Kaspar KL, Khoo C, Derrig LH, Schild AL, Gupta K. Consumption of a cranberry juice beverage lowered the number of clinical urinary tract infection episodes in women with a recent history of urinary tract infection. *Am J Clin Nutr*. 2016;103(6):1434-1442. doi:10.3945/ajcn.116.130542
11. Jepson RG, Williams G, Craig JC. Cranberries for preventing urinary tract infections. *Cochrane Database Syst Rev*. 2012;10(10):CD001321. doi:10.1002/14651858.CD001321.pub5

12. Mantzorou M, Giaginis C. Cranberry consumption against urinary tract infections: clinical state-of-the-art and future perspectives. *Curr Pharm Biotechnol*. 2018;19(13):1049-1063. doi:10.2174/1389201020666181206104129
13. Foxman B, Cronenwett AEW, Spino C, Berger MB, Morgan DM. Cranberry juice capsules and urinary tract infection after surgery: results of a randomized trial. *Am J Obstet Gynecol*. 2015;213(2):194.e1-194.e8. doi:10.1016/j.ajog.2015.04.003
14. Barbosa-Cesnik C, Brown MB, Buxton M, Zhang L, DeBusscher J, Foxman B. Cranberry juice fails to prevent recurrent urinary tract infection: results from a randomized placebo-controlled trial. *Clin Infect Dis*. 2011;52(1):23-30. doi:10.1093/cid/ciq073
15. McMurdo MET, Argo I, Phillips G, Daly F, Davey P. Cranberry or trimethoprim for the prevention of recurrent urinary tract infections: a randomized controlled trial in older women. *J Antimicrob Chemother*. 2009;63(2):389-395. doi:10.1093/jac/dkn489
16. Wing DA, Rumney PJ, Preslicka CW, Chung JH. Daily cranberry juice for the prevention of asymptomatic bacteriuria in pregnancy: a randomized, controlled pilot study. *J Urol*. 2008;180(4):1367-1372. doi:10.1016/j.juro.2008.06.016
17. McMurdo MET, Bissett LY, Price RJG, Phillips G, Crombie IK. Does ingestion of cranberry juice reduce symptomatic urinary tract infections in older people in hospital: a double-blind, placebo-controlled trial. *Age Ageing*. 2005;34(3):256-261. doi:10.1093/ageing/afi101
18. Linsenmeyer TA, Harrison B, Oakley A, Kirshblum S, Stock JA, Millis SR. Evaluation of cranberry supplement for reduction of urinary tract infections in individuals with neurogenic bladders secondary to spinal cord injury: a prospective, double-blinded, placebo-controlled, crossover study. *J Spinal Cord Med*. 2004;27(1):29-34. doi:10.1080/10790268.2004.11753727
19. Babar A, Moore L, Leblanc V, et al. High dose versus low dose standardized cranberry proanthocyanidin extract for the prevention of recurrent urinary tract infection in healthy women: a double-blind randomized controlled trial. *BMC Urol*. 2021;21(1):44. doi:10.1186/s12894-021-00811-w
20. Kontiokari T, Sundqvist K, Nuutinen M, Pokka T, Koskela M, Uhari M. Randomised trial of cranberry-lingonberry juice and Lactobacillus GG drink for the prevention of urinary tract infections in women. *BMJ*. 2001;322(7302):1571. doi:10.1136/bmj.322.7302.1571
21. Stapleton AE, Dziura J, Hooton TM, et al. Recurrent urinary tract infection and urinary Escherichia coli in women ingesting cranberry juice daily: a randomized controlled trial. *Mayo Clin Proc*. 2012;87(2):143-150. doi:10.1016/j.mayocp.2011.10.006
22. Di Martino P, Agniel R, David K, et al. Reduction of Escherichia coli adherence to uroepithelial bladder cells after consumption of cranberry juice: a double-blind randomized placebo-controlled cross-over trial. *World J Urol*. 2006;24(1):21-27. doi:10.1007/s00345-005-0045-z
23. Lee BB, Haran MJ, Hunt LM, et al. Spinal-injured neuropathic bladder antisepsis (SINBA) trial. *Spinal Cord*. 2007;45(8):542-550. doi:10.1038/sj.sc.3101974
24. Hooton TM, Vecchio M, Iroz A, et al. Effect of increased daily water intake in premenopausal women with recurrent urinary tract infections: a randomized clinical trial. *JAMA Intern Med*. 2018;178(11):1509-1515. doi:10.1001/jamainternmed.2018.4204
25. Menten JC, Culp K. Reducing hydration-linked events in nursing home residents. *Clin Nurs Res*. 2003;12(3):210-225. doi:10.1177/1054773803252996
26. Tan-Kim J, Shah NM, Do D, Menefee SA. Efficacy of vaginal estrogen for recurrent urinary tract infection prevention in hypoestrogenic women. *Am J Obstet Gynecol*. 2023;229(2):143.e1-143.e9. doi:10.1016/j.ajog.2023.05.002
27. Stamm WE. Estrogens and urinary-tract infection. *J Infect Dis*. 2007;195(5):623-624. doi:10.1086/511526
28. Simunić V, Banović I, Ciglar S, Jeren L, Pavčić Baldani D, Sprem M. Local estrogen treatment in patients with urogenital symptoms. *Int J Gynaecol Obstet*. 2003;82(2):187-197. doi:10.1016/S0020-7292(03)00200-5
29. McVicker L, Labeit AM, Coupland CAC, et al. Vaginal estrogen therapy use and survival in females with breast cancer. *JAMA Oncol*. 2024;10(1):103-108. doi:10.1001/jamaoncol.2023.4508
30. Crandall CJ, Hovey KM, Andrews CA, et al. Breast cancer, endometrial cancer, and cardiovascular events in participants who used vaginal estrogen in the Women's Health Initiative Observational Study. *Menopause*. 2018;25(1):11-20. doi:10.1097/GME.0000000000000956
31. Harding C, Chadwick T, Homer T, et al. Methenamine hippurate compared with antibiotic prophylaxis to prevent recurrent urinary tract infections in women: the ALTAR non-inferiority RCT. *Health Technol Assess*. 2022;26(23):1-172. doi:10.3310/QOIZ6538

32. Botros C, Lozo S, Iyer S, et al. Methenamine hippurate compared with trimethoprim for the prevention of recurrent urinary tract infections: a randomized clinical trial. *Int Urogynecol J*. 2022;33(3):571-580. doi:[10.1007/s00192-021-04849-0](https://doi.org/10.1007/s00192-021-04849-0)
33. Wolff BJ, Price TK, Joyce CJ, Wolfe AJ, Mueller ER. Oral probiotics and the female urinary microbiome: a double-blinded randomized placebo-controlled trial. *Int Urol Nephrol*. 2019;51(12):2149-2159. doi:[10.1007/s11255-019-02282-3](https://doi.org/10.1007/s11255-019-02282-3)
34. Toh SL, Boswell-Ruys CL, Lee BSB, Simpson JM, Clezy KR. Probiotics for preventing urinary tract infection in people with neuropathic bladder. *Cochrane Database Syst Rev*. 2017;9(9):CD010723. doi:[10.1002/14651858.CD010723.pub2](https://doi.org/10.1002/14651858.CD010723.pub2)
35. Toh SL, Lee BB, Ryan S, et al. Probiotics [LGG-BB12 or RC14-GR1] versus placebo as prophylaxis for urinary tract infection in persons with spinal cord injury [ProSCIUTT]: a randomised controlled trial. *Spinal Cord*. 2019;57(7):550-561. doi:[10.1038/s41393-019-0251-y](https://doi.org/10.1038/s41393-019-0251-y)
36. Abdullatif VA, Sur RL, Eshaghian E, et al. Efficacy of probiotics as prophylaxis for urinary tract infections in premenopausal women: a systematic review and meta-analysis. *Cureus*. 2021;13(10):e18843. doi:[10.7759/cureus.18843](https://doi.org/10.7759/cureus.18843)
37. Ala-Jaakkola R, Laitila A, Ouwehand AC, Lehtoranta L. Role of D-mannose in urinary tract infections—a narrative review. *Nutr J*. 2022;21(1):18. doi:[10.1186/s12937-022-00769-x](https://doi.org/10.1186/s12937-022-00769-x)
38. Porru D, Parmigiani A, Tinelli C, et al. Oral D-mannose in recurrent urinary tract infections in women: a pilot study. *J Clin Urol*. 2014;7(3):208-213. doi:[10.1177/2051415813518332](https://doi.org/10.1177/2051415813518332)
39. Kranjčec B, Papeš D, Altarac S. D-mannose powder for prophylaxis of recurrent urinary tract infections in women: a randomized clinical trial. *World J Urol*. 2014;32(1):79-84. doi:[10.1007/s00345-013-1091-6](https://doi.org/10.1007/s00345-013-1091-6)
40. Hayward G, Mort S, Hay AD, et al. D-mannose for prevention of recurrent urinary tract infection among women: a randomized clinical trial. *JAMA Intern Med*. 2024;184(6):619-628. doi:[10.1001/jamainternmed.2024.0264](https://doi.org/10.1001/jamainternmed.2024.0264)
41. Phé V, Pakzad M, Haslam C, et al. Open label feasibility study evaluating D-mannose combined with home-based monitoring of suspected urinary tract infections in patients with multiple sclerosis. *Neurourol Urodyn*. 2017;36(7):1770-1775. doi:[10.1002/nau.23173](https://doi.org/10.1002/nau.23173)
42. Domenici L, Monti M, Bracchi C, et al. D-mannose: a promising support for acute urinary tract infections in women: a pilot study. *Eur Rev Med Pharmacol Sci*. 2016;20(13):2920-2925.
43. Cooper TE, Teng C, Howell M, Teixeira-Pinto A, Jaure A, Wong G. D-mannose for preventing and treating urinary tract infections. *Cochrane Database Syst Rev*. 2022;8(8):CD013608. doi:[10.1002/14651858.CD013608.pub2](https://doi.org/10.1002/14651858.CD013608.pub2)
44. Lenger SM, Bradley MS, Thomas DA, Bertolet MH, Lowder JL, Sutcliffe S. D-mannose vs other agents for recurrent urinary tract infection prevention in adult women: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2020;223(2):265.e1-265.e13. doi:[10.1016/j.ajog.2020.05.048](https://doi.org/10.1016/j.ajog.2020.05.048)
45. Simerville JA, Maxted WC, Pahira JJ. Urinalysis: a comprehensive review. *Am Fam Physician*. 2005;71(6):1153-1162.
46. Advani SD, Polage CR, Fakih MG. Deconstructing the urinalysis: a novel approach to diagnostic and antimicrobial stewardship. *Antimicrob Steward Healthc Epidemiol*. 2021;1(1):e6. doi:[10.1017/ash.2021.167](https://doi.org/10.1017/ash.2021.167)
47. Roberts KB; Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. *Pediatrics*. 2011;128(3):595-610. doi:[10.1542/peds.2011-1330](https://doi.org/10.1542/peds.2011-1330)
48. Bhat RG, Katy TA, Place FC. Pediatric urinary tract infections. *Emerg Med Clin North Am*. 2011;29(3):637-653. doi:[10.1016/j.emc.2011.04.004](https://doi.org/10.1016/j.emc.2011.04.004)
49. Mena Lora AJ, Hua J, Ali M, Krill C, Takhsh E, Bleasdale SC. Changing the culture: impact of a diagnostic stewardship intervention for urine culture testing and CAUTI prevention in an urban safety-net community hospital. *Antimicrob Steward Healthc Epidemiol*. 2024;4(1):e14. doi:[10.1017/ash.2024.12](https://doi.org/10.1017/ash.2024.12)
50. Werneburg GT, Rhoads DD. Diagnostic stewardship for urinary tract infection: a snapshot of the expert guidance. *Cleve Clin J Med*. 2022;89(10):581-587. doi:[10.3949/ccjm.89a.22008](https://doi.org/10.3949/ccjm.89a.22008)
51. O'Grady NP, Alexander E, Alhazzani W, et al. Society of Critical Care Medicine and the Infectious Diseases Society of America Guidelines for evaluating new fever in adult patients in the ICU. *Crit Care Med*. 2023;51(11):1570-1586. doi:[10.1097/CCM.0000000000006022](https://doi.org/10.1097/CCM.0000000000006022)

52. Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM; Infectious Diseases Society of America; American Society of Nephrology; American Geriatric Society. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis*. 2005;40(5):643-654. doi:10.1086/427507
53. Nicolle LE, Gupta K, Bradley SF, et al. Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2019;68(10):1611-1615. doi:10.1093/cid/ciz021
54. Flokas ME, Andreatos N, Alevizakos M, Kalbasi A, Onur P, Mylonakis E. Inappropriate management of asymptomatic patients with positive urine cultures: a systematic review and meta-analysis. *Open Forum Infect Dis*. 2017;4(4):ofx207. doi:10.1093/ofid/ofx207
55. Stamm WE, Counts GW, Running KR, Fihn S, Turck M, Holmes KK. Diagnosis of coliform infection in acutely dysuric women. *N Engl J Med*. 1982;307(8):463-468. doi:10.1056/NEJM198208193070802
56. Hooton TM, Roberts PL, Cox ME, Stapleton AE. Voided midstream urine culture and acute cystitis in premenopausal women. *N Engl J Med*. 2013;369(20):1883-1891. doi:10.1056/NEJMoa1302186
57. Tullus K. Defining urinary tract infection by bacterial colony counts: a case for less than 100,000 colonies/mL as the threshold. *Pediatr Nephrol*. 2019;34(10):1651-1653. doi:10.1007/s00467-019-04291-x
58. Kass EH. Asymptomatic infections of the urinary tract. *Trans Assoc Am Physicians*. 1956;69:56-64.
59. Szlachta-McGinn A, Douglass KM, Chung UYR, Jackson NJ, Nickel JC, Ackerman AL. Molecular diagnostic methods versus conventional urine culture for diagnosis and treatment of urinary tract infection: a systematic review and meta-analysis. *Eur Urol Open Sci*. 2022;44:113-124. doi:10.1016/j.euros.2022.08.009
60. Hilt EE, McKinley K, Pearce MM, et al. Urine is not sterile: use of enhanced urine culture techniques to detect resident bacterial flora in the adult female bladder. *J Clin Microbiol*. 2014;52(3):871-876. doi:10.1128/JCM.02876-13
61. Lewis DA, Gumede LYE, van der Hoven LA, et al. Antimicrobial susceptibility of organisms causing community-acquired urinary tract infections in Gauteng Province, South Africa. *S Afr Med J*. 2013;103(6):377-381. doi:10.7196/SAMJ.6722
62. Wolfe AJ, Toh E, Shibata N, et al. Evidence of uncultivated bacteria in the adult female bladder. *J Clin Microbiol*. 2012;50(4):1376-1383. doi:10.1128/JCM.05852-11
63. Hugon P, Dufour JC, Colson P, Fournier PE, Sallah K, Raoult D. A comprehensive repertoire of prokaryotic species identified in human beings. *Lancet Infect Dis*. 2015;15(10):1211-1219. doi:10.1016/S1473-3099(15)00293-5
64. Neugent ML, Hulyalkar NV, Nguyen VH, Zimmern PE, De Nisco NJ. Advances in understanding the human urinary microbiome and its potential role in urinary tract infection. *mBio*. 2020;11(2):e00218-e00220. doi:10.1128/mBio.00218-20
65. Kim Y, Seo MR, Kim SJ, et al. Usefulness of blood cultures and radiologic imaging studies in the management of patients with community-acquired acute pyelonephritis. *Infect Chemother*. 2017;49(1):22-30. doi:10.3947/ic.2017.49.1.22
66. Soulen MC, Fishman EK, Goldman SM, Gatewood OM. Bacterial renal infection: role of CT. *Radiology*. 1989;171(3):703-707. doi:10.1148/radiology.171.3.2655002
67. Pierce C, Keniston A, Albert RK. Imaging in acute pyelonephritis: utilization, findings, and effect on management. *South Med J*. 2019;112(2):118-124. doi:10.14423/SMJ.0000000000000936
68. Enikeev DV, Glybochko P, Alyaev Y, Enikeev M, Rapoport L. Imaging technologies in the diagnosis and treatment of acute pyelonephritis. *Urologia*. 2017;84(3):179-184. doi:10.5301/uj.5000234
69. Johnson JR, Russo TA. Acute pyelonephritis in adults. *N Engl J Med*. 2018;378(1):48-59. doi:10.1056/NEJMcip1702758
70. Faletti R, Cassinis MC, Fonio P, et al. Diffusion-weighted imaging and apparent diffusion coefficient values versus contrast-enhanced MR imaging in the identification and characterisation of acute pyelonephritis. *Eur Radiol*. 2013;23(12):3501-3508. doi:10.1007/s00330-013-2951-6
71. Leyendecker JR, Clingan MJ. Magnetic resonance urography update—are we there yet? *Semin Ultrasound CT MR*. 2009;30(4):246-257. doi:10.1053/j.sult.2009.03.004
72. Tambyah PA, Maki DG. The relationship between pyuria and infection in patients with indwelling urinary catheters: a prospective study of 761 patients. *Arch Intern Med*. 2000;160(5):673-677. doi:10.1001/archinte.160.5.673
73. Warren JW, Tenney JH, Hoopes JM, Muncie HL, Anthony WC. A prospective microbiologic study of bacteriuria in patients with chronic indwelling urethral catheters. *J Infect Dis*. 1982;146(6):719-723. doi:10.1093/infdis/146.6.719



74. Abdel-Latif M, Mosbah A, El Bahnasawy MS, Elsayy E, Shaaban AA. Asymptomatic bacteriuria in men with orthotopic ileal neobladders: possible relationship to nocturnal enuresis. *BJU Int*. 2005;96(3):391-396. doi:10.1111/j.1464-410X.2005.05637.x
75. Morris EJ, Bracken RB, Hopfer RL, Mills K, Rodriguez DB. Urinary findings in 20 asymptomatic patients with an ileal conduit. *J Enterostomal Ther*. 1982;9(2):24-27. doi:10.1097/00152192-198203000-00022
76. Gupta K, Hooton TM, Naber KG, et al; Infectious Diseases Society of America; European Society for Microbiology and Infectious Diseases. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*. 2011;52(5):e103-e120. doi:10.1093/cid/ciq257
77. Hooton TM, Bradley SF, Cardenas DD, et al; Infectious Diseases Society of America. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. *Clin Infect Dis*. 2010;50(5):625-663. doi:10.1086/650482
78. Huttner A, Kowalczyk A, Turjeman A, et al. Effect of 5-day nitrofurantoin vs single-dose fosfomycin on clinical resolution of uncomplicated lower urinary tract infection in women: a randomized clinical trial. *JAMA*. 2018;319(17):1781-1789. doi:10.1001/jama.2018.3627
79. Park DW, Peck KR, Chung MH, et al. Comparison of ertapenem and ceftriaxone therapy for acute pyelonephritis and other complicated urinary tract infections in Korean adults: a randomized, double-blind, multicenter trial. *J Korean Med Sci*. 2012;27(5):476-483. doi:10.3346/jkms.2012.27.5.476
80. Kaye KS, Gupta V, Mulgirigama A, et al. Antimicrobial resistance trends in urine *Escherichia coli* isolates from adult and adolescent females in the United States from 2011 to 2019: rising ESBL strains and impact on patient management. *Clin Infect Dis*. 2021;73(11):1992-1999. doi:10.1093/cid/ciab560
81. Raz R, Schiller D, Nicolle LE. Chronic indwelling catheter replacement before antimicrobial therapy for symptomatic urinary tract infection. *J Urol*. 2000;164(4):1254-1258. doi:10.1016/S0022-5347(05)67150-9
82. Tenney J, Hudson N, Alnifaidy H, Li JTC, Fung KH. Risk factors for acquiring multidrug-resistant organisms in urinary tract infections: a systematic literature review. *Saudi Pharm J*. 2018;26(5):678-684. doi:10.1016/j.jsps.2018.02.023
83. Larramendy S, Deglaire V, Dusollier P, et al. Risk factors of extended-spectrum beta-lactamases-producing *Escherichia coli* community acquired urinary tract infections: a systematic review. *Infect Drug Resist*. 2020;13:3945-3955. doi:10.2147/IDR.S269033
84. Brown DG, Worby CJ, Pender MA, et al. Development of a prediction model for the acquisition of extended spectrum beta-lactam-resistant organisms in US international travellers. *J Travel Med*. 2023;30(6):taad028. doi:10.1093/jtm/taad028
85. Kadry N, Natarajan M, Bein E, Kim P, Farley J. discordant clinical and microbiological outcomes are associated with late clinical relapse in clinical trials for complicated urinary tract infections. *Clin Infect Dis*. 2023;76(10):1768-1775. doi:10.1093/cid/ciad010
86. Zaoutis T, Shaikh N, Fisher BT, et al. Short-course therapy for urinary tract infections in children: the SCOUT randomized clinical trial. *JAMA Pediatr*. 2023;177(8):782-789. doi:10.1001/jamapediatrics.2023.1979
87. Lafaurie M, Chevret S, Fontaine JP, et al; PROSTASHORT Study Group. Antimicrobial for 7 or 14 days for febrile urinary tract infection in men: a multicenter noninferiority double-blind, placebo-controlled, randomized clinical trial. *Clin Infect Dis*. 2023;76(12):2154-2162. doi:10.1093/cid/ciad070
88. Lawrenson RA, Logie JW. Antibiotic failure in the treatment of urinary tract infections in young women. *J Antimicrob Chemother*. 2001;48(6):895-901. doi:10.1093/jac/48.6.895
89. Efstathiou SP, Pefanis AV, Tsioulos DI, et al. Acute pyelonephritis in adults: prediction of mortality and failure of treatment. *Arch Intern Med*. 2003;163(10):1206-1212. doi:10.1001/archinte.163.10.1206
90. Pertel PE, Haverstock D. Risk factors for a poor outcome after therapy for acute pyelonephritis. *BJU Int*. 2006;98(1):141-147. doi:10.1111/j.1464-410X.2006.06222.x
91. Karve S, Ryan K, Peeters P, et al. The impact of initial antibiotic treatment failure: real-world insights in patients with complicated urinary tract infection. *J Infect*. 2018;76(2):121-131. doi:10.1016/j.jinf.2017.11.001
92. Rosa R, Abbo LM, Raney K, Tookes HE III, Supino M. Antimicrobial resistance in urinary tract infections at a large urban ED: factors contributing to empiric treatment failure. *Am J Emerg Med*. 2017;35(3):397-401. doi:10.1016/j.ajem.2016.11.021
93. Jorgensen S, Zurayk M, Yeung S, et al. Risk factors for early return visits to the emergency department in patients with urinary tract infection. *Am J Emerg Med*. 2018;36(1):12-17. doi:10.1016/j.ajem.2017.06.041

94. Pujades-Rodriguez M, West RM, Wilcox MH, Sandoe J. Lower urinary tract infections: management, outcomes and risk factors for antibiotic re-prescription in primary care. *EClinicalMedicine*. 2019;14:23-31. doi:10.1016/j.eclinm.2019.07.012
95. Eliakim-Raz N, Babitch T, Shaw E, et al; RESCUING Study Group. Risk factors for treatment failure and mortality among hospitalized patients with complicated urinary tract infection: a multicenter retrospective cohort study (RESCUING study group). *Clin Infect Dis*. 2019;68(1):29-36. doi:10.1093/cid/ciy418
96. Martischang R, Godycki-Ćwirko M, Kowalczyk A, et al. Risk factors for treatment failure in women with uncomplicated lower urinary tract infection. *PLoS One*. 2021;16(8):e0256464. doi:10.1371/journal.pone.0256464
97. Trautner BW, Kaye KS, Gupta V, et al. Risk factors associated with antimicrobial resistance and adverse short-term health outcomes among adult and adolescent female outpatients with uncomplicated urinary tract infection. *Open Forum Infect Dis*. 2022;9(12):ofac623. doi:10.1093/ofid/ofac623
98. Dunne MW, Puttagunta S, Aronin SI, Brossette S, Murray J, Gupta V. Impact of empirical antibiotic therapy on outcomes of outpatient urinary tract infection due to nonsusceptible *Enterobacterales*. *Microbiol Spectr*. 2022;10(1):e0235921. doi:10.1128/spectrum.02359-21
99. Lamas Ferreiro JL, Álvarez Otero J, González González L, et al. *Pseudomonas aeruginosa* urinary tract infections in hospitalized patients: mortality and prognostic factors. *PLoS One*. 2017;12(5):e0178178. doi:10.1371/journal.pone.0178178
100. Michael M, Hodson EM, Craig JC, Martin S, Moyer VA. Short versus standard duration oral antibiotic therapy for acute urinary tract infection in children. *Cochrane Database Syst Rev*. 2003;(1):CD003966. doi:10.1002/14651858.CD003966
101. Fitzgerald A, Mori R, Lakhanpaul M, Tullus K. Antibiotics for treating lower urinary tract infection in children. *Cochrane Database Syst Rev*. 2012;2012(8):CD006857. doi:10.1002/14651858.CD006857.pub2
102. Moreira MVB, de Freitas LR, Fonseca LM, et al. Shorter versus longer-course of antibiotic therapy for urinary tract infections in pediatric population: an updated meta-analysis. *Eur J Pediatr*. 2024;183(5):2037-2047. doi:10.1007/s00431-024-05512-8
103. Goodlet KJ, Benhalima FZ, Nailor MD. A systematic review of single-dose aminoglycoside therapy for urinary tract infection: is it time to resurrect an old strategy? *Antimicrob Agents Chemother*. 2018;63(1):e02165-e18. doi:10.1128/AAC.02165-18
104. Strohmeier Y, Hodson EM, Willis NS, Webster AC, Craig JC. Antibiotics for acute pyelonephritis in children. *Cochrane Database Syst Rev*. 2014;7. doi:10.1002/14651858.CD003772.pub4
105. Montini G, Tessitore A, Console K, Ronfani L, Barbi E, Pennesi M; STOP Trial Group. Short oral antibiotic therapy for pediatric febrile urinary tract infections: a randomized trial. *Pediatrics*. 2024;153(1):e2023062598. doi:10.1542/peds.2023-062598
106. Fox MT, Amoah J, Hsu AJ, Herzke CA, Gerber JS, Tamma PD. Comparative effectiveness of antibiotic treatment duration in children with pyelonephritis. *JAMA Netw Open*. 2020;3(5):e203951. doi:10.1001/jamanetworkopen.2020.3951
107. Afolabi TM, Goodlet KJ, Fairman KA. Association of antibiotic treatment duration with recurrence of uncomplicated urinary tract infection in pediatric patients. *Ann Pharmacother*. 2020;54(8):757-766. doi:10.1177/1060028019900650
108. Huttner A, Verhaegh EM, Harbarth S, Muller AE, Theuretzbacher U, Mouton JW. Nitrofurantoin revisited: a systematic review and meta-analysis of controlled trials. *J Antimicrob Chemother*. 2015;70(9):2456-2464. doi:10.1093/jac/dkv147
109. Kim DK, Kim JH, Lee JY, et al. Reappraisal of the treatment duration of antibiotic regimens for acute uncomplicated cystitis in adult women: a systematic review and network meta-analysis of 61 randomised clinical trials. *Lancet Infect Dis*. 2020;20(9):1080-1088. doi:10.1016/S1473-3099(20)30121-3
110. Christiaens TCM, De Meyere M, Verschraegen G, Peersman W, Heytens S, De Maeseneer JM. Randomised controlled trial of nitrofurantoin versus placebo in the treatment of uncomplicated urinary tract infection in adult women. *Br J Gen Pract*. 2002;52(482):729-734.
111. Trienekens TA, Stobberingh EE, Winkens RA, Houben AW. Different lengths of treatment with co-trimoxazole for acute uncomplicated urinary tract infections in women. *BMJ*. 1989;299(6711):1319-1322. doi:10.1136/bmj.299.6711.1319
112. Gossius G, Vorland L. A randomised comparison of single-dose vs three-day and ten-day therapy with trimethoprim-sulfamethoxazole for acute cystitis in women. *Scand J Infect Dis*. 1984;16(4):373-379. doi:10.3109/00365548409073963

113. Hooton TM, Latham RH, Wong ES, Johnson C, Roberts PL, Stamm WE. Ofloxacin versus trimethoprim-sulfamethoxazole for treatment of acute cystitis. *Antimicrob Agents Chemother*. 1989;33(8):1308-1312. doi:10.1128/AAC.33.8.1308
114. Neringer R, Forsgren A, Hansson C, Ode B; The South Swedish Loxex Study Group. Lomefloxacin versus norfloxacin in the treatment of uncomplicated urinary tract infections: three-day versus seven-day treatment. *Scand J Infect Dis*. 1992;24(6):773-780. doi:10.3109/00365549209062463
115. Trienekens TA, London NH, Houben AW, De Jong RA, Stobberingh EE. Treating acute urinary tract infections: an RCT of 3-day versus 7-day norfloxacin. *Can Fam Physician*. 1993;39:514-518.
116. Arredondo-García JL, Figueroa-Damián R, Rosas A, et al; uUTI Latin American Study Group. Comparison of short-term treatment regimen of ciprofloxacin versus long-term treatment regimens of trimethoprim/sulfamethoxazole or norfloxacin for uncomplicated lower urinary tract infections: a randomized, multicentre, open-label, prospective study. *J Antimicrob Chemother*. 2004;54(4):840-843. doi:10.1093/jac/dkh414
117. Vogel T, Verreault R, Gourdeau M, Morin M, Grenier-Gosselin L, Rochette L. Optimal duration of antibiotic therapy for uncomplicated urinary tract infection in older women: a double-blind randomized controlled trial. *CMAJ*. 2004;170(4):469-473.
118. Bahman H, Hyaide O, Omid N, et al. Comparison of 3-day and 7-day ciprofloxacin regimen for the treatment of uncomplicated urinary tract infection in women: a randomized double-blind clinical trial. *Iranian J Clin Infect Dis*. 2010;55(2):70-74.
119. Boerema JB, Willems FT. Fosfomycin trometamol in a single dose versus norfloxacin for seven days in the treatment of uncomplicated urinary infections in general practice. *Infection*. 1990;18(suppl 2):S80-S88. doi:10.1007/BF01643433
120. Crocchiolo P; Multicenter Group of General Practitioners. Single-dose fosfomycin trometamol versus multiple-dose cotrimoxazole in the treatment of lower urinary tract infections in general practice. *Chemotherapy*. 1990;36(suppl 1):37-40. doi:10.1159/000238815
121. Selvaggi FP, Dittono P, Traficante A, Battaglia M, Di Lorenzo V. Fosfomycin trometamol (Monuril) versus norfloxacin in single dose for adult female uncomplicated UTIs: multicenter randomized, double-blind study. *Chemotherapy*. 1990;36(suppl 1):31-33. doi:10.1159/000238813
122. Naber KG, Thyroff-Friesinger U. Fosfomycin trometamol versus ofloxacin/co-trimoxazole as single dose therapy of acute uncomplicated urinary tract infection in females: a multicentre study. *Infection*. 1990;18(suppl 2):S70-S76. doi:10.1007/BF01643431
123. de Jong Z, Pontonnier F, Plante P. Single-dose fosfomycin trometamol (Monuril) versus multiple-dose norfloxacin: results of a multicenter study in females with uncomplicated lower urinary tract infections. *Urol Int*. 1991;46(4):344-348. doi:10.1159/000282164
124. Van Pienbroek E, Hermans J, Kaptein AA, Mulder JD. Fosfomycin trometamol in a single dose versus seven days nitrofurantoin in the treatment of acute uncomplicated urinary tract infections in women. *Pharm World Sci*. 1993;15(6):257-262. doi:10.1007/BF01871127
125. Elhanan G, Tabenkin H, Yahalom R, Raz R. Single-dose fosfomycin trometamol versus 5-day cephalixin regimen for treatment of uncomplicated lower urinary tract infections in women. *Antimicrob Agents Chemother*. 1994;38(11):2612-2614. doi:10.1128/AAC.38.11.2612
126. Minassian MA, Lewis DA, Chattopadhyay D, Bovill B, Duckworth GJ, Williams JD. A comparison between single-dose fosfomycin trometamol (Monuril) and a 5-day course of trimethoprim in the treatment of uncomplicated lower urinary tract infection in women. *Int J Antimicrob Agents*. 1998;10(1):39-47. doi:10.1016/S0924-8579(98)00021-1
127. Ceran N, Mert D, Kocdogan FY, et al. A randomized comparative study of single-dose fosfomycin and 5-day ciprofloxacin in female patients with uncomplicated lower urinary tract infections. *J Infect Chemother*. 2010;16(6):424-430. doi:10.1007/s10156-010-0079-z
128. PIVYA. Highlights of prescribing information. US Food and Drug Administration; 2024. Accessed May 25, 2024. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2024/216483s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/216483s000lbl.pdf)
129. Richards HH. Comparative efficacy of 3-day and 7-day chemotherapy with twice-daily pivmecillinam in urinary tract infections seen in general practice. *Curr Med Res Opin*. 1984;9(3):197-203. doi:10.1185/03007998409109580
130. Pitkääjärvi T, Pyykönen ML, Kannisto K, Piippo T, Viita P. Pivmecillinam treatment in acute cystitis: three versus seven days study. *Arzneimittelforschung*. 1990;40(10):1156-1158.

131. Ferry SA, Holm SE, Stenlund H, Lundholm R, Monsen TJ. Clinical and bacteriological outcome of different doses and duration of pivmecillinam compared with placebo therapy of uncomplicated lower urinary tract infection in women: the LUTIW project. *Scand J Prim Health Care*. 2007;25(1):49-57. doi:10.1080/02813430601183074
132. Jansåker F, Thønnings S, Hertz FB, et al. Three versus five days of pivmecillinam for community-acquired uncomplicated lower urinary tract infection: a randomised, double-blind, placebo-controlled superiority trial. *EClinicalMedicine*. 2019;12:62-69. doi:10.1016/j.eclinm.2019.06.009
133. Wagenlehner F, Perry CR, Hooton TM, et al. Oral gepotidacin versus nitrofurantoin in patients with uncomplicated urinary tract infection (EAGLE-2 and EAGLE-3): two randomised, controlled, double-blind, double-dummy, phase 3, non-inferiority trials. *Lancet*. 2024;403(10428):741-755. doi:10.1016/S0140-6736(23)02196-7
134. Dinh A, Davido B, Etienne M, et al. Is 5 days of oral fluoroquinolone enough for acute uncomplicated pyelonephritis? The DTP randomized trial. *Eur J Clin Microbiol Infect Dis*. 2017;36(8):1443-1448. doi:10.1007/s10096-017-2951-6
135. Peterson J, Kaul S, Khashab M, Fisher AC, Kahn JB. A double-blind, randomized comparison of levofloxacin 750 mg once-daily for five days with ciprofloxacin 400/500 mg twice-daily for 10 days for the treatment of complicated urinary tract infections and acute pyelonephritis. *Urology*. 2008;71(1):17-22. doi:10.1016/j.urology.2007.09.002
136. Klausner HA, Brown P, Peterson J, et al. A trial of levofloxacin 750 mg once daily for 5 days versus ciprofloxacin 400 mg and/or 500 mg twice daily for 10 days in the treatment of acute pyelonephritis. *Curr Med Res Opin*. 2007;23(11):2637-2645. doi:10.1185/030079907X233340
137. Eliakim-Raz N, Yahav D, Paul M, Leibovici L. Duration of antibiotic treatment for acute pyelonephritis and septic urinary tract infection—7 days or less versus longer treatment: systematic review and meta-analysis of randomized controlled trials. *J Antimicrob Chemother*. 2013;68(10):2183-2191. doi:10.1093/jac/dkt177
138. Talan DA, Stamm WE, Hooton TM, et al. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis in women: a randomized trial. *JAMA*. 2000;283(12):1583-1590. doi:10.1001/jama.283.12.1583
139. Sandberg T, Skoog G, Hermansson AB, et al. Ciprofloxacin for 7 days versus 14 days in women with acute pyelonephritis: a randomised, open-label and double-blind, placebo-controlled, non-inferiority trial. *Lancet*. 2012;380(9840):484-490. doi:10.1016/S0140-6736(12)60608-4
140. Ode B, Bröms M, Walder M, Cronberg S. Failure of excessive doses of ampicillin to prevent bacterial relapse in the treatment of acute pyelonephritis. *Acta Med Scand*. 1980;207(4):305-307. doi:10.1111/j.0954-6820.1980.tb09725.x
141. Jernelius H, Zbornik J, Bauer CA. One or three weeks' treatment of acute pyelonephritis: a double-blind comparison, using a fixed combination of pivampicillin plus pivmecillinam. *Acta Med Scand*. 1988;223(5):469-477. doi:10.1111/j.0954-6820.1988.tb15899.x
142. Mensa J, Moreno-Martinez A, Martinez J. Treatment of acute uncomplicated pyelonephritis (AUP): a randomized trial comparing 7- vs. 14-day therapy. Presented at: American Society for Microbiology Abstracts of the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy. September 1999; San Francisco, CA.
143. Wagenlehner FM, Umeh O, Steenberg J, Yuan G, Darouiche RO. Ceftolozane-tazobactam compared with levofloxacin in the treatment of complicated urinary-tract infections, including pyelonephritis: a randomised, double-blind, phase 3 trial (ASPECT-cUTI). *Lancet*. 2015;385(9981):1949-1956. doi:10.1016/S0140-6736(14)62220-0
144. Langford BJ, Daneman N, Diong C, et al. Antibiotic Selection and duration for catheter-associated urinary tract infection in non-hospitalized older adults: a population-based cohort study. *Antimicrob Steward Healthc Epidemiol*. 2023;3(1):e132. doi:10.1017/ash.2023.176
145. Yahav D, Franceschini E, Koppel F, et al; Bacteremia Duration Study Group. Seven versus 14 days of antibiotic therapy for uncomplicated gram-negative bacteremia: a noninferiority randomized controlled trial. *Clin Infect Dis*. 2019;69(7):1091-1098. doi:10.1093/cid/ciy1054
146. von Dach E, Albrich WC, Brunel AS, et al. Effect of C-reactive protein-guided antibiotic treatment duration, 7-day treatment, or 14-day treatment on 30-day clinical failure rate in patients with uncomplicated gram-negative bacteremia: a randomized clinical trial. *JAMA*. 2020;323(21):2160-2169. doi:10.1001/jama.2020.6348
147. Molina J, Montero-Mateos E, Praena-Segovia J, et al; SHORTEN trial team. Seven-versus 14-day course of antibiotics for the treatment of bloodstream infections by Enterobacterales: a randomized, controlled trial. *Clin Microbiol Infect*. 2022;28(4):550-557. doi:10.1016/j.cmi.2021.09.001

148. Turjeman A, von Dach E, Molina J, et al. Duration of antibiotic treatment for gram-negative bacteremia—systematic review and individual participant data (IPD) meta-analysis. *EClinicalMedicine*. 2022;55:101750. doi:10.1016/j.eclinm.2022.101750
149. Al Lawati H, Blair BM, Larnard J. Urinary tract infections: core curriculum 2024. *Am J Kidney Dis*. 2024;83(1):90-100. doi:10.1053/j.ajkd.2023.08.009
150. Liu F, MacDonald B, Jain R, et al. Prevalence and treatment of asymptomatic bacteriuria at academic and critical-access hospitals—opportunities for stewardship efforts. *Infect Control Hosp Epidemiol*. 2023;44(6):979-981. doi:10.1017/ice.2022.143
151. Petty LA, Vaughn VM, Flanders SA, et al. Risk factors and outcomes associated with treatment of asymptomatic bacteriuria in hospitalized patients. *JAMA Intern Med*. 2019;179(11):1519-1527. doi:10.1001/jamainternmed.2019.2871
152. Petty LA, Vaughn VM, Flanders SA, et al. Assessment of testing and treatment of asymptomatic bacteriuria initiated in the emergency department. *Open Forum Infect Dis*. 2020;7(12):ofaa537. doi:10.1093/ofid/ofaa537
153. Smaill FM, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. *Cochrane Database Syst Rev*. 2019;2019(11):CD000490. doi:10.1002/14651858.CD000490.pub4
154. Henderson JT, Webber EM, Bean SI. Screening for asymptomatic bacteriuria in adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2019;322(12):1195-1205. doi:10.1001/jama.2019.10060
155. Grabe M, Forsgren A, Hellsten S. The effect of a short antibiotic course in transurethral prostatic resection. *Scand J Urol Nephrol*. 1984;18(1):37-42. doi:10.3109/00365598409182161
156. Grabe M, Forsgren A, Björk T, Hellsten S. Controlled trial of a short and a prolonged course with ciprofloxacin in patients undergoing transurethral prostatic surgery. *Eur J Clin Microbiol*. 1987;6(1):11-17. doi:10.1007/BF02097183
157. Sayin Kutlu S, Aybek Z, Tekin K, et al. Is short course of antimicrobial therapy for asymptomatic bacteriuria before urologic surgical procedures sufficient? *J Infect Dev Ctries*. 2012;6(2):143-147. doi:10.3855/jidc.1781
158. Lightner DJ, Wymer K, Sanchez J, Kavoussi L. Best practice statement on urologic procedures and antimicrobial prophylaxis. *J Urol*. 2020;203(2):351-356. doi:10.1097/JU.0000000000000509
159. Moehring RW, Yarrington ME, Warren BG, et al; Centers for Disease Control and Prevention's Prevention Epicenters Program. Evaluation of an opt-out protocol for antibiotic de-escalation in patients with suspected sepsis: a multicenter, randomized, controlled trial. *Clin Infect Dis*. 2023;76(3):433-442. doi:10.1093/cid/ciac787
160. Leone M, Bechis C, Baumstarck K, et al; AZUREA Network Investigators. De-escalation versus continuation of empirical antimicrobial treatment in severe sepsis: a multicenter non-blinded randomized noninferiority trial. *Intensive Care Med*. 2014;40(10):1399-1408. doi:10.1007/s00134-014-3411-8
161. Chopra V, O'Horo JC, Rogers MAM, Maki DG, Safdar N. The risk of bloodstream infection associated with peripherally inserted central catheters compared with central venous catheters in adults: a systematic review and meta-analysis. *Infect Control Hosp Epidemiol*. 2013;34(9):908-918. doi:10.1086/671737
162. Chopra V, Anand S, Krein SL, Chenoweth C, Saint S. Bloodstream infection, venous thrombosis, and peripherally inserted central catheters: reappraising the evidence. *Am J Med*. 2012;125(8):733-741. doi:10.1016/j.amjmed.2012.04.010
163. Chopra V, Flanders SA, Saint S. The problem with peripherally inserted central catheters. *JAMA*. 2012;308(15):1527-1528. doi:10.1001/jama.2012.12704
164. Chopra V, Anand S, Hickner A, et al. Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. *Lancet*. 2013;382(9889):311-325. doi:10.1016/S0140-6736(13)60592-9
165. Tamma PD, Avdic E, Li DX, Dzintars K, Cosgrove SE. Association of adverse events with antibiotic use in hospitalized patients. *JAMA Intern Med*. 2017;177(9):1308-1315. doi:10.1001/jamainternmed.2017.1938
166. Rybak MJ, Le J, Lodise TP, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: a revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. *Am J Health Syst Pharm*. 2020;77(11):835-864. doi:10.1093/ajhp/zxaa036
167. Keller SC, Williams D, Gavani M, et al. Rates of and risk factors for adverse drug events in outpatient parenteral antimicrobial therapy. *Clin Infect Dis*. 2018;66(1):11-19. doi:10.1093/cid/cix733



168. Rieger KL, Bosso JA, MacVane SH, Temple Z, Wahlquist A, Bohm N. Intravenous-only or intravenous transitioned to oral antimicrobials for enterobacteriaceae-associated bacteremic urinary tract infection. *Pharmacotherapy*. 2017;37(11):1479-1483. doi:10.1002/phar.2024
169. Gamble KC, Rose DT, Sapozhnikov J. Intravenous to oral antibiotics versus intravenous antibiotics: a step-up or a step-down for extended spectrum  $\beta$ -lactamase (ESBL)-producing urinary tract infections without concomitant bacteraemia? *Int J Antimicrob Agents*. 2022;59(3):106541. doi:10.1016/j.ijantimicag.2022.106541
170. Mouwen AMA, Dijkstra JA, Jong E, Buijtel PCAM, Pasker-de Jong PCM, Nagtegaal JE. Early switching of antibiotic therapy from intravenous to oral using a combination of education, pocket-sized cards and switch advice: a practical intervention resulting in reduced length of hospital stay. *Int J Antimicrob Agents*. 2020;55(1):105769. doi:10.1016/j.ijantimicag.2019.07.020
171. Gandhi K, Wrzesinski M, Bunnell K, Gible A. Oral antibiotic step-down therapy for nonstaphylococcal gram-positive bloodstream infections. *Diagn Microbiol Infect Dis*. 2023;107(4):116068. doi:10.1016/j.diagmicrobio.2023.116068
172. Olson J, Franz-O'Neal E, Cipriano FA, Ou Z, Presson AP, Thorell EA. Impact of early oral antibiotic therapy in infants with bacteremic urinary tract infections. *Hosp Pediatr*. 2022;12(7):632-638. doi:10.1542/hpeds.2021-006479
173. McAlister MJ, Rose DT, Hudson FP, Padilla-Tolentino E, Jaso TC. Oral  $\beta$ -lactams vs fluoroquinolones and trimethoprim/sulfamethoxazole for step-down therapy for *Escherichia coli*, *Proteus mirabilis*, and *Klebsiella pneumoniae* bacteremia. *Am J Health Syst Pharm*. 2023;80(suppl 1):S33-S41. doi:10.1093/ajhp/zxac202
174. Eron LJ, Passos S. Early discharge of infected patients through appropriate antibiotic use. *Arch Intern Med*. 2001;161(1):61-65. doi:10.1001/archinte.161.1.61
175. Khan DA, Banerji A, Blumenthal KG, et al; Chief Editor(s); Workgroup Contributors; Joint Task Force on Practice Parameters Reviewers. Drug allergy: a 2022 practice parameter update. *J Allergy Clin Immunol*. 2022;150(6):1333-1393. doi:10.1016/j.jaci.2022.08.028
176. Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. Antibiotic allergy. *Lancet*. 2019;393(10167):183-198. doi:10.1016/S0140-6736(18)32218-9
177. Blumenthal KG, Li Y, Banerji A, Yun BJ, Long AA, Walensky RP. The cost of penicillin allergy evaluation. *J Allergy Clin Immunol Pract*. 2018;6(3):1019-1027.e2. doi:10.1016/j.jaip.2017.08.006
178. Hayden DA, White BP, Neely S, Bennett KK. Impact of fluoroquinolone susceptibility suppression on discharge prescribing for acute uncomplicated cystitis. *Open Forum Infect Dis*. 2023;10(10):ofad459. doi:10.1093/ofid/ofad459
179. Langford BJ, Seah J, Chan A, Downing M, Johnstone J, Matukas LM. Antimicrobial stewardship in the microbiology laboratory: impact of selective susceptibility reporting on ciprofloxacin utilization and susceptibility of gram-negative isolates to ciprofloxacin in a hospital setting. *J Clin Microbiol*. 2016;54(9):2343-2347. doi:10.1128/JCM.00950-16
180. Langford BJ, Daneman N, Diong C, et al. Antibiotic susceptibility reporting and association with antibiotic prescribing: a cohort study. *Clin Microbiol Infect*. 2021;27(4):568-575. doi:10.1016/j.cmi.2020.10.001
181. Nicolle LE. Asymptomatic bacteriuria in the elderly. *Infect Dis Clin North Am*. 1997;11(3):647-662. doi:10.1016/S0891-5520(05)70378-0
182. Ariathianto Y. Asymptomatic bacteriuria—prevalence in the elderly population. *Aust Fam Physician*. 2011;40(10):805-809.
183. Lin YT, Chen LK, Lin MH, Hwang SJ. Asymptomatic bacteriuria among the institutionalized elderly. *J Chin Med Assoc*. 2006;69(5):213-217. doi:10.1016/S1726-4901(09)70221-7
184. Childs SJ, Egan RJ. Bacteriuria and urinary infections in the elderly. *Urol Clin North Am*. 1996;23(1):43-54. doi:10.1016/S0094-0143(05)70292-5
185. Boscia JA, Kobasa WD, Knight RA, Abrutyn E, Levison ME, Kaye D. Epidemiology of bacteriuria in an elderly ambulatory population. *Am J Med*. 1986;80(2):208-214. doi:10.1016/0002-9343(86)90011-2
186. Boscia JA, Kobasa WD, Abrutyn E, Levison ME, Kaplan AM, Kaye D. Lack of association between bacteriuria and symptoms in the elderly. *Am J Med*. 1986;81(6):979-982. doi:10.1016/0002-9343(86)90391-8
187. Ostrow O, Prodanuk M, Foong Y, et al. Decreasing misdiagnoses of urinary tract infections in a pediatric emergency department. *Pediatrics*. 2022;150(1):e2021055866. doi:10.1542/peds.2021-055866
188. Choi DM, Heo TH, Yim HE, Yoo KH. Evaluation of new American Academy of Pediatrics guideline for febrile urinary tract infection. *Korean J Pediatr*. 2015;58(9):341-346. doi:10.3345/kjp.2015.58.9.341



189. Brandström P, Lindén M. How Swedish guidelines on urinary tract infections in children compare to Canadian, American and European guidelines. *Acta Paediatr*. 2021;110(6):1759-1771. doi:10.1111/apa.15727
190. 't Hoen LA, Bogaert G, Radmayr C, et al. Update of the EAU/ESPU guidelines on urinary tract infections in children. *J Pediatr Urol*. 2021;17(2):200-207. doi:10.1016/j.jpuro.2021.01.037
191. Azzarone G, Liewehr S, O'Connor K. Cystitis. *Pediatr Rev*. 2007;28(12):474-476. doi:10.1542/pir.28.12.474
192. Raszka WV Jr, Khan O. Pyelonephritis. *Pediatr Rev*. 2005;26(10):364-370. doi:10.1542/pir.26.10.364
193. SUBCOMMITTEE ON URINARY TRACT INFECTION. Reaffirmation of AAP Clinical Practice Guideline: the diagnosis and management of the initial urinary tract infection in febrile infants and young children 2-24 months of age. *Pediatrics*. 2016;138(6):e20163026. doi:10.1542/peds.2016-3026
194. Tullus K, Shaikh N. Urinary tract infections in children. *Lancet*. 2020;395(10237):1659-1668. doi:10.1016/S0140-6736(20)30676-0
195. Karavanaki K, Koufadaki AM, Soldatou A, et al. Fever duration during treated urinary tract infections and development of permanent renal lesions. *Arch Dis Child*. 2019;104(5):466-470. doi:10.1136/archdischild-2017-314576
196. Massanyi EZ, Preece J, Gupta A, Lin SM, Wang MH. Utility of screening ultrasound after first febrile UTI among patients with clinically significant vesicoureteral reflux. *Urology*. 2013;82(4):905-909. doi:10.1016/j.urology.2013.04.026
197. Nelson CP, Johnson EK, Logvinenko T, Chow JS. Ultrasound as a screening test for genitourinary anomalies in children with UTI. *Pediatrics*. 2014;133(3):e394-e403. doi:10.1542/peds.2013-2109
198. Alon US, Ganapathy S. Should renal ultrasonography be done routinely in children with first urinary tract infection? *Clin Pediatr (Phila)*. 1999;38(1):21-25. doi:10.1177/000992289903800103
199. Shaikh N, Spingarn RB, Hum SW. Dimercaptosuccinic acid scan or ultrasound in screening for vesicoureteral reflux among children with urinary tract infections. *Cochrane Database Syst Rev*. 2016;7(7):CD010657. doi:10.1002/14651858.CD010657.pub2
200. Jahnukainen T, Honkinen O, Ruuskanen O, Mertsola J. Ultrasonography after the first febrile urinary tract infection in children. *Eur J Pediatr*. 2006;165(8):556-559. doi:10.1007/s00431-006-0113-4
201. Battula V, Krupanandan RK, Nambi PS, Ramachandran B. Safety and feasibility of antibiotic de-escalation in critically ill children with sepsis—a prospective analytical study from a pediatric ICU. *Front Pediatr*. 2021;9:640857. doi:10.3389/fped.2021.640857
202. Ibrahim NA, Bakry MM, Ching SE, Tahir NM, Shah NN. Early empiric antibiotic de-escalation in suspected early onset neonatal sepsis. *Indian J Pharm Sci*. 2019;81(5):913-921. doi:10.36468/pharmaceutical-sciences.586
203. Antonio MEE, Cassandra BGC, Emiliano RJD, et al. Treatment of asymptomatic bacteriuria in the first 2 months after kidney transplant: a controlled clinical trial. *Transpl Infect Dis*. 2022;24(6):e13934. doi:10.1111/tid.13934
204. Alexopoulos E, Memmos D, Sakellariou G, Paschalidou E, Kyrou A, Papadimitriou M. Urinary tract infections after renal transplantation. *Drugs Exp Clin Res*. 1985;11(2):101-105.
205. Khosravi AD, Abasi Montazeri E, Ghorbani A, Parhizgari N. Bacterial urinary tract infection in renal transplant recipients and their antibiotic resistance pattern: a four-year study. *Iran J Microbiol*. 2014;6(2):74-78.
206. Goldman JD, Julian K. Urinary tract infections in solid organ transplant recipients: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019;33(9):e13507. doi:10.1111/ctr.13507
207. Amano M, Shimizu T. Emphysematous cystitis: a review of the literature. *Intern Med*. 2014;53(2):79-82. doi:10.2169/internalmedicine.53.1121
208. Wu SY, Yang SSD, Chang SJ, Hsu CK. Emphysematous pyelonephritis: classification, management, and prognosis. *Tzu Chi Med J*. 2022;34(3):297-302. doi:10.4103/tcmj.tcmj\_257\_21
209. Somani BK, Nabi G, Thorpe P, Hussey J, Cook J, N'Dow J; ABACUS Research Group. Is percutaneous drainage the new gold standard in the management of emphysematous pyelonephritis: evidence from a systematic review. *J Urol*. 2008;179(5):1844-1849. doi:10.1016/j.juro.2008.01.019
210. Thomas AA, Lane BR, Thomas AZ, Remer EM, Campbell SC, Shoskes DA. Emphysematous cystitis: a review of 135 cases. *BJU Int*. 2007;100(1):17-20. doi:10.1111/j.1464-410X.2007.06930.x
211. Rubilotta E, Balzarro M, Lacola V, Sarti A, Porcaro AB, Artibani W. Current clinical management of renal and perinephric abscesses: a literature review. *Urologia*. 2014;81(3):144-147. doi:10.5301/urologia.5000044
212. Lee SH, Jung HJ, Mah SY, Chung BH. Renal abscesses measuring 5 cm or less: outcome of medical treatment without therapeutic drainage. *Yonsei Med J*. 2010;51(4):569-573. doi:10.3349/ymj.2010.51.4.569

213. Siegel JF, Smith A, Moldwin R. Minimally invasive treatment of renal abscess. *J Urol*. 1996;155(1):52-55. doi:[10.1016/S0022-5347\(01\)66536-4](https://doi.org/10.1016/S0022-5347(01)66536-4)
214. Coelho RF, Schneider-Monteiro ED, Mesquita JLB, Mazzucchi E, Marmo Lucon A, Srougi M. Renal and perinephric abscesses: analysis of 65 consecutive cases. *World J Surg*. 2007;31(2):431-436. doi:[10.1007/s00268-006-0162-x](https://doi.org/10.1007/s00268-006-0162-x)
215. Shu T, Green JM, Orihuela E. Renal and perirenal abscesses in patients with otherwise anatomically normal urinary tracts. *J Urol*. 2004;172(1):148-150. doi:[10.1097/01.ju.0000132140.48587.b8](https://doi.org/10.1097/01.ju.0000132140.48587.b8)
216. Meng MV, Mario LA, McAninch JW. Current treatment and outcomes of perinephric abscesses. *J Urol*. 2002;168(4 Pt 1):1337-1340. doi:[10.1016/S0022-5347\(05\)64443-6](https://doi.org/10.1016/S0022-5347(05)64443-6)
217. Etienne M, Chavanet P, Sibert L, et al. Acute bacterial prostatitis: heterogeneity in diagnostic criteria and management: retrospective multicentric analysis of 371 patients diagnosed with acute prostatitis. *BMC Infect Dis*. 2008;8:12. doi:[10.1186/1471-2334-8-12](https://doi.org/10.1186/1471-2334-8-12)
218. McNaughton Collins M, Fowler FJ Jr, Elliott DB, Albertsen PC, Barry MJ. Diagnosing and treating chronic prostatitis: do urologists use the four-glass test? *Urology*. 2000;55(3):403-407. doi:[10.1016/S0090-4295\(99\)00536-1](https://doi.org/10.1016/S0090-4295(99)00536-1)
219. Gamé X, Vincendeau S, Palascak R, Milcent S, Fournier R, Houlgatte A. Total and free serum prostate specific antigen levels during the first month of acute prostatitis. *Eur Urol*. 2003;43(6):702-705. doi:[10.1016/S0302-2838\(03\)00158-1](https://doi.org/10.1016/S0302-2838(03)00158-1)
220. Gill BC, Shoskes DA. Bacterial prostatitis. *Curr Opin Infect Dis*. 2016;29(1):86-91. doi:[10.1097/QCO.0000000000000222](https://doi.org/10.1097/QCO.0000000000000222)
221. Bradshaw AW, Pe M, Bechis SK, et al. Antibiotics are not necessary during routine cystoscopic stent removal: a randomized controlled trial at UC San Diego. *Urol Ann*. 2020;12(4):373-378. doi:[10.4103/UA.UA\\_130\\_19](https://doi.org/10.4103/UA.UA_130_19)
222. Westhoff N, Anokhin A, Patroi P, Neuberger M, Siegel F, Pfalzgraf D. Prospective evaluation of antibiotic management in ureteral stent and nephrostomy interventions. *Urol Int*. 2022;106(4):411-418. doi:[10.1159/000517546](https://doi.org/10.1159/000517546)
223. Bonkat G, Bartoletti R, Bruyere F. EAU Guidelines on Urological Infections 2022. Published online 2022. Accessed September 20, 2023. <https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Urological-Infections-2022.pdf>
224. Yang C, Wei H, Zhan H, et al. Effect of preoperative prophylactic antibiotic use on postoperative infection after percutaneous nephrolithotomy in patients with negative urine culture: a single-center randomized controlled trial. *World J Urol*. 2023;41(12):3687-3693. doi:[10.1007/s00345-023-04623-5](https://doi.org/10.1007/s00345-023-04623-5)
225. Darenkov AF, Derevianko II, Martov AG, Kotliarova GA, Kondrat'eva EM, Siniukhin VN. [The prevention of infectious-inflammatory complications in the postoperative period in percutaneous surgical interventions in patients with urolithiasis]. *Urol Nefrol (Mosk)*. 1994;(2):24-26.
226. Jung HD, Cho KS, Moon YJ, Chung DY, Kang DH, Lee JY. Antibiotic prophylaxis for percutaneous nephrolithotomy: an updated systematic review and meta-analysis. *PLoS One*. 2022;17(4):e0267233. doi:[10.1371/journal.pone.0267233](https://doi.org/10.1371/journal.pone.0267233)
227. Levy MM, Fink MP, Marshall JC, et al; SCCM/ESICM/ACCP/ATS/SIS. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med*. 2003;31(4):1250-1256. doi:[10.1097/01.CCM.0000050454.01978.3B](https://doi.org/10.1097/01.CCM.0000050454.01978.3B)
228. Bag S, Kumar S, Taneja N, Sharma V, Mandal AK, Singh SK. One week of nitrofurantoin before percutaneous nephrolithotomy significantly reduces upper tract infection and urosepsis: a prospective controlled study. *Urology*. 2011;77(1):45-49. doi:[10.1016/j.urology.2010.03.025](https://doi.org/10.1016/j.urology.2010.03.025)
229. Mariappan P, Smith G, Moussa SA, Tolley DA. One week of ciprofloxacin before percutaneous nephrolithotomy significantly reduces upper tract infection and urosepsis: a prospective controlled study. *BJU Int*. 2006;98(5):1075-1079. doi:[10.1111/j.1464-410X.2006.06450.x](https://doi.org/10.1111/j.1464-410X.2006.06450.x)
230. Fisher JF, Sobel JD, Kauffman CA, Newman CA. Candida urinary tract infections—treatment. *Clin Infect Dis*. 2011;52(suppl 6):S457-S466. doi:[10.1093/cid/cir112](https://doi.org/10.1093/cid/cir112)
231. Mathers MJ, Lazica DA, Roth S. [Non-bacterial cystitis: principles, diagnostics and etiogenic therapy options]. *Aktuelle Urol*. 2010;41(6):361-368. doi:[10.1055/s-0030-1262615](https://doi.org/10.1055/s-0030-1262615)
232. Luciani LG, Mattevi D. Urinary tract infections: virus. *Encyclopedia Infection Immunity*. 2022;3:32-43. doi:[10.1016/B978-0-12-818731-9.00139-7](https://doi.org/10.1016/B978-0-12-818731-9.00139-7)
233. Hirsch HH. BK virus: opportunity makes a pathogen. *Clin Infect Dis*. 2005;41(3):354-360. doi:[10.1086/431488](https://doi.org/10.1086/431488)

234. Allen CW, Alexander SI. Adenovirus associated haematuria. *Arch Dis Child*. 2005;90(3):305-306. doi:10.1136/adc.2003.037952

235. Sawinski D, Goral S. BK virus infection: an update on diagnosis and treatment. *Nephrol Dial Transplant*. 2015;30(2):209-217. doi:10.1093/ndt/gfu023

236. Ambalathingal GR, Francis RS, Smyth MJ, Smith C, Khanna R. BK polyomavirus: clinical aspects, immune regulation, and emerging therapies. *Clin Microbiol Rev*. 2017;30(2):503-528. doi:10.1128/CMR.00074-16

237. Krajewski W, Kamińska D, Poterek A, et al. Pathogenicity of BK virus on the urinary system. *Cent European J Urol*. 2020;73(1):94-103. doi:10.5173/cej.2020.0034

SUPPLEMENT.

- eAppendix 1. Prophylaxis and Prevention
- eAppendix 2. Diagnosis and Diagnostic Stewardship
- eAppendix 3. Empiric Treatment
- eAppendix 4. Definitive Treatment and Antimicrobial Stewardship
- eAppendix 5. Special Populations and Genitourinary Syndromes
- eTable 1. Overview of Author Selection and Section Assignments
- eTable 2. Comprehensive List of Authors, Specialties, and Nationalities
- eFigure 1. Empiric Treatment Assessment Framework for Adults
- eFigure 2. Empiric Treatment Assessment Framework for Pediatrics