

Clinical Practice Guideline by Infectious Diseases Society of America (IDSA): 2025 Guideline on Management and Treatment of Complicated Urinary Tract Infections: Introduction and Methods

Barbara W. Trautner,¹ Nicolás W. Cortés-Penfield,² Kalpana Gupta,³ Elizabeth B. Hirsch,⁴ Molly Horstman,⁵ Gregory J. Moran,⁶ Richard Colgan,⁷ John C. O'Horo,⁸ Muhammad S. Ashraf,⁹ Shannon Connolly,¹⁰ Dimitri Drekonja,¹¹ Larissa Grigoryan,¹² Angela Huttner,¹³ Gweneth B. Lazenby,¹⁴ Lindsay Nicolle,¹⁵ Anthony Schaeffer,¹⁶ Sigal Yawetz,¹⁷ Valéry Lavergne,^{18,19}

¹Division of Infectious Diseases, Department of Medicine, Washington University School of Medicine, St. Louis, MO, ²Division of Infectious Diseases, University of Nebraska Medical Center, Omaha, NE, USA, ³Section of Infectious Diseases, Boston VA Health Care System, Boston University School of Medicine, Boston, MA, USA, ⁴Department of Experimental and Clinical Pharmacology, University of Minnesota College of Pharmacy, Minneapolis, MN, USA, ⁵Center for Innovations in Quality, Effectiveness, and Safety, Michael E. DeBakey VA Medical Center, Department of Medicine, Baylor College of Medicine, Houston, TX, USA, ⁶Professor of Clinical Emergency Medicine, David Geffen School of Medicine at UCLA, Olive View-UCLA Medical Center, Los Angeles, CA, USA, ⁷Department of Family and Community Medicine, University of Maryland School of Medicine, Baltimore, MD, USA, ⁸Division of Public Health, Infectious Diseases and Occupational Medicine, Mayo Clinic, Rochester, MN, USA, ⁹Division of Infectious Diseases, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, USA, ¹⁰Associate Medical Director, Planned Parenthood of Orange and San Bernardino Counties, Orange, CA, USA, ¹¹Infectious Disease Section, Minneapolis VA Health Care System, University of Minnesota Medical School, Minneapolis, MN, USA, ¹²Department of Family and Community Medicine, Baylor College of Medicine, Houston, TX, USA, ¹³Division of Infectious Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland, ¹⁴Departments of Obstetrics and Gynecology and Medicine Division of Infectious Diseases, Medical University of South Carolina, Charleston, SC, USA, ¹⁵Faculty of Health Sciences, University of Manitoba School of Medicine, Winnipeg, Manitoba, Canada, ¹⁶Department of Urology, Feinberg School of Medicine Northwestern University, Chicago, IL, USA, ¹⁷Division of Infectious Diseases, Brigham and Women's Hospital, Boston, MA, USA, ¹⁸Division of Medical Microbiology and Infection Control, Department of Pathology & Laboratory Medicine, Vancouver General Hospital, University of British Columbia, Vancouver, BC, Canada, ¹⁹Department of Clinical Affairs and Practice Guidelines, Infectious Diseases Society of America (IDSA), Arlington, VA, USA

Introduction

Reasons to Update the UTI Guidelines

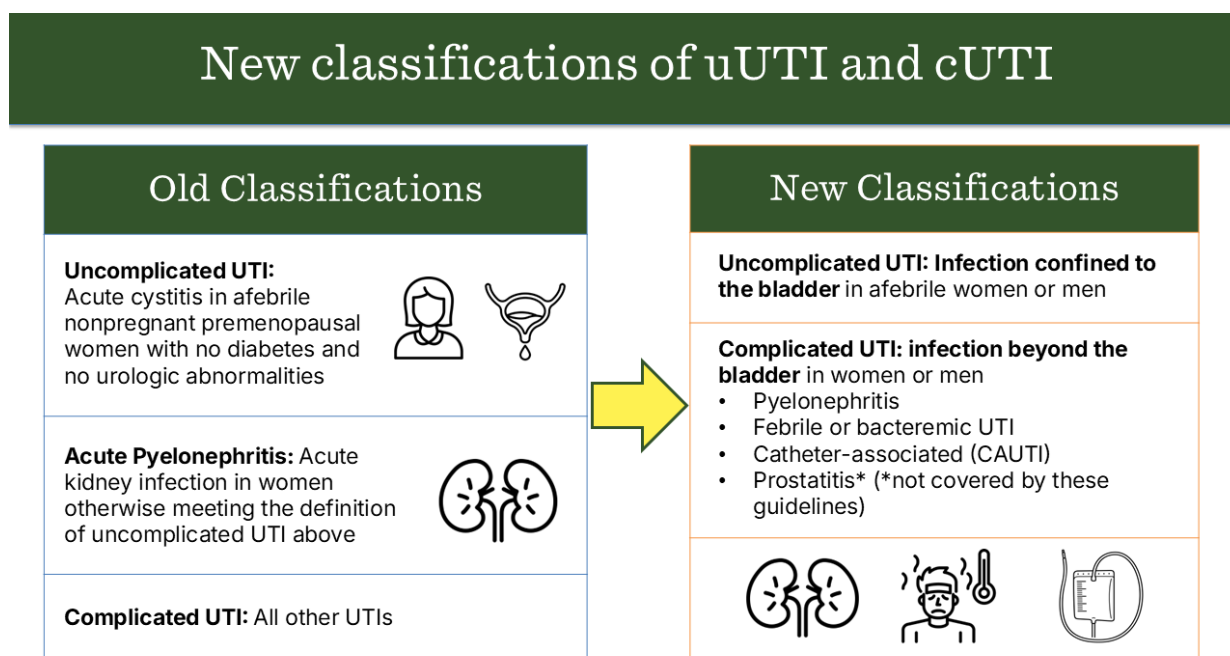
Magnitude of the burden of urinary tract infection: Urinary tract infection (UTI) is one of the most frequent reasons for clinic, emergency room, and hospital visits, with an estimated annual global burden of 404.61 million cases and 236,790 deaths in 2021.¹ Consequently, UTI is one of the most common infections managed by primary care clinicians, urgent and emergency care clinicians, hospitalists, general internists, gynecologists, and geriatricians. In 2021, an estimated 7.7 million visits to United States (US) emergency departments were for genitourinary issues, the majority presumably for UTI.² A summary of the National Inpatient Sample (NIS) database in 2018 reported that among 35.5 million hospitalizations in the US, 2.8 million had any UTI ICD-10 diagnosis code, and 626,520 met their definition of complicated UTI.³ Of the complicated UTI diagnoses, only 126,520 (20%) had coding documentation of a urinary catheter and thus met their definition of catheter-associated UTI (CAUTI).

UTI is also the leading cause of gram-negative bacteremia, accounting for 48% of gram-negative bacteremia reported by 24 US hospitals in 2021.⁴⁻⁶ Many but not all healthcare-associated UTIs are related to urinary catheters. A point prevalence survey of patients in US acute care hospitals in 2015 found that UTI accounted for 9.1% of all healthcare-associated infections, with an estimated 62,700 healthcare-associated UTIs annually.⁵ Of these healthcare-associated UTIs, 62% were related to an indwelling transurethral urinary catheter, thus meeting the surveillance definition for CAUTI. Unfortunately, estimates of the burden of complicated urinary tract infections (cUTIs) are uncertain, for several reasons. Documentation of urinary catheter use is often missing, and thus database studies tend to underestimate CAUTI. On the other hand, CAUTI may be over diagnosed in asymptomatic patients with bladder colonization. National surveillance for healthcare associated infections in acute care settings requires reporting of CAUTI but not of UTIs that develop in the absence of a urinary catheter, so the true incidence of UTI cases occurring in hospitalized patients is hard to quantitate.⁶

Need to expand the scope of prior UTI guidelines: The prior version of the IDSA UTI guidelines focused on uncomplicated cystitis and pyelonephritis in women, omitting complicated UTI (cUTI) and UTI in men.⁷ Since the publication of those guidelines, many randomized, controlled trials assessing new antimicrobials for cUTI in both women and men have been published. Although UTI is more common in women, m. Women have a lifetime risk of 53% of experiencing UTI. While UTI is uncommon in men prior to age 50, their lifetime risk is a nontrivial 14%.⁸ Risk of experiencing a UTI increases with age in both sexes.⁹ Given the aging US population, UTI in men is a salient issue, as is UTI in women. Fortunately, a reasonable evidence base now exists to support guidelines for treatment of cUTI in men and women. As a caveat, throughout these guidelines, “women” and “men” refer to persons’ biological sex (assigned at birth), as data from transgender persons are lacking in UTI clinical trials, and genitourinary anatomy is likely relevant for UTI risk and treatment response.

The bacteria that are isolated from UTI are becoming increasingly resistant to antibiotics: Gram-negative urinary organisms collected from outpatients across all regions of the United States now have antimicrobial resistance rates above the thresholds recommended for using antibiotics as empiric treatment of UTI in the 2010 guidelines.⁷ Specifically, these guidelines recommended avoiding empiric use of trimethoprim-sulfamethoxazole for acute cystitis if the local resistance rates of uropathogens are known to exceed 20% and avoiding empiric use of fluoroquinolones alone for pyelonephritis if the resistance of community uropathogens to fluoroquinolones is known to exceed 10%. Enterobacterales (formerly Enterobacteriaceae) is the order of gram-negative bacteria that includes many of the organisms typically causative of UTI (i.e., *Escherichia coli*, *Klebsiella* species, *Proteus* species) but does not include *Pseudomonas* species. Among Enterobacterales urinary isolates from US adult patients in ambulatory settings from 2018-2020, resistance was 21.6% to fluoroquinolones, 22.4% to trimethoprim-sulfamethoxazole, and 21.6% to nitrofurantoin. Corresponding inpatient urinary isolates had resistance rates of 27.5%, 25.4%, and 27% to fluoroquinolones, trimethoprim-sulfamethoxazole, and nitrofurantoin, respectively.¹⁰ In the face of these concerning high rates of resistance, the evidence needed to guide empiric choice of antibiotics for treating UTIs needs to be reevaluated.

Figure 1.0. Comparing prior and updated classifications of uncomplicated and complicated UTI



Need to update the classifications of uncomplicated and complicated UTI: We perceived a need to update the classifications of uncomplicated and complicated UTI to better align with clinical practice, become more congruent with the available data on male UTI, and better guide management decisions. The clinical distinctions between subcategories of complicated UTI, such as pyelonephritis and febrile UTI, are not standardized or clearly understood from a pathogenesis point of view.^{11,12} We therefore focused our revised classifications of uncomplicated and complicated UTI on the presence or absence of localized or systemic symptoms, particularly fever, that would suggest the infection had progressed beyond the bladder. We also focused the revised classifications on factors that would be readily apparent to the treating clinician at the point of care (e.g., vital signs and catheterization) rather than factors that might not be apparent without a urologic evaluation (e.g., anatomic abnormalities or urinary retention). These updated classifications align with the current clinical terminology of simple cystitis versus complicated UTI. Our updated classifications also align the European Urologic Association's (EUA) recently published classifications of UTI as localized or systemic.¹³ We likewise agree with the EUA that risk factors for treatment failure (and subsequent complications) are relevant to both uncomplicated (localized) or complicated (systemic), and the clinician must consider each patient's risk factors in addition to determining whether the infection is presenting as a localized or systemic infection. Furthermore, all patients diagnosed with UTI need to have signs or symptoms related to the organisms in the bladder (or spreading beyond the bladder); otherwise the patient actually has asymptomatic bacteriuria (ASB) and does not need antibiotic treatment.

Classifications

Classifications of complicated and uncomplicated UTI: Our understanding of what constitutes uncomplicated and complicated urinary tract infection has evolved since the 2010 publication of the IDSA guidelines (**Figure 1.0**). Clinical practice and considerations for management of the infectious syndrome have largely driven these changes. The classifications that we have chosen for the purposes of these guidelines focus on whether or not the infection is likely to be confined to the bladder, on initial evaluation. If so, the infection is defined as an uncomplicated UTI. Systemic signs of illness, such as fever or bacteremia, suggest that the infection has extended beyond the bladder and is thus defined as a complicated UTI. Evidence of renal parenchymal involvement (e.g. costovertebral angle tenderness), or a prostatic abscess, would also demonstrate that the infection has extended beyond the bladder. Subsequent discovery of obstruction in the upper urinary tract, such as from a stone, would render the infection complicated. Therefore, our categorization focuses on the extent and clinical severity of the illness, which in turn will drive management considerations.

Patients who have underlying urologic abnormalities (such as benign prostatic hypertrophy or a cystocele), diabetes, or immunocompromise are not automatically classified as having a complicated UTI. If such patients appear to have infection confined to the bladder and are not systemically ill, their infection would be considered an uncomplicated UTI (uUTI). By this classification, both men and women can have uncomplicated UTI, but choice of antibiotics and duration of treatment for uncomplicated UTI may differ for men and women. Duration of treatment for uUTI will be addressed in the subsequent uUTI guidelines. While we acknowledge that patients with underlying urologic abnormalities, diabetes, or immunocompromise may be at higher risk for severe infection and may merit closer observation, these beliefs should be balanced against the lack of robust data indicating said populations benefit from longer antibiotic duration for UTI. On the other hand, a patient with new onset hydronephrosis related to obstruction along the urinary tract would be expected to have a cUTI with systemic symptoms.

In general, acute prostatitis, should be considered and excluded before classifying UTI as uncomplicated in a male patient, as prostatitis can affect choice of therapy and duration.¹⁴ Our clinical questions and accompanying search strategies did not encompass prostatitis, epididymitis, or orchitis, and the management of these conditions is outside the scope of these guidelines.

Our updated classifications should help avoid the difficulty in clinical practice of determining which patients have an underlying urologic abnormality (such as chronic urolithiasis), as such information is often unavailable at the point of care when treating UTI.

Box 1: Complicated UTI classifications for guidelines purposes (intended to guide treatment not diagnosis)

- Clinical presentation:
 - o Complicated UTI is accompanied by symptoms which suggest an infection extending beyond the bladder, including:
 - Fever
 - Other signs or symptoms of systemic illness (including chills, rigors, or hemodynamic instability)
 - Flank pain
 - Costovertebral angle tenderness
 - o Pyelonephritis is encompassed in complicated UTI.
 - o UTI with systemic symptoms associated with transurethral, suprapubic, or intermittent catheterization is encompassed in complicated UTI.
- Populations:
 - o Patients with complicated UTIs may have an indwelling urinary catheter, neurogenic bladder, urinary obstruction, or urinary retention as an underlying condition.
 - o These guidelines are not intended to apply to bacterial prostatitis, epididymitis, or orchitis.

Conversely, patients with long-term indwelling urinary catheters, stents, or percutaneous nephrostomy tubes and symptoms related to the presence of bacteria in the urinary tract are considered to have a complicated UTI, as the presence of a medical device/foreign body is readily apparent and impacts multiple aspects of the treatment approach. For our purposes, urinary catheters include transurethral (Foley) catheters, suprapubic catheters, and daily intermittent use of urinary catheters because all can be associated with bladder colonization, biofilm formation, bladder/urethral trauma, and chronic sediment or stones in the urinary tract. However, we acknowledge that a subset of patients with CAUTI without systemic symptoms may be treated as simple cystitis, particularly those in which the catheter has only been in place for a short while, thus minimizing the bladder injury. In a patient with a long-term urinary catheter who does not have signs or symptoms of infection beyond the bladder, the clinician should carefully consider whether the patient has UTI or asymptomatic bacteriuria (ASB). ASB is covered in the IDSA guidelines on this topic.¹⁵ Urinary catheters can cause urethral and bladder discomfort, which needs to be distinguished from the bladder pain of cystitis.

“note that the classifications of uncomplicated and complicated UTI chosen for these guidelines are intended to guide management of UTI, not diagnosis. Details of our classifications appear in **Figure 1.0** and **Boxes 1 and 2**.

Our classifications of uncomplicated and complicated UTI differ from the Food and Drug Administration (FDA) guidance definitions. The FDA guidance defines uncomplicated UTI as occurring in a female patient with lower urinary tract symptoms and pyuria, and microbiologic confirmation via culture is recommended. Many of the clinical trials that form the evidence base for these guideline recommendations were designed per the FDA definitions. Therefore, trials designed to study a new drug for uncomplicated cystitis excluded men, and trials focused on complicated UTI may have enrolled men with simple, acute cystitis. Another important implication of our updated classifications is that studies focused on women with “uncomplicated

Box 2: Uncomplicated UTI classifications for guidelines purposes (intended to guide treatment, not diagnosis)

- Clinical presentation:
 - A clinical syndrome characterized by local bladder signs and symptoms such as dysuria, urgency, frequency, and suprapubic pain.
 - Uncomplicated UTI is presumed to be confined to the bladder and is defined by absence of signs or symptoms which suggest an infection extending beyond the bladder:
 - No fever, unless explained by a non-UTI cause
 - No other signs or symptoms of systemic illness (including chills, rigors, or unstable vital signs), unless explained by a non-UTI cause
 - No flank pain
 - No costovertebral angle tenderness
- Populations:
 - Uncomplicated UTI can occur in females or males, patients with underlying urologic abnormalities, patients with immunocompromise, and persons with diabetes. Recurrent UTI can be uncomplicated.
 - Patients with urinary catheters (including transurethral, suprapubic, and intermittent catheterization), stents, and percutaneous nephrostomy tubes generally do not have uncomplicated UTI.
 - These guidelines are not intended to apply to bacterial prostatitis, epididymitis, or orchitis.

pyelonephritis,” including cases of mild pyelonephritis that could be managed in the outpatient setting, became part of our evidence base for management of complicated UTI. Pyelonephritis in a premenopausal woman without other urinary tract abnormalities is clearly a different scenario than pyelonephritis in an older woman with a staghorn calculus; nuances of the management of pyelonephritis will be addressed under the text of the clinical questions. Implications of these definitional differences are discussed under each guideline recommendation.

A few other points of clarification may help in understanding these updated classifications and resulting guideline recommendations. Hospitalized patients can develop an uncomplicated UTI, so the term “healthcare-associated UTI,” typically referring to a UTI acquired in a healthcare setting, does not define whether the UTI is uncomplicated or complicated.¹⁶ Additionally, recurrent episodes of UTI can be uncomplicated or complicated. Our guidelines address empiric treatment of individual episodes of UTI without addressing preventive strategies for recurrent UTI. Uncomplicated UTI will be addressed in a subsequent set of guidelines.

Please note that these classifications are intended to help clinicians choose the best course of action, but there are cases in which the clinical presentation might not completely fit into one of these two categories. Clinical judgment is required for application of these categories and guidelines to patient care.

Definitions of “male” and “female”: UTI research is largely limited to cisgender male-bodied persons and female-bodied persons and largely fails to distinguish between gender identity and biological sex. Reference in the literature to “men” or “males” and “women” or “females”, often used interchangeably, suggests gender identities that participants may or may not have for themselves and omits people with nonbinary identities. The terms “male” and “female” are sex-based terms that refer to binary biological characteristics and exclude those whose bodies do not fit the binary. Acknowledging these limitations in language and past research, we will use language employed in original research studies. Throughout the text, we will use terms employed by the original studies to describe their participants when describing the research literature.

Scope: Population

The population encompassed in these guideline recommendations is adults with complicated urinary tract infections (cUTI). Patients with renal transplantation or who are pregnant, lactating, or neutropenic are not specifically addressed in this guideline, because these populations were excluded from the clinical trials that form the evidence base for these guidelines. Clinicians must use their judgment to determine whether and when our recommendations can be generalized to individual patients in these populations. That said, we do not have any reason to believe that lactating women should be treated for a different duration of antibiotics, or that the IV to oral switch data would not apply to them. For antibiotic choice in lactating women, excretion into the milk is a factor to consider. Advice on antibiotic choices during lactation can be found through the American College of Obstetrics and Gynecology guidelines¹⁷ and the online Drugs and Lactation Database (LactMed®).¹⁸

Clinical trials contributing to the evidence base typically limited enrollment to ages 18 and up, leading to exclusion of adolescents and children. Other populations rarely included in randomized, controlled trials of cUTI management include catheterized patients, patients with pyogenic infection (abscesses) of the urinary tract, men with acute prostatitis, patients with renal failure, patients who are immunocompromised for reasons other than neutropenia, patients with urinary obstruction, patients with nephrostomy tubes or urinary stents, and patients with urinary stones. Data on cUTI outcomes in these populations are, therefore, very limited. Of note, few studies attempted to determine if men with febrile UTI had prostatic involvement, nor is there a single widely agreed-upon approach for ruling out prostatitis in men with febrile UTI. Details of which cUTI treatment duration trials included men with prostatitis versus excluded men with prostatitis are discussed in clinical question 3 (duration of treatment for cUTI) and the supplementary materials for clinical question 3. Our guidelines also recognize that several populations were not formally studied due to limited identification of these study populations in trials, including patients with external (condom) catheters and transgender or gender diverse persons; these groups may have been represented within study populations yet not

documented as such. Finally, many patients who are treated for cUTI do not actually have a UTI and instead have another etiology for their presenting symptoms, including fever or sepsis.

Scope: Audience

Appropriate treatment of cUTI requires a correct diagnosis; however, diagnosis of cUTI, including overdiagnosis of cUTI in people with asymptomatic bacteriuria, will be covered in a future set of guidelines. We focused this initial guideline on cUTI treatment because this infection is common and the IDSA has not previously published clinical practice guidelines for cUTI. Additionally, many new drugs have recently received FDA approval for cUTI, and their registration trials provide an appropriate evidence base for cUTI guidelines. New treatment recommendations for uncomplicated UTI are in progress and will be subsequently released. For management of asymptomatic bacteriuria, please refer to the IDSA guidelines on management of asymptomatic bacteriuria.¹⁵

The intended target audience for these guidelines is the healthcare clinicians who most often treat cUTI in the emergency department, urgent care clinics, and hospital wards, including hospitalists, primary care clinicians, and emergency room clinicians. We also considered the perspectives of infectious disease specialists and pharmacists. The four practice questions this guideline addresses are: 1) how to best approach selection of empiric antibiotics for cUTI, 2) whether and when antibiotics for cUTI can be switched from the parenteral to oral route, 3) the appropriate duration of antibiotic treatment for cUTI, and 4) the role of imaging for evaluation of a patient presenting with suspected cUTI. Clinical questions 1, 2, and 3 will be presented here; clinical question 4, focused on the role of imaging, will follow later.

Methods

Clinical Practice Guidelines

Clinical Practice Guidelines are statements that include recommendations intended to optimize patient care by assisting practitioners and patients in making shared decisions about appropriate healthcare for specific clinical circumstances. These are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options. The “IDSA Handbook on Clinical Practice Guideline Development” provides more detailed information on the processes followed throughout the development of this guideline.¹⁹ The guideline was developed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) framework to prioritize clinical questions, identify patient-centered outcomes, and conduct an evidence synthesis.²⁰ The guideline panel used the Evidence-to-Decision framework to develop recommendations and provide implementation considerations for clinical practice.²¹

Guideline Panel Composition

The IDSA leadership selected the two co-chairs of the guideline panel. The co-chairs selected a total of 17 panelists from among volunteer applicants, including physicians and a pharmacist. Expertise represented among our panelists included infectious diseases, medical microbiology, hospital medicine, primary care, emergency medicine, gynecology-obstetrics, urology, and pharmacology. Panelists were diverse in gender, geographic distribution, and years of clinical experience. An IDSA guideline methodologist oversaw all methodological aspects of the guideline development. IDSA staff oversaw all administrative and logistical issues related to the guideline panel.

Disclosure and Management of Potential Conflict of Interest

All expert panel members complied with the IDSA policy on conflict of interest (COI), which requires disclosure of any financial, intellectual, or other interest that might be construed as constituting an actual, potential, or apparent conflict. Evaluation of such relationships as potential conflicts of interest was determined by a review process that included assessment by the Standards and Practice Guideline Subcommittee (SPGS) Chair, and if necessary, the Executive Committee of the Board. This assessment of disclosed relationships for possible COI was based on the relative weight of the financial relationship (i.e., monetary amount) and the relevance of the relationship (i.e., the degree to which an independent observer might reasonably interpret an association as related to the topic or recommendation of consideration).

In the event that a prohibited conflicts are disclosed during the course of the guideline development process, an internal investigation will be conducted to determine if the conflict introduced bias to the process and whether the panelist may continue to serve, provided the conflict can be appropriately managed. The reader of these guidelines should be mindful of this when reviewing the list of disclosures. See the COI summary at the end of the guideline for the disclosures reported to IDSA.

Formulating Clinical Questions

The clinical practice guideline development started in 2019. In line with the National Academy of Medicine standards on trustworthy guidelines,²² the GRADE approach was used to assess the certainty of evidence and strength of recommendation. Clinical questions were formulated using the “PICO” format (Patient/Population [P]; Intervention/Indicator [I]; Comparator/Control [C]; Outcome [O]) questions.

Determining Outcomes of Interest

All outcomes of interest were identified *a priori* and explicitly rated for their relative importance for decision-making. Each clinical question was assigned to a subgroup of panelists. Ranking of the outcomes by importance for decision-making was determined by consensus within the panel in collaboration with patient representatives for each clinical question question. In situations where a clinical question compared the use of one specific antibiotic regimen to

another (e.g., comparing spectrum of activity, route of administration, or duration of therapy) and the beneficial effects of the two regimens were similar, then the undesirable outcomes could be ranked as critical for decision-making, but several other considerations might have also been taken into account, such as antimicrobial stewardship issues for appropriate use, tolerability, as well as costs and resources.

Panel's judgment on clinical cure versus microbiologic cure: We judged the most important outcome in interventional treatment trials for cUTI to be mortality; however, mortality was rare in the identified clinical trials. In this context, the panel (in collaboration with patient representatives) judged that clinical cure at test-of-cure (TOC) was most critical for decision-making (meaning that this outcome was the main driver of whether an antibiotic should be preferred versus other agents for cUTI).²³ The panel also judged that recurrence of infection at late follow-up, which is influenced by many factors beyond initial antimicrobial therapy (e.g., comorbidities), was important for decision-making about the choice of empiric therapy and the switch from IV to oral therapy. Taking into account the values and preferences of our patient representatives, recurrence of infection was judged to be critical for making decisions about duration of therapy.

In contrast to the FDA guidance on clinical trials for cUTI, the panel decided that clinical cure alone rather than a composite outcome of clinical and microbiologic cure should be the primary metric for comparing antimicrobials for empiric treatment of cUTI. The panel judged that microbiologic eradication was important but not critical for decision-making. The GRADE methodology is outcome-centric and focuses on patient-important outcomes. Clinical cure is the most important outcome to patients and was set as our critical outcome for decision-making when choosing among empiric antibiotics for initial treatment of cUTI. Our analysis placed less emphasis on microbiologic cure for several reasons. First, if the patient no longer has urinary symptoms, from the patient's perspective, the UTI episode is resolved. Second, detecting microbiologic cure or failure requires a urine culture after cessation of antibiotic therapy, and in practice, test of cure urine cultures are discouraged in asymptomatic patients.¹⁵ Third, the majority of the trials that contributed to this cUTI evidence base did not report the outcome of symptomatic recurrence, and very few confirmed whether the organisms causing recurrence were the same as those isolated at microbiologic failure. Another issue is that microbiologic cure or eradication was variably defined as a test-of-cure urine culture with fewer than 10⁴ colony-forming units per mL (CFU/mL) or fewer than 10³ CFU/mL of the baseline uropathogen, therefore the definition of microbiologic failure also varies. Women with 10² CFU/mL can still have symptoms of acute cystitis.

We acknowledge that multiple studies with varying degrees of adjustment for potential confounders show that patients with microbiologic failure might also be more likely to have clinical recurrence.^{24,25} This finding is not surprising in light of decades of evidence from uUTI studies that women with asymptomatic bacteriuria (ASB) are also more likely to develop symptomatic UTI. However, the anatomical and immunologic risk factors predisposing to ASB in these patients cannot be corrected by antibiotics and treatment of ASB in multiple populations (e.g., young women, catheterized patients, diabetic patients, renal transplant patients, and nursing home residents) has consistently failed to prevent subsequent bouts of ASB or

symptomatic UTI.¹⁵ Whether or not this finding also applies to the patients in cUTI studies is unknown because, to the knowledge of the panel, no trial has yet randomized patients with microbiologic failure at TOC to antibiotic treatment versus no treatment. That said, we considered microbiologic cure in the decision-making process but did not value it as highly as clinical cure.

Panel's judgment on clinical decision threshold: The panel judged that the clinical decision threshold (or a minimally important difference) would consist of an increase of more than 10% in clinical failure. For example, if the treatment with a specific antibiotic leads to an increase in clinical failure of more than 10% than the comparator antibiotic(s), the panel would judge this difference as clinically unacceptable and important enough to decide to recommend against this antibiotic. Despite not being considered a critical outcome, microbiologic cure was also examined using a decision threshold of 10%. All other outcomes were compared based on statistical difference.

Evidence Review and Synthesis

Search strategy

After scoping the available literature, the panel decided to conduct multiple systematic reviews to summarize and synthesize the evidence for all clinical questions included in the guideline. Two librarians specialized in systematic review designed the literature searches and MeSH terms for Ovid Medline, for EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL), and Cochrane Database of Systematic Reviews. Searches were limited to studies published in English and restricted to two different sets of years of publication: from 2000 up to September 2024 for general concepts (for example, for timing of IV to oral switch or impact of inappropriate empiric antibiotic therapy) or from 2008 up to September 2024 if updating data from the prior IDSA uncomplicated UTI guidelines 2010 (for example, empiric choice of antibiotics).⁷ These cut offs (2000 and 2008) were chosen based on concerns about generalizability of older studies to current practice. The initial formal literature search was initially performed in October 2020 and last updated in September 2024. All search strategies are available in the Supplementary materials.

Study selection

A subgroup of panelists screened titles and abstracts of all identified citations. Two panel members independently screened each relevant title and abstract retrieved from the search using Covidence software (Covidence Systematic Review Software VHI, Melbourne, Australia. Available at www.covidence.org). A third reviewer resolved disagreements about relevance. All potentially relevant citations were subjected to a full-text review using predefined inclusion and exclusion criteria tailored to meet the specific population, intervention, and comparator of each clinical question. Abstracts and conference proceedings, letters to the editor, editorials, review articles, and unpublished data were excluded. When acceptable RCTs of effectiveness were found, no additional non-randomized studies or non-comparative evidence (i.e., single-arm case series) were sought. The literature search results were supervised and thoroughly reviewed by

the guideline methodologist for the final selection of the relevant articles. Panel members reviewed the final set of included articles for accuracy.

Data collection and extraction

Once the articles were selected, the guideline methodologist, in conjunction with panelists, extracted the data for patient-important outcomes. Reviewers extracted relevant information into a standardized data extraction form, including study characteristics, study design, participant characteristics, details of the intervention and comparison, outcomes reported and funding source. The numbers of events and total sample sizes were extracted for all dichotomous outcomes, and means with standard deviations were calculated for continuous outcomes.

Data analysis

The quantitative data from RCTs or non-randomized studies with a control arm were combined to obtain a relative risk (RR) for dichotomous outcomes and a mean difference for continuous outcomes and reported with 95% confidence intervals (95% CI). We used the Mantel-Haenszel random-effects model to pool the relative effects unless the number of studies was too small to allow precise estimation of between-study variance, in which case we used the fixed-effects model. The statistical heterogeneity in the pooled estimates was assessed by visual inspection of the forest plots and the I² statistic. Statistical heterogeneity was deemed substantial if I² was greater than 50%.²⁶ When a sufficient number of studies were presented with no substantial heterogeneity, we planned to assess for publication bias using funnel plot asymmetry tests.²⁷ All quantitative analyses were performed using RevMan.²⁸

Risk of bias assessment

In collaboration with the subgroup, the guideline methodologist assessed the risk of bias. The risk of bias was assessed by using the Cochrane risk of bias tool for RCTs, the ROBINS-I²⁹ for observational studies, QUIPS for prognostic studies,³⁰ and the QUADAS-2 tool for diagnostic test accuracy studies.³¹

Certainty of evidence assessment

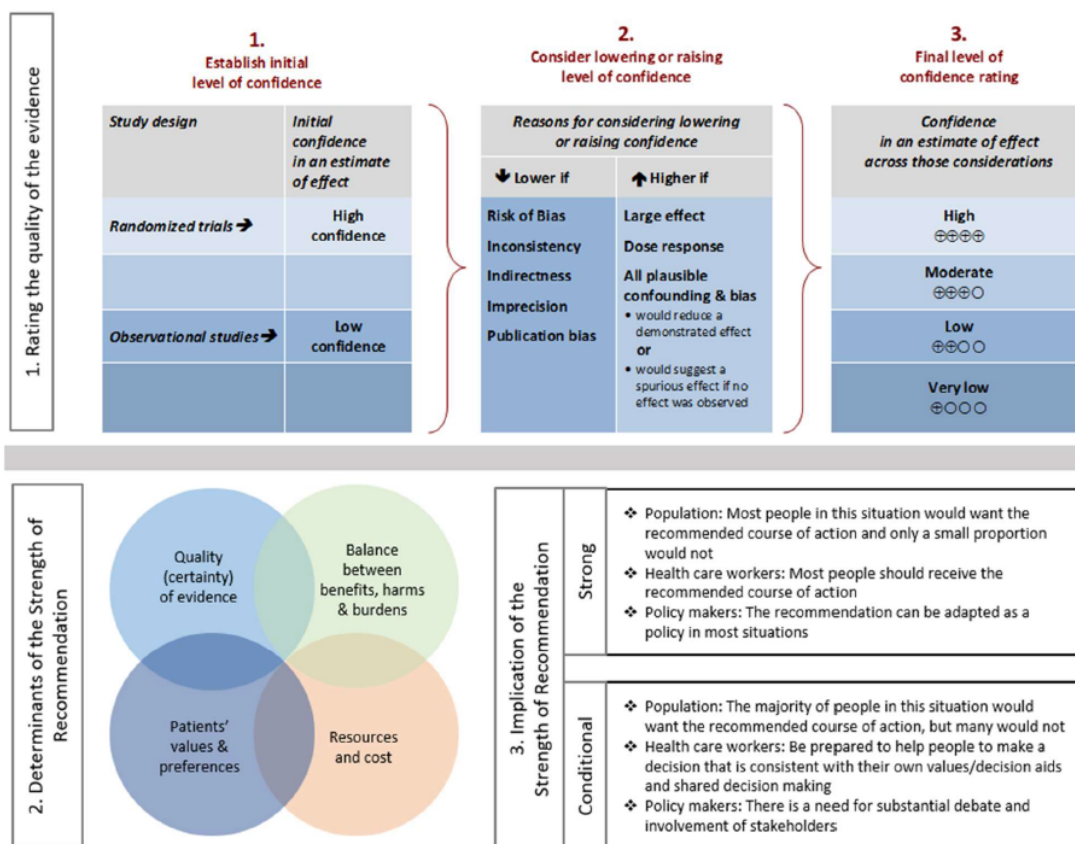
The certainty of the evidence was determined for each critical and important outcome and then for each recommendation using the GRADE approach to rating the confidence in the evidence.^{20,32} Within GRADE, the body of evidence across each outcome is assessed for domains that may reduce or increase one's certainty in the evidence. Factors that may reduce one's certainty include risk of bias (study limitations), inconsistency (unexplained heterogeneity across study findings), indirectness (applicability or generalizability to the research question), imprecision (the confidence in the estimate of an effect to support a particular decision) or publication bias (selective publication of studies). One's certainty in the evidence may be strengthened if the following considerations are present: large or very large magnitude of effect, evidence of a dose-response gradient, or opposing residual confounding. GRADE evidence profile and summary of findings tables were developed in GRADEpro Guideline Development Tool.³³ All summary tables were reviewed by subgroup of panelists responsible and edited as appropriate.

Evidence to Recommendations

The panel considered core elements of the GRADE evidence in the decision process, including Certainty of evidence and balance between desirable and undesirable effects. Additional domains were acknowledged where applicable (feasibility, resource use, acceptability). All recommendations were labeled as either “strong” or “conditional” according to the GRADE approach.¹⁹ The words “we recommend” indicate strong recommendations, and the words “we suggest” indicate conditional recommendations. **Figure 2.0** provides the suggested interpretation of strong and conditional recommendations for patients, clinicians, and healthcare policymakers. For recommendations where the comparator treatment or tests are not formally stated, the comparison of interest is implicitly referred to as “not using the intervention” (not using either a specific treatment or a diagnostic test). According to the GRADE guidance on discordant recommendations, strong recommendations in the setting of lower certainty of evidence were assigned only when the panelists believed they conformed to one of the five accepted paradigmatic conditions.³⁴ According to the GRADE working group, appropriate identification and wording choices were followed for recommendations regarding good practice statements.³⁵ A good practice statement represents a message the guideline panel perceives as necessary regarding current healthcare practice. It is supported by a large body of indirect evidence that is difficult to summarize and indicates that implementing this recommendation would clearly result in large net positive consequences. “Research Needs” were noted for recommendations as deemed appropriate by the panel.

Final presentation of evidence summaries and the development of the recommendations were conducted through a series of video teleconferences by the whole panel. All members of the panel participated in the preparation of the draft guideline and approved the recommendations. Literature search strategies, PRISMA flow diagram detailing the search results, evidence profiles tables, EtD framework, and additional data, such as quantitative analysis and modeling when appropriate, can be found in the Supplementary Material.

Figure 2.0. Approach and implications to rating the quality of evidence and strength of recommendations using GRADE methodology (*unrestricted use of figure granted by the U.S. GRADE Network*)



Section on oral empiric antibiotics for cUTI

The external review process highlighted the readership's need for more information on oral empiric antibiotics; thus, the section discussing oral empiric antibiotics for cUTI was considerably expanded after completion of the initial formulation of recommendations. The section and associated dosing table are based on a mapping review of clinical studies that compared different oral antibiotics when transitioning from IV in populations either treated for cUTI or Gram-negative bacteremia of predominately urinary origin. The evidence identified from that search was not assessed as per the GRADE methodology and no formal recommendations are made for use of these oral antibiotics as empiric initial therapy cUTI.

Public Patient Involvement

As per the 2011 Institute of Medicine, AGREE II and GIN standards, patients' representatives were involved in the development of this guideline.³⁶ Public patient involvement was advertised through the MyIDSA website as well as through the social media account of the

UTI Global Alliance. IDSA patient representatives are unpaid. Patient representatives willing to give of their time and effort often are those who suffer most from the disease under study. Patients' representatives were selected if they had a prior history of UTI and were not part of an advocacy group potentially at risk of intellectual or financial COI with the guideline. Patients were involved at different steps of the process, mainly providing feedback for the ranking patient-important outcomes, on patients' values and preferences for the different clinical questions reviewed, and on the final recommendations and potential related implementation issues. A narrative section can be found at the end of the document to highlight concerns expressed by patients experiencing UTIs.

Revision process

Feedback was obtained from three external peer expert reviewers, and involved organizations, i.e. SIDP (Society of Infectious Diseases Pharmacists), AAFP (American Academy of Family Physicians), SHM (Society of Hospital Medicine), AUA (American Urological Association), ASM (American Society of Microbiology), SAEM (Society for Academic Emergency Medicine), ACOG (American College of Obstetricians and Gynecologists), AMMI-CA (Association of Medical Microbiology and the Infectious Disease Canada), European Society of Clinical Microbiology and Infectious Diseases (ESCMID). In addition, the guideline was reviewed by the IDSA Standards and Practice Guidelines Subcommittee (SPGS), the IDSA Quality Subcommittee, and the IDSA Board of Directors. After review and approval by the various organizations and reviewers, the guideline was posted online prior to publication to facilitate a public comment period requesting feedback on the full guideline. The panel reviewed the feedback from the public comment phase and updated the guideline prior to final approval by the IDSA SPGS and Board of Directors.

Notes

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Disclaimer

It is important to recognize that guidelines cannot always account for individual variation among patients. They are assessments of current scientific and clinical information provided as an educational service; are not continually updated and may not reflect the most recent

evidence (new evidence may emerge between the time information is drafted and when it is published or read); should not be considered inclusive of all proper methods of care, or as a statement of the standard of care; do not mandate any course of medical care; and are not intended to supplant clinician judgment with respect to particular patients or situations. Whether to follow guidelines and to what extent is voluntary, with the ultimate determination regarding their application to be made by the clinician in the light of each patient's individual circumstances. While IDSA makes every effort to present accurate, complete, and reliable information, these guidelines are presented "as is" without any warranty, either express or implied.

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Possible conflicts of interest

Evaluation of relationships as potential conflicts of interest is determined by a review process. The assessment of disclosed relationships for possible COIs is based on the relative weight of the financial relationship (i.e., monetary amount) and the relevance of the relationship (i.e., the degree to which an association might reasonably be interpreted by an independent observer as related to the topic or recommendation of consideration). The following panelists have reported relationships with indicated companies since 2019, when the guideline work began. **B.T.** served as an advisor for Genentech, GSK, PhioGen Pharma, and Paratek Pharmaceuticals; received research funding from Genentech and Zambon Pharmaceuticals; received grant funding from the MacDonald Research Foundation, Agency for Healthcare Research and Quality, VA HSR&D, CDC, NIH, Mike Hogg Foundation, Neilsen Foundation, and VA RR&D; engaged in activity with Infectious Diseases Board Review Course, Warren Alpert School of Brown University Department of Medicine, Baylor College of Medicine PriMed, and UpToDate; owns

intellectual property for PhioGen Pharma; and owned stocks in Abbott Laboratories, Bristol Meyers Squibb, Abbvie, and Pfizer (all divested when BT learned of the individual stock ownership). **N.C.P.** received funding from Duke University. **K.G.** served as a consultant for Iterum Therapeutics, Tetrphase Pharmaceutical, Paratek Pharmaceutical, First Light Diagnostics, Ocean Spray Inc, Shionogi Inc, Nabriva Therapeutics, Utility Therapeutics, Qiagen Diagnostics, Rebiotix, Spero Therapeutics; serves as a consultant for GlaxoSmithKline, PhenUtest (Innotive), CarbX and PRIME Education; receives remuneration from Up to Date, Inc. Pri-Med and PRIME Education; owned equities in Pfizer Pharmaceutical (past), and Fidelity Managed Investment Account; received research grant funding from VA Health Services Research & Development, VA Cooperative Studies Program, NIAID, and NIH. **E.H.** receives funding from Cystic Fibrosis Foundation; receives honoraria from SIDP; served as an advisor for Nabriva Pharmaceuticals, Merck, GlaxoSmithKlin, Paratek Pharmaceuticals and MeMed; received funding from Merck; engages in activity with SIDP and CLSI. **M.H.** received research grants from AHA, VA QUERI, Veterans Affairs Health Systems Research, National Institute on Aging, Society to Improve Diagnosis in Medicine, and Michael E. DeBakey VA Medical Center; receives funding from Veterans Affairs Health Systems Research. **G.M.** served as an advisor for Light AI and Qiagen; received funding from Light AI, Contrafect, Nabriva, and NIH; engaged in activity with Annals of Emergency Medicine; owns stock in Light AI; receives funding from Abvacc. **R.C.** served as an advisor for the GlaxoSmithKlin, Biofire and Rebiotix. **J.O.** received funding from MITRE Corporation. **M.S.A.** received funding from Merck & Co. Inc and Nebraska DHHS HAI/AR Program (through CDC grants); served as a member and vice chair of PALTmed's Infection Advisory Committee (IAC) and chair of PALTmed's IAC UTI workgroup; served as a member of ASCP's AS and Infection Control committee; served as vice president and president for Nebraska Infection Control Network; served as a member of SHEA's education committee and Learning CE committee; and served as member of IDSA antimicrobial resistance committee; serves as board member and immediate past president for Nebraska Infection Control Network; serves as chair of PALTmed's infection prevention and control committee (previously infection advisory committee) and member of PALTmed's state advocacy committee (previously state based policy and advocacy subcommittee) and clinical practice steering committee; serves as a member of CSTE HAI/AR subcommittee; is member of the SHEA Long-Term Care Special Interest Group, was a member of the COVID-19 State Collaboration Task Force of PALTmed; worked on development of infection control guidance for nursing homes with SHEA and is working on development of infection control guidance for LTACHs and antibiotic initiation guidance for nursing homes with SHEA and also on nursing home infection control educational module development for front-line staff with SHEA; and accepted invitation to serve on HICPAC but onboarding was not completed. **D.D.** received funding from VA CSP, VA Merit Review, VA Cooperative Studies Program, CDC Tuberculosis Trials Consortium, and honoraria from UpToDate. **L.G.** received funding from Antibacterial Resistance Leadership Group, NIH, Zambon Pharmaceuticals, VA Health Services Research & Development, Rebiotix, and AHRQ; receives funding from AHRQ; Neilsen Foundation, VA Health Services Research & Development and Micheal E. DeBakey Veterans Affairs Seed Grant. **S.C.** Received honoraria for the development of sexual and reproductive health educational materials for family physicians from the American Academy of Family Physicians and California Academy of Family Physicians. Received honoraria for the development of training materials on sexual health from Quest Diagnostics. **A.H.** received funding from Swiss National Science Foundation, and serves as the ESCMID representative on the panel. **G.L.** received honoraria from UpToDate; received funding from Lupin Pharmaceutical, NeuMoDx, CDC, NACCHO, NIH, HRSA, DHHS, State Office of Victims Assistance, and IDSOG. **L.N.**

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