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ORIGINAL ARTICLE

Lack of uniformity among United States recommendations for diagnosis and management of acute, uncomplicated cystitis

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Abstract

Introduction and hypothesis Acute, uncomplicated cystitis is one of the most common bacterial infections seen in clinical practice. Quality improvement and antibiotic stewardship efforts to optimize cystitis management rely on clinicians managing patients in a manner recommended by experts and guidelines. However, it is unclear if recent recommendations for cystitis from experts and guidelines from US medical societies that provide recommendations are well aligned.

Methods We examined recommendations and guidelines for acute, symptomatic cystitis in women published in US medical societies' journals from January 1, 2008, to December 31, 2016, within the fields of family medicine, obstetrics and gynecology, internal medicine, female pelvic medicine and reconstructive surgery, and infectious diseases.

Results All recommendations endorsed the use of symptoms and urine dipstick to diagnose cystitis. Some societies did not recommend urine dipstick in patients with recurrent urinary tract infection (UTI), classic UTI symptoms, or a lack of underlying conditions or competing diagnoses. All endorsed nitrofurantoin, trimethoprim-sulfamethoxazole, and fosfomycin as first-line agents. Some guidelines classified fluoroquinolones as second- or third-line, while others considered them first-line treatment for UTI. Avoiding use of amoxicillin and ampicillin, antibiotic agents with high prevalence of resistance in the US, was recommended by some societies.

Conclusions US recommendations differed in their approach to the treatment of acute, uncomplicated cystitis. Lack of uniformity likely contributes to clinical management variance for patients with UTI and hampers quality improvement and antibiotic stewardship efforts aimed at promoting optimal management. Our findings emphasize the need for more consistent recommendations for cystitis management.

Keywords Antimicrobial treatment · Diagnosis · Management · Recommendations · Urinary tract infection

Introduction

Uncomplicated urinary tract infection (UTI) is defined as infection involving only the bladder and is not associated with anatomical or functional abnormalities or foreign bodies in the urinary tract. UTIs are one of the most common conditions encountered in US outpatient facilities, totaling over 8.6 million visits in 2007 alone [1], and uncomplicated UTI (cystitis) is the most common category. The prevalence of UTIs in women aged 18 years of age or older has been estimated to be 11–13% over a 12-month time period [2, 3]. Over one third of all US women are diagnosed with a UTI by the age of 24, 50% are diagnosed with a UTI by the age of 35, and the lifetime risk of UTI is 60% [3]. An estimated $1.6 billion is spent per year in the US on the associated costs of uncomplicated UTI [4, 5].

The most common etiologic agent of cystitis is *Escherichia coli*, causing 72% of cases [6]. Additional agents contributing to uncomplicated UTI in women aged 15–50 in the US, along with their susceptibility patterns, are shown in Table 1 [6]. While most *E. coli* isolates associated with UTI remain susceptible to nitrofurantoin and fosfomycin, antibiotic resistance is increasing to trimethoprim-sulfamethoxazole and other antibiotics commonly prescribed for UTI [7]. Although recommendations have been published in a number of relevant

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Table 1 Etiologic agents and susceptibility patterns in uncomplicated cystitis in women aged 15–50 in the US

Uropathogen	Frequency	TMP/SMX susceptible	Nitrofurantoin susceptible	Ciprofloxacin susceptible	Levofloxacin susceptible	Ampicillin susceptible
E. coli	72%	82%	99%	99%	99%	60%
Klebsiella species	6%	94%[a]	60%[a]	90%[a]	95%[a]	51%[a]
Enterococcus species	5%					
Proteus species	4%					
Coagulase-negative staphylococci	3%					
Enterobacter species	2%					
Other gram-negative rods	2%					
Staphylococcus aureus	2%					
Staphylococcus saprophyticus	2%					
Pseudomonas aeruginosa	1%					
Other isolate	1%					

[a] Rates of US antimicrobial susceptibility for all non-*E. coli* uropathogens

medical specialties, adherence to these recommendations remains suboptimal. For example, in an urban emergency department in Washington, DC, 63.1% of patients received antibiotics for uncomplicated UTI that were non-adherent with Infectious Disease Society of America (IDSA) guidelines, and an Arizona study found that less than 25% of patients with uncomplicated UTI received treatment adherent to IDSA guidelines in a family practice setting [8, 9].

Expert recommendations from publications and guidelines of US medical societies regarding the diagnosis and management of acute, uncomplicated cystitis have not previously been compared. Assessment of quality of care and efforts to promote antibiotic stewardship rely on adherence to commonly agreed upon standards. Inconsistent recommendations make development of quality metrics extremely challenging to achieve. In this review, we examined and compared US expert recommendations and guidelines for the diagnosis and therapeutic management of acute, uncomplicated cystitis.

Methods

US clinical recommendations were acquired based on a PubMed search of keywords, "urinary tract infection," "recommendations," and "guideline." Additionally, the official websites of professional organizations were accessed in search of specialty-specific published recommendations. The data were reviewed independently by two individuals (MAM and LNW). The following specialties were selected for the presence of recommendations based on the physicians in that specialty treating acute, symptomatic cystitis in adult women: emergency medicine, family medicine, infectious disease, internal medicine, obstetrics and gynecology, and urology. Societies with evidence-based publications, recommendations, or best-practice statements were included. All available recommendations published from January 1, 2008, to December 31, 2016, were included.

All identified recommendations were extracted for content on UTI diagnosis and therapeutic management of acute, uncomplicated cystitis. Portions of the recommendations that deal with asymptomatic bacteriuria, complicated or recurrent UTI, acute pyelonephritis, and UTI in postmenopausal women were not included in this review.

Approval by the UCLA institutional review board was not obtained, as published literature from professional medical organizations was examined.

Results

We found guidelines on UTI treatment from the American College of Obstetricians and Gynecologists (ACOG), 2008 (reaffirmed in 2016) [10], and the IDSA, 2011 [11]. Of note, IDSA guidelines contained no discussion of diagnostics. While no formal guidelines exist from the American Academy of Family Physicians (AAFP), the American College of Physicians (ACP), and the American Urogynecologic Society (AUGS), clinical recommendations were available for AAFP, published in 2011 [12], ACP, published in 2012 [13], and AUGS, published in 2011 [14]. No professional societies in the fields of emergency medicine or urology published specific UTI guidelines or recommendations. For the purpose of this review, we use the name of the medical society that published the journal that contained expert recommendation or guidelines as the recommending source.

Diagnostic recommendations

Acute, uncomplicated cystitis was typically defined as a UTI in premenopausal, immunocompetent, non-pregnant females,

although the specific patient population of cystitis differed across recommendations (Table 2). All recommendations outlined an increased pretest probability for acute, uncomplicated cystitis in patients with dysuria, urinary frequency, and urinary urgency. The ACP and AUGS include hematuria as an important diagnostic sign [13, 14]. Recommendations other than those published by ACOG included the absence of vaginal discharge as an important diagnostic criterion for UTI [10].

The presence of suprapubic or abdominal tenderness on physical examination was considered typical in acute, uncomplicated cystitis in all, but is not discussed in recommendations from the ACP. Additionally, the presence of costovertebral angle (CVA) tenderness was detailed as a warning sign by all societies [10, 12, 14, 15]. Pelvic examination was recommended by AUGS when entertaining a diagnosis of UTI [14].

All guidelines and recommendations were consistent in their inclusion of the urine dipstick as a possible diagnostic test, with an emphasis on the presence of nitrites and leukocyte esterase. However, some society recommendations provided a more critical review of dipstick results. AUGS described urine dipstick as a rapid and inexpensive mode for detecting UTI, although its high false-positive and -negative rates make it only one of three diagnostic tools to consider in diagnosing UTI, with microscopy and culture being the other two [14]. Similarly, the ACP stated that dipstick is used for diagnostic confirmation only, and patients with classic symptoms of cystitis (i.e., dysuria, urgency, and frequency), who lack an underlying condition and symptoms of an alternative diagnosis, do not require dipstick testing [13]. The ACP recommended diagnostic testing in patients presenting with a more complex history.

All recommendations stated that sending urine specimens for culture and sensitivity (C&S) is not standard practice in the diagnosis of acute uncomplicated cystitis, with varying caveats. AUGS and AAFP emphasized that urine C&S is not necessary in classic presentations of acute, uncomplicated cystitis, with AAFP detailing C&S requirement only for patients that present with atypical symptoms, if pyelonephritis is suspected, or for patients with symptoms that have not resolved 2 to 4 weeks after treatment [12, 14]. ACOG recommended urine C&S if dipstick results are negative and symptoms are present, if symptoms persist > 48 h after treatment, or if pyelonephritis is suspected [10]. The ACP outlined the highest number of exceptions in which urine C&S may be indicated: if diagnosis of cystitis is unclear, if a resistant or unusual organism is suspected, if treatment failure or a recurrent episode is suspected, if treatment options are limited by antibiotic intolerances, or if the patient is pregnant [15].

Recommendations were consistent in their emphasis on the safety of self-treatment and out-of-office UTI diagnostics. ACOG, ACP, and AUGS state that patients with recurrent UTI may be prescribed an antimicrobial agent to be self-administered at the onset of symptoms (or after self-testing results in a positive urine dipstick) [10, 14, 15]. ACOG stated that clinical follow-up is only needed if symptoms persist > 48 h after self-treatment [10]. Both AAFP and ACP considered telephone diagnosis safe for prescribing antimicrobials to patients with classic symptoms of cystitis lacking an underlying condition or symptoms of an alternative diagnosis [12, 15].

Treatment recommendations

Multiple antibiotic regimens are available for the management of acute, uncomplicated cystitis among US guidelines and recommendations (Table 3). Although the American College of Emergency Physicians (ACEP) does not have a policy for UTI management, it published a review of the 2011 IDSA guidelines [16]. Similarly, the Society for Academic Emergency Medicine (SAEM) does not have its own UTI management policy, but co-sponsored the 2011 IDSA guidelines. Professional societies within urology also do not have unique UTI guidelines. The Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) does not have a policy for UTI diagnosis or treatment, and the American Urological Association (AUA) does not have a policy for non-catheter-associated UTI. However, the AUA co-sponsored the 2011 IDSA guidelines, and its recommendations for adult UTI management available to medical students mirrors those set by the IDSA [17].

All recommendations reviewed endorsed empiric antibiotic therapy based on the diagnostic criteria detailed in Table 2, including the presence of symptoms, physical examination findings, and dipstick results. Recommendations for prescribing antimicrobial agents across medical societies were largely based upon the content of the IDSA's 2011 guidelines, with some variability.

There is a broad consensus that nitrofurantoin monohydrate, trimethoprim/sulfamethoxazole (TMP/SMX), and fosfomycin trometamol are all first-line therapies for acute, uncomplicated cystitis. All, with varying emphasis, highlighted that nitrofurantoin is highly effective based on its ability to concentrate in urine and the low rates of resistance among *E. coli* urinary isolates. However, the IDSA guidelines noted that nitrofurantoin should not be prescribed if pyelonephritis is suspected, as it has poor tissue penetration [11]. Resistance to TMP/SMX is emerging in some US regions, particularly among the elderly [10–12, 14, 15, 18]. Fosfomycin is discussed as less widely available and less effective than nitrofurantoin and TMP/SMX, but still considered first line [10–12, 14, 15]. Due to its low resistance rates, pivmecillinam was included as first-line therapy in several guidelines and is widely used in some European countries, although it is not available in the US [11, 14].

Second-line therapy for acute uncomplicated cystitis was also modeled after the 2011 IDSA guidelines by most of the societal recommendations regarding fluoroquinolones and

Table 2 Clinical recommendations for diagnosis of acute uncomplicated cystitis

Organization	Patient population	Common symptoms	Physical examination	Urine dipstick	Urine C&S	Out-of-office diagnosis
American Urogynecologic Society (AUGS) (via *Female Pelvic Medicine & Reconstructive Surgery)*	Young, nonpregnant women	• Dysuria • Urinary frequency • Urinary urgency • Hematuria • Absence of vaginal discharge • Lower abdominal or suprapubic pain	Pelvic and abdominal exam should be performed	Nitrites and leukocyte esterase are screening tools	• Complicated UTI suspected	Self-treatment for recurrent UTI acceptable (3-day antibiotic)
American Academy of Family Physicians (AAFP)	Premenopausal, nonpregnant, immunocompetent women with no comorbidities or urologic abnormalities	• Dysuria • Urinary frequency • Urinary urgency • Absence of vaginal discharge or irritation	Normal (80–90%) or suprapubic tenderness (10–20%)	Nitrites and leukocyte esterase are diagnostic tools	• **Pyelonephritis suspected** • **Atypical symptoms** • **Symptoms have not resolved 2–4 weeks after treatment**	Telephone diagnosis acceptable
American College of Obstetricians & Gynecologists (ACOG)	Pre- and **postmenopausal** women with no urologic abnormalities or prior urologic surgery	• Dysuria • Urinary frequency • Urinary urgency • Suprapubic pain or pressure	N/A	Nitrites and leukocyte esterase are diagnostic tools	• **Pyelonephritis suspected** • **Negative dipstick with symptoms present** • **No symptom improvement 48 h after treatment**	Self-treatment for recurrent UTI acceptable with or without dipstick self-administered dipstick testing (3-day antibiotic given)
American College of Physicians (ACP) (via *Annals of Internal Medicine)*	Premenopausal, non-catheterized women	• Dysuria • Urinary frequency • Urinary urgency • Hematuria • Absence of vaginal discharge or irritation	N/A	Nitrites and leukocyte esterase confirm the diagnosis **Patients with classic symptoms, without an underlying condition or a likely alternative diagnosis do not require dipstick testing**	• **Cystitis diagnosis is unclear** • **Resistant or unusual organism suspected** • **Treatment failure or recurrent episode suspected** • **Treatment options limited by antibiotic intolerances** • **Pregnant**	Self-treatment for recurrent UTI acceptable (antibiotic given) Telephone diagnosis acceptable

Diagnostic recommendations from the American Urogynecologic Society via *Female Pelvic Medicine & Reconstructive Surgery* are listed as the primary guideline with notable differences among other societies highlighted in bold. No guidelines for the diagnosis of acute, uncomplicated UTI exist from the IDSA

Table 3 Clinical recommendations for treatment of acute uncomplicated cystitis

Organization	First-line treatment	Second-line treatment	Third-line treatment	Treatments to avoid
American Urogynecologic Society (AUGS) (via *Female Pelvic Medicine & Reconstructive Surgery)*	Nitrofurantoin monohydrate/macrocrystals (100 mg bid × 5 days) Trimethoprim/sulfamethoxazole (160/800 mg bid × 3 days)[a] Fosfomycin trometamol (3 g single dose) Pivmecillinam (400 mg bid × 3–7 days)[b]	Ofloxacin, ciprofloxacin, or levofloxacin (3-day regimen) Beta-lactams (3–7 day regimen)	N/A	Amoxicillin or ampicillin alone
American Academy of Family Physicians (AAFP)	Fosfomycin trometamol (3 g single dose) Nitrofurantoin monohydrate/ macrocrystals (100 mg bid × 5 days) Trimethoprim/ sulfamethoxazole (160/800 mg bid × 3 days)[a]	Ciprofloxacin (250 mg bid × 3 days) Ciprofloxacin, extended release (500 mg daily × 3 days) Levofloxacin (250 mg daily × 3 days) Ofloxacin (200 mg daily × 3 days OR 400 mg single dose)	**Amoxicillin/clavulanate (500/125 mg bid × 7 days)** **Cefdinir (300 mg bid × 10 days)** **Cefpodoxime (100 mg bid × 7 days)**	Amoxicillin or ampicillin alone
American College of Obstetricians & Gynecologists (ACOG)	Trimethoprim/sulfamethoxazole (160/800 mg bid × 3 days)[a] Trimethoprim (100 mg bid × 3 days) **Ciprofloxacin (250 mg bid × 3 days)** **Levofloxacin (250 mg daily × 3 days)** **Norfloxacin (400 mg bid × 3 days)** **Gatifloxacin (200 mg daily × 3 days)** Nitrofurantoin monohydrate/macrocrystals (100 mg bid × **7 days**) Nitrofurantoin macrocrystals (50–100 mg qid × **7 days**) Fosfomycin tromethamine (3 g single dose)	Beta-lactams (dosage not listed) Sulfonamides (dosage not listed)	N/A	N/A
American College of Physicians (ACP) (via *Annals of Internal Medicine)*	Nitrofurantoin monohydrate/macrocrystals (100 mg bid × 5 days) Trimethoprim/sulfamethoxazole (160/800 mg bid × 3 days)[a] Fosfomycin trometamol (3 g single dose)	Ofloxacin, ciprofloxacin or levofloxacin (3-day regimen) Beta-lactams (5–7 day regimen)	N/A	N/A
Infectious Diseases Society of America (IDSA)	Nitrofurantoin monohydrate/macrocrystals (100 mg bid × 5 days) Trimethoprim/sulfamethoxazole (160/800 mg bid × 3 days)[a] Fosfomycin trometamol (3 g single dose) **Pivmecillinam (400 mg bid × 3–7 days)[b]**	Ofloxacin, ciprofloxacin, or levofloxacin (3-day regimen) Beta-lactams (amoxicillin-clavulanate, cefdinir, cefaclor, and cefpodoxime-proxetil) (3–7-day regimen)	N/A	Amoxicillin or ampicillin alone

[a] Only recommended if local resistance rates are < 20% and TMP/SMX has not been used for treatment in the past 3 months. Treatment recommendations from the American Urogynecologic Society via *Female Pelvic Medicine & Reconstructive Surgery* are listed as the primary guideline with notable differences among other societies highlighted in bold

[b] Pivmecillinam is not licensed or available in the US

beta-lactams. Despite their high efficacy, fluoroquinolones were considered second-line therapy based on their propensity for adverse side effects, including gastrointestinal toxicity, central nervous system effects, *Clostridium difficile* colitis, and tendinopathy [11]. Beta-lactam agents were considered second-line based on their lower efficacy rates [11].

While there was consensus on the risks and benefits of fluoroquinolone and beta-lactam antibiotics, recommendations on when to prescribe them varied among societies. ACOG outlines ciprofloxacin, levofloxacin, norfloxacin, and gatifloxacin as first-line therapies for treatment of acute, uncomplicated cystitis [10]. ACOG described that their preferred first-line therapy is TMP/SMX, but, if its local resistance rates exceed 20%, then use of a fluoroquinolone is considered equivalent [10]. Beta lactams, including amoxicillin-clavulanate, cefdinir, cefaclor, and cefpodoxime-proxetil, were considered second-line therapy for acute uncomplicated cystitis by the IDSA, ACP, and AUGS [11, 14, 15]. Ampicillin and amoxicillin alone were beta-lactams to avoid entirely, as described by the AAFP, IDSA, and AUGS [11, 12, 14]. Yet, ampicillin, amoxicillin and first-generation cephalosporin antibiotics were recommended as alternative therapies to first-line treatments by ACOG [10].

Dosage was largely uniform across the medical specialties. However, ACOG recommends the use of nitrofurantoin monohydrate at 100 mg, twice daily for 7 days, while all other guidelines and recommendations prefer its use at 100 mg, twice daily for 5 days [10–12, 14, 15].

Discussion

Clinical guidelines and recommendations for the diagnosis and therapeutic management of acute, uncomplicated cystitis published by professional medical societies in the US have important differences. Those reviewed, as well as the articles and endorsements of professional societies within the urology and emergency medicine communities, utilize the 2011 IDSA treatment standards as the foundation for their cystitis treatment recommendations.

Content common to all included the diagnosis of uncomplicated cystitis based on the presence of dysuria, urinary frequency, and urinary urgency, along with a dipstick positive for nitrites and leukocyte esterase. However, dipstick urine testing was not considered important by ACOG in the work-up of a recurrent UTI patient or by the ACP in an instance of a patient with classic UTI symptoms without an underlying condition or competing diagnosis. Urine C&S testing was not recommended in classic presentations of acute, uncomplicated cystitis by any, with a few exceptions that varied across the medical societies. Pelvic examination was recommended by AUGS when entertaining a diagnosis of UTI. North European guidelines on UTI diagnosis in adult women varied more widely than US guidelines, particularly regarding urinalysis, as German and Belgian guidelines outlined algorithms for further diagnostics based on the presence or absence of nitrites and leukocyte esterase, guidelines from The Netherlands focused solely on the presence of nitrites, and Norwegian guidelines advised against urinalysis entirely in UTI diagnostics [19]. However, a similar approach to urine C&S exists between US and North European guidelines, as C&S is indicated only in cases of suspected complicated UTI, recurrent infection, or negative dipstick results in both US and European guidelines [19]. Authors of the North European guidelines expressed various opinions as the basis for their recommendations, some citing fast and efficient care as a priority and others emphasizing shared decision-making as crucial for UTI management [19].

In terms of treatment, nitrofurantoin, TMP/SMX, and fosfomycin were commonly recommended as first-line options for acute, uncomplicated cystitis in the articles we reviewed. All of the recommendations reviewed were critical of fluoroquinolone usage, detailing its contribution to multidrug-resistant organisms and rising rates of resistant bacteria, with almost all guidelines outlining fluoroquinolone prescription as second line, with one exception; ACOG recommended utilizing fluoroquinolones as first-line therapy when resistance to TMP/SMX is greater than 15–20%. In 2008 and 2013, the US Food and Drug Administration (FDA) issued and amended, respectively, a black box warning for fluoroquinolones because of their association with tendon rupture and peripheral neuropathy [20]. Of note, in 2016, the FDA recommended avoiding fluoroquinolones in uncomplicated UTI, unless an alternative therapy does not exist [20]. Health education platforms aimed at consumers, including Choosing Wisely, led by the American Board of Internal Medicine (ABIM), publicize that fluoroquinolones should not be used as first-line therapy for uncomplicated UTI, based on recommendations from the AUA, in order to stimulate conversations between patients and their providers and, ultimately, attenuate the adverse effects and medical misuse of fluoroquinolones [21]. Beta-lactams were outlined as less effective than nitrofurantoin and TMP/SMX and as having many adverse effects by all societies, delegating them as second- or third-tier therapy for acute, uncomplicated cystitis.

The 2011 IDSA guidelines were used as the foundation for many US recommendations, which emphasizes a basis for cystitis management that addresses the benefits and potential risks of broad-spectrum antimicrobials. The IDSA's guidelines reveal that their choices for antibiotic treatment in acute, uncomplicated cystitis are guided by an interplay of antibiotic in vitro resistance patterns, patient history and presentation, and antibiotic efficacy in clinical trials [11]. The IDSA described each drug's potential for risk, or the adverse public health effects of antimicrobial therapy, including the development of multidrug-resistant organisms, in which the IDSA weighed risk more heavily than antimicrobial efficacy [11].

For example, the IDSA recommends fosfomycin and pivmecillinam as first-line agents, despite their lower efficacy, because they have a substantially lower potential for harm [11]. Utilization of IDSA recommendations throughout professional medical specialty guidelines for acute, uncomplicated cystitis points to a shift in the evaluation of antibiotic treatment from merely the benefits and drawbacks to the individual patient to include society at large as well.

These UTI guidelines and recommendations were published in national and international journals in the case of the IDSA guidelines. It is thus illuminating to correlate the differences in diagnostic and treatment expectations of these recommendations with numerous studies that detail a lack of adherence in in- and outpatient practices in the US. Adherence to UTI recommendations across specialties is remarkably low, with over-prescription of second- and third-line antimicrobials and over-treatment with fluoroquinolones documented in previous studies, as evidenced by local studies in Arizona and Washington, DC [8, 9]. A US cross-sectional study from 1996 to 2001 of uncomplicated UTI using data from the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHMCS) revealed that 24.2% of patients received ciprofloxacin and 11.2% received another fluoroquinolone as first-line therapy for UTI, which is attributed to a lack of guideline knowledge and the influence of antimicrobial costs on physician decision-making [22]. As *E. coli* isolates resistant to TMP/SMX and fluoroquinolones, including extended spectrum beta-lactamase strains (ESBLs), continue to rise worldwide [23], there is a sense of urgency for increased attention to antibiotic stewardship [24]. A focus group of Irish general practitioners who treat UTI revealed several strategies to promote antibiotic stewardship, including the incorporation of antimicrobial resistance discussions into UTI patient encounters to justify delayed treatment strategies and avoidance of overtreatment [25]. Antibiotic stewardship is unlikely to result from one-time interventions on physician practices and instead require a combination of interactive workshops, audits, and feedback reports on antibiotic prescribing and guideline adherence to elicit changes in management [25].

Antibiotic stewardship is critical for making sure clinicians prescribe the right antibiotic for the appropriate duration [26]. While there have been efforts to promote antibiotic stewardship for UTIs [27–29], the high rates of non-adherence to "standards" [8, 9] may stem in part from clinicians who have sought guidance from published expert opinion that is not consistent with other published opinions or societal guidelines. Likewise, quality indicators, which are a commonly used means to improve processes and outcomes of care [30, 31], cannot be developed or expected to achieve consensus if there is heterogeneity of recommendations.

Despite the drawbacks of a heterogeneity of antimicrobial therapies for the management of acute, uncomplicated cystitis, they remain the mainstay of successful symptomatic and microbiologic resolution of UTI. Trials of non-steroidal anti-inflammatory drugs (NSAIDs), including ibuprofen and diclofenac, have been tested against fosfomycin and norfloxacin therapy, respectively, in randomized controlled trials; however, both trials resulted in significantly higher symptom scores and rates of pyelonephritis in those in the NSAID groups [32, 33]. Statistics such as these elucidate the risks of developing a complicated UTI from antimicrobial-sparing strategies, emphasizing that antimicrobials remain the backbone of UTI therapy and should be administered prudently, rather than eliminated entirely, from the therapeutic regimen.

The rapid increase in antibiotic resistance among uropathogenic *E. coli* and other organisms causing UTI suggests that empiric use of antimicrobials in acute, uncomplicated cystitis may eventually be considered inappropriate in some patients. It can be anticipated that future cystitis guidelines may recommend routine urine culture and sensitivity testing or rapid UTI diagnostic methods in patients with risk factors for infection due to antibiotic resistant organisms, such as recent antibiotic therapy, recent hospitalization, or residence in a long-term healthcare facility [34]. As we move closer to this paradigm, it should be recognized that urine culture and sensitivity, a gold standard diagnostic, is not without its limitations. A US study conducted in Washington and Florida comparing midstream urine specimens to catheterized urine samples in women with symptoms consistent with acute cystitis revealed that while low colony counts of *E. coli* (10 to 10^2 CFU/ml) colonizing the bladder were detected in midstream urine samples, gram-positive organisms, such as *Enterococci* and *Group B Streptococcus*, were often detected in midstream urine samples, yet were not grown in catheter-collected samples [35]. This discrepancy reveals that *Enterococci* and *Group B Streptococcus* are infrequent contributors to UTI, despite growth in midstream urine specimens, resulting in inappropriate treatment, while an underlying *E. coli* infection of the bladder goes undetected [35].

Limitations of our review include the focus on clinical recommendations for the management of acute, uncomplicated cystitis rather than other types of UTI. The evidence for and against their content was not critically assessed, although the most recent guidelines for UTIs from the IDSA did not comment on pyelonephritis thus making a meaningful comparison of guidelines and expert opinion not ideal.

In summary, there are important differences among US professional society guidelines and expert recommendations for the diagnosis and treatment for acute, uncomplicated cystitis. The lack of uniformity makes efforts to measure quality and implement antibiotic stewardship programs problematic. Future directions should be aimed at development of multidisciplinary consensus guidelines that are easy to operationalize for quality improvement purposes. This key development

would be critical to measuring and improving clinician adherence to guidelines that could reduce patient harm and overutilization of already scarce antibiotics in an era where antibiotic resistance grows increasingly more important.

Compliance with ethical standards

Conflicts of interest None.

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