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Proposing the 'Continuum of Urinary Tract Infection (UTI)' for a Nuanced Approach to Diagnosis and Management of UTIs

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UTI continuum workgroup

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Abstract

Purpose: Patients with suspected urinary tract infections (UTIs) are categorized into three clinical phenotypes based on current guidelines: no UTI, asymptomatic bacteriuria (ASB), or UTI. However, all patients may not fit neatly into these groups. Our objective was to characterize clinical presentations of patients who receive urine tests using the 'continuum of UTI' approach.

Materials and Methods: This was a retrospective cohort study of a random sample of adult non-catheterized inpatient and ED encounters with paired urinalysis and urine cultures from five hospitals in three states between 01/01/2017 and 12/31/2019. Trained abstractors collected clinical (e.g., symptom) and demographic data. A focus group discussion with multidisciplinary experts was conducted to define the 'continuum of UTI', a 5-level classification scheme that includes two new categories: lower urinary tract symptoms/other urologic symptoms (LUTS/OUS) and

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bacteriuria of unclear significance (BUS). The newly defined 'continuum of UTI' categories were compared to current UTI classification scheme.

Results: Of 220,531 encounters, 3392 randomly selected encounters were reviewed. Based on the current classification scheme, 32.1% (n=704) had ASB and 53% (n=1614) did not have a UTI. When applying the 'continuum of UTI' categories, 68% of patients (n=478) with ASB were reclassified as BUS and 29% of patients (n=467) with 'no UTI' were reclassified to LUTS/OUS.

Conclusions: Our data suggest the need to reframe our conceptual model of UTI vs. ASB to reflect the full spectrum of clinical presentations, acknowledge the diagnostic uncertainty faced by front line clinicians, and promote a nuanced approach to diagnosis and management of UTIs.

Plain Language Summary

Our large multicenter study of adult inpatients revealed that current practice guidelines for urinary tract infection (UTI) do not accurately classify patients with asymptomatic bacteriuria (ASB) and lower urinary tract symptoms. These findings suggest the need to reframe how we define ASB and UTIs to reflect the full spectrum of patient presentations.

Keywords

Bacteriuria of unclear significance; BUS; bacteriuria; LUTS; asymptomatic bacteriuria; urinary tract infection; antibiotic stewardship

Background:

Practice guidelines recommend against antibiotic treatment for asymptomatic bacteriuria (ASB), which occurs in up to 50% of hospitalized patients. Despite this strong recommendation, a large proportion of patients with ASB are treated with antimicrobials for a urinary tract infection (UTI). Treatment of ASB is associated with increased length of stay, antibiotic resistance, and *Clostridioides difficile* infection (CDI). However, two major challenges exist with appropriate management of patients with suspicion of UTI.

First, patients with positive urine cultures have historically been diagnosed with ASB or UTI based on absence or presence of symptoms referrable to the urinary tract. The Infectious Diseases Society of America (IDSA) guidelines recommend against antimicrobials in older adults with cognitive impairment and delirium in the absence of localized genitourinary symptoms or other systemic signs of infection. However, many hospitalized patients, especially older adults, often present to the emergency department (ED) with non-specific symptoms like fever, hypotension, and delirium in the setting of abnormal urine tests. Because of the diagnostic uncertainty in these cases, front-line clinicians perceive these patients to be symptomatic and often treat with antimicrobials for UTI. Antibiotic stewardship teams, on the other hand, classify these patients as ASB and recommend withholding antibiotics. These clinical scenarios highlight differences between the front line clinicians' and antibiotic stewardship teams' definitions of 'asymptomatic', highlighting the ambiguity of the term 'ASB'.

Second, urine culture thresholds of 100,000 colony forming units per milliliter (CFU/ml) have been recommended for diagnosis of cystitis and ASB by regulatory agencies and IDSA^{1,9,10} This cut-off of 100,000 CFU/ml is based on one study performed over 60 years ago. ¹¹ Since then, several studies have identified subsets of women who present with pyuria and symptoms consistent with a UTI, but who have colony counts <100,000 CFU/mL in voided urine. ^{12,13} Furthermore, lower colony counts may be treated as contamination or colonization and may not even be reported by laboratories, despite potential clinical significance. ¹⁴

Our objectives were (1) to understand the clinical presentation of patients who receive urine tests in a cohort of diverse hospitals and (2) to characterize the 'continuum of UTI' and compare with the current classification scheme.

Methods:

Study Design and Setting:

This retrospective cohort study was conducted across five study hospitals (one academic medical center, four community hospitals) in three states (North Carolina, Virginia, Georgia). Sites that performed reflex urinalysis to culture orders were excluded due to variability in reflex criteria. This study was considered exempt by Duke University Institutional Review Board (IRB, protocol no. 00107418). We also received IRB exemption for this project from the other sites.

Study Population:

Patients were eligible for inclusion if (1) they were hospitalized or seen in the ED of one of the five study hospitals between January 1, 2017 and December 31, 2019, and (2) received a urinalysis and urine culture order within 24 hours of each other. Exclusion criteria included age less than 18 years and presence of an indwelling urinary catheter. Duplicate or repeat patient encounters were also excluded. A random number generator was used to select patient encounters from each site for chart review.

Chart Review Process:

All abstractors were trained using a standardized chart review protocol prior to initiating chart reviews. Trained abstractors collected data from selected patients into a 60-question electronic Redcap survey (Supplement 1). Objective data abstracted from medical records included demographics, laboratory and radiographic findings, as well as clinical signs and symptoms. Symptoms were collected from clinician and nursing documentation 48hrs before and after urine culture collection. A standardized data dictionary was created and random audits of 10% of charts were conducted by the lead investigator to ensure data integrity. The lead investigator (SDA) held biweekly virtual meetings with abstractors to review any discrepancies from audits and address questions.

Focus Group Discussion:

The lead investigator led an hour-long semi-structured discussion to gather different insights and perspectives regarding the categorization of UTIs. Focus group discussion details and

themes are described in Supplement 2. Based on this discussion, a new classification scheme was proposed that includes the three current phenotypes (UTI, ASB, no UTI) and two new categories: Lower Urinary Tract Symptoms/ Other Urologic Symptoms (LUTS/OUS) and Bacteriuria of Unclear Significance (BUS, see Table 1 and Supplement 4)).

Categorization:

We classified no UTI, ASB and UTI based on American Urologic Association (AUA), Centers for Disease Control and Prevention, and Infectious Diseases Society of America (IDSA) guidelines, ^{1,17}, but did not differentiate between complicated and uncomplicated UTIs due to forthcoming updates to the IDSA guidelines, as well as differences in the IDSA, AUA, and American Urogynecologic Society definitions of complicated UTI^{17–19}. Our focus group discussion of experts (Supplement 2) defined objective criteria for case classification based on current definitions (table 1, Supplement 5).

Primary outcomes:

The primary outcome studied was the distribution of patients along the 'continuum of UTI' categories: no UTI, LUTS/OUS, ASB, BUS and UTI. Secondary outcomes included length of stay, CDI within 7 days, 30-day readmission, 30-day mortality, and repeat urine culture test within 7 days.

Analysis:

The 'continuum of UTI' categories were descriptively compared to the current UTI classification scheme by reporting patient frequencies. As a sensitivity analysis, we also described the 'continuum of UTI' categories with patient frequencies when a lower bacterial colony count threshold (<100,000 CFU/ml) was used to define ASB, BUS, and UTI. Continuous variables were reported as median (interquartile range, IQR) and categorical variables were reported as n (%). Comparisons were evaluated by Kruskal Wallis tests and chi-square tests separately for No UTI vs LUTS/OUS and ASB vs BUS vs UTI, with statistical significance determined at the α =0.05 level. Data analyses were performed using SAS software, version 9.4 (SAS Institute, Inc., Cary, NC, USA).

Results:

During the study period, 220,531 encounters met study criteria. Of these, a random sample of 3392 encounters were reviewed and included for analysis.

Baseline variables (Entire cohort):

Median age across the entire cohort was 67 years (IQR: 54–79 years) and 2021 (59.6%) patients were female. Additionally, 627 (18.5%) patients had private insurance, and 817 (24.2%) patients had an underlying immunocompromising condition. Of the 3392 patient encounters, 1427 (42.1%) urine cultures grew organisms 100,000 CFU/ml, 1038 (30.6%) were negative, 578 (17%) grew mixed flora, and 349 (10.3%) grew 1000–99,999 CFU/ml. Forty percent of urine cultures were obtained in the ED, 28.2% in medical wards, 11.3% in surgical wards, and 6.8% each from intensive care units and medical/surgical wards.

Comparison of Continuum of UTI categories:

Using the current UTI classification scheme, 723 (21.3%) patients met criteria for UTI, 704 (20.8%) met criteria for ASB, and 1614 (47.6%) met criteria for 'no UTI'. On applying the new 'continuum of UTI' categories, the prevalence of ASB decreased to 226 due to reassignment of 478 patients to BUS. The prevalence of 'no UTI' patients decreased to 1147 due to reassignment of 467 patients to LUTS/OUS. (Table 2). Three hundred and fifty-one (10.3%) patients with <100,000 CFU/ml growth in urine cultures were not classified in any category, initially, as there is no consistent guidance on whether to classify them as 'no UTI' or ASB or contamination. In a sensitivity analysis, lowering the bacterial threshold to <100,000 CFU/ml classified 152 cases as UTI (increased UTI cases to 875 from 723). The remaining 199 encounters were classified as ASB (n=50) or BUS (n=149) (Figure 1). These data have been stratified by sex in Supplement 3.

Baseline variables (continuum of UTI):

Sociodemographic variables, clinical characteristics, and laboratory data across the five categories of the continuum of UTI are described in Table 3. When comparing ASB, BUS, and UTI, statistically significant differences were detected in the distributions of age (p=0.022), sex (p=0.049), and levels of pyuria on urinalysis (p=0.001), with estimates suggesting that patients with ASB tended to be older, of female sex, and have lower levels of pyuria than patients with BUS or UTI. Significant differences were also detected in the distributions of age (p=0.013), ethnicity (p=0.013), body mass index (BMI, p=0.017), levels of pyuria (p<0.001), and presence of nitrite (p=0.002) on urinalysis between patients with no UTI vs. LUTS/OUS, with estimates suggesting that patients with LUTS tended to be older, of lower BMI, and have higher levels of pyuria and positive nitrite as compared to patients with no UTI (Table 3).

Secondary Outcomes:

A statistically significant difference was detected in the length of stay distributions for ASB, BUS, and UTI (p=0.013), with estimates suggesting that patients with BUS tended to have longer hospital stays than patients with ASB or UTI. Additionally, there is a statistically significant difference in the likelihood of patients having a repeat urine culture after 7 days (p=0.004), with estimates suggesting the likelihood is higher for patients with BUS or UTI. There was no statistically significant difference for 30-day mortality, 30-day readmission, or CDI test at 7 days (Table 4).

Discussion:

Our large retrospective cohort study of patients who underwent urine testing in five hospitals reveals three important findings related to diagnostic workup of patients with suspected UTI. First, almost two thirds of patients who undergo testing for UTI did not have signs or symptoms localizing to the urinary tract. Using our "continuum of UTI" approach, bacteriuric patients with non-localizing symptoms or those unable to provide symptom data were reclassified as BUS. This newly defined BUS category acknowledges clinical signs or symptoms that are significant to front line clinicians and patients, even if not classified as UTI by the current classification scheme. Patients with BUS based on our classification also

tended to have longer hospital stays than patients with ASB or UTI, which may reflect some combination of higher severity of illness, more diagnostic uncertainty, or receipt of more healthcare interventions. Hence, reclassifying patients as BUS may provide an opportunity to acknowledge diagnostic uncertainty and need for additional monitoring than ASB patients so as to promote a nuanced and patient-centered approach to diagnosis and management.

Second, almost a third of patients initially diagnosed as 'no UTI' based on culture results were reclassified into LUTS/OUS based on symptoms. In prior studies, 20% of patients with urinary symptoms had negative cultures and were historically referred to as having the 'urethral syndrome'.^{20,21} In our cohort, we classified patients with negative urine cultures with symptoms referable to the urinary tract as LUTS/OUS. In practice, LUTS is a broad term referring to voiding or obstructive symptoms (hesitancy, poor and/or intermittent stream, dribbling, etc) and storage or irritative symptoms (frequency, urgency, urge incontinence, and nocturia).^{21,22,23} In most of these LUTS/OUS cases, further work-up is needed to determine which of these patients would benefit from symptomatic treatment, antibiotic therapy, further diagnostic evaluation by requesting species level identification of mixed flora, additional testing for pathogens that do not grow readily in culture, or examining the laboratory's urine culture diagnostic threshold if suspicion for true UTI exists^{24,25}.

Third, our sensitivity analysis suggested that lowering the bacterial threshold in some symptomatic patients may capture additional patients with UTI whose symptoms may be dismissed due to concern for contamination or attributed to LUTS rather than infection. However, current UTI and ASB guidelines use 100,000 CFU/ml as the cut-off for diagnosing bacteriuria. 1,9,18,19 This diagnostic threshold has been widely accepted since the 1956 landmark study by Kass¹¹, who compared urine specimens from adult women with pyelonephritis and 3 groups of asymptomatic women. He demonstrated that 1% of adult women had colony counts between 10,000 and 100,000 CFU/ml in random urine samples. However, in patients with clinical pyelonephritis, colony counts rapidly increased from 10,000 to more than 1,000,000 CFU/ml. In the 1980s, Stamm et al. questioned this bacterial threshold of 100,000 CFU/ml in his analysis of symptomatic women and proposed cut-off rates as low as 100 CFU/mL for symptomatic UTI.¹² Recently, Hooton et al. confirmed that low counts of *Escherichia coli* in midstream urine was predictive of clinically significant bacteriuria, not contamination.¹² Additional research is needed to determine whether better CFU thresholds exist to guide clinical care, or if recently described enhanced culture and culture-independent methods may enhance diagnostic accuracy. ^{26,27}

Our findings suggest the need to reframe our conceptual model of UTI vs. ASB to recognize clinical uncertainty and reflect the full spectrum of clinical presentations. Recent data suggest that UTI may present as a bidirectional continuum from asymptomatic bladder colonization to a symptomatic bladder infection. Some populations (e.g., older adults, catheterized patients) may not present with signs or symptoms referable to the urinary tract or may have chronic lower urinary tract symptoms that makes differentiating ASB from UTI difficult. The use of dichotomous terminology (UTI vs ASB) may strain the relationship between stewardship teams and clinicians, cause anxiety among patients and caregivers, and lead to workarounds like prescribing antibiotics at discharge. Some populations (e.g., older adults, catheterized patients) may not present with signs or symptoms referable to the urinary tract or may have chronic lower urinary tract symptoms that makes differentiating ASB from UTI difficult. Some populations (e.g., older adults, catheterized patients) may not present with signs or symptoms referable to the urinary tract or may have chronic lower urinary tract symptoms that makes differentiating ASB from UTI difficult. Some populations (e.g., older adults, catheterized patients) may not present with signs or symptoms referable to the urinary tract or may have chronic lower urinary tract symptoms and signs of symptoms and signs of symptoms and symptoms and symptoms are symptoms.

Prior expert commentaries have recommended the use of alternative terms for patients that do not meet ASB or UTI definition like "pseudo-UTI", bacteriuria pyuria of clinically undetermined significance (BPCUS), subclinical UTI, etc. ^{8,28,32} However, terms like "pseudo" may carry a negative association, while other terms have not gained consensus across multiple specialties. We chose "focus group" methodology as our goal was to explore different opinions from experts across multiple specialties, leverage group interactions, and enhance communication among participants. Our focus group discussion concluded that labeling the diagnostic uncertainty in patients with bacteriuria or chronic lower urinary tract symptoms (BUS or LUTS), will allow for improved communication with teams in addition to nuanced and patient-focused treatment approaches (e.g., watchful waiting, symptomatic therapy, etc).

Our study has limitations. First, this is a retrospective observational study and we were limited in assessment of symptoms and signs of UTI by chart review. This process was standardized by collection of objective data only, while adjudication to different "continuum of UTI" categories was done during analysis. This cohort only included patients that received urine tests and, hence, findings from this study should not be used to estimate prevalence rates of LUTS, BUS, ASB or UTI in the general population. The study population does not include children. Finally, our findings are primarily descriptive and should be interpreted with caution. Specifically, our statistical analysis is based on definitions from our focus group discussion by a group of multi-disciplinary experts, and will need future validation using a modified-Delphi approach, assessment of feasibility and acceptability, as well as nuances of implementation.

Conclusions

Our study highlights the complexity of UTI diagnosis and the challenges faced by clinicians in applying consistent definitions. The goal of classifying patients as having "BUS" as opposed to ASB or UTI, is not to promote antimicrobial therapy in these cases. Instead, our categorization scheme recognizes signs and symptoms significant to front line clinicians and patients to improve communication and promote patient centered interventions. These finds are meant to contribute to the ongoing dialogue on refining ASB and UTI definitions, rather than replacing current definitions, particularly for tested populations that do not fit within existing criteria. In the future, our objective criteria can be used to develop a UTI risk calculator to determine which patients with BUS would benefit from antimicrobial treatment. Further research and collaboration among professional societies are warranted to address these discrepancies and establish clearer guidelines to enhance clinical practice and patient care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of Interest:

Dr Advani reports support from the Centers for Disease Control and Prevention (grant nos. 5U54CK000616-02 and SHEPheRD 75D30121D12733-D5-E003), the Society for Healthcare Epidemiology of America, and the Duke Claude D. Pepper Older Americans Independence Center (National Institute on Aging grant no. P30AG028716), as well as consulting fees from Locus Biosciences (ended), Sysmex America (ended), GlaxoSmithKline, bioMérieux, and the Infectious Diseases Society of America. Dr. North reports support from the Centers for Disease Control and Prevention (SHEPheRD 75D30121D12733-D5-E003), the Duke Claude D. Pepper Older Americans Independence Center (National Institute on Aging grant no. P30AG028716)

References:

- 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):e83–e110. [PubMed: 30895288]
- 2. Fakih MG, Advani SD, Vaughn VM. Diagnosis of urinary tract infections: need for a reflective rather than reflexive approach. Infect Control Hosp Epidemiol. 2019:1–2.
- 3. 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. [PubMed: 33324723]
- 4. Mody L, Juthani-Mehta M. Urinary tract infections in older women: a clinical review. JAMA. 2014;311(8):844–854. [PubMed: 24570248]
- 5. Rowe TA, Juthani-Mehta M. Diagnosis and management of urinary tract infection in older adults. Infect Dis Clin North Am. 2014;28(1):75–89. [PubMed: 24484576]
- 6. Crnich CJ, Jump RL, Nace DA. Improving Management of Urinary Tract Infections in Older Adults: A Paradigm Shift or Therapeutic Nihilism? J Am Geriatr Soc. 2017;65(8):1661–1663. [PubMed: 28653467]
- 7. McKenzie R, Stewart MT, Bellantoni MF, Finucane TE. Bacteriuria in individuals who become delirious. Am J Med. 2014;127(4):255–257. [PubMed: 24439075]
- 8. Gomolin IH. When Asymptomatic Bacteriuria is not Asymptomatic or "Pseudo-Urinary Tract Infection". J Am Geriatr Soc. 2018;66(11):2223. [PubMed: 30289984]
- CDC. National Healthcare Safety Network (NHSN) Patient Safety Component Manual. https://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual_current.pdf. Published January 2017. Accessed January 1, 2017.
- FDA. Uncomplicated Urinary Tract Infections: Developing Drugs for Treatment Guidance for Industry. https://www.fda.gov/media/129531/download. Published 2019. Accessed Aug 22,, 2022.
- 11. Kass EH. Asymptomatic infections of the urinary tract. Trans Assoc Am Physicians. 1956;69:56–64. [PubMed: 13380946]
- 12. 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. [PubMed: 7099208]
- 13. 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. [PubMed: 24224622]
- Smith MA, Lamb MJ, Baillie L, Simor A, Leis JA. Clinical Significance of Low Colony-Count Urine Cultures Among Hospitalized Inpatients. Infect Control Hosp Epidemiol. 2018;39(4):488–489. [PubMed: 29428000]

15. Folaranmi T, Harley C, Jolly J, Kirby A. Clinical and microbiological investigation into mixed growth urine cultures. J Med Microbiol. 2022;71(5).

- 16. Whelan P, Nelson A, Kim CJ, et al. Investigating Risk Factors for Urine Culture Contamination in Outpatient Clinics: A New Avenue for Diagnostic Stewardship. Antimicrob Steward Healthc Epidemiol. 2022;2(1).
- 17. Nicolle LE, Bradley S, Colgan R, et al. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis. 2005;40(5):643–654. [PubMed: 15714408]
- 18. Anger J, Lee U, Ackerman AL, et al. Recurrent Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Guideline. J Urol. 2019;202(2):282–289. [PubMed: 31042112]
- 19. Gupta K, Hooton TM, Naber KG, et al. 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):e103–120. [PubMed: 21292654]
- Aspevall O, Hallander H, Gant V, Kouri T. European guidelines for urinalysis: a collaborative document produced by European clinical microbiologists and clinical chemists under ECLM in collaboration with ESCMID. Clin Microbiol Infect. 2001;7(4):173–178. [PubMed: 11422238]
- 21. Stamm WE, Wagner KF, Amsel R, et al. Causes of the acute urethral syndrome in women. N Engl J Med. 1980;303(8):409–415. [PubMed: 6993946]
- 22. Coyne KS, Sexton CC, Thompson CL, et al. The prevalence of lower urinary tract symptoms (LUTS) in the USA, the UK and Sweden: results from the Epidemiology of LUTS (EpiLUTS) study. BJU Int. 2009;104(3):352–360. [PubMed: 19281467]
- 23. Zhang AY, Xu X. Prevalence, Burden, and Treatment of Lower Urinary Tract Symptoms in Men Aged 50 and Older: A Systematic Review of the Literature. SAGE Open Nurs. 2018;4:2377960818811773.
- Patel R, Polage CR, Dien Bard J, et al. Envisioning Future Urinary Tract Infection Diagnostics. Clin Infect Dis. 2022;74(7):1284–1292. [PubMed: 34463708]
- 25. Nyayadhish R, Mishra K, Kumar M, Saigal K. Identification of Probable Urinary Tract Infection in Children Using Low Bacterial Count Thresholds in Urine Culture. Indian Pediatr. 2023;60(5):369–372. [PubMed: 36756998]
- 26. 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. [PubMed: 36093322]
- 27. Price TK, Dune T, Hilt EE, et al. The Clinical Urine Culture: Enhanced Techniques Improve Detection of Clinically Relevant Microorganisms. J Clin Microbiol. 2016;54(5):1216–1222. [PubMed: 26962083]
- 28. Trautner BW. Urinary Tract Infections as a Continuum: Implications for Diagnostic and Antibiotic Stewardship. Clin Infect Dis. 2021;72(8):1339–1341. [PubMed: 32179895]
- 29. Tjilos M, Drainoni ML, Burrowes SAB, et al. A qualitative evaluation of frontline clinician perspectives toward antibiotic stewardship programs. Infect Control Hosp Epidemiol. 2023:1–7.
- 30. Boiko O, Gulliford MC, Burgess C. Revisiting patient expectations and experiences of antibiotics in an era of antimicrobial resistance: Qualitative study. Health Expect. 2020;23(5):1250–1258. [PubMed: 32666579]
- 31. Vaughn VM, Gandhi TN, Chopra V, et al. Antibiotic Overuse After Hospital Discharge: A Multihospital Cohort Study. Clin Infect Dis. 2021;73(11):e4499–e4506. [PubMed: 32918077]
- 32. Johnson JR, Drekonja DM. Bacteriuria/Pyuria of Clinically Undetermined Significance (BPCUS): Common, but Currently Nameless. Am J Med. 2017;130(5):e201–e204. [PubMed: 28011317]
- 33. Gupta S, Preece J, Haynes A, Becknell B, Ching C. Differentiating Asymptomatic Bacteriuria From Urinary Tract Infection in the Pediatric Neurogenic Bladder Population: NGAL As a Promising Biomarker. Top Spinal Cord Inj Rehabil. 2019;25(3):214–221. [PubMed: 31548788]
- 34. Nanda N, Juthani-Mehta M. Novel biomarkers for the diagnosis of urinary tract infection-a systematic review. Biomark Insights. 2009;4:111–121. [PubMed: 19707519]

35. Edwards G, Seeley A, Carter A, et al. What is the Diagnostic Accuracy of Novel Urine Biomarkers for Urinary Tract Infection? Biomark Insights. 2023;18:11772719221144459.

36. Slade SC, Molloy E, Keating JL. The dilemma of diagnostic uncertainty when treating people with chronic low back pain: a qualitative study. Clin Rehabil. 2012;26(6):558–569. [PubMed: 21971757]

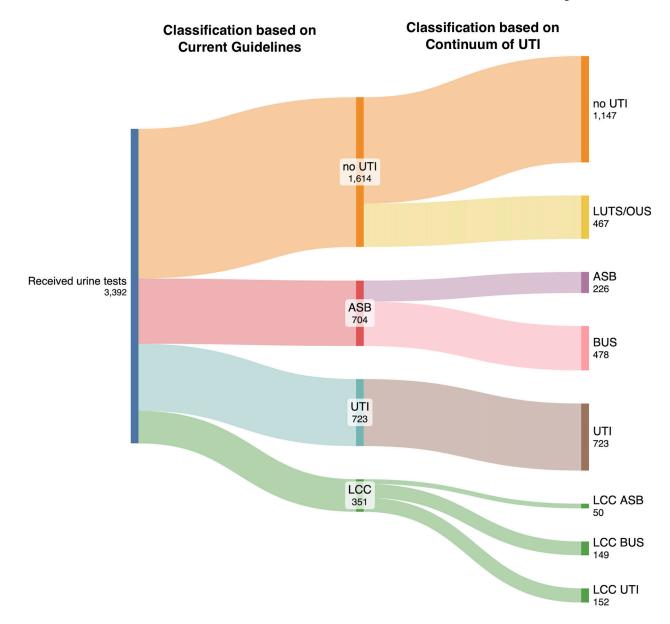


Figure 1:Comparison of Urinary Tract Infection (UTI) categories based on current IDSA guidelines and new "continuum of UTI" definition

UTI: Urinary Tract Infection, ASB: Asymptomatic bacteriuria, LUTS/OUS: Lower urinary tract symptoms/ other urologic symptoms, BUS: bacteriuria of unclear significance

Table 1:Definitions used for different clinical presentations in patients who receive urine tests

	Culture results	Signs and symptoms per IDSA/AUA guidelines	Signs and symptoms per continuum of UTI
No UTI	Negative or mixed urine culture	All patients	Without any lower or upper urinary tract symptoms
Lower Urinary Tract Symptoms/ Other Urologic Symptoms (LUTS/OUS)		NA	With upper or lower urinary symptoms OR Any urologic criteria
Asymptomatic Bacteriuria (ASB)	Positive urine culture 100,000CFU/ml (1000 CFU/ml in sensitivity analysis)	Without specific signs or symptoms of a urinary tract infection (may have clinical criteria)	Without specific signs or symptoms of a urinary tract infection or any clinical criteria
Bacteriuria of Unclear Significance (BUS)		NA	One clinical criterion with or without other cause OR cannot express symptoms (may have urologic criteria without clinical criteria)
Urinary Tract Infection (UTI)		Specific signs or symptoms of a urinary tract infection: Lower or upper urinary tract symptoms OR Two clinical criteria without other cause (e.g., fever + confusion) OR one clinical criterion + one urologic criterion (eg fever + hematuria)	Specific signs or symptoms of a urinary tract infection: Lower or upper urinary tract symptoms OR two clinical criteria without other cause OR one clinical criterion + one urologic criterion

Specific signs or symptoms of a urinary tract infection: dysuria, urgency, frequency, suprapubic pain or tenderness, flank pain or tenderness

Urologic criteria: urologic procedure or surgery causing mucosal bleeding, urologic obstruction, e.g., stones or active urogynecologic malignancy; retention or incontinence; urologic trauma causing hematuria (catheter trauma; stent placement, etc)

Clinical criteria: These include constitutional or non-specific signs or symptoms that do not localize to the urinary tract like fever, rigors, hypotension, hypothermia, shock, nausea, vomiting, or confusion

PS: no catheterized patients included

Table 2:

Comparison of Urinary Tract Infection (UTI) categories based on current IDSA guidelines and new "continuum of UTI" definition.

	UTI Classification base	d on current I	DSA guidelines	(n, %)		
Category	Low bacterial colony count	No	UTI	А	SB	UTI
Population	Positive culture <100,000CFU/ml	Mixed + Neg	gative cultures	Positive cult	ure cut off 100	0,000 CFU/ml
All patients (N=3392)	351 (10.3)	1614	(47.6)	704	(20.8)	723 (21.3)
	New Definition	of Continuum	of UTI (n, %)			
Category	Low bacterial colony count	No UTI	LUTS/OUS	ASB	BUS	UTI
Population	Positive culture <100,000CFU/ml	Mixed + Neg	gative cultures	Positive cult	ure cut off 100	0,000 CFU/ml
All patients (N=3392)	351 (10.3)	1147 (33.8)	467 (13.8)	226 (6.7)	478 (14.1)	723 (21.3)
Sensiti	ivity Analysis: Continuum of UTI u	sing lower pos	itive urine cultı	ire threshold	1000 cfu/ml	
Category	NA	No UTI	LUTS/OUS	ASB	BUS	UTI
Population		Mixed + Neg	gative cultures	Any g	growth on urine	culture
All patients (N=3392)		1147 (33.8)	467 (13.8)	276 (8.1)	627 (18.5)	875 (25.8)

ASB- Asymptomatic bacteriuria, LUTS/OUS- Lower Urinary Tract Symptoms/ Other Urologic Symptoms, BUS- Bacteriuria of Unclear Significance, CFU/ml- colony forming units per milliliter

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Table 3.

Patient and Laboratory Characteristics by Continuum of UTI Categories

Characteristic (N, % unless stated)	No UTI (N=1147)	LUTS/OUS (N=467)	ASB (N=226)	BUS (N=478)	(N=723)
Age, Median (IQR)	63 (51, 74)	66 (51, 78)	73 (61, 83)	71 (59, 82)	70 (57, 81)
BMI, Median (IQR)	27.3 (23, 32.6)	26.5 (22.7, 31.2)	27.6 (23.3, 34.4)	26.5 (22.5, 32.4)	27.1 (23, 33.9)
Female	563 (49.1)	240 (51.4)	171 (75.7)	318 (66.5)	501 (69.3)
Race					
Black or African American	356 (31.0)	129 (27.6)	63 (27.9)	143 (29.9)	217 (30)
White	717 (62.5)	305 (65.3)	153 (67.7)	321 (67.2)	466 (64.5)
Other	(0.9) 69	32 (6.9)	10 (4.4)	14 (2.9)	40 (5.5)
Hispanic Ethnicity	38 (3.3)	28 (6.0)	3 (1.3)	6 (1.3)	21 (2.9)
Private Insurance	293 (25.5)	106 (22.7)	20 (8.8)	66 (13.8)	89 (12.3)
Immunosuppressed	353 (30.8)	130 (27.8)	31 (13.7)	92 (19.2)	123 (17.0)
Urinalysis Pyuria (WBCs/hpf)					
< 5	656 (57.2)	241 (51.6)	29 (12.8)	73 (15.3)	58 (8.0)
5–9	132 (11.5)	52 (11.1)	24 (10.6)	50 (10.5)	58 (8.0)
10–14	62 (5.4)	26 (5.6)	23 (10.2)	36 (7.5)	61 (8.4)
15–19	37 (3.2)	13 (2.8)	16 (7.1)	23 (4.8)	36 (5.0)
20–29	32 (2.8)	25 (5.4)	28 (12.4)	54 (11.3)	71 (9.8)
> 30	119 (10.4)	82 (17.6)	101 (44.7)	234 (49.0)	430 (59.5)
Urinalysis Nitrite Present	47 (4.1)	37 (7.9)	113 (50)	216 (45.2)	347 (48)
Clinical Characteristics of Patients					
Lower UTI symptoms	0 (0)	143 (30.6)	0 (0)	0 (0)	329 (45.5)
Upper UTI symptoms	0 (0)	61 (13.1)	0 (0)	0 (0)	112 (15.5)
Suprapubic tenderness	0 (0)	24 (5.1)	0 (0)	0 (0)	53 (7.3)
Flank tenderness	0 (0)	35 (7.5)	0 (0)	0 (0)	83 (11.5)
Clinical Criteria *					
Fever (>=100.4F)	308 (26.9)	129 (27.6)	0 (0)	46 (9.6)	282 (39.0)
Chills or Rigors	102 (8.9)	61 (13.1)	(0) 0	8 (1.7)	161 (22.3)

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Characteristic (N, % unless stated)	No UTI (N=1147)	LUTS/OUS (N=467)	ASB (N=226)	BUS (N=478)	UTI (N=723)
Hypothermia (<95F)	13 (1.1)	10 (2.1)	0 (0)	(0) 0	8 (1.1)
Hypotension (< 90/60)	120 (10.4)	49 (10.5)	0 (0)	19 (4.0)	112 (15.5)
Confusion/Delirium	192 (16.7)	85 (18.2)	0 (0)	154 (32.2)	223 (30.8)
Nausea or vomiting	199 (17.4)	109 (23.3)	0 (0)	74 (15.5)	240 (33.2)
Abdominal tendemess (generalized)	141 (12.3)	95 (20.3)	0 (0)	62 (13.0)	148 (20.5)
Abdominal distension	85 (7.4)	24 (5.14)	0 (0)	34 (7.1)	33 (4.6)
Leukocytosis	141 (12.3)	56 (12.0)	0 (0)	57 (11.9)	62 (8.6)
Could not express symptoms	193 (16.8)	85 (18.2)	0 (0)	267 (55.8)	235 (32.5)
Urologic Criteria st			(0) 0		
Recent urologic procedure or trauma (e.g. catheter trauma)	0 (0)	110 (23.6)	0 (0)	8 (1.7)	39 (5.4)
Obstruction in and around the urinary tract (e.g. nephrolithiasis)	0 (0)	146 (31.3)	(0) 0	26 (54.4)	77 (10.7)
Functional problems in the urinary tract (e.g. incontinence)	0 (0)	269 (57.6)	(0) 0	65 (13.6)	165 (22.8)
Urine Culture results Positive 100,000 CFU/ml Negative Mixed flora	0 (0) 737 (64.3) 410 (35.7)	0 (0) 300 (64.2) 167 (35.8)	226 (100) 0 (0) 0 (0)	478(100) 0 (0) 0 (0)	723 (100) 0 (0) 0 (0)
Prior categorization	IIU oN	No UTI (N=1614)	ASB (I	ASB (N=704)	UTI (N=723)

UTI: urinary tract infection, LUTS/OUS: Lower Urinary Tract Symptoms/ Other Urologic Symptoms, ASB: Asymptomatic bacteriuria, BUS: Bacteriuria of Unclear Significance., CFU-ml: colony forming units per milliliter

 $\ensuremath{^*}$ Patients may have more than one criteria present

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Table 4.

Patient Outcomes by Continuum of UTI categories

Characteristic (N, % unless stated otherwise) No UTI (N=1147) LUTS/OUS (N=467) ASB (N=226) BUS (N=478) UTI (N=723)	No UTI (N=1147)	LUTS/OUS (N=467)	ASB (N=226)	BUS (N=478)	UTI (N=723)
Length of Stay, Median (IQR)	7 (4, 14)	7 (4, 12)	5 (3, 9)	6 (4, 12)	5 (4, 10)
30-day mortality	145 (12.6)	49 (10.5)	10 (4.4)	37 (7.7)	51 (7.1)
30-day readmission	253 (22.1)	106 (22.7)	37 (16.4)	84 (17.6)	134 (18.5)
C difficile test (7 days after urine culture)	8 (0.7)	7 (1.5)	2 (0.9)	4 (0.8)	8 (1.1)
Repeat urine culture in 7 days	121 (10.5)	52 (11.1)	11 (4.9)	38 (7.9)	84 (11.6)

UTI: urinary tract infection, LUTS/OUS: Lower Urinary Tract Symptoms/ Other Urologic Symptoms, ASB: Asymptomatic bacteriuria, BUS: Bacteriuria of Unclear Significance.

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