

## Carolina Antimicrobial Stewardship Program Guideline

# Urinary Tract Infection Diagnosis & Management in Adolescents & Adults at UNC Medical Center

This guidance document provides best practice recommendations for the diagnosis and antimicrobial treatment of urinary tract infections (UTIs). These recommendations apply to adolescents ( $\geq 13$  years of age) and adults.

### Table of Contents

- I. [Diagnosis](#)
  - a. [Types of Urinary Tract Infections](#)
  - b. [Signs & Symptoms of UTI](#)
  - c. [UA and Urine Culture Interpretation](#)
- II. [Algorithms](#)
  - a. [Urine Diagnostic Guide](#)
  - b. [Altered Mental Status](#)
  - c. [UTI Treatment](#)
  - d. [Urine Culture Interpretation](#)
- III. [Frequently Asked Questions](#)

### Key Points

- **Diagnosis**
  - Decision to workup for UTI (UA or urine culture) should be based on patient symptoms.
  - Inappropriate urine culture ordering often leads to misdiagnosis and unnecessary antibiotics.
- **Treatment** of asymptomatic bacteriuria is **NOT** recommended as it offers no benefit and may cause harm.
- **Bottom Line:** unnecessary testing and treatment of asymptomatic bacteriuria can lead to antibiotic resistance, adverse drug effects, and *C. difficile* infection.

### Questions?

Page the Carolina Antibiotic Stewardship Program at 216-2398

This document is intended for educational purposes and does not replace the medical decision and diagnosis of a treating provider. Although we have made a good faith effort to provide accurate information as of the date of creation, we make no representation or warranty regarding its accuracy and have no obligation to update the guidelines as new medical information becomes available.

## I. Diagnosis

### Types of UTIs:

- **Urinary Tract Infection (UTI):**
  - **Cystitis:** infection of the bladder.
  - **Pyelonephritis:** infection involving the kidneys and upper urinary tract.
  - **Catheter-Associated UTI (CAUTI):** presence of an indwelling urinary catheter with signs and symptoms of UTI with positive urine culture and no other identified source of infection
- **Asymptomatic Bacteriuria (ASB):** isolation of bacteria in the urine at levels often regarded as clinically significant (i.e. > 100,000 CFU/mL) +/- pyuria, in patients without symptoms of UTI.

**Table 1: Symptoms suggestive of UTI**

Classification/Diagnosis	Symptoms
<b>ASB</b>	None!
<b>Cystitis</b>	Dysuria, new or worsening frequency or urgency, suprapubic pain
<b>Pyelonephritis</b>	Cystitis symptoms + chills, flank pain or tenderness, fever
<b>CAUTI</b>	Chills, flank pain or tenderness, fever

The following symptoms are **NOT** specific/suggestive of UTI\*: malodorous or cloudy urine, increased urine sediment

Altered mental status (AMS) may be present in certain populations with UTI. Reference [AMS Algorithm](#).

\*Consider alternative, non-UTI diagnosis, such as dehydration.

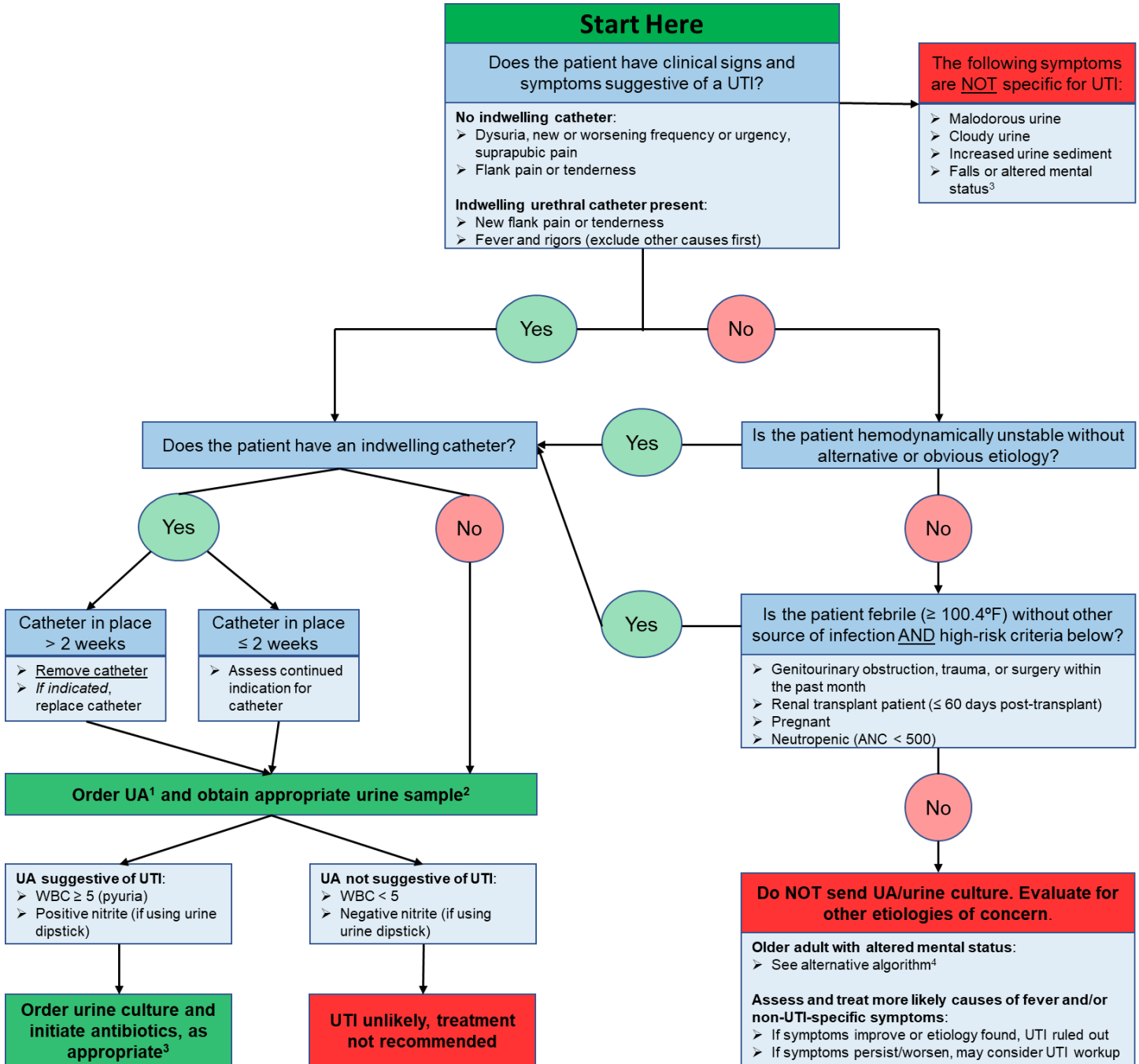
**Table 2: Urinalysis Interpretation**

UA Factor	Normal	Abnormal	Interpretation	Caveats
<b>WBC</b>	< 5	≥ 5	<ul style="list-style-type: none"> <li>•<b>Normal:</b> UTI unlikely, negative predictive value &gt;90%</li> <li>•<b>Abnormal:</b> nonspecific to UTI*; may occur in other conditions, including STIs or genital dermatitis.</li> </ul>	<ul style="list-style-type: none"> <li>•Less sensitive in neutropenic patients (i.e. ANC &lt; 500 cells/μL).</li> </ul>
<b>Leukocyte Esterase</b>	Absent	Present (any)	<ul style="list-style-type: none"> <li>•<b>Normal:</b> UTI unlikely</li> <li>•<b>Abnormal:</b> nonspecific*. Indicates WBCs in urine.</li> </ul>	<ul style="list-style-type: none"> <li>• Less specific than WBC for UTI.</li> </ul>
<b>Nitrite</b>	Absent	Positive	<ul style="list-style-type: none"> <li>•<b>Normal:</b> does not rule out UTI (low sensitivity)</li> <li>•<b>Abnormal:</b> indicates presence of certain bacteria, including <i>E. coli</i>. Does not differentiate between ASB, contamination, or infection.</li> </ul>	<ul style="list-style-type: none"> <li>•Certain bacteria do not produce nitrite, including <i>Enterococcus</i>.</li> </ul>
<b>Bacteria</b>	Absent	Present	<ul style="list-style-type: none"> <li>•<b>Normal:</b> no bacteria seen. Low sensitivity.</li> <li>•<b>Abnormal:</b> indicates presence of bacteria. Does not differentiate between ASB, contamination, or infection.</li> </ul>	

\*Non-infectious causes of WBC and leukocyte esterase in urine include STIs, genital dermatitis, inflammatory and autoimmune disease (Kawasaki's disease, systemic lupus erythematosus, etc.), presence or recent urinary catheter. Sometimes no cause is identified.

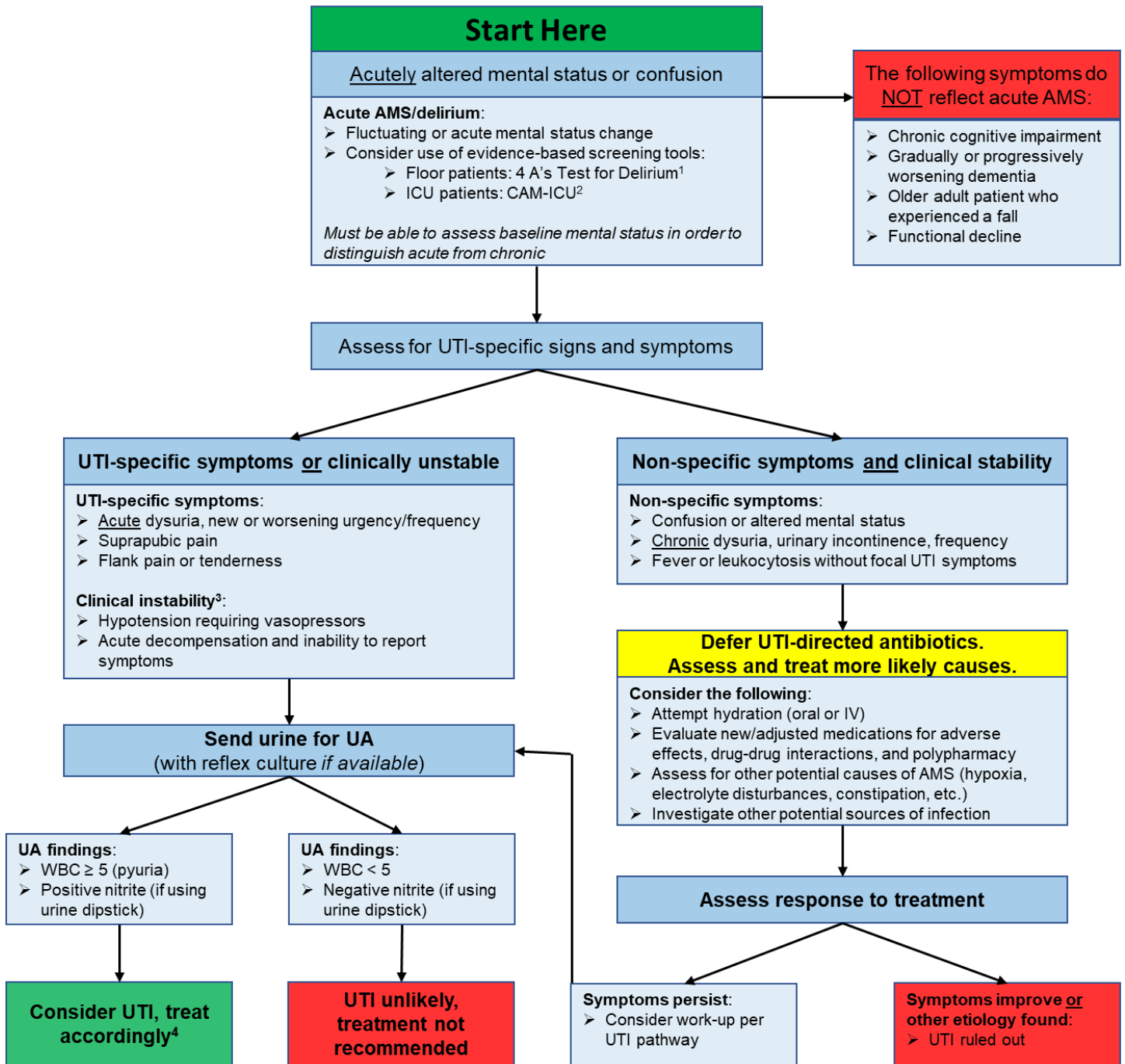
## II. Algorithms

### A. Urine Diagnostic Guide Algorithm



- If available, may order UA with reflex culture (Epic order available for ED and outpatients). Consider ordering UA and culture simultaneously in the following scenarios:
  - Neutropenic (ANC ≤ 500 cells/μL)
  - Hemodynamic instability (order prior to initiating empiric antibiotics)
- Reference [PolicyStat](#) (Specimen Acceptability/Rejection Criteria - Micro Processing) for urine specimen criteria. If urine is collected from an indwelling Foley catheter, the specimen must be processed as "Catheterized Urine." Urine specimens obtained from a Foley bag are never appropriate for adult patients and processing will therefore be rejected by the lab.
- [UTI Treatment Algorithm](#)
- [AMS Algorithm](#)

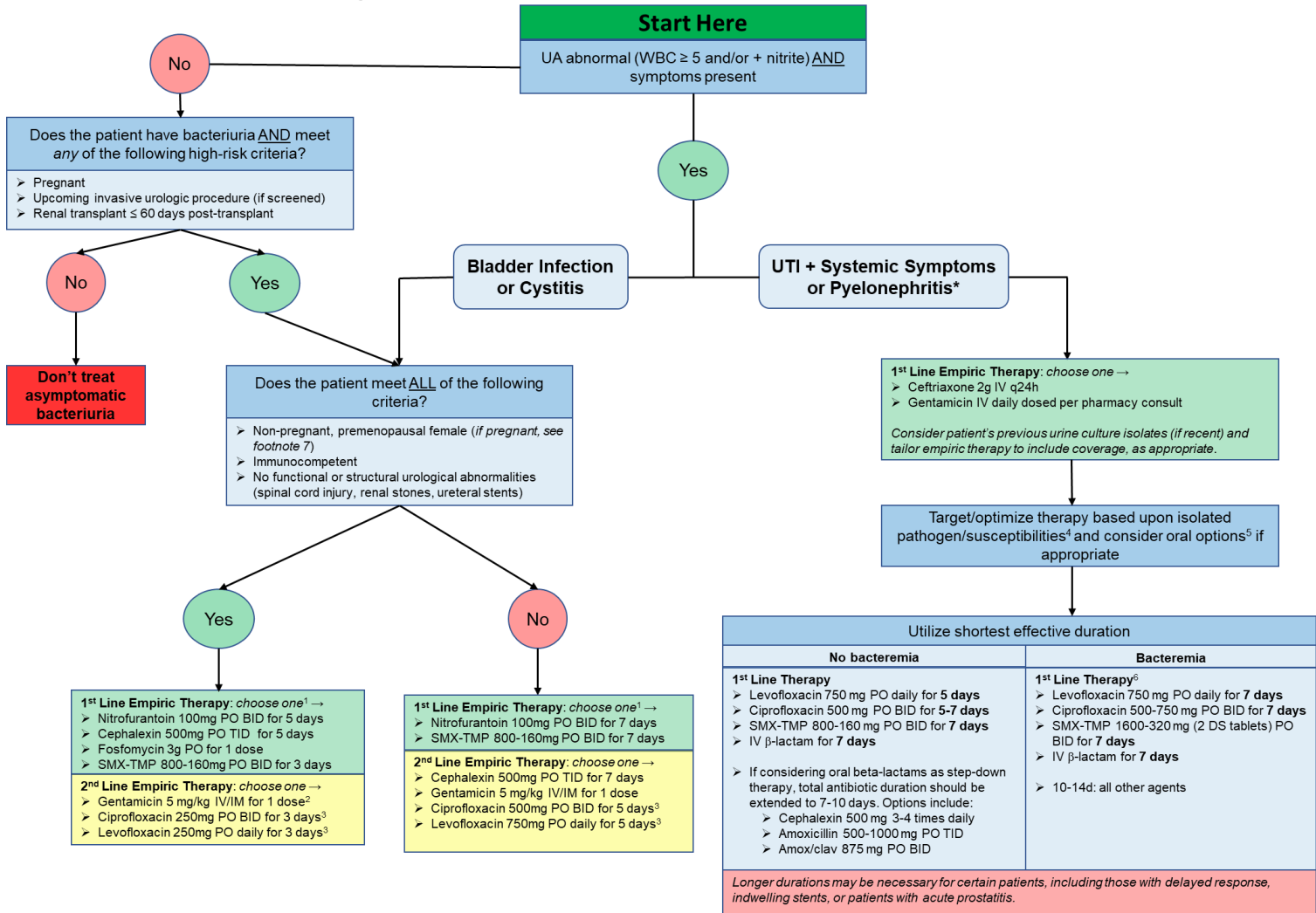
## B. Altered Mental Status Algorithm



Algorithm adapted from: Mody L, et al. *JAMA*. 2014;311(8):844-54.

1. [4 A's Test for Delirium Screening](#) or [3D-CAM](#)
2. [CAM-ICU](#) (Confusion Assessment Method for the ICU)
3. Sepsis is a common ED diagnosis, based upon non-specific SIRS criteria (below). While many patients with sepsis are not considered "clinically unstable" per the criteria in the algorithm, prompt administration of antimicrobials and infectious work-up are often indicated. Urinalyses and urine cultures may be appropriate in this setting. However, if UTI is ruled-out, consider discontinuation of UTI-directed antibiotics in these patients.
  - a. SIRS criteria:  $\geq 2$  of the following  $\rightarrow$  Temp  $>38^{\circ}\text{C}$  ( $100.4^{\circ}\text{F}$ ) or  $<36^{\circ}\text{C}$  ( $96.8^{\circ}\text{F}$ ); HR  $> 90$  bpm; RR  $> 20$ ; or WBC  $>12,000/\text{mm}^3$ ,  $<4,000/\text{mm}^3$ , or  $>10\%$  bands
4. [UTI Treatment Algorithm](#)

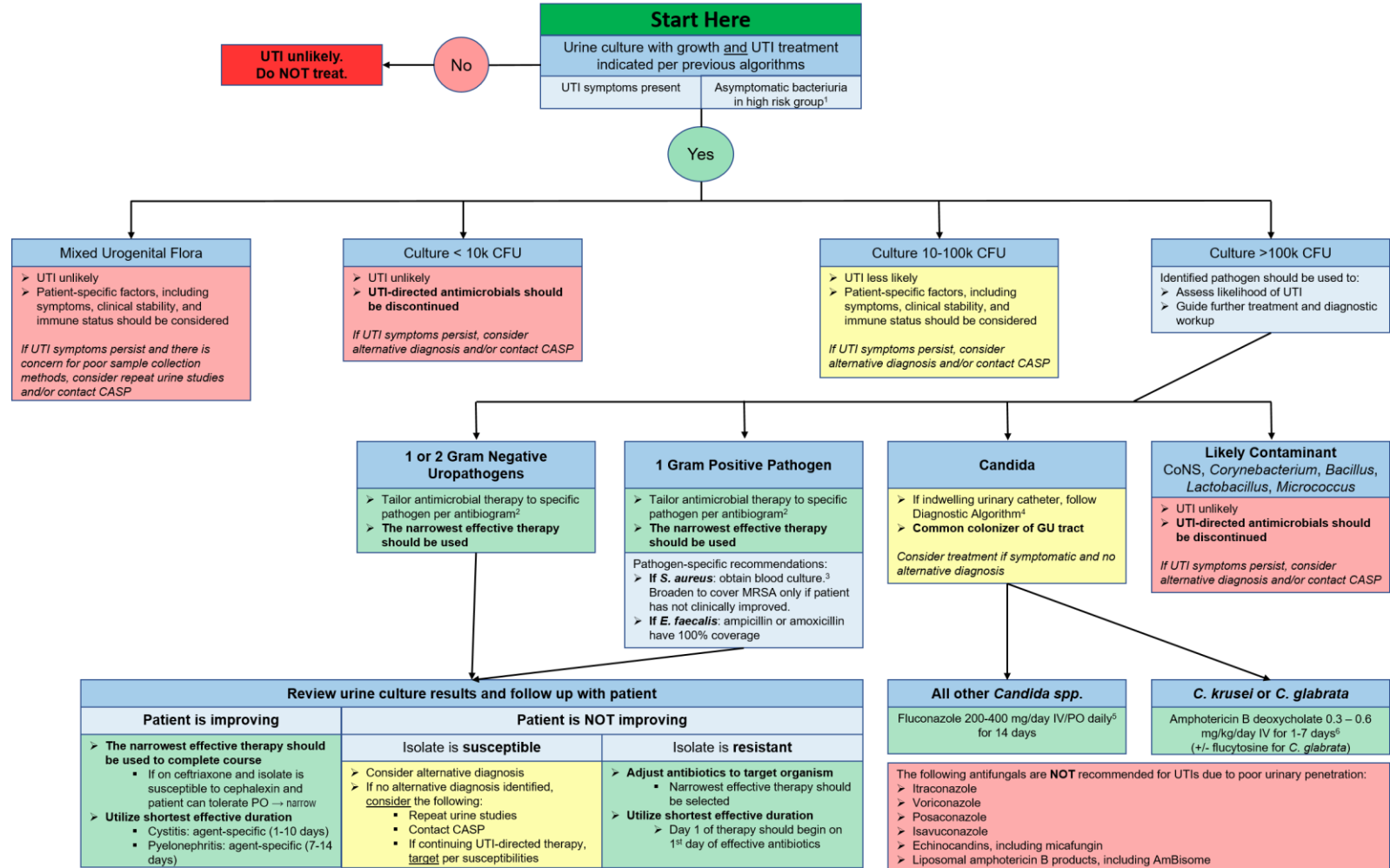
## C. UTI Treatment Algorithm



\*CAUTI most often presents with systemic UTI symptoms that are indistinguishable from pyelonephritis

1. [UNC Antibiotic Dosing Guide](#) (normal renal function, renal insufficiency, hemodialysis) and [CRRT Dosing Guide](#)
2. Gentamicin could serve as an effective, broad-spectrum, single dose option for cystitis in individuals with a history of a multi-drug resistant UTI or those with antimicrobial allergies or intolerances.
  - a. [Reference](#): Goodlett KJ, et al. *Antimicrob Agents Chemother.* 2018;63(1):e02165-18.
3. Fluoroquinolones have poor local susceptibility rates for the most likely uropathogens. Refer to UNC Antibiogram.
4. Utilize current [UNC Antibiogram](#) on CASP website, under CASP Resource page
5. Oral antibiotics should be considered for patients that meet the following criteria: able to tolerate enteral medication, signs of clinical improvement (defervesced, normal or down-trending WBC, etc.), and availability of an effective oral antibiotic (per confirmed susceptibility data or comparable spectrum of activity).
6. Shorter treatment durations of 7 days are recommended only for patients with gram-negative bacteremia that are considered uncomplicated (identified source, source control obtained, immunocompetent, clinical improvement within 72 hours of effective antibiotic treatment).
  - a. [Reference](#): Heil E, et al. *Open Forum Infect Dis.* 2021;8(10):ofab434.
  - b. [Reference](#): Yahav D, et al. *Clin Infect Dis.* 2019;69(7):1091-1098.
7. Recommendations for pregnant women requiring antimicrobial therapy for cystitis or asymptomatic bacteriuria are listed below:
  - a. First line (regardless of trimester): beta-lactam agents, such as amoxicillin +/- clavulanate or cephalexin
  - b. Second line:
    - i. Any trimester: fosfomycin
    - ii. Not at term (i.e. pre-38<sup>th</sup> week) and not near/at delivery: nitrofurantoin
  - c. Contact pharmacy if considering alternative antibiotics in a pregnant patient, including SMX-TMP.

## D. Urine Culture Interpretation Algorithm



- High risk groups warranting treatment of asymptomatic bacteriuria: pregnant, upcoming invasive urologic procedure, ≤ 60 days post-renal transplant
- Antibiogram – [UNC Medical Center Antibiogram](#)
- S. aureus* is not a common urinary pathogen. Its presence in the urine should raise the suspicion for hematogenous spread. Blood cultures should be obtained and other potential foci of infection should be evaluated (ed: renal abscess, etc.).
- [Diagnostic Algorithm](#) for catheter retention or removal
- Fluconazole requires renal adjustment for CrCl ≤ 50 ml/min ([UNC Antibiotic Dosing Guide](#)). Dosing for cystitis is 3 mg/kg (200mg) and for pyelonephritis is 3-6 mg/kg (200-400mg).
- Amphotericin B requires pre-medication with IV fluid (NS), acetaminophen, and diphenhydramine. Bladder irrigation is discouraged due to limited data supporting clinical benefit; should only be used in consultation with CASP and/or pharmacy. Consider ID consult for all *C. krusei* or *C. glabrata* UTIs if considering treatment.

### III. Frequently Asked Questions (FAQs)

**1. A patient has a positive urine culture, but the UA is normal. Should this patient be treated with antibiotics?**

No, this should not be treated with antibiotics. The absence of pyuria (>5 WBC/hpf on UA) has a high negative predictive value. A normal WBC on the UA is useful in ruling out a UTI.

Asymptomatic bacteriuria is common in many patient populations and the prevalence increases with age. Screening and treatment is appropriate for pregnant women and patients prior to certain urologic procedures. Otherwise, asymptomatic bacteriuria should not be treated, as treatment offers no clinical benefit but does pose risk to the patient.

**2. A patient has a positive UA (>5 WBC/hpf), but the urine culture has no growth. Should I treat this with antibiotics?**

Pyuria alone is not an indication for treatment with antibiotics. Pyuria is a common finding and can be seen in many conditions including catheter use, interstitial nephritis, and sexually transmitted infections. Pyuria should be interpreted in conjunction with the urine culture and patient symptoms for the diagnosis of UTI.

**3. A patient is sedated in the ICU or is non-verbal at baseline and can't report symptoms. How do I know if this patient has a UTI?**

When the usual lower urinary tract symptoms (dysuria, frequency, etc.) cannot be assessed, suspect UTI when other signs and symptoms of infection are present with no other identified cause (i.e. fever with no other identified cause). See [AMS Algorithm](#) and [UA interpretation criteria](#) for additional guidance.

**4. If a patient appears septic and is unable to report symptoms (and has no other identified source of infection), should I send a UA with reflex to urine culture?**

Yes, in this instance a reflex culture is appropriate because it is important to send the UA with reflex to culture prior to starting antibiotics, and antibiotics should be administered in a timely manner. Antibiotics should not be withheld while awaiting UA interpretation.

**5. A patient has *E. coli* pyelonephritis with concurrent *E. coli* bacteremia. What should the treatment duration be?**

Patients with pyelonephritis may translocate bacteria to the blood causing a bacteremia. This may happen without causing a sepsis-like picture. Patients should be treated for the same duration that they would have been treated for pyelonephritis, which is generally 7 days. If patient has rapid clinical response, repeat blood cultures to document clearance are not necessary.

References:

- Yahav D, Franceschini E, Koppel F, et al. Seven versus 14 days of antibiotic therapy for uncomplicated gram-negative bacteremia: a noninferiority randomized controlled trial. *Clin Infect Dis*. 2019;69(7):1091-1098. doi:10.1093/cid/ciy1054.
- Tansarli GS, Andreatos N, Pliakos EE, Mylonakis E. A systematic review and meta-analysis of antibiotic treatment duration for bacteremia due to Enterobacteriaceae. *Antimicrob Agents Chemother*. 2019;63(5):e02495-18. doi:10.1128/AAC.02495-18.
- Heil EL, Bork JT, Abbo LM, et al. Optimizing the management of uncomplicated gram-negative bloodstream infections: consensus guidance using a modified delphi process. *Open Forum Infect Dis*. 2021;8(10):ofab434. doi:10.1093/ofid/ofab434.

**6. A patient has more than one bacteria growing in the same urine culture. How should I manage this patient?**

This can be common for patients with indwelling foley catheters and often represents colonization or contamination. This generally should not be treated with antibiotics. The presence of 3 or more species in the urine is suggestive of contamination and a new specimen should be obtained if a UTI is suspected. See [Urine Culture Interpretation Algorithm](#).

**7. In which patients would fosfomycin be an appropriate antimicrobial option?**

- Fosfomycin could be considered for cystitis due to either *E. coli* or *E. faecalis*. Given that *E. coli* is the most common UTI pathogen, fosfomycin is an appropriate empiric option. The data to support fosfomycin for the treatment of UTI due to other organisms is lacking. However, if a patient is treated with fosfomycin and they clinically improve despite growing a resistant organism (i.e. *Klebsiella pneumoniae*), additional antimicrobial treatment is likely not necessary.
  - The microbiology lab at UNC is unable to perform fosfomycin susceptibility testing, thus all use is empiric.
- The recommended dose for cystitis is 3g PO as a single dose. Multidose regimens of 3g PO q48-72 hours for 2 doses can be considered for cystitis in patients other than young, healthy women. GI adverse effects are more common with these multidose regimens. Use caution in patients with impaired renal function (CrCl < 30 ml/min), as fosfomycin elimination may be prolonged.
- Fosfomycin should NOT be considered a preferred option for the treatment of pyelonephritis due to limited renal distribution. If considering fosfomycin for this indication or any indication other than cystitis, please contact CASP.

**8. When can oral cephalosporins be used for UTIs caused by *Enterobacterales* based on the cefazolin susceptibility result?**

- For cystitis due to *E. coli*, *K. pneumoniae*, or *P. mirabilis*, cefazolin is used as a surrogate to predict susceptibility to a variety of oral cephalosporins, including cephalexin.
- The typical cefazolin breakpoint for these organisms is  $\leq 2$  mcg/mL, but that breakpoint is increased to  $\leq 16$  mcg/mL for cystitis due to the excellent urinary penetration of oral cephalosporins.
- This means that an *E. coli* isolate from a urine culture with a cefazolin MIC of 8 mcg/mL will be reported as:

Urine Culture, >100,000 CFU/mL Escherichia coli !  
 Comprehensive Specimen Source: Clean Catch  
 Resulting Agency: UNCH MCL

**Susceptibility**

	Escherichia coli MIC SUSCEPTIBILITY RESULT	
Amoxicillin + Clavulanate	Susceptible	
Ampicillin	Resistant	
Ampicillin + Sulbactam	Susceptible	
Cefazolin	Resistant	
Cephalexin	Susceptible <sup>1</sup>	
Ciprofloxacin	Resistant	
Gentamicin	Susceptible	
Levofloxacin	Resistant	
Nitrofurantoin	Susceptible	
Piperacillin + Tazobactam	Susceptible	
Tetracycline	Resistant <sup>2</sup>	
Tobramycin	Susceptible	
Trimethoprim + Sulfamethoxazole	Resistant	

<sup>1</sup> For uncomplicated UTI's only.

- Clinical interpretation of this resistance pattern should be based upon the patient's diagnosis:
  - If cystitis: cephalexin is an appropriate therapeutic option. Cephalexin is preferred over cefdinir for susceptible isolates given favorable adverse effect profile, narrower spectrum of activity, and cost.
  - If pyelonephritis with or without concurrent bacteremia: Oral fluoroquinolones or TMP/SMX is preferred, but oral beta-lactams may be considered for step-down therapy in clinically improved patients. Refer to UTI Treatment Algorithm C (p.5) for dosing and duration recommendations.