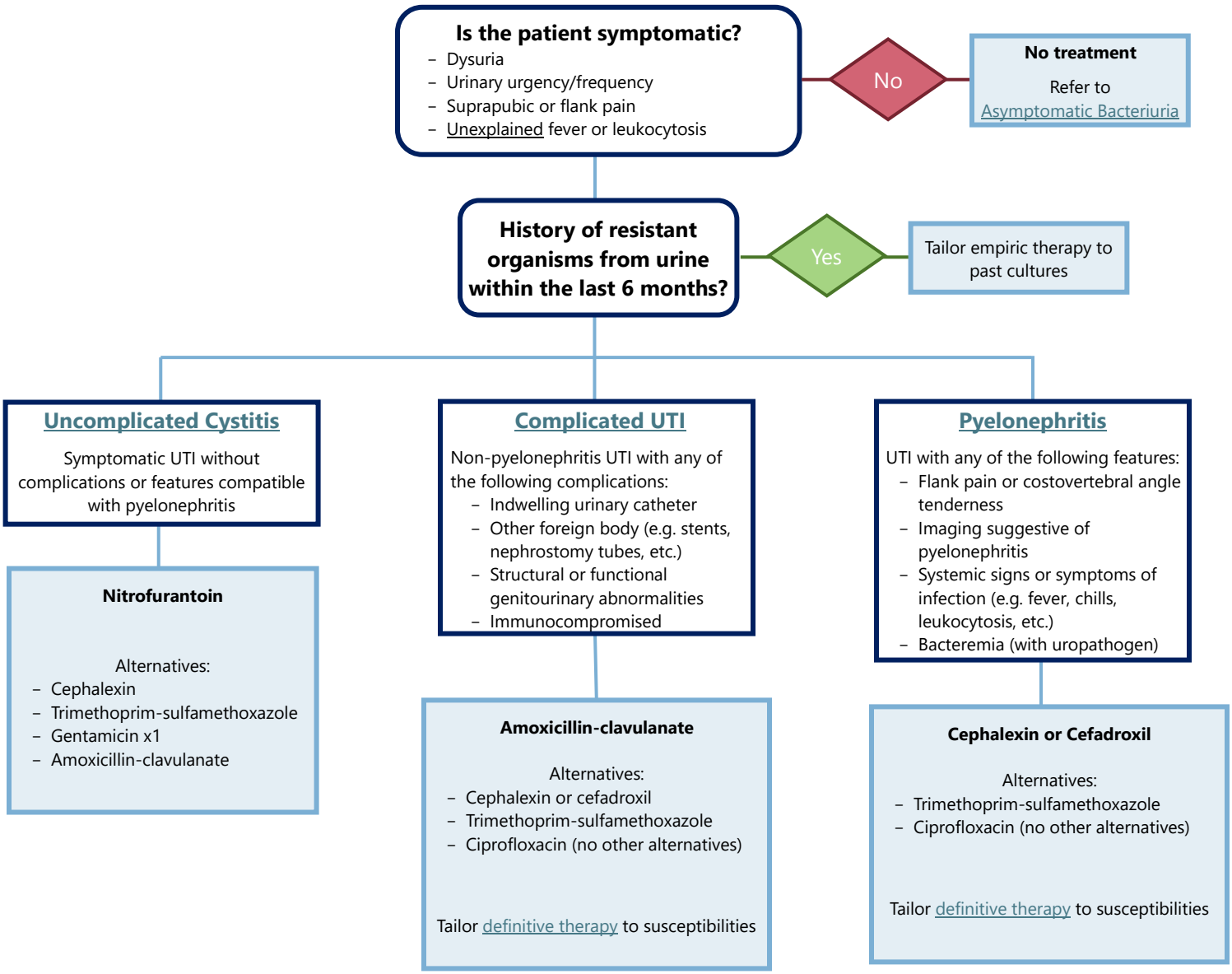
CARILION CLINIC Antimicrobial Stewardship

Outpatient: Adult Urinary Tract Infection Guidance

Updated: May 2025



FDA warning: Fluoroquinolones should be reserved for use in patients who have no other treatment options for urinary tract infections because the risk of serious side effects may outweigh the benefits.

- Some side effects include: aortic aneurysm and dissection, tendinitis, tendon rupture, confusion/altered mental status, prolonged QTc

Refer to the Carilion Clinic Adult Antimicrobial Renal Dosing Protocol for dosing recommendations

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Microbiology:

Figure 1. 2024 Distribution of Organisms from Outpatient Urine Cultures

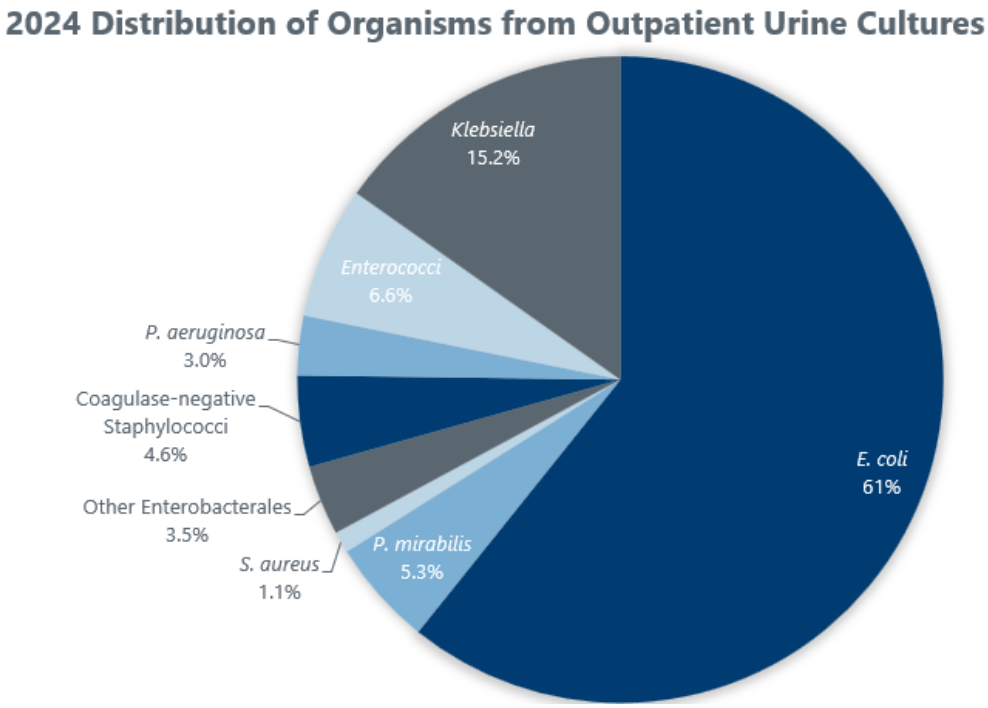
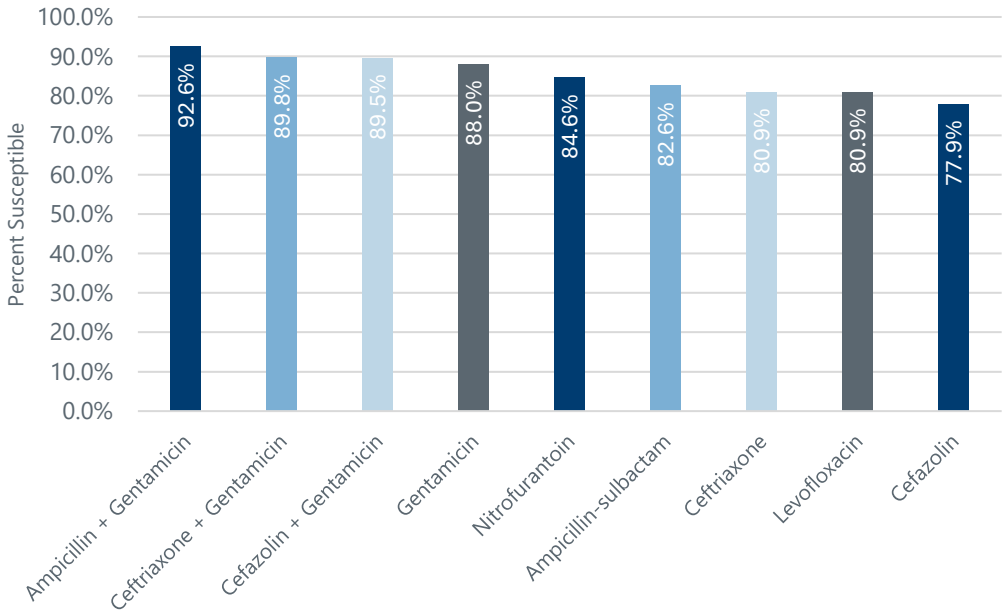


Figure 2. 2024 Outpatient Combination Urine Antibiogram (excluding *Pseudomonas aeruginosa*)



Diagnosis: Urinary tract infection (UTI) is *clinical diagnosis*

Refer to the Carilion Clinic Adult Antimicrobial Renal Dosing Protocol for dosing recommendations

- Urinary symptoms are the most sensitive and specific findings associated with UTIs. In contrast, neither the presence of bacteriuria nor abnormal urinalysis (UA) are reliably capable of distinguishing between colonization and infection.
- **UA and/or culture findings in patients without urinary symptoms should not be treated.** Refer to Asymptomatic Bacteriuria for exceptions and additional information.

Urinary Symptoms:

- Dysuria
- Urinary urgency or frequency
- Suprapubic pain or flank pain/costovertebral angle tenderness
- Fever or *unexplained* leukocytosis

Non-specific Symptoms: Gross hematuria, delirium, malodorous urine, cloudy urine

- These symptoms are unreliable *independent* indicators of infection with very low specificity.[1,2]
- In the absence of urinary symptoms (e.g. dysuria, urinary urgency, etc.), alternative causes of these non-specific symptoms should be thoroughly investigated prior to considering a diagnosis of UTI since treatment can be associated with significant harm (see Asymptomatic Bacteriuria).
- Refer to Neurogenic Bladder/Spinal Cord Injury for recommendations regarding the assessment of symptoms in challenging patient populations.

Urinalysis (UA): The diagnostic utility of UA is limited but it can be a helpful tool to *rule out* UTIs in immunocompetent patients. **An abnormal UA does not diagnose UTI on its own.**

- Individual components of the UA (i.e. leukocyte esterase and nitrites) have wide ranges of sensitivity and specificity in the literature demonstrating a lack of correlation to true infection. Leukocyte esterase and nitrites have a limited role in the diagnosis of UTIs.
- Pyuria may indicate that an immunocompetent patient is responding to the presence of microorganisms in the genitourinary (GU) tract. However, pyuria has a poor positive predictive value of <60% due to the multitude of non-infectious causes of GU inflammation, especially in the elderly. The negative predictive value of pyuria ranges from 83-95% indicating its utility in *excluding* a diagnosis of UTI.[1,3,4]

Role of Imaging:[1] Imaging can support a diagnosis, but negative findings do not rule out UTI in symptomatic patients. CT or MRI may assist in the identification of complications such as abscess, stones, or other anatomic/pathological features.

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Asymptomatic Bacteriuria (ASB): The identification of bacteria in the urine *without* symptoms attributable to urinary tract infections (i.e. fever or unexplained leukocytosis, dysuria, urinary urgency/frequency, suprapubic/CVA pain)

- Urine is not sterile. ASB has a reported prevalence of up to 16% in most patients. The prevalence of ASB in the elderly and long-term care facility residents ranges from 50% to as high as 100% in chronically catheterized patients.[2]
- **Treatment of ASB has not demonstrated any clinical benefit in most patient populations and is significantly associated with harm.** Patients who receive antibiotics experience higher rates of adverse events, *Clostridioides difficile* infections, antibiotic resistance, and subsequent symptomatic UTIs.[1,2,5–9]

Delirium or Foul-smelling/Cloudy Urine:

- New-onset delirium or altered mental status, and malodorous or cloudy urine are highly non-specific for UTIs and are unreliable individual indicators of infection.[1,2]
- In patients with delirium as their only symptom, studies show that treatment is associated with no clinical benefit or improvement in mental status.[9–11] Patients who received treatment also experienced *worse* functional outcomes and increased incidence of *Clostridioides difficile* infections.[12,13]
- In the absence of other true urinary symptoms, thorough work-up for alternative causes of delirium and urine changes should be pursued prior to considering antibiotic therapy.

Neurogenic Bladder/Spinal Cord Injury:

- The prevalence of ASB in patients with neurogenic bladder exceeds 50%, especially in patients with urinary catheter use.[14,15] Diagnosis of UTI is challenging in this population since patients are often bacteriuric with GU symptoms at baseline.
- In patients with pyuria and new, *unexplained* onset of non-specific symptoms (e.g., malaise/lethargy, incontinence/leaking, spasticity, malodorous/cloudy urine, etc.), treatment of ASB can be considered once alternative causes have been ruled out. The decision to treat should be balanced against the protective effect of bacteriuria and risks of treating ASB, including antibiotic resistance.

Treatment of ASB:

Population	Recommendations
Most Patients	No treatment
Pregnancy	Treat with pathogen-directed therapy for 3-5 days
Patients Undergoing Invasive Urologic Procedures (e.g. TURP, TURB, percutaneous stone surgery)	Pre-operative prophylaxis with pathogen-directed therapy for ≤24 hours

Abbreviations: TURP, transurethral resection of the prostate; TURB, transurethral resection of the bladder
Pathogen-directed therapy: Antibiotics targeted at the isolated pathogen(s) based on susceptibility testing results

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Uncomplicated Cystitis: Symptomatic UTI (i.e., fever or unexplained leukocytosis, dysuria, urinary urgency/frequency, suprapubic/CVA pain) without complications or features compatible with pyelonephritis.

Male Patients:

- **Male patients with UTIs should NOT be considered complicated by default.**
- Male patients are less likely than female patients to develop UTIs due to baseline anatomical differences between sexes. As a result, male patients who contract UTIs are more likely to have actual complications (e.g., catheters, foreign bodies, etc.) than female patients. This dynamic has been mis-interpreted, historically, by categorizing all male UTIs as complicated.
- However, **male patients with uncomplicated cystitis do not require longer durations of therapy or broader therapy** to adequately treat the infection. In general, antibiotics do not have major differences in physiochemical properties or urine exposure in males compared to females. Thus, sex should not play a major role in agent selection or duration of therapy for UTIs.

Empiric Treatment of Simple Cystitis: Refer to Pathogen-directed Therapy for guidance once susceptibilities are available.

Population	Preferred	Alternatives (in order of preference)
Most Patients	Nitrofurantoin x5d	- Amoxicillin-clavulanate x5d - Cephalexin or cefadroxil x5d - Trimethoprim-sulfamethoxazole x 3-5d - Gentamicin 5mg/kg IM x1 dose
Hemodialysis or CrCL<30 mL/min	Amoxicillin-clavulanate x5d	- Cephalexin or cefadroxil x5d - Trimethoprim-sulfamethoxazole x3-5d
Anaphylaxis to Penicillin	Nitrofurantoin x5d	- Gentamicin 5mg/kg IM x1 dose - Trimethoprim-sulfamethoxazole x3-5d - Cephalosporin x5d*
History of recent organisms from urine within the last 6 months	Tailor empiric therapy to past cultures x5d	

* Cross-reactivity between penicillins and cephalosporins is <5% unless the drugs share an identical R1 side chain (e.g., ampicillin and cephalexin, etc.)

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Complicated Urinary Tract Infection: Non-pyelonephritis UTI with complicating features

- Indwelling urinary catheters
- Presence of other foreign bodies (e.g. stents, nephrostomy tubes, etc.)
- Structural or functional genitourinary abnormalities (including abscesses, fistulous connections, etc.)
- Immunocompromised

In general, complicated UTIs do not require broader coverage than simple cystitis or pyelonephritis. Instead, the presence of complications necessitates attention to source control, which is often coupled with a longer, more nuanced duration of therapy. This also applies to male patients, who should NOT be categorized as complicated based on sex alone.

Empiric Treatment of Complicated UTIs: Refer to Pathogen-directed Therapy for guidance once susceptibilities are available.

<table>
<tr><th>Population</th><th>Preferred</th><th>Alternatives
(in order of preference)</th><th>Duration</th></tr>
<tr><td>Catheter-associated UTIs</td><td>Remove/replace catheter

Amoxicillin-clavulanate x 5d</td><td colspan="2">- Nitrofurantoin x5d
- Trimethoprim-sulfamethoxazole x3d
- Cephalexin or cefadroxil x5d
- Gentamicin x1 dose

Patients with retained catheters may require longer durations of therapy</td></tr>
<tr><td>Presence of other foreign bodies (e.g., stents, nephrostomy tubes)</td><td rowspan="2">Amoxicillin-clavulanate</td><td rowspan="2">- Cephalexin or cefadroxil
- Trimethoprim-sulfamethoxazole
- Ciprofloxacin</td><td rowspan="2">7-14d**</td></tr>
<tr><td>Genitourinary abnormalities (e.g., abscesses, fistulous connections, abnormal anatomy)</td></tr>
<tr><td>History of recent organisms from urine within the last 6 months</td><td colspan="2">Tailor empiric therapy to past cultures</td><td>7-14d**</td></tr>
</table>

IV alternatives are permissible, when necessary (e.g., ampicillin may be substituted for amoxicillin, cefazolin for cephalexin, etc.)
*Risk factors for nosocomial organisms: Receipt of IV antibiotics within last 90d AND either hospitalization for ≥48h OR receipt of medical care outside of the US
**Duration of therapy varies based on clinical scenario and achievement of source control. Reach out to antimicrobial stewardship for patient-specific guidance.

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Pyelonephritis: UTI with any of the following features:

- Flank pain or costovertebral angle tenderness
- Imaging suggestive of pyelonephritis
- Systemic signs or symptoms of infection (e.g., fever, chills, leukocytosis, etc.)
- Bacteremia (with uropathogen or organism with suspected urinary source)

Empiric Treatment of Pyelonephritis: Refer to Pathogen-directed Therapy for guidance once susceptibilities are available.

<table>
<tr><th>Population</th><th>Preferred</th><th>Alternatives
(in order of preference)</th><th>Duration</th></tr>
<tr><td>Uncomplicated Pyelonephritis</td><td rowspan="3">Cephalexin</td><td rowspan="3">- Trimethoprim-sulfamethoxazole
- Ciprofloxacin</td><td>7d</td></tr>
<tr><td>Presence of Other Foreign Bodies (e.g., stents, nephrostomy tubes)</td><td rowspan="2">7-14d*</td></tr>
<tr><td>Genitourinary abnormalities (e.g., abscesses, fistulous connections, abnormal anatomy)</td></tr>
<tr><td>History of recent organisms from urine within the last 6 months</td><td colspan="2">Tailor empiric therapy to past cultures</td><td>7-14d*</td></tr>
</table>

*Duration of therapy varies based on clinical scenario and achievement of source control. Reach out to antimicrobial stewardship for patient-specific guidance.

Candida Urinary Tract Infections:[26]

- *Candida* is normal human genitourinary flora. **In asymptomatic patients, candiduria almost exclusively represents colonization and should not be treated.** Candiduria does not lead to candidemia, and treatment does not improve outcomes, even in the kidney transplant population. However, there is some limited evidence to support treatment in patients undergoing invasive urologic procedures or neutropenia.
- Treatment for candiduria can be considered in *symptomatic* patients once alternative (i.e., bacterial) causes have been assessed. Reach out to antimicrobial stewardship or infectious diseases for patient-specific guidance.
- Complications and secondary sources should be addressed diligently. This includes urinary catheters, obstructions, nephrostomy tubes, stents, abscesses, emphysematous infection, and fungal balls. **Lack of source control precludes successful treatment with antifungal therapy alone.**

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Pathogen-directed Therapy:

- Once the causative pathogen(s) and susceptibilities are known, therapy should be completed with targeted antimicrobial therapy. Patients who have already completed a full course with active empirical therapy **(including gentamicin x1 for cystitis)** do not require additional treatment.
- Selecting "narrower" spectrum antimicrobials and shorter treatment durations lessens selective pressure for resistance and is often more efficacious than broad-spectrum treatment.

Preferred Therapy for Select Pathogens/Resistance:

Pathogen	Resistance Pattern	Preferred PO Agents
Enterobacterales (e.g., *E. coli*, *K. pneumoniae*, *P. mirabilis*, etc.)	Pan-susceptible	- Nitrofurantoin (cystitis only) - Amoxicillin - Cephalexin or cefadroxil
	Cefazolin-resistant	- Nitrofurantoin (cystitis only) - Trimethoprim-sulfamethoxazole - Amoxicillin or amoxicillin-clavulanate - Cefpodoxime (ONLY if susceptibility confirmed) - Levofloxacin
	Ceftriaxone-resistant	- Nitrofurantoin (cystitis only) - Trimethoprim-sulfamethoxazole - Levofloxacin
E. cloacae, *C. freundii*, or *K. aerogenes*	Ceftriaxone-susceptible	
	Ceftriaxone-resistant	
ESBL E. coli	Fosfomycin-susceptible	-Fosfomycin x 1 -Gentamicin or Tobramycin IM x 1
Enterococcus spp.	Ampicillin-susceptible	Amoxicillin
	Ampicillin-resistant	- Amoxicillin (cystitis only) - Linezolid
	Vancomycin-resistant	- Linezolid
P. aeruginosa	Pan-susceptible	- Levofloxacin - Ciprofloxacin - Tobramycin IM x1 (cystitis only)

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