



Clear the Stream: cUTI Guideline Updates

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Disclosures

The planners and speaker have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

Abbreviation Key

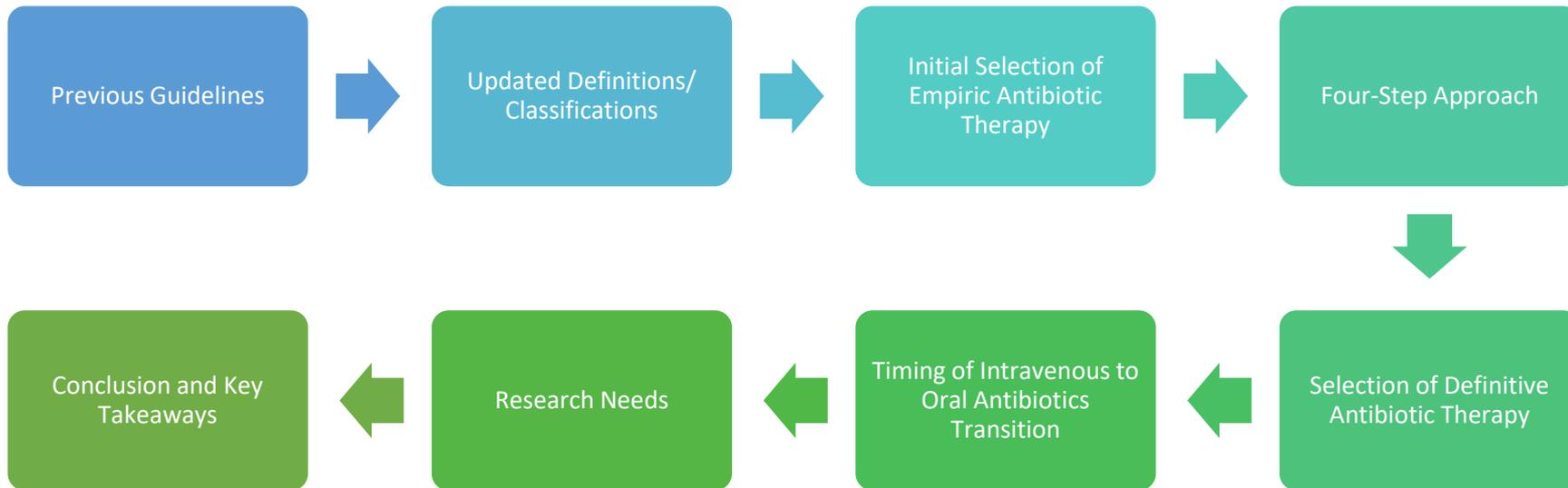
- BLBLI: beta-lactam beta-lactamase inhibitor
- BSI: bloodstream infection
- cUTI: complicated urinary tract infection
- ED: emergency department
- ESBL: extended spectrum beta-lactamase
- FQ: fluoroquinolone
- g/mg: grams/milligrams
- ICU: intensive care unit
- ID: Infectious Diseases
- IV: intravenous
- LGH: Lutheran General Hospital
- MDR: multi-drug resistant
- PO: by mouth
- SGLT2i: sodium glucose co-transporter 2 inhibitor
- SIRS: systemic inflammatory response syndrome
- SOFA: sequential organ failure assessment
- TMP-SMX: trimethoprim-sulfamethoxazole
- uUTI: uncomplicated urinary tract infection
- UTI: urinary tract infection

Learning Objectives

At the end of this session, learners should be able to:

1. Differentiate uncomplicated and complicated urinary tract infections using the updated guideline-defined criteria.
2. Identify recommended empiric antimicrobial therapies for complicated urinary tract infections.
3. Select appropriate definitive therapy including drug choice and duration using culture results.
4. Apply the four-step approach to formulate evidence-based treatment plans for patients with complicated urinary tract infections.

Presentation Outline



Previous IDSA Guideline

Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women

- Excluded:
 - Men
 - Explicit guidance on complicated UTI

Why the Update?

Increased antimicrobial resistance rates have made empiric choices increasingly uncertain



Newer antibiotics have received FDA approval for cUTI treatment



Impacts:

Empiric antibiotic choices

Route of therapy

Duration of treatment

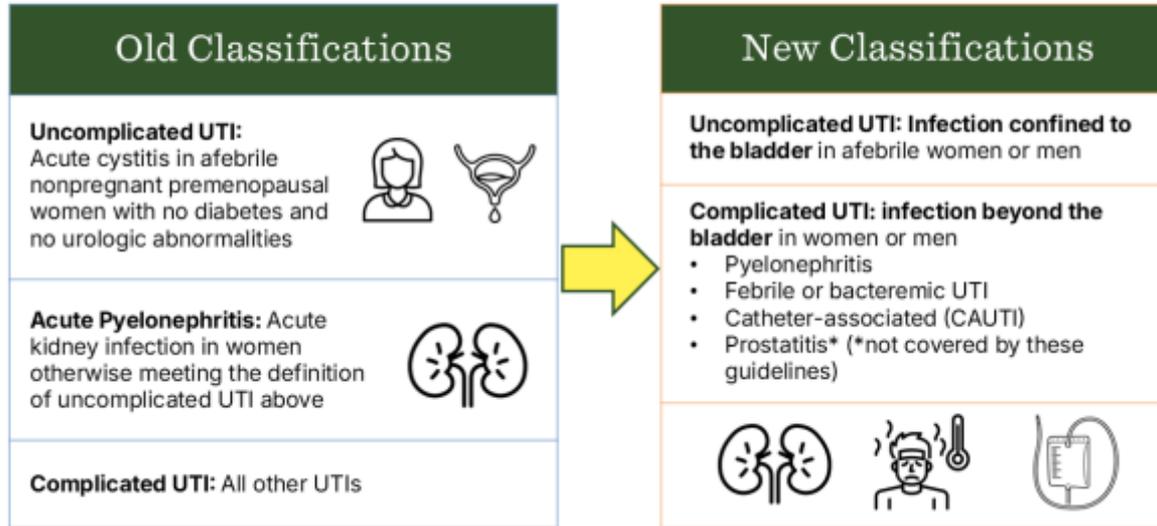


Prevents:

Overtreatment

Updated Classifications

New classifications of uUTI and cUTI



uUTI Classification

Definition:

- Clinical syndrome, confined to the bladder, with the absence of signs/symptoms that extend beyond the bladder

Clinical Presentation:

- Signs/ symptoms include
 - Dysuria
 - Urgency
 - Frequency
 - Suprapubic pain

cUTI Classification

Definition:

- UTI with symptoms extending systemically

Clinical Presentation:

- Signs and symptoms include
 - Fever
 - Flank pain
 - Costovertebral angle tenderness
 - Other systemic illness symptoms
 - Chills
 - Rigors
 - Hemodynamic instability

This Guideline Doesn't Apply To

Bacterial
prostatitis

Epididymitis

Orchitis

Assessment Question #1

Assessment Question #1

GT is a 68-year-old male who presents to the ED with flank pain that began 2 days ago. He notes he has urinary urgency and frequency and has not taken his BP meds in 2 days. No other issues or complaints.

PMH: hypertension and type 2 diabetes

Vitals: HR 95, BP 112/74, Temp 38.4C

What type of urinary tract infection does GT most likely have?

- a. Acute on chronic UTI
- b. Complicated UTI
- c. Uncomplicated UTI
- d. GT doesn't have a urinary tract infection

Predominant Pathogens & Risk Factors

Predominant Pathogens

Gram negative bacteria – most commonly:

Escherichia coli
(70-80%)

Klebsiella pneumoniae

Klebsiella oxytoca

Proteus mirabilis



Increasing prevalence of ESBL and FQ resistant strains

UTI Risk Factors

Previous UTI

Urologic
instrumentation/
surgery

Neurogenic bladder

Renal
transplantation

Treatment of
asymptomatic
bacteriuria

Urinary
incontinence

Impaired cognitive
function

Exposure to
medications

- SGLT2i
- Antimicrobials

Empiric Use of Antibiotics

Empiric Antibiotic Summary

Condition of the Patient	Preferred	Alternative
Sepsis with or without shock	3 rd or 4 th generation cephalosporins Carbapenems Piperacillin-tazobactam Fluoroquinolones	Novel BLBLI Cefiderocol Plazomicin Older aminoglycosides
Without sepsis, IV route of therapy	3 rd or 4 th generation cephalosporins Piperacillin-tazobactam Fluoroquinolones	Carbapenems Newer agents (BLBLI, cefiderocol, plazomicin) Older aminoglycosides
Without sepsis, oral route of therapy	Fluoroquinolones or trimethoprim-sulfamethoxazole	Amoxicillin-clavulanate or oral cephalosporins

3rd & 4th Generation Cephalosporins

Ceftriaxone, and by extension third and fourth generation cephalosporins, remain one of the **preferred** classes of antibiotics for empiric treatment of cUTI without sepsis

Third or fourth generation cephalosporins may be used in patients with sepsis if not excluded based on patient-specific factors

3rd/4th Generation Cephalosporins: Dosing

Drug	Dose	Notes
Ceftriaxone	1-2 g IV once daily	Highly albumin bound, consider alternative if hypoalbuminemia present
Ceftazidime	1-2 g IV every 8 hours	

Live as of 12/18/25	Cefepime (Maxipime)										
	Population	Duration	>60 mL/min	30-60 mL/min	11-29 mL/min	≤10 mL/min	HD	CRRT	PD		
	Septic Shock, CNS, Cystic Fibrosis, HAP/VAP, Febrile Neutropenia, Bone and Joint, Gram-negative MIC ≥4, <i>Pseudomonas aeruginosa</i> Bacteremia, or Endocarditis	240 min	2g q8h	1g q8h	1g q12h	1g q24h	1g q24h ¹	2g q8h	1g q24h		
	Load with 2g over 30 minutes for all regardless of renal function										
Other Indications	240 min	1g q8h	1g q12h	1g q24h	500mg q24h	500mg q24h ¹	---	1g q24h			
Load with 1 g over 30 minutes for all regardless of renal function											
If 30 min infusion required due to line access, may change to 30 min infusion with the same dose and frequency											
12g TIWeek post HD (1800) also available if transitioning to outpatient											

Ceftriaxone: Patient Considerations

Once daily
administration

- Facilitates outpatient antibiotic therapy
- Ease of dosing

Low cost

Intramuscular
administration

Piperacillin-tazobactam

Extended spectrum penicillin and beta-lactamase inhibitor combination

Piperacillin-tazobactam remains one of the **preferred** antibiotics for empiric treatment of cUTI without sepsis

Piperacillin-Tazobactam (Zosyn)							
Live as of 11/20/25	Population	Duration	≥ 20 mL/min	<20 mL/min	HD	CRRT	PD
	BMI>40, Septic Shock, Cystic Fibrosis, HAP/VAP, Febrile Neutropenia, Bone and Joint, Gram-negative MIC >8, <i>Pseudomonas aeruginosa</i> Bacteremia, or Endocarditis	240 min	4.5g q8h	3.375g q12h	3.375g q12h	4.5g q8h	3.375g q12h
	Load with 4.5g over 30 min for all regardless of renal function						
	Other indications	240 min	3.375g q8h	3.375g q12h	3.375g q12h	3.375g q8h	3.375g q12h
	Load with 3.375g over 30 minutes for all regardless of renal function						
If 30-min infusion is required due to line access, see Appendix							
	Population	Duration	≥ 20 mL/min		<20 mL/min		
	Invasive <i>Pseudomonas</i> MIC >8	Continuous over 24 hours	18 g		13.5 g		
Not delegated authority – reach out to pharmacy for assistance with ordering this dosing scheme							

Piperacillin-tazobactam: Patient Considerations

Prolonged or continuous infusions

- To enhance the time : MIC ratio

May create challenge for patient, nursing staff, etc.

Medium cost

Challenges to effectiveness include rising rates of:

- ESBL-producing organisms
- Multi-drug-resistant *Pseudomonas*

Antibiogram: Aurora St. Lukes Medical Center



ANNUAL REPORT OF SUSCEPTIBILITY PATTERNS

January 1 - December 31, 2025

Percent of isolates susceptible¹ to antimicrobial agents at attainable concentrations

Gram Negative	# Isolates ²	ESBL ³	Penicillins			Cephalosporins								Carbapenems			Quinolones		Aminoglycosides			Other							
			Ampicillin	Ampicillin/sulbactam	Piperacillin/tazobactam	Cefazolin (Urine) ⁴	Cefazolin	Cefuroxime axetil	Cefepodoxime	Ceftazidime	Ceftriaxone	Cefepime	Ceftazidime/avibactam ^{5,6}	Ceftolozane/tazobactam ^{5,6}	Ertapenem ⁶	Meropenem ⁶	Mono-bactam	Aztreonam ⁷	Ciprofloxacin ⁷	Levofloxacin ⁷	Gentamicin	Tobramycin	Amikacin	Nitrofurantoin ⁸	Trimethoprim/sulfamethoxazole	Fosfomycin ^{5,6,9}	Colistin ⁵	Minocycline ^{5,6}	
ENTEROBACTERALES																													
<i>Citrobacter freundii</i> complex ¹¹	80				68					68	63	98					98	100	65	92			97		100	89	90		
<i>Citrobacter koseri</i>	42				97				51	94	100	100	100				100	100	100	97			97		100	84	97		
<i>Enterobacter cloacae</i> complex ¹²	223				73					70	72	67	92	99			83	99	72	87			96	95	100	29	88		
<i>Escherichia coli</i> ¹⁰	2126	17	48	59	94	81	57	74	76	88	83	91	100				99	99	87	68			90	83	97	94	73		
<i>Klebsiella (Enterobacter) aerogenes</i>	72				75					73	76	98					96	100	75	94			98		100	15	97		
<i>Klebsiella oxytoca</i> ¹⁰	120	9			70	88		0	82	86	95	89	95	95			96	98	95	92			95	97	100	78	90		
<i>Klebsiella pneumoniae</i> ¹⁰	673	17			76	90	82	69	75	81	83	82	89	100			97	98	81	79			92	87	99	27	82		
<i>Morganella morganii</i>	43				9	86						67	100				96	97	71	72			88		100		76		
<i>Proteus mirabilis</i>	362				80	91	100	93	16	94	98	97	96	99	100		100	99	98	83			96	98	99		85		
<i>Providencia rettgeri</i>																													
<i>Providencia stuartii</i>																													
<i>Serratia marcescens</i>	100									93	91	100	100				97	97	98	93			99	87	98		100		
NONFERMENTERS																													
<i>Acinetobacter baumannii</i> complex ^{13,14}																													
<i>Pseudomonas aeruginosa</i>	564				87					89		89	99	98			92	81					87	84		98	99		
<i>Stenotrophomas maltophilia</i>	34																										100		94

Not reported due to intrinsic resistance or susceptibility panel restrictions.

Antibiogram: Lutheran General Hospital



ANNUAL REPORT OF SUSCEPTIBILITY PATTERNS

January 1 - December 31, 2025

Percent of isolates susceptible¹ to antimicrobial agents at attainable concentrations

Gram Negative	# Isolates ²	ESBL ³	Penicillins			Cephalosporins							Carbapenems			Meno- cyclams	Quinolones		Aminoglycosides			Other														
			Ampicillin	Ampicillin/sulbactam	Piperacillin/tazobactam	Cefazolin (Urine) ⁴	Cefazolin	Cefuroxime axetil	Cefepodoxime	Ceftazidime	Ceftriaxone	Cefepime	Ceftazidime/avibactam ^{5,6}	Ceftolozane/tazobactam ^{5,6}	Ertapenem ⁶		Mero- penem ⁶	Aztreonam ⁷	Ciprofloxacin ⁷	Levofloxacin ⁷	Gentamicin	Tobramycin	Amikacin	Nitrofurantoin ⁸	Trimethoprim/sulfamethoxazole	Fosfomycin ^{5,6,9}	Colistin ⁵	Minocycline ^{5,6}								
AAH Lutheran General Hospital* 2025																																				
ENTEROBACTERALES																																				
<i>Citrobacter freundii</i> complex ¹¹	55				65									58	92	100			92	96			87			96	90	100	94	92						
<i>Citrobacter koseri</i>	61				98								96	96	100	100			100	100	96	96				98	94	100	91	100						
<i>Enterobacter cloacae</i> complex ¹²	149				81					77	81	76	93	100					87	98	81	91				97	97	100	35	90						
<i>Escherichia coli</i> ¹⁰	2128	17	49	61	92	80	49	72	74	87	81	91	90	100					99	99	85	63				88	83	96	96	75	83					
<i>Klebsiella (Enterobacter) aerogenes</i>	78				74														90	96	72	94				100	96	98	21	97						
<i>Klebsiella oxytoca</i> ¹⁰	88	3		80	92			0	89	100	98	92	98	97					98	100	92	97				97	97	100	92	95						
<i>Klebsiella pneumoniae</i> ¹⁰	647	19		67	82	75	54	66	69	74	74	81	96						89	91	73	71				91	79	93	25	74						
<i>Morganella morganii</i>	61			16	93						72	80	96	97					94	100	84	62				86	97	98		70						
<i>Proteus mirabilis</i>	434		62	82	98	91	10	84	82	85	89	95	99						99	99	98	56				85	77	94		68						
<i>Providencia rettgeri</i>																																				
<i>Providencia stuartii</i>	63				84					51	26	53	79	79					84	90	86	7						67		66						
<i>Serratia marcescens</i>	73										85	82	95	98					95	97	86	82				93	77	88		93						
NONFERMENTERS																																				
<i>Acinetobacter baumannii</i> complex ¹³	89			47	14															16						15									85 [#]	83
<i>Pseudomonas aeruginosa</i>	502				69															74	76	76	71					91	97							
<i>Stenotrophomas maltophilia</i>	54																														92					92

Not reported due to intrinsic resistance or susceptibility panel restrictions.

Antibiogram: Wake Forest Baptist

ATRIUM HEALTH WAKE FOREST BAPTIST ANTIBIOTIC SUSCEPTIBILITY REPORT %SUSCEPTIBLE: INPATIENTS (January-December 2025)

GRAM NEGATIVE RODS	Number Tested	Cefazolin	Ceftriaxone	Cefepime	Ciprofloxacin	Levofloxacin	Ertapenem	Meropenem	Ampicillin + Sulbactam	Piperacillin + Tazobactam	Trimethoprim Sulfamethoxazole	Minocycline	Amikacin	Gentamicin	Tobramycin
<i>Escherichia coli</i>	1255	70	78	81	68	—	99	99	58	96	69	—	99	86	83
<i>Klebsiella pneumoniae</i>	465	66	72	73	69	—	98	99	64	93	70	—	100	84	82
<i>Proteus mirabilis</i>	239	78	90	92	71	—	99	99	90	98	76	—	99	89	87
<i>Serratia marcescens</i>	138	—	83	96	77	—	97	99	—	86	97	—	99	98	75
<i>Enterobacter cloacae</i> complex	129	—	—	89	87	—	87	99	—	79	86	—	100	96	96
<i>Klebsiella aerogenes</i>	81	—	—	95	92	—	93	98	—	74	96	—	100	98	100
<i>Klebsiella oxytoca</i>	61	22	78	86	86	—	98	98	59	85	80	—	98	85	85
<i>Citrobacter freundii</i> complex	50	—	80	98	94	—	92	98	—	86	92	—	100	94	94
<i>Providencia</i> species	35	—	—	71	57	—	100	100	48	80	88	—	97	77	68
<i>Pseudomonas aeruginosa</i>	450	—	—	90	83	—	—	90	—	89	—	—	—	—	—
<i>Stenotrophomonas maltophilia</i>	102	—	—	—	—	91	—	—	—	—	98	47	—	—	—
<i>Acinetobacter baumannii</i> complex	34	—	—	64	58	—	—	61	91	—	91	—	94	70	88

Antibiogram: Carolinas Medical Center

Atrium Health – CMC INPATIENTS 2024 Antibiotic Susceptibility Surveillance Report

Gram Negative Organisms ¹	# of Isolates Tested	Penicillins				Cephems						Miscellaneous									
		Ampicillin	Ampicillin-Subactam ⁷	Piperacillin-Tazob ⁶	Cefazolin	Ceftazidime	Ceftiaxone	Cefepime ⁶	Aztreonam	Ertapenem	Meropenem	Gentamicin	Tobramycin	Amikacin	Ciprofloxacin	Levofloxacin	Nitrofurantoin ²	Tetracycline ³	Trimethoprim-Sulfa	Fosfomycin ⁵	Ceftolozane/Tazob
Escherichia coli - Total	1352	44	51	92	63		83	85	83	99	99	88	87	99	71	74	96	67	68		
<i>Escherichia coli</i> - ESBL ⁴	185									99	100	65	60	94	18	26	93	39	35	97	
Klebsiella pneumoniae - Total	546		74	90	76		85	86	84	98	98	93	93	99	83	90	54	77	82		
<i>Klebsiella pneumoniae</i> - ESBL ⁴	72									100	100	59	54	100	23	56	37	44	19		
<i>Klebsiella aerogenes</i>	99			84			71	95	77	95	97	100	100	100	97	97	34	74	100		
<i>Enterobacter cloacae</i> complex	197			77			59	85	67	85	99	97	96	100	91	94	29	92	100		
<i>Proteus mirabilis</i> - Total	258	86	91	98	80		96	96	95	100	99	94	95	100	82	83				86	
<i>Proteus vulgaris</i> - Total	34		64	100			35	82	73	100	100	100	100	100	94	97				97	
<i>Serratia marcescens</i>	142			78			67	92	71	100	100	97	78	99	90	97				98	
<i>Citrobacter freundii</i> complex	65			84			53	90	54	93	96	96	93	100	90	90	93		89	93	
<i>Citrobacter koserii</i>	33			100	100		100	100	100	100	100	100	100	100	100	100	83		100	100	
<i>Morganella morganii</i>	51			94			76	96	72	100	100	96	96	100	68	70			50	68	
<i>Providencia</i> species	50			94			80	86	72	100	100	52	52	98	70	66			0	66	
Pseudomonas aeruginosa - Total	472			90				90	82		93			97 ⁴	84	79					
<i>Pseudomonas aeruginosa</i> - MDRO ⁴	74			31				31	10		71			90 ⁴	55	33					94
<i>Stenotrophomonas maltophilia</i>	58														93						100
<i>Acinetobacter</i> species	54		96				92	75	96			100	94	96	100	92	98				96
<i>Acinetobacter baumannii</i> complex ⁴	35		97				97	68	91			100	88	97	100	94	97				94

Assessment Question #2

Assessment Question #2

GT is a 68-year-old male who presents to the ED with flank pain that began 2 days ago. He notes he has urinary urgency and frequency and has not taken his blood pressure medications in 2 days. He has no other issues or complaints. He has not been recently hospitalized and has no history of urinary tract infections.

PMH: hypertension and type 2 diabetes mellitus
Vitals: HR 95, BP 112/74, Temp 38.4°C

GT is diagnosed with a cUTI with pyelonephritis and will be admitted for intravenous antibiotics. Based on his presentation, which of the following is the most appropriate empiric antibiotic therapy?

- A. Ceftriaxone
- B. Cefazolin
- C. Meropenem
- D. Vancomycin

Title: Antimicrobial Prescribing Use Criteria (Enterprise)

Published Date: 11/17/2025

Last Review / Revised Date: 11/1/2025

Document Type:
 Policy Procedure Guideline Other

Content Applies to Patient Care:
 Adults Pediatrics (Under 18) N/A

Scope: Enterprise

 Division(s):

 Area Name:

 Entity Name:

 Department Name:

Restricted Antimicrobials

Amphotericin B (liposomal)	Ceftolozane - Tazobactam	Foscarnet	Linezolid	Paxlovid
Artesunate	Ciprofloxacin	Fosfomycin	Maribavir	Peramivir
Aztreonam	Dalbavancin	Ibrexafungerp	Meropenem	Posaconazole
Cefiderocol	Daptomycin	Imipenem - Cilastatin	Meropenem - Vaborbactam	Remdesivir
Cefotaxime	Eravacycline	Imipenem - Cilastatin - Relebactam	Micafungin	Sulbactam - Durlobactam
Ceftaroline	Ertapenem	Isavuconazole	Minocycline (IV)	Tigecycline
Ceftazidime - Avibactam	Fidaxomicin	Levofloxacin	Moxifloxacin	Voriconazole

Antimicrobial Prescribing Use Criteria

Enterprise Antimicrobial Prescribing Use Criteria, 2026.

Fluoroquinolones

Class remains one of the **preferred** for empiric cUTI treatment in those without sepsis and low resistance rates

Long history in treatment of urinary tract infections

Widespread use and overuse has led to resistance rate **increases**

2024 Enterprise Antibioqram Data

Location (Site/Source)	Pathogen	Total	Cefazolin (UTI)	Ceftriaxone	Ciprofloxacin
Carolinas Medical Center (Non-ICU/All Sources)	<i>E. coli</i>	1352	-	83	71
	<i>K. pneumoniae</i>	546	-	85	83
	<i>P. mirabilis</i>	258	-	96	82
Lutheran General (Inpatient/All Sources)	<i>E. coli</i>	2147	79	81	66
	<i>K. pneumoniae</i>	639	73	72	69
	<i>P. mirabilis</i>	461	87	87	50
St. Lukes (Inpatient/All Sources)	<i>E. coli</i>	2198	84	85	73
	<i>K. pneumoniae</i>	657	86	85	83
	<i>P. mirabilis</i>	398	96	96	81
Wake Forest Baptist (Inpatient/Urine)	<i>E. coli</i>	843	81	82	72
	<i>K. pneumoniae</i>	251	71	73	65
	<i>P. mirabilis</i>	117	87	90	62

Fluoroquinolones: Dosing & Considerations

Drug	Dose	Comments
Levofloxacin	500-750 mg PO/IV every 24 hours	Reserve use for patients without fluoroquinolone exposure in the past 3 to 12 months or without history of fluoroquinolone-resistant urinary isolate
Ciprofloxacin	500-750 mg PO every 12 hours 400 mg IV every 12 hours	
Moxifloxacin	Not recommended for urinary tract infections (inadequate urinary distribution)	

Excellent bioavailability

Ease of administration

Low – medium cost

Adverse side effects: QTc prolongation, tendonitis, CNS effects, arthralgia, phototoxicity

Carbapenems

Carbapenems are **preferred** for the treatment of cUTI with sepsis

In those without sepsis, carbapenems are **not** first-line

Broad-spectrum of activity, stable against many beta-lactamases

Carbapenems: Dosing

Drug	Dose	Comments
Meropenem	1-2g IV every 8 hours over 180 minutes	Preferred empiric agent from this class due to broad coverage Formulary restricted
Ertapenem	1g IV once daily	Gap in coverage: <i>Pseudomonas aeruginosa</i> Formulary restricted
Imipenem-cilastatin	500 mg – 1g IV every 6 hours	Formulary non-stock

Meropenem/ertapenem: ID consult or clinical pharmacist review against established criteria

Imipenem-cilastatin: ID consult and clinical pharmacist review against established criteria

Carbapenems: Patient Considerations

No oral options

Reserve for critically-ill patients

- Healthcare-associated infections
- Risk factors for resistant pathogens (e.g. ESBL producing organisms)

Medium cost

Important antimicrobial stewardship priority

- To preserve their effectiveness

Novel β -lactam/ β -lactamase inhibitors

Crucial role against multidrug-resistant pathogens

Restricted to septic shock patients in which preferred antimicrobials are likely inappropriate due to

- Previous culture data
- Risk factors

Reserve for:

- Known multi-drug-resistant pathogens
- Carbapenem resistant pathogens

High cost

BLBLI's: Dosing

Drug	Dosing	Comments
Ceftazidime-Avibactam	2.5g IV every 8 hours	Treatment limited to: <ul style="list-style-type: none">- Carbapenem-resistant Enterobacterales- Difficult-to-treat <i>Pseudomonas aeruginosa</i> with documented susceptibility Preferred for ESBL-producing gram-negative infections in those unable to tolerate carbapenems (e.g. DDI with valproic acid)
Ceftolozane-Tazobactam	1.5g IV every 8 hours over 4 hours	Treatment limited to: <ul style="list-style-type: none">- Difficult-to-treat <i>Pseudomonas aeruginosa</i>
Meropenem-Vaborbactam	4g IV every 8 hours	Treatment limited to: <ul style="list-style-type: none">- Carbapenem-resistant Enterobacterales- <i>Klebsiella pneumoniae</i> carbapenemases producing Enterobacterales- Isolates resistant to ceftazidime/avibactam

All BLBLI's are formulary restricted: ID consult and clinical pharmacist review against established criteria

Cefiderocol

Alternative antibiotic to empirically treat cUTI due to:

- Stewardship considerations
- Uncertainties about real-world effectiveness

Resistance already emerging

Reserve for infections with metallo-beta-lactamase carbapenemases

Dosing: 2g IV every 6 hours

Formulary restricted for MDR Gram-negative pathogens with documented resistance to all front-line antimicrobials

Susceptibility testing is required (not required at the time of initiation)

Older Aminoglycosides

Amikacin, gentamicin, and tobramycin are an **alternative** for empiric treatment of cUTI

- Use in populations with increasing rates of ESBL-producing organisms
- Extended interval dosing = cUTI
- One-time dose = uUTI

Class-wide adverse drug effects: nephrotoxicity, ototoxicity

Therapeutic drug monitoring essential

Oral Empiric Antibiotics

No specific preferred guideline recommendation

Ideal for outpatient management candidates

Oral Antibiotic Options

Antibiotic	Oral Absorption	Urinary Excretion	Dose (normal renal function)
Amoxicillin-clavulanate	80%	A 50-70%, C 25-40%	875/125 mg every 8-12 hours
Cefpodoxime	50%	80%	200-400 mg every 12 hours
Cefuroxime	52%	90%	500 mg every 12 hours
Cephalexin	90%	90%	500-1000 mg every 6 hours
Ciprofloxacin	70%	40-50%	500-750 mg every 12 hours
Levofloxacin	99%	64-100%	500-750 mg daily
Other oral b-lactams (amoxicillin, cefadroxil, cefaclor, cefdinir)	More limited data on clinical outcomes compared to higher bioavailable alternatives, use with caution if alternatives not available		
Trimethoprim-sulfamethoxazole	70-90%	T 66%, S 84%	800/160 mg every 12 hours

Oral Antibiotics: Patient Considerations

Decrease unnecessary hospital admission rates

High resistance rates to fluoroquinolones

Utilize prior urine cultures to guide treatment choice

Assess both oral absorption and urinary excretion

Optimize dosing of oral-beta lactams with low bioavailability

Assessment Question #3

Assessment Question #3

AH is a 78-year-old male who presents with altered mental status, hypotension, tachycardia, and dysuria. Patient met sepsis criteria and the rapid blood culture panel resulted with DTR *Pseudomonas aeruginosa* with documented resistance to ceftazidime-avibactam. He will be admitted for antibiotic treatment.

PMH: HTN, HLD, GERD

Vital Signs: BP 90/50, HR 110, T 38°C

What is the most appropriate empiric antibiotic?

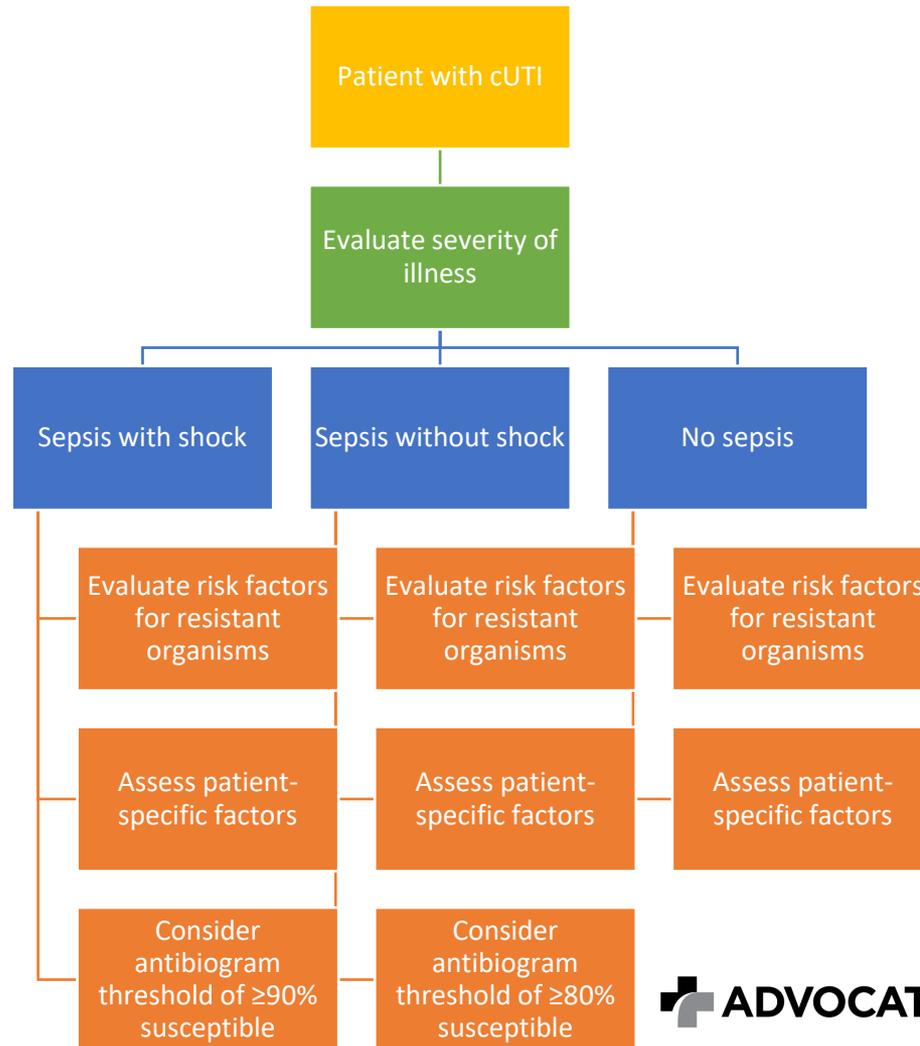
- A. Ceftolozane-tazobactam
- B. Cefiderocol
- C. Amoxicillin-clavulanate
- D. Ertapenem

Empiric Antibiotic Summary

Condition of the Patient	Preferred	Alternative
Sepsis with or without shock	3 rd or 4 th generation cephalosporins Carbapenems Piperacillin-tazobactam Fluoroquinolones	Novel BLBLI Cefiderocol Plazomicin Older aminoglycosides
Without sepsis, IV route of therapy	3 rd or 4 th generation cephalosporins Piperacillin-tazobactam Fluoroquinolones	Carbapenems Newer agents (BLBLI, cefiderocol, plazomicin) Older aminoglycosides
Without sepsis, oral route of therapy	Fluoroquinolones or trimethoprim-sulfamethoxazole	Amoxicillin-clavulanate or oral cephalosporins

How to Select Empiric Therapy: Four Step Approach

Empiric Antibiotic Selection



Four-Step Approach

Assess the following:

Severity of
illness

Risk factors for
resistance

Patient-
specific
considerations

If septic,
consider the
antibiogram

Step 1: Severity of Illness

Inappropriate empiric antibiotics have impact on mortality

Does the patient have sepsis?

- Life-threatening organ dysfunction caused by a dysregulated host response to infection
- SOFA score increase in 2 points
 - In hospital mortality >10%
- SIRS criteria more sensitive than specific
 - Do not correlate as well with severity of illness/ outcomes as SOFA criteria

Step 2: Resistant Organisms

More recent urine cultures may be a better guide than distant urine cultures

- Median of 3-6 months

Most recent antibiotic exposure

FQ exposure in past 12 months

- Strong predictor of resistance
- More recent exposure (< 3 months) = stronger resistance prediction

Step 3: Patient Considerations

Assess other patient-specific considerations

- Risk of allergic reaction
- Contraindications
- Drug-drug interactions

Step 4: Antibiogram

Assess antibiogram for patients with sepsis

Antibiogram needs to be:

- Local
- Recent
- Relevant to the patient

Application to Pharmacy Practice

You receive an order for cefepime for RT, a 50-year-old male patient being transferred from the ED to the ICU for sepsis due to suspected UTI, you follow the four-step approach to determine antibiotic appropriateness:

Severity of
illness

Risk factors for
resistance

Patient-specific
considerations

If septic,
consider the
antibiogram

Step 1

Severity of illness

You see that the provider selected cefepime from the sepsis order set

ED Inpatient Severe Sepsis Treatment

Urinary Tract

Urinary Community Acquired (Limited or No Antibiotic Exposure in Last 90 Days)

Urinary Hospital or Healthcare-Acquired or Extensive Outpatient Antibiotic Exposure in Last 90 Days

Standard regimen (ceFEPIme IVPB OR piperacillin/tazobactam IVPB)

cefepime IVPB

cefepime 2,000 mg once followed by 2,000 mg every 8 hours

ceFEPIme (MAXIPIME) 2,000 mg in sodium chloride 0.9 % 100 mL IVPB
2,000 mg ONCE, Intravenous, Administer over 0.5 Hours, today at 0845, For 1 dose
First dose STAT if not given in the ED.
* MINIBAG PLUS - Mix before hanging *
Hospice coverage not set

ceFEPIme (MAXIPIME) 2,000 mg in sodium chloride 0.9 % 100 mL IVPB
2,000 mg EVERY 8 HOURS SCHEDULED (3 times per day), Intravenous, Administer over 4 Hours, First dose today at 1245, For 5 days
* MINIBAG PLUS - Mix before hanging *
Hospice coverage not set

Steps 2 & 3

Risk factors for resistance

You investigate the patient's history and find that he spends half of every year abroad.

Patient-specific considerations

You also find that RT was seen in urgent care 1 month ago for urinary frequency and had ESBL *E. coli* for which he was prescribed TMP-SMX. He has no antibiotic allergies or drug-drug interactions.

Step 4

If septic, consider the antibiogram

Under typical circumstances, cefepime would be an extremely reliable treatment option.



ANNUAL REPORT OF SUSCEPTIBILITY PATTERNS

January 1 - December 31, 2025

Percent of isolates susceptible¹ to antimicrobial agents at attainable concentrations

Gram Negative	# Isolates ²	ESBL ³	Penicillins		Cephalosporins								Carbapenems		Micro-bactam	Quinolones		Aminoglycosides			Other						
			Ampicillin	Ampicillin/sulbactam	Piperacillin/tazobactam	Cefazolin (Urine) ⁴	Cefazolin	Cefuroxime axetil	Cefepodoxime	Ceftazidime	Ceftriaxone	Cefepime	Ceftazidime/avibactam ^{5,6}	Ceftolozane/tazobactam ^{5,6}	Ertapenem ⁶	Meropenem ⁶	Aztreonam ⁷	Ciprofloxacin ⁷	Levofloxacin ⁷	Gentamicin	Tobramycin	Amikacin	Nitrofurantoin ⁸	Trimethoprim/sulfamethoxazole	Fosfomycin ^{5,6,9}	Colistin ⁹	Minocycline ^{5,6}
ENTEROBACTERIALES																											
<i>Citrobacter freundii</i> complex ¹¹	80				68										98	100	65	92		97		100		89	90		
<i>Citrobacter koseri</i>	42				97		51	94	100	100	100				100	100	100	100		97		100		84	97		
<i>Enterobacter cloacae</i> complex ¹²	223				73			70	72	67	92	99			83	99	72	87		96	95	100		29	88		
<i>Escherichia coli</i> ¹³	2126	17	48	59	94	81	57	74	76	88	83	91	100		99	99	87	68		90	83	97	94	73			
<i>Klebsiella (Enterobacter) aerogenes</i>	72				75					73	76	98			96	100	75	94		98		100		15	97		
<i>Klebsiella oxytoca</i> ¹⁰	120	9		70	88		0	82	86	95	89	95	95		96	98	95	92		95	97	100		78	90		
<i>Klebsiella pneumoniae</i> ¹⁰	673	17		76	90	82	69	75	81	83	82	89	100		97	98	81	79		92	87	99		27	82		
<i>Morganella morganii</i>	43			9	86						67	100			96	97	71	72		88		100			76		
<i>Proteus mirabilis</i>	362		80	91	100	93	16	94	98	97	96	99	100		100	99	98	83		96	98	99			85		
<i>Providencia rettgeri</i>																											
<i>Providencia stuartii</i>																											
<i>Serratia marcescens</i>	100														97	97	98	93		99	87	98			100		
NONFERMENTERS																											
<i>Acinetobacter baumannii</i> complex ^{13,14}																											
<i>Pseudomonas aeruginosa</i>	564				87					89		89	99	98		92	81	87	84				98	99			
<i>Stenotrophomonas maltophilia</i>	34																								100		94

Not reported due to intrinsic resistance or susceptibility panel restrictions.

10. Includes both ESBL and non-ESBL isolates.

Assessment Question #4

Assessment Question #4

After completing your patient assessment of RT using the four-step approach, which of the following recommendations would you discuss with the provider?

- A. Change to ceftriaxone since the patient doesn't have a cephalosporin allergy
- B. Change to meropenem-vaborbactam since he's 50 years old and has a history of ESBL *E. coli*
- C. Change to meropenem since he has a recent history of ESBL *E. coli*
- D. No change needed

Transitioning to Definitive Therapy

Definitive Therapy Selection

De-escalating antibiotics should be based on urine culture:

- Identification
- Susceptibilities

Optimizing the effectiveness of therapy:

- Improve clinical cure
- Reduce recurrence of infection

De-escalation Considerations

Antibiotic
stewardship

IV vs PO

Cost of
treatment
options

Administration
resources

Therapeutic
drug
monitoring

Inpatient vs
outpatient

- Culture call-back

Timing of IV to PO Antibiotic Transition

Timing of IV to PO Transition

cUTI **without** bacteremia and:

- Treated initially with parenteral therapy
- Clinically improving
- Able to take oral medication
- Effective oral option available

→ Transition to PO antibiotics

Why? Reduces

- Reduces avoidable IV catheter-related ADRs
- Reduces costs/ resources
- Improved practicality of administration

Timing of IV to PO Transition

cUTI **with** Gram-negative bacteremia and:

- Treated initially with parenteral therapy
- Clinically improving
- Able to take oral medication
- Effective oral option available

Before transitioning, patients should be:

- Afebrile
- Hemodynamically stable
- Achieved source control

→ Transition to PO antibiotics

IV/PO Stepdown Study #1

Study Type	Multicenter observational cohort study, between Jan 2016 and Dec 2022, 759 patients
Outcome	60-day recurrence of infection
Intervention	IV β -lactam to oral stepdown therapy within 7 days using FQ, TMP-SMX, or high-bioavailability β -lactams (HBBLs: amoxicillin, amoxicillin-clavulanate, and cephalexin)
Baseline Characteristics	Mean age 70 years, female 55%, pyelonephritis 40%, <i>E. coli</i> 82%, <i>Klebsiella</i> species 17%
Results	Effectiveness differences: FQs (adjusted hazard ratio, 1.09 [95% confidence interval, .49-2.43]) TMP-SMX (1.44 [.54-3.87]) HBBLs (3.83 [1.76-8.33])
Conclusion	FQs and TMP-SMX have similar effectiveness as IV β -lactams, HBBLs associated with higher recurrence rates Limitation: HBBLs not optimally dosed for bacteremia

IV/ PO Stepdown Study #2

Study Type	Retrospective, multicenter, cohort study from July 2016 to July 2018, n =372 hospitalized patients with BSI due to <i>E. coli</i> , <i>K. pneumoniae</i> , or <i>P. mirabilis</i>
Outcome(s)	Composite of treatment failure (30-day readmission due to recurrence, 30-day all-cause mortality, and change in oral antibiotic)
Intervention	Oral stepdown therapy with either FQ, TMP-SMX, or β -lactam
Baseline Characteristics	B-lactam group: 200 patients, FQ or TMP-SMX: 197 patients, female 66%, duration of IV therapy 5 days, <i>E. coli</i> 82.8%, urinary source of infection 85%
Results	Median total duration of therapy: 14 days in both groups Treatment failure composite: - FQ or TMP-SMX 5.8% compared to β -lactam 7% (p= 0.561)
Conclusion	No difference in treatment failure rates in those receiving oral β -lactams compared to oral FQ or TMP-SMX for step-down therapy

Drug	Dose
Amoxicillin	1000 mg every 8 hours
Amoxicillin-clavulanate	875/125 mg every 12 hours
Cephalexin	1000 mg every 6 hours
Ciprofloxacin	750 mg every 12 hours
TMP-SMX	160/800 mg every 12 hours
Levofloxacin	750 mg every 24 hours

IV/PO Stepdown Study #3

Study Type	Retrospective, multicenter, observational cohort from 3 Michigan hospitals from Feb 2020 to Oct 2022 194 patients with gram negative bacteremia from a urinary source
Outcome	Composite recurrent bacteremia or mortality within 30 days of therapy
Intervention	Active empiric intravenous antibiotics and transitioned to appropriately dosed oral cephalexin, amoxicillin, FQ, or TMP-SMX
Baseline Characteristics	Mean age 71 years, more females in standard therapy group, median 11 days treatment (4 days IV, 7 days PO), <i>E. coli</i> 77%, <i>Klebsiella</i> spp. 17%
Results	Primary outcome occurred in beta-lactam group 1.3% vs standard therapy 1.7%, OR 1.27 [95% CI 0.11-14.2]
Conclusion	High-dose oral b-lactams are as safe and effective as oral FQ and TMP-SMX for the treatment of bacteremia from a urinary source

Title: Adult IV to Oral Antimicrobial Step-Down Therapy Guidelines (IL & WI Divisions)		Published Date: 11/06/2025
		Last Review / Revised Date: 11/06/2025
Document Type: <input type="checkbox"/> Policy <input type="checkbox"/> Procedure <input checked="" type="checkbox"/> Guideline <input type="checkbox"/> Other		Content Applies to Patient Care: <input checked="" type="checkbox"/> Adults <input type="checkbox"/> Pediatrics (Under 18) <input type="checkbox"/> N/A
Scope: <input type="checkbox"/> Enterprise	<input checked="" type="checkbox"/> Division(s): IL & WI Divisions	
<input type="checkbox"/> Area Name:	<input type="checkbox"/> Entity Name:	<input type="checkbox"/> Department Name:

APPENDIX B – Duration of Antibiotic Therapy in Uncomplicated Enterobacterales Bacteremia

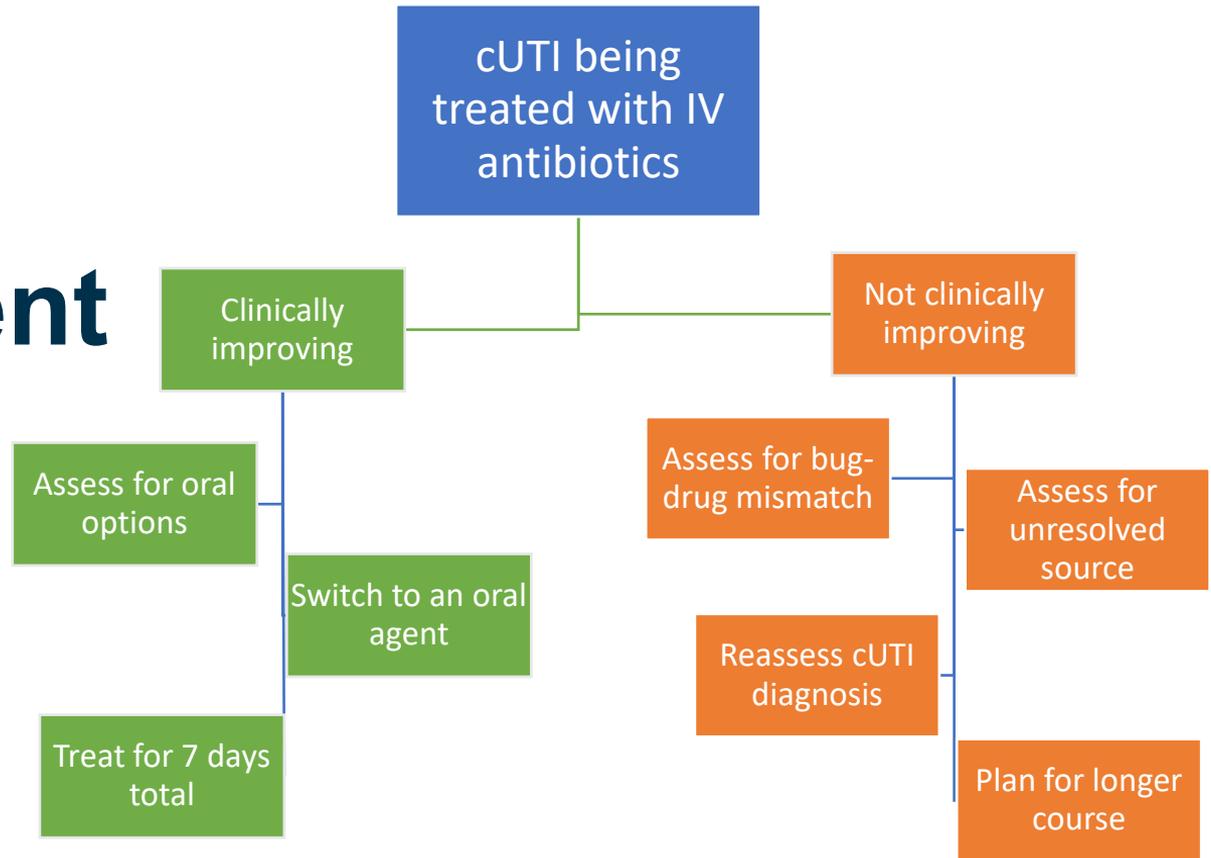
Table 1. Source & Severity of Bacteremia: Percent of Total Cohort¹

Source of Bacteremia (n=1,769)		Severity of Infection (n=1,769)
Urinary Tract 39.6%	Catheter Associated 16.6%	ICU Admission on Day 1 of Bacteremia: 29.2%
GI 19.7%	Pneumonia 8.2%	Pitt Bacteremia Score: Median 2 (IQR 1-3)
Biliary 12.2%	Skin and Soft Tissue 1%	Inadequate Source Control During Therapy: 2.2%

Table 2. Oral Therapy: Usual Doses – Normal Renal Function³

Oral Step Down with clinical improvement & source control Longer duration (10-14 days) has been suggested for oral beta-lactams	
Amoxicillin 1g PO TID	Cefpodoxime 400mg PO BID ^b
Amoxicillin/Clavulanate 875/125mg TID up to Amox/Clav ER 2 tabs BID	Ciprofloxacin 750mg PO BID
Cephalexin 1g PO QID or Cefadroxil 1g PO BID ^{a,b}	TMP/SMX 5 mg/kg (TMP) PO BID ^c

IV to PO Switch Assessment



Duration of Antibiotics

cUTI Treatment Duration

cUTI without associated bacteremia and clinically improving on effective therapy

Fluoroquinolone: 5-7 days total

Non-fluoroquinolone: 7-10 days

cUTI Treatment Duration

cUTI with associated Gram-negative bacteremia and clinically improving on effective therapy

Typical Duration: 7 days

Those who would benefit from 14 days:

- Suspected acute bacterial prostatitis
- Lack of source control

Future Needs & Conclusions

Research Needs

Optimal use of antibiograms

- Specifically in non-septic cUTI patients

Oral beta-lactams

- Optimal dosing
- Effectiveness

Management of underrepresented populations

- Immunocompromised
- Severe CKD
- Indwelling catheters
- Recent urologic procedures

Key Takeaways & Conclusions

New cUTI classifications

Empiric treatment depends on presence/
absence of sepsis

Four-step approach to choosing empiric therapy

Transition to definitive therapy once
susceptibilities have resulted

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Questions?

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