Stewardship strategies for interpretation of novel urinary diagnostics

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Lauren Biehle, PharmD, BCPS, BCIDP
CDPHE Antimicrobial Stewardship Pharmacy Lead

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Objectives

- Describe methods for evaluating urinary diagnostics in the nursing home setting.

- Compare rapid diagnostics, such as polymerase chain reaction, to traditional culture and sensitivity.

- Apply principles of antimicrobial and diagnostic stewardship to the nursing home setting.

Patient case

- You receive a call about an 86 year-old resident who has a positive result from a urine sample. You are told that the patient has four organisms detected:

    - *Enterococcus faecalis.*
    - *Proteus mirabilis.*
    - *Pseudomonas aeruginosa.*
    - *Staphylococcus aureus.*

- What are your next steps?

Antibiotics in nursing homes

- Estimated 50-79% of nursing home residents receive antibiotics annually.

- Up to 75% of antibiotic use in nursing homes may be inappropriate.

  - Greatest contributor is misuse of antibiotics for asymptomatic bacteriuria.
  - Antibiotics exhibit second highest rate of adverse drug events after antipsychotic medications.

Appaneal H, et al. Infect Control Hosp Epidemiol. 2019; 40(10): 1087–1093.
Beeber AS, et al. J Am Med Dir Assoc. 2021; 22(1): 156–163.
CMS. Available at: https://qsep.cms.gov/data/251/DEVELO1.PDF
Nace DA, et al. JAMA Intern Med 2020; 180(7): 1–9.
Weber BR, et al. Infect Control Hosp Epidemiol 2019;40(1):18-23..

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Antibiotics in nursing homes

- Being a resident of a long-term care setting is a risk factor for colonization with multidrug resistant organisms and *C. difficile*.

- High rates of antibiotic use in nursing homes associated with increased rates of adverse events among all facility residents, not just those receiving antibiotics.

- CDC and CMS identified nursing homes as priority areas for improved antimicrobial stewardship.

Appaneal H, et al. Infect Control Hosp Epidemiol. 2019; 40(10): 1087–1093.
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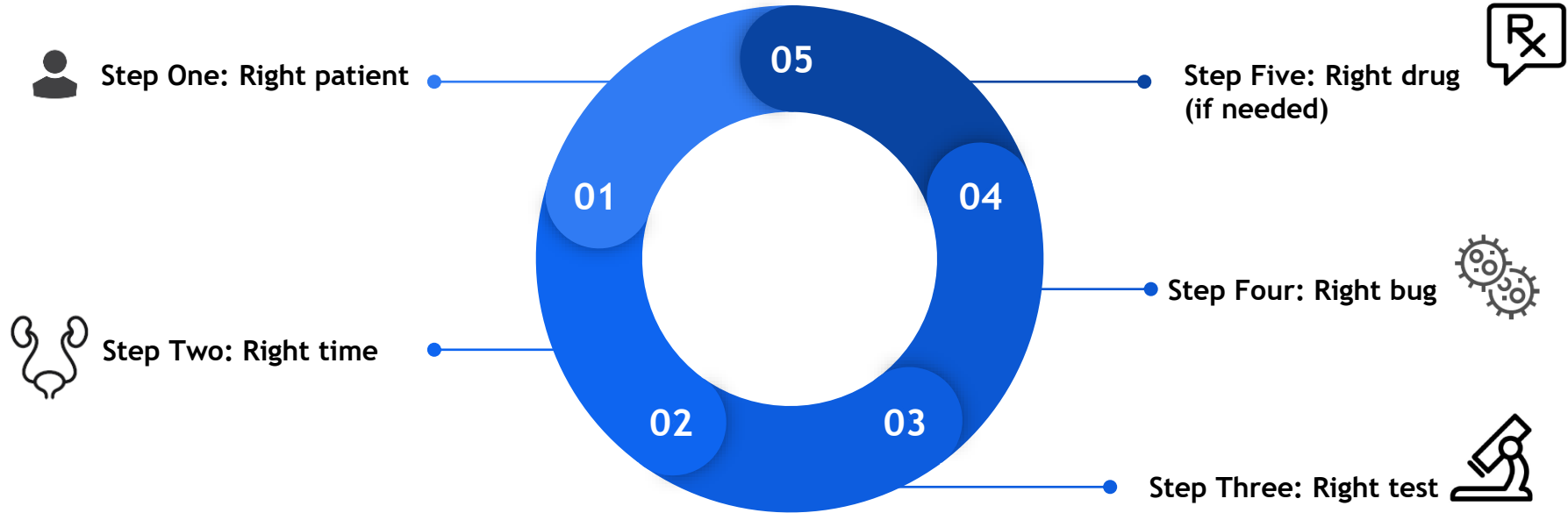CMS. Available at: https://qsep.cms.gov/data/251/DEVELO1.PDF
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Five steps of urinary diagnostics interpretation

Step One: Right patient

Step Two: Right time

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Step Five: Right drug (if needed)

Step Four: Right bug

Step Three: Right test

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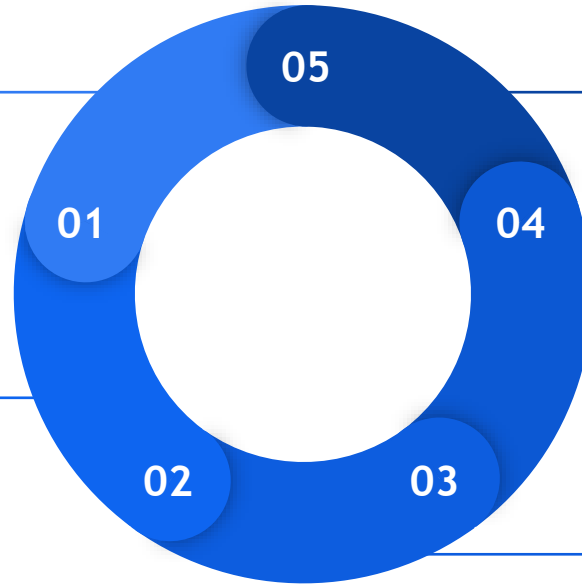# Five steps of urinary diagnostics interpretation

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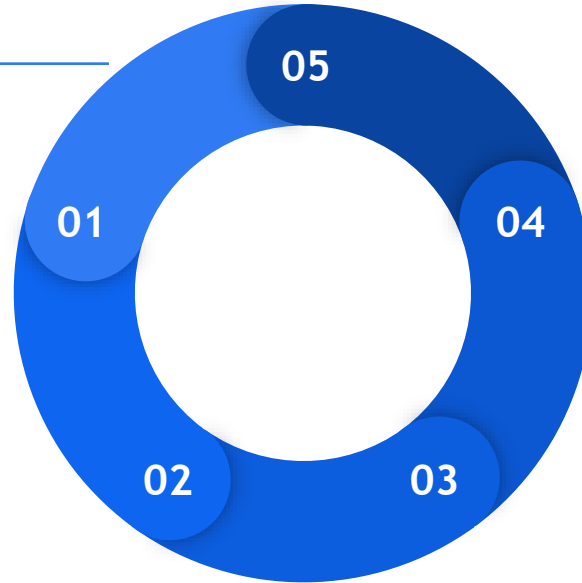
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What quantitative data is available?
If polymicrobial, should test be re-collected?

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Step One: Right patient

UTI syndrome	Diagnostic findings	Treatment and duration	Notes
Asymptomatic bacteriuria	≥100,000 CFU/mL of bacteria, no s/s localized to genitourinary tract.	**No antibiotics.**	
Simple cystitis	≥100,000 CFU/mL of bacteria or ≥100 CFU in specimen by straight catheter. **Localized symptoms**: Acute dysuria, suprapubic tenderness, new/worsening incontinence, frequency, urgency, gross hematuria.	Nitrofurantoin x five days. TMP-SMX x three days. Beta-lactams x 3-7 days. Fosfomycin x one dose. Fluoroquinolones x three days.	FQ use should be minimized, not considered first-line.
Catheter-associated UTI	Systemic such as fever, rigors, chills, or localized symptoms as above + suprapubic/CVA tenderness or acute pain/swelling/tenderness of testes, epididymis, prostate.	If symptoms resolve quickly, seven days. If delayed response, 10-14 days.	If acute pain/swelling/tenderness, evaluate for prostatitis or epididymitis.

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Asymptomatic Bacteriuria

- "Bacteria recovered from a urine sample in a person <u>without localized</u> urinary tract signs or symptoms."

- Screening for and treatment of asymptomatic bacteriuria (ASB) is not recommended in nursing home residents.
  - Culture likely to be positive at any time.
  - Bacteriuria present in 50% of female residents, 40% of male residents.

$$\text{ASB} \neq \text{UTI}$$

Ashraf MS, et al. JAMDA 2020; 21:12e24.

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Asymptomatic Bacteriuria

- Antibiotics only recommended in pregnancy or immediately prior to urologic procedure associated with mucosal trauma (i.e. transurethral resection of prostate).

- Does not increase morbidity or mortality.

- Can lead to unnecessary antibiotic exposure and adverse effects.

$$ASB \neq UTI$$

Ashraf MS, et al. JAMDA 2020; 21:12e24.

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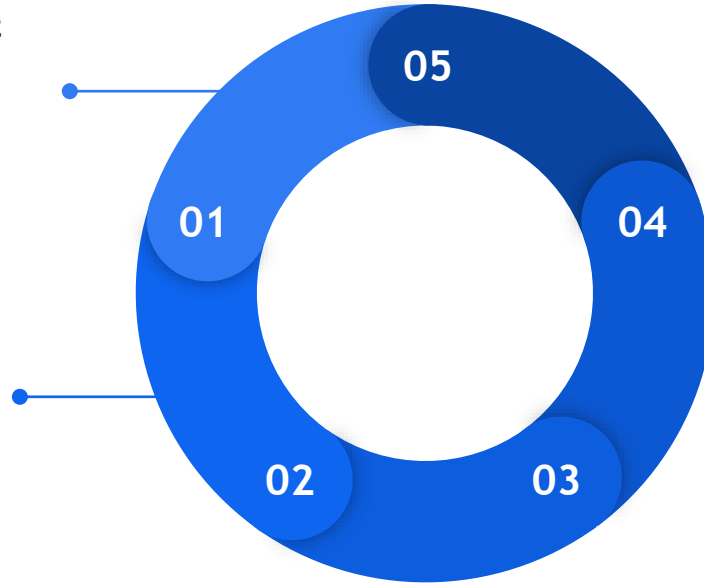# Five steps of urinary diagnostics interpretation

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Step Two: Right time

- Loeb criteria developed in 2001.
- Minimum criteria for initiating antibiotics in long-term care residents with possible infection.

		Fever	Symptoms
Without indwelling catheter	Acute dysuria OR	Fever >37.9C (100F) or 1.5C-2.4F increase above baseline temp AND	Urgency. Frequency. Suprapubic pain. Gross hematuria. Costovertebral angle (CVA) tenderness. Urinary incontinence.
With indwelling catheter	At least one of these:	Fever >37.9C (100F) or 1.5C-2.4F increase above baseline temp OR	New CVA tenderness. Rigors. New onset of delirium.

Ashraf MS, et al. JAMDA 2020; 21:12e24.
Katz MJ, et al. JAMA Network Open. 2022;5(2):e220181.
Loeb M, et al. Infect Control Hosp Epidemiol 2001;22:120e124.

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Suspected UTI action tool

ACTION TOOL

"Does the resident have new or worsening signs or symptoms that meet one of three criteria for suspected urinary tract infection?"

Link:https://cdphe.colorado.gov/antimicrobial-stewardship
CDPHE Toolkits for Long-term Care Facilities

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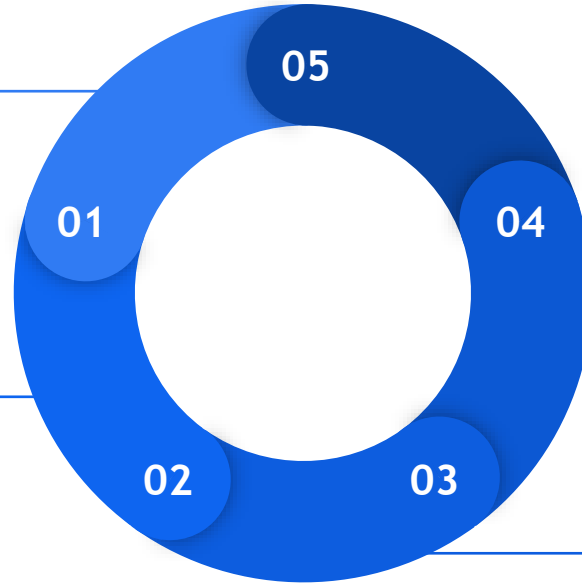
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Step Three: Right test

	Has disease	Does not have disease	
Test positive	True positive (Sensitivity)	False positive	Positive predictive value=TP/TP + FP
Test negative	False negative	True negative (Specificity)	Negative predictive value=TN/TN + FN

- Higher prevalence of disease within population→ higher positive predictive value.

- Higher sensitivity of test→ higher risk of false positives.

- Interpret test results in context of probability that infection is present (localized signs/symptoms of infection).

Examples of diagnostics for UTI

Technology	Methodology	FDA approved	Use	Pros	Cons
Dipstick	Nitrite and leukocyte esterase	Yes	Urinalysis	Quick, inexpensive, point of care	Poor specificity, limited information
Urine culture	Agar, automated systems (i.e. Vitek, Microscan)	Yes	Identification, susceptibilities	Gold standard, can detect slow-growing, fastidious pathogens	Longer time to result, does not distinguish ASB from infection
PCR	Nucleic acid amplification	No	Identification, antibiotic resistance genes	Rapid identification, highly sensitive	Provides resistance genes, does not provide susceptibilities, does not distinguish ASB from infection, may provide polymicrobial results

Harris M, et al. J Lab Med 2022; 46(1): 3–15.

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Multiplex PCR

- **Pros**
  - Multiple primers to detect several targets simultaneously.
  - High sensitivity.
  - Identified pathogens 43 hours sooner than culture and sensitivity (C&S).

- **Cons**
  - Cannot fully replace urine culture.
  - Polymicrobial results (29% vs. 7% in C&S).
  - Less quantitative data to distinguish colonization vs. infection.
  - Unable to provide susceptibilities.
    - Only provides results of resistance genes tested.
  - Higher cost.
  - Consistency of report formatting.

Wojno, et al. Urology 2020; 136: 119–126.
Xu, R. et al. Diagnostics 2021, 11, 479.

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Sample Report

Organisms Detected
Common pathogens in bold
- **Enterococcus faecalis**
- **Proteus mirabilis**
- **Pseudomonas aeruginosa**
- **Staphylococcus aureus**

Resistance Detected
Macrolide
Macrolide/Clindamycin
Methicillin
TMP-SMX
Antimicrobial Resistance **ARKSCORE**
LO ▮▮▮▮▮▮ [7] HI

No Allergies Reported

Drug Information

Fosfomycin
Dosing Req ☑ Renal ☐ Hepatic
Side Effects Diarrhea
Interactions Metoclopramide
Adverse Reaction **ARKSCORE**
LO [1] ▮▮▮▮▮▮ HI

Linezolid
Dosing Req ☐ Renal ☐ Hepatic
Side Effects Mylosuppresion
Interactions SSRI's
Adverse Reaction **ARKSCORE**
LO ▮▮▮ [4] ▮▮▮ HI

Infection Complexity **ARKSCORE**
LOW ▮▮▮▮▮▮▮ [7] HIGH

ONECHOICE®

Fosfomycin 3 gm PO x 1 dose & Linezolid dose not defined x 5 days for possible acute UTI*

Alternative Treatment Options with Adverse Reaction ArkScore™

Due to the presence of Pseudomonas and MRSA, antibiotic options are limited. Fosfomycin has variable activity. The combination of levofloxacin **ARKSCORE 5** with linezolid may have activity. Levofloxacin should be used with caution due to FDA warnings. Combination therapy may increase the risk of adverse reactions. Piperacillin/tazobactam IV **ARKSCORE 4** with vancomycin IV **ARKSCORE 3** is a possible option, however, pip/taz, vancomycin, and linezolid are used off-label for UTIs.‡

Why is this the OneChoice?

The detected organisms can be pathogenic when found in urine samples with a suspected diagnosis of UTI. Resistance genes were detected in six classes, of which four affects the treatment of some or all of the detected pathogens, limiting available options. ‡

When should this be treated?

Asymptomatic bacteriuria does not typically need treatment, and microbe detection may not indicate infection. However, treatment may be necessary during pregnancy or prior to urological procedures. Simple UTIs are typically treated for 3 days (fluoroquinolones/TMP-SMX), or 5 days (beta-lactams). In more complicated cases therapy may be extended to 7-14 days. STI treatment is specific to the microbe being treated and antimicrobial being used.‡

Are there any special considerations?

Multiple microbes detected may indicate contamination or colonization. Enterococcus faecalis and Pseudomonas may have intrinsic resistance to certain antimicrobials, making them difficult to treat. Enterococcus faecalis, Pseudomonas, and Staph aureus may require modified dosing and duration. Staph aureus may lead to infections in other sites of the body, have associated syndromes, or may present differently depending on the clinical scenario.‡

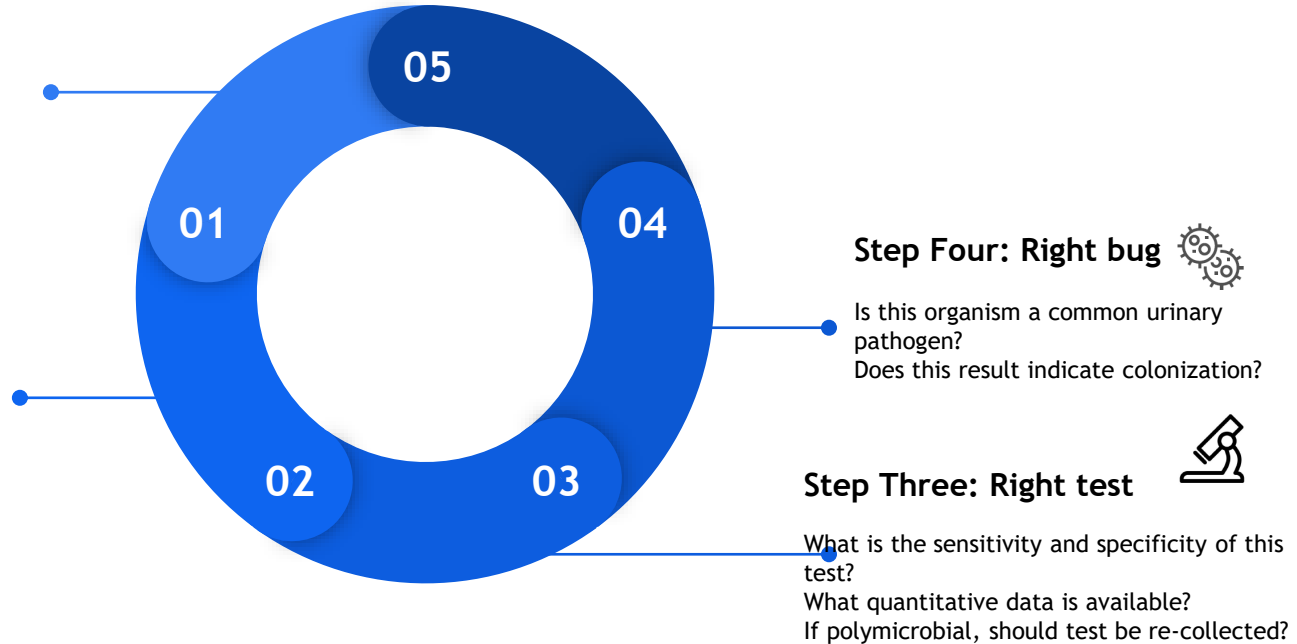# Five steps of urinary diagnostics interpretation

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What quantitative data is available?
If polymicrobial, should test be re-collected?

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Sample urine PCR report

Organisms Detected
Common pathogens in bold

- **Enterococcus faecalis**
- **Proteus mirabilis**
- **Pseudomonas aeruginosa**
- **Staphylococcus aureus**
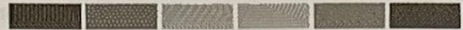
Resistance Detected

Macrolide
Macrolide/Clindamycin
Methicillin
TMP-SMX

Antimicrobial Resistance **ARKSCORE**

LO ▮▮▮▮▮▮ **7** HI

Infection Complexity **ARKSCORE**

LOW ▮▮▮▮▮▮ **7** HIGH

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Evaluation of rapid diagnostic results

- Is quantitative data available to assist in determining causative organism?
- Which resistance genes were tested?
  - PCR does not perform sensitivities
- Do these results indicate colonization or infection?
- What are the most likely organisms causing infection? Are these common urinary pathogens?
  - Aim to treat the most likely causative organism, rather than all pathogens detected.
  - Antibiotic recommendations in report likely to be overly broad in order to treat all pathogens.
- If high suspicion for infection and polymicrobial results, should the test be re-collected?
  - Similar to a mixed flora/dirty catch result from a culture.

Langford BJ, et al. Am J Infect Control 2019; 47:1409–1414.

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Pathogens Detected (B: Bacterial, V: Virus, P: Parasite, F: Fungal)		
🚩 HIGH	NONE DETECTED	
⚠️ MODERATE	NONE DETECTED	
🔵 LOW	B - Enterococcus spp., B - Prevotella bivia, B - Serratia marcescens	
NOT DETECTED	B - Acinetobacter baumannii, B - Klebsiella pneumoniae, B - Klebsiella michiganensis / oxytoca, F - Candida parapsiliosis, F - Candida albicans, B - Bacteroides fragilis, B - Staphylococcus saprophyticus, B - Morganella morganii, F - Candida krusei, B - Citrobacter freundii/braakii, B - Staphylococcus aureus, F - Candida dublinensis, F - Candida glabrata, B - Citrobacter koseri, B - Staphylococcus epidermidis, F - Candida tropicalis, B - Klebsiella Aerogenes, B - Pseudomonas aeruginosa, B - Mycoplasma genitalium, B - Enterobacter cloaca, B - Streptococcus pyogenes (Group A), B - Mycoplasma hominis, B - Escherichia coli, B - Streptococcus agalactiae (GBS), B - Proteus mirabilis, B - Ureaplasma urealyticum	

Legend					
🚩 HIGH	Likely active infection, discuss treatment options.	HIGH	Bacterial Load = 100,000 (=10^5)	Blank Box	Drug Not Indicated for Treatment
⚠️ MODERATE	May choose to recommend treatment in the presence of symptoms.	Moderate	Bacterial Load < 100,000 & =10,000 and (<10^5 & =10^4)	+	Recommended Treatment
🔵 LOW	Monitor for infection, may choose to treat if symptomatic.	Low	Bacterial Load < 10^4	R	Resistant to Antibiotic Class

Antibiotic Resistance Marker(s)/Gene(s) Detected	Possibly Ineffective Antibiotics
Antibiotic Resistance Panel	
Trimethoprim (dfrA)	Primsol

Antibiotic Treatment Options				
Antibiotic Support	**Enterococcus spp.**	**Prevotella bivia**	**Serratia marcescens**		
Amoxicillin	+				
Ampicillin	+				
Ceftriaxone		+			
Doripenem			+		
Ertapenem			+		
Linezolid	+				
Metronidazole		+			
Penicillin G	+				
Pip-Tazo			+		
Teicoplanin	+				
Vancomycin	+				

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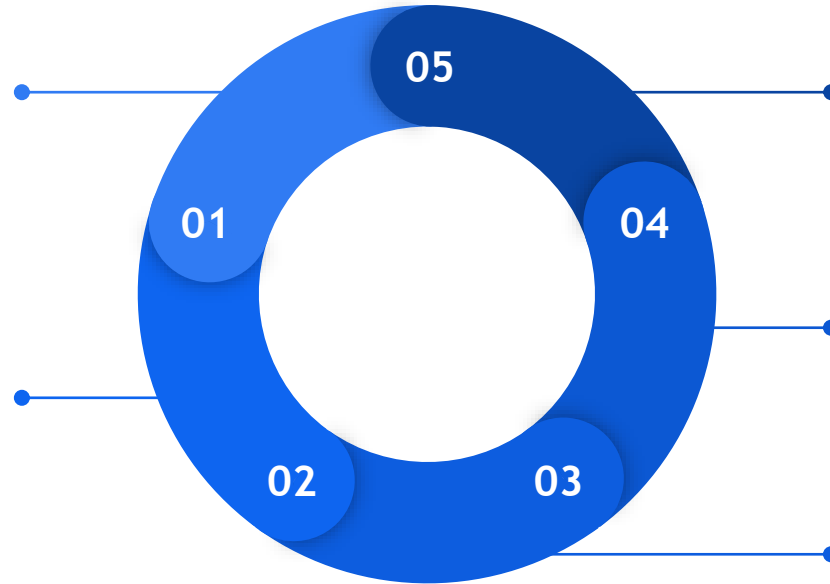# Five steps of urinary diagnostics interpretation

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Step Four: Right bug

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Does this result indicate colonization?

Step Three: Right test

What is the sensitivity and specificity of this test?
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AMDA diagnosis and treatment of UTI

UTI syndrome	Diagnostic findings	Treatment and duration	Note
Asymptomatic bacteriuria	≥100,000 CFU/mL of bacteria, no s/s localized to genitourinary tract.	No antibiotics	
Simple cystitis	≥100,000 CFU/mL of bacteria or ≥100 CFU in specimen by straight catheter. Localized symptoms: acute dysuria, suprapubic tenderness, new/worsening incontinence, frequency, urgency, gross hematuria.	Nitrofurantoin x five days. TMP-SMX x three days. Beta-lactams x 3-7 days. Fosfomycin x one dose. Fluoroquinolones x three days.	FQ use should be minimized, not considered first-line
Catheter-associated UTI	Systemic such as fever, rigors, chills or localized symptoms as above + suprapubic/CVA tenderness or acute pain/swelling/tenderness of testes, epididymis, prostate.	If symptoms resolve quickly, seven days; if delayed response, 10-14 days.	If acute pain/swelling/tenderness, evaluate for prostatitis or epididymitis.
Pyelonephritis	≥100,000 CFU/mL of bacteria or ≥100 CFU in specimen by straight catheter. Systemic: Fever, rigors/chills, fatigue/malaise, nausea/vomiting, dysuria, suprapubic tenderness, CVA tenderness, local symptoms above.	TMP-SMX x 14 days Beta-lactams x 10-14 days FQ x seven days.	If pelvic or perineal pain in men, evaluate for prostatitis.

Ashraf MS, et al. JAMDA 2020; 21:12e24.
Katz MJ, et al. JAMA Network Open. 2022;5(2):e220181.

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Active monitoring

- If Loeb criteria not met, consider initiating active monitoring orders:
  - Encourage _____ ounces of liquid intake _____ daily until urine is light yellow in color.
  - Record fluid intake every _____ hours for _____ hours.
  - Assess vital signs, including temp, every _____ hours for _____ hours.
  - Request notification if symptoms worsen or if unresolved in _____ hours.
  - Consult pharmacist to review medication regimen.
- AMDA recommends increased hydration as supportive care for UTI.

AHRQ. Available at: https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK1_T1-SBAR_UTI_Final.pdf.
Ashraf MS, et al. JAMDA 2020; 21:12e24.

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Stewardship and UTIs in nursing homes

Core element	Examples
Leadership commitment	Prioritize appropriate diagnosis and treatment of UTI. Communication priority to staff, clinicians, residents, families.
Accountability	Establish facility-specific policies and procedures for diagnosis and treatment of UTI including specific signs/symptoms, collection of specimens, catheter use, and communication.
Pharmacy expertise	Engage consultant pharmacist in selection of antibiotics, dose, duration, and potential drug-drug interactions. Develop facility-specific treatment guidelines and antibiogram.
Action	Implement SBAR tool for communication about suspected UTI. Establish orders for active monitoring in suspected UTI.
Tracking	Assess documentation for specific urinary signs/symptoms. Track DOT and rates of UTIs per 1000 resident days and/or catheter days.
Reporting	Report documentation of specific urinary signs/symptoms. Report DOT and rates of UTIs to prescribers, QAPI team, staff.
Education	Provide in-service on ASB. Utilize reporting data to target education.

Ashraf MS, et al. JAMDA 2020; 21:12e24.

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LEVEL 2 NGS REPORT

COMPREHENSIVE IDENTIFICATION NEXT-GEN DNA SEQUENCING RESULTS with PRIOR **PCR** RESULTS.

ANTIMICROBIALS FOR CONSIDERATION

COMPLETE (NGS & PCR RESULTS) BACTERIAL LOAD	DNA copies (N/A) Med	NGS %	Gram Stain	Respiration	Carbapenems e.g. Merrem (IV)	Aminoglycosides e.g. Amikacin (IV)	Anti-Pseudomonal penicillins/Beta-lactamase inhibitors e.g. Zosyn	Fluoroquinolones e.g. Levofloxacin (PO)	Glycopeptides e.g Vancomycin (IV)	Extended spectrum penicillins/Beta-lactamase inhibitors e.g. Augmentin (PO)	Clindamycin (PO)	Penicillins e.g. Penicillin (PO)	Ampicillin/Amoxicillin (PO)	Cephalosporins Fourth Gen e.g. Maxipime (IV)	Cephalosporins Third Gen e.g. Suprax (PO)	Fosfomycin (PO)	Linezolid (Zyvox) (PO)	Anti-Pseudomonal Penicillins e.g. Mezlin (IV)	Lipopeptides e.g. Cubicin (IV)
Pseudomonas aeruginosa	Low	22%	-	Ae	√	√	√	√											
Streptococcus agalactiae	Low	19%	+	FAn	√				√	√	√	√	√	√	√	√	√	√	
Corynebacterium striatum	NGS	17%	+	FAn					√										√
Finegoldia magna	NGS	11%	+	An					√	√	√	√	√						
Anaerococcus vaginalis	NGS	11%	+	An					√	√	√	√							
Proteus mirabilis	NGS	6%	-	FAn	√	√	√	√		√			√	√	√	√			
Peptoniphilus harei	NGS	5%	+	An	√				√		√	√						√	
Peptoniphilus coxii	NGS	2%	+	An	√				√	√	√	√						√	

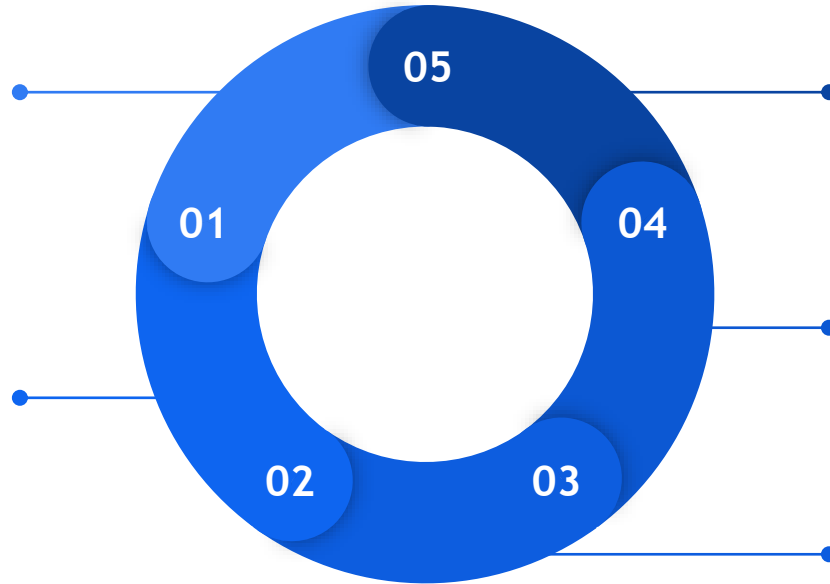# Five steps of urinary diagnostics interpretation

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Summary

- Evaluate each urinary diagnostic with five steps:
  - Right patient.
  - Right time.
  - Right test.
  - Right bug.
  - Right drug (if needed).
- Utilize Loeb criteria and local urinary symptoms to treat infection, do not treat colonization or asymptomatic bacteriuria.
- Evaluate quantitative results available in addition to qualitative, particularly for polymicrobial results.
- Incorporate diagnostic stewardship.
- Action, tracking, and reporting with individual audit and feedback.

Langford BJ, et al. Am J Infect Control 2019; 47:1409–1414.

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