Common Sense Evaluation for Infections in Hospitalized Patients

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- No intelligence, artificial or otherwise was used to create this talk

Objectives

- Describe how diagnostic testing influences antibiotic use
- Identify non-infectious syndromes which mimic infection
- Define evidence-based diagnostic testing strategies for common hospital infections

Case

- 50 yo female with history of DVT and recurrent pharyngitis over last 3 months treated with multiple courses of antibiotics
- Presented to ED with 36 hours of progressively worsening right neck and throat pain with swelling in neck and fever to 103.
- Tonsils enlarged, red, with exudate
- WBC 13.8, CRP 3.3, procalcitonin <0.05, POC strep testing negative
- CT Neck – diffuse edema and phlegmonous change right peritonsillar, parapharyngeal, and retropharyngeal space. No abscess or fluid. Reactive LAD.
- ENT evaluated and no surgical intervention
- Started on vancomycin and ampicillin-sulbactam
- ID consulted next day – some improvement in symptoms, fever down, changed vancomycin to linezolid, recommend throat culture

The Next Day

- Fever overnight to 39.1 and complaining of headache in AM
- Team very concerned and asking about escalating to pip-tazo
- Why is she “worse?!”
- What to do in this situation?
  - More imaging?
  - More cultures?
  - Change antibiotics?
  - More clinical data?

More Data

- Patient reports moderate headache but neck pain and swelling seems further improved (although not a huge amount)
- WBC 7.2
- BP normal, not tachycardic
- No neck stiffness on exam nor any signs of meningismus
- Elected to monitor, not obtain additional testing and next day substantially improved

Things to consider when patients are not improving or worsening

Is this the typical course of the disease

Have I achieved source control

- Abdominal infection – do we need to drain something
- Pneumonia – is there a parapneumonic effusion
- SSTI – did they develop an abscess
- UTI – is there a stone obstructing things
- Device-associated infection – did you remove the infected device

Impact of Timing of Source Control on Mortality in Sepsis and Septic Shock

Population	Definition of Early Source Control	Impact on Mortality
ICU patients with IAI (N=1077)	2-6 hours	Early source control: OR 0.50 (95% CI 0.34-0.73)
Community-acquired sepsis requiring source control (N=4962)	<6 hours	Early source control: aOR 0.71 (95%CI 0.63-0.80)
ICU patients with sepsis requiring surgical source control (N=1595)	NA	Septic shock patients aOR 1.01 (95%CI 1.01-1.07) per hour delay
Patients with septic shock in ED (N=524)	<6 hours	Delated source control aOR 1.42 (95%CI 0.72-2.8)

"For adults with sepsis or septic shock and a specific anatomical diagnosis or source of infection that requires source control, we "suggest" early source control over late source control, ideally within 6 hr of diagnosis of sepsis or septic shock requiring source control."

De Waele JJ. *J Intensive Med*. 2024;4:281-6.
Prescott HC, et al. *Crit Care Med*. 2026;54:725-812.

Things to consider when patients are not improving or worsening

Is this the typical course of the disease

Have I achieved source control

Am I giving the right drug at the right dose for the site of infection?

- Is this the right drug for this site
- Could there be resistance to this antibiotics?
- Am I giving an adequate dose to the patient

Average US BMI = 26 with 42% obese, 9% severe obesity (BMI 40+)

Cephalexin Recommended Adult Dosing

Usual dosage range: Oral: 250 mg to 1 **g** every 6 hours or 500 mg every 12 hours (maximum: 4 **g**/day).

https://www.cdc.gov/obesity/adult-obesity-facts/index.html

Things to consider when patients are not improving or worsening

- Is this the typical course of the disease
- Have I achieved source control
- Am I giving the right drug at the right dose for the site of infection?
- Do I have the right diagnosis?

Diagnostic Errors that Lead to Inappropriate Antimicrobial Use

Infect Control Hosp Epidemiol. 2015;36:949-56.

Gregory A. Filice, MD;[1,2] Dimitri M. Drekonja, MD;[1,2] Joseph R. Thurn, MD;[1,2] Galen M. Hamann, RN;[1] Bobbie T. Masoud, PharmD;[1] James R. Johnson, MD[1,2]

- Evaluated 500 inpatient antimicrobial courses
- Judged accuracy of initial provider diagnosis and appropriateness of antibiotics

Reasons that Antimicrobial Courses Were Not Appropriate According to Accuracy of Provider Initial Diagnosis

		Reason antimicrobial course not appropriate, No. (%, row)				
Accuracy of Provider Initial Diagnosis	Antimicrobial Course Appropriate	Incorrect Drug	Incorrect Dose	Incorrect Duration	Other	Antimicrobial Not Indicated
Correct (n = 291)	181 (62)	81 (28)	5 (2)	43 (15)	1 (0)	10 (3)
Correct, but sign or symptom rather than a syndrome or disease (n = 31)	2 (7)	6 (19)	1 (3)	1 (3)	1 (3)	25 (81)
Incorrect (n = 156)	6 (4)	21 (14)	1 (1)	5 (3)	0 (0)	131 (84)
Indeterminate (n = 22)	2 (9)	4 (18)	0 (0)	7 (32)	0 (0)	11 (50)

NOTE. Percentages sum to >100% because some courses involved multiple errors.

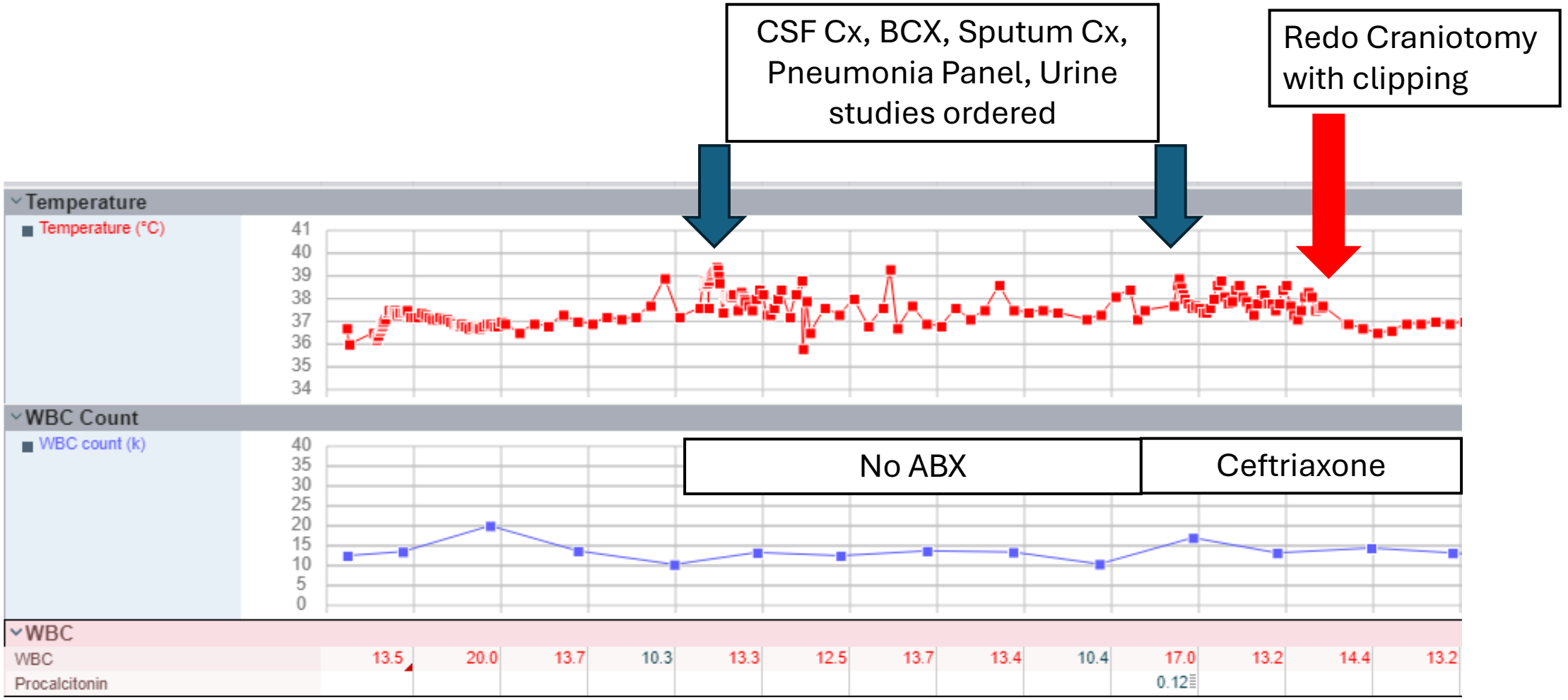
If you have the wrong diagnosis, it his highly likely you will treat inappropriately

Case

- A 57 yo female is transferred to the ICU from her small-town hospital after developing severe headache and confusion
- Imaging shows a SAH and she is intubated and has an EVD placed
- Developed fever 72 hours after admission

- What evaluation for infection is appropriate?
- Is this from her CNS event?

Case


CSF Cx, BCX, Sputum Cx, Pneumonia Panel, Urine studies ordered
Redo Craniotomy with clipping
Temperature
Temperature (°C)
41
40
39
38
37
36
35
34
WBC Count
WBC count (k)
40
35
30
25
20
15
10
5
0
No ABX
Ceftriaxone
WBC
WBC 13.5 20.0 13.7 10.3 13.3 12.5 13.7 13.4 10.4 17.0 13.2 14.4 13.2
Procalcitonin 0.12

AMERICAN THORACIC SOCIETY DOCUMENTS

Antibiotic Stewardship in the Intensive Care Unit

An Official American Thoracic Society Workshop Report in Collaboration with the AACN, CHEST, CDC, and SCCM

Ann Am Thorac Soc Vol 17, No 5, pp 531–540, May 2020

Richard G. Wunderink, Arjun Srinivasan, Philip S. Barie, Jean Chastre, Charles S. Dela Cruz, Ivor S. Douglas,

Up to 70% of patients in the ICU receive antibiotics with 30-60% of those antibiotics being considered inappropriate or unneeded

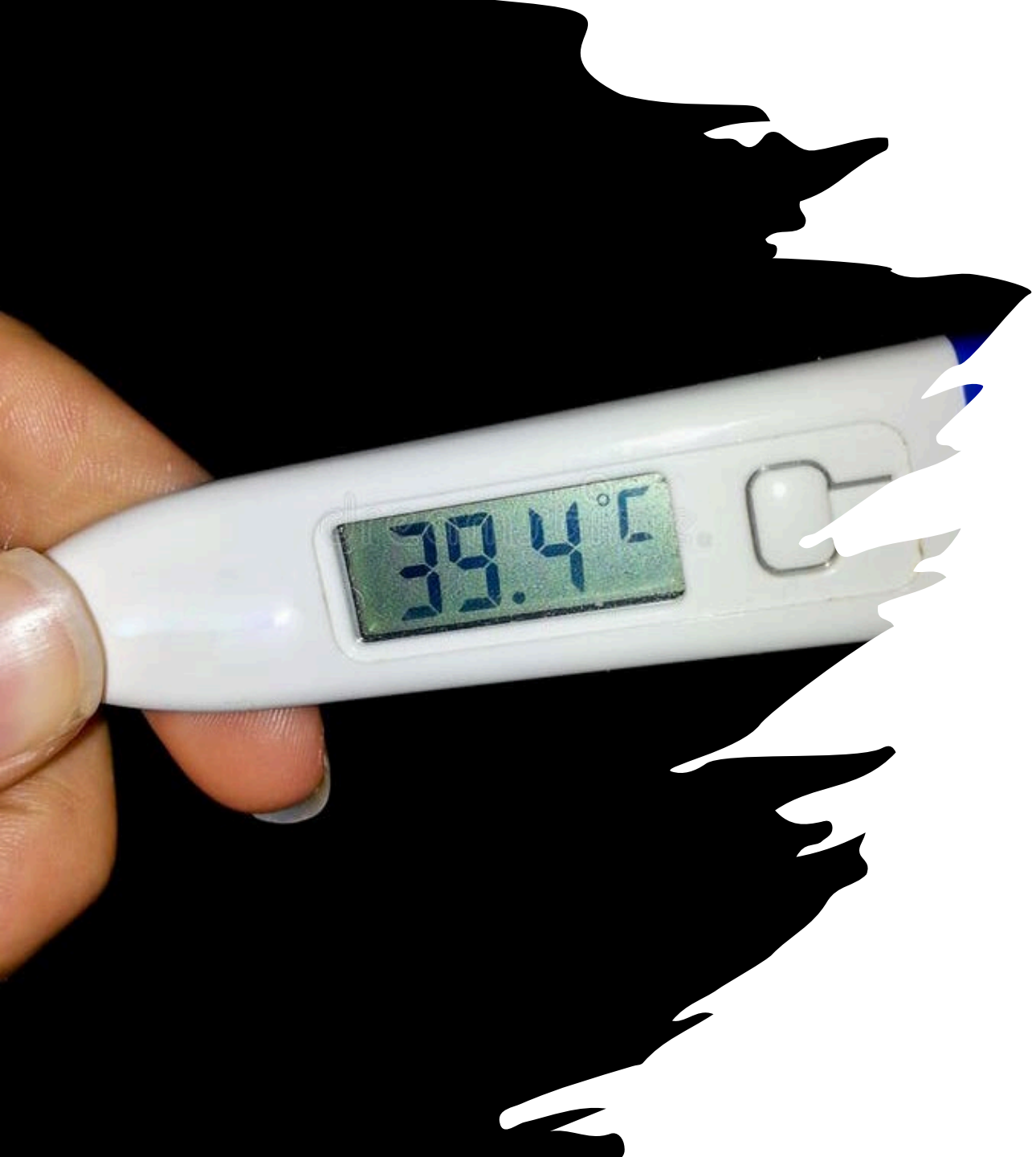
- **Critical care practitioners are important causes and potential solutions** to the crisis of antibiotic resistance.
- Antibiotic stewardship should be a core competency of critical care practitioners.
- **Antibiotic stewardship must address the fear of inadequate empirical treatment to be effective**.
- The adverse effect of excessive antibiotic treatment on individual patients needs greater emphasis.
- A shift in emphasis to an individualized approach to antibiotic therapy is needed.

Cognitive Errors Lead to Antibiotic Misuse

- We think everything is infection

Causes of Fever in the Hospital

Infectious Causes of Fever	Non-Infectious Causes of Fever
• Meningitis • Sinusitis • CVC or PIV related bloodstream infection • Endocarditis • Pneumonia • Empyema • Cholecystitis or other intra-abdominal infection • *C. difficile* infection • UTI – Catheter-associated or pyelonephritis • Cellulitis • Wound infection (surgical, sacral) • Septic arthritis • Respiratory virus infection	• Intracranial bleeding (SAH, IVH) • CNS tumor or stroke • Aspiration or ARDS • Blood product transfusion • Drug fever • Malignant hyperthermia/neuroleptic malignant syndrome/Serotonin syndrome • Withdrawal – alcohol, opioids, etc. • Seizure • Pancreatitis • Ischemic colitis • Venous thromboembolism/PE • Pulmonary infarction/contusion • Endocrine (thyrotoxicosis, adrenal insufficiency) • Gout • Tumor lysis • Transplant rejection • Inflammatory conditions (vasculitis, etc.)



Evaluating Fever or Change in Status

The first step is a through patient assessment including an exam

- Evaluate for symptoms/signs of infection as well as other causes
- Examine all IV catheter sites
- Look at trends → temperature, oxygenation, WBC, procalcitonin
- Look at recent events → procedures, blood products

Original Investigation

Indicators of Central Fever in the Neurologic Intensive Care Unit

JAMA Neurology. 2013;70:1499-1504.

Sara E. Hocker, MD; Lin Tian; Guangxi Li; James M. Steckelberg, MD; Jay N. Mandrekar, PhD; Alejandro A. Rabinstein, MD

- Neurologic ICU patients with T>38.3 for 2 days (N=526)
  - 47% were determined to be central
- Predictors of central fever
  - SAH, IVH, tumor present (strongest predictor)
  - Persistent (>6 hours for 2+ days), occurred within 72 hours of admission
  - Blood transfusion
  - No infiltrate on CXR
- Longer time fever free before developing a fever and longer duration mechanical ventilation predicted against central fever

Cognitive Errors Lead to Antibiotic Misuse

- We think everything is infection
- We assume antibiotics are the “safe” option
  - “It looks like heart failure, but I will antibiotics to cover my bases”

Antibiotics Aren't the "Safer" Option

- Patients admitted with clear decompensated heart failure (N=144)
- Compared those treated with IV Abx (N=56) and not treated (N=88)

Variable	No Antibiotics	Antibiotics	P
Mean Length of Stay	3.0 days	6.6 days	<.001
Readmission Rate	10.1%	22.2%	.043
Furosemide Given	320 mg	930 mg	<.001

- Antibiotic arm received additional 1381 mg/d of sodium

Frisbee J, et al. *Open Forum Infect Dis*. 2019;6(6):ofz220.

Sodium Content of Various Antibiotic Preparations

Antibiotic (usual dose)	Sodium per Dose in 50 mL NS (mg)	Daily Sodium Load (mg/day)
Penicillin G potassium 4 MU	213	2,340
Ampicillin 2 g*	~486	2,910
Ampicillin-sulbactam 3 g*	~584	2,340
Oxacillin 2 g	376	3,320
Piperacillin-tazobactam 3.375 g	392	2,280
Cefazolin 1 g	225	1,200
Ceftriaxone 2 g	411	1,180
Cefepime 2 g	212	1,170
Ertapenem 1 g	349	530
Meropenem 1 g	267	1,330
Ceftaroline 600 mg	247	1,270
Daptomycin 500 mg	212	390
Levofloxacin	280	280

Wang N, et al. *Open Forum Infect Dis*. 2019;6(12)ofz508.

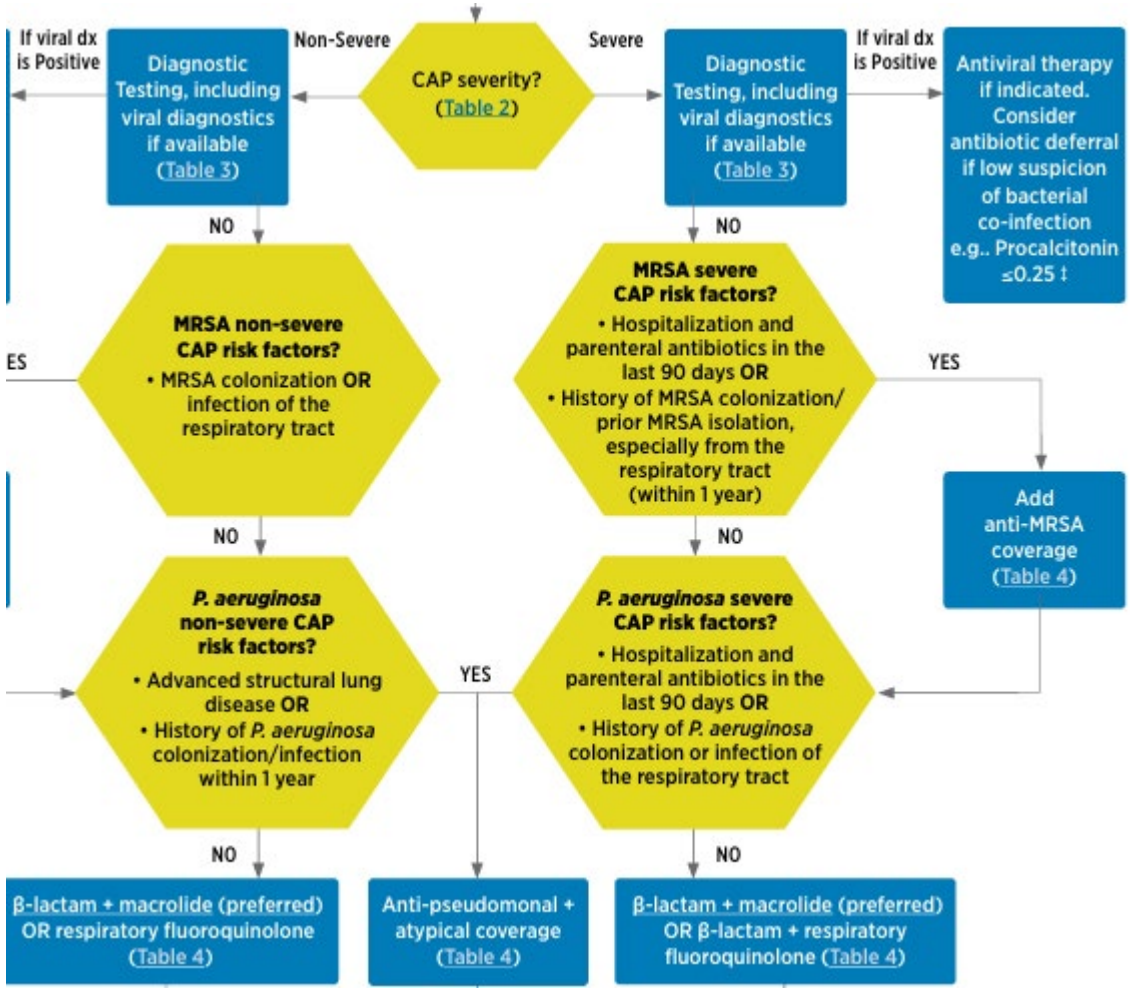
Cognitive Errors Lead to Antibiotic Misuse

- We think everything is infection
- We think antibiotics are the “safe” option
  - “It looks like heart failure, but I will antibiotics to cover my bases”
- We think broader spectrum antibiotics are better
  - “This patient with community-acquired pneumonia is really sick. I better start vancomycin/linezolid and cefepime/meropenem/piperacillin-tazobactam.”

Broader Isn't Recommended

IDSA/ATS CAP Guidelines:

"We recommend clinicians only cover empirically for MRSA or *P. aeruginosa* in adults with CAP if locally validated risk factors for either pathogen are present (strong recommendation, moderate quality of evidence)."



Metlay JP, et al. Am J Resp Crit Care Med. 2019;200:e45-67.
https://www.idsociety.org/globalassets/idsa/practice-guidelines/community-acquired-pneumonia-in-adults/cap-clinical-pathway-final-online.pdf

Broader Isn't Better

JAMA Internal Medicine | Original Investigation

Empirical Anti-MRSA vs Standard Antibiotic Therapy and Risk of 30-Day Mortality in Patients Hospitalized for Pneumonia

Barbara Ellen Jones, MD, MSc; Jian Ying, PhD; Vanessa Stevens, PhD; Candace Haroldsen, MPH; Tao He, MS; McKenna Nevers, MPH; Matthew A. Christensen, MD; Richard E. Nelson, PhD; Gregory J. Stoddard, MS; Brian C. Sauer, PhD; Peter M. Yarbrough, MD; Makoto M. Jones, MD, MSc; Matthew Bidwell Goetz, MD; Tom Greene, PhD; Matthew H. Samore, MD

2020;180:552-60.

- Retrospective cohort >88,000 patients hospitalized VA with pneumonia
- Compared those who received anti-MRSA therapy (38%) with standard therapy to standard therapy alone
  - Used propensity adjustment

Table 2. Adjusted Risk Ratios for 30-Day Mortality Among Primary and Subgroup Inverse Probability–Weighted Analyses

Group	Adjusted Risk Ratio (95% CI)	
	Anti-MRSA Therapy Plus Standard Antibiotics	Anti-MRSA Therapy Without Standard Antibiotics
All patients	1.4 (1.3-1.5)	1.5 (1.4-1.6)
Patients admitted to ICU	1.3 (1.2-1.5)	1.4 (1.2-1.5)
High clinical risk for MRSA	1.2 (1.1-1.4)	1.3 (1.1-1.4)
MRSA surveillance PCR positive	1.6 (1.3-1.9)	1.8 (1.4-2.3)
MRSA culture positive	1.1 (0.8-1.4)	1.2 (0.9-1.6)

Also increased risk of kidney injury, CDI, VRE, and secondary GNR infection

Estimating Daily Antibiotic Harms

Umbrella Review and Meta-Analysis

Public Health Ontario | Santé publique Ontario

35 Systematic Reviews

71 Short vs. Long Antibiotic Duration Trials

92% studies evaluated respiratory tract and urinary tract infections

23,174 patients evaluated

Adverse Events	N=20,345	4%↑ odds ratio/day
Antibiotic Resistance	N=2,330	3%↑* odds ratio/day
Super-infections	N=5,776	2%↓* odds ratio/day

Each Additional Day Can Cause Harm

5 vs 3 Days → **9%↑ odds ratio** Of adverse events

7 vs 3 Days → **19%↑ odds ratio** Of adverse events

* Non-statistically significant difference

Source: Curran J et al. Estimating daily antibiotic harms: An Umbrella Review with Individual Study Meta-analysis Clin Micro Infect. 2021

Ontario Agency for Health Protection and Promotion | Agence de protection et de promotion de la santé

Why Talk About Testing?

If we want to improve antibiotic use, we must focus on the drivers of inappropriate treatment

Testing drives treatment

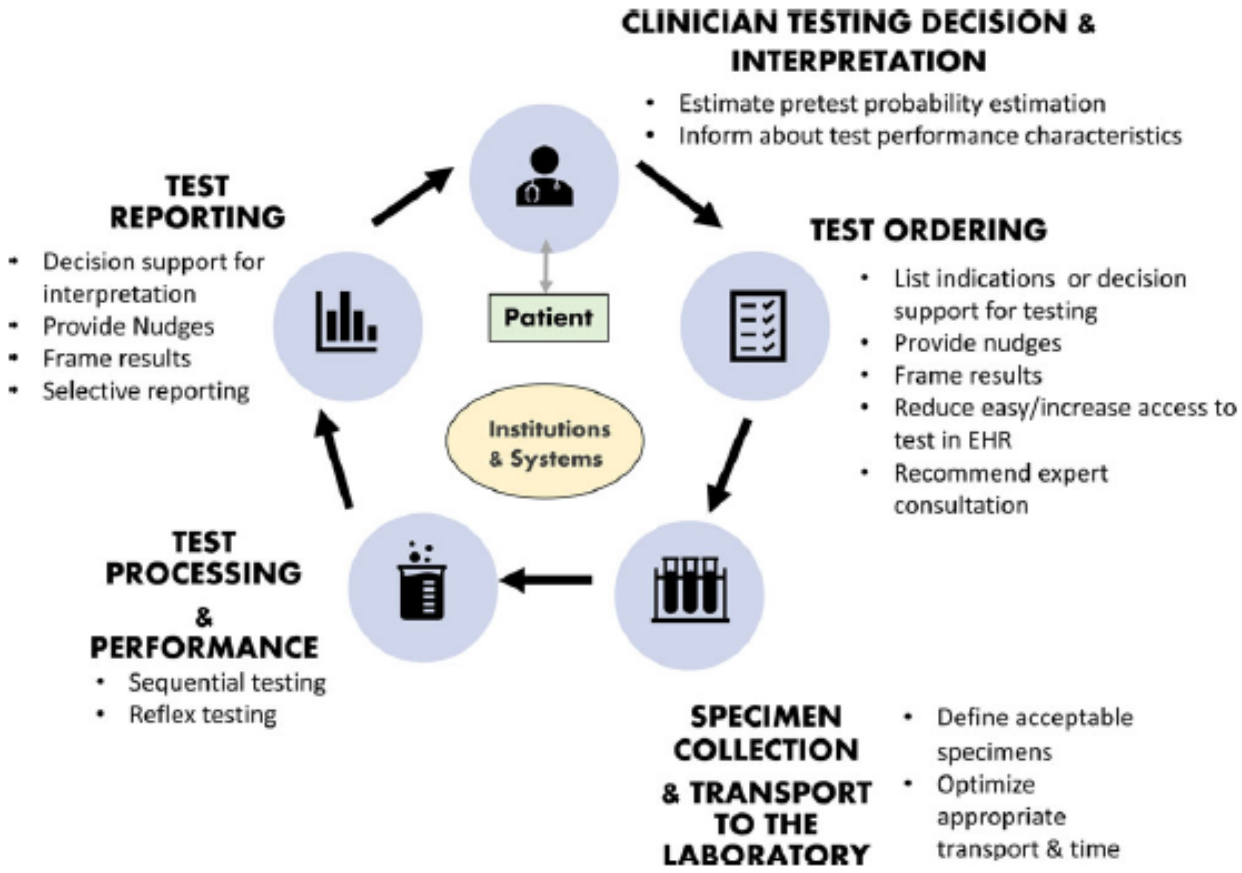
Positive tests result lead to

- Treatment initiation
- Treatment adjustment
- Additional interventions

Diagnostic Stewardship

Modifying the ordering, performing, or reporting of diagnostic tests to improve the diagnosis of and treatment of infections and other conditions.

- Improve patient care and outcomes
- Avoid patient harm
- Optimize antimicrobial use
- Improve efficiency of care
- Improve institutional costs and metrics



Fabre V, et al. *Infect Control Hosp Epidemiol*. 2023;44:178-85.

Case

- You are called to an RRT where a 68 yo patient admitted for diabetic foot infection developed new onset atrial fibrillation with hypotension
  - The primary surgical team was not responding to nursing pages and so RRT was called
  - Temp 37.7, P 140-155, RR 22, BP 80s/50s
- Patient has been on ceftriaxone and metronidazole for 36 hours
  - Large wound with drainage but no increasing erythema
  - WBC this morning was 15
- The phlebotomists asks if you want blood cultures with the other labs they are drawing???

Blood Culture Stewardship

Why is BCX Stewardship Important

- BCX are overused
  - Most blood cultures are negative and
  - Obtained when likelihood of contamination (2-3%) is equivalent to bacteremia
- Contaminated BCX results represent 20-40% of all positive results
- False positive BCX are harmful
  - Unnecessary antibiotic use (+ 1.5 days antibiotic)
  - Increased hospital LOS (+1-3 days)
  - Further testing (+0.6 BCX) and cost (+$3-6,000)
  - Unnecessary CVC/device removal, consultations
  - Cancelled surgical procedures
  - Iatrogenic anemia/blood transfusion
  - Diagnostic delay via anchoring bias
  - NHSN-defined CLABSI

Fabre V et al. Blood Culture Utilization in the Hospital Setting: a Call for Diagnostic Stewardship. *J Clin Microbiol*. 2022
Doern GV et al. Practical Guidance for Clinical Microbiology Laboratories: A Comprehensive Update on the Problem of Blood Culture Contamination and a Discussion of Methods for Addressing the Problem. *Clin Microbiol Rev*. 2019.

Common Inappropriate Blood Culture Reasons

- Clinicians order them when bad things happen that make you sick
  - GI bleed, Cardiac event, Seizure
- To evaluate isolated findings without other signs of infection
  - Hypotension, leukocytosis, or fever
- Obtained when BCX have recently been sent

Blood cultures are for evaluating life threatening infections

If a patient is sick enough to consider BCX they should be evaluated clinically

Order BCX based on clinical assessment and likelihood of infection

Do NOT	Consider	Follow	Use
Reflexively order based on change in status	Is bacteremia likely and will its detection change management? When were BCX last obtained?	BCX guidance Obtain 2 BCX Avoid line BCX except when infection concern Obtain before antibiotics	Site specific cultures which have higher yield • UTI = urine culture • Pneumonia = respiratory culture • IAI and SSTI = abscess drainage

INDICATIONS FOR INITIAL BLOOD CULTURES (BCx) in ADULTS*

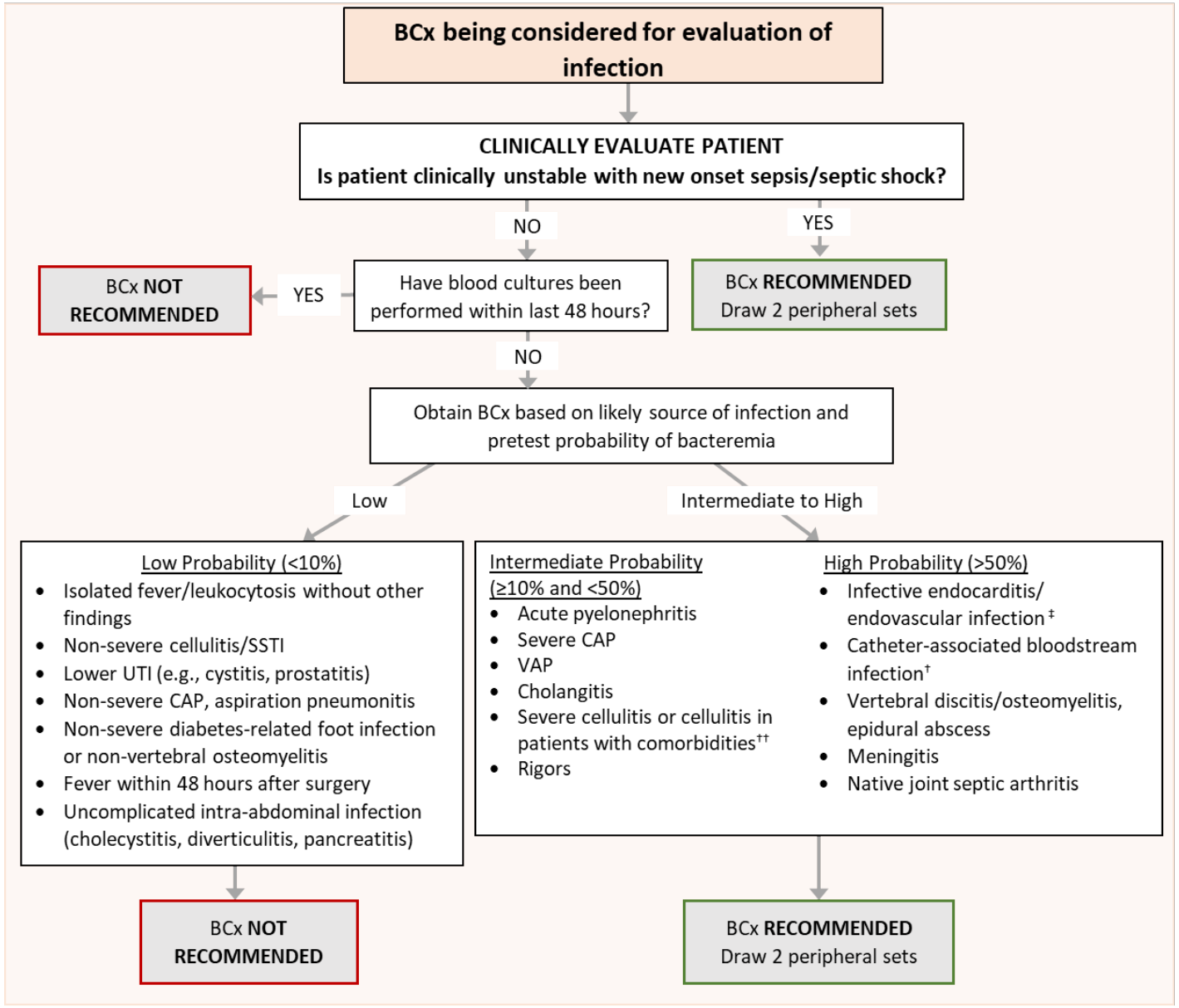


Table 1: Indications for INITIAL Blood Cultures (BCx) in Adult Patients*

Step 1: Evaluate patient clinically, assess hemodynamic stability, and identify possible sources of infection

Step 2: If unstable (sepsis/septic shock), obtain BCx and strongly consider empiric antibiotics.

Step 3: If stable, evaluate for potential source of infection and determine if BCx and/or empiric antibiotics are indicated

BCx NOT Indicated	BCx Indicated

• Syndromes with low risk of bacteremia (<10%):
  ○ Non-severe cellulitis/skin and soft tissue infection (SSTI)
  ○ Lower urinary tract infection (e.g., cystitis, prostatitis)
  ○ Non-severe community-acquired pneumonia (CAP)
  ○ Non-severe diabetes-related foot infection
  ○ Colitis (including *C. difficile*)
  ○ Aspiration pneumonitis
  ○ Uncomplicated cholecystitis, diverticulitis, or pancreatitis
• Fever or leukocytosis explained by a non-infectious cause (e.g., drug withdrawal, trauma, pulmonary embolism, etc.)
• Isolated fever and/or leukocytosis without other findings
• Post-operative fever within 48 hours
• Persistent fever or leukocytosis in patient with negative BCx in past 48-72 hours without new localizing signs of infection
  ○ Other cultures or imaging more appropriate than blood cultures
  ○ Consider expert consultation
• All forms of surveillance blood cultures in patients without suspicion of bacteremia (e.g., from central line prior to TPN initiation, prior to central line placement)
	• Sepsis/septic shock
	• Systemic signs of infection AND asplenia
	• Syndromes with high risk of bacteremia (≥50%):
	  ○ Infective endocarditis/endovascular infection (septic thrombophlebitis, infected cardiac/vascular devices)
	  ○ Catheter-related bloodstream infection
	  ○ Vertebral discitis/osteomyelitis
	  ○ Epidural abscess
	  ○ Native joint septic arthritis
	  ○ Meningitis
	• Syndromes with intermediate risk of bacteremia (>10% - <50%)
	  ○ Cholangitis
	  ○ Pyelonephritis
	  ○ Severe pneumonia (CAP and VAP)
	  ○ Severe cellulitis/SSTI or with severe comorbidities (necrotizing soft tissue infection, severe immunocompromise, end-stage renal or liver disease)

Peripheral BCx are preferred over central lines blood cultures due to improved specificity.
Always draw 2 peripheral sets (i.e., 4 bottles with 8-10cc/bottle).
***Excludes severely immunosuppressed patients (neutropenia, hematopoietic stem cell or solid organ transplant)**

INDICATIONS FOR FOLLOW UP BLOOD CULTURES (BCx) IN ADULTS*

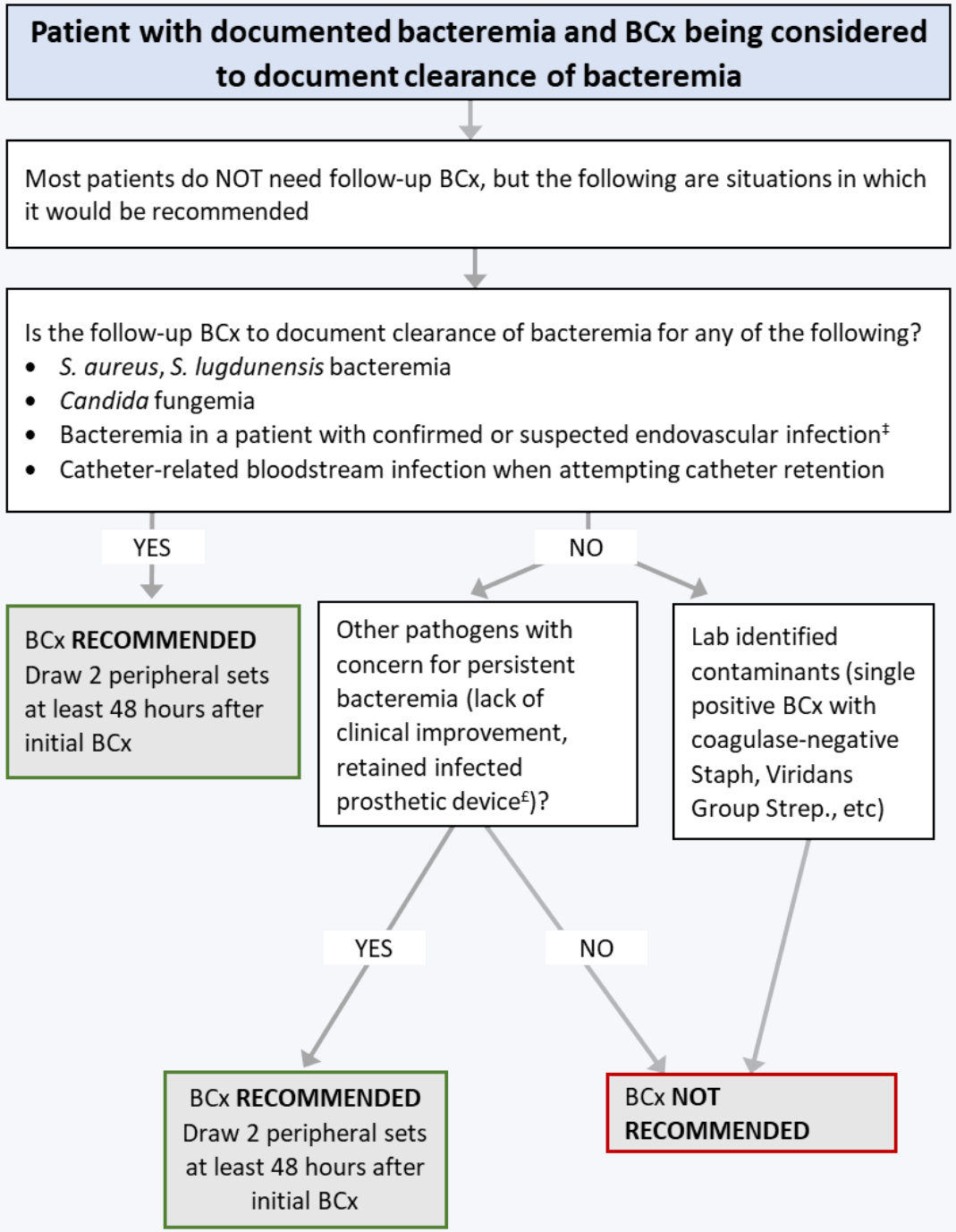


Table 2: Indications for FOLLOW-UP Blood Cultures (BCx) in Adult Patients* with Positive BCx

BCx Not Indicated	Follow-Up BCx Indicated
• Single positive blood culture with skin flora (i.e., coagulase-negative Staphylococci, *Cutibacterium acnes*, *Micrococcus*, viridans group Streptococci, *Corynebacterium* spp, *Aerococcus* spp, *Bacillus* spp) • Examples of syndromes which do not need FU BCx if clinically improving: ○ *Enterococcus* bacteremia from urinary or biliary source ○ *S. pneumoniae* bacteremia from pulmonary source ○ Gram-negative bacteremia from urinary/abdominal source ○ Cases likely to represent contamination (e.g., single BCX with coagulase-negative staphylococci • ***Note:*** *Strep* other than *S. pneumoniae* or beta-hemolytic streptococci (i.e., *S. pyogenes*) are potential infective endocarditis pathogens. Assess patient risk factors for endovascular infection and clinical presentation to determine significance of *Streptococci* in blood and need for repeat BCx (see below).	• All bacteremia/fungemia cases due to: ○ *S. aureus* ○ *S. lugdunensis* ○ *Candida spp.* • All cases with suspected endovascular infection ○ Infective endocarditis ○ Septic thrombophlebitis ○ Implantable cardioverter defibrillator (ICD)/pacemaker lead infections ○ LVAD line infections ○ Vascular graft infections • Select cases in patients at risk of endovascular infection, particularly with gram positive bacteremia ○ ICD/pacemaker ○ Vascular graft ○ Prosthetic valves ○ History of infective endocarditis ○ Valvulopathy in heart transplant recipient • Infected prosthetic device that is retained (catheter or other prosthetic) • Concern for persistent bacteremia due to lack of clinical improvement after 48 hours of effective therapy **Draw 2 peripheral sets at least 48 hours after initial BCx.** **Single sets are not adequate to detect bacteremia.**

Peripheral BCx are preferred over central lines blood cultures due to lower false positive results.
Always draw 2 peripheral sets (i.e., 4 bottles with 8-10cc/bottle).
***Excludes severely immunosuppressed patients (neutropenia, hematopoietic stem cell or solid organ transplant)**

JAMA Pediatrics | Original Investigation

Association of Diagnostic Stewardship for Blood Cultures in Critically Ill Children With Culture Rates, Antibiotic Use, and Patient Outcomes

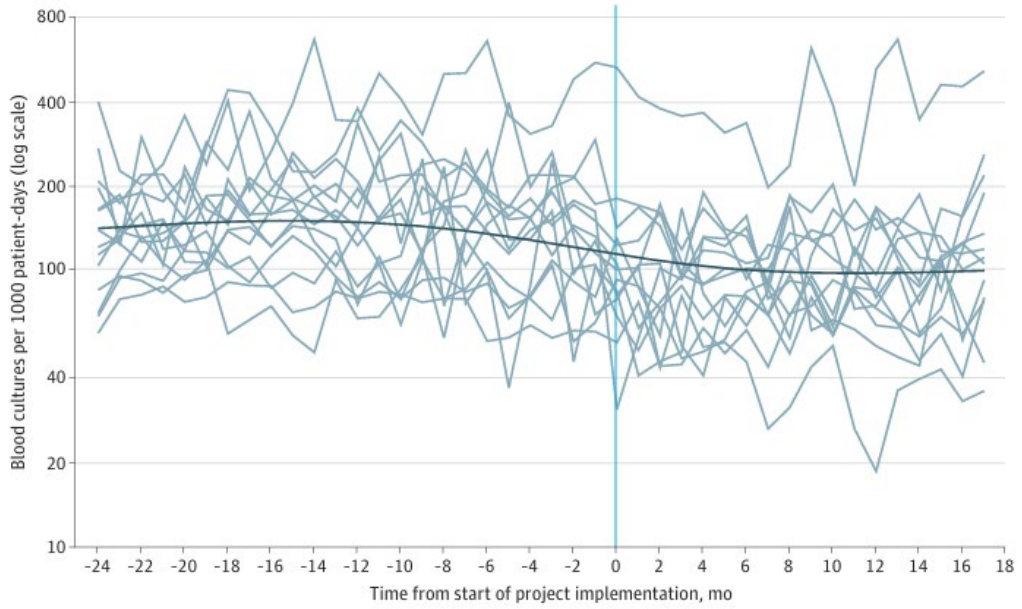
Results of the Bright STAR Collaborative

2022;176:690-98.

Charlotte Z. Woods-Hill, MD, MSHP; Elizabeth A. Colantuoni, PhD; Danielle W. Koontz, MA, MS; Annie Voskertchian, MPH; Anping Xie, PhD; Cary Thurm, PhD; Marlene R. Miller, MD, MSc; James C. Fackler, MD; Aaron M. Milstone, MD, MHS; and the Bright STAR Authorship Group

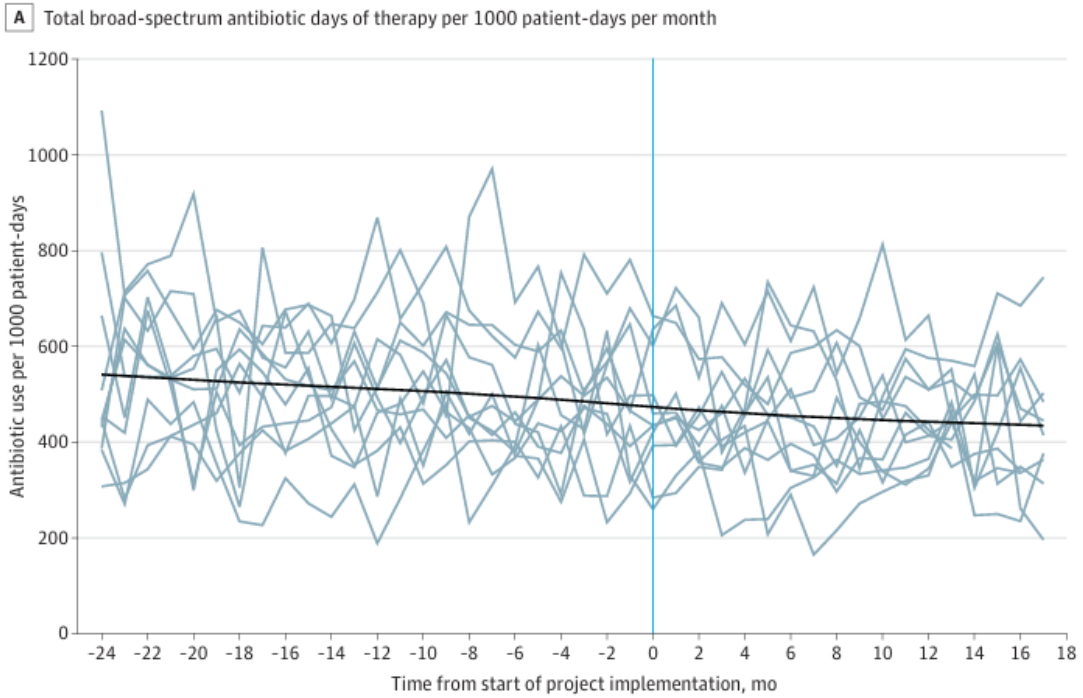
- Prospective QI collaborative 14 PICUs
- Local QI work to improve BCX use
- Median monthly BCX per 1000 PD decreased from 146 to 99 (-33%)

Figure 2. Monthly Blood Cultures per 1000 Patient-Days for Each of the 14 Bright STAR (Testing Stewardship for Antibiotic Reduction) Sites



- Antibiotic use decreased 13%
- Broad-spectrum antibiotic starts decreased 8%
- CLABSI decreased 36%
- No change mortality, LOS, readmissions
- Reviewed 792 bacteremias and one may have had a slight delay in detection

Figure 3. Antibiotic Use for Each of the 11 Bright STAR (Testing Stewardship for Antibiotic Reduction) Sites That Participate in the Children's Hospital Association Pediatric Health Information System



Case

- A 54 yo with paraplegia is admitted for decubitus ulcer and possible UTI. They are treated with ceftriaxone, wound debridement and remain in the hospital for wound care.
- Hospital day 7 they have an episode of witnessed aspiration and become hypoxic, tachycardic, tachypneic
  - CXR shows new bilateral lower lobe infiltrates – atelectasis vs developing consolidation

Should you start antibiotics?
Should you obtain a sputum culture or other pneumonia microbiologic diagnostic testing?

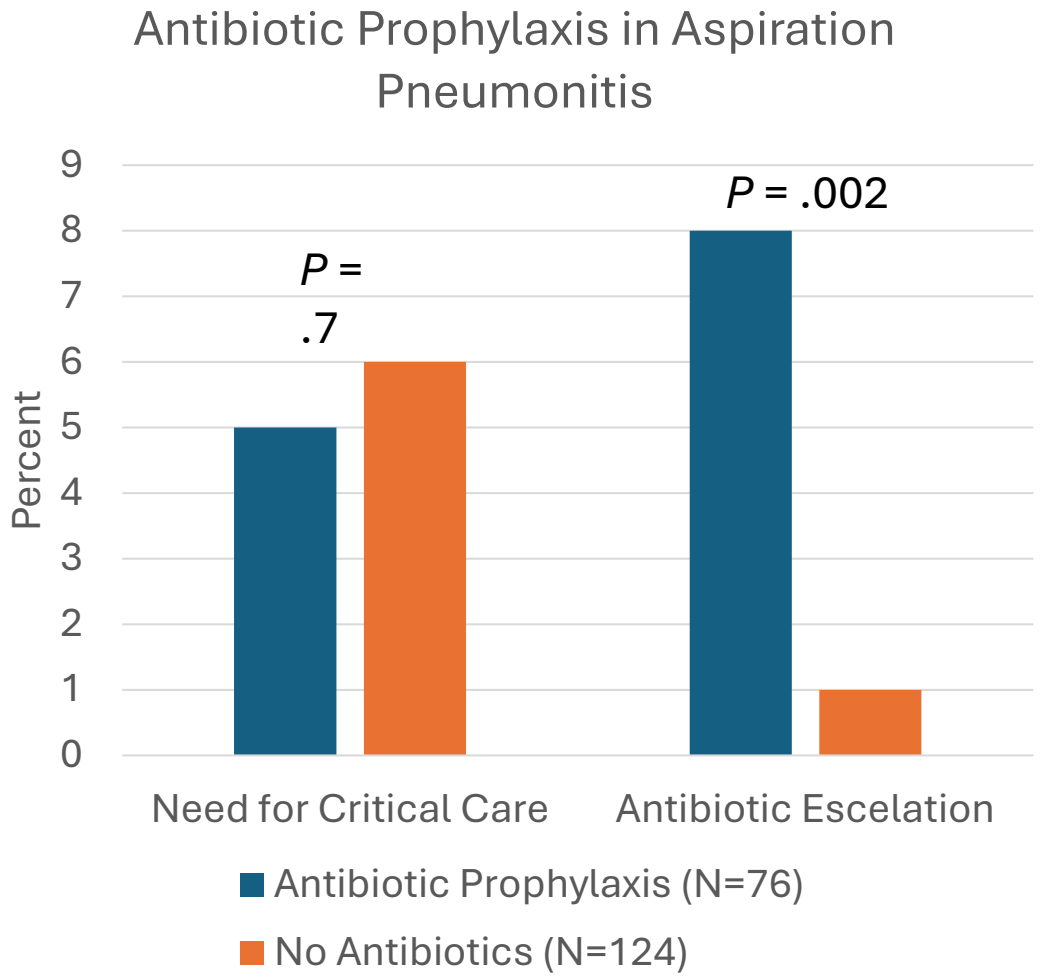
Case

- You started Zosyn
- Sputum culture growing *E. coli* and MRSA two days later
- Patient off 02 within 24 hours of event, CXR shows improved infiltrates, no other findings of infection

Should you have started antibiotics?
Should you continue antibiotics?

Antibiotics in Aspiration

- NO clinical benefit on mortality, need for ICU care
  - Increase subsequent antibiotic use
- No need to add “anaerobic coverage”
  - Only increases CDI risk
- If started and oxygenation rapidly improves → it isn’t pneumonia
  - STOP the antibiotics



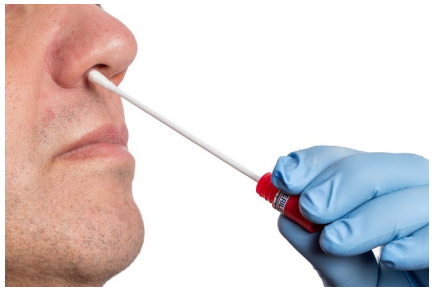
Bai AD, et al. *Chest*. 2024;166;:39-48.
Dragan V, et al. *Clin Infect Dis*. 2018;67:513-8.

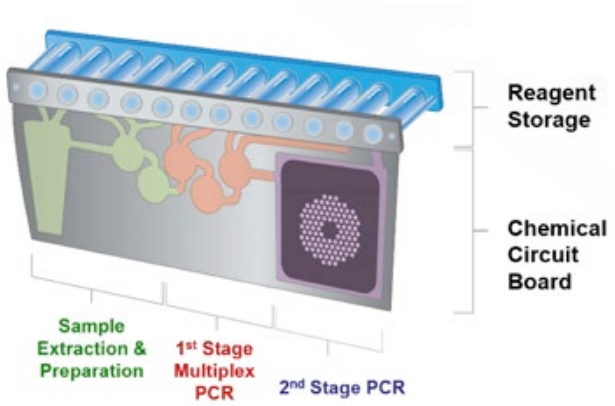
Case

- Same patient but you didn't start antibiotics. Patient improved within 24 hours and off O2 with improved but not normal CXR.
- 3 days later patient reports increased cough and sputum and requiring 2L of oxygen
- Temp 38.4, P 110s, RR 20-24, BP 118/78
- WBC is 19 with mild left shift, PCT 3.74
- CXR – resolution left sided infiltrate but RLL infiltrate is increased

Should you start antibiotics?
Should you obtain a sputum culture or other pneumonia microbiologic diagnostic testing?

What Microbial Diagnostics Are Available?





What is the Role of Microbiologic Testing in Pneumonia Diagnosis?

Microbiologic tests do not diagnose pneumonia!!

- Pneumonia diagnosed based on clinical and imaging findings
- Microbiologic tests define the etiology

What is the Role of Microbiologic Testing in Pneumonia Diagnosis?

Only order testing when patients have clinical evidence of pneumonia!!

- Positive microbiologic testing is common in ventilated patients
  - >70% chronic tracheostomy
  - >40% endotracheal tube, increases the longer on ventilator
- More cultures associated with more antibiotics given
- Do not treat positive respiratory tract cultures (or pneumonia panels) in patients without clinical evidence of pneumonia
- Stop antibiotics in patients where another diagnosis is more likely than pneumonia

Morrison JM, et al. Pediatr Pulmonol. 2025;59:2761-71.
Jeng M, et al. Crit Care Explor. 1012;5:e1008.
Prinzi A, et al. JAMA Netw Open 212;4:e2140378.

Why do testing for the etiology of pneumonia?

CAP/HAP/VAP guidelines recommend antibiotics in all patients

De-escalation of therapy is poorly implemented

Only 13% on broad spectrum antibiotics for pneumonia had them stopped by hospital at day 4

Positive microbiologic results are associated with increased de-escalation (improved outcomes too!)

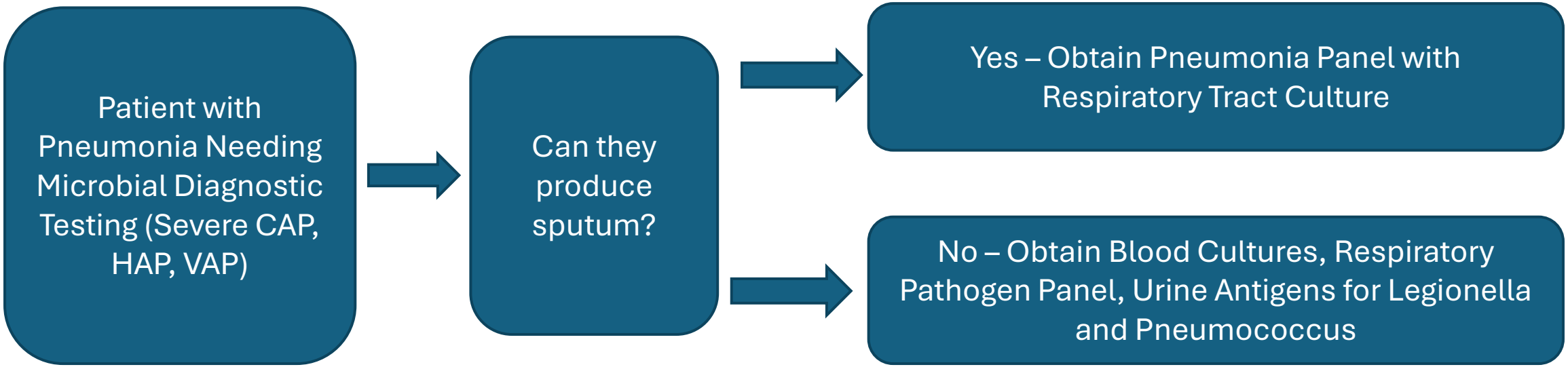
Stewardship feedback is associated with de-escalation

Magill SS, et al. *JAMA Network Open*. 2021;4:e212007
Deshpande A, et al. *Clin Infect Dis*. 2021;72:1314-22.
Abelenda-Alonso G, et al. *Clin Micro Infect*. 2022;28:1602.
Schweitzer VA, et al. *Lancet Infect Dis*. 2022;22:274-83.

When to Use a Respiratory Tract Diagnostic Testing in Pneumonia

<u>Where pathogen identification is most likely to provide benefit:</u>

- Very sick → Patients with severe CAP (admitted to ICU, respiratory failure, etc.)
- Using broad spectrum therapy →
  - CAP patients on expanded-spectrum therapy (vancomycin, cefepime, etc.)
  - Patients with hospital-acquired or ventilator-associated pneumonia
- Not getting better → Patients not responding to typical therapy



Metlay JP, et al. *Am J Respir Crit Care Med* 2019;200:e45-e67.

Kalil AC, et al. *Clin Infect Dis*. 2016;63:e61-111.

How to Improve Respiratory Tract Testing

Guidance

- When to use
  - HAP/VAP, severe CAP, etc.
- In whom to use →
- What to obtain and how
  - Limited vs extended viral testing
  - Pneumonia panel
  - Urine antigens
  - Blood cultures
  - Sputum vs. tracheal aspirate vs. BAL

BrighT STAR Guidelines on Obtaining Endotracheal Aspirate Cultures

Clinical Signs Considered for Evaluation of Bacterial Lower Respiratory Tract Infections

Systemic signs of infection
- Temperature instability (fever, hypothermia)
- Elevation in inflammatory markers (e.g., C-reactive protein or procalcitonin)
- Abnormal WBC count: leukocytosis or leukopenia
- Hemodynamic instability

Reliable signs of bacterial lower respiratory tract infection
- New increased work of breathing (e.g., increased accessory muscle use)
- New focal signs on auscultation (e.g., decreased breath sounds, crackles/rales)
- Persistent[a], increased[b] endotracheal secretion volume
- Sustained worsening of gas exchange[c] with increase in ventilator settings or oxygen requirement[d]
  - "Sustained" worsening in gas exchange > 6 hr duration
  - "Increase" in oxygen requirement is an increase of > 10% absolute increase in F_{IO_2} and/or an increase in positive end-expiratory pressure
- New chest imaging findings consistent with pneumonia (e.g., opacities concerning infiltrates, consolidations, cavities, and air bronchograms)

6	Consider obtaining an EAC if the patient has at least one new reliable sign of a bacterial lower respiratory tract infection and at least one systemic sign of an infection (parent statement)	**94** (36/38)
6.1	Consider obtaining an EAC if the patient has a sustained worsening gas exchange with increase in ventilator settings or oxygen requirement and at least one systemic sign of an infection	**97** (37/38)

Sick-Samuels A, et al. *Pediat Crit Care Med*. 2025;26:e569-82.

Hospital-Acquired Pneumonia (HAP) is not present on admission and arises more than 48 hours after admission.

Ventilator-Acquired Pneumonia (VAP) arises more than 48 hours after endotracheal intubation.

HAP/VAP management guideline and HAP/VAP infographicare available for reference

☑ HAP/VAP

Microbial diagnostic testing does not diagnose pneumonia; but defines etiology. Use only when clinical evidence of pneumonia is present.

Blood cultures	Pneumonia Panel	Respiratory Tract Culture	Respiratory Pathogen Panel (RPP)	Urine Antigens
If not performed in last 24 hours	All patients (couple with respiratory tract culture)	All patients	Only if unable to obtain pneumonia panel	Only if unable to obtain pneumonia panel

☑ Diagnostic Tests

☐ Blood Cultures: 2 Sets - Peripheral Draw NO Suspected line infection

☑ Pneumonia panel + sputum culture

Pneumonia panel restricted to ICU patients and ID/Pulmonary use

- If outside the ICU, order sputum culture alone
- Pneumonia panel should not be repeated on sputum within 3 days or on BAL within 7 days
- Pneumonia panel does not detect SARS-CoV-2 causing COVID19

- Pneumonia Panel Testing Guidance

☑ Pneumonia panel
Once, today at 1114, For 1 occurrence
Source: Sputum
Pt. Portal result release timeframe: Auto Release Standard

Sputum Culture

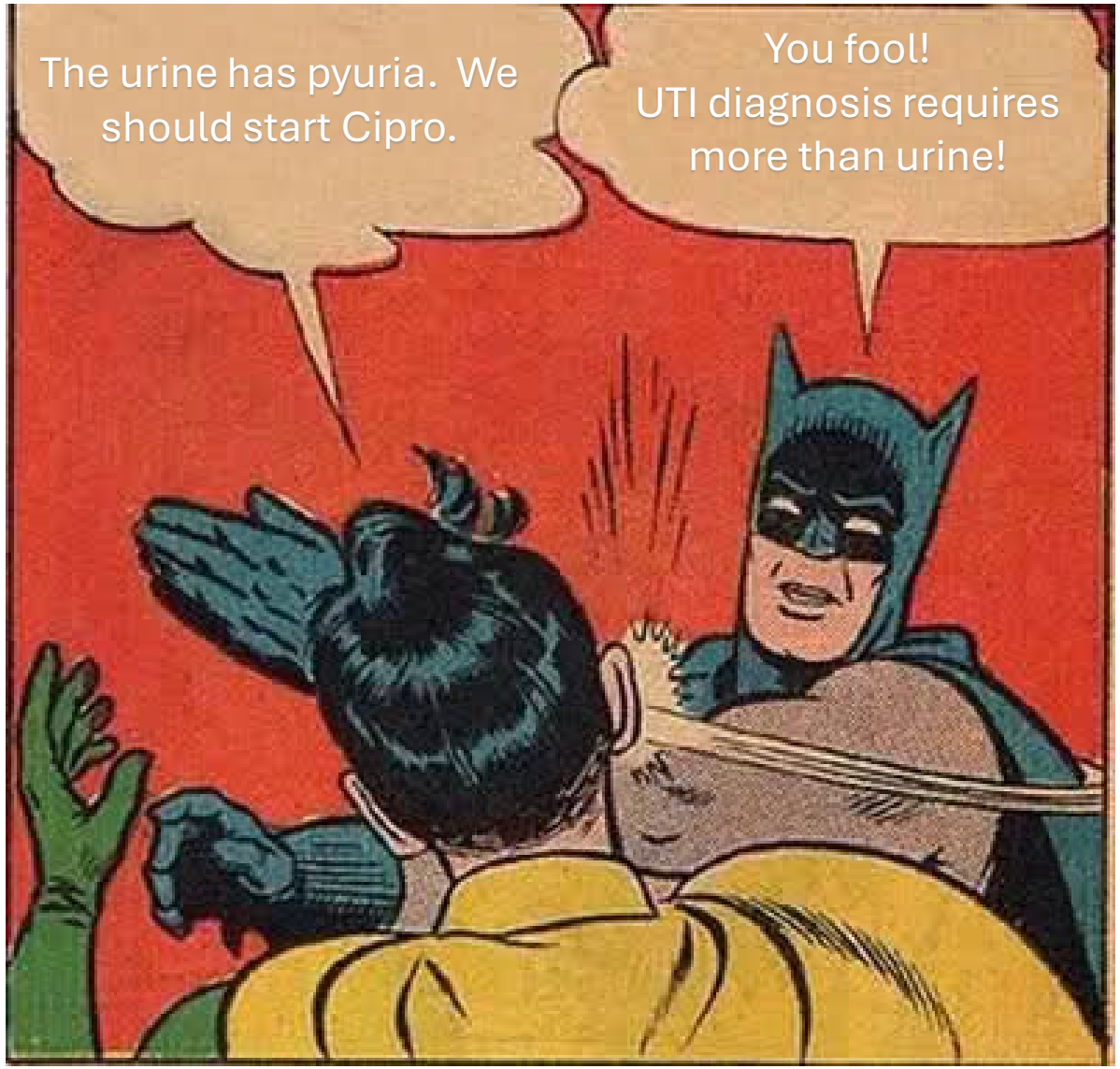
◉ Sputum culture ($22)
Once, today at 1114, For 1 occurrence
Sputum

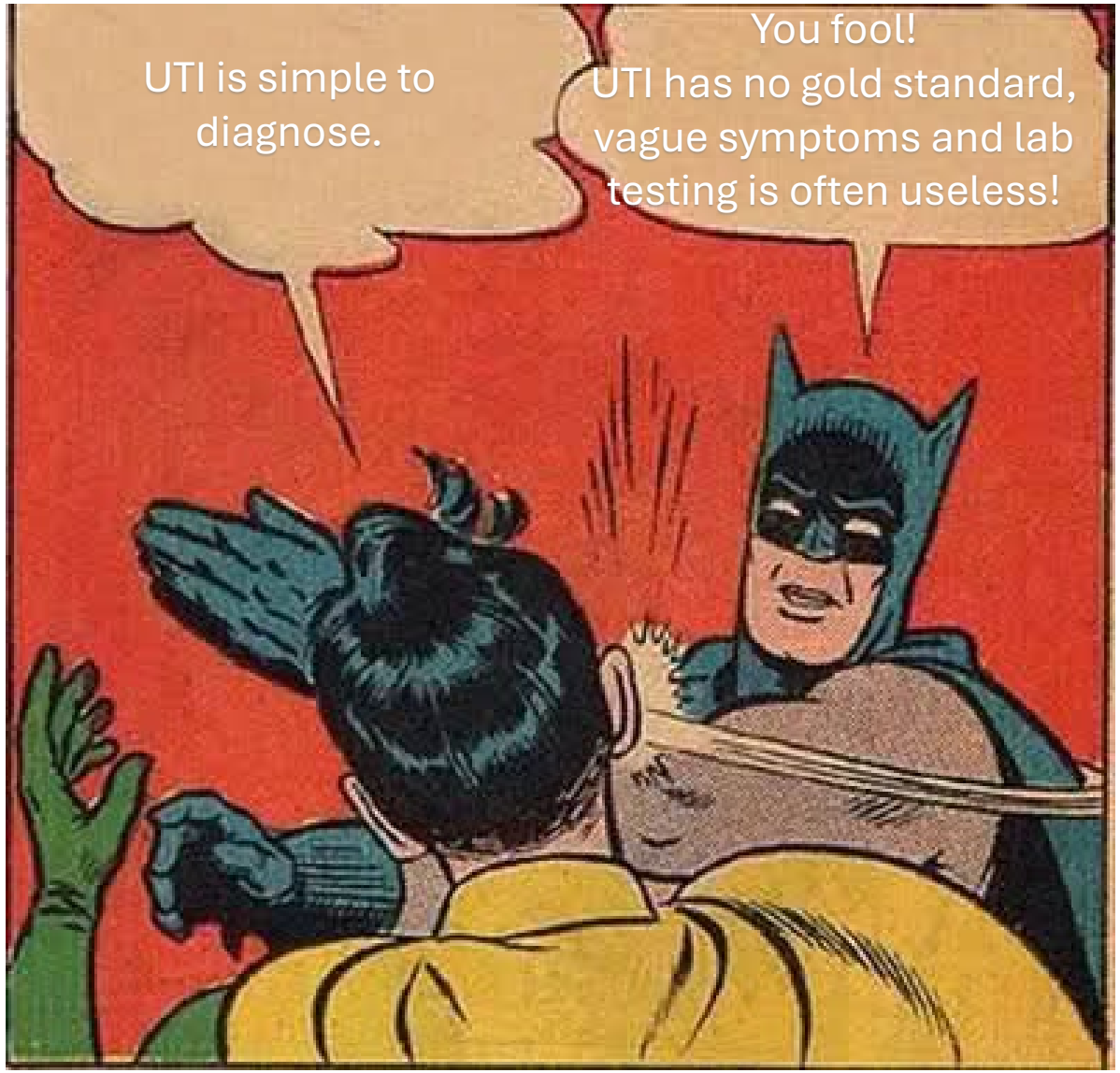
○ Sputum culture for cystic fibrosis and/or lung transplant patients ($60)

☐ Legionella antigen, urine ($34)

☐ Streptococcus pneumoniae antigen, urine ($23)

☐ Respiratory pathogen panel


The urine has pyuria. We should start Cipro.
You fool! UTI diagnosis requires more than urine!


UTI is simple to diagnose.
You fool! UTI has no gold standard, vague symptoms and lab testing is often useless!

How Useful are Urinalysis Findings for UTI Diagnosis?

Great for ruling out; pretty useless for ruling in

Table 4. Urinalysis vs Urine Culture Positivity

Variable	Data
Urinalysis positive, n	
Urine culture negative	71
Urine culture positive	19
Urinalysis negative, n	
Urine culture negative	140
Urine culture positive	2
Estimated value, %	
Prevalence	9.1
Sensitivity	90.4
Specificity	66.3
Positive predictive value	21.1
Negative predictive value	98.5

- Pyuria is highly prevalent in elderly patients, especially women
- Positive predictive value of abnormal UA (positive LE or nitrites) 5-14%

Abnormal UA ≠ UTI
Normal UA = NO UTI

Stovall RT, et al. *J Am Coll Surg*. 2013;217:162-6.
Latour K, et al. *BMC Geriatrics*. 2022;22:187.

Presenting Features Suggestive of UTI

Table 1. Baseline Characteristics, Presenting Features, and Culture Results

Characteristic	Total N = 265	UTI n = 150	Non-UTI n = 115	*P*-Value UTI vs Non-UTI
Presenting features				
Urinary tract symptoms, n (%)				
Dysuria	35 (12.1)	31 (20.7)	4 (3.5)	<.001
Hematuria	3 (1.1)	3 (2.0)	0	.13
Frequency	27 (10.2)	22 (14.7)	5 (4.3)	.002
Urgency	6 (2.3)	3 (2.0)	3 (2.6)	.64
Retention	18 (6.8)	17 (11.3)	1 (0.9)	.0004
Suprapubic pain	15 (5.7)	12 (8.0)	3 (2.6)	.03
Flank pain	9 (3.4)	9 (6.0)	0	.007
Rigors	16 (6.0)	14 (9.3)	2 (1.7)	.005
Any of the above	85 (32.1)	73 (48.7)	12 (10.4)	<.001

Woodford HJ et al. J Am Geriatr Soc 57:107–114, 2009

Non-Specific Signs and Symptoms are Not Diagnostic for UTI

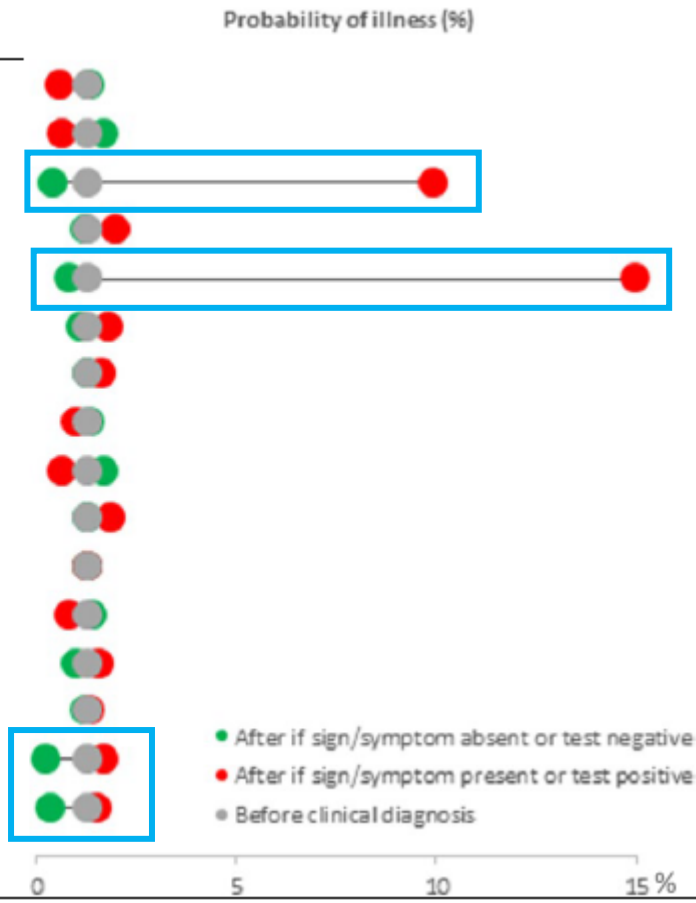
Table 1. Baseline Characteristics, Presenting Features, and Culture Results

Characteristic	Total N = 265	UTI n = 150	Non-UTI n = 115	*P*-Value UTI vs Non-UTI
Geriatric syndromes, n (%)				
Falls	79 (29.8)	47 (31.3)	32 (27.8)	.42
New or worsened confusion	117 (44.2)	70 (46.7)	47 (40.9)	.21
New or worsened urinary incontinence	27 (10.2)	17 (11.3)	10 (8.7)	.38
Functional decline	108 (40.7)	66 (44.0)	42 (36.5)	.11
Any geriatric syndrome	205 (77.4)	117 (78.0)	88 (76.5)	.70
Clinical signs, n (%)				
Suprapubic tenderness	29 (10.9)	20 (13.3)	9 (7.8)	.08
Costovertebral angle tenderness	7 (2.6)	7 (4.7)	0	.02
Pyrexia > 37°C	87 (32.8)	60 (40.0)	27 (23.5)	< .001
Urine pungent	24 (9.1)	14 (9.3)	10 (8.7)	.82
Urine discolored	11 (4.2)	9 (6.0)	2 (1.7)	.05
Patient smells of urine	15 (5.7)	8 (5.3)	7 (6.1)	.71

Woodford HJ et al. J Am Geriatr Soc 57:107–114, 2009

Performance of Sign/symptoms, Urine dipstick, and CRP for diagnosing UTI

	Sens (95% CI)	Spec (95% CI)	LR+ (95% CI)	LR- (95% CI)
Fever (reported sign) or rigors	2.94 (0.308-22.9)	93.9 (88.1-96.9)	0.475 (0.0290-8.01)	1.03 (0.941-1.14)
Acute change in mental or functional status	18.8 (6.59-43.0)	62.8 (53.9-70.9)	0.505 (0.177-1.44)	1.29 (0.985-1.70)
Acute dysuria	68.8 (44.4-85.8)	90.9 (84.5-94.8)	7.56 (3.94-14.5)	0.343 (0.166-0.713)
Acute costovertebral angle pain or tenderness	6.25 (1.11 -28.3)	95.9 (90.7-98.2)	1.54 (0.188-12.1)	0.977 (0.857-1.12)
Acute suprapubic pain	37.5 (18.5-61.4)	96.7 (91.8-98.7)	11.4 (3.58-35.9)	0.646 (0.442-0.946)
New or marked increase in incontinence, urgency or frequency	37.5 (18.5-61.4)	72.7 (64.2-79.9)	1.37 (0.685-2.76)	0.860 (0.579-1.28)
Gross haematuria	6.25 (1.11-28.3)	95.0 (89.6-97.7)	1.26 (0.162-9.81)	0.986 (0.864-1.13)
Change in character of urine (excl. blood)	12.5 (3.50-36.0)	83.5 (75.8-89.0)	0.758 (0.195-2.94)	1.05 (0.857-1.28)
Strong or foul smelling urine	18.8 (6.59-43.0)	62.0 (53.1-70.1)	0.495 (0.173-1.40)	1.31 (0.997-1.72)
Purulent discharge from around the catheter	2.94 (0.308-22.9)	98.0 (93.6-99.4)	1.45 (0.0720-28.6)	0.991 (0.909-1.08)
Marked loss of appetite, tiredness or fatigue	25.0 (10.2-49.5)	75.2 (66.8-82.0)	1.01 (0.408-2.49)	0.997 (0.738-1.35)
Marked restlessness or agitation	12.5 (3.50-36.0)	80.2 (72.2-86.3)	0.631 (0.164-2.42)	1.09 (0.889-1.34)
CRP value of ≥ 5 mg/L	60.0 (35.7-80.2)	50.9 (41.9-59.8)	1.22 (0.776-1.92)	0.786 (0.413-1.50)
Positive nitrite urine dipstick	56.3 (33.2-76.9)	45.8 (37.0-54.7)	1.04 (0.653-1.65)	0.954 (0.530-1.72)
Positive leukocyte esterase urine dipstick	93.8 (71.7-98.9)	29.1 (21.6-37.8)	1.32 (1.11-1.57)	0.213 (0.0320-1.465)
Combined nitrite and leukocyte esterase urine dipstick (one or both positive)	93.8 (71.7-98.9)	20.7 (14.3-28.9)	1.18 (1.01-1.38)	0.300 (0.0440-2.08)



Latour K, et al. *BMC Geriatrics*. 2022;22:187.

UTI is a Clinical Diagnosis

Signs/symptoms

Exam findings

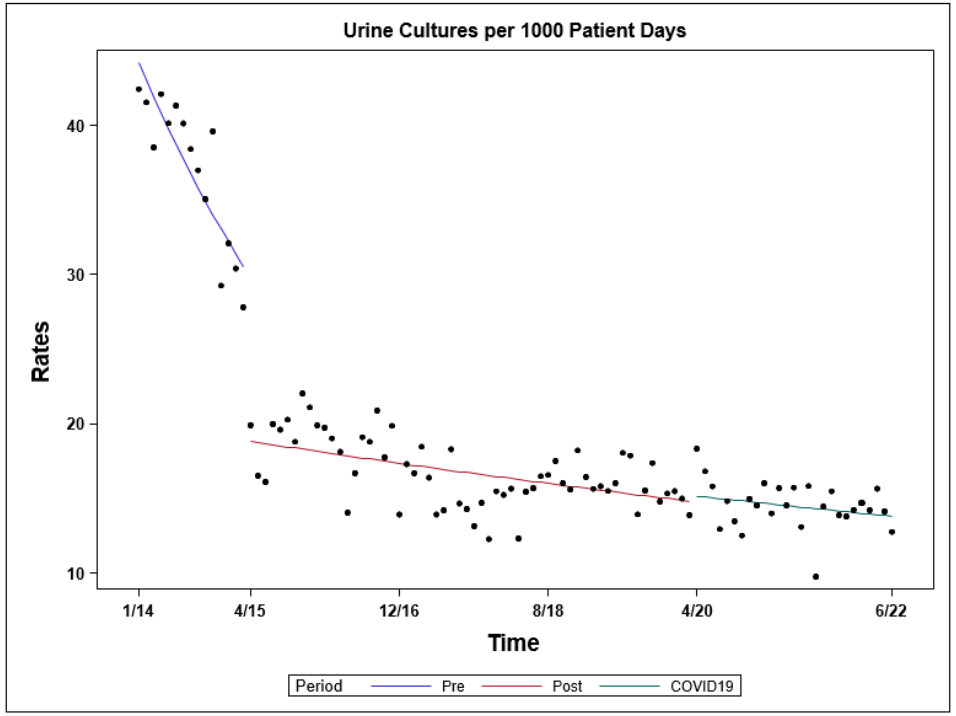
Urine studies (urinalysis and culture)

Urine studies cannot rule in UTI but can rule it out

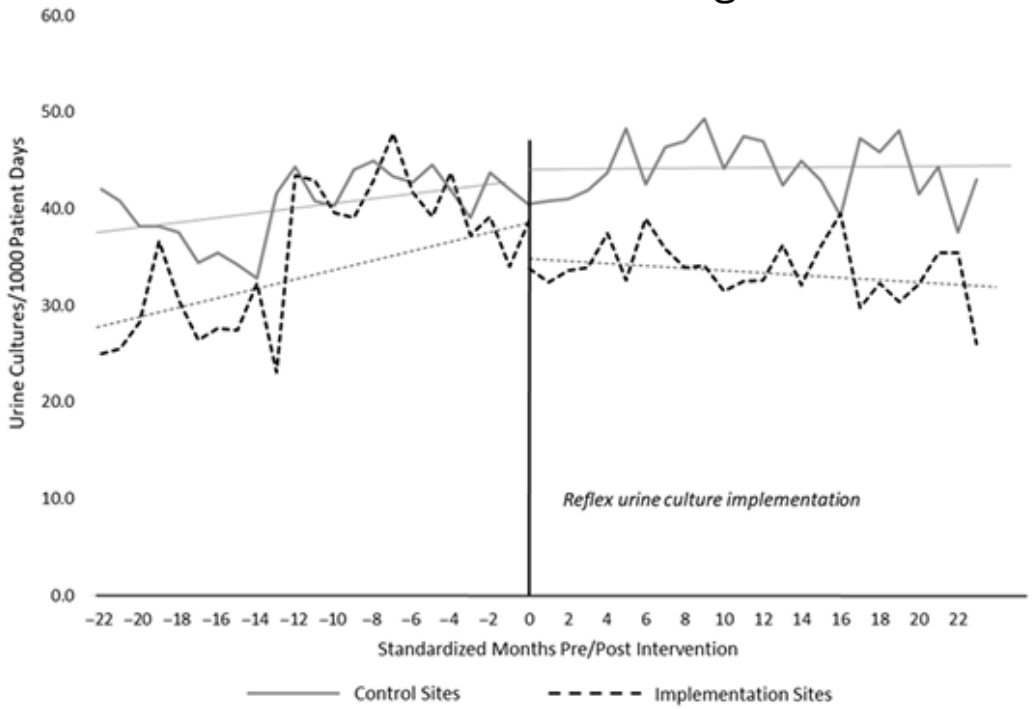
Reflex Urine Cultures Can Be Useful

Goal of reflex urine culture is to only perform culture in patients where it will grow something and mean something (hopefully)

Monthly rates of urine cultures before and after implementation of reflex UC Nebraska Medicine (<100 Squamous cells and >10 WBC required)



Urine Cultures per Month, Pre- vs. Post-Reflex Culture Change



Claeys KC, et al. *Infect Control Hosp Epidemiol*. 2021;42:176-81.
Torres C, et al. *Infect Control Hosp Epidemiol*. 2025;46:377-83.

If You Use it Correctly

Impact of discontinuing automatic reflex urine culture after urinalysis: a diagnostic and antibiotic stewardship initiative

Blaine Berger[1,2], Janell Lukey[1], Chetan Jinadatha[3,4] and Dhammika H. Navarathna[1*]

- Measured UCX and Antibiotic use for 3 years after dropping reflex testing
- 42% reduction in urine specimens undergoing culture and sensitivity testing
- Significant reduction in ciprofloxacin use, increase in nitrofurantoin use

- Only preform conditional urine culturing when UTI is suspected
- Evaluate the criteria you are using to trigger testing
  - Pyuria preferred

Frontiers Cell and Infect Microbiol. 2025;15:1572936.

Use Common Sense When Evaluating for Infection

- Don’t assume everything is infection. Evaluate clinically before testing.
- Utilize microbiologic testing based on patient assessment
- BCX are for evaluating life threatening illness
- Respiratory diagnostic testing should be performed only when pneumonia is present
- Urine studies should only be ordered when symptoms/signs of UTI are present

It is safe and appropriate to withhold antibiotics in clinically stable patients pending your investigation

Questions, Comments and Critiques?