

Diagnostic Stewardship: A Prerequisite to Successful Antimicrobial Stewardship

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Presentation Objectives

1. Define diagnostic stewardship
2. Identify key diagnostic stewardship areas that can improve patient care and promote antimicrobial stewardship
3. Recommend strategies to implement diagnostic stewardship

Case Vignette

- 77 yo man with history of benign prostate hyperplasia (BPH), hypertension, and coronary artery disease presents to the hospital with 2 days of dizziness after an upper respiratory tract infection.
- Patient denies burning sensation with urination. His urinary urgency and frequency not changed since BPH diagnosis a year ago.
- Vital signs and lab data:
 - Afebrile
 - Urinalysis: 9 WBC/hpf, positive for bacteria
 - Urine culture: > 100,000 cfu/mL *E coli*, resistant to cefazolin
- Patient is started on ciprofloxacin and discharged on ciprofloxacin to complete 10-day course for UTI.
- A month later, the patient is readmitted with severe diarrhea. He is diagnosed with *C. difficile* colitis and undergoes colectomy. However, the patient dies from complications.

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This patient had **asymptomatic bacteriuria**.
Urine culture should **not** have been obtained.
Antibiotic treatment should **not** have been administered.
Death was **preventable**.

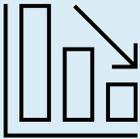
Define Diagnostic Stewardship

Definition of Diagnostic Stewardship

- **SHEA 2023:** Interventions prioritizing the right test, for the right patient, to prompt the right action
- **ISAC 2023:** Appropriate use of the right diagnostic tools for every patient, to limit overuse and guide timely patient management
- **WHO 2016:** Coordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions

SHEA, Society for Healthcare Epidemiology of America; **ISAC**, International Society of Antimicrobial Chemotherapy; **WHO**, World Health Organization

Objectives of Diagnostic Stewardship

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

Optimal Patient Journey

1. Patient presents to healthcare with illness
2. Clinical assessment
3. **Diagnostic stewardship**
 - Right test
 - Right patient
 - Right interpretation
4. **Antimicrobial stewardship**
 - Right antimicrobial
 - Right patient
 - Right dose and duration
5. Patient treated **appropriately**

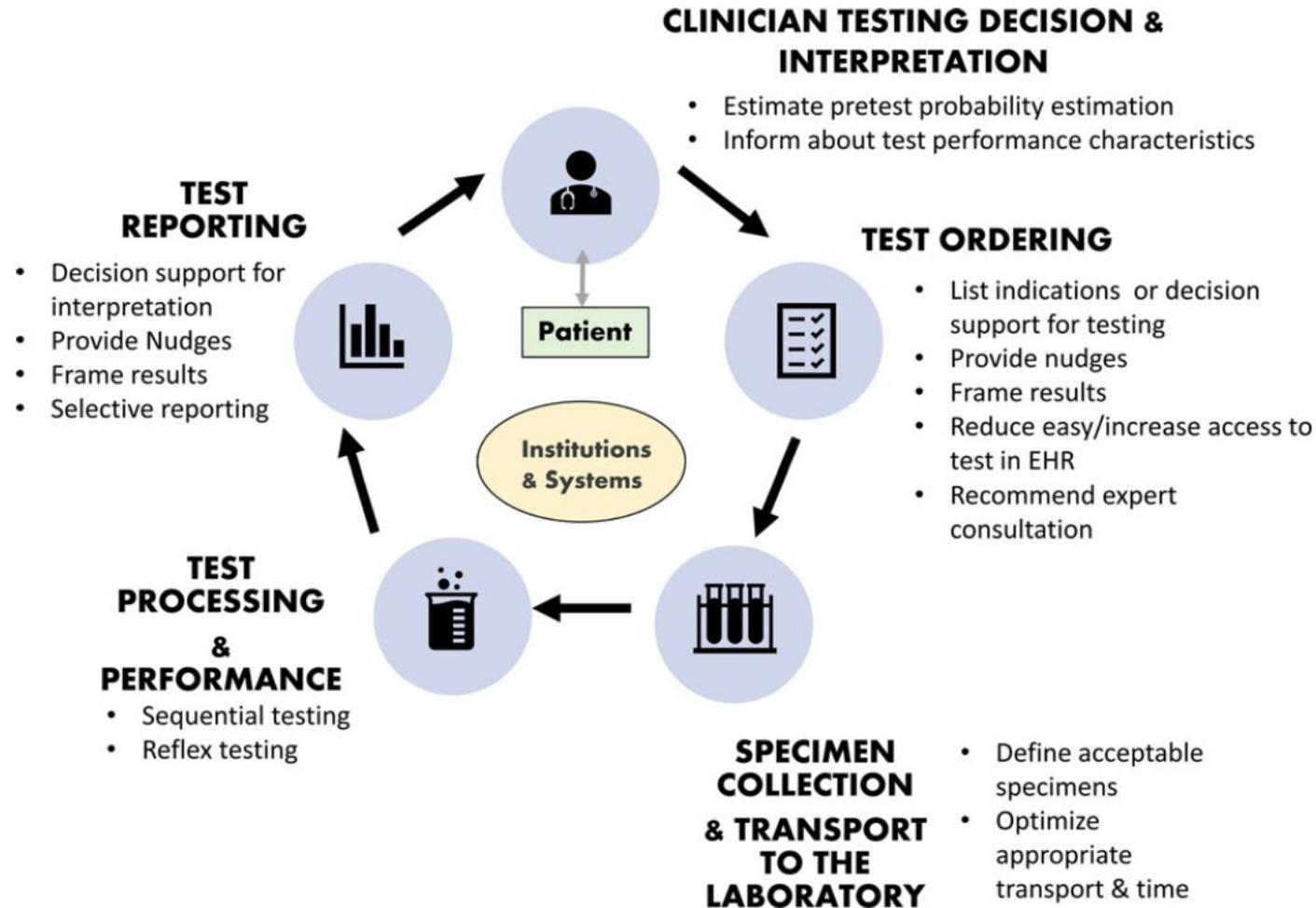


Suboptimal Patient Journey

1. Patient presents to healthcare with illness
2. Clinical assessment
3. **Inappropriate diagnostics**
 - Inappropriate test
 - Inappropriate patient
 - Inappropriate interpretation
4. **Inappropriate antimicrobials**
 - Inappropriate antimicrobial
 - Inappropriate patient
 - Inappropriate dose or duration
5. Patient treated **inappropriately**



Diagnostic Pathway



Common Barriers to Appropriate Diagnostic Utilization

- Lack of **clinical guidance** on appropriate diagnostic testing
- Lack of awareness on importance of **pretest probability** of infection
- Underestimation of **consequences** of overtesting and overtreatment
- Competing demands
- Patient insistence
- Concern for missing an infection
- Fee-for-service reimbursement systems

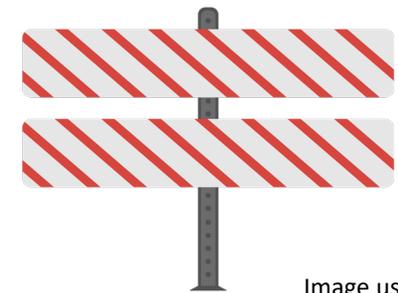


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Consequences of Inappropriate Diagnostic Use



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Inappropriate testing can lead to diagnostic errors

- **Overtesting (most common)** results in:
 - Overdiagnosis
 - Missing the true diagnosis
 - Unnecessary antimicrobial treatment
 - Excess cost
- **Undertesting** results in:
 - Missed diagnoses

Choosing Wisely to Improve Care and Prevent Harm

- Attention to overtesting in healthcare is growing
- In addition to asking “*what more can we do to prevent patient harm?*” we should also be asking “*how can we safely do less?*”

Do you really need that
medical test or treatment?
The answer may be no.



Talk to your doctor about which tests
and treatments you need – and which
ones you don't need.

Identify Key Diagnostic Stewardship Areas that Can Improve Patient Care and Promote Antimicrobial Stewardship

Diagnostic Stewardship Priorities

- At a minimum, institutions should develop strategies for optimal practices of:
 - **Blood cultures**
 - **Respiratory cultures**
 - **Urine cultures**
 - *C. difficile* testing

Why Focus on Blood Culture Stewardship?

- Only ~10% of blood cultures are positive with up to 50% representing contamination.
- Inappropriate testing increases risk of false-positives and:
 - Unnecessary antibiotic therapy
 - Additional testing
 - Overestimation of CLABSI rates
 - Unnecessary removal of central venous catheters
 - Longer hospital stay
 - Higher cost
- Common barriers are **lack of clinical guidance** and perception that blood culture is **standard component** of fever workup.

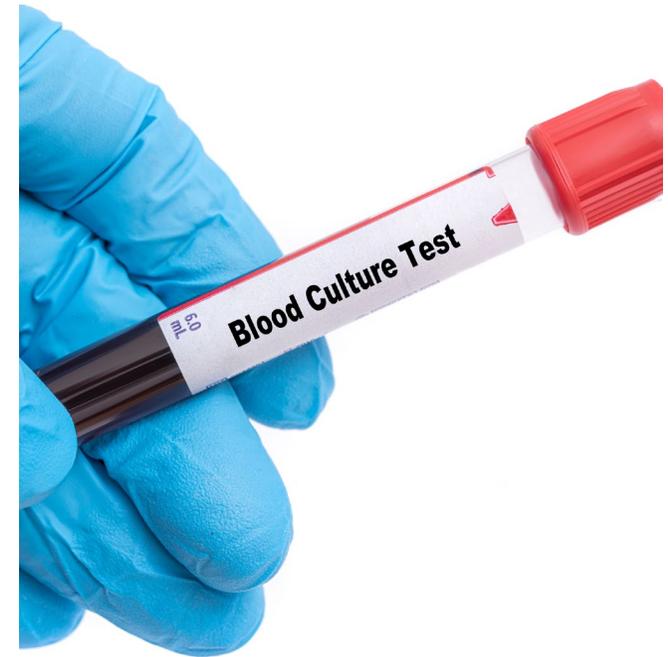


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CLABSI, central line associated bloodstream infection

Pretest Probability of Bacteremia in Hospitalized Nonneutropenic Adults

≥ 50% High	20% to < 50% Moderate	10% to < 20% Low-moderate	< 10% Low	< 5% Very Low
Septic shock	Severe sepsis	Cellulitis in patients with severe comorbidities	Uncomplicated cellulitis including periorbital cellulitis	Fever within first 48 h of surgery
Endovascular infection	Acute pyelonephritis	VAP	Cystitis/prostatitis	Isolated fever
Meningitis	Cholangitis		Non severe CAP	
Epidural abscess	Pyogenic liver abscess		HCAP	
Ventriculoatrial shunt infection	Severe CAP			
Acute nontraumatic native septic joint	Nonvascular shunt infection			
Discitis and NVO	Shaking chills in febrile patient			

CAP, community-acquired pneumonia; **HCAP**, healthcare-associated pneumonia; **NVO**, native vertebral osteomyelitis
UTI, urinary tract infection; **VAP**, ventilator-associated pneumonia

Initial Blood Culture Recommendations in Nonneutropenic Adults

BCx recommended

- Severe sepsis/septic shock
- **High** ($\geq 50\%$) pretest probability of bacteremia
- **Intermediate** (≥ 10 and $< 50\%$) pretest probability of bacteremia **AND** at risk of endovascular infection, primary site of infection inaccessible **or** BCx results likely to impact management

BCx NOT recommended

- **Low** ($< 10\%$) pretest probability of bacteremia
- **Intermediate** (≥ 10 and $< 50\%$) pretest probability of bacteremia **and NOT** at risk of endovascular infection, primary site of infection accessible **or** BCx results will not likely impact management

BCx, blood culture

Follow-up Blood Culture Recommendations in Nonneutropenic Adults

BCx recommended

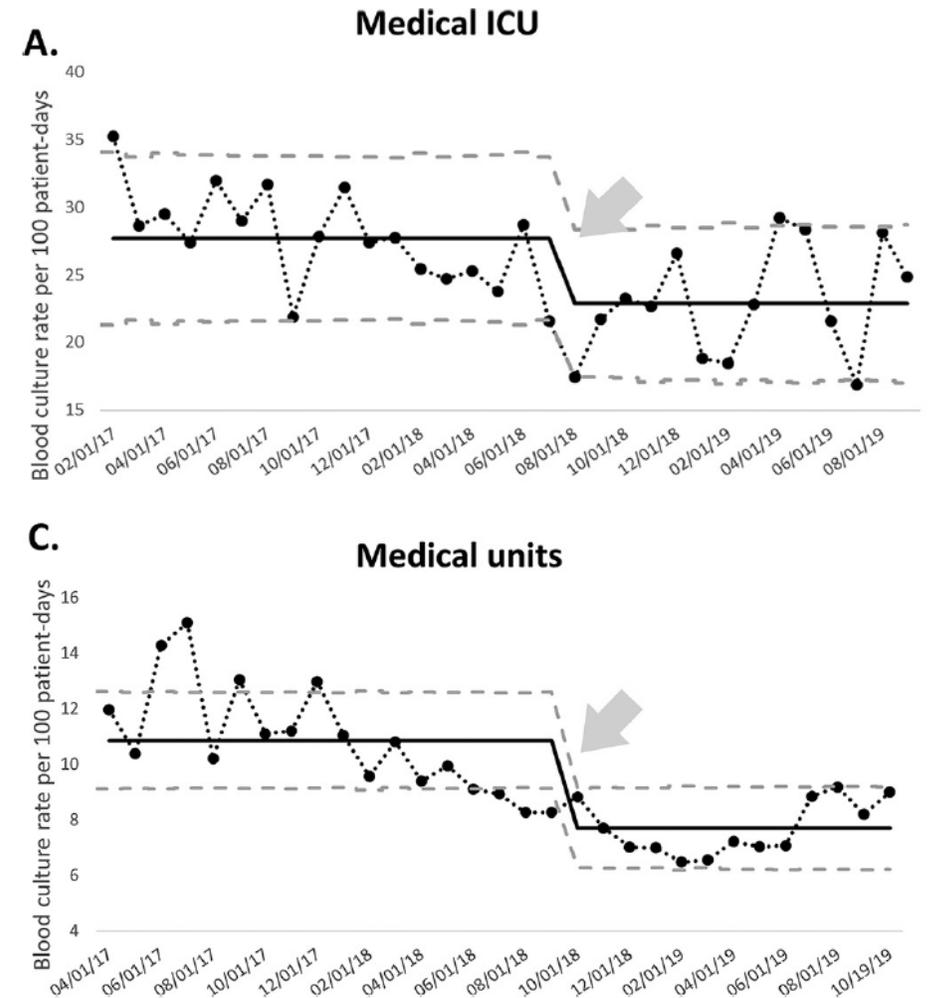
- Concern for persistent bacteremia in absence of source control
- Single positive BCx with skin flora and patient at high risk of endovascular infection
- Documenting clearance:
 - *S. aureus* or *S. lugdunensis* bacteremia
 - Before catheter placement in catheter related bloodstream infection
 - Suspected or high risk of endovascular infection

BCx NOT recommended

- All other

DISTRIBUTE Study in Hospitalized Nonneutropenic Adults

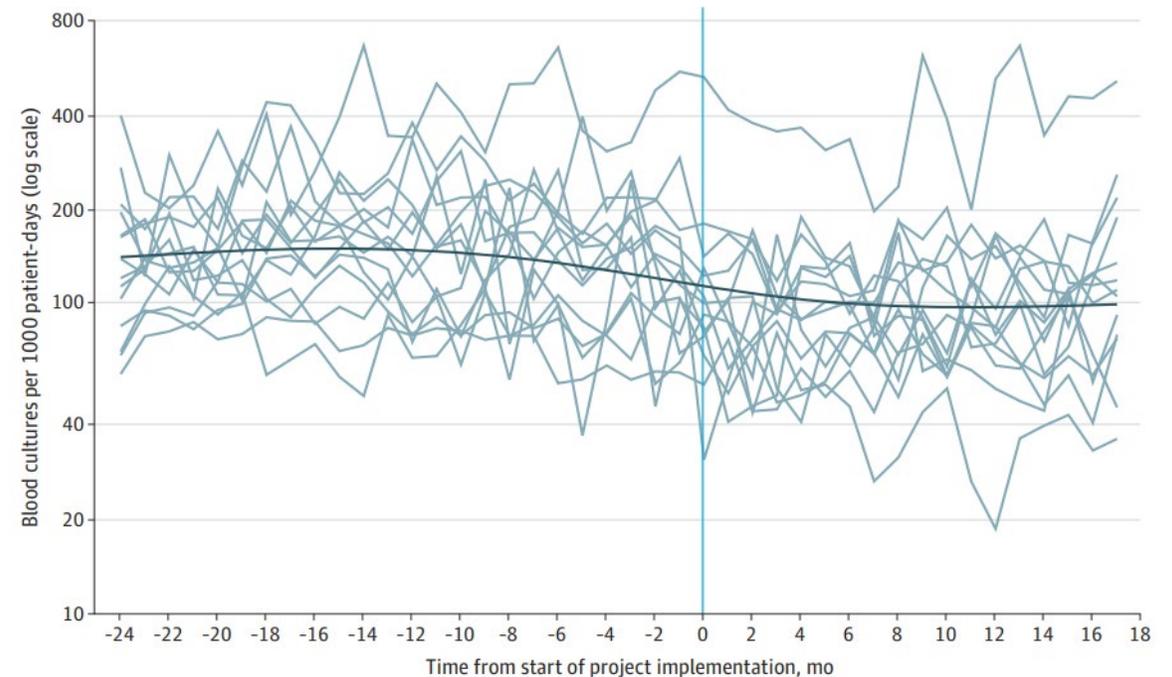
- Impact of **algorithm** and **education** on BCx rates
- **18%** ↓ in medical ICU BCx rates ($P < 0.001$)
- **30%** ↓ medical units BCx rates ($P < 0.001$)
- No change in sepsis quality metrics or mortality



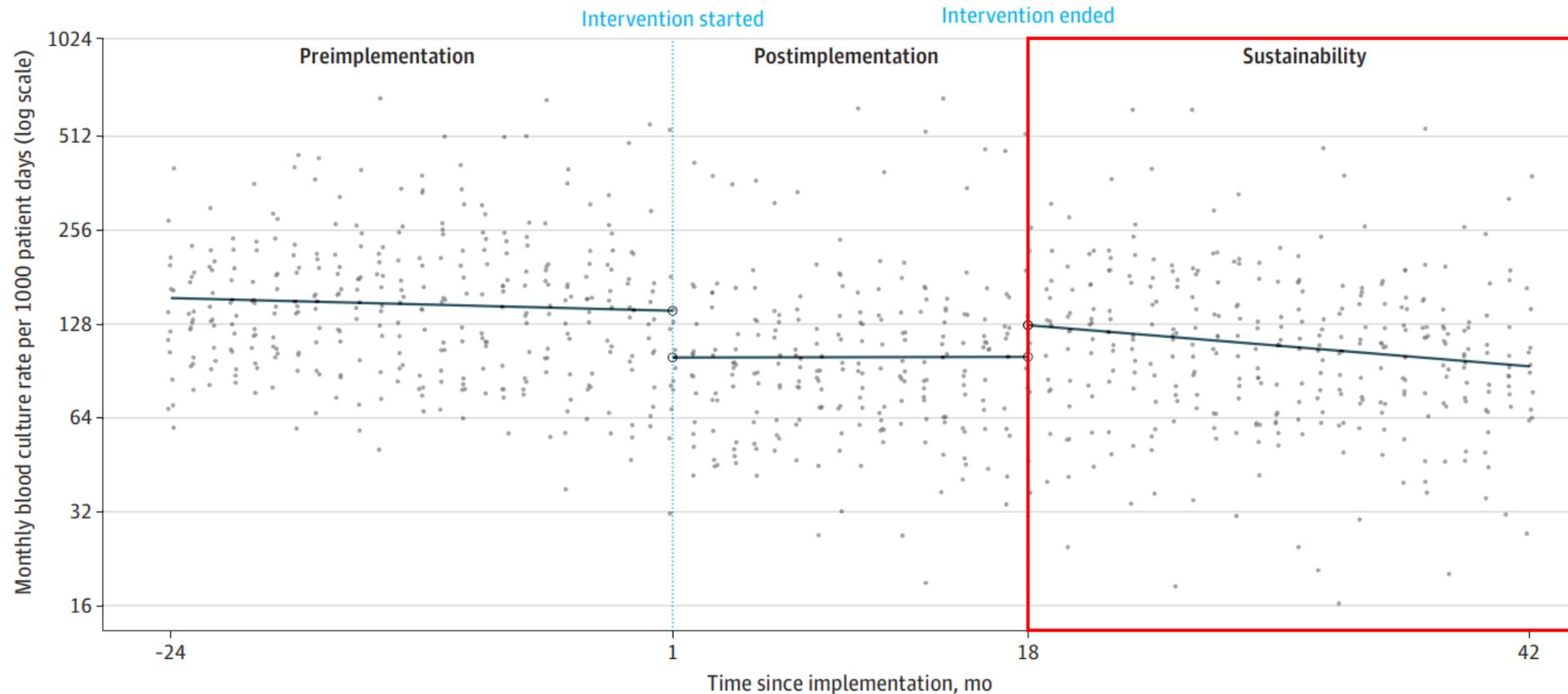
ICU, intensive care unit

Bright STAR Blood Culture Study in Critically Ill Children

- 14-site multidisciplinary BCx collaborative
- Site-specific BCx **algorithms** and **education**
- **33%** ↓ in pediatric ICU BCx rates ($P < 0.001$)
- **36%** ↓ in CLABSI rates ($P < 0.001$)
- **13%** ↓ broad-spectrum abx use ($P < 0.001$)
- No change in mortality, length of stay, readmission, severe sepsis/septic shock



Bright STAR Blood Culture Study in Critically Ill Children



BCx rate remained **27% lower** during 24-month **sustainability period** than during preimplementation period

Consensus Recommendations for Blood Culture Use in Critically Ill Children

Before blood culture decision

- Review clinical data (vital signs, lab/imaging, recent cultures, antimicrobial therapy)
- Examine patient
- Discuss clinical status of patient with bedside nurse

If no signs of sepsis, **AVOID** blood cultures for any of the following

- New fever within 24 hours of surgery with or without CVC
- Surveillance on ECMO, CRRT, or immunocompromised patients with or without CVC
- Asymptomatic patients with inadvertent CVC disconnection or broken/cracked CVC

CVC, central venous catheter

Consensus Recommendations for Blood Culture *Avoidance* in Critically Ill Children

If no signs of sepsis, AVOID blood cultures for any of the following

***Immunocompetent* children without CVC**

- New fever and symptoms of sedative/opioid withdrawal
- Viral syndrome and fever within expected time for viral infection
- Localized bacterial source of infection with persistent and expected fever and ≥ 1 negative BCx since start of fever

***Immunocompetent* children with CVC**

- New fever and symptoms of sedative/opioid withdrawal responsive to withdrawal treatment
- Viral syndrome and fever within expected time and ≥ 1 negative BCx since start of fever
- Localized bacterial source of infection (e.g. UTI) with persistent and expected fever and BCx negative to date obtained within last 48 hours

Consensus Recommendations for Blood Culture *Avoidance* in Critically Ill Children

If no signs of sepsis, *AVOID* repeat blood cultures for any of the following *Immunocompromised* children with or without CVC

- Persistent fever, multiple prior negative BCx, and no plan to change current antimicrobial therapy
- Persistent fever, negative initial set of blood cultures from all CVC lumens → do not repeatedly culture more than one lumen

Diagnostic Stewardship Strategies for Blood Cultures

Diagnostic Phase	Strategy
Ordering	<ul style="list-style-type: none"> • Evidence-based guidelines with culture indications and best practices • Real-time clinical decision support • Removal of test from order sets for infections with low pretest probability for bacteremia (e.g. lower UTI) • Inclusion of test in order sets for infections with high pretest probability for bacteremia (e.g. septic shock) • No surveillance cultures • When appropriate, automation of follow-up cultures • Monitoring and reporting of adherence to best clinical and lab practices
Collection	<ul style="list-style-type: none"> • Blood specimen collection site specification • No collection via intravascular catheters unless catheter is likely source of bacteremia • Designated team or dedicated phlebotomists for blood culture collection • Appropriate skin disinfection • Blood culture bottle cap disinfection • Appropriate blood specimen volume used for each culture bottle • Blood sample diversion technique or devices
Processing	<ul style="list-style-type: none"> • Rapid transport time at room temperature • 24/7 processing of positive cultures
Reporting	<ul style="list-style-type: none"> • Test result interpretation guidance (eg, “likely skin contaminant”; “<i>Staphylococcus aureus</i>, likely pathogen consider infectious diseases consult”) • No antimicrobial susceptibility testing for contaminants • Selective and cascade antibiotic susceptibility reporting

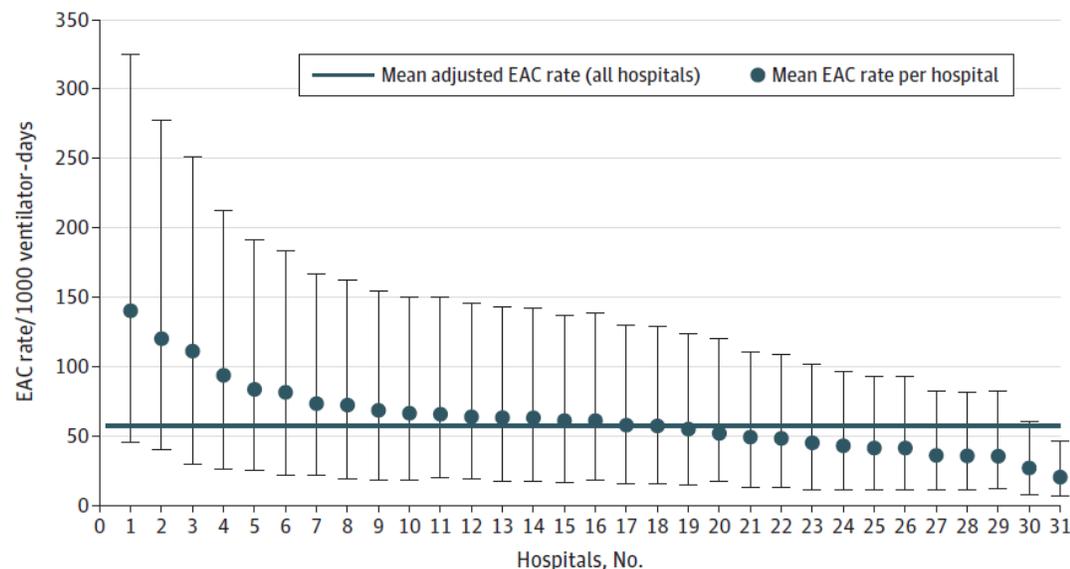
Why Focus on Respiratory Culture Stewardship?

- Respiratory tract is not sterile
- **Positive respiratory culture \neq Respiratory infection**
 - >50% of endotracheal cultures positive within 2 days of intubation **regardless** of clinical symptoms
 - Biofilms and bacteria persist despite treatment
- Accurate diagnosis of pneumonia is challenging
- Positive cultures contribute to inappropriate antibiotic use
- Common barriers include **fear of missing infection, variable practice**, and perceived **insufficient evidence** that cultures can be reduced safely.

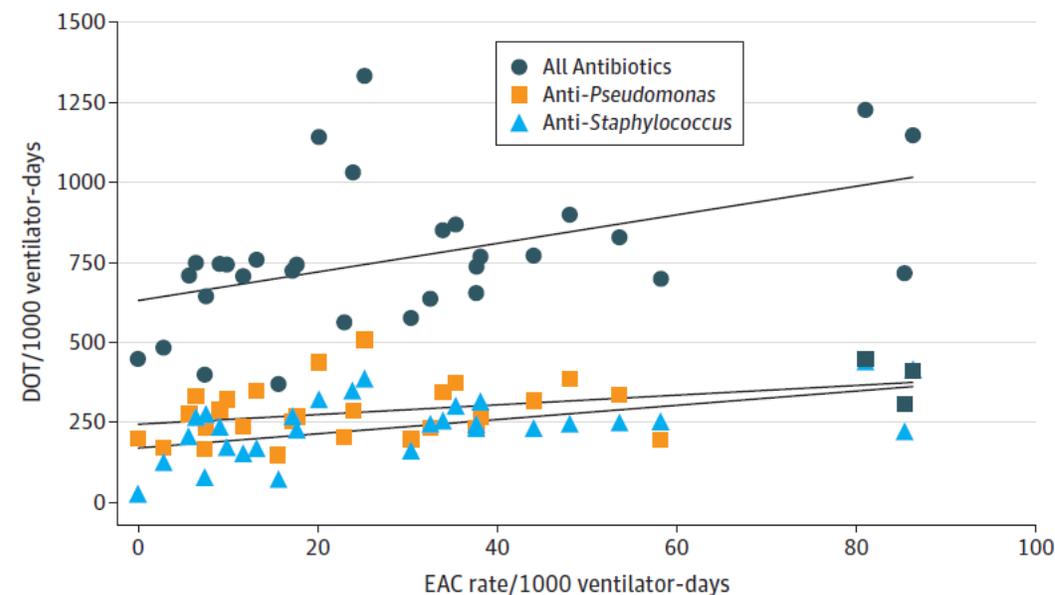


Respiratory Cultures are Associated with Antibiotic Use

Interhospital variability in endotracheal Cx rates



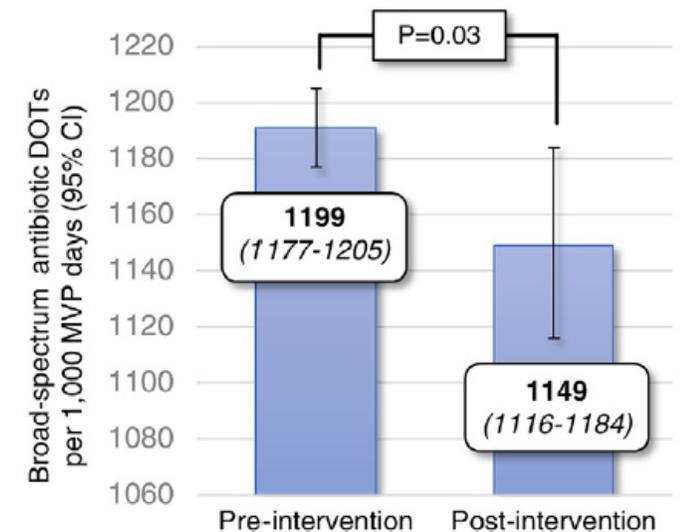
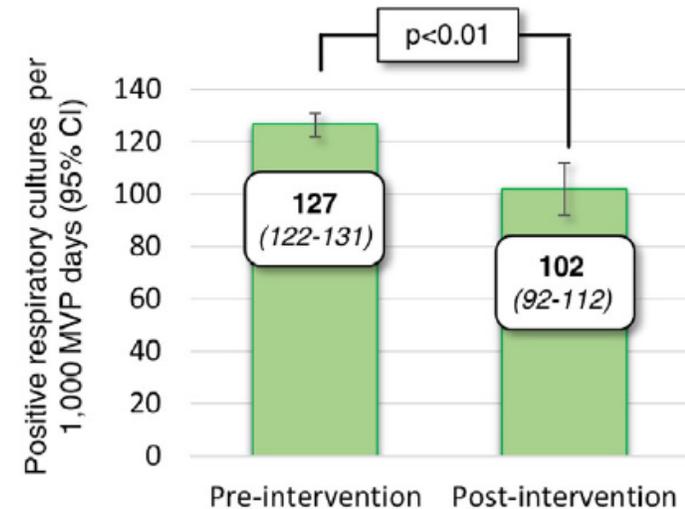
Correlation between endotracheal Cx rates and antibiotic use



EAC: Endotracheal aspirate culture; **DOT:** Antibiotic days of therapy

DIVA Study Reduced VAP Overdiagnosis and Overtreatment in Adults

- Impact of **bundled respiratory Cx stewardship intervention** on respiratory Cx rates
- **20%** ↓ in positive respiratory Cx rates ($P < 0.01$)
- **8%** ↓ in broad-spectrum antibiotic use ($P = 0.03$)
- No change in mortality, duration of mechanical ventilation, or ventilator-associated events

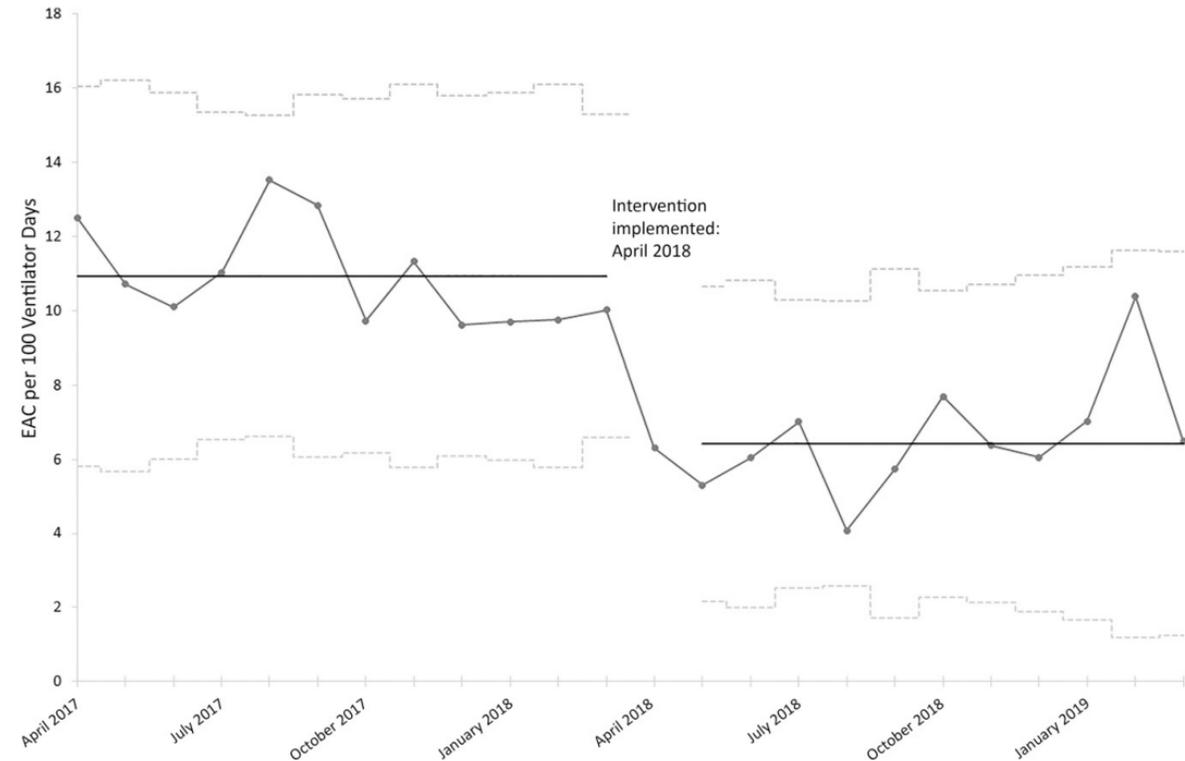


DIVA Bundled Respiratory Culture Stewardship Interventions

Diagnostic Phase	Intervention	Details
Ordering	Required selection of valid indication for Cx collection: <ul style="list-style-type: none"> • New infiltrate on CXR or chest CT • Purulent endotracheal secretions • Worsening PEEP and/or FiO₂ 	Prompt against Cx collection if low pretest probability of pneumonia: <ul style="list-style-type: none"> • Isolated fever or leukocytosis • Atelectasis or pulmonary edema • Thickened or increased non-purulent secretions • Transient worsening of PEEP and/or FiO₂ that rapidly improves
Collection	Preferred use of bronchoalveolar lavage (BAL) when no contraindications present	Contraindications to BAL: <ul style="list-style-type: none"> • Major lung surgery in prior 30 days • Gross blood in ET secretions • INR > 2 or platelet count <50k • P/F ratio <80
Reporting	<ul style="list-style-type: none"> • BAL culture results automatically reported only if PMN% >50% • BAL culture results with PMN% <50% suppressed 	Prompt for suppressed BAL results: “Culture results suppressed due to <50% PMNs.... Please call the Lab within 7 days if identification or antimicrobial susceptibility testing is needed.”

Endotracheal Culture Stewardship Reduced Culture Utilization in Children

- Single center study
- Endotracheal Cx **algorithm** and **education**
- **41%** ↓ in Cx rates ($P < 0.001$)
- **59%** ↓ in antibiotic-treated VAIs
- No change in mortality, hospital and ICU length of stay, readmissions
- 26K annual cost savings



VAI, ventilator-associated infections (includes VAP and ventilator-associated tracheobronchitis)

Algorithm for Obtaining Endotracheal Cultures from Mechanically Ventilated Children

Patient has increased **quantity of secretions** from baseline

Clinical decision making

Patient has at least **one** additional supporting sign of infection:

- Sustained increase in ventilator settings (pressure or FiO₂) due to poor oxygenation or ventilation *for* ≥ 6 hrs **or**
- Fever $>38^{\circ}\text{C}$ or Hypothermia $<36^{\circ}\text{C}$ (sustained $\times 2$) **or**
- New Leukocytosis $\geq 12\text{k}$ or Leukopenia $< 4\text{k}$ **or**
- Increase in CRP **or**
- New opacity on chest X-ray concerning for pneumonia

Specimen collection

*Cx should **not** be sent if patient **not** creating enough secretions to obtain sample.
Do **not** instill saline to generate a sample.

It has been more than **3 days** since last endotracheal culture

Microbiology lab

Consider obtaining Cx

Low-yield Scenarios for Obtaining Respiratory Cultures

- During surveillance bronchoscopies
- Following macroaspiration events
- Mild, transient respiratory decompensations in patients with mechanical airways
- Established viral respiratory infections without biphasic clinical decompensation
- As part of “pan-culture” workup for fever without changes in respiratory status

Why Focus on Urine Culture Stewardship?

- Nonsterile site and easy to contaminate
- **Positive urine culture \neq UTI infection**
- ASB should not be screened or treated in most patients.
- Unnecessary ASB treatment frequent in hospital and nursing home settings
- Low specificity of cultures for UTI diagnosis: catheterized or elderly patients, young children
- Inappropriate testing can overestimate CAUTIs



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CAUTI, catheter-associated
urinary tract infection

Common Variables Associated with Inappropriate Decision to Test or Treat



Labs without context of patient's symptoms and risk

- Abnormal urinalysis
- Urine culture colony count $> 10^5$ CFU/mL
- Leukocytosis
- Resistant organisms

Urine

- Foul smelling urine
- Dark urine
- Sediment in urine

Patient

- Older age
- Prior UTI diagnosis
- Dementia
- Vague malaise/weakness
- Urinary incontinence

Urine Culture Stewardship in Adults

Study and Setting	Intervention	Outcomes
<p>Trautner et al. JAMA Intern Med 2015;175:1120-27</p> <p>2 VA Healthcare systems, USA</p>	<p>Testing decision and interpretation CAUTI diagnostic algorithm with indications for UCx, management guidance, prospective audit and feedback of cases</p>	<ul style="list-style-type: none"> • 71% ↓ in UCx rate • 75% ↓ in treatment of ASB
<p>Watson et al. ICHE 2020;41:564-70</p> <p>Inpatient and ED in 5 hospitals (1 academic, 4 community), USA</p>	<p>Ordering Indication for UCx required upon order placement with clinical decision support for guidance: 1) UA without reflex to UCx; 2) UA with reflex to UCx; 3) UA and UCx together</p>	<ul style="list-style-type: none"> • 40% ↓ in UCx rate • 15% ↓ in abx DOT/1000 pt days for UTI
<p>Sang et al. ICHE 2016; 37:448-54</p> <p>7 adult ICUs, USA</p>	<p>Processing UA performed first. UCx performed reflexively only if urine WBC count >10 per high power field (hpf).</p>	<ul style="list-style-type: none"> • 30% ↓ in UCx rate • ↓ proportion of patients started on abxs: 41% pre vs. 23% post.
<p>Daley et al. ICHE 2018;39:814-19</p> <p>2 tertiary academic hospitals, Canada</p>	<p>Reporting No reporting UCx results for nonpregnant noncatheterized inpatients and asking clinicians to call lab for results if UTI suspected</p>	<ul style="list-style-type: none"> • ↑ appropriate treatment (abx for UTI; no abx for ASB) vs. standard reporting: 80% vs. 53% • No increase in adverse events

Abx, antibiotics; **ASB**, asymptomatic bacteriuria; **DOT**, days of therapy; **CAUTI**, catheter-associated UTI; **UA**, urinalysis; **UCx**, urine culture; **UTI**, urinary tract infection

Consensus Urine Culture Recommendations in Adults

Ordering	Processing	Reporting
<p>Appropriate practices</p> <ul style="list-style-type: none"> • Require documentation of UTI s/s • Discourage ordering UCx in absence of s/s • Utilize conditional reflex UCx • Cancel UCx repeated within 5 days of positive UCx during same hospitalization or within 7 days for LTC residents. 	<p>Appropriate practices</p> <ul style="list-style-type: none"> • Use urine WBC count as criterion to reflex to UCx • Require documentation of collection site 	<p>Appropriate practices</p> <ul style="list-style-type: none"> • Nudges/framing <ul style="list-style-type: none"> • High colony counts may not represent UTI • Do not treat ASB or mixed flora • Withhold UCx results if >2 bacterial strains • Selective and cascade reporting <ul style="list-style-type: none"> • Preferentially report IDSA–recommended abx if susceptible • Withhold FQN susceptibilities unless resistance to preferred abx
<p>Inappropriate practices</p> <ul style="list-style-type: none"> • Include UCx in standard order sets (e.g. ED, hospital admission, inpatient pre-op, assessment of falls in LTC) • Order UCx based on urine characteristic changes 	<p>Inappropriate practices</p> <ul style="list-style-type: none"> • Automatically reflex routine UA to UCx if not requested 	<p>Inappropriate practices</p> <ul style="list-style-type: none"> • Nudge clinicians to not treat if <100,000 CFU/mL of bacteria • Withhold information about UCx organism identification or susceptibilities unless clinician contacts lab

Excludes pregnancy, renal transplantation, severely immunocompromised status

Abx, antibiotics; **AMS**, altered mental status; **ASB**, asymptomatic bacteriuria; **ED**, emergency department; **FQN**, fluoroquinolone; **IDSA**, Infectious Diseases Society of America; **LTC**, long-term care; **WBC**, white blood cell; **UA**, urinalysis; **UCx**, urine culture; **UTI**, urinary tract infection

Consensus Urinary Tract Infection Symptoms in Adults

<p>Patients WITHOUT urinary catheters</p>	<p>Appropriate Dysuria, suprapubic pain, flank pain, costovertebral angle (CVA) tenderness, or septic shock</p>	<p>Uncertain Fever or systemic leukocytosis with no other known cause</p>	<p>Inappropriate Altered mental status, or change in urine characteristics (color, sediment, smell)</p>
<p>Patients WITH urinary catheters</p>	<p>Appropriate Dysuria, suprapubic pain, flank pain, costovertebral angle (CVA) tenderness, or septic shock</p>	<p>Uncertain Fever, systemic leukocytosis with no other known cause, or delirium</p>	<p>Inappropriate Change in urine characteristics (color, sediment, smell)</p>

Diagnostic Stewardship Strategies for Urine Cultures

Diagnostic Phase	Strategy
Ordering	<ul style="list-style-type: none"> • Guidelines and algorithms with best practices • Real-time clinical decision support • Education on prevalence of asymptomatic bacteriuria in catheterized patients • Best practice alert to evaluate for symptoms of UTI when ordering urine culture • Discouraging testing in asymptomatic patients • Required indications for urine cultures • Removal of order from ED triage, hospital admission, and presurgical evaluation order sets (“order set hygiene”) • Discouraging follow-up testing for urinary bacterial clearance • No surveillance cultures • Monitoring and reporting of adherence to best clinical and lab practices
Collection	<ul style="list-style-type: none"> • Nurse education and training on proper specimen collection • Newly inserted catheter preferred • Urinary catheter replacement prior to culture if in place >7 days • Catheter sample from collection port (not collection bag) • Urine specimen collection site specification
Processing	<ul style="list-style-type: none"> • No delays in transport, refrigerate if >1 hour delay • Collection device containing preservative (eg, boric acid) • Conditional reflex urine culture (eg, culture only if pyuria present)
Reporting	<ul style="list-style-type: none"> • Comment that many hospitalized patients have asymptomatic bacteriuria • Comment advising against treatment of asymptomatic bacteriuria • Interpretative guidance on polymicrobial cultures (“multiple organisms indicating likely contamination”) • Suppression of organism identification if multiple organisms present • No antimicrobial susceptibility testing for contaminants (e.g. “mixed flora, no further work-up”) • Selective and cascade antibiotic susceptibility reporting

Summary

- There is growing evidence that blood, respiratory, and urine culture practices can be optimized **effectively** and **safely** with evidence-based guidance and clinical decision support in ordering, collection, processing, and reporting phases of diagnostic pathway.
- Further work needed to better define optimal diagnostic stewardship across patient populations (e.g. geriatrics, immunocompromised, pediatrics) and settings (ambulatory, emergency, inpatient, long-term care).

Recommend Strategies to Implement Diagnostic Stewardship

Diagnostic Stewardship: Getting started

- Identify and prioritize diagnostic stewardship opportunity
- Get numbers to make a case
- Partner with key stakeholders and champions
- Investigate local drivers (e.g. lack of guidance, order sets, time)
- Build momentum and **gain trust**



Diagnostic Stewardship: Implementation

- Propose a **change**
- Define a **clear goal**
- Involve **all** relevant stakeholders including end users
- Define **measures** to track impact of intervention
- Ensure leadership support
- Decide go-live date and **educate**
- **Track** and **report** impact of intervention
- Assess need for modifications
- Consider how will **sustain** practice change



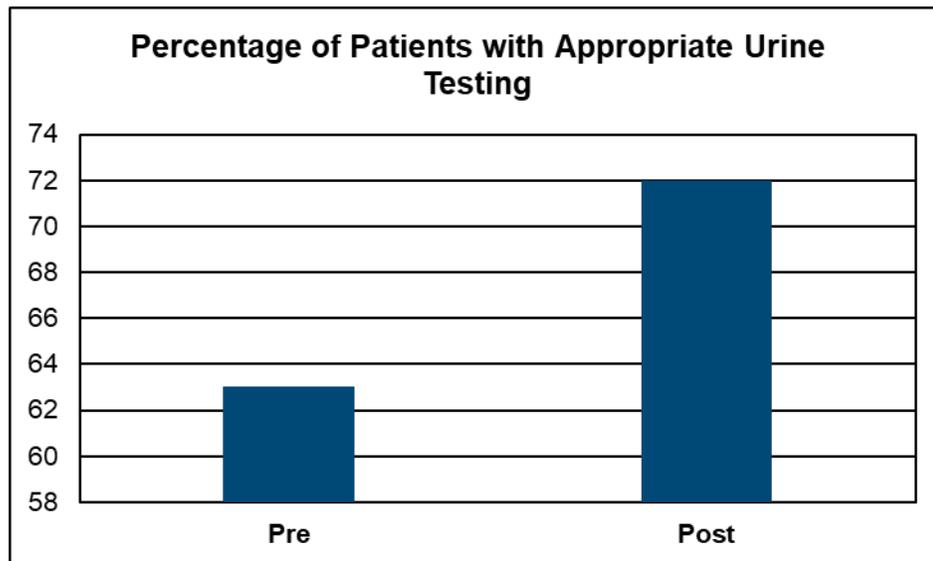
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Quality Improvement Data Analysis

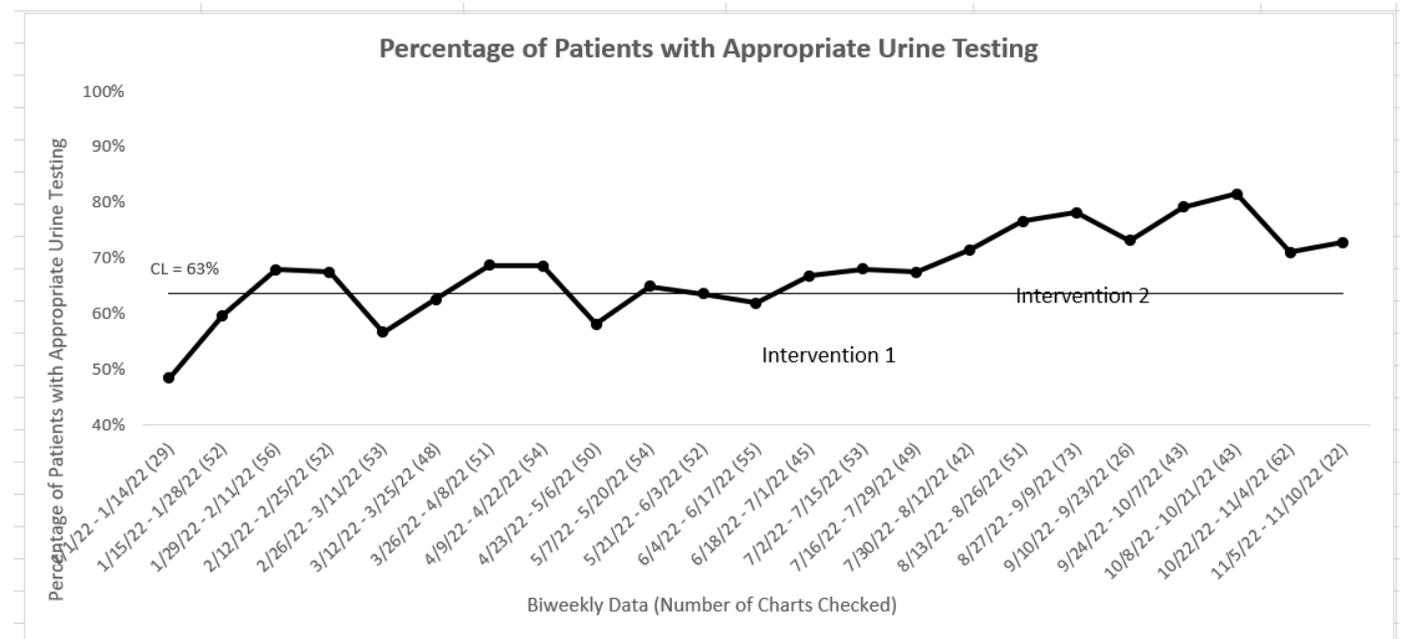
- **Run charts** and **statistical process control (SPC) charts** are **backbone** of QI data analysis
- Run and SPC charts are **preferred** over pre- and post-intervention data:
 - Collecting **static** pre- and postintervention data does **not** reflect entire process.
 - Data points **over time** provide more **dynamic** and **accurate** process representation.
 - Run and SPC charts allow interpretation of data points relative to central line

Quality Improvement Data Graphing

Static pre- and postintervention data



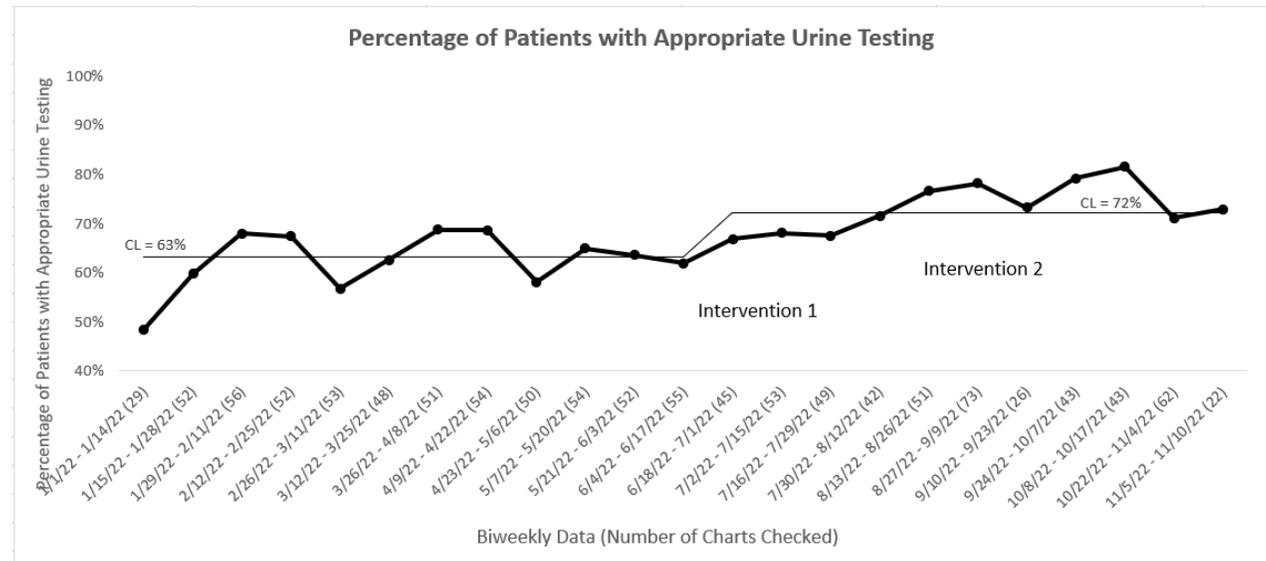
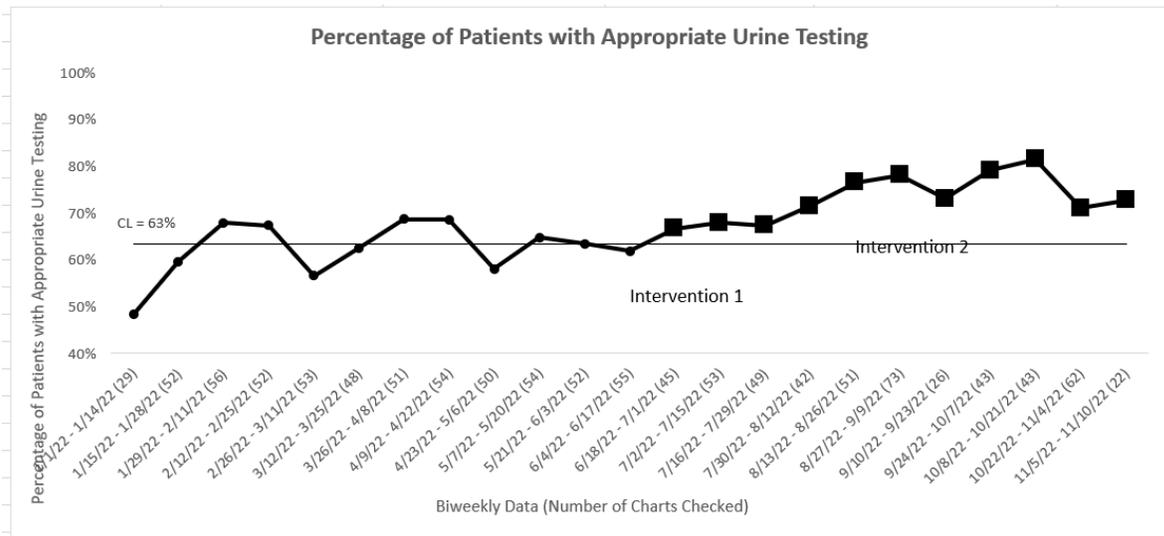
Run chart depicts temporal relation between interventions and outcomes



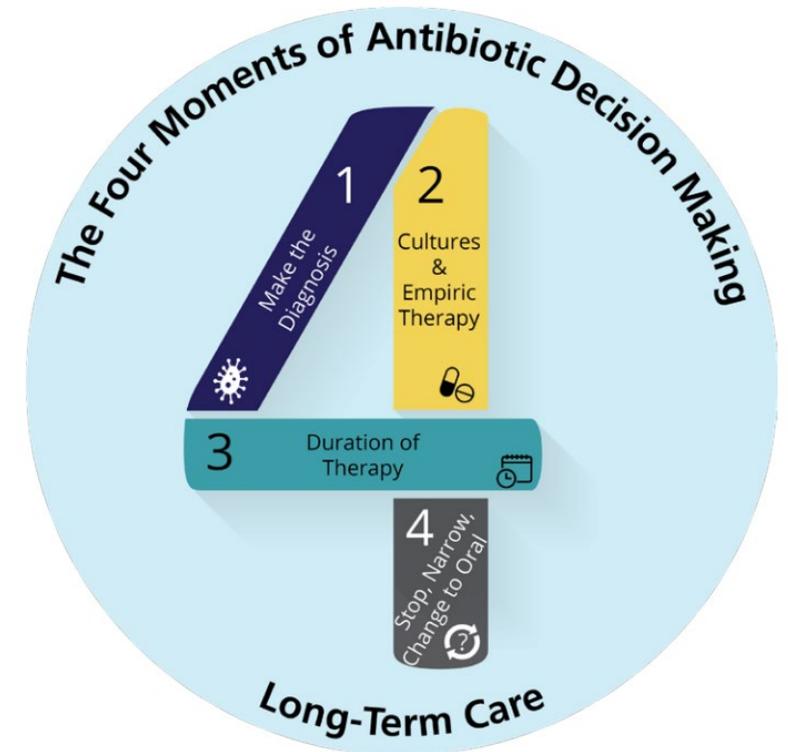
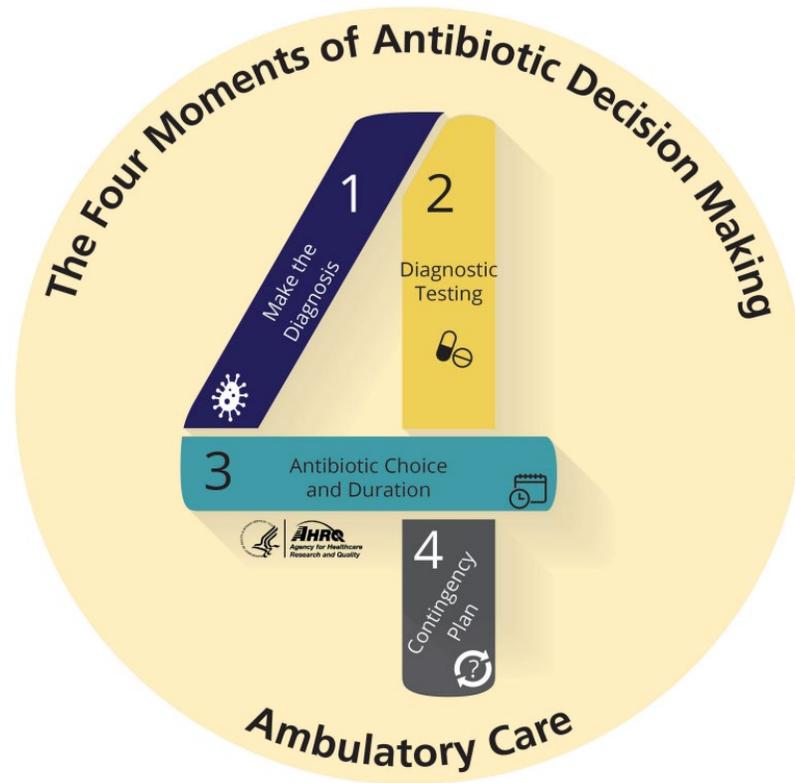
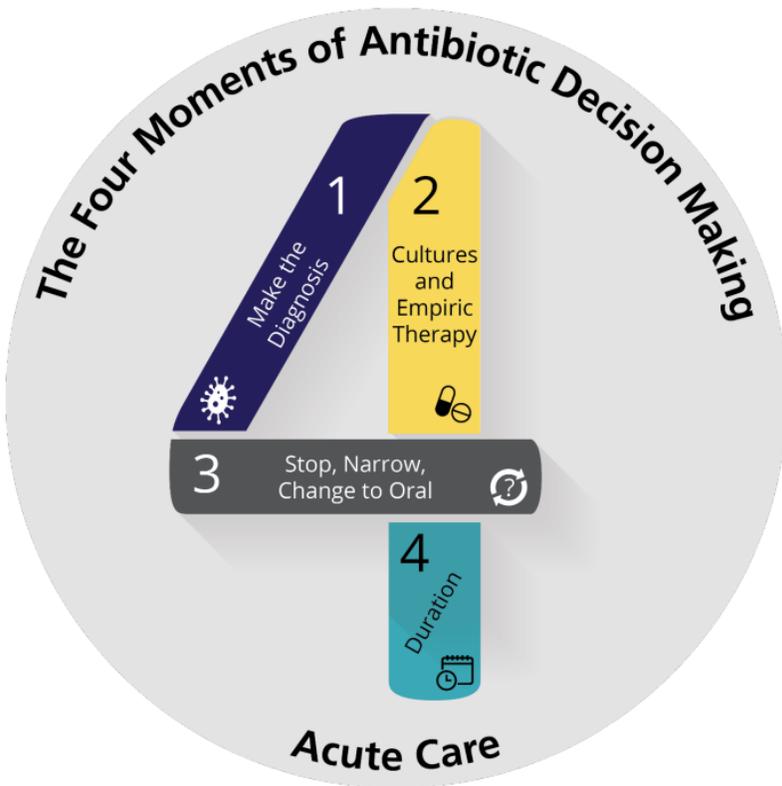
Run Chart Interpretation

- At least 10 data points of intervention data should be used
- Run charts identify **nonrandom** signals of **change**, e.g.:
 - **Shift:** 6–9 or more points above or below the median
 - **Trend:** ≥ 5 consecutively increasing or decreasing points
- If shift or trend identified, nonrandom change has occurred, indicating $< 5\%$ chance this data pattern occurred by chance

More Run Charts



The Four Moments of Antibiotic Decision Making



Take Home Points

- Diagnostic stewardship is critical to preventing downstream antimicrobial overuse.
- **Diagnostic** stewardship and **antimicrobial** stewardship are **synergistic**. They can improve patient care while optimizing healthcare resources.
- Relevant stakeholders should work together to identify opportunities for diagnostic stewardship and optimize testing.



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Thank you

