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Diagnostic Stewardship and Lower Respiratory Cultures

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Disclosures

I have the following financial relationships with the manufacturer(s) and/or provider(s) of commercial services discussed in this activity:

- Contracted research with:
  - Pfizer (pediatric nirmatrelvir-ritonavir)
  - Pfizer (maternal RSV vaccine)
  - Merck (monoclonal antibody for RSV prevention)

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

Diagnostic Stewardship: Why?

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- Most infectious diseases diagnostics have imperfect specificity and positive predictive value
  - Patients can have C-diff colonization, urinary tract colonization, ET tube or trach colonization, Group A Strep colonization, CVC colonization…
- False-positives:
  - Mask the patient's true problem
  - Cause unnecessary antibiotic exposure
  - Overcount HAIs
- Not the goal: missing HAIs, saving money

Diagnostic Stewardship Principles

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- Perform infectious diseases diagnostic testing *appropriately*
- Only send testing when infection reasonably suspected
  - Avoid false-positives
  - Especially nonsterile sites
- Examples: reject C-diff testing on formed stools; check urinalysis before sending urine culture, etc

Diagnostic Stewardship Stakeholders

Frontline staff

Obtain most samples for testing

Often suggest testing to providers

Microbiology lab

Assess sample adequacy (rejecting formed stools, rejecting “sputum” that’s all spit)

Reporting algorithms

Ordering providers and pharmacists

Order diagnostic tests and make treatment decisions

Respiratory Culture Diagnostic Stewardship

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- Respiratory cultures from airway devices have poor specificity and PPV
  - Can be improved with sampling method and lab rejection criteria

- False-positive cultures → treatment courses
  - Often repetitively in one patient
  - Usually broad-spectrum

Ventilator-Associated Respiratory Infection: Stewardship Importance

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- One of the most common causes of nosocomial infection in ICUs
- In one academic hospital, treatment of suspected VAP accounted for nearly half (47%) of the total antibiotic treatment days in the PICU
- MDROs common: MRSA, ESBLs, *Pseudomonas*, *Stenotrophomonas*, *Acinetobacter*, CRE, etc.

Respiratory Tract Sampling

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Approach	Advantages	Disadvantages
ET tube aspirate	✓ Fast, easy, noninvasive	x Poorest specificity x Often detects ET tube or tracheostomy tube colonizers

ET Tube and Trach Aspirates: Sample Processing

- Samples should be rejected if Gram stain shows:
  - Low numbers of neutrophils and/or
  - No bacteria
- Labs should:
  - Report oropharyngeal flora (viridans streptococci, nonpathogenic *Neisseria*, etc) as OP flora – do not name OP flora species!

Poor Specificity

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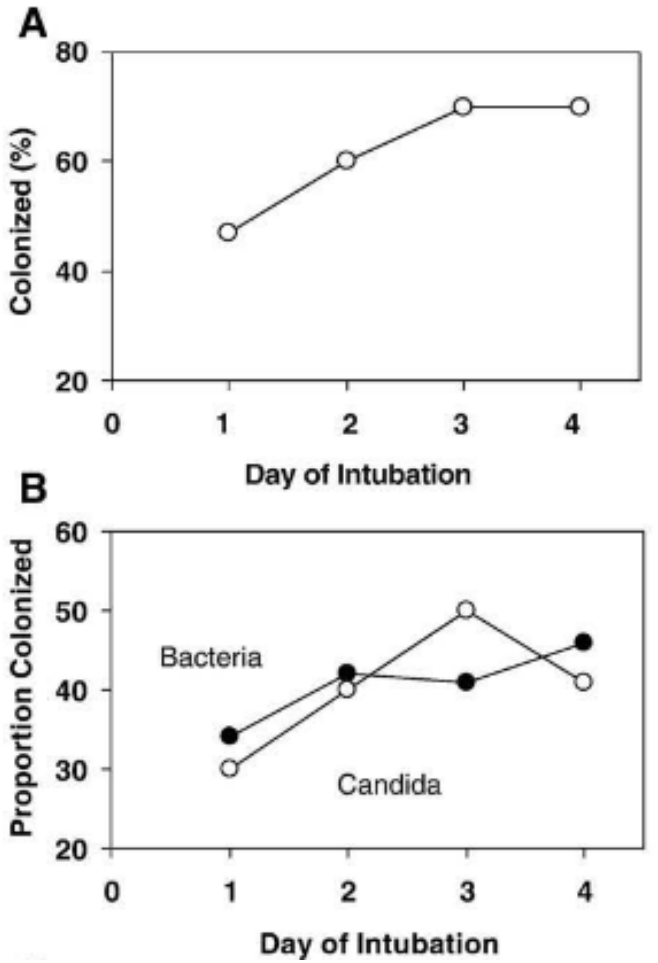
Patterns and density of early tracheal colonization in intensive care unit patients☆,☆☆

Lakshmi Durairaj MD[a,*], Zeinab Mohamad MS[a], Janice L. Launspach RN[a], Alix Ashare MD[a], James Y. Choi MD[b], Srinivasan Rajagopal MD[b], Gary V. Doern PhD[c], Joseph Zabner MD[a]

- Tracheal aspirates in patients for four consecutive days after intubation
- Bacterial and fungal colonization was almost immediate
- Almost all patients were receiving antibiotics



Journal of Critical Care, 2009

Poor Specificity

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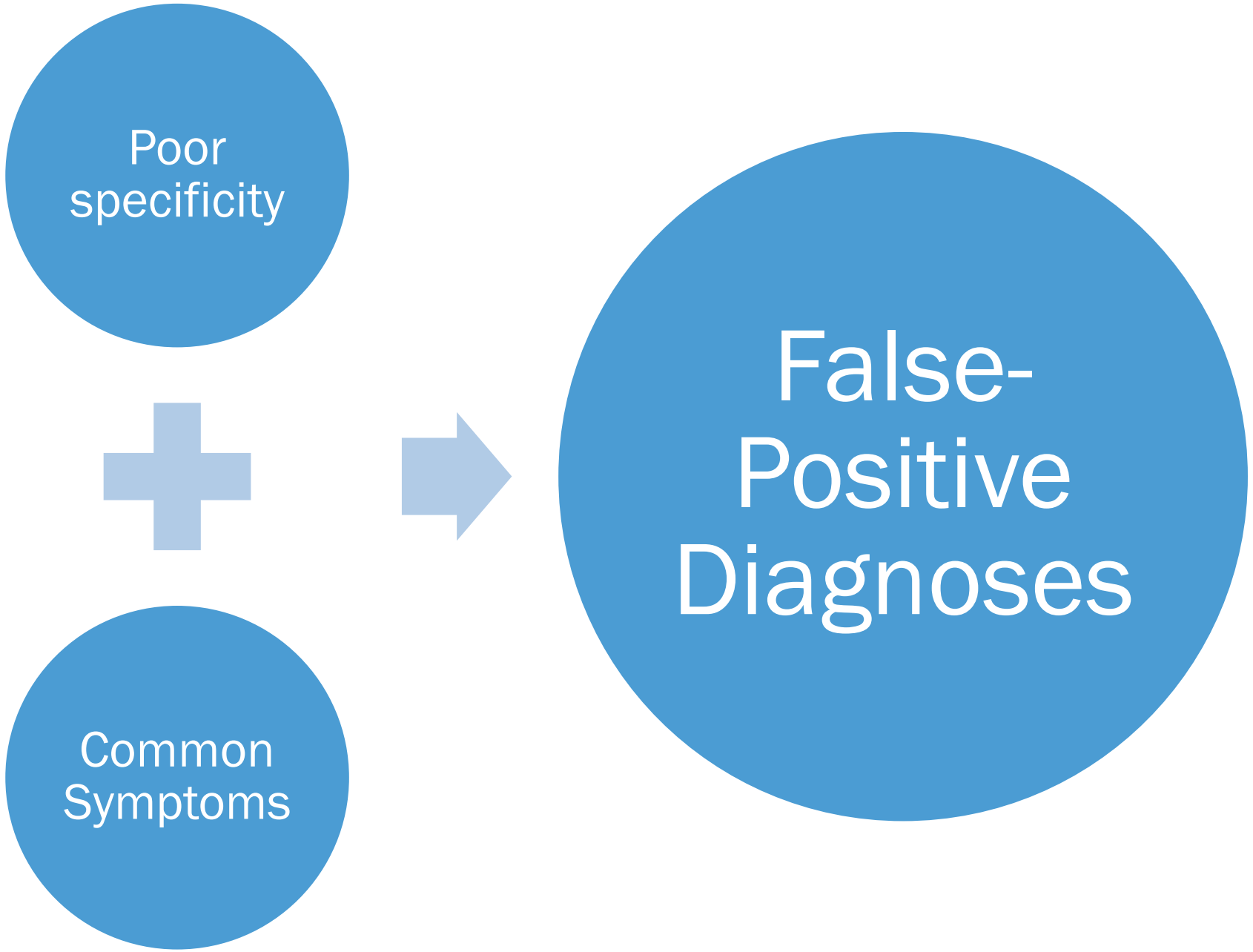
Physical Findings	Sensitivity	Specificity
Fever	66.4%	53.9%
Purulent Secretions	77%	39%
Infiltrate on Chest X-ray	88.9%	26.1%

Sample Type	Sensitivity	Specificity
Sputum from Endotracheal Aspirate	75.7%	67.9%
Protected Specimen Brush	61.4%	76.5%
Bronchoalveolar Lavage (BAL)	71.1%	79.6%

Fernando SM, et al. Diagnosis of ventilator-associated pneumonia in critically ill adult patients—a systematic review and meta-analysis. Intensive Care Med. 2020;46(6):1170–1179. PMCID: PMC7223448


Poor specificity
Common Symptoms
False-Positive Diagnoses

Respiratory Cultures Diagnostic Stewardship Project

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- Population:
  - <= 21 years, admitted to the hospital >48 hours (including OSH)
- To justify respiratory cultures in ventilated patient, must have:
  - Evidence of inflammation (fever, high or low WBC, sepsis) PLUS
  - Increased/purulent sputum OR increased oxygen/MAP requirement
- Definitions:
  - VAP: with new pulmonary infiltrate
  - VAT (tracheobronchitis): without pulmonary infiltrates

Diagnostic Stewardship Project

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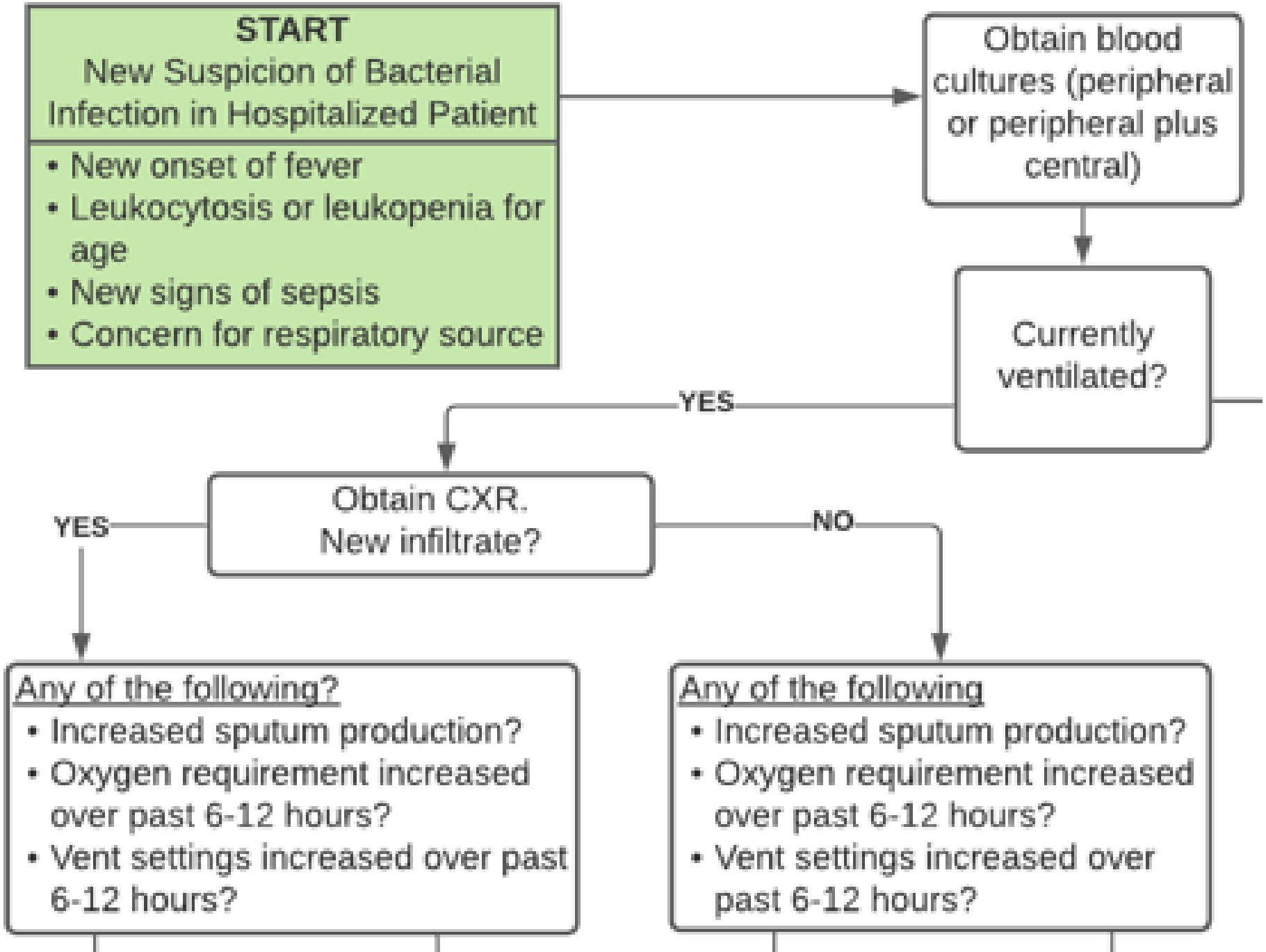
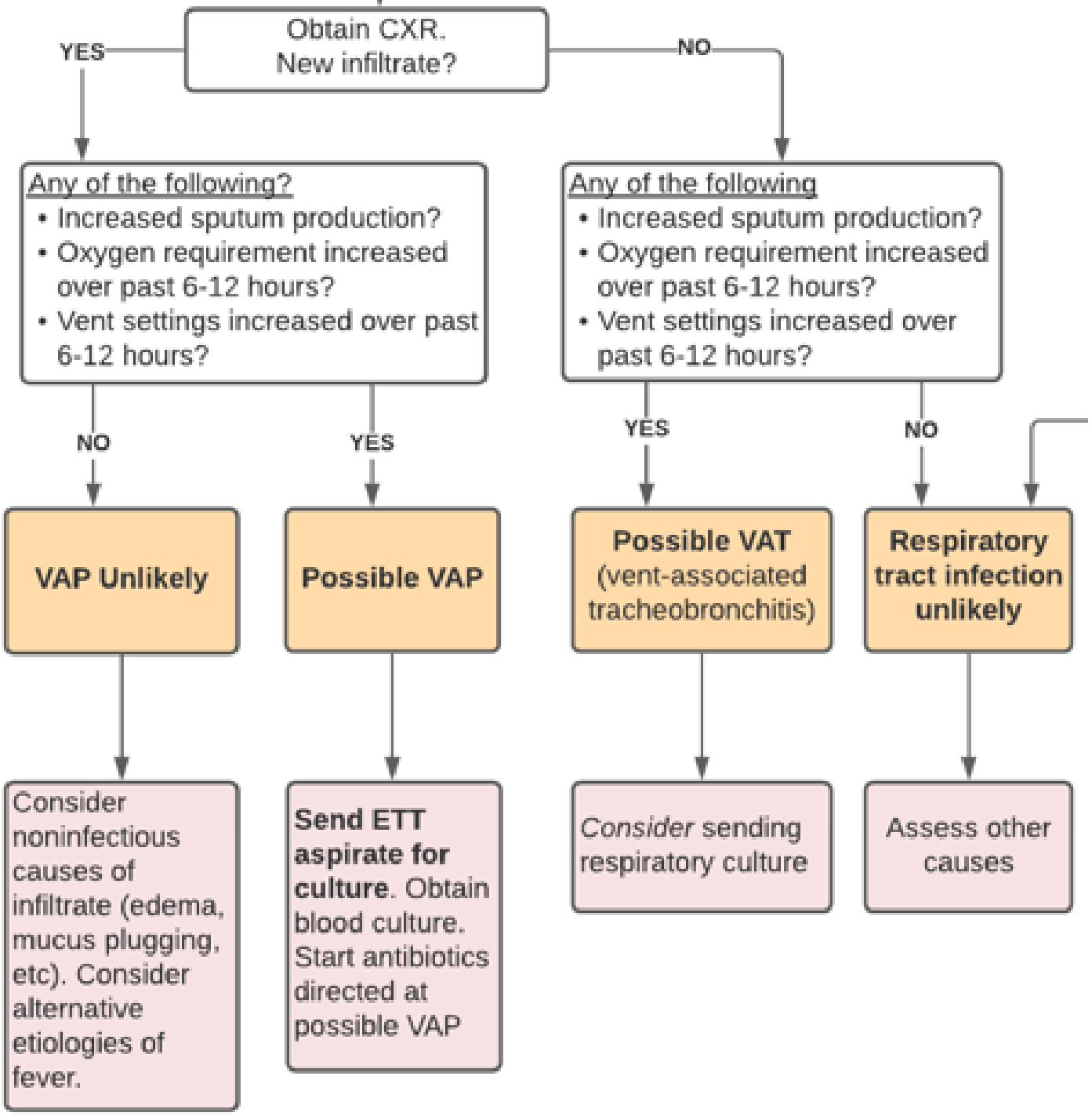
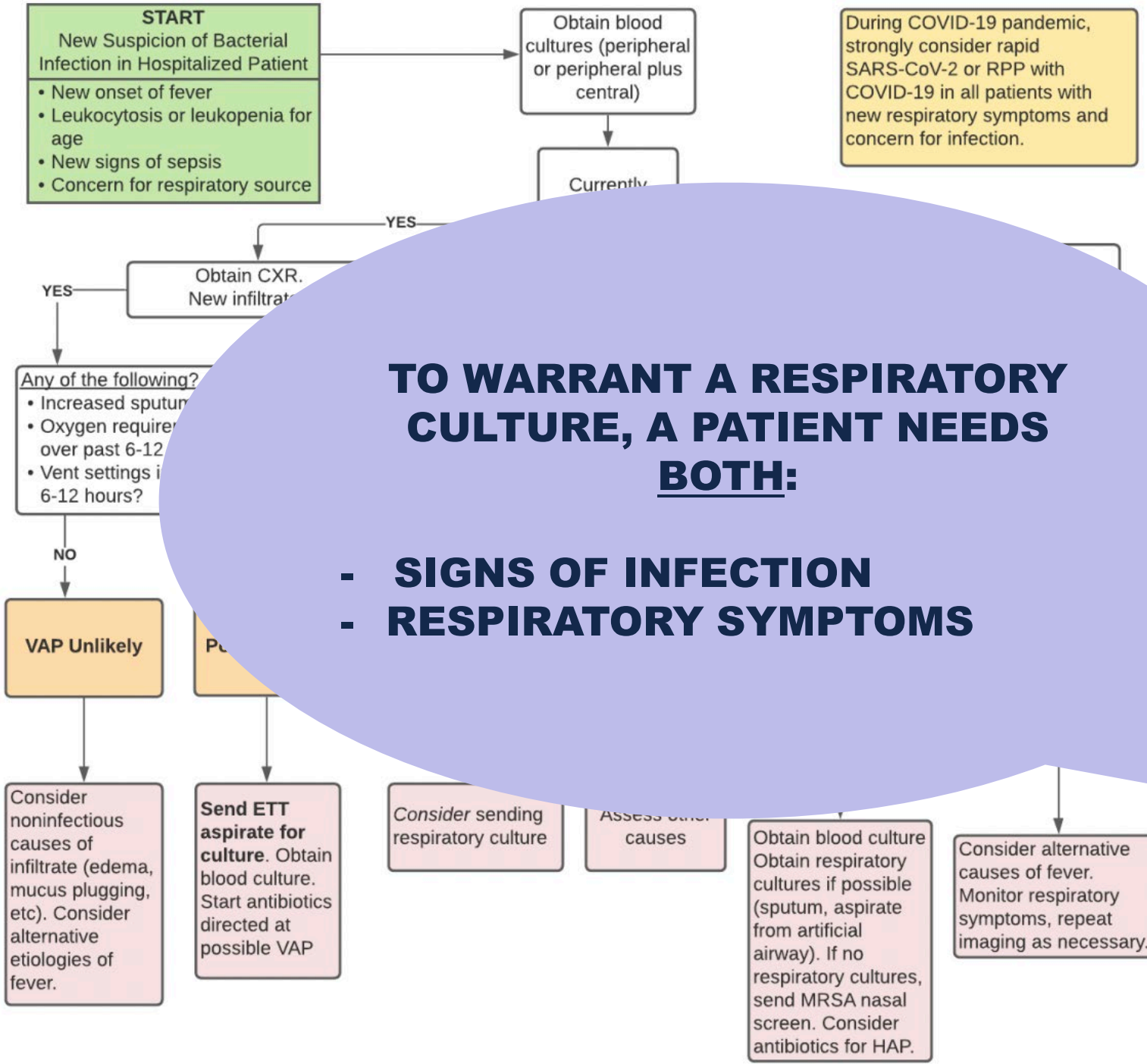
- Education provided to PICU before launch
- Audited every respiratory culture sent from patients in PICU
  - 9/1/21-12/31/22 (15 months)
    - 3 months pre- and 12 months post-intervention.
  - Cultures assessed as guideline-concordant or –discordant
    - Systemic signs of illness (fever, leukocytosis, etc) PLUS respiratory symptoms (persistently increased PEEP/FiO2, CXR changes, purulent ETT output)
- Periodic feedback to PICU providers

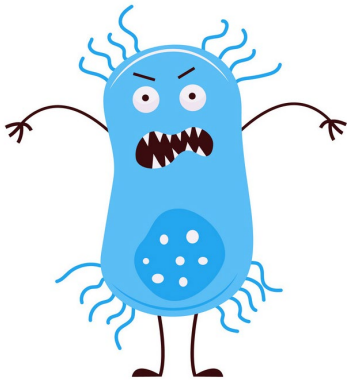

START
New Suspicion of Bacterial Infection in Hospitalized Patient
• New onset of fever
• Leukocytosis or leukopenia for age
• New signs of sepsis
• Concern for respiratory source
Obtain blood cultures (peripheral or peripheral plus central)
Currently ventilated?
YES
Obtain CXR.
New infiltrate?
YES
NO
Any of the following?
• Increased sputum production?
• Oxygen requirement increased over past 6-12 hours?
• Vent settings increased over past 6-12 hours?
Any of the following
• Increased sputum production?
• Oxygen requirement increased over past 6-12 hours?
• Vent settings increased over past 6-12 hours?


Obtain CXR.
New infiltrate?
YES
NO
Any of the following?
• Increased sputum production?
• Oxygen requirement increased over past 6-12 hours?
• Vent settings increased over past 6-12 hours?
Any of the following
• Increased sputum production?
• Oxygen requirement increased over past 6-12 hours?
• Vent settings increased over past 6-12 hours?
NO
YES
YES
NO
VAP Unlikely
Possible VAP
Possible VAT (vent-associated tracheobronchitis)
Respiratory tract infection unlikely
Consider noninfectious causes of infiltrate (edema, mucus plugging, etc). Consider alternative etiologies of fever.
Send ETT aspirate for culture. Obtain blood culture. Start antibiotics directed at possible VAP
Consider sending respiratory culture
Assess other causes



TO WARRANT A RESPIRATORY CULTURE, A PATIENT NEEDS BOTH:

- **SIGNS OF INFECTION**
- **RESPIRATORY SYMPTOMS**



Proportion of Respiratory Cultures that were Guideline-Concordant

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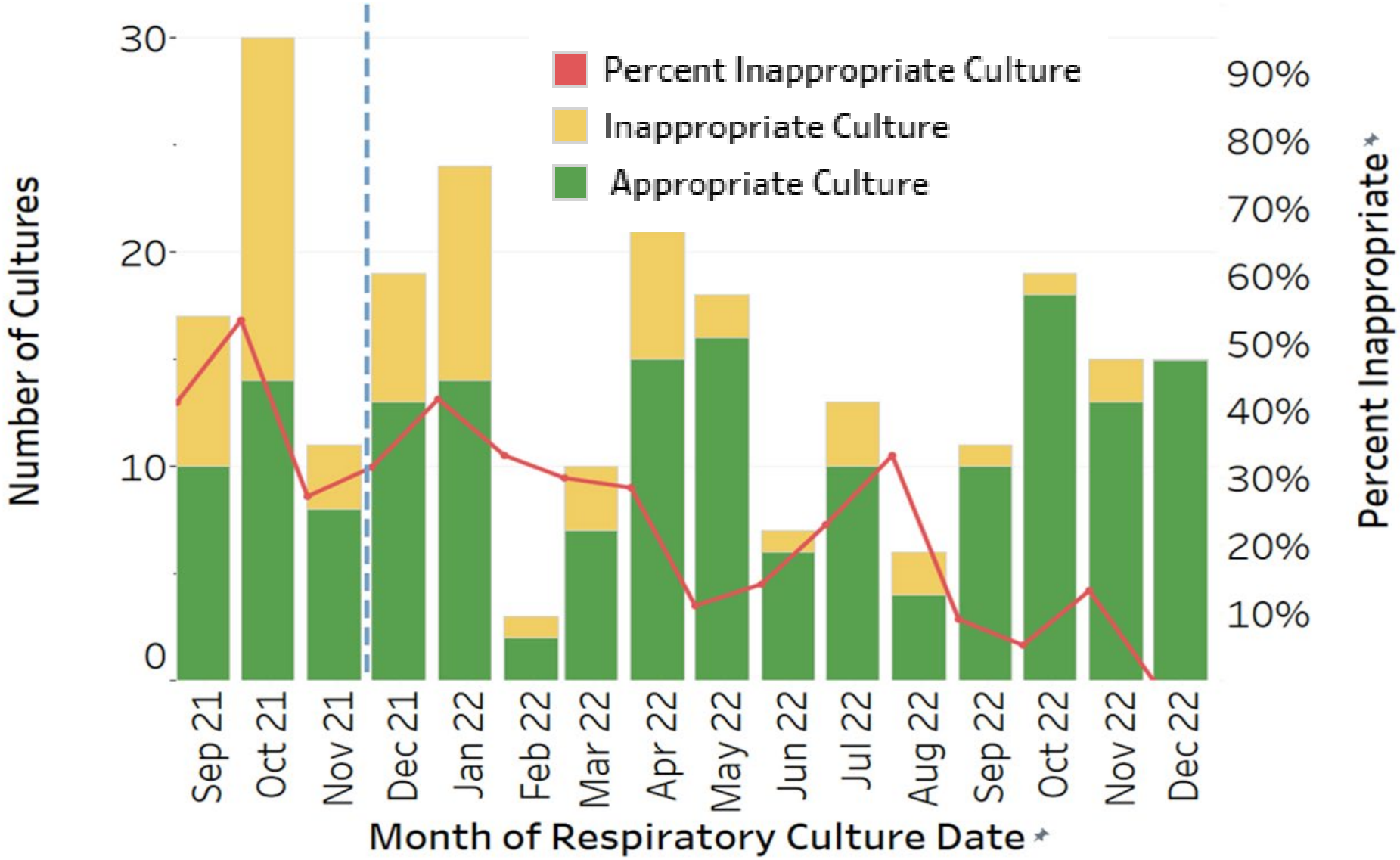

Results of Guideline-Discordant Cultures

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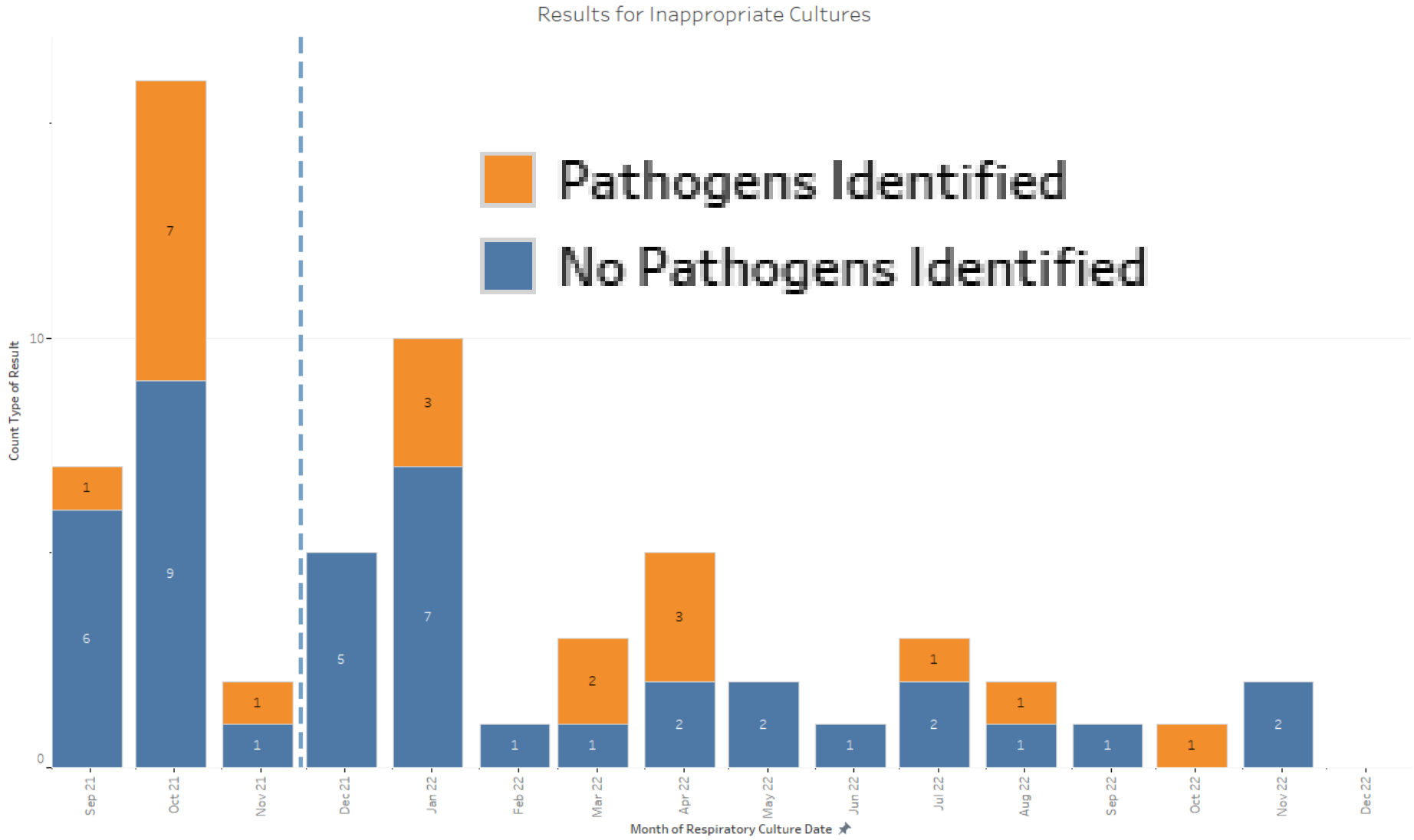
Orange: cultures that grew pathogens

Blue: cultures that did not grow



The plot of count of Combined Type of Resp Culture Result (copy 2) for Respiratory Culture Date Month. Color shows details about Combined Inappropriate Type of Resp Culture Result (copy). The marks are labeled by count of Combined Type of Resp Culture Result (copy 2). The data is filtered on Location, which keeps PCICU and PICU. The view is filtered on Combined Inappropriate Type of Resp Culture Result (copy), which excludes Null.

Guideline-Discordant Cultures Treated with Antibiotics

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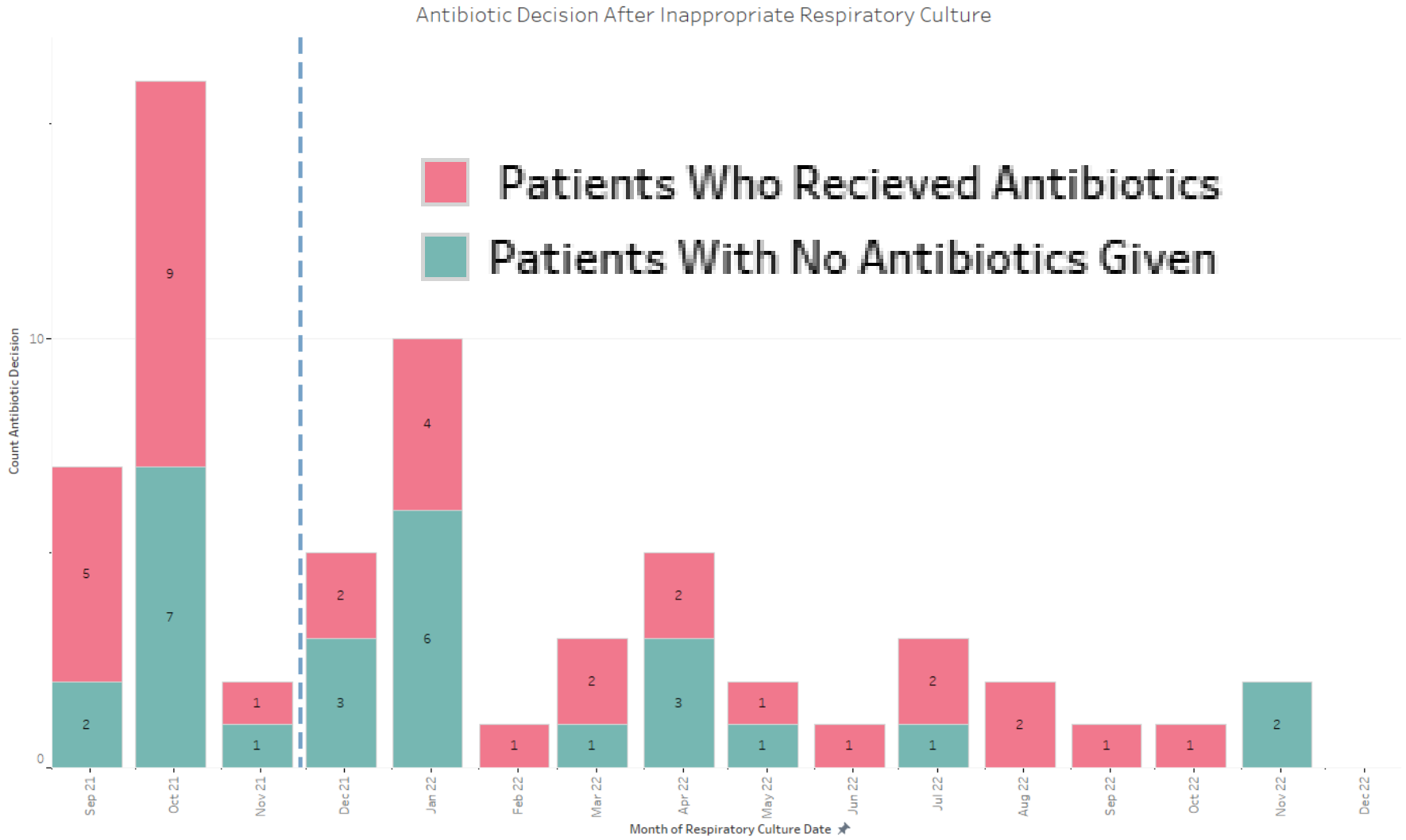
Salmon: Number of guideline-discordant cultures treated with antibiotics



The plot of count of Were Antibiotics Given For Patients With Inappropriate Cultures? for Respiratory Culture Date Month. Color shows details about Were Antibiotics Given For Patients With Inappropriate Cultures?. The marks are labeled by count of Were Antibiotics Given For Patients With Inappropriate Cultures?. The data is filtered on Location, which keeps PCICU and PICU. The view is filtered on Were Antibiotics Given For Patients With Inappropriate Cultures?, which excludes Null.

Cultures Most Often "Inappropriate" When:

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- Recent respiratory culture (<72 hours) was negative or not processed
- Recent respiratory culture (7-10 days) was positive and treated
- No blood culture sent
- Limited systemic signs of infection
- Respiratory status stable or improving
  - "Send LRCx" and "Extubate today" in same note
- Resp culture sent, antibiotics started only when it returned positive

Challenging Scenarios

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- Chronically colonized tracheostomy tubes
- Constantly changing CXRs
  - “Shifting atelectasis,” pulmonary edema
- ECMO – difficult to assess systemic signs, respiratory status
- Suctioning sputum that is:
  - “thick” and/or “tan”

Culture Interpretation

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- Always consider a pathogen:
  - *Streptococcus pneumoniae*, *Haemophilus influenzae*, Group A Strep
  - Probably *Moraxella catarrhalis*
- Almost always a pathogen:
  - Staph aureus (occasionally a colonizer)
  - Enteric Gram-negative rods (*E coli*, *Klebsiella, Enterobacter, Serratia,* etc)
    - *Serratia* tends to be very persistent after treatment
- Often a pathogen, often a colonizer
  - *Pseudomonas aeruginosa*, *Acinetobacter*
- Usually a colonizer, sometimes a pathogen
  - *Stenotrophomonas maltophilia*
- Respiratory Tract Non-Pathogens
  - *Candida* spp., *Neisseria* (non-*meningitidis* or *gonorrhoeae*), Coag-negative Staph, etc.

Diagnostic Stewardship Recommendations

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- Scenarios
  - C-diff, urine cultures, respiratory cultures, blood cultures, respiratory pathogen panels…
- Use diagnostic testing only when pre-test probability is sufficiently high
- Encourage high-specificity diagnostic sampling
  - No blood cultures off PIVs, arterial lines, etc.
  - Urine sampling from indwelling urinary catheters
  - Etc

Clinical Practice Recommendations for Frontline Clinicians

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- Be thoughtful about respiratory cultures
  - Signs of infection PLUS signs referring to respiratory tract
- Be skeptical when the patient grows the same thing as before
  - Very difficult to discern colonization and true infection
- When appropriate, bronchoscopy is more accurate and often therapeutic
- Reasonable to be more aggressive with cultures when:
  - Immunocompromised (Hem/Onc, transplant patients, etc)
  - Infants, especially under 3 months of age
- If suspicion for infection and intubating, send a culture!
  - (Unless you know it's not pneumonia, this is rare)
- Use short courses for "tracheitis" – 5 days maximum

Respiratory Culture Stewardship

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- Design diagnostic protocols that require systemic *and* respiratory symptoms before obtaining respiratory cultures
- Emphasize higher-specificity specimens (BAL vs ETT aspirate)
- Avoid repeat culturing after recent positive
- Make sure your lab is:
  - Rejecting low-quality samples
  - Not naming OP flora species

References

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Questions?