VAP

DIAGNOSING AND MANAGING
VENTILATOR-ASSOCIATED PNEUMONIA

A SELF STUDY
COURSE FOR CREDIT

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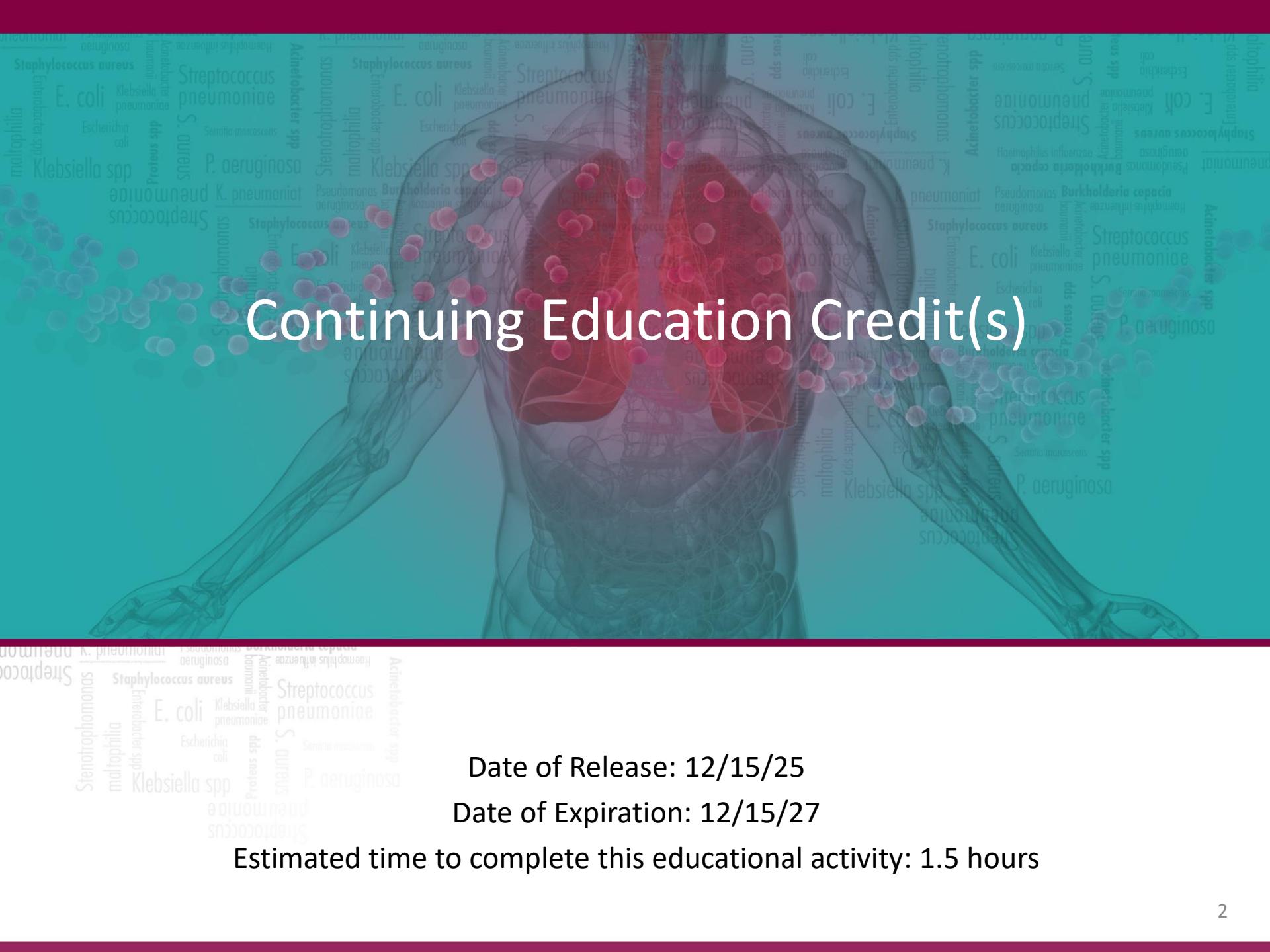
Continuing Education Credit(s)

Date of Release: 12/15/25

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Estimated time to complete this educational activity: 1.5 hours

Continuing Education Credit(s)

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Disclosures

There are no disclosures for this learning activity.

Statement of Need

Ventilator-associated pneumonia (VAP) is a subtype of hospital-acquired pneumonia (HAP) which occurs in people receiving mechanical ventilation.

Ventilator-associated pneumonia is difficult to diagnose and surveillance is curtailed by the subjectivity of many components of the surveillance definition.

This learning activity will describe how bedside analyte testing may assist with therapeutic decision-making and improve the prognosis for patients with VAP.

Intended Audience

The primary audience for this learning activity is healthcare professionals (physicians, nurses, respiratory therapists, and laboratory professionals) involved in the testing, diagnosis, treatment, and management of ventilator-associated pneumonia and who are interested in the role of biomarkers to improve care for these patients.

Learning Objectives

After completing this activity, the participant should be able to:

1. Identify the risk factors of VAP.

2. Review the epidemiology of VAP.

3. Describe guidelines and recommendations used in the diagnosis and treatment of VAP.

4. Identify the benefits and limitations of point-of-care testing in VAP patients.

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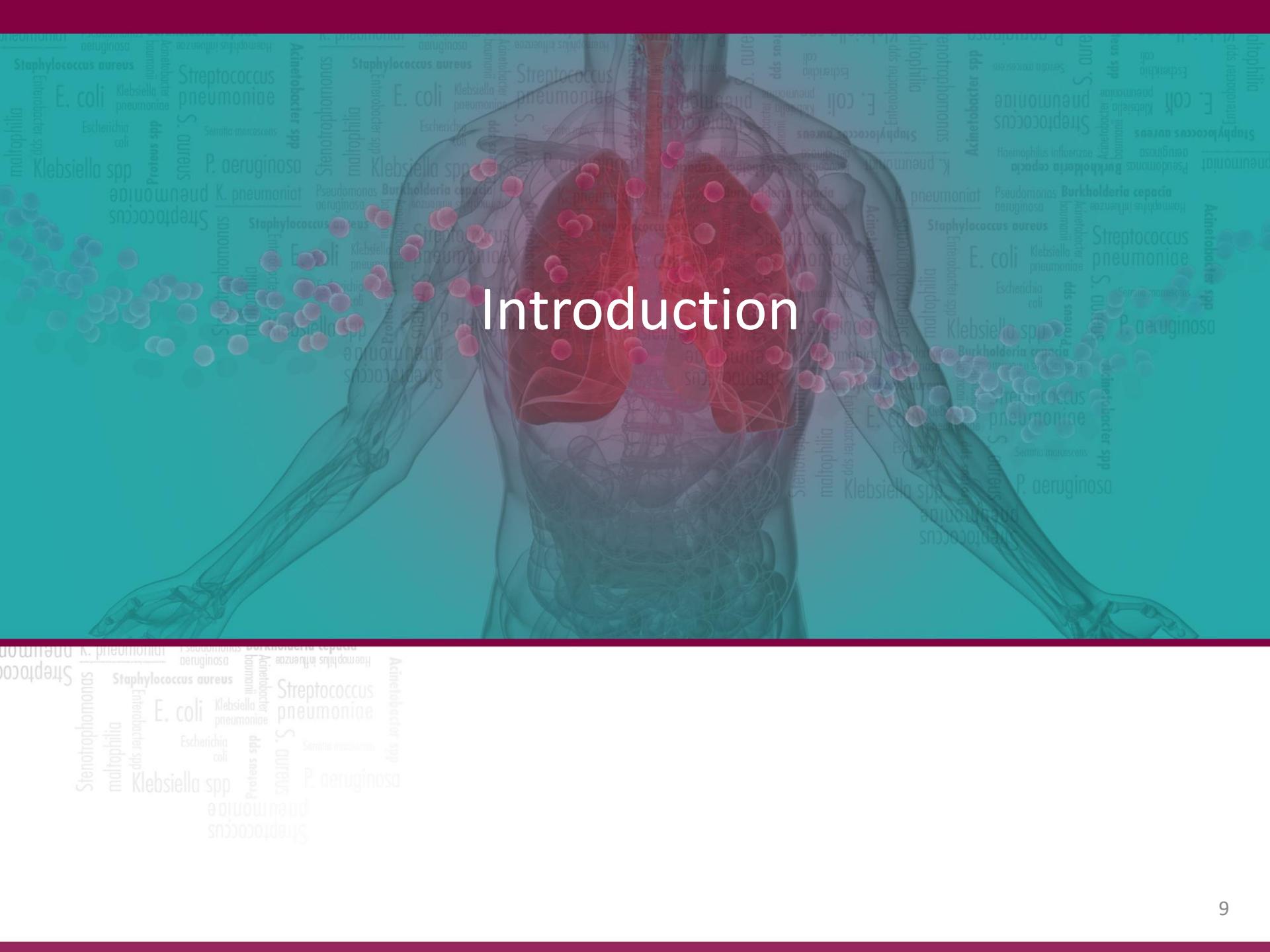
Introduction

Ventilator-Associated Pneumonia

- Ventilator-associated pneumonia (VAP) can develop in any patient on a ventilator

- VAP is one of the most common of the hospital-acquired infections (HAI) in the intensive care unit (ICU)

**Intubation
or mechanical ventilation**

| 24 hrs | 48 hrs | 72 hrs |

Onset of VAP

Papazian L, et al. *Intens Care Med*. 2020;1-19.
Kohbodi GNA, Rajasurya V, Noor A. Ventilator-Associated Pneumonia. [Updated 2023 Sep 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507711/

# Ventilator-Associated Pneumonia: Characterization

Intubation or mechanical ventilation

24 hrs

48 hrs

72 hrs
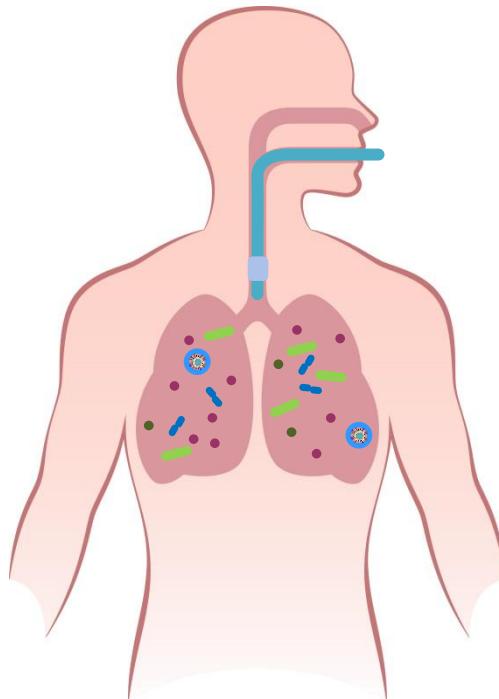
Onset of VAP

- Presence of a new or progressive infiltrate
- Signs of systemic infection (fever, altered white blood cell count)
- Changes in sputum characteristics
- Detection of a causative agent

Yao J, et al. *Medicine*. 2020;99:e19716.

# National Healthcare Safety Network Definitions

Ventilator-Associated Event (VAE)	Criteria
Ventilator-Associated Condition (VAC) (Baseline period + ≥ 1 respiratory criteria)	Baseline Period • ≥ 2 calendar days of stable or decreasing daily minimum FiO2 or PEEP values Respiratory Criteria • ≥ 0.20 increase in FiO_2 • ≥ 3 cm H_2O increase in PEEP
Infection-Related Ventilator-Associated Complication (IVAC) (Temperature OR WBC criteria + antimicrobial agent criteria)	• Temperature < 36 or > 38°C • WBC ≤ 4,000 or ≥ 12,000 cells/mm • One or more new antimicrobial agent required and continued for ≥ 4 days
Possible Ventilator-Associated Pneumonia (PVAP) (VAC + IVAC criteria + ≥ 1 PVAP criteria)	• Positive culture from either ETA ≥ 10^5 CFU/mL, BAL ≥ 10^4 CFU/mL, lung tissue ≥ 10^4 CFU/mL, or protected specimen brush ≥ 10^4 CFU/mL WITHOUT purulent respiratory secretions • Purulent respiratory secretions + positive identification from sputum, ETA, BAL, lung tissue, protected specimen brush • Organism identified from pleural fluid, lung histopathology, diagnostic test for *Legionella* species, or diagnostic test on respiratory secretions for influenza, respiratory syncytial virus, adenovirus, parainfluenza, rhinovirus, human metapneumovirus, coronavirus

FiO_2: fraction of inspired oxygen; PEEP: positive end-expiratory pressure; ETA: endotrachial aspiration; BAL: bronchoalveolar lavage

2025 NHSN Ventilator-Associated Event Checklist. CDC. January 2025.

Risk Factors for VAP
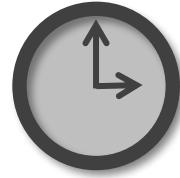
- Duration of intubation
- Reintubation

- Trauma admission
- Tracheostomy
- Enteral feeding/NG tube
- COPD

- Prior use of antibiotics
- Neuromuscular blockers
- H2 blockers

ICU
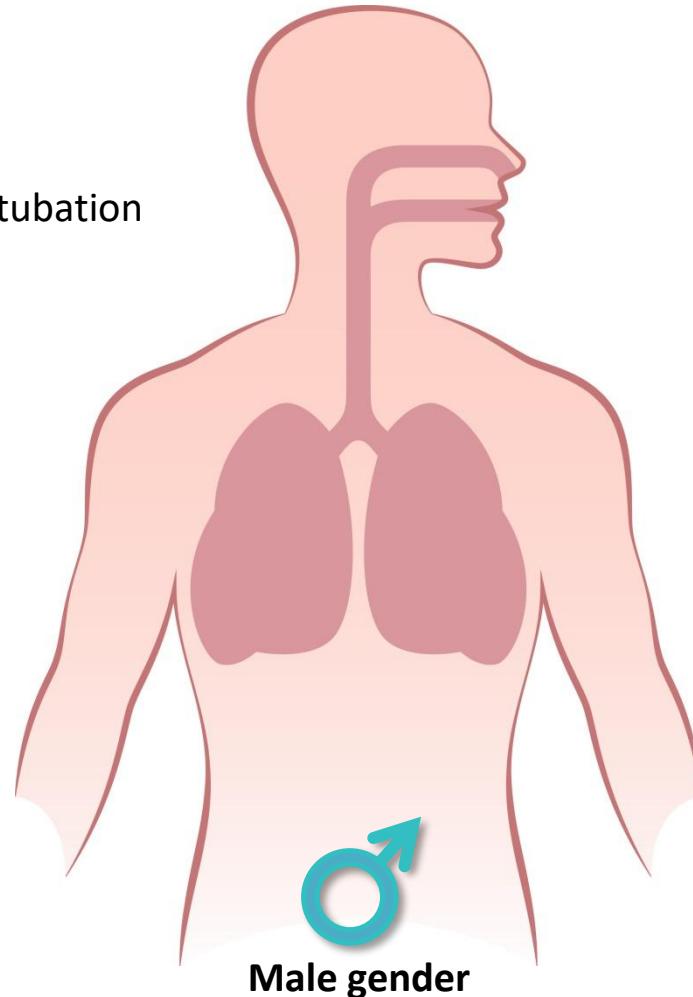
- Severity of illness
- Supine positioning

Male gender

Ochoa P, et al. *BMC Pulm Med*. 2025 Oct 6;25(1):453.
Papazian L, et al. *Intens Care Med*. 2020;1-19.

Methods of Contamination
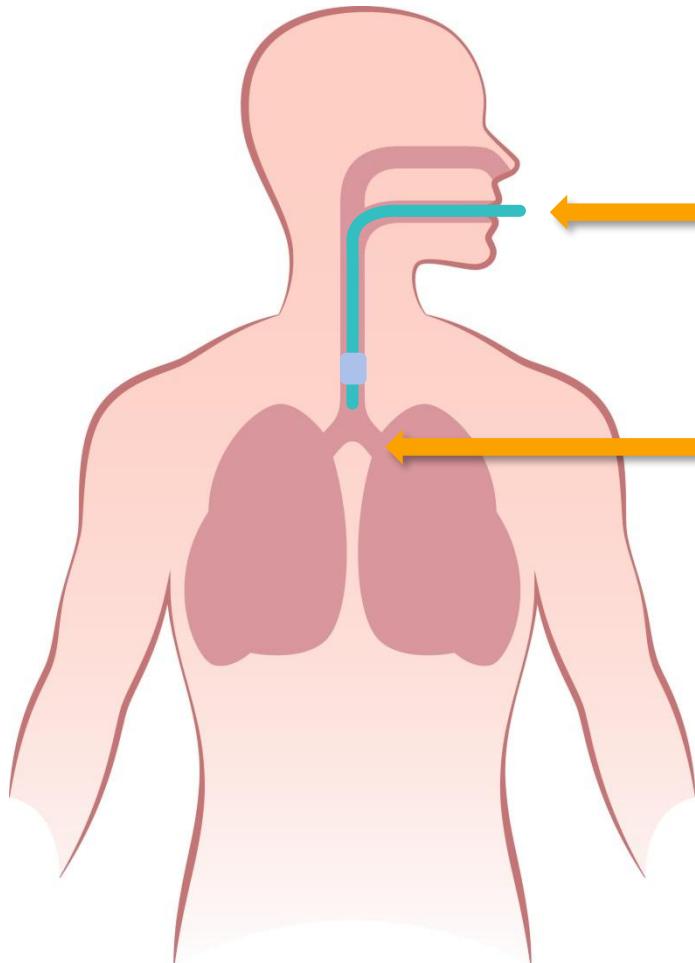
- Inoculation during the intubation process

- Contaminated aerosol or ventilator condensate

- Endotracheal tube biofilm

- Aspiration from sinus, oropharyngeal, or gastric fluids around the tube

Póvoa HC, et al. *Infect Dis Ther*. 2020;9(3):417–420.

Microbe Types

Bacteria

Gram negative bacteria are the most common type seen in VAP

May be gram positive during MRSA outbreak

Viruses

COVID-19 associated, but other viral causes are not as common as bacterial causes
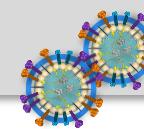
Fungi

Occasionally seen in immunodeficient patients, rarely causative

Monomicrobial

Only one pathogen type

Polymicrobial

Most common VAP infection type
Multiple pathogens

Póvoa HC, et al. *Infect Dis Ther*. 2020;9(3):417–20.
Blonz G, et al. *Crit Care*. 2020;25:72.

Hospital Costs

- Due to increased length of stay and ventilator time, hospital costs are also increased with VAP

- Incremental costs associated with VAP have been estimated at between $25,000 and $28,000 per diagnosis

$1.45 billion annually

VAP increases medical costs.

Ladbrook E, et al. *J Infect Control*. 2020. https://doi.org/10.1016/j.ajic.2020.11.027.
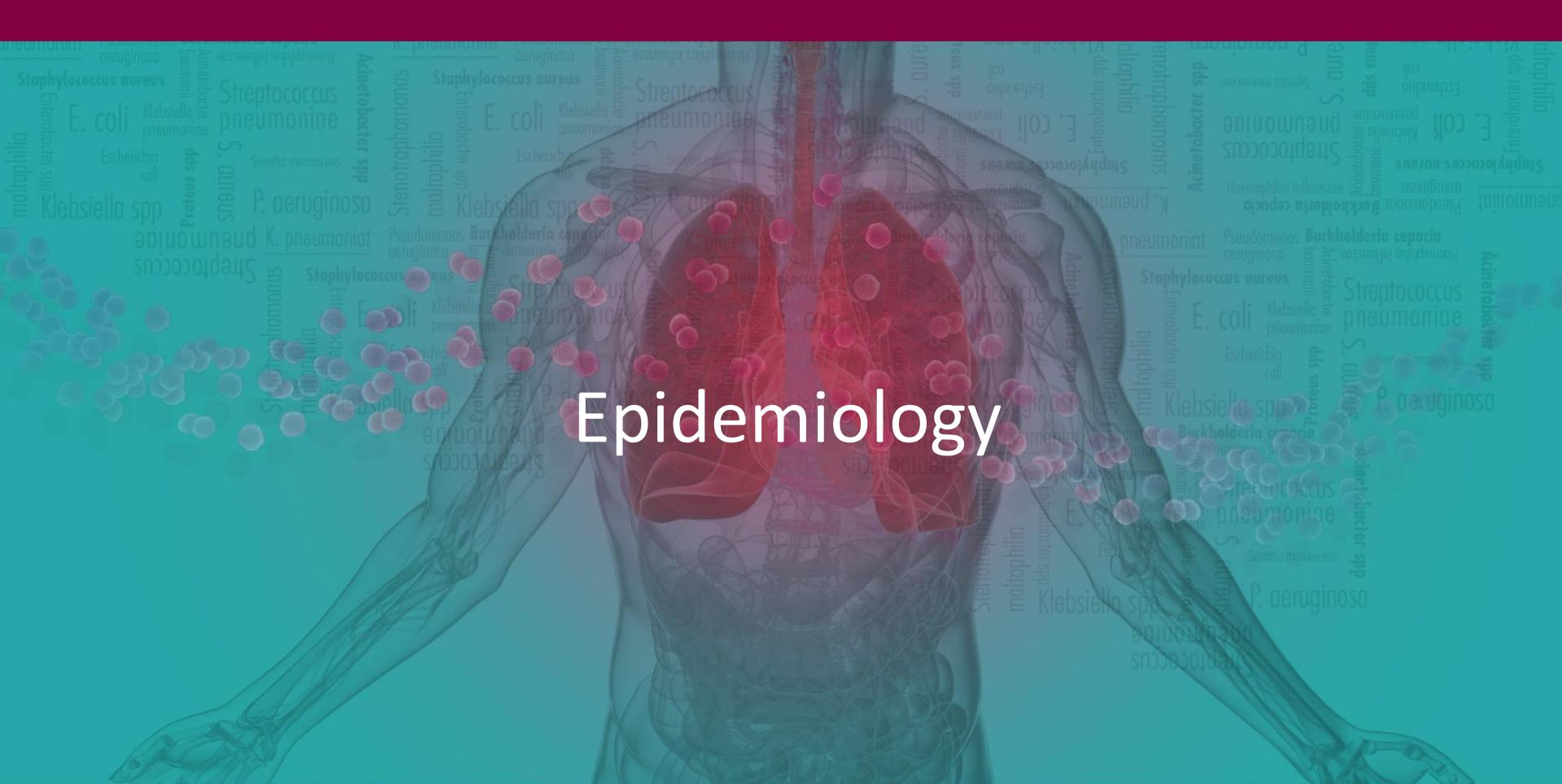
Epidemiology

Incidence of VAP

- 300,000 patients are ventilated each year in the U.S.

- 0.1 to 4.4 cases per 1,000 ventilation days

- Up to 24.5/1,000 in cancer patients

- 18% of trauma patients
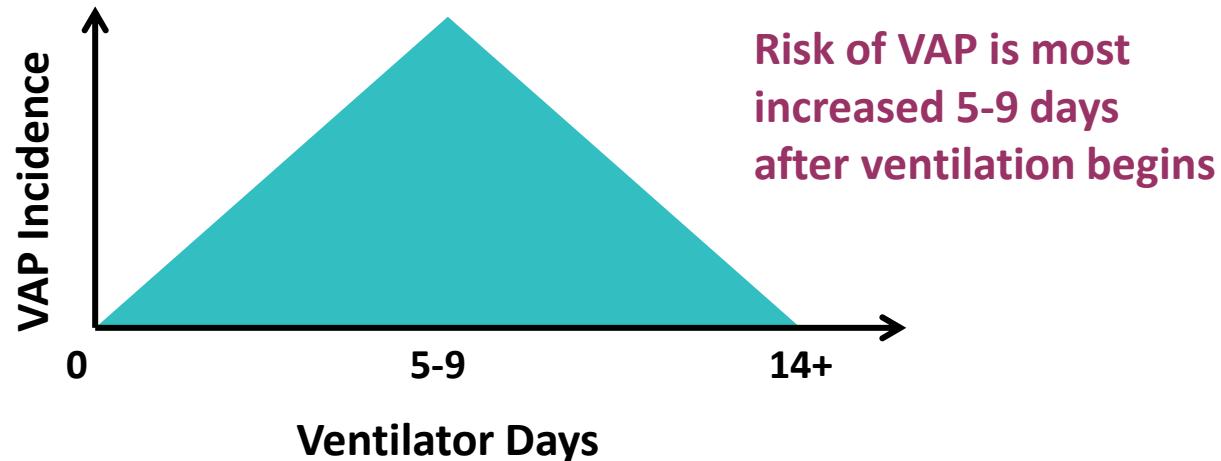
Risk of VAP is most increased 5-9 days after ventilation begins

VAP Incidence — Ventilator Days (0, 5-9, 14+)

Papazian L, et al. *Intens Care Med*. 2020;1-19.
https://www.cdc.gov/nhsn/pdfs/pscmanual/10-vae_final.pdf. Accessed May 8, 2021.

VAP Odds Ratios Increase With Comorbidities

Risk Factors	# Studies	Heterogeneity I^2 (%)	Pooled OR/MD (95% CI)	*p*
Patient-related factors				
Gender (male)	16	0	OR 1.30 (1.18, 1.44)	**< 0.05**
COPD	10	75	OR 1.52 (1.10, 2.09)	**< 0.05**
Impaired consciousness at hospital admission	5	83	OR 3.14 (1.28, 7.69)	**< 0.05**
Poisoning	6	0	OR 1.04 (0.70, 1.53)	0.86
Smoking	5	0	OR 0.97 (0.78, 1.21)	0.79
Use of corticosteroids	13	52	OR 1.22 (0.99, 1.51)	0.06
Diabetes mellitus	10	65	OR 1.0 (0.79, 1.28)	0.97
Cardiac disease	7	38	OR 0.98 (0.76, 1.27)	0.89
Age	14	84	MD 0.04 (−1.57, 1.65)	0.96
Trauma	7	0	OR 1.47 (1.12, 1.93)	**< 0.05**
Chronic kidney disease	6	24	OR 0.88 (0.68, 1.13)	0.31
APACHE II	7	90	MD 2.01 (0.60, 3.43)	< 0.05
SAPS II	4	85	MD 0.70 (−2.84, 4.23)	0.7

OR Odds ratio, MD Mean difference, APACHE Acute Physiology And Chronic Health Evaluation, SAPS II Simplified Acute Physiology Score II, COPD Chronic Obstructive Pulmonary Disease, Values in bold indicate statistical significance

Ochoa P, et al. *BMC Pulm Med*. 2025 Oct 6;25(1):453.

VAP Odds Ratios Increase With Comorbidities

Risk Factors	# Studies	Heterogeneity I^2 (%)	Pooled OR/MD (95% CI)	p
Treatment-related factors				
H2 blocker	6	0	OR 2.24 (1.50, 3.37)	**< 0.05**
Tracheostomy	11	77	OR 3.44 (2.00, 5.92)	**< 0.05**
Prior antibiotic treatment	5	57	OR 1.52 (1.08, 2.15)	**< 0.05**
Reintubation	6	77	OR 5.11 (2.29, 11.42)	**< 0.05**
Enteral feeding	6	57	OR 4.73 (2.54, 8.78)	**< 0.05**
Nasogastric tube	5	20	OR 2.94 (1.56, 5.53)	**< 0.05**
Neuromuscular blocker use	3	0	OR 1.30 (1.13, 1.49)	**< 0.05**
Days of intubation prior to VAP	5	98%	MD 6.20 (1.09, 11.30)	**< 0.05**
Emergency intubation	3	74	OR 2.39 (0.36, 15.67)	0.36
Previous surgery	10	13	OR 1.09 (0.88, 1.34)	0.43

OR Odds ratio, MD Mean difference, Values in bold indicate statistical significance

Ochoa P, et al. *BMC Pulm Med*. 2025 Oct 6;25(1):453.

Mortality

- Crude mortality rates for VAP are around 10-40%

- In acute respiratory distress syndrome (ARDS), crude mortality rates for VAP are 42% compared to 31% in patients without VAP

Papazian L, et al. *Intens Care Med*. 2020;1-19.
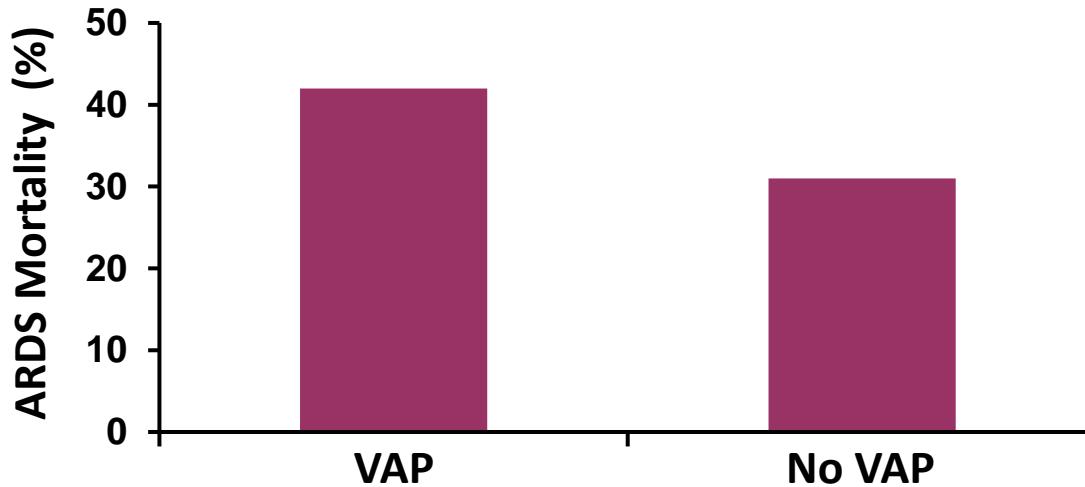
Factors Associated With VAP Mortality

Type of Patient
- Surgical
- Trauma
- Respiratory distress syndrome

Organisms
- Mono versus polymicrobial
- Gram positive vs. Gram negative
- *Pseudomonas, Acinetobacter, E. coli, Klebsiella*

Hospital Factors
- Diagnostic criteria
- Treatments available
- Methods for treating resistant microbes

Yao J, et al. *Medicine*. 2020;99:e19716.
Papazian L, et al. *Intens Care Med*. 2020;1-19.
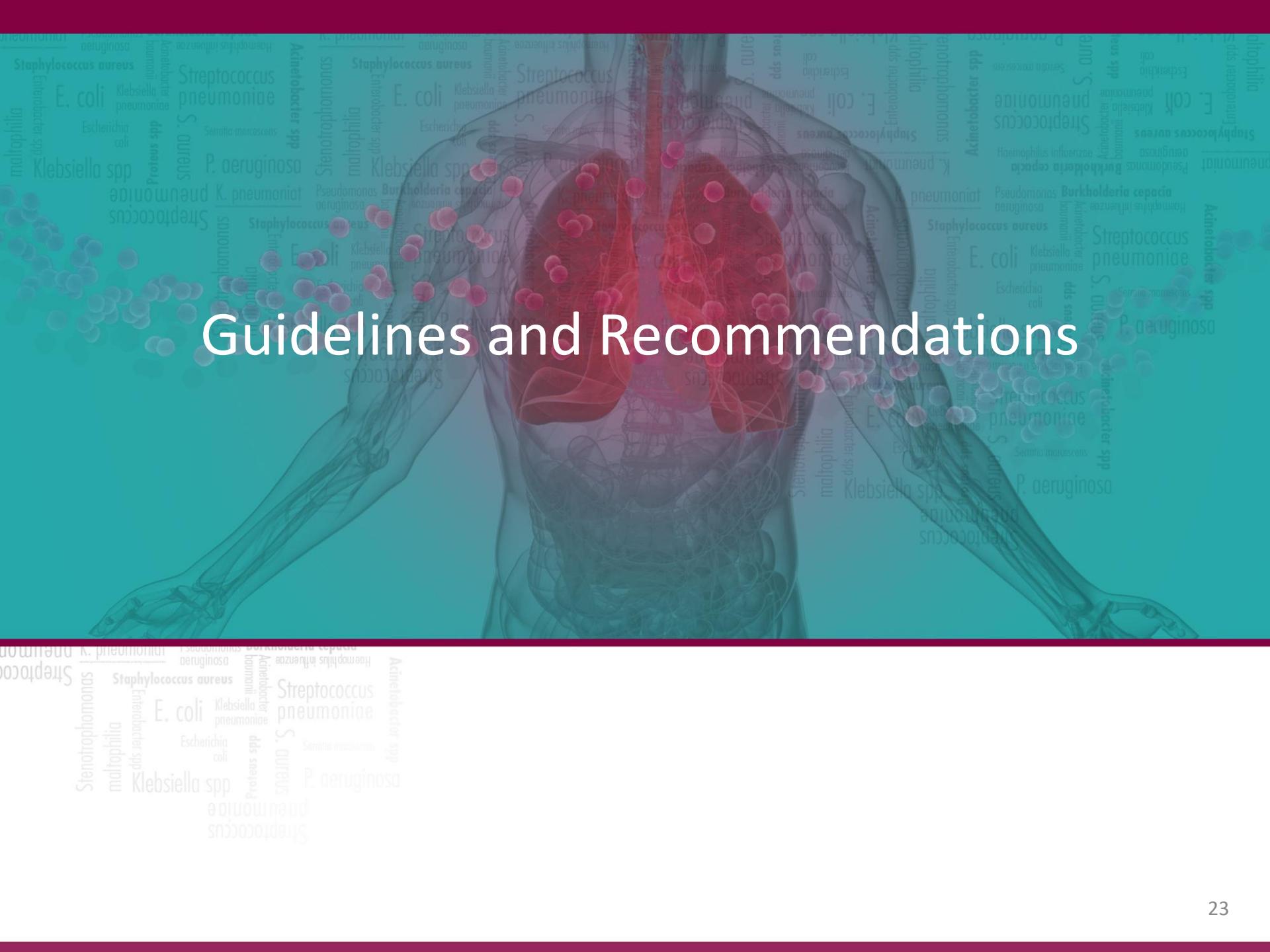
Guidelines and Recommendations

Guidelines

- In 2011 the CDC convened a Working Group for VAP and other ventilator-associated events (VAE)

- VAE surveillance definition algorithm implemented in 2013
  - Based on objective, streamlined, and potentially automatable criteria that identify a broad range of conditions and complications occurring in mechanically-ventilated adult patients

- There are three definition tiers within the VAE algorithm
  - Ventilator-Associated Condition (VAC)
  - Infection-related Ventilator-Associated Complication (IVAC)
  - Possible and probable VAP

CDC. National Healthcare Safety Network. 2025. https://www.cdc.gov/nhsn/PDFs/pscManual/10-VAE_FINAL.pdf.

CDC VAE Algorithm

Patient has a baseline period of stability or improvement on the ventilator, defined by ≥ 2 calendar days of stable or decreasing daily minimum* FiO_2 or PEEP values. The baseline period is defined as the 2 calendar days immediately preceding the first day of increased daily minimum PEEP or FiO_2.

*Daily minimum defined by lowest value of FiO_2 or PEEP during a calendar day maintained for at least 1 hour.

After a period of stability or improvement on the ventilator, the patient has at least one of the following indicators of worsening oxygenation:

1) Increase in daily minimum* FiO_2 of ≥ 0.20 (20 points) over the daily minimum FiO_2 in the baseline period, sustained for ≥ 2 calendar days.

2) Increase in daily minimum* PEEP values of ≥ 3 cm H_2O over the daily minimum PEEP in the baseline period†, sustained for ≥ 2 calendar days.

*Daily minimum defined by lowest value of FiO_2 or PEEP in a calendar day maintained ≥ 1 hour.

†Daily minimum PEEP values of 0-5 cm H_2O are equivalent for the purposes of surveillance.

Ventilator-Associated Condition

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, the patient meets both of the following two criteria:

1) Temperature > 38° C or < 36° C, OR white blood cell count ≥ 12,000 cells/mm³ or ≤ 4,000 cells/mm³ AND

2) A new antimicrobial agent(s) is started and is continued for ≥ 4 qualifying antimicrobial days.

Infection-related Ventilator-Associated Complication

CDC VAE Algorithm

Infection-Related Ventilator-Associated Complication

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met:

1) Criterion 1: Positive culture of one of the following specimens, meeting quantitative or semi-quantitative thresholds, without requirement for purulent respiratory secretions:

Endotracheal aspirate (ETA), ≥ 10^5 CFU/mL or corresponding semi-quantitative result; bronchoalveolar lavage (BLA), ≥ 10^4 CFU/mL or corresponding semi-quantitative result; lung tissue (LT) , ≥ 10^4 CFU/g or corresponding semi-quantitative result; protected specimen brush (PSB), ≥ 10^3 CFU/mL or corresponding semi-quantitative result

1) Criterion 2: Purulent respiratory secretions (secretions from the lungs, bronchi, or trachea that contain ≥ 25 neutrophils and ≤ 10 squamous epithelial cells per low power field [lpf, x100]) plus organism identified from one of the following specimens (to include qualitative culture, or quantitative/semi-quantitative culture without sufficient growth to meet criterion #1): Sputum, ETA, BLA, LT, PSB

2) Criterion 3: One of the following positive tests:

Organism identified from pleural fluid (where specimen was obtained during thoracentesis or initial placement of chest tube and NOT from an indwelling chest tube); lung histopathology, defined as:

1) abscess formation or foci of consolidation with intense neutrophil accumulation in bronchioles and alveoli;

2) evidence of lung parenchyma invasion by fungi (hyphae, pseudohyphae or yeast forms);

3) evidence of infection with the viral pathogens listed below based on results of immunohistochemical assays, cytology, or microscopy performed on lung tissue; diagnostic test for *Legionella* species; diagnostic test on respiratory secretions for influenza virus, respiratory syncytial virus, adenovirus, parainfluenza virus, rhinovirus, human metapneumovirus, coronavirus

Possible Ventilator-Associated Pneumonia

CDC. National Healthcare Safety Network. 2025. https://www.cdc.gov/nhsn/PDFs/pscManual/10-VAE_FINAL.pdf.

Guidelines

Society for Healthcare Epidemiology of America/ Infectious Diseases Society of America

Section 1: Rationale and Statement of Concern
Section 2: Background on detection of VAP, VAE, and NV-HAP
Section 3: Background on prevention of VAP, VAE, and NV-HAP
Section 4: Recommended strategies to prevent VAP, VAE, and NV-HAP
Section 5: Performance Measures
Section 6: Implementation of VAP, VAE, and NV-HAP prevention strategies

VAP, ventilator-associated pneumonia; VAE, ventilator-associated event;
NV-HAP, non-ventilator-associated hospital-acquired pneumonia

Klompas M, et al. *Infect Control Hosp Epidemiol*. 2022 Jun;43(6):687-713.

Recommendations: VAP Surveillance

Hospitals are advised to conduct active surveillance for VAE, using CDC definitions and surveillance protocols. The CDC's VAE module requires surveillance for all definition tiers (VAC, IVAC, possible VAP, and probable VAP).

1. The CDC recommends that hospitals conduct surveillance for VAE in lieu of VAP using CDC definitions and surveillance protocols.

2. The VAE definitions are amenable to partial or complete automation using electronic data. Facilities seeking to automate VAE detection should work with their information technology personnel and/or electronic health record vendor(s).

3. Infection preventionists should work with their critical care, respiratory therapy, and/or information technology staff to develop efficient means to gather and aggregate ventilator data (daily minimum PEEP and daily minimum F_{io2}) from all patients ventilated for greater than or equal to 4 days. Temperature, white blood cell count, and antibiotic exposure data are needed only for the subset of patients who fulfill VAC criteria to determine if they fulfill IVAC criteria. Pulmonary specimen Gram stains and microbiology test results are required only for the subset of patients who meet IVAC criteria to determine if they fulfill possible or probable VAP criteria.

Klompas M, et al. *Infect Control Hosp Epidemiol*. 2022 Jun;43(6):687-713.

Recommendations: VAP Prevention

Basic practices to prevent VAP and other VAE in adult patients: interventions with little risk of harm that decrease duration of mechanical ventilation, length of stay, mortality, and/or costs.

A. **Avoid intubation if possible**
   1. Use high-flow nasal oxygen or non-invasive positive pressure ventilation (NIPPV) as appropriate whenever safe | and feasible (Quality of Evidence: HIGH)
   2. Placing nonintubated patients with COVID-19 acute hypoxemic respiratory failure in the prone position may lower the risk of intubation compared to standard care (Quality of Evidence: MODERATE)

B. **Minimize sedation**
   1. Minimize sedation of ventilated patients whenever possible (Quality of Evidence: HIGH)
   2. Preferentially use multimodal strategies and medications other than benzodiazepines to manage agitation (Quality of Evidence: HIGH)
   3. Implement a ventilator liberation protocol (Quality of Evidence: HIGH)

C. **Maintain and improve physical conditioning**
   1. Provide early exercise and mobilization (Quality of Evidence: MODERATE)

D. **Elevate the head of the bed**
   1. Elevate the head of the bed to 30–45° (Quality of Evidence: LOW)

E. **Provide oral care with toothbrushing but without chlorhexidine**
   1. Provide daily oral care with toothbrushing but without chlorhexidine (Quality of Evidence: MODERATE)

F. **Provide early enteral rather than parenteral nutrition**
   1. Provide early enteral rather than parenteral nutrition (Quality of Evidence: HIGH)

G. **Maintain ventilator circuits**
   1. Change the ventilator circuit only if visibly soiled or malfunctioning (Quality of Evidence: HIGH)

Klompas M, et al. *Infect Control Hosp Epidemiol*. 2022 Jun;43(6):687-713.

Some Cases May Be Missed

- The National Healthcare Safety Network replaced traditional VAP surveillance with VAE surveillance in 2013.

- Studies have found VAE surveillance missed many cases of VAP.

- Population characteristics identified by the two surveillance paradigms differed.

  VAE surveillance may not accurately detect cases of VAP.

Haribhai S, Mahboobi SK. Ventilator Complications. [Updated 2022 Sep 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560535/
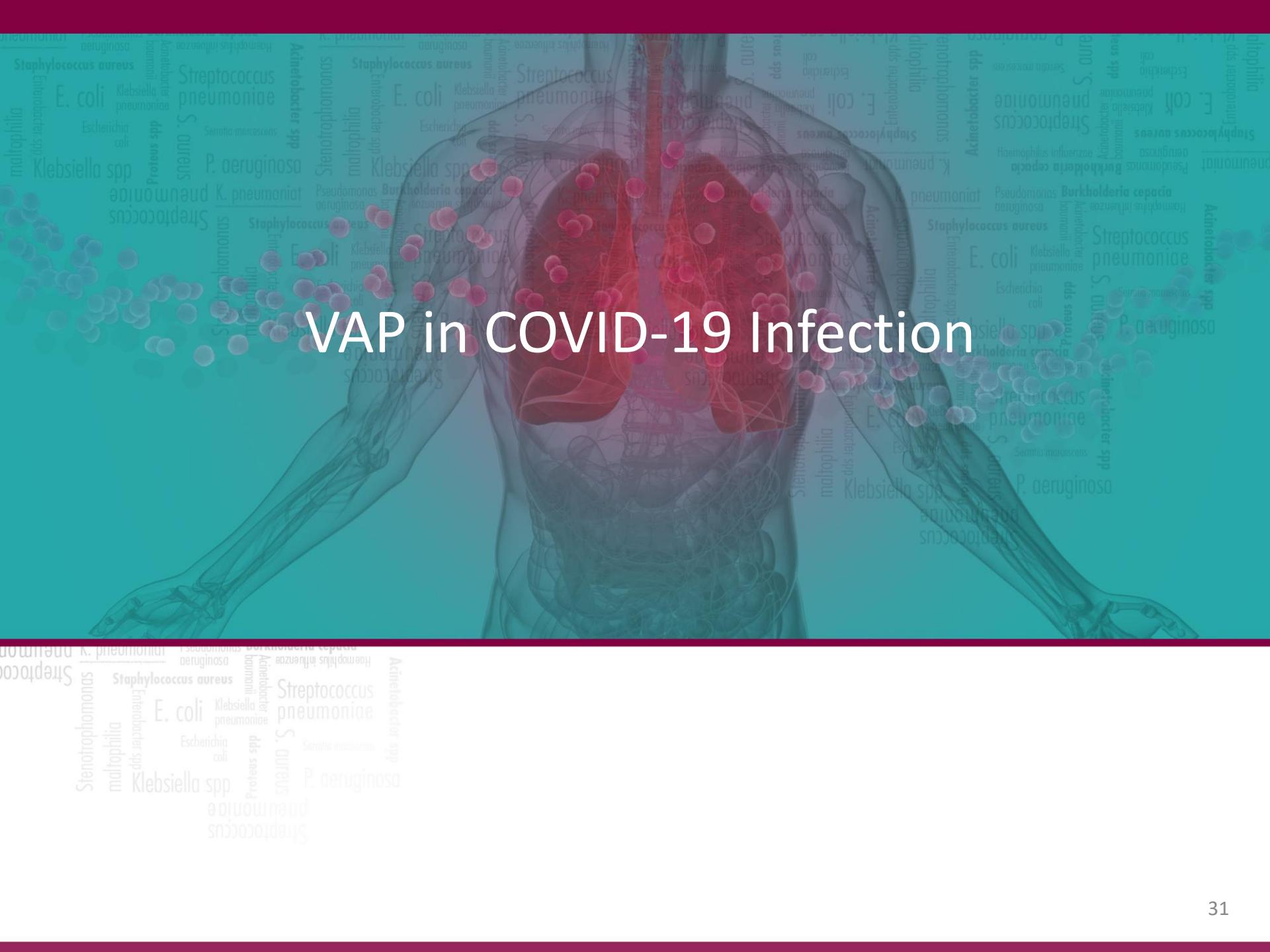
VAP in COVID-19 Infection

VAP Development in COVID-19

Endotracheal tube interface is a route for pathogens

Mechanical ventilation is a predisposing factor for VAP.

Mechanical ventilation is a common supportive treatment for COVID-19 infection with ARDS.

Biofilm formation

Tube interference with mucociliary clearance

Increased risk of VAP

Prevention and early identification of VAP in COVID-19 can improve outcomes.

Póvoa HC, et al. *Infect Dis Ther*. 2020;9(3):417–420.

Patients with VAP and COVID-19 Have Reduced Survival Rates

P = 0.0015
HR 2.01 (95% CI 1.14-3.54)

Non-COVID

COVID-19

VAP-Free Survival

Days

Maes M, et al. *Crit Care*. 2021;25:25.
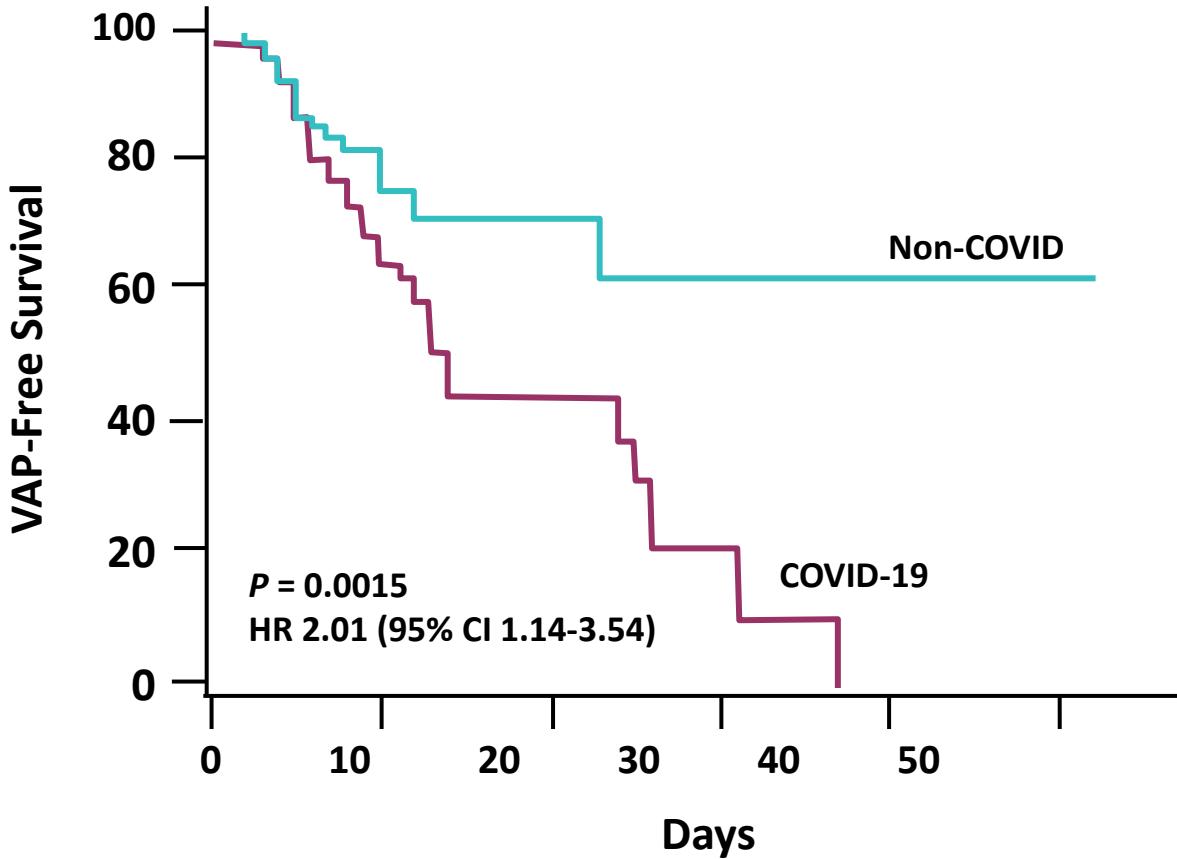
Co-Infection Isolates of COVID-19-Associated VAP

| Organism	ETA (≥ 10^5 CFU/ml)	BAL culture (≥ 10^4 CFU/ml)	BAL PCR (≤ Ct 32)
Gram negative			
Burkholderia cepacia	1		
Citrobacter freundii		1	*
Citrobacter koseri	1	1	*
Coliform (not further specified)	1		
Escherichia coli	5	3!	4!
Enterobacter asburiae	1		*
Enterobacter cloacae	3		
Enterobacteraeciae (not further specified)			2
Haemophilus influenzae	1		4
Klebsiella aerogenes	2	1	*
Klebsiella pneumoniae	2	3	5
Klebsiella oxytoca	3	1	*
Proteus mirabilis	1		1$
Pseudomonas aeruginosa	7	3	2
Serratia liquefaciens	1		
Serratia marcescens	1	2	5
Stenotrophomonas maltophilia	3	4	4
Gram positive			
Staphylococcus aureus	2	2	1
Fungi			
Aspergillus fumigatus			1

*Sequence for the organism in question not present on the TAC. !1 *E. coli* was detected by culture but not TAC in a patient, 2 *E. coli* detected by TAC without growth on culture. $Sequence on TAC is for *Proteus* spp. rather than species specific

Maes M, et al. *Crit Care*. 2021;25:25.

World Health Organization COVID-19 Guidelines for Reducing VAP

Oral intubation is preferable to nasal.

Semi-recumbent position (head of bed elevation 30 to 45º).

Closed suctioning system with periodic draining.

New ventilator circuit for each patient.

WHO COVID-19 Clinical Management. 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1
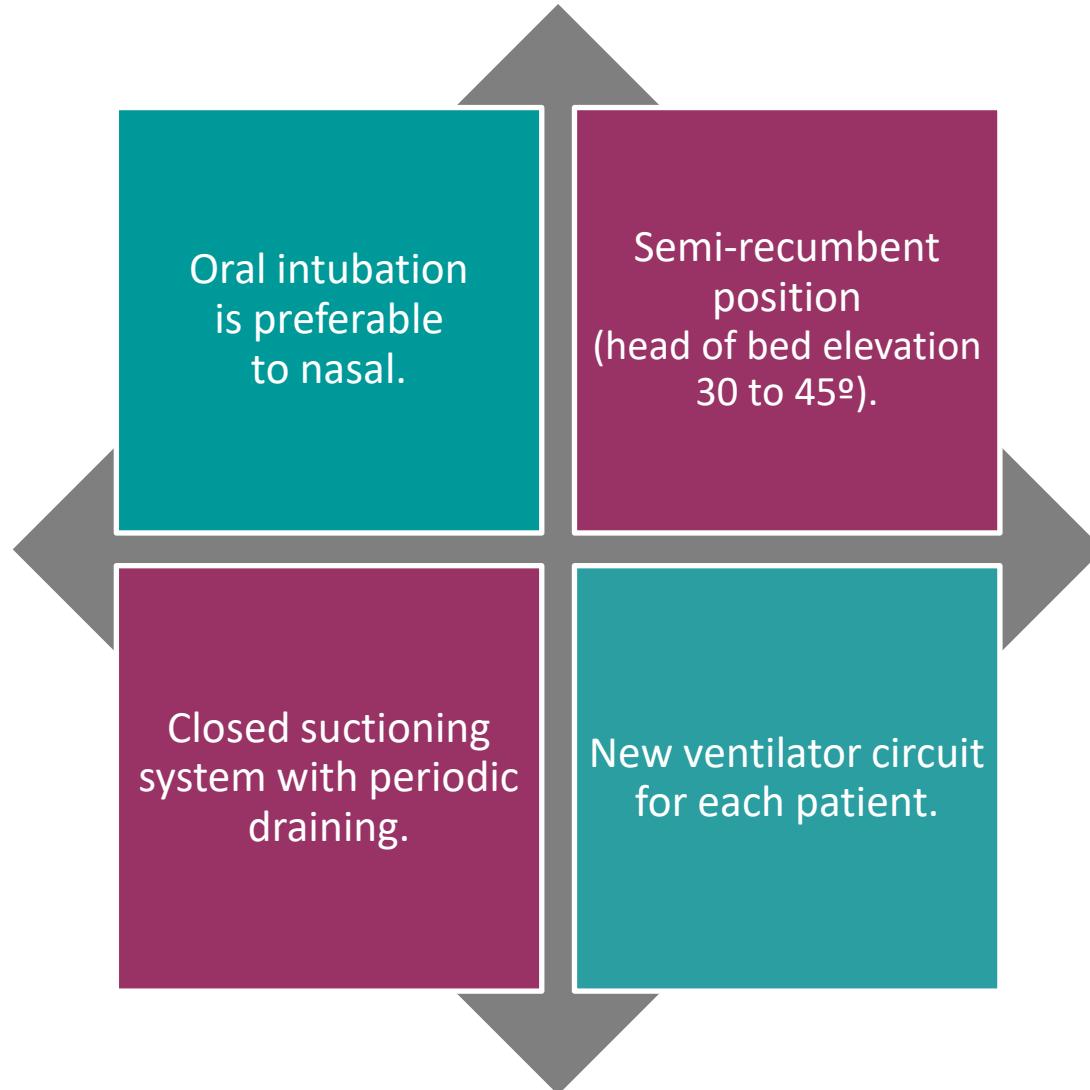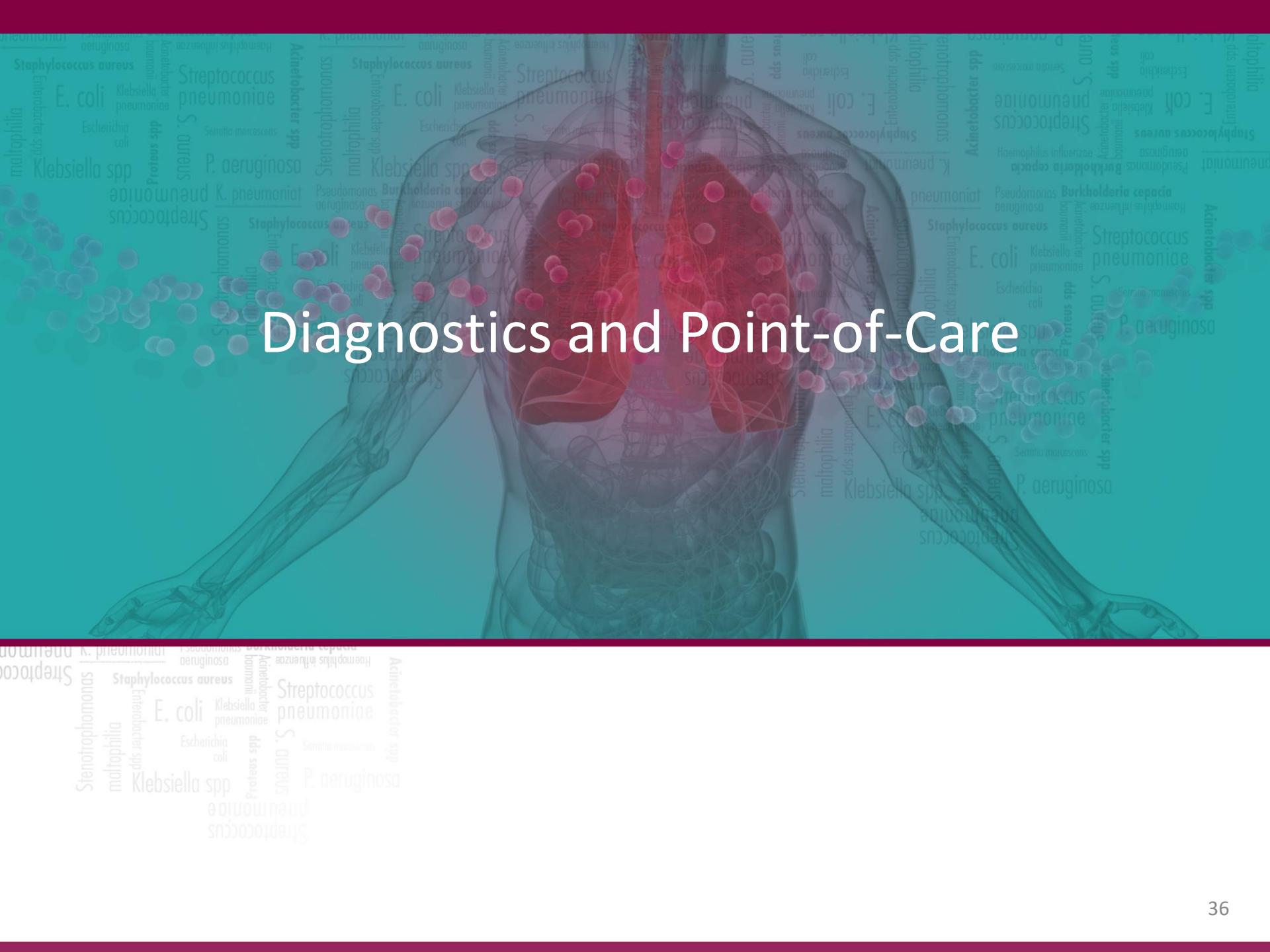
Diagnostics and Point-of-Care

2016 Clinical Practice Guideline by the IDSA and the American Thoracic Society

General recommendation:

Noninvasive sampling with semiquantitative cultures to diagnose VAP, rather than invasive sampling with quantitative cultures and rather than noninvasive sampling with quantitative cultures

If invasive sampling is performed:

For patients with suspected VAP whose invasive quantitative culture results are below the diagnostic threshold for VAP, we suggest that antibiotics be withheld rather than continued

Kalil AC, et al. *Clin Infect Dis*. 2016;63(5):e61–e111.

2016 Clinical Practice Guideline by the IDSA and the American Thoracic Society

If diagnostic tests for VAP are positive:

A 7-day course of antimicrobial therapy rather than a longer duration is recommended.

Antibiotic therapy should be de-escalated rather than fixed

Kalil AC, et al. *Clin Infect Dis*. 2016;63(5):e61–e111.
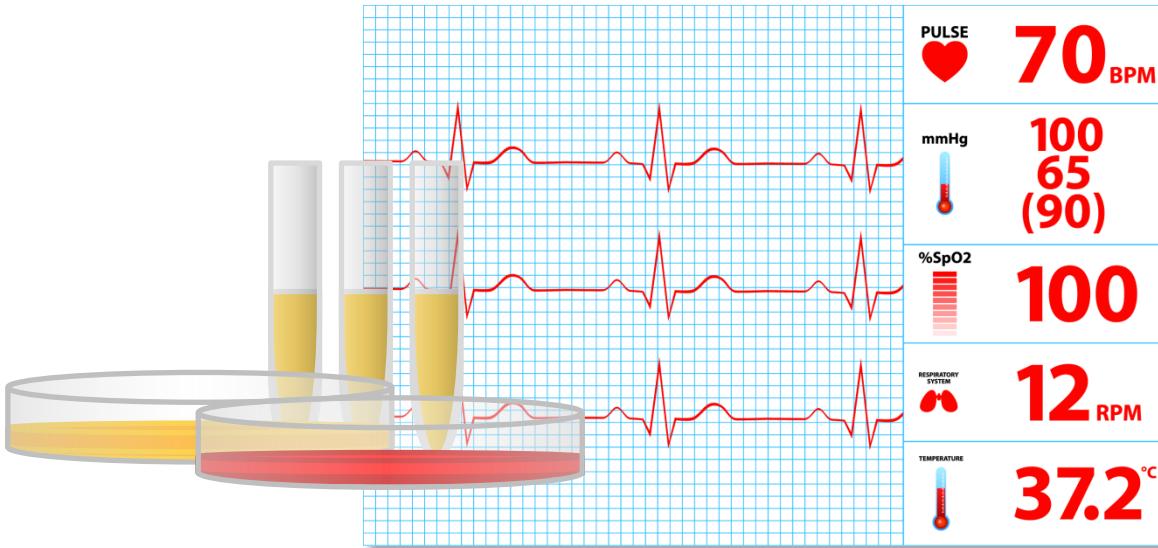
Up to 2/3 of clinical VAP diagnoses turn out to be incorrect. Core clinical signs are neither sensitive nor specific.

Klompas M. *Respir Care*. 2024 Jun 28;69(7):854-868.

VAP Clinical Criteria

Accepted clinical criteria for pneumonia
are of limited diagnostic value in definitively
establishing the presence of VAP.

Johanson Criteria	Presence of a new or progressive radiographic infiltrate
	Plus at least two of three clinical features:
	• Fever > 38ºC
	• Leukocytosis or leukopenia
	• Purulent secretions

Koenig SM, et al. *Clin Microbiol Rev*. 2006;19(4):637-57.
Rea-Neto A, et al. *Critical Care.* 2008;12:R56.

VAP Clinical Criteria

Clinical Pulmonary Infection Score (CPIS)	Temperature	Oxygenation (PaO2/FiO2)	Tracheal Secretions (Score)
	0 point: 36.5–38.4ºC	0 point: > 240 or ARDS	0 point: < 14
	1 point: 38.5–38.9ºC	2 points: < 240, No evidence of ARDS	1 point: > 14
	2 points: < 36 or > 39ºC		2 points: Purulent sputum
	Blood Leukocytes (Cells/µL)	Pulmonary Radiography	Tracheal Aspirate Culture
	0 point: 4000–11000	0 point: No infiltrate	0 point: Minimal growth
	1 point: < 4000 or > 11000	1 point: Diffuse or patchy infiltrates	1 point: Moderate or more growth
	2 points: > 500 band forms	2 points: Localized infiltrate	2 points: Moderate or greater growth

ARDS = acute respiratory distress syndrome

## VAP Score > 6

Rea-Neto A, et al. *Critical Care.* 2008;12:R56.

Inaccuracy of the Clinical Diagnosis of VAP
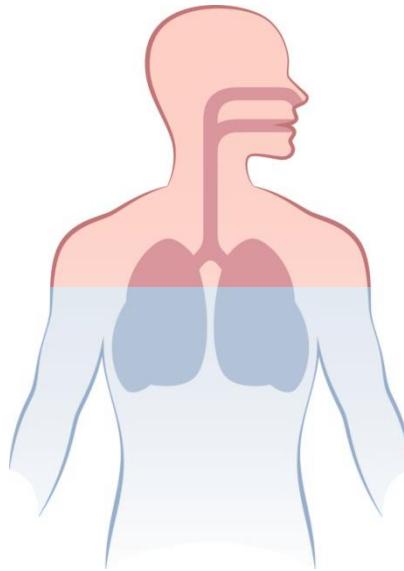
50%
Cases show
no evidence
of pneumonia
at autopsy.
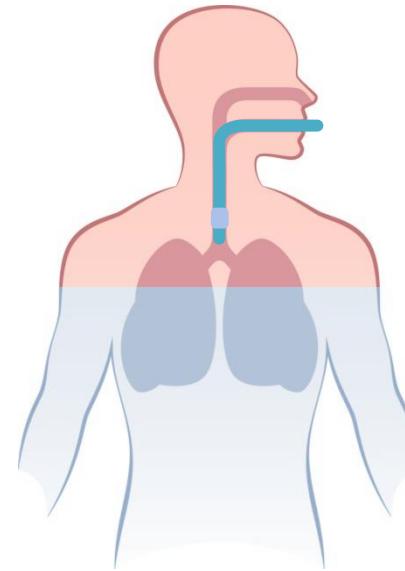
50%
Could not be
confirmed by
microbiological
cultures.

https://emcrit.org/ibcc/vap/. Accessed December 2, 2025..
Torres A, et al. *Nat Rev Dis Primers*. 2021;7:25.

Microbiological Methods for VAP Diagnosis

Endotracheal aspirate

Lung tissue

Protected specimen brush

Bronchoalveolar lavage

CDC. *Device Associated Module*. 2021.
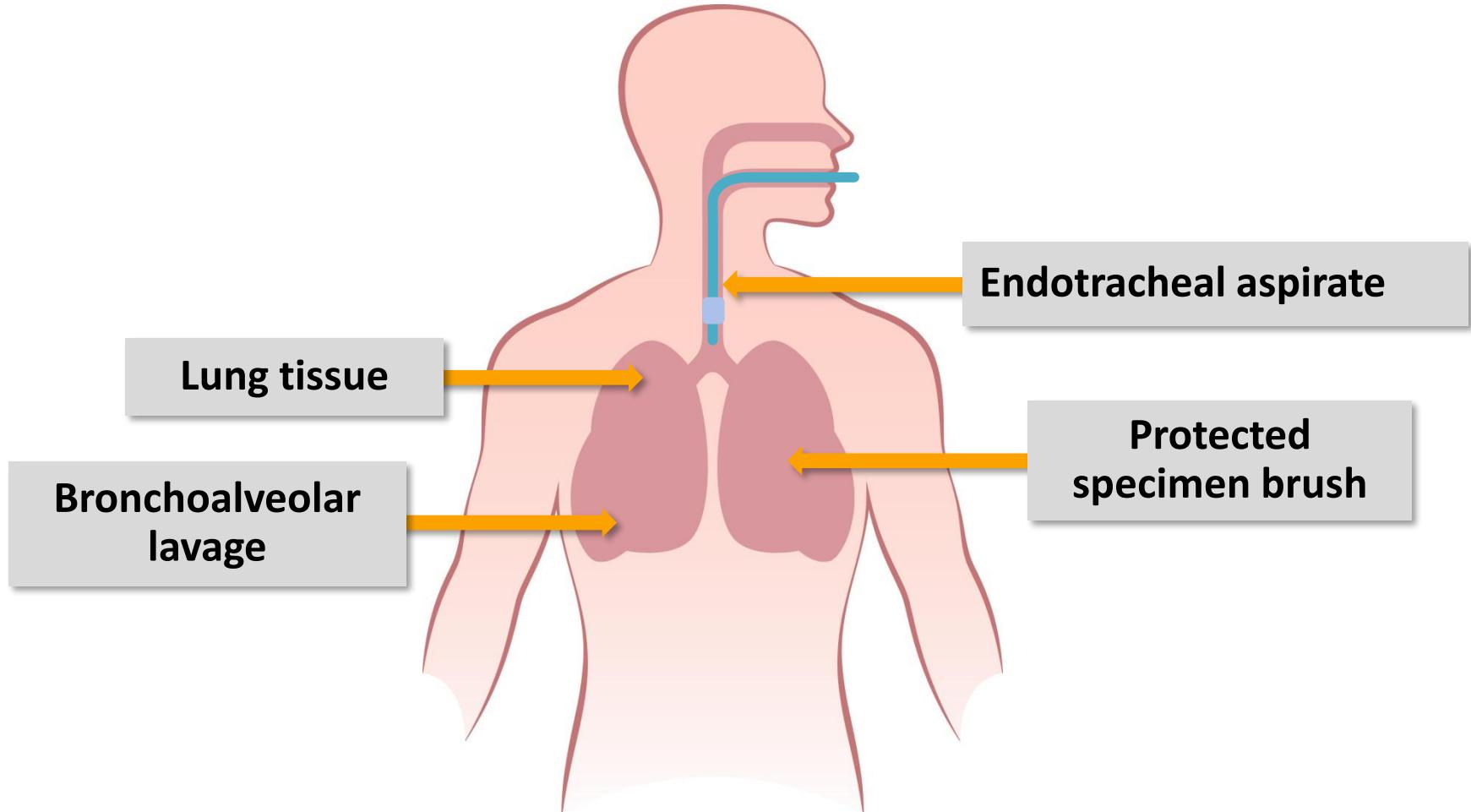
Specimen Threshold Values for Diagnosis

Specimen collection/technique	Values
Lung tissue	$\geq 10^4$ CFU/g tissue*
Bronchoscopically (B) obtained specimens	
Bronchoalveolar lavage (B-BAL)	$\geq 10^4$ CFU/ml*
Protected BAL (B-PBAL)	$\geq 10^4$ CFU/ml*
Protected specimen brushing (B-PSB)	$\geq 10^3$ CFU/ml*
Non-bronchoscopically (BN) obtained (blind) specimens	
NB-BAL	$\geq 10^4$ CFU/ml*
NB-PSB	$\geq 10^3$ CFU/ml*
Endotracheal aspirate (ETA)	$\geq 10^5$ CFU/ml*

CFU = colony forming units, g = gram, ml = milliliter,
*Or corresponding semi-quantitative result

Microbiological Method: Impact on Incidence

- Incidence of VAP varies widely in the literature

- Clinical variability
  - Patient populations
  - Pathogens
  - ICU type
  - Diagnostic methods
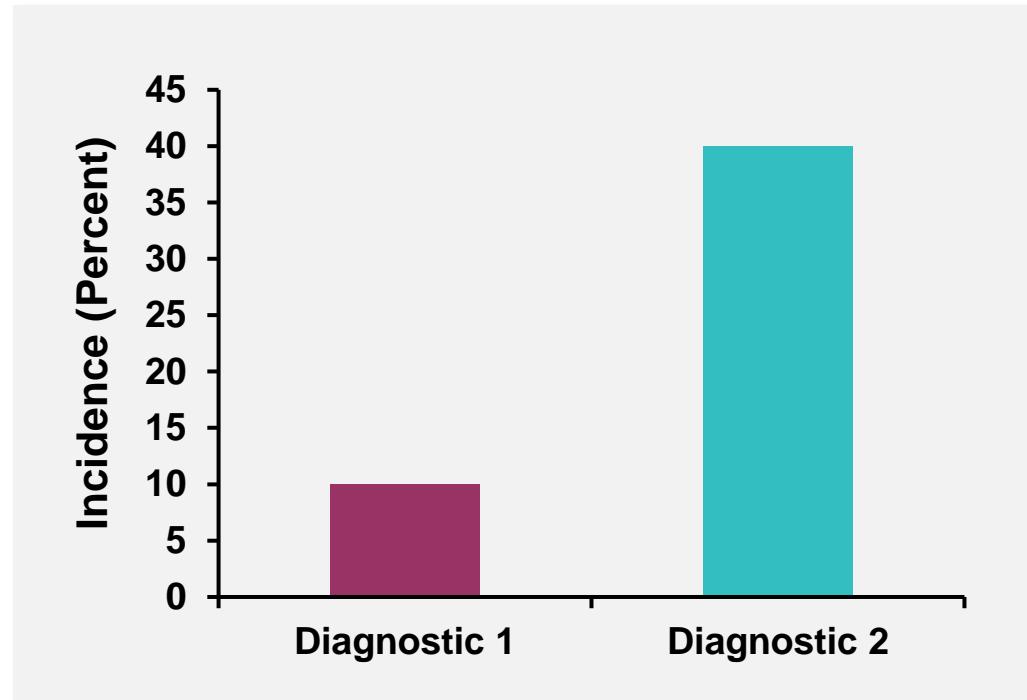
A single hospital can report a 4-fold increase in incidence by changing diagnostic criteria.

Klompas M. *Respir Care*. 2019;64(8):953-61.

Diagnosis of VAEs vs. VAP

VAEs

Clinically Diagnosed VAP

Fluid overload

ARDS

Aspiration pneumonitis

Pulmonary embolism

Atelectasis

Transfusion-associated injury

Hypersensitivity pneumonitis

Sepsis

Clinically-diagnosed VAP *with* sustained increases in ventilator support

Clinically-diagnosed VAP *without* sustained increases in ventilator support

VAP mimickers

Tracheobronchitis

Klompas M. *Respir Care*. 2019;64(8):953-61.

Qualitative vs. Quantitative

- Qualitative
  - Advantages
    - Reproducible without special equipment
  - Disadvantages
    - Does not add to clinical diagnosis and often results in overdiagnosis
    - Airways are colonized by pathogenic bacteria hours after intubation, regardless of presence of pneumonia

- Quantitative
  - Advantages
    - Limits false positives and associated incorrect antibiotic use
  - Disadvantages
    - Questions of withholding antibiotics if quantitative numbers are below threshold

Papazian L, et al. *Intens Care Med*. 2020;1-19.

Colonization Does Not Equal Causation

- Bacterial colonization is common in critical care and represents a continuum to VAP in ICU patients.

- Colonization may not be equivalent to infection of distal airways.

- Bacterial eradication from endotracheal aspirates is a poor marker for clinical response.

Microbiological criteria alone are not reliable.

Howroyd F, et al. *Nat Commun*. 2024 Jul 31;15(1):6447.

Advantages and Disadvantages of Clinical and Radiological Assessment of VAP

	Advantages	Disadvantages
Bedside Clinical Symptoms	• Inexpensive • Rapid, bedside assessment • Any clinician/grade • Foundation of clinical suspicion	• Nonspecific to the cause of infection • Overlap with many disease processes • Confounded by ICU imposed factors • Inconclusive
Radiological Diagnosis	CT	
	• 3D imaging • High resolution of different densities • Accurate	• Radiation risk • Transfer risks • Time delay • Cost
	CXR	
	• Portable enabling a bedside assessment • Rapid • Pragmatic • Inexpensive	• 2D imaging only • Patient positioning limited • Difficult interpretation • Overlap with many disease processes • Benefits from comparison images
	Lung Ultrasound	
	• Portable enabling a bedside assessment • Rapid • Inexpensive • Minimal radiation • Dynamic exploration	• Specialist training • Limitations - body habitus and subcutaneous emphysema • Not a recognized or validated tool

Howroyd F, et al. *Nat Commun*. 2024 Jul 31;15(1):6447.

Advantages and Disadvantages of Microbiological Assessment of VAP

	Advantages	Disadvantages
Microbiological Diagnosis	Non-invasive techniques	
	• Simple • Safe • Rapid/efficient to obtain a sample • Obtained by a breadth of ICU staff groups • Does not require extensive training	• Cross-contamination risk • Unable to isolate lower respiratory tract
	Invasive techniques	
	• Targets the lower respiratory tract, therefore, more specific	• Not routinely available over 24 h • Requires specialist training • Risk of patient instability
	Qualitative techniques	
	• Simple • Quicker and more efficient than quantitative methods	• Not specific to the exact organism
	Quantitative techniques	
	• Specific • Allows for targeted antibiotic therapy	• Timely • Costly • Laboratory resources • Expertise required

Howroyd F, et al. *Nat Commun*. 2024 Jul 31;15(1):6447.

Biomarkers

- Identification of biomarkers may eliminate disadvantages of common VAP diagnostic techniques.

  - Procalcitonin (PCT)

  - suPAR (Soluble Urokinase-type Plasminogen Activator Receptor)

  - C-reactive protein (CRP)

  - MR-proADM

- Biomarkers are not a useful replacement for VAP diagnostic criteria.

- Biomarkers such has procalcitonin may guide antibiotic treatment in VAP.

Torres A, et al. *Intens Care Med*. 2021;47:97–100.

Indications and Pitfalls of Common VAP Biomarkers

PCT

Indications:

- Shorten antibiotic duration with other parameters

Pitfalls:

- Delta values are necessary
- Inaccurate in renal failure or dialysis

CRP

Indications:

- Delta value increases are useful to predict poor evolution of VAP
- Delta values can predict VAP up to 3 days before clinical evidence

Pitfalls:

- Increased in non-infectious conditions

suPAR

Indications:

- Prediction of VAP

Pitfalls:

- Moderate prediction only

Torres A, Artigas A, Ferrer R. *Intensive Care Med*. 2021 Jan;47(1):97-100.

CRP Shows Promise for VAP Prediction

	Good Response	Poor Response	P-Value
Leukocytes	13,514 ± 5,264	15,685 ± 42,563	0.033
Temperature °C	36.2 ± 0.55	37.1 ± 0.71	0.039
CRP Ratio	15.7 ± 5.26	19.65 ± 4.21	0.042

Mohamed WSA. *Res Opin Anesth Intens Care.* 2020;7:20-24.
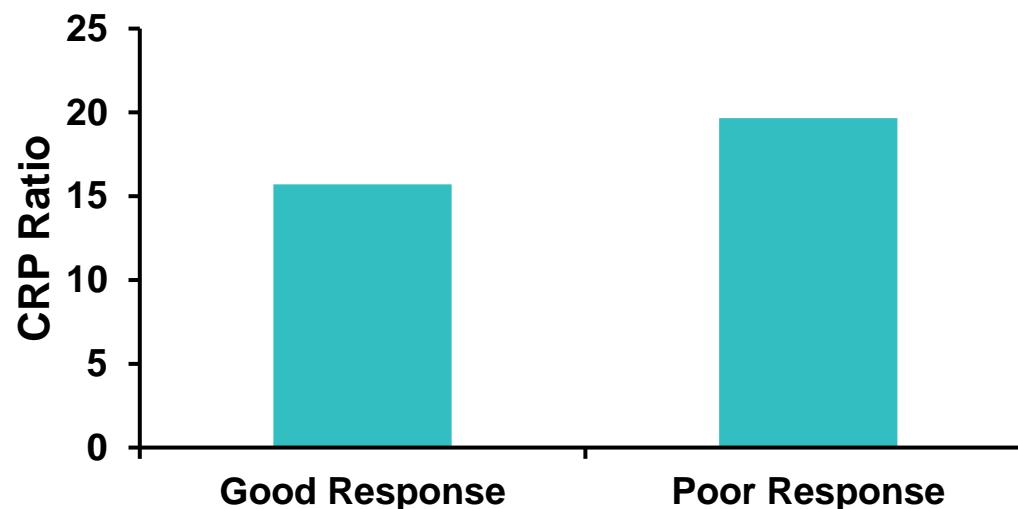
PCT Associated With VAP Mortality in COVID-19

AUC 71.7%, *P* = 0.002

Sensitivity (%)

100%-Specificity (%)

Côrtes MF, et al. *Diagn Microbiol Infect Dis.* 2021;115344.
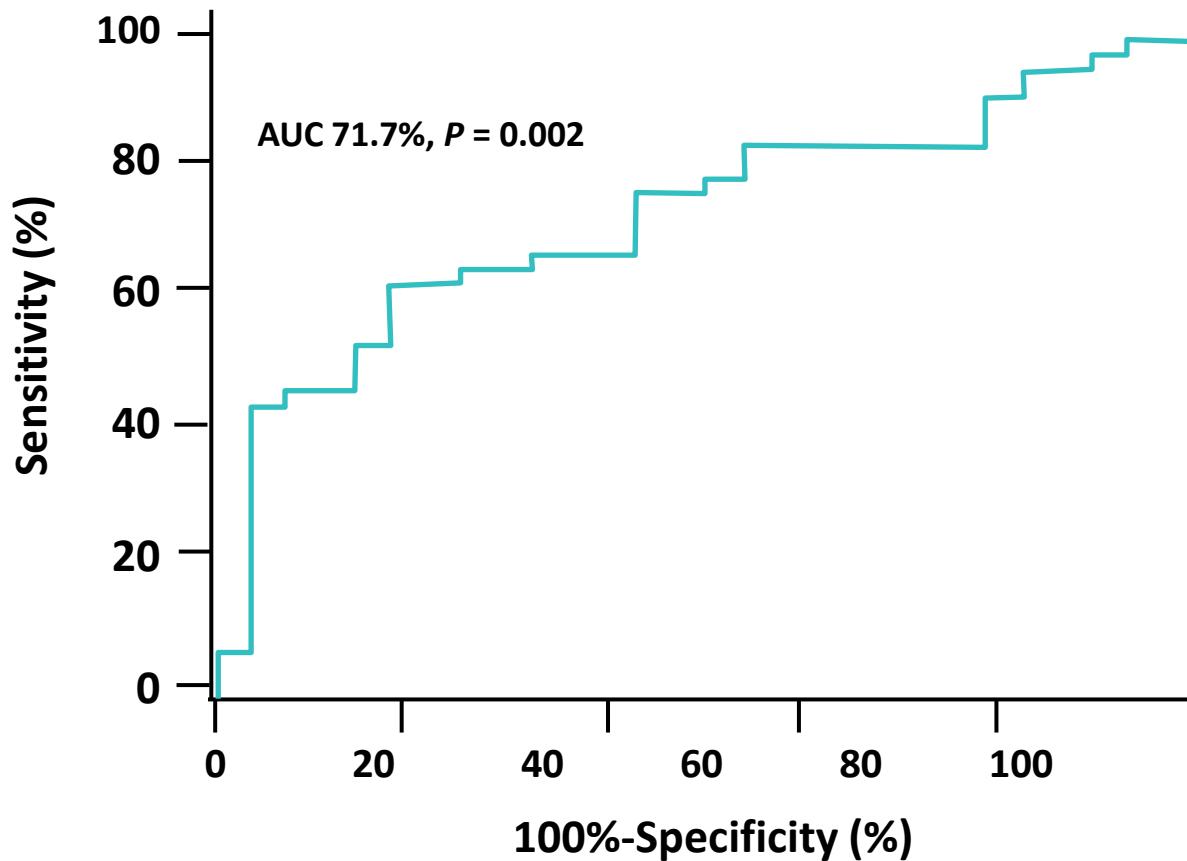
2016 Clinical Practice Guideline by the IDSA and the American Thoracic Society

Use clinical criteria alone, rather than using PCT, CRP, or sTREM-1 or clinical pulmonary infection score (CPIS) plus clinical criteria, to decide whether or not to *initiate* antibiotic therapy.

Use PCT levels plus clinical criteria to guide the *discontinuation* of antibiotic therapy, rather than clinical criteria alone.

Do not use CPIS to guide the *discontinuation* of antibiotic therapy.

Kalil AC, et al. *Clin Infect Dis*. 2016;63(5):e61–e111.

VAP Timeline:
Implications for Point-of-Care Testing

0-6 Hours

Antibiotic golden hours

6-24 Hours

Changing antibiotics may improve outcome

> 24 Hrs

No proven improvement when changing antibiotics

Testing Most Beneficial

Dhesi Z, et al. *ACS Pharmacol Transl* Sci. 2020 May 12;3(3):401-417.
Millot G, et al. *Ann Transl Med.* 2017;5(22):451.

VAP Timeline:
Implications for Point-of-Care Testing

Traditional Testing

CRP PCT sTREM1	Gram stain	Conventional cultures

0-6 Hours

Antibiotic golden hours

6-24 Hours

Changing antibiotics may improve outcome

> 24 Hrs

No proven improvement when changing antibiotics

CRP PCT

MPCR

Automated microscopy

POC Testing

Dhesi Z, et al. *ACS Pharmacol Transl* Sci. 2020 May 12;3(3):401-417.
Millot G, et al. *Ann Transl Med.* 2017;5(22):451.

Summary

- Any patient on a ventilator for more than 48 hours is at risk for VAP.

- The CDC has provided an algorithm as well as recommendations for surveillance and prevention of VAP and other VAE.

- Biomarkers and other point-of-care analytes, may assist in VAP diagnosis as well as reducing time on mechanical ventilation.
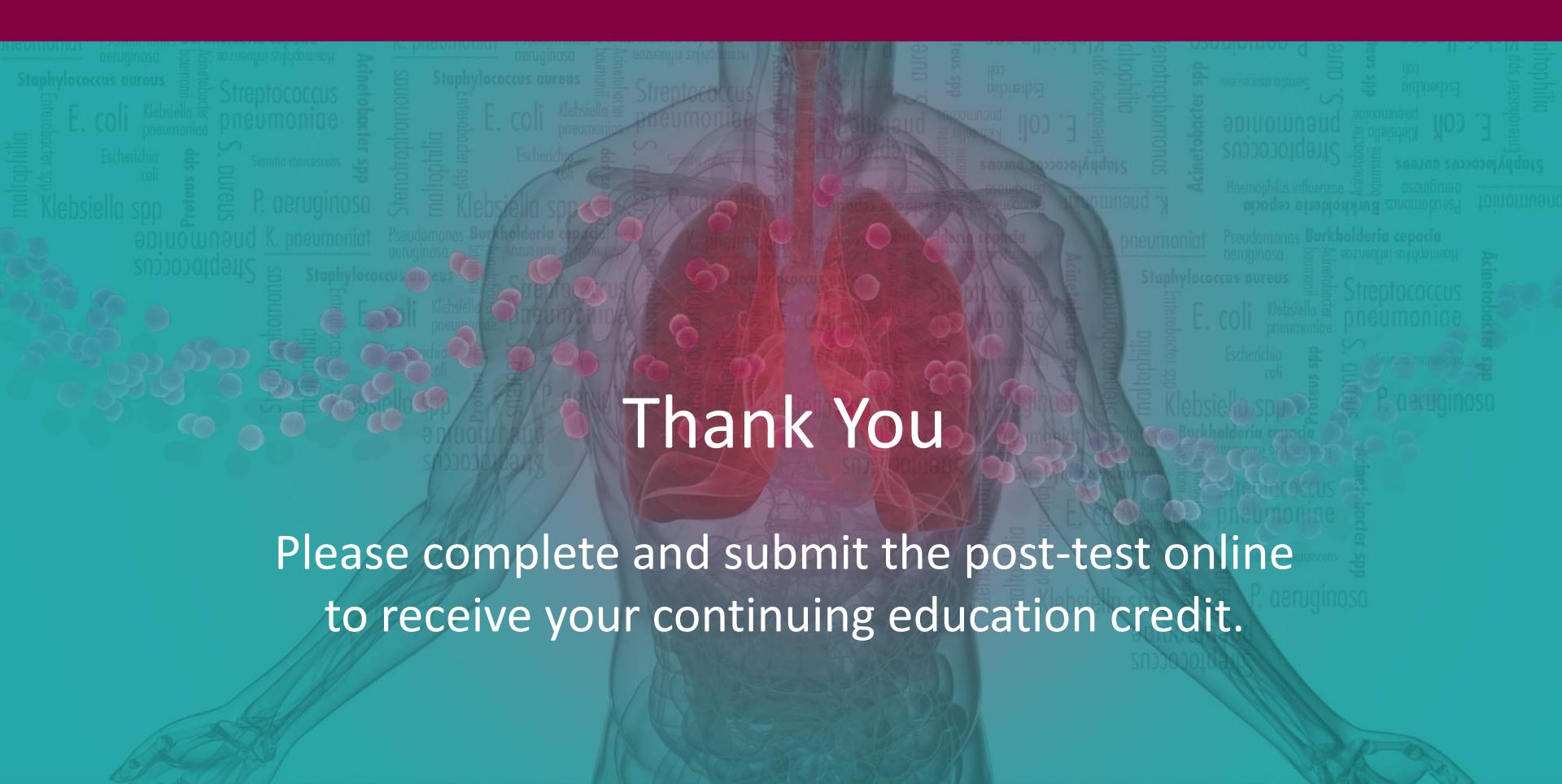
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