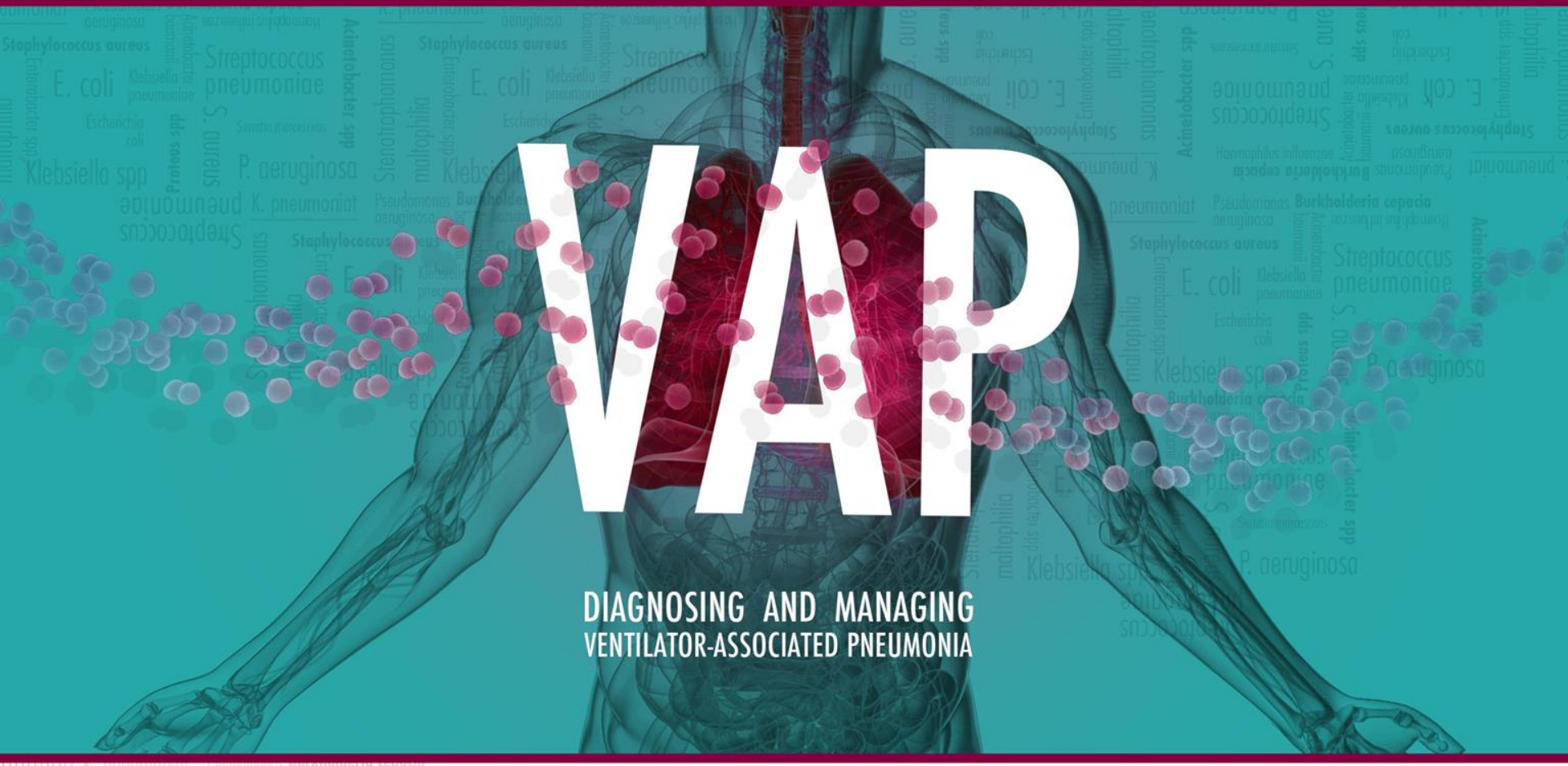
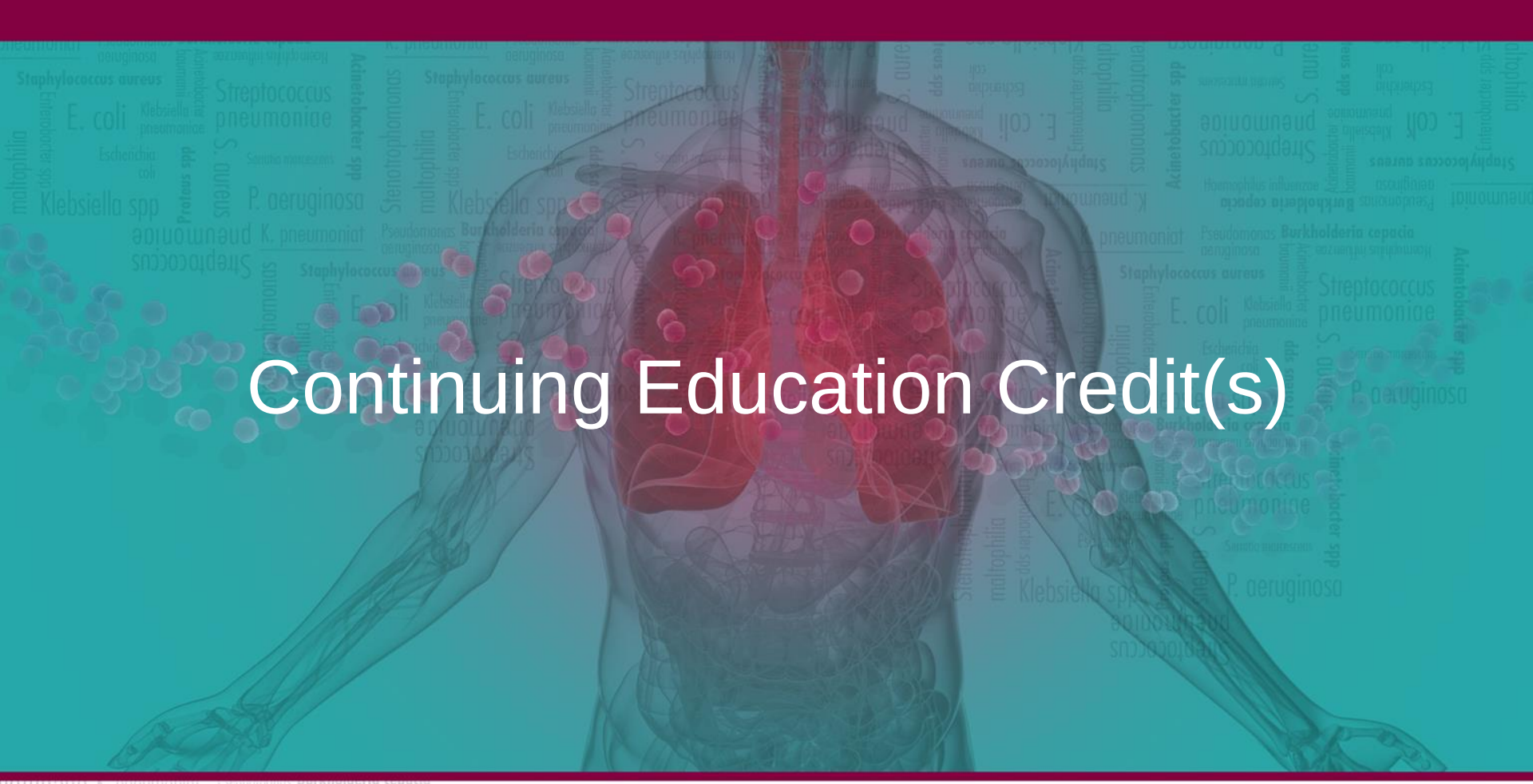


DIAGNOSING AND MANAGING VENTILATOR-ASSOCIATED PNEUMONIA

A SELF STUDY
COURSE FOR CREDIT

FIND OUT MORE AT VAPEDUCATION.COM



Continuing Education Credit(s)

Date of Release: 7/1/23

Date of Expiration: 7/1/25

Estimated time to complete this educational activity: 1.5 hours

Continuing Education Credit(s)

Physicians - This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through Synativ. Synativ is accredited by the ACCME to provide continuing medical education for physicians. Synativ designates this educational activity for a maximum of 1 AMA PRA Category 1 Credit(s)™ toward the AMA Physician's Recognition Award. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Nursing - Educational Review Systems is an approved provider of continuing education in nursing by ASNA, an accredited provider by the ANCC/Commission on Accreditation. Provider #5-115. This program is approved for one and a half (1.5) credit hours. Educational Review Systems is also approved for nursing continuing education by the State of California and the District of Columbia.

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Laboratory Professionals - Educational Review Systems is approved as a provider of continuing education programs in the clinical laboratory sciences by the ASCLS P.A.C.E. Program. This program is approved for one and a half (1.5) hours of continuing education credit.

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

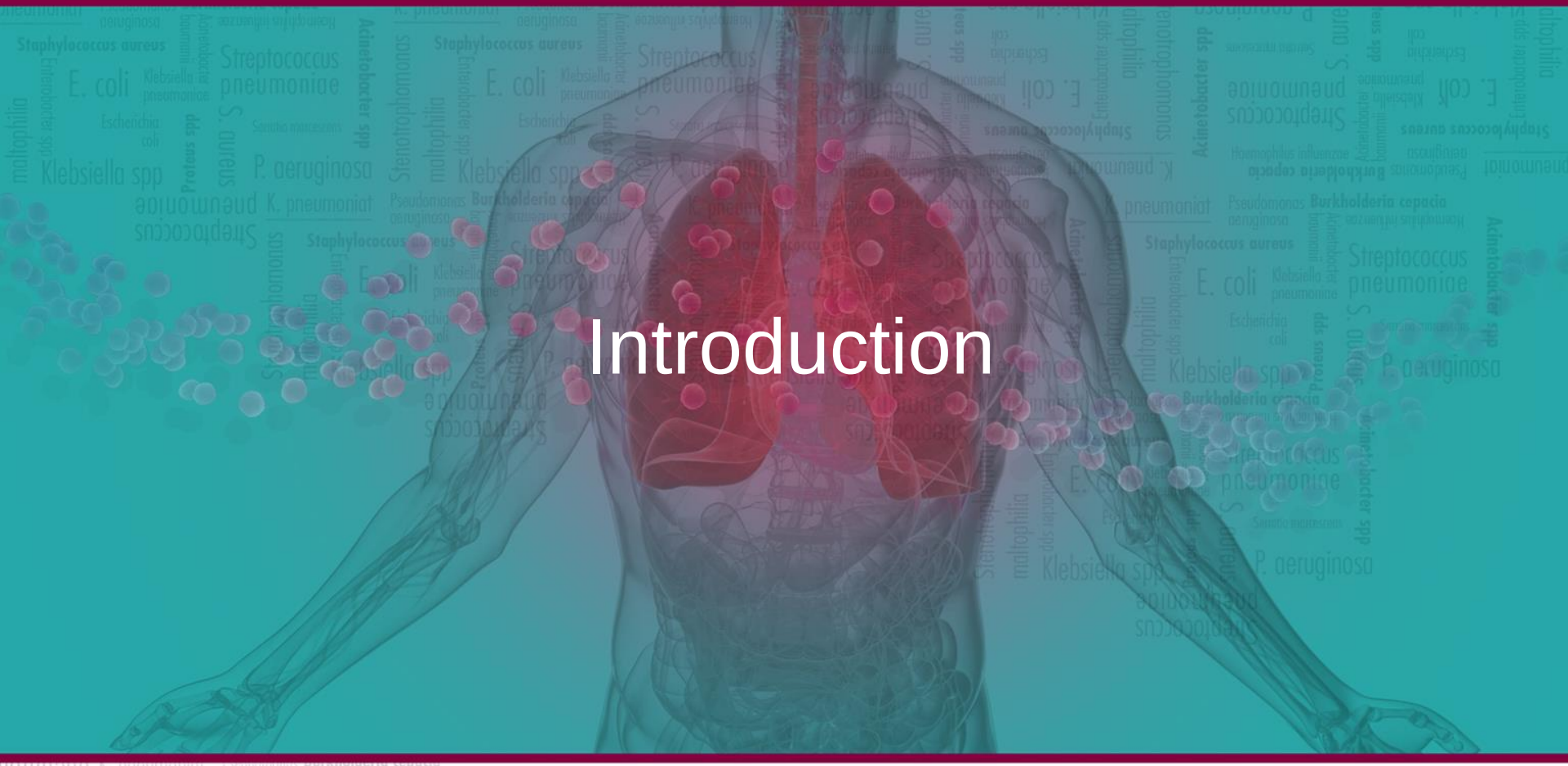
The primary audience for this learning activity is healthcare professionals (physicians, nurses, respiratory therapists, and laboratory professionals) involved in the testing, diagnosis, treatment, and management of ventilator-associated pneumonia and who are interested in the role of biomarkers to improve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

Learning Objectives

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

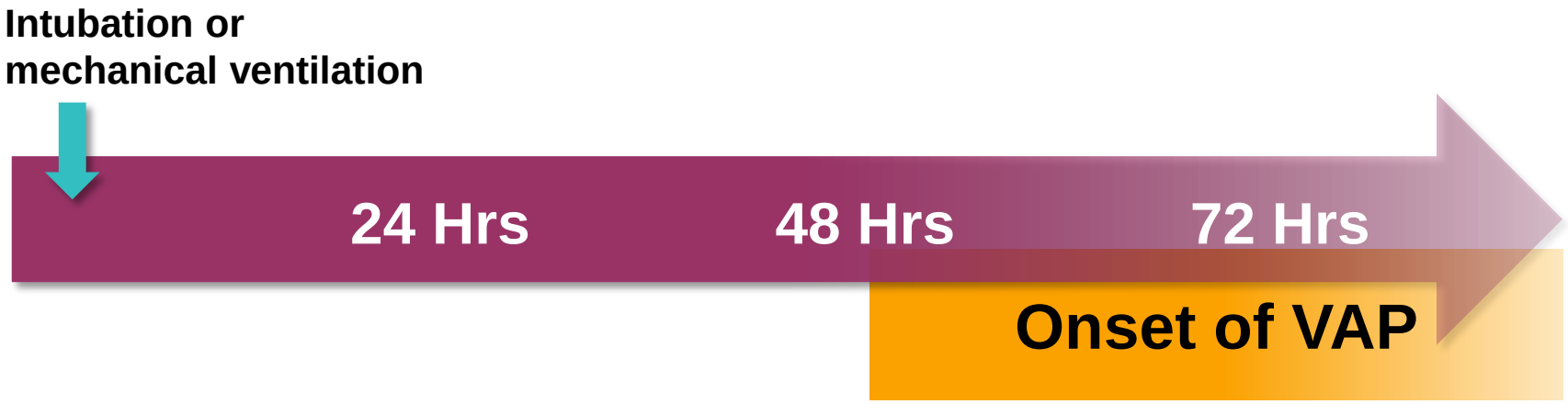
1. Identify the risk factors of VAP.
2. Review the epidemiology of VAP.
3. Describe guidelines and recommendations used in the diagnosis and treatment of VAP.
4. Identify the benefits and limitations of point-of-care testing in VAP patients.

Table of Contents


Introduction

Ventilator-Associated Pneumonia

- Ventilator-associated pneumonia (VAP) can develop in any patient on a ventilator
- VAP is the most common of the hospital-acquired infections (HAI) in the intensive care unit (ICU)

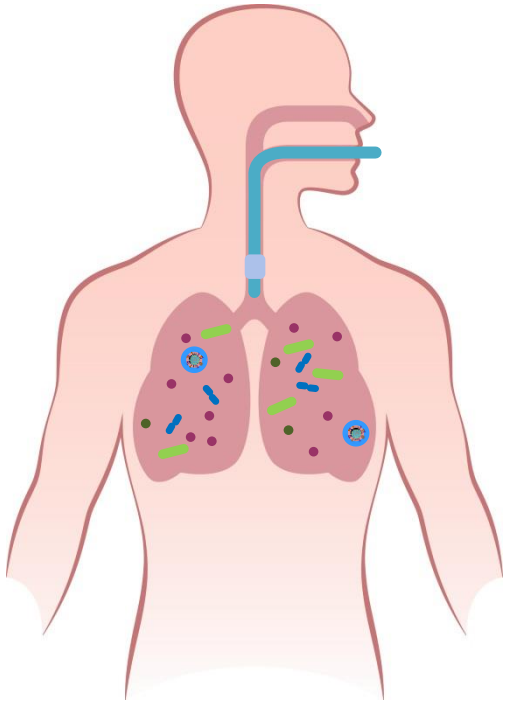


Papazian L, et al. *Intens Care Med*. 2020;1-19.

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.

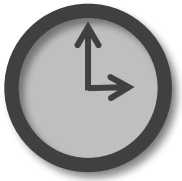
National Healthcare Safety Network Definition

Respiratory Status	• ≥ 0.20 increase in FiO_2 • ≥ 3 cm H_2O increase in PEEP
Infection/Inflammation	• 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
Additional Data	• Gram stain showing ≥ neutrophils and ≤ 10 epithelial cells • Positive culture from either ETA or BAL

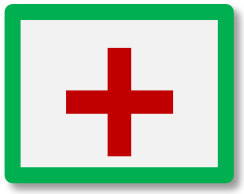
FiO_2: fraction of inspired oxygen; PEEP: positive end-expiratory pressure; ETA: endotrachial aspiration; BAL: bronchoalveolar lavage

Nora D, et al. *Ann Transl Med.* 2017;5(22):450.

Risk Factors

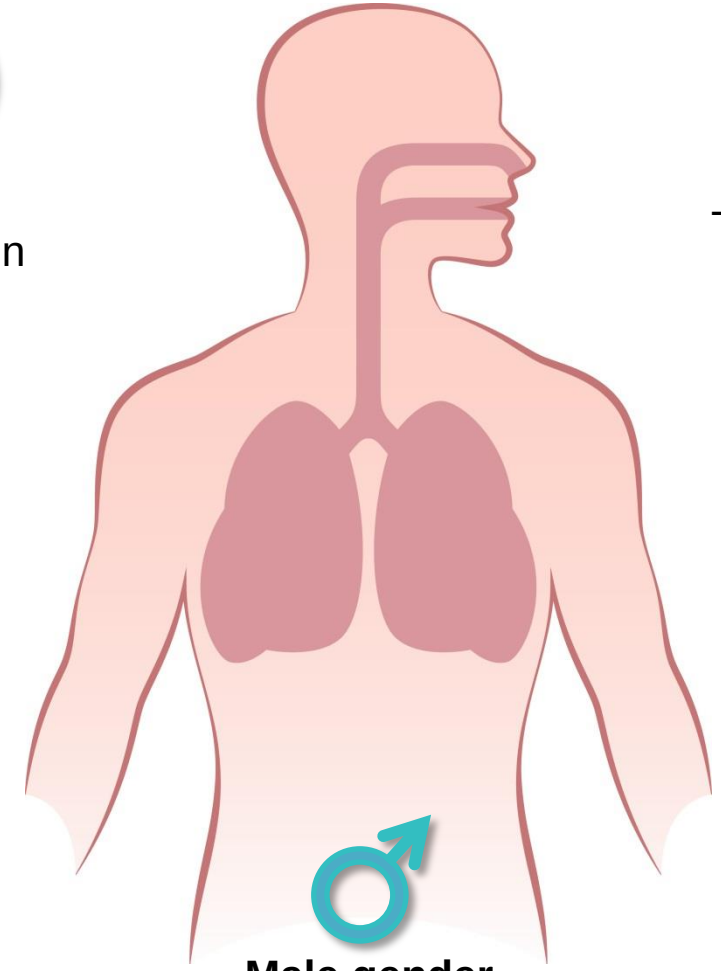


Duration
of intubation



Trauma admission

Prior use of antibiotics



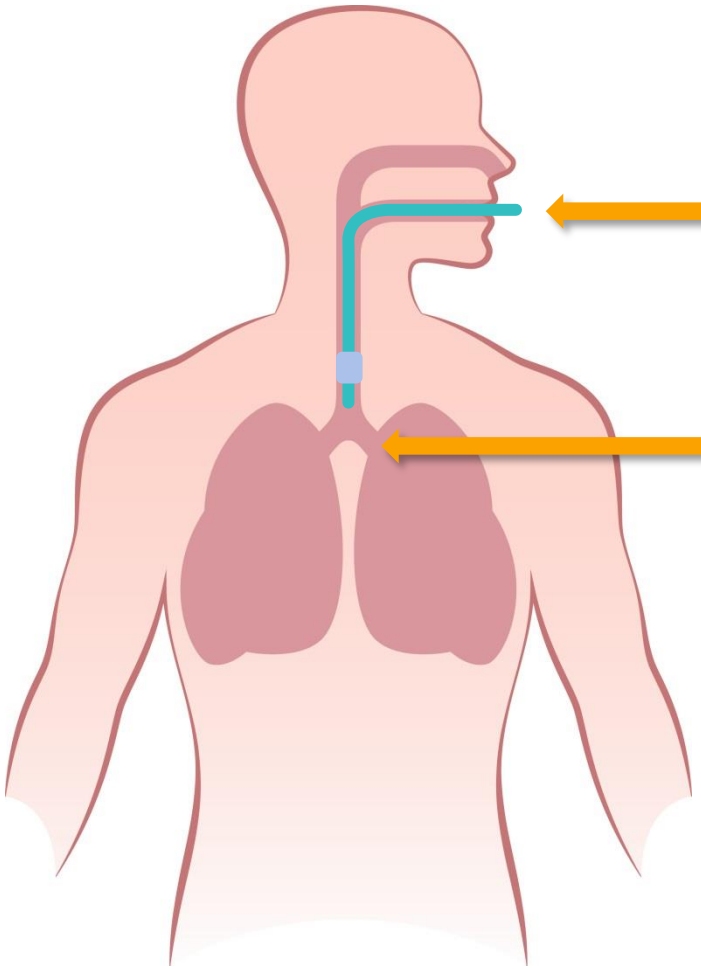
Male gender

Severity of illness

Supine positioning

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

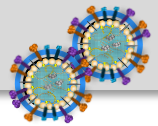
Bacteria

Gram negative bacteria are the most common type seen in VAP

May be gram positive during MRSA outbreak

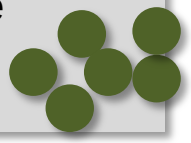
Viruses

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



Fungi

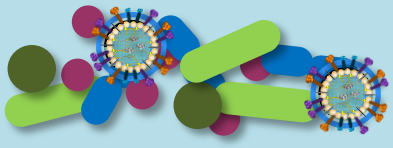
Occasionally seen in immunodeficient patients, rarely causative



Monomicrobial

Only one pathogen type

Polymicrobial



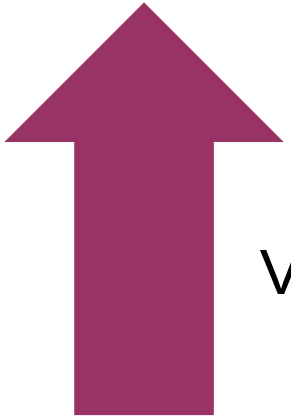
Most common VAP infection type
Multiple pathogens

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.

VAP Increases ICU Cost & Mortality Compared to Other Ventilator Associated Respiratory Infections (VARI)

	VAP (N = 37)	VARI Without VAP (N = 55)	No VARI (N = 286)
ICU length of stay (days)*	25 (19–37)	27 (25–38)	16 (10–28)
ICU cost (USD)*	7213 (3011–8329)	4196 (2726–7193)	2534 (1493–4407)
Hospital length of stay (days)*	31 (22–46)	39.5 (29.5–49)	25 (14–39)
Hospital cost (USD)*	4522 (2716–7990)	4167 (2658–6985)	2639 (1555–4576)
In-hospital mortality	13/37 (35.1%)	4/54 (7.4%)	54/277 (19.5%)

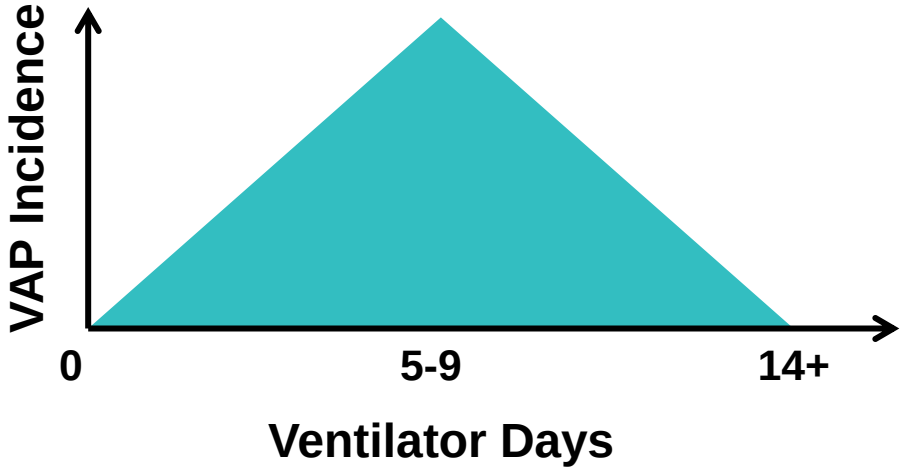
*$P < 0.01$; VARI: ventilator associated respiratory infection

Phu VD, et al. *J Inten Care*. 2017;5:69.

Epidemiology

Incidence

- 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



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

	VAP (N = 5012)		
	Odds Ratio	**LCL**	**UCL**
PPH admission	0.335	0.295	0.381
Comorbid conditions			
Congestive heart failure	1.781	1.636	1.938
Pulmonary circulation disorders	1,944	1.687	2.239
Hypertension	0.577	0.541	0.616
Paralysis	2.899	2.514	3.342
Diabetes without chronic complication	0.699	0.645	0.758
Renal failure	1.904	1.755	2.065
Obesity	1.431	1.306	1.567
Weight loss	2.892	2.652	3.153

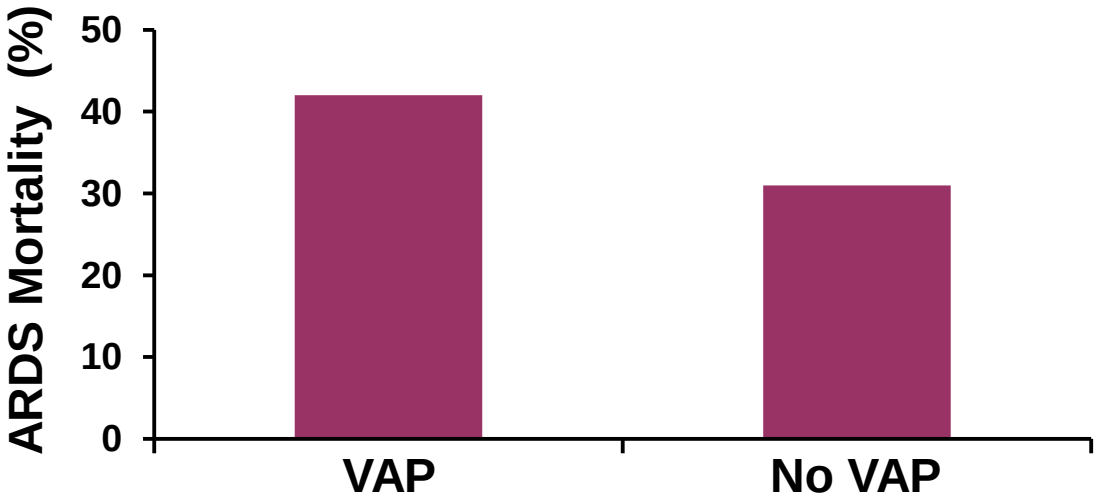
All odds ratios significant at $P < 0.001$.
PPH: potentially preventable hospitalization; LCL: lower confidence limit; UCL: upper confidence limit

Lorden AL, et al. *Health Serv Res Man Epidemiol.* 2017;4:1-9.

Mortality

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

- In 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

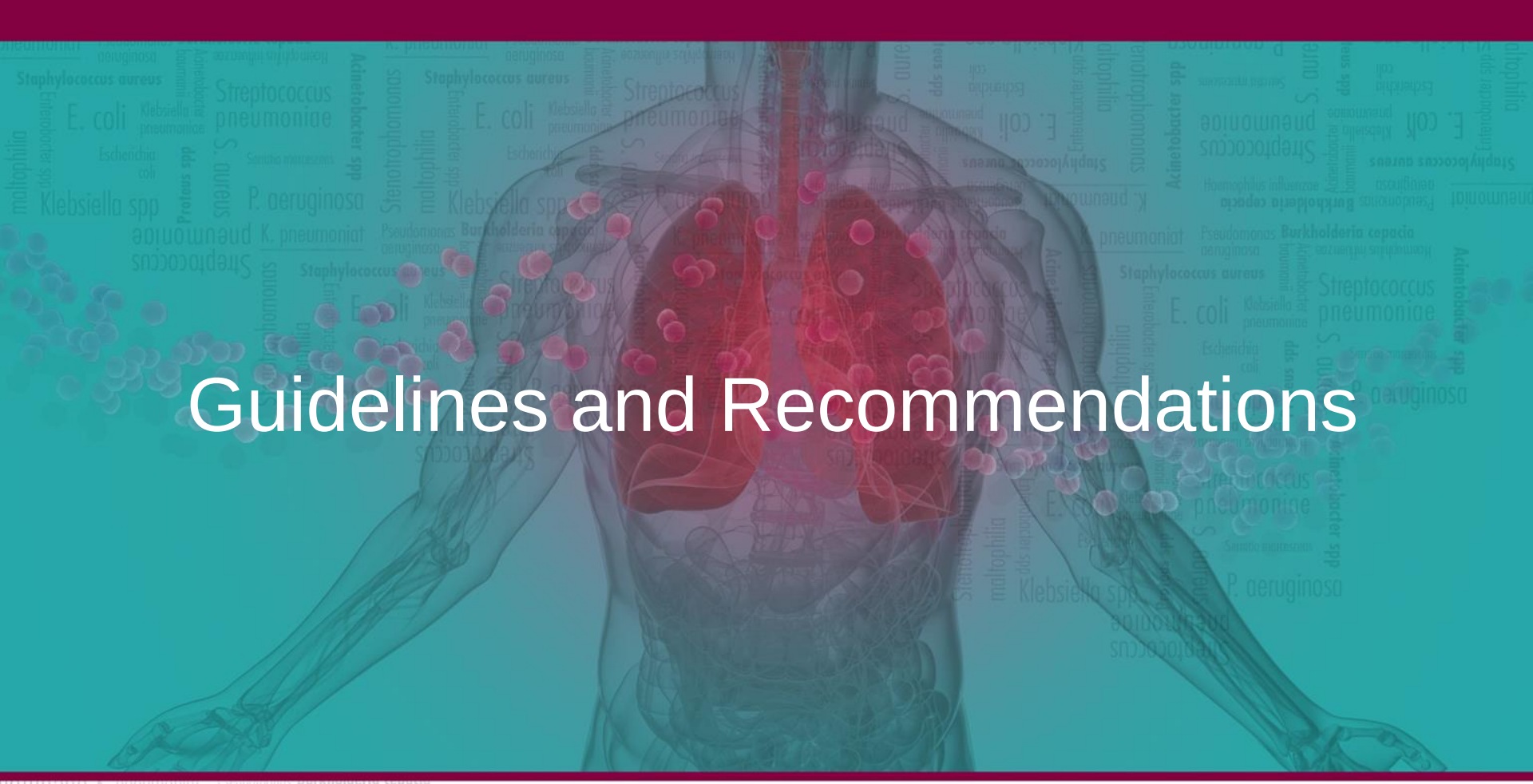
Organisms

- 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. 2021. 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* FiO2 or PEEP values. The baseline period is defined as the 2 calendar days immediately preceding the first day of increased daily minimum PEEP or FiO2.

***Daily minimum defined by lowest value of FiO2 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* FiO2 of ≥ 0.20 (20 points) over the daily minimum FiO2 in the baseline period, sustained for ≥ 2 calendar days.

2) Increase in daily minimum* PEEP values of ≥ 3 cmH2O over the daily minimum PEEP in the baseline period†, sustained for ≥ 2 calendar days.

***Daily minimum defined by lowest value of FiO2 or PEEP during a calendar day that is maintained at least 1 hour.**

†Daily minimum PEEP values of 0-5 cmH2O are considered equivalent for the purposes of VAE 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. National Healthcare Safety Network. 2021. https://www.cdc.gov/nhsn/pdfs/pscmanual/10-vae_final.pdf

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 as outlined in protocol, without requirement for purulent respiratory secretions:

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

2) Criterion 2: Purulent respiratory secretions (defined as 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, endotracheal aspirate, bronchoalveolar lavage, lung tissue, protected specimen brush

3) 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. 2021. 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 Concerns
Section 2: Background—Strategies to Detect VAP and Other VAE
Section 3: Background—Strategies to Prevent VAP and Other VAE
Section 4: Recommendations for Prevention of VAP and Other VAE
Section 5: Performance Measures
Section 6: Implementation Strategies

Klompas K, et al. *Infect Control Hosp Epidemiol*. 2014;35:915-36.

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. 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.
2. Organizing daily ventilator data into "line lists" for every patient, with 1 row of data per patient per calendar day, facilitates VAC detection by allowing the surveyor to vertically scan daily ventilator settings to look for sustained increases that cross the threshold for VAC. Surveyors can also enter raw data into the CDC's online "VAE calculator" to assist with case identification (http://www.cdc.gov/nhsn/VAE-calculator /index.html).

   a. 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).

Klompas K, et al. *Infect Control Hosp Epidemiol*. 2014;35:915-36.

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 noninvasive positive pressure ventilation (NIPPV) whenever feasible (quality of evidence: I)

B. Minimize sedation

1. Manage ventilated patients without sedatives whenever possible (quality of evidence: II)
2. Interrupt sedation once a day (spontaneous awakening trials) for patients without contraindications (quality of evidence: I)
3. Assess readiness to extubate once a day (spontaneous breathing trials) in patients without contraindications (quality of evidence: I)
4. Pair spontaneous breathing trials with spontaneous awakening trials (quality of evidence: I)

C. Maintain and improve physical conditioning

1. Provide early exercise and mobilization (quality of evidence: II)

D. Minimize pooling of secretions above the endotracheal tube cuff

1. Provide endotracheal tubes with subglottic secretion drainage ports for patients likely to require greater than 48 or 72 hours of intubation (quality of evidence: II)

E. Elevate the head of the bed

1. Elevate the head of the bed to 30–45 (quality of evidence: III)

F. Maintain ventilator circuits

1. Change the ventilator circuit only if visibly soiled or malfunctioning (quality of evidence: I)
2. Follow CDC/Healthcare Infection Control Practices Advisory Committee guidelines for sterilization and disinfection of respiratory care equipment (quality of evidence: II)

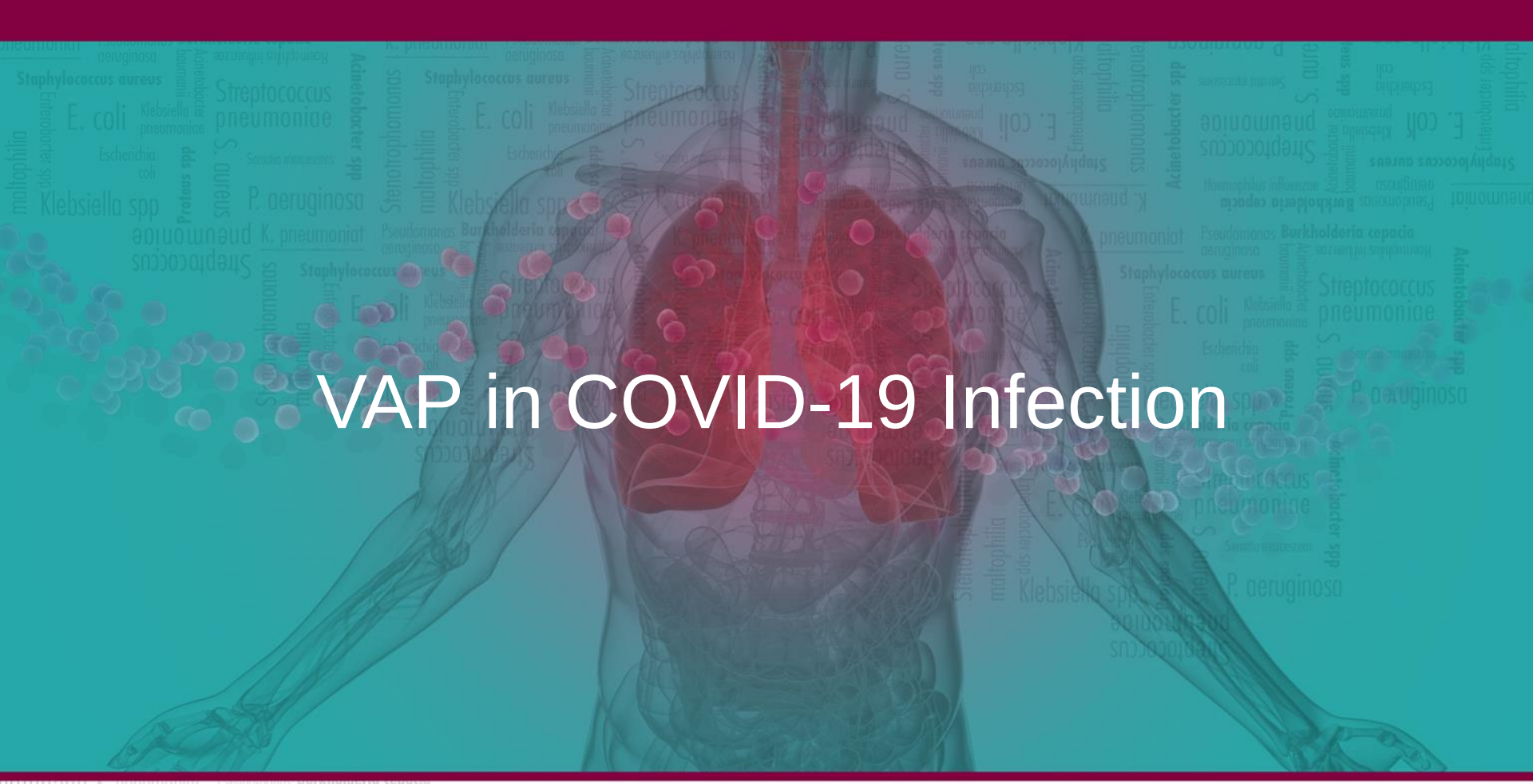
Klompas K, et al. *Infect Control Hosp Epidemiol*. 2014;35:915-36.

Some Cases May Be Missed

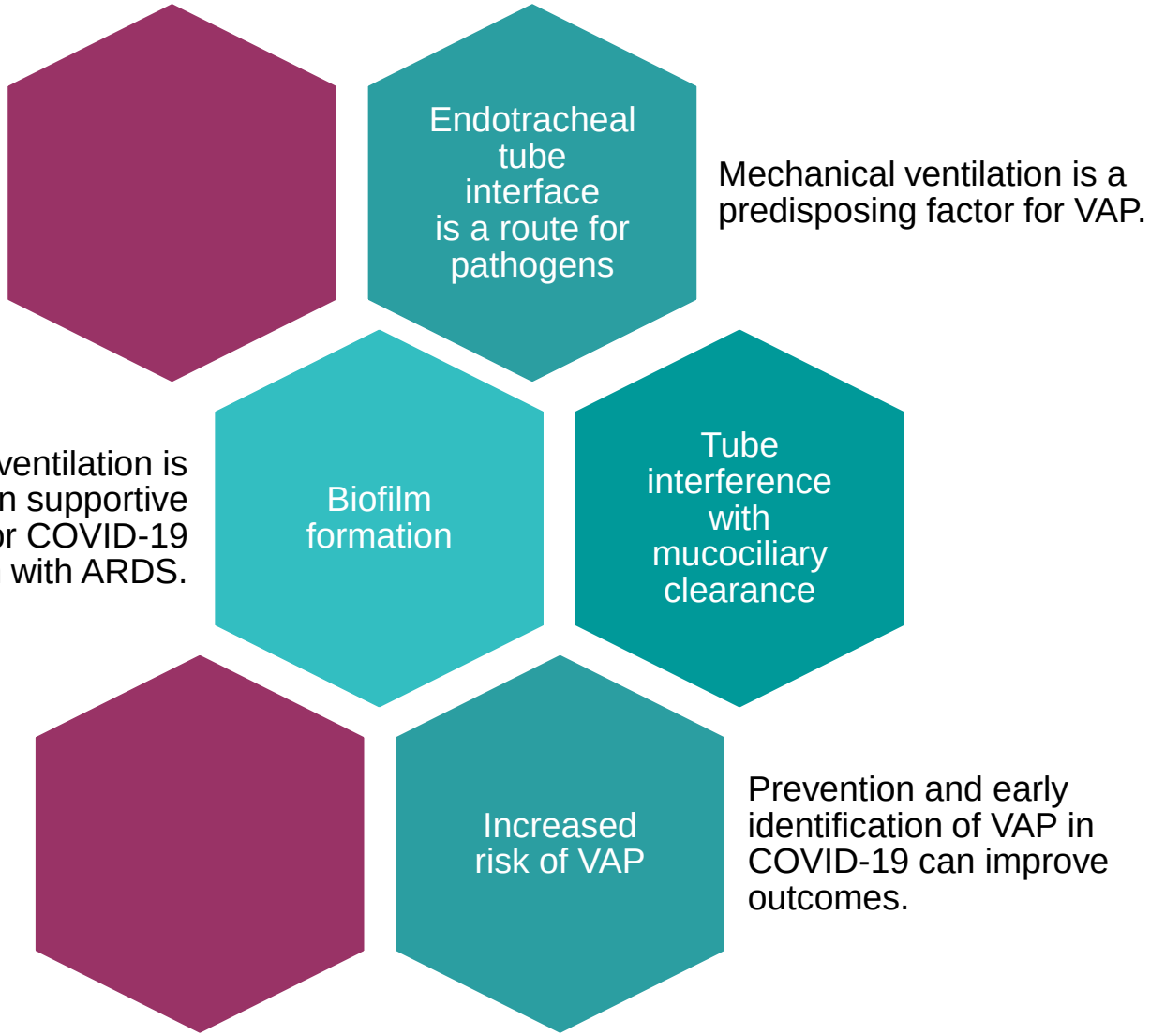
- The National Healthcare Safety Network replaced traditional VAP surveillance with VAE surveillance in 2013.
- Studies have found VAE surveillance missed many cases of VAP.
- Population characteristics identified by the two surveillance paradigms differed.

VAE surveillance may not accurately detect cases of VAP.

Haribhai S, et al. Ventilator Complications. 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560535/. Accessed May 9, 2021.


VAP in COVID-19 Infection

VAP Development in COVID-19



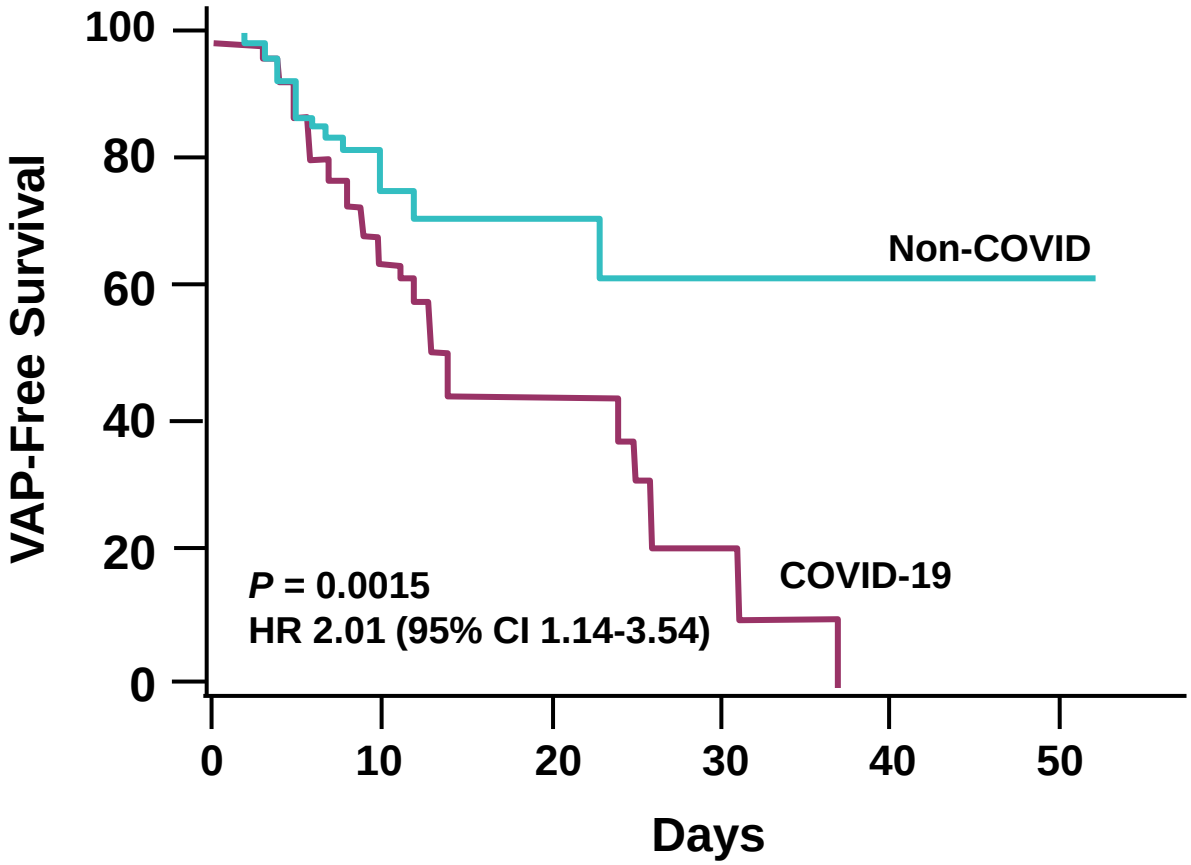
Mechanical ventilation is a predisposing factor for VAP.

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

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



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

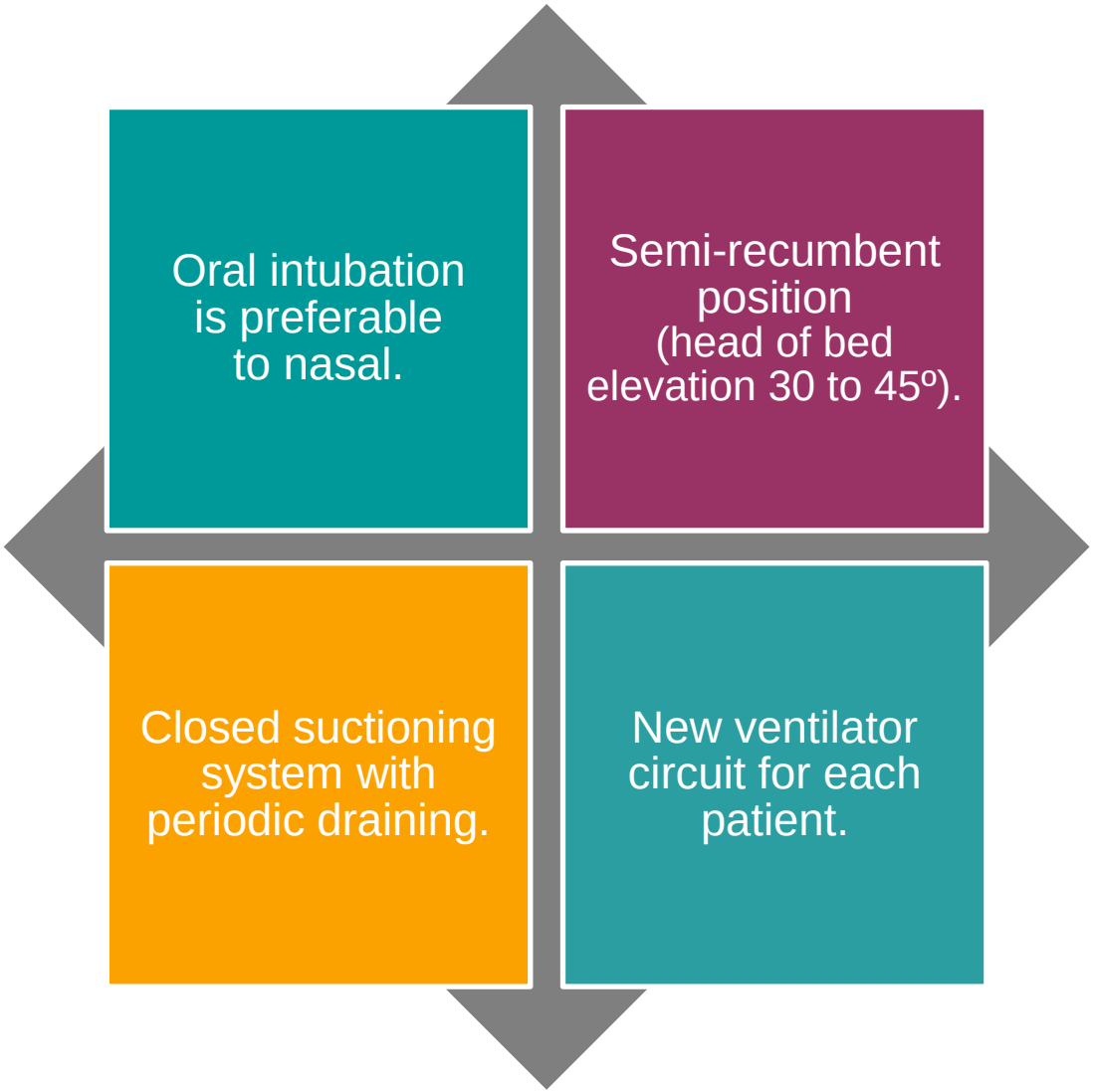
Co-Infection Isolates of COVID-19-Associated VAP

Organism	ETA ($\geq 10^5$ CFU/ml)	BAL culture ($\geq 10^4$ CFU/ml)	BAL PCR ($\leq$ 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

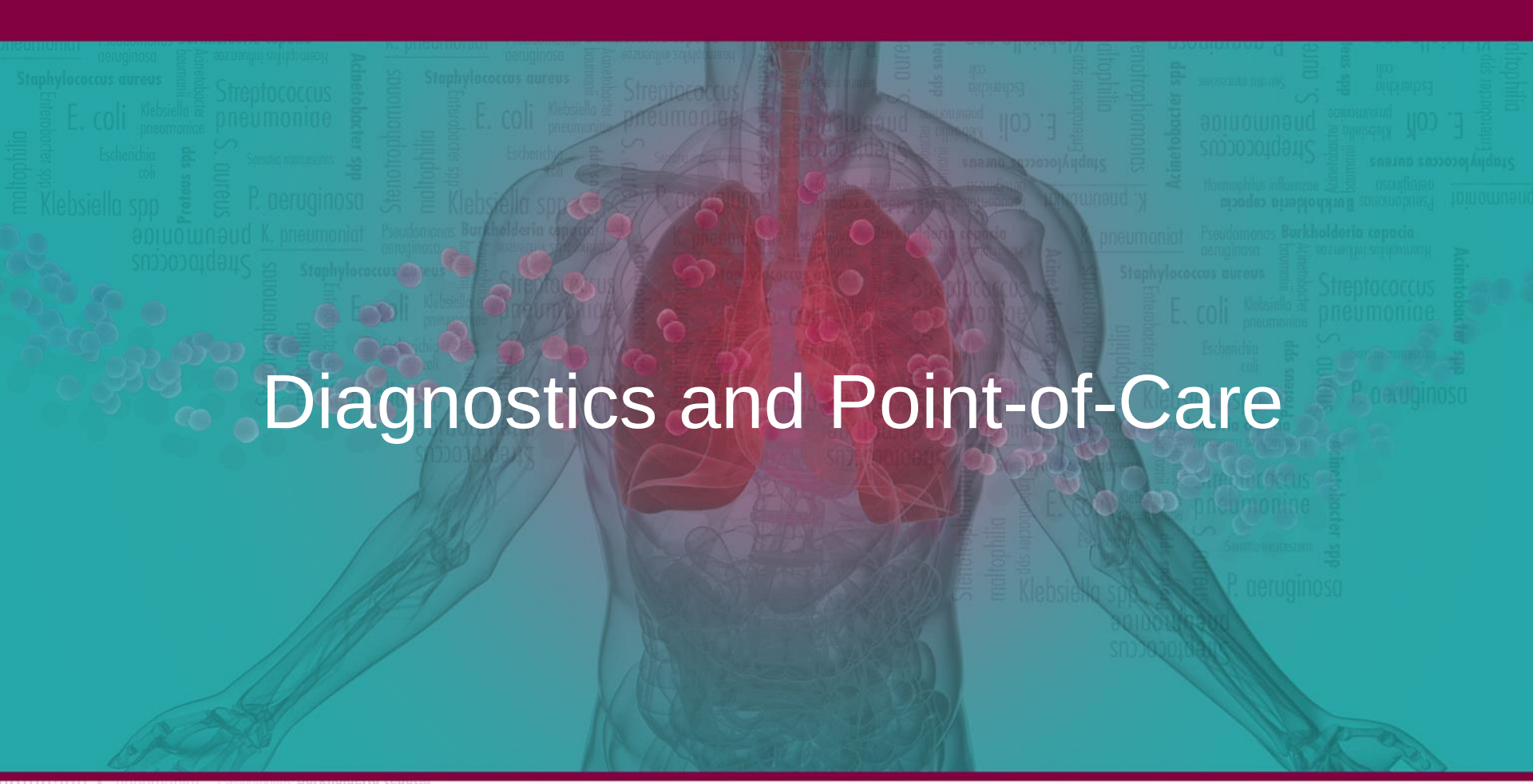
*Sequence for the organism in question not present on the TAC. !1 *E. coli* was detected by culture but not TAC in a patient, 2 *E. coli* detected by TAC without growth on culture. $Sequence on TAC is for *Proteus* spp. rather than species specific

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

World Health Organization COVID-19 Guidelines for Reducing VAP



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

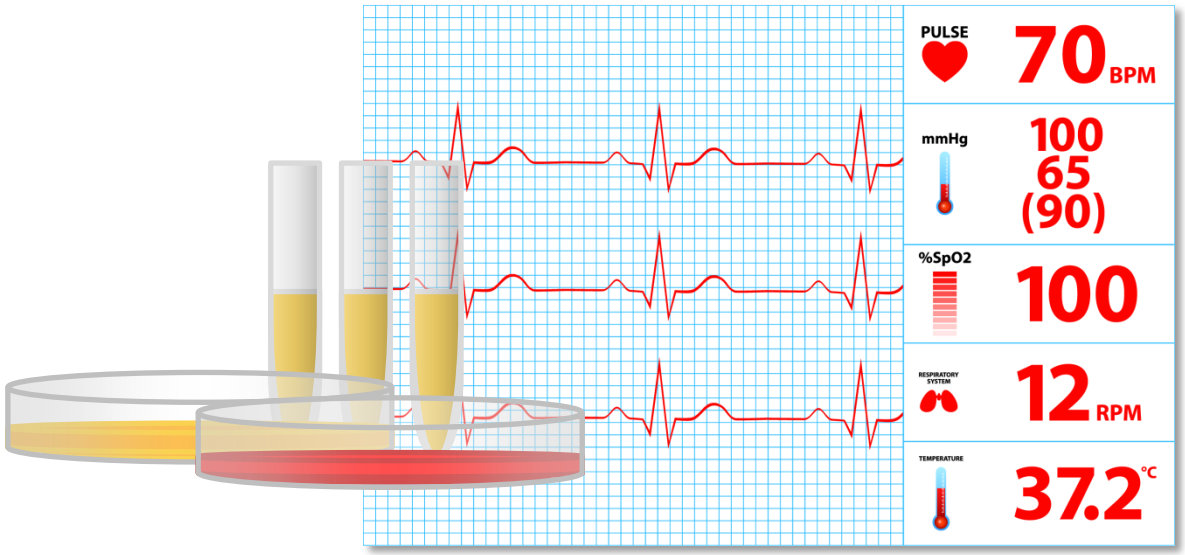
If diagnostic tests for VAP are positive:

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.

Diagnostic Methods



Diagnosing VAP requires a high clinical suspicion combined with bedside examination and microbiologic analysis of respiratory secretions.

http://ccsconline.org/high-value-care/vaevap. Accessed May 1, 2021.

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

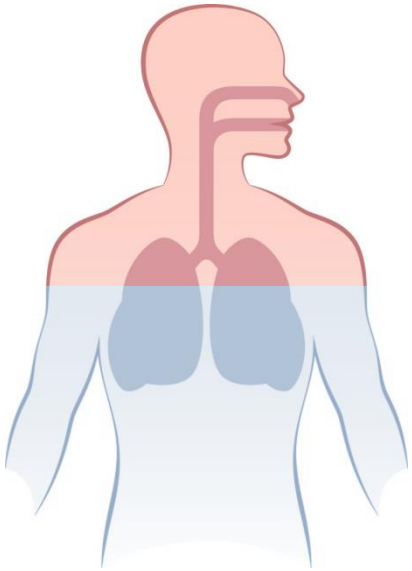
Clinical Pulmonary Infection Score (CPIS)	Temperature	Oxygenation (PaO2/FiO2)	Tracheal Secretions (Score)
	0 point: 36.5–38.4ºC	0 point: > 240 or ARDS	0 point: < 14
	1 point: 38.5–38.9ºC	2 points: < 240, No evidence of ARDS	1 point: > 14
	2 points: < 36 or > 39ºC		2 points: Purulent sputum
	Blood Leukocytes (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

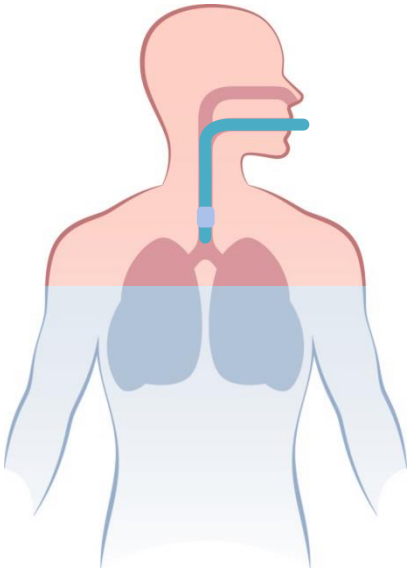
VAP Score > 6

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

Inaccuracy of Clinical Diagnosis of VAP



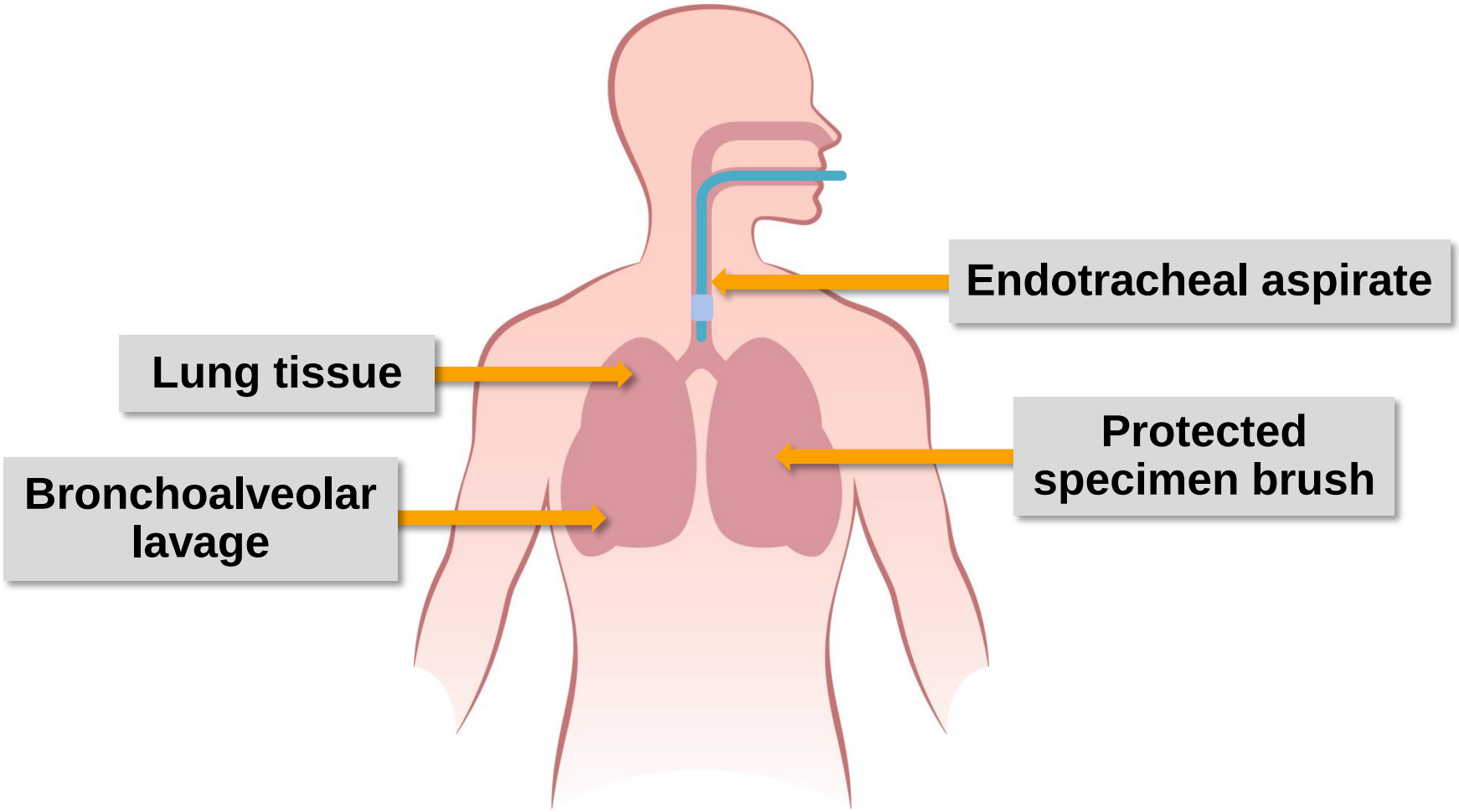
50%
Cases show no evidence of pneumonia at autopsy.



50%
Could not be confirmed by microbiological cultures.

https://emcrit.org/ibcc/vap/. Accessed May 1, 2021.
Torres A, et al. *Nat Rev Dis Primers*. 2021;7:25.

Microbiological Methods



CDC. *Device Associated Module*. 2021.

Specimen Threshold Values for Diagnosis

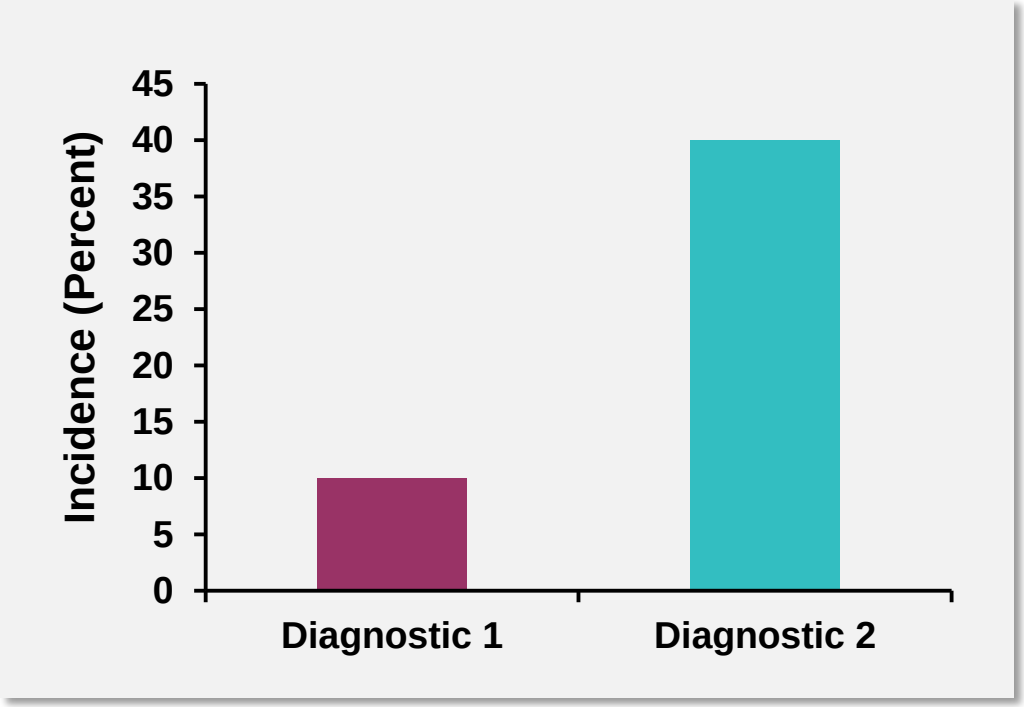
Specimen collection/technique	Values
Lung tissue	≥ 10^4 CFU/g tissue*
Bronchoscopically (B) obtained specimens	
Bronchoalveolar lavage (B-BAL)	≥ 10^4 CFU/ml*
Protected BAL (B-PBAL)	≥ 10^4 CFU/ml*
Protected specimen brushing (B-PSB)	≥ 10^3 CFU/ml*
Non-bronchoscopically (BN) obtained (blind) specimens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

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

CDC. National Healthcare Safety Network. 2021. https://www.cdc.gov/nhsn/pdfs/pscmanual/10-vae_final.pdf

Microbiological Method: Impact on Incidence

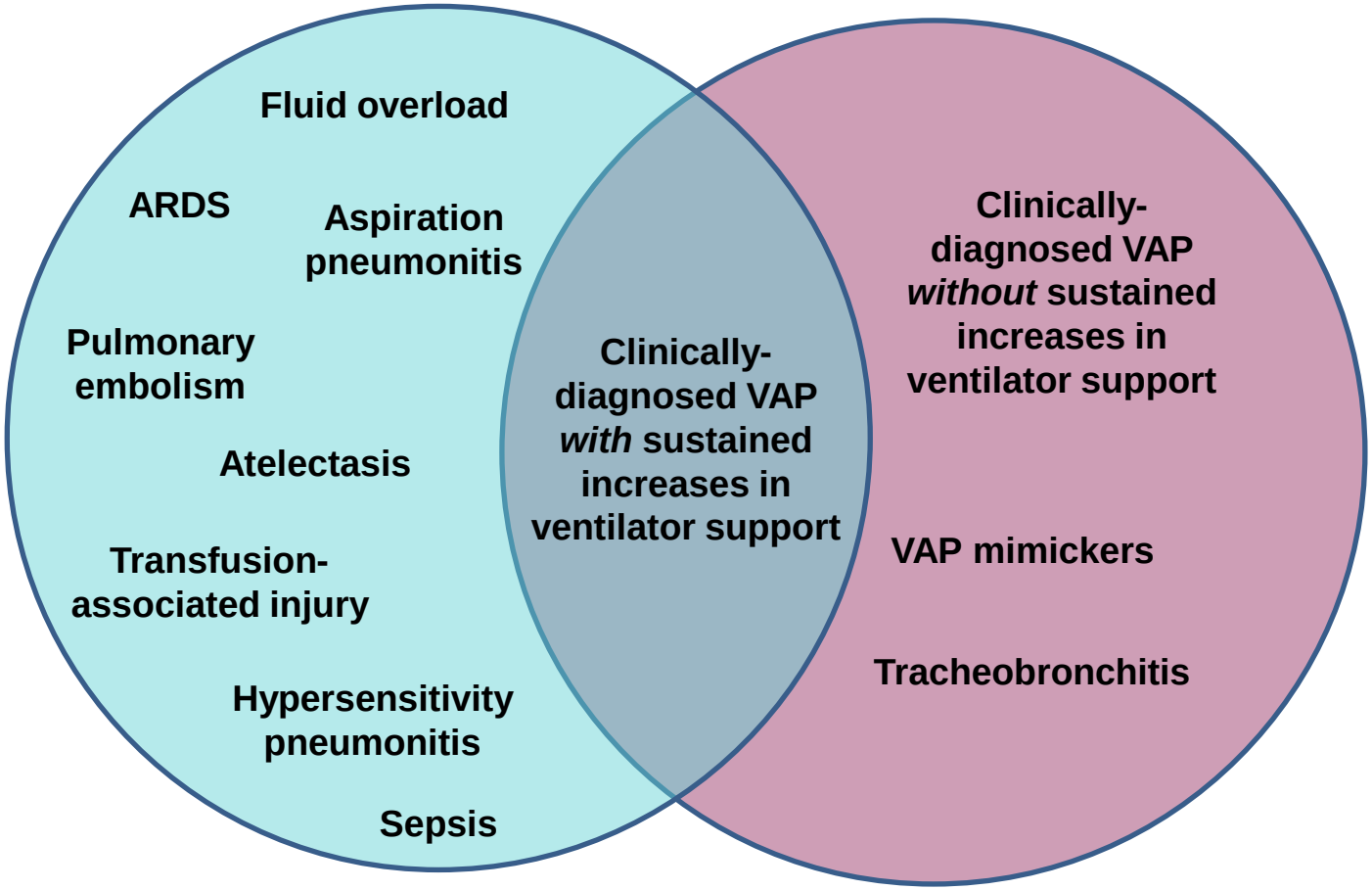
- Incidence of VAP varies widely in the literature
- Clinical variability
  - Patient populations
  - Pathogens
  - ICU type
  - Diagnostic methods



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



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 and should not be used to justify a prolonged antibiotic course, as clinical cure does not equate to microbiological eradication.

Zilahi G, et al. *J Thorac Dis.* 2016;8(12):3774-80.|
Messika J, et al. *Ann Transl Med*. 2018;6(21):426.

Diagnosis and Poor Clinical Response

Unusual or Resistant Pathogens

- Mycobacteria
- Virus
- Fungus

Incorrect Diagnosis

- Atelectasis
- Pulmonary
- Embolism
- ARDS
- Alveolar
- Hemorrhage
- Neoplasia

Complications

- Emphysema
- Lung Abscess
- *Clostridium difficile*
- Other infections

Inadequate Antimicrobial Therapy

- Short Duration
- Long Duration

Zilahi G, et al. *J Thorac Dis.* 2016;8(12):3774-80.

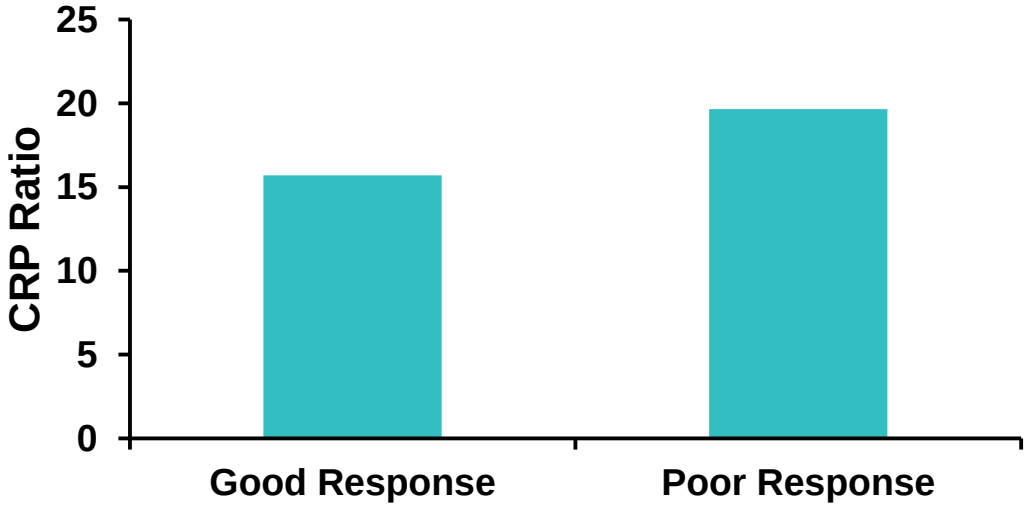
Biomarkers

- 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.

CRP Shows Promise for VAP Prediction

	Good Response	Poor Response	P-Value
Leukocytes	13,514 ± 5,264	15,685 ± 42,563	0.033
Temperature ºC	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.

CRP and Modified CPIS Scores Are Associated With Gradual Development of VAP

	AUC	95%CI	*P*-Value	Sensitivity	Specificity	Likelihood Ratio	
						Positive	Negative
PCT ≥ 0.5 ng/mL	0.505	0.332–0.677	0.953	65	40	1.08	0.88
CRP ≥ 54 mg/dL	0.678	0.493–0.863	0.047	60	49	1.22	0.86
mCPIS > 5 points	0.67	0.545–0.796	0.016	44	92	6.67	0.6

CRP = C-reactive protein, mCPIS = modified Clinical Pulmonary Infection Score, PCT = procalcitonin

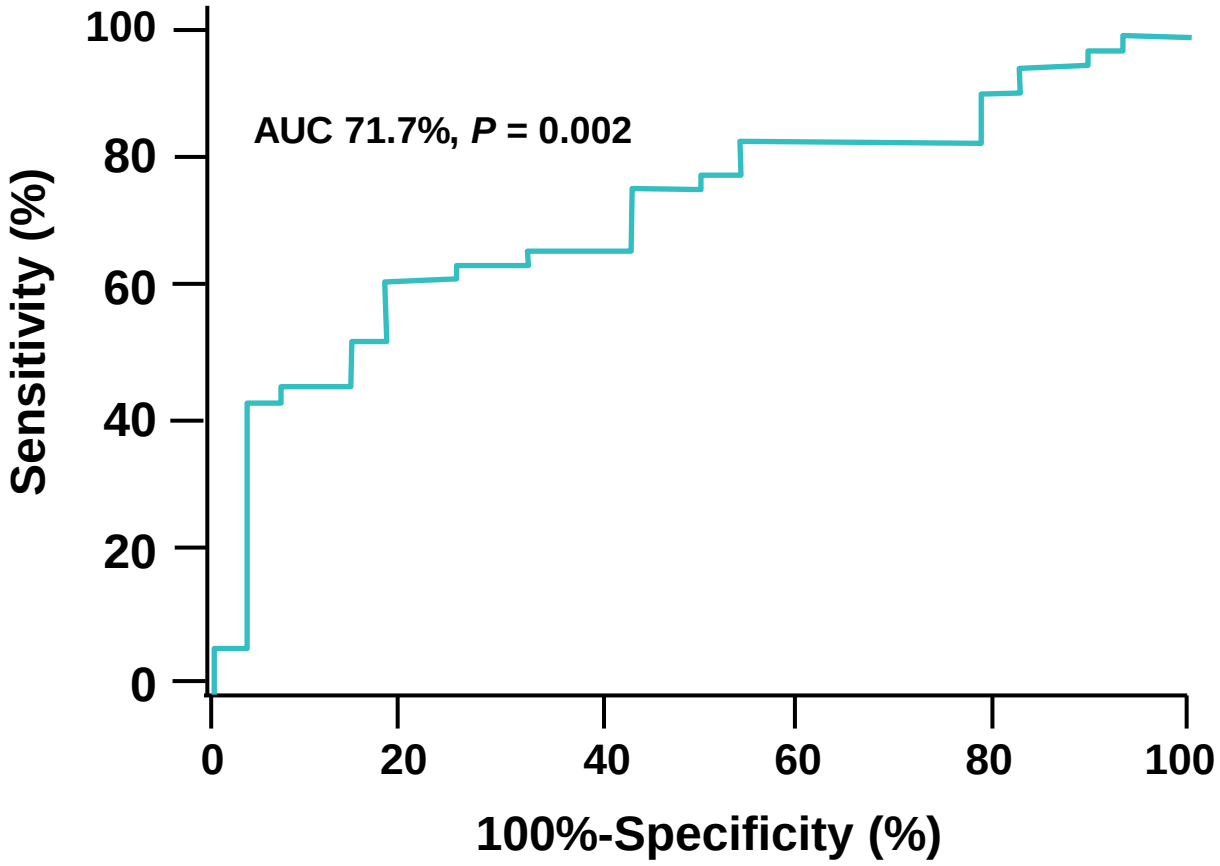
Ramirez P, et al. *Critical Care.* 2016;20:169.

Gradual VAP Biomarker Kinetics

	Pre-VAP CRP (mg/dl)	VAP CRP (mg/ml)	*P* Value	Pre-VAP PCT (ng/dl)	VAP PCT (ng/ml)	*P* Value
Non-gradual VAP	76 [9.75–186]	200 [99–347]	0.565	0.78 [0.25–9.09]	1.41 [0.5–6.2]	0.006
Gradual VAP	159 [80–210]	132 [67.7–268.5]	0.502	0.9 [0.42–2.35]	1.42 [0.56–4.21]	0.008

Ramirez P, \et al. *Crit Care*. 2016;20:169.

PCT Associated With VAP Mortality in COVID-19



Côrtes MF, et al. *Diagn Microbiol Infect Dis.* 2021;115344.

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

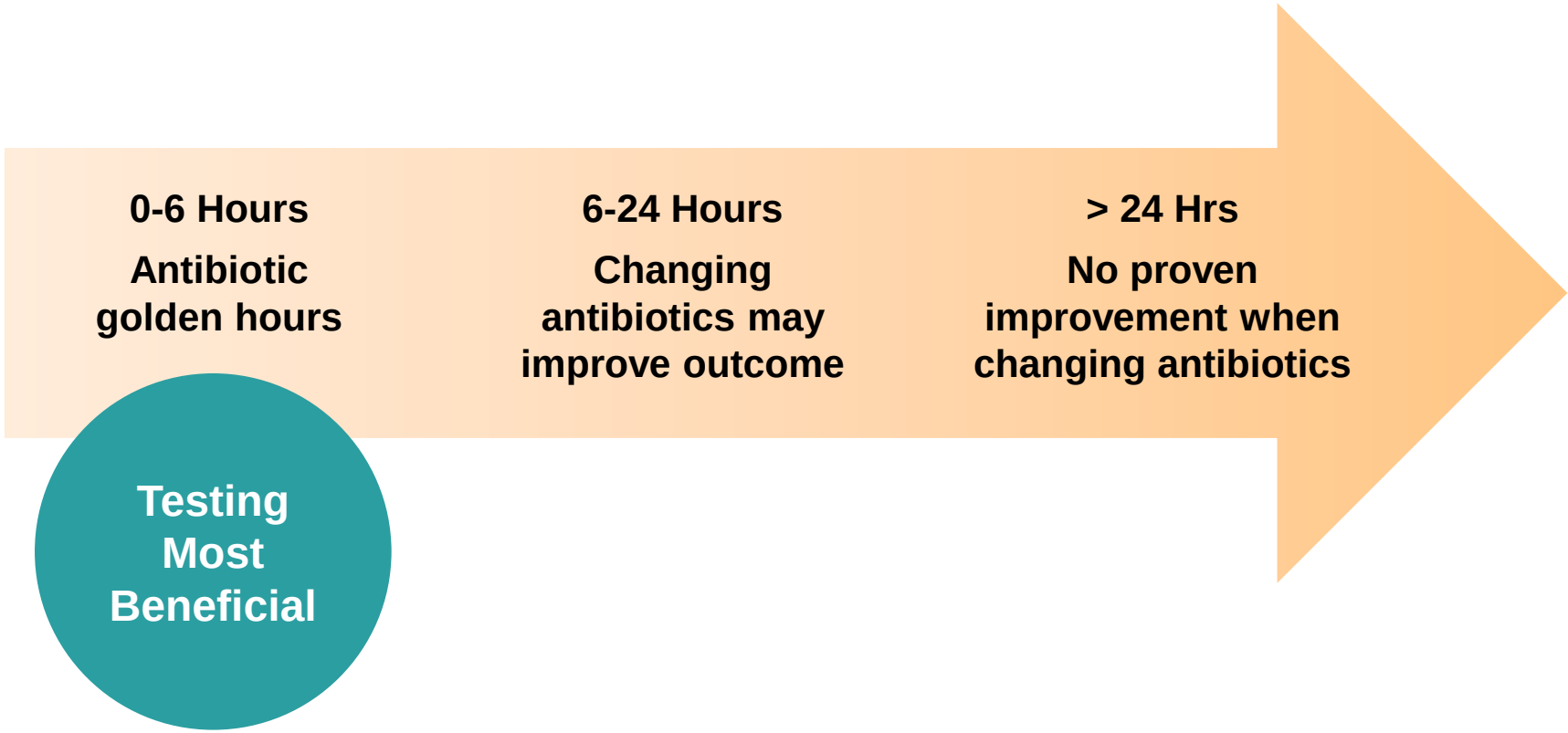
Use clinical criteria alone, rather than using PCT, CRP, or sTREM-1 or clinical pulmonary infection score (CPIS) plus clinical criteria, to decide whether or not to *initiate* antibiotic therapy.

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.

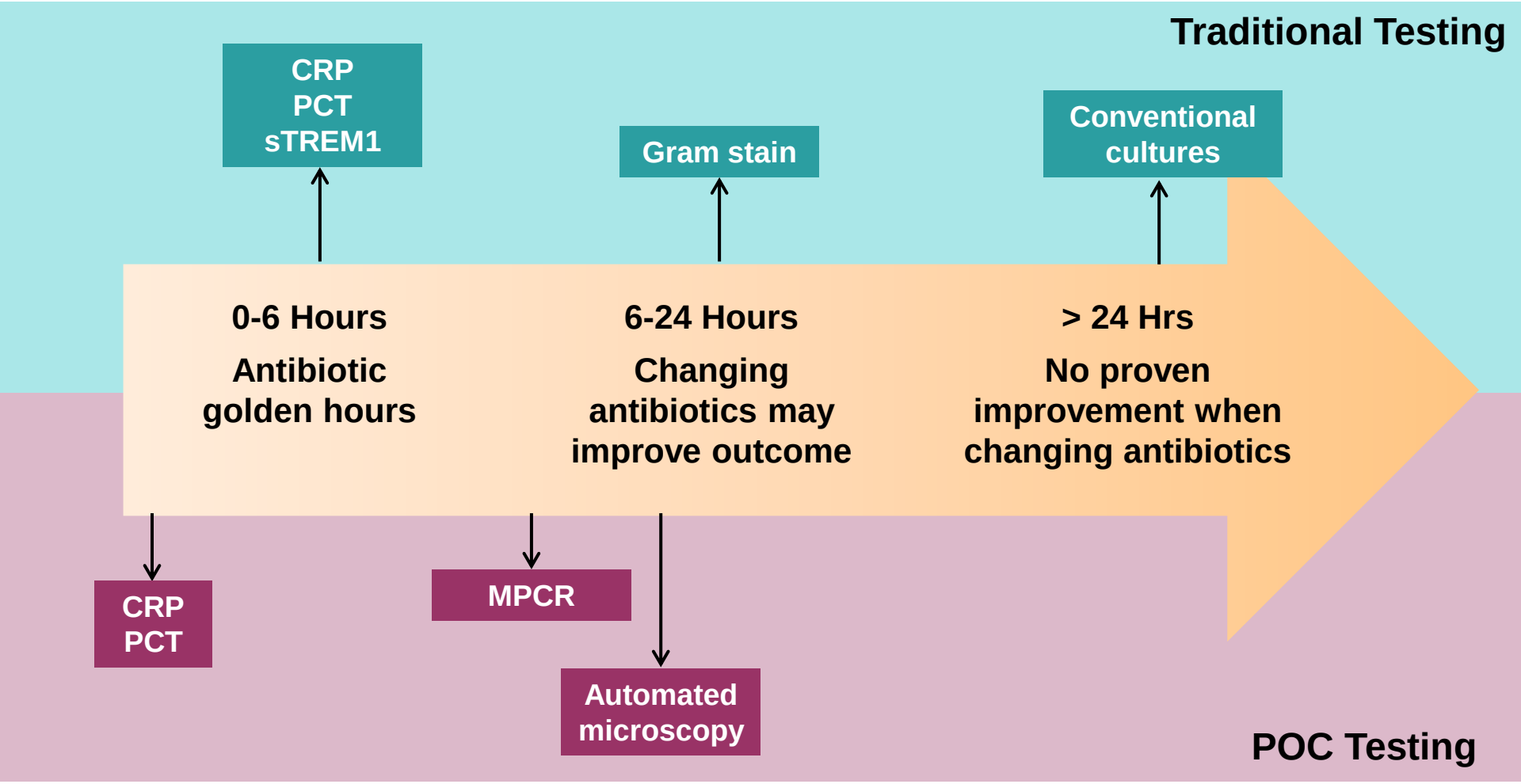
Kalil AC, et al. *Clin Infect Dis*. 2016;63(5):e61–e111.

VAP Timeline: Implications for Point-of-Care Testing



Millot G, et al. *Ann Transl Med.* 2017;5(22):451.

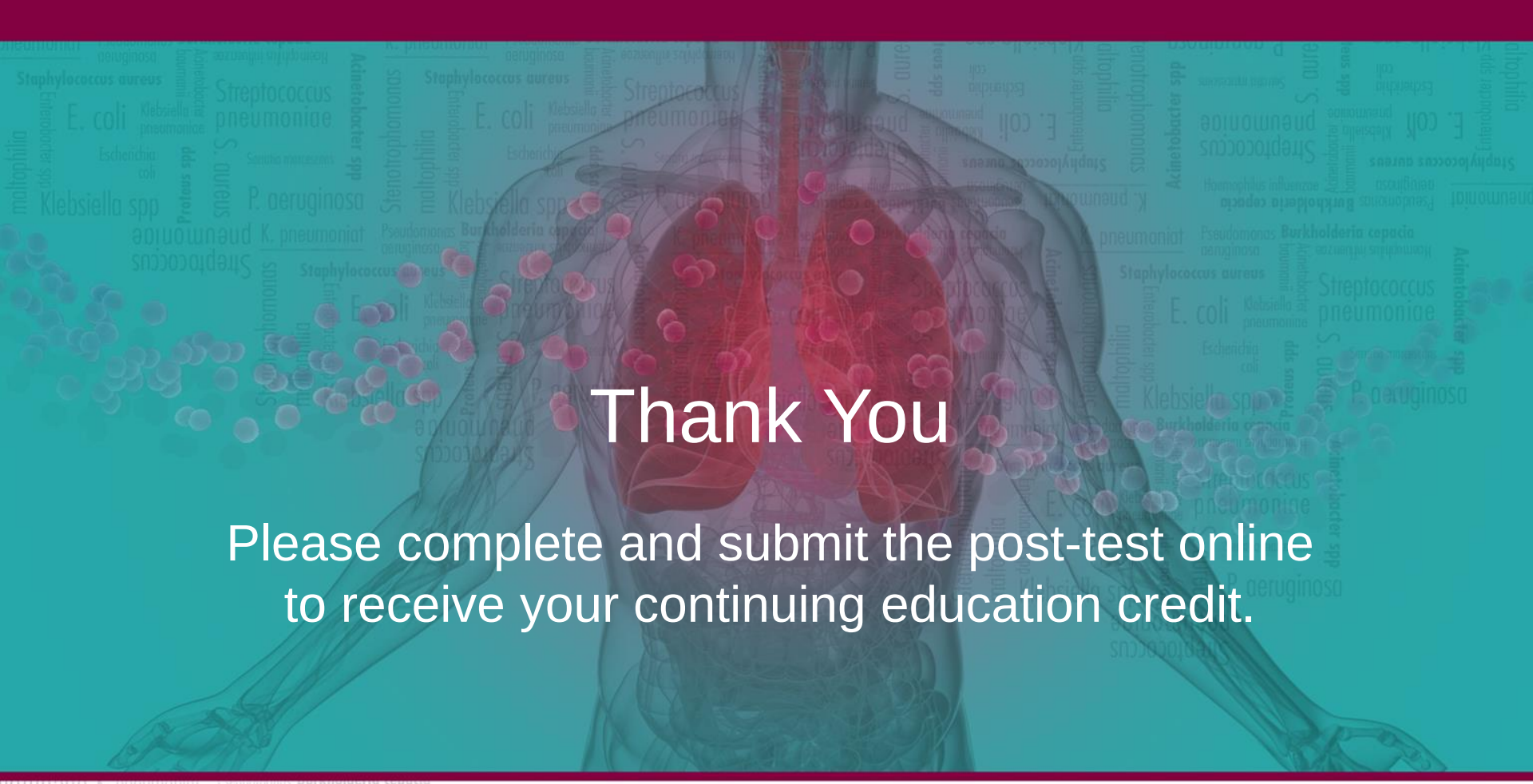
VAP Timeline: Implications for Point-of-Care Testing



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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