



# How should we define VAP to get a reliable diagnosis and monitoring?

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# COIs

- Nothing related to this presentation



# VAP for individual diagnosis and/or collective usage?

Individual:

- Early diagnosis and early appropriate treatment
- Estimation of Patients' outcomes (mortality, Duration of stay, QoL...)

Global:

- Identification of population at risk
- Case-mix adjusted strategies of improvement of Quality of Care
- Case-Mix adjustment for benchmarking

# VAP: a benchmark tools?

*Uçkay I – Clin Infect Dis 2008; 46:557*

- CON: Benchmarking VAP rates as outcome parameters between institutions is hazardous and potentially misleading.
- PRO: That is not because VAP is very difficult to diagnose that we must ignore it...

*Donabedian A– ICHE 1990:11:117*

# Appropriate end-point for clinicians and healthcare practitioners

**Crucial for treating patients, and for successful interpretation of an IC program or an intervention**

Definition of VAP should comply with the following characteristics

1. Objective (little variability in measurement between observers)
2. Frequent (powerful to detect variations)
3. Easy to measure
4. Internal validity (related to the disease being studied or related to a true patient-related (or healthcare system) outcome)
5. External validity (valid to target population outside of the study)

# Impact of Diagnostic Criteria on the Incidence of Ventilator-Associated Pneumonia

Amédée Ego, MD; Jean-Charles Preiser, MD, PhD; and Jean-Louis Vincent, MD, PhD, FCCP

## 89 possibility of combination to diagnose VAP...

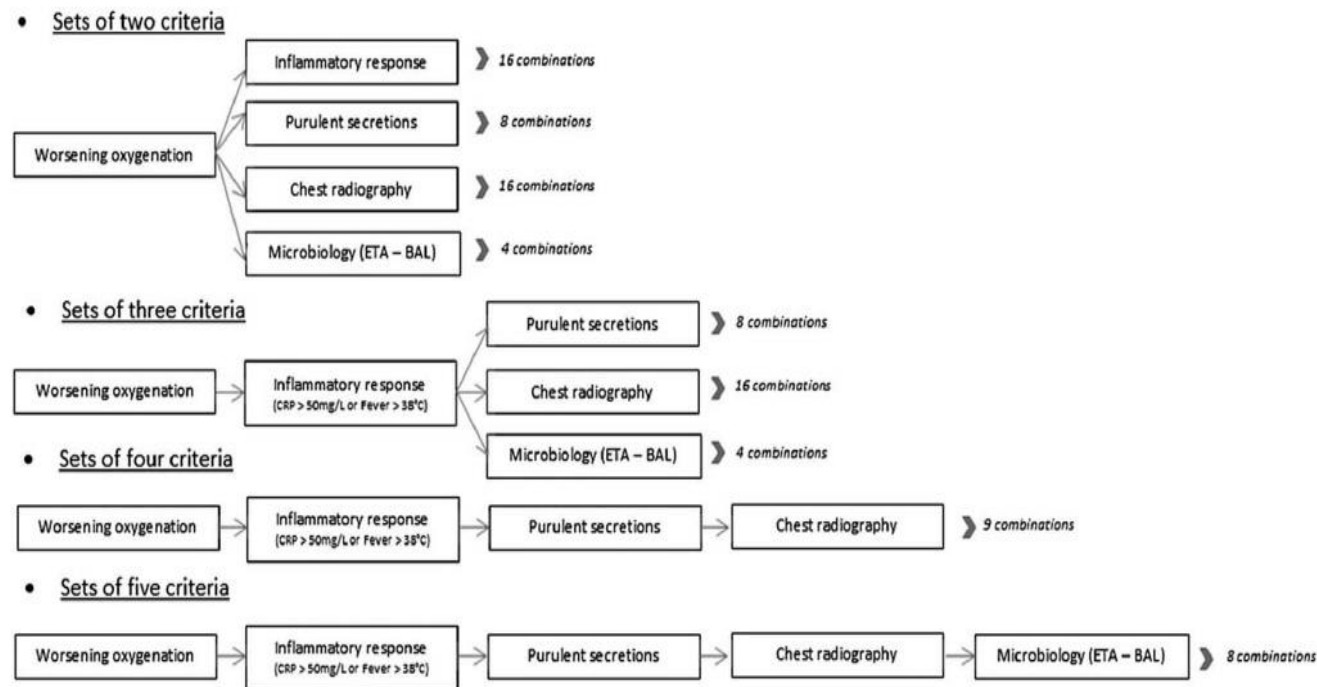


Figure 1 – Construction of the 89 sets of criteria. See also e-Table 1. CRP = C-reactive protein; ETA = endotracheal aspirate.

TABLE 2 | Criteria Used to Build the 89 Sets

Worsening oxygenation
PEEP > 2 cm H <sub>2</sub> O or Fio <sub>2</sub> > 0.15
PEEP > 5 cm H <sub>2</sub> O or Fio <sub>2</sub> > 0.30
PEEP > 2 cm H <sub>2</sub> O or Fio <sub>2</sub> > 0.15 for two successive days
PEEP > 5 cm H <sub>2</sub> O or Fio <sub>2</sub> > 0.30 for two successive days
Inflammatory response
Leukopenia < 4,000 mm <sup>3</sup> or leukocytosis > 12,000/mm <sup>3</sup>
CRP > 50 mg/L
Neutrophils > 7,700/mm <sup>3</sup>
Pyrexia > 38°C
Tracheal aspirates
Purulent
Type 5 ETA <sup>a</sup> (< 25 leukocytes, > 10 epithelial cells per field)
Chest radiography
Diffuse infiltrates
Consolidation
Worsening infiltrates
Microbiology (qualitative culture)
ETA positive
BAL positive

CRP = C-reactive protein; ETA = endotracheal aspirate. See Table 1 legend for expansion of other abbreviation.

<sup>a</sup>Bartlett classification.<sup>18</sup>

# Impact of Diagnostic Criteria on the Incidence of Ventilator-Associated Pneumonia

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Ego A et al - CHEST 2015; 147( 2 ): 347- 355

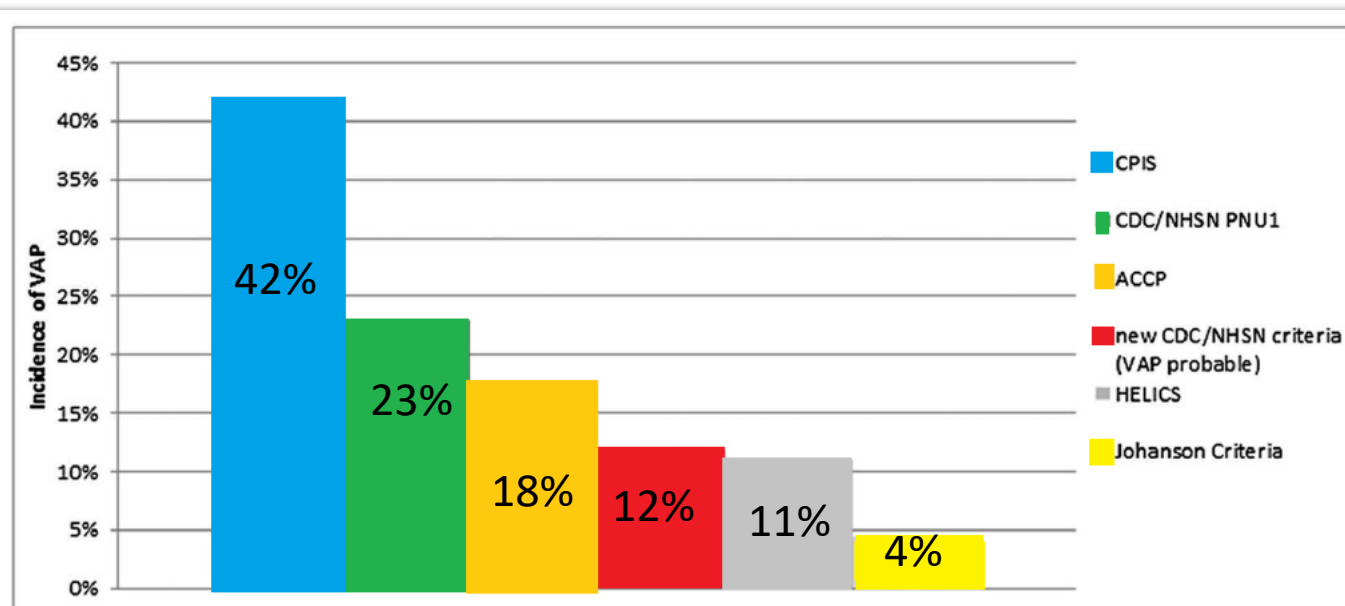


Figure 3 – Incidence of VAP according to the published algorithms. CDC/NHSN PNU1 = US Centers for Disease Control and Prevention/National Healthcare Safety Network clinically defined pneumonia; ACCP = American College of Chest Physicians; CPIS = Clinical Pulmonary Infection Score; HELICS = Hospital in Europe Link for Infection Control through Surveillance; VAP = ventilator-associated pneumonia.

TABLE 4 ] Agreement Between Published Criteria<sup>a</sup>

Published Criteria	CDC/NHSN PNU1	HELICS	CPIS	CHEST	Johanson's Criteria
New CDC/NHSN VAP probable	0.23	0.24	0.27	0.22	0.26
CDC/NHSN PNU1	...	0.43	0.35	0.56	0.27
HELICS	...	...	0.09	0.38	0.09
CPIS	...	...	...	0.31	0.12
CHEST	...	...	...	...	0.14

See Table 1 legend for expansion of abbreviations.

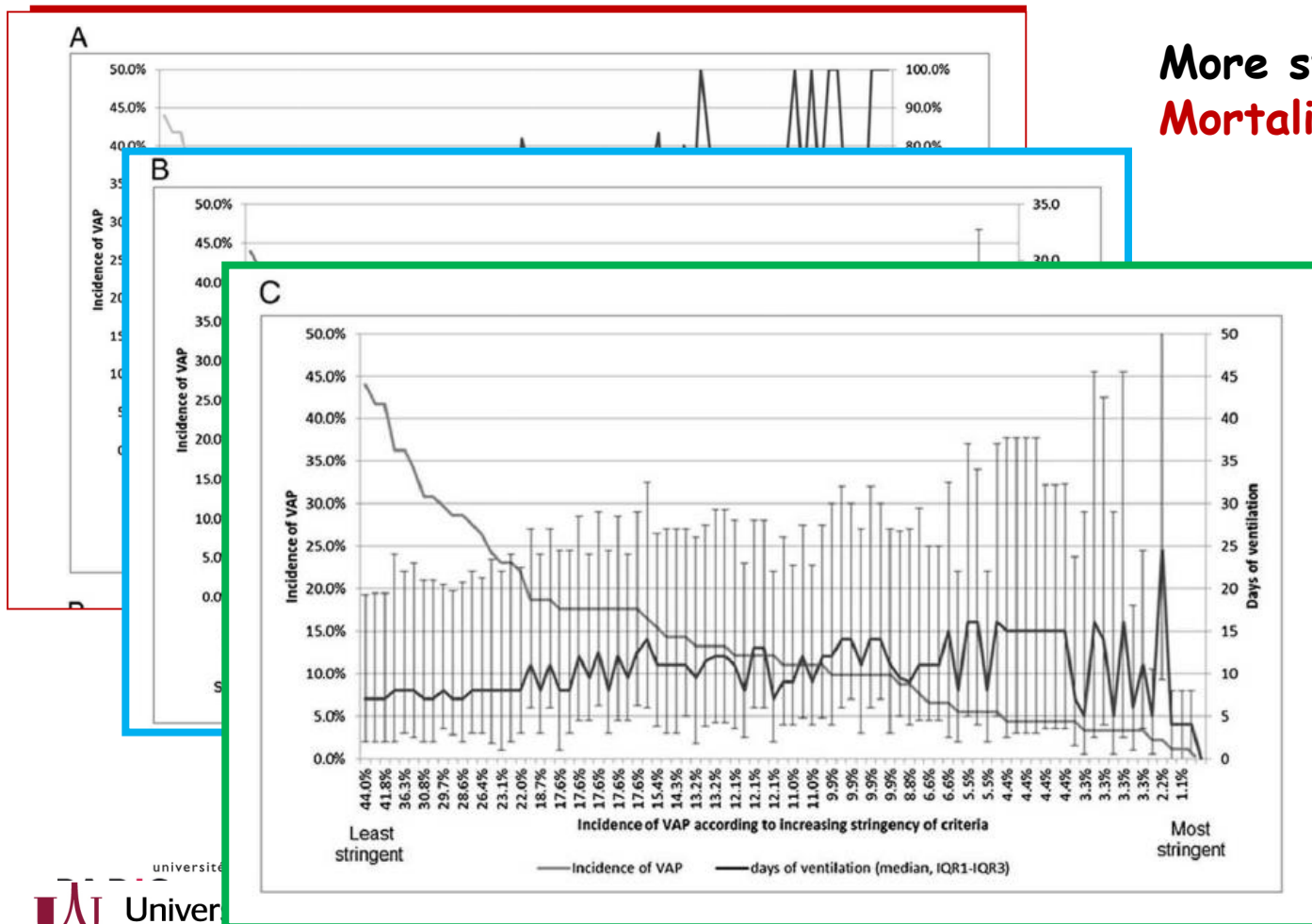
<sup>a</sup>Assessed using Cohen κ (0-0.20: very low agreement; 0.21-0.40: low; 0.41-0.60: moderate; 0.61-0.80: strong; 0.81-1: almost perfect).

**Various results  
Poorly correlated**



# Impact of Diagnostic Criteria on the Incidence of Ventilator-Associated Pneumonia

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More stringent criteria=  
Mortality increase 50 → 80%

Later Diagnosis 4 → 8 days

Increased  
Duration of  
stay

# IVAC is easy to collect automatically but with a poor internal- validity

## ***Ventilator-associated conditions (VACs):***

MV worsening after at least 2 days of stable MV status (PEEP/FiO<sub>2</sub>)

## ***Infection-related ventilator-associated complications (IVACs):***

VAC + T°C or abnormal WBC AND at least one new antibiotics continued for at least 4 days.

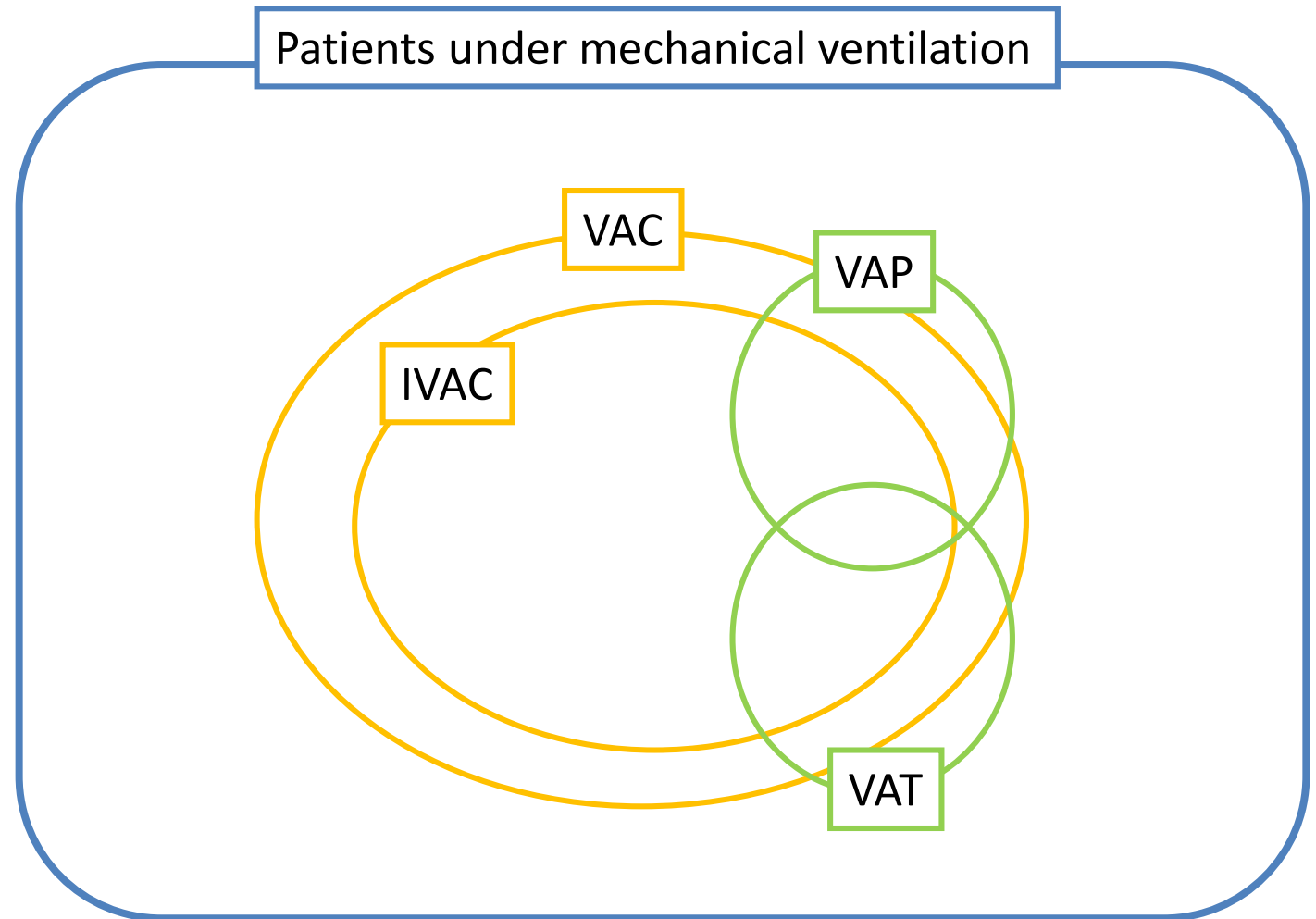
## ***Possible ventilator-associated pneumonia (VAP) (CDC):***

IVAC plus + culture / purulent secretion or empyema/legionella.lung histopathology

**VAP:** New infiltrates+ systemic criteria (abn T°, WBC), + pulm criteria (purulent aspirates or worsening blood gases)

## ***Ventilator-associated tracheobronchitis (VAT):***

Criteria for VAP but without radiographic criteria.



# External validity should take into account the case-mix

- Intubated/tracheostomized
- Preexisting pulmonary diseases (COPD, ARDS...)
- ECMO
- Immunocompromized hosts (neutropenia, others)

# Other issues for ICP

- First episode only?
- Definition of relapse, recurrence?
- Denominators? (number patients, duration of MV before the 1st episode, global duration of MV.....)



MI<sup>2</sup>

- **Clinical diagnosis**
- Microbiological diagnosis
- Non microbiological diagnosis
- Diagnostic strategy



# Who need to be suspected of VAP?

- ' Is there a:
  - new 'sepsis' or an increase in catecholamines?
  - ' New or worsening respiratory status (oxygenation)?'
  - New and persistent infiltrates?
  - ' Modification and purulence of expectorations/aspirates
- For which patients may diagnostic microbiological tests NOT be performed?

# Clinical radiological and biological signs are of limited values

Klompas M – JAMA 2007; 297:1583

Finding	Se %	Sp%
Fever	45-67	33-76
Abnormal WBC	50-86	7-76
Sputum purulence	50-79	33-67
Crepitation on auscultation	73	40
Hypoxemia	64	40
New infiltrates	78-100	33-75

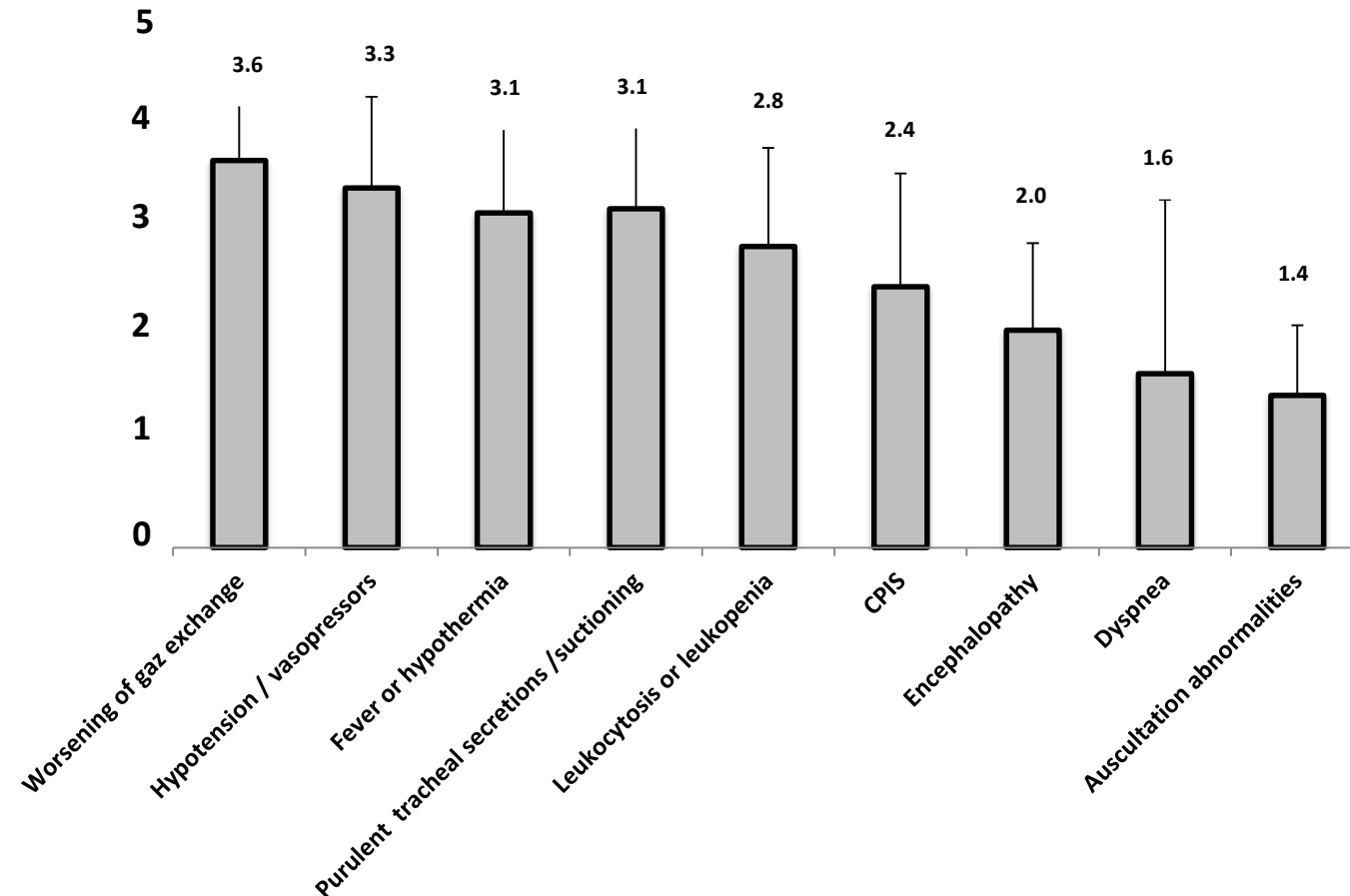
# Main criteria for suspicion of VAP

(Delphi process international expert panel)

Weiss E et al – Clin Infect Dis. 2019 Nov 13;69(11):1912-1918

A

Agreement on VAP suspicion criteria



The traditional signs of clinical VAP are no longer the most accurate ones for experts



# Biomarkers (CRP/PCT) should not be used for diagnosis

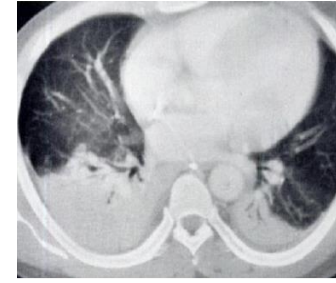
**VI. In Patients With Suspected HAP/VAP, Should C-Reactive Protein (CRP) Plus Clinical Criteria, or Clinical Criteria Alone, Be Used to Decide Whether or Not to Initiate Antibiotic Therapy?**

*Recommendation*

1. For patients with suspected HAP/VAP, we recommend using clinical criteria alone rather than using CRP plus clinical criteria, to decide whether or not to initiate antibiotic therapy (*weak recommendation, low-quality evidence*).



# Radiology



- Chest X ray:
  - Poor specificity (30%) and intermediate sensitivity (60%)
  - Subjective interpretation and high interobserver variability
- Value of?
  - CT-scan: good NPV
  - Thoracic US: idem CT scan?

*Klompas AJIC 2010*

*Winner, Radiology 1998*

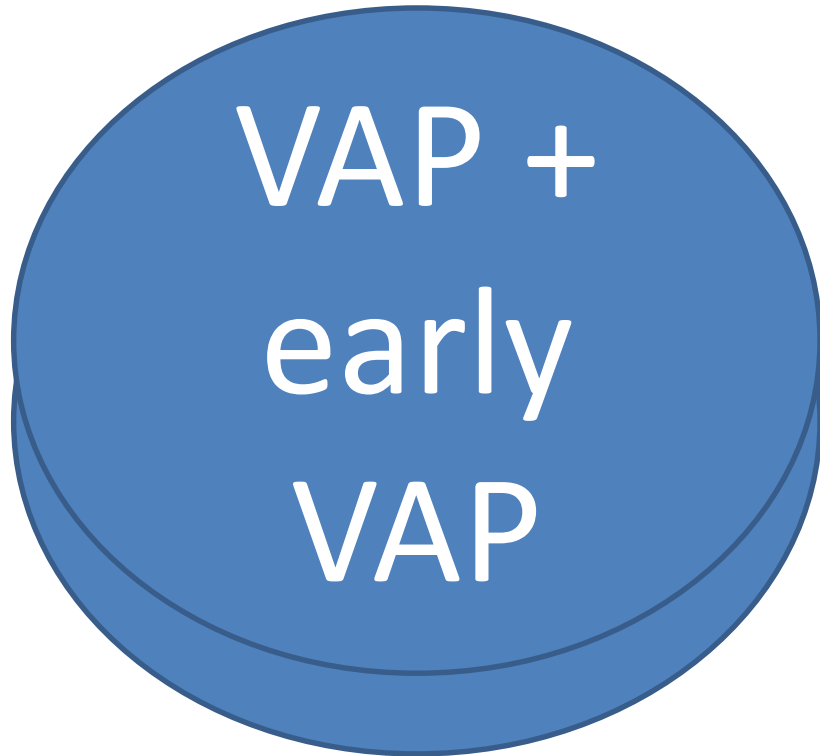
*Bouhemad, Crit Care Med 2010.*

*Mongodi S et al – Chest 2016; 969*

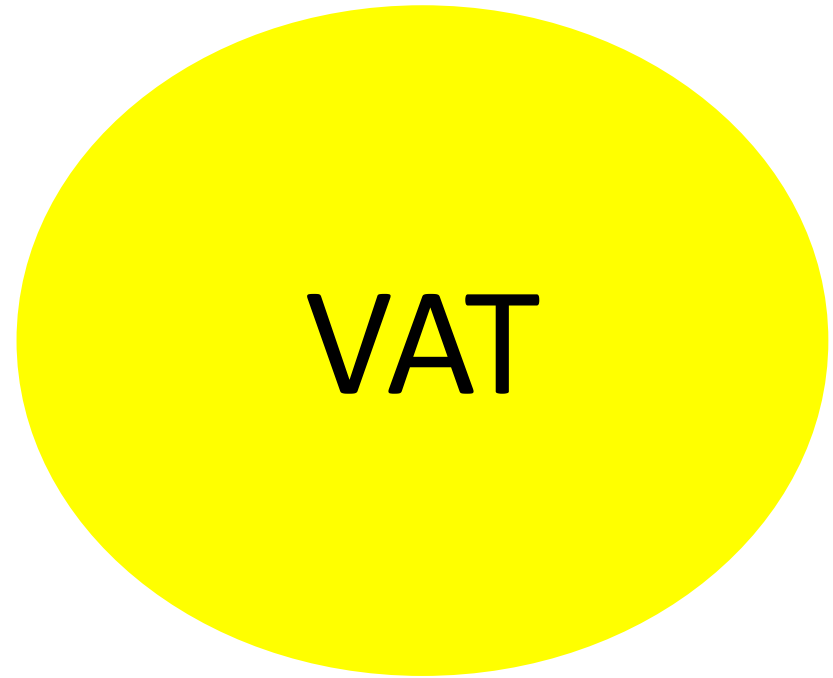


VAP

VAT



VAT not  
requiring therapy



## VAT-VAP a continuum?

- Distinct prognosis/ similar ICU LOS
- Younger patients, Lower severity
- Only 1/3 of untreated VAT → VAP
- Mortality of VAT similar to mortality of MV patients > 48 hours

**Important consequence for the counting process:**  
*overuse of VAT to decrease procecssion risk.....*



# Agenda

1. Who are the patients with a clinical suspicion of HAP-VAP?
- 2. Should we perform bacterial exams?**
3. Which ones? (quantitative or not, distal of proximal)
4. When to accept the absence of VAP and to stop antibiotics?
5. Impact of strategies on patients' outcome and antimicrobial consumption

# We should perform bacteriological exams



**R2.2 – We suggest collecting microbiological airway samples, regardless of type, before initiation of or any change in antibiotic therapy.**

**GRADE 2+, STRONG AGREEMENT**

“Therefore, both sampling and culture methods are left to the discretion of clinicians according to strategic choices at the unit, department or institutional levels.”

Anaesth Crit Care Pain Med 37 (2018) 83–98



We recommend obtaining a lower respiratory tract sample (distal quantitative or proximal quantitative or qualitative culture) to focus and narrow the initial empiric antibiotic therapy. (Strong recommendation, low quality of evidence.)

**III. In Patients With Suspected HAP (Non-VAP), Should Treatment Be Guided by the Results of Microbiologic Studies Performed on Respiratory Samples, or Should Treatment Be Empiric?**

*Recommendation*

1. We suggest that patients with suspected HAP (non-VAP) be treated according to the results of microbiologic studies performed on respiratory samples obtained noninvasively, rather than being treated empirically (*weak recommendation, very low-quality evidence*).

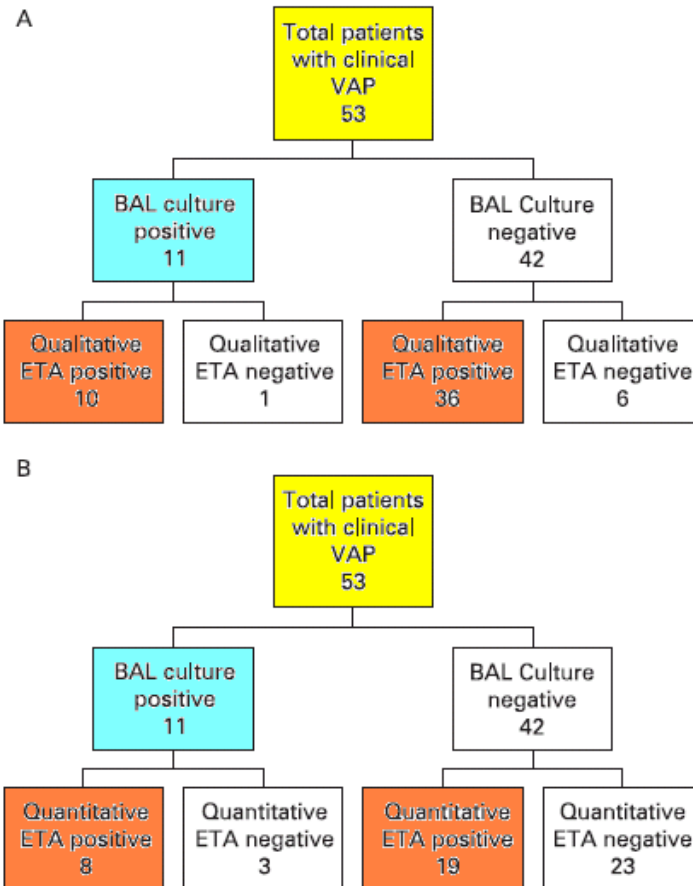




# Agenda

1. Who are the patients with a clinical suspicion of HAP-VAP?
2. Should we perform bacterial exams?
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# Variation of incidence with definitions



**Table 1** Classification of ventilator-acquired pneumonia by the HELICS criteria

Code	Diagnostic method
PN1	Positive quantitative culture from minimally contaminated LRT specimen—BAL $\geq 10^4$ CFU
PN2	Positive quantitative culture of LRT (tracheal aspirate) or sputum—not available within our laboratory
PN3	Positive culture related to no other source—positive pleural fluid culture OR pulmonary abscess with positive needle aspiration OR positive histology OR positive exams for virus
PN4	Positive sputum culture or non-quantitative LRT (tracheal aspirate) specimen culture
PN5	No positive microbiology including BAL with $< 10^4$ CFU

11 PN1  
 27 PN2  
 46 PN4!!!  
 53 clinical VAP

# Microbiologic diagnosis



- DO NOT sample patients who are not suspected having VAP
- Sample all the patients suspected having VAP
- Take Samples before any CHANGE of antimicrobials
  - Risk of over treatment because negative samples are uneasy to interpret
  - Risk of masking another disease mimicking pneumonia

*Question: What is the impact of prophylactic inhaled or IV antibiotic therapy????*

→ My opinion: Sample quantitatively *(to improve reliability and the ability to stop antimicrobials)*

# What is the place of molecular methods: mPCR?

## What do we know?

Biologically accurate

Some microorganisms are not targetted by syndromic mPCR++

## What is still open issues?

Role of viruses?

Role of the quantification???

Impact of previous antimicrobial therapy on mPCR results?

Evolution of mPCR with therapy?



MI<sup>2</sup>

**Radiological**

New or worsening infiltrates on Chest X-ray or CT thorax

AND

**Clinical**

AND at least one of the following:

- fever > 38°C with no other cause
- leukopenia (< 4 000 WBC/mm<sup>3</sup>) or leucocytosis (≥ 12 000 WBC/mm<sup>3</sup>).
- and at least one of the following
  - new onset of purulent sputum, or change in character of sputum (colour, odour, quantity, consistency)
  - suggestive auscultation (rales or bronchial breath sounds), rhonchi, wheezing
  - worsening gas exchange (e.g. O<sub>2</sub> desaturation or increased oxygen requirements or increased ventilation demand)

AND

**Microbiological**

Bacteriologic diagnostic performed by:

- a) positive quantitative culture from minimally contaminated LRT specimen (PN 1)
  - broncho-alveolar lavage (BAL) with a threshold of ≥ 10<sup>4</sup> colony forming units (CFU)/ml
  - detection by TaqMan array with Ct ≤ 32
- OR
- Positive quantitative culture from possibly contaminated LRT specimen (PN 2)
- Quantitative culture of LRT specimen (e.g. endotracheal aspirate) with a threshold of 10<sup>5</sup> CFU/ml.

**Table 2 Organisms identified by culture and PCR testing (BAL only) in patients with confirmed VAP**

Organism	ETA (≥ 10 <sup>5</sup> CFU/ml)	BAL culture (≥ 10 <sup>4</sup> CFU/ml)	BAL PCR (≤ Ct32)
<b>Gram negative</b>			
<i>Burkholderia cepacia</i>	1		
<i>Citrobacter freundii</i>		1	*
<i>Citrobacter koseri</i>	1	1	*
Coliform (not further specified)	1		
<i>Escherichia coli</i>	5	3 <sup>1</sup>	4 <sup>1</sup>
<i>Enterobacter asburiae</i>	1		*
<i>Enterobacter cloacae</i>	3		
Enterobacteraeiae (not further specified)			2
<i>Haemophilus influenzae</i>	1		4
<i>Klebsiella aerogenes</i>	2	1	*
<i>Klebsiella pneumoniae</i>	2	3	5
<i>Klebsiella oxytoca</i>	3	1	*
<i>Proteus mirabilis</i>	1		1 <sup>§</sup>
<i>Pseudomonas aeruginosa</i>	7	3	2
<i>Serratia liquefaciens</i>	1		
<i>Serratia marcescens</i>	1	2	5
<i>Stenotrophomonas maltophilia</i>	3	4	4
<b>Gram positive</b>			
<i>Staphylococcus aureus</i>	2	2	1
<b>Fungi</b>			
<i>Aspergillus fumigatus</i>			1
<b>Non-pathogenic organisms</b>			
<i>Candida albicans</i>	6	4	4
<i>Candida spp.</i>			1
Coagulase negative <i>Staphylococci</i>		1	4
<i>Enterococcus faecium</i>		2	7
<i>Streptococcus spp.</i> (non-pneumoniae, non-pyogenes)			4
Herpes simplex virus			2



**« PICK A DEFINITION OF VAP FOR YOUR INSTITUTION  
AND APPLY IT CONSISTENTLY »**

# Appropriate end-point for clinicians and healthcare practitioners

MI<sup>2</sup>

1. Objective (little variability in measurement between observers)
  - Do not use routine surveillance culture
  - The more you sample the more you increase antimicrobial consumption
  - Sampling before AB start (always the same sample)
  - Add clinically documented VAP (AB start and no positive sample)
  - VAT with AB start is a VAP
2. Frequent (powerful to detect variations)
3. Easy to measure
  - IVAC is easy but do not accurately reflect VAP
4. Internal validity (related to the disease being studied or related to a true patient-related (or healthcare system) outcome)
  - collect also vital status, LOS, length of MV, duration of AB use
5. External validity (valid to target population outside of the study)
  - Case-mix issues (ECMO, ARDS, Surg/MED, immunocomp. severity scores)



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