VAP Marker and Quality

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What is a Marker of Quality

Selection of KPI

- Relevance to overall framework
- Availability of automated data
- Reliability of available data
- Comparability of data across clusters
- Materiality of selected KPIs in affecting behavior of managers or clinicians
- Impact on service outcome & cost efficiency
- Burden of diseases in clinical services

What is Ventilator-associated Pneumonia (VAP)?

- VAP refers to pneumonia that arise more than 48-72 hours after endotracheal intubation and is type of HAP [1,2]
- VAP represent a conspicuous **clinical conundrum** [3]
- Classic clinical signs [4]:
  - Fever, leucocytosis, purulent secretions, worsening oxygenation, infiltrates, and pathogenic cultures
  - These signs are neither sensitive nor specific
- The clinical diagnosis and surveillance **definitions of VAP could be controversial** [5]

1. Uptodate - Marin H Kollef. Clinical presentation and diagnosis of ventilator-associated pneumonia – accessed 13 May 2015
2. ATS/IDSA Official Guideline for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia, 2004
3. Zilberberg MD and Shorr AF. Ventilator-Associated Pneumonia: the Clinical Pulmonary Infection Score as a Surrogate for Diagnostics and Outcome. Clin infect Dis 2010: 51 (S1):S131-S135
4. Mandell 8th edition– Michael Klompas. Chapter 303 Nosocomial pneumonia. Page 3325 – 3333
5. McMullen KM, Boyer AF, Schoenberg N et al. Surveillance versus clinical adjudication: Differences persist with new ventilator-associated event definition. Am J Infect Control. 2015(43): 581-91

Pathophysiology

- The fundamental obstacle to the diagnosis of VAP is the **absence of a uniform gold standard** [3]
- The **histological hallmark of VAP is heterogeneity** [4]
  - Autopsies of ventilated patients' lungs are often notable for widely scattered, patchy areas of inflammation. Lesions vary significantly in age and severity, ranging from bronchiolitis to bronchopneumonia to frank abscess, often within the same lung
  - Different organisms can be cultured from different lung segments of the same patient
  - Cultures of histologically benign-appearing lung segments are often positive

3. Zilberberg MD and Shorr AF. Ventilator-Associated Pneumonia: the Clinical Pulmonary Infection Score as a Surrogate for Diagnostics and Outcome. Clin infect Dis 2010: 51 (S1):S131-S135
4. Mandell 8th edition– Michael Klompas. Chapter 303 Nosocomial pneumonia. Page 3325 - 3333

Prerequisite of a standardized system for VAP diagnosis [3]

- Valid
  - its presence represents the presence of the disease that it is intended to identify
- Reliable
  - its evolution corresponds to the biologic evolution of the disease
- Reproducible
  - no major differences in its derivation either between different observes or b the same observer at different times

3. Zilberberg MD and Shorr AF. Ventilator-Associated Pneumonia: the Clinical Pulmonary Infection Score as a Surrogate for Diagnostics and Outcome. Clin infect Dis 2010: 51 (S1):S131-S135

The ideal VAP markers should also

1. Be non-invasive
2. Facilitate rapid diagnosis
3. Prompt earlier therapy
4. Help avoid excess antibiotic use
5. Identify patients early during the disease course who may experience treatment failure or who are not responding to treatment
6. Assist in the conduct of clinical research

3. Zilberberg MD and Shorr AF. Ventilator-Associated Pneumonia: the Clinical Pulmonary Infection Score as a Surrogate for Diagnostics and Outcome. Clin infect Dis 2010: 51 (S1):S131-S135

Possible markers for VAP

1. Signs and Symptoms
2. Mechanical ventilation settings
3. Chest Imaging
4. Microbiological analysis
5. Histology

Birth of a standard…

Am Rev Respir Dis. 1991 May;143(5 Pt 1):1121-9.

Diagnosis of ventilator-associated pneumonia by bacteriologic analysis of bronchoscopic and nonbronchoscopic "blind" bronchoalveolar lavage fluid.

Pugin J[1], Auckenthaler R, Mili N, Janssens JP, Lew PD, Suter PM.

Author information

Abstract

Substantial efforts have been devoted to improving the means for early and accurate diagnosis of ventilator-associated (VA) pneumonia in intensive care unit (ICU) patients because of its high incidence and mortality. A good diagnostic yield has been reported from quantitative cultures of bronchoalveolar lavage (BAL) fluid or a protected specimen brush, both obtained by fiberoptic bronchoscopy. As bronchoscopy requires specific skills and is costly, we evaluated a simpler method to obtain BAL fluid, that is, by a catheter introduced blindly into the bronchial tree. Quantitative cultures from bronchoscopically sampled BAL (B-BAL) and blindly nonbronchoscopically collected BAL (NB-BAL) were assessed for sensitivity, specificity, and predictive value for the diagnosis of VA pneumonia. A total of 40 pairs of samples were examined in 28 patients requiring prolonged mechanical ventilation and presenting a high risk of developing pneumonia. For comparison with bacteriologic data we defined a clinical score for pneumonia ranging from zero to 12 using the following variables: body temperature, leukocyte count, volume and character of tracheal secretions, arterial oxygenation, chest X-ray, Gram stain, and culture of tracheal aspirate. To quantify the bacteria in BAL the bacterial index (BI) was used, defined as the sum of the logarithm of the number of bacteria cultured per milliliter of BAL fluid. A good correlation between clinical score and quantitative bacteriology was observed (r = 0.84 for B-BAL and 0.76 for NB-BAL; p less than 0.0001). Similar to studies in baboons, patients with pulmonary infection could be distinguished by a BI greater than or equal to 5 with a sensitivity of 93% and a specificity of 100% (B-BAL).(ABSTRACT TRUNCATED AT 250 WORDS)

PMID: 2024824 [PubMed - indexed for MEDLINE]

Clinical Pulmonary Infection Score Calculation

	Parameter	Points
1	Temperature, °C	
	36.5–38.4	0
	38.5–38.9	1
	⩾39.0 and ⩽36.0	2
2	Blood leukocyte level, leukocytes/mm^{-3}	
	4000–11,000	0
	<4000 or >11000	1
	Plus band forms ⩾500	2
3	Tracheal secretions	
	<14+	0
	⩾14+	1
	Plus purulence	2
4	Oxygenation, PaO_2:FiO_2, mm Hg	
	>240 or ARDS	0
	⩽240 and no ARDS	2
5	Pulmonary radiograph finding	
	No infiltrate	0
	Diffuse or patchy infiltrate	1
	Localized infiltrate	2
6	Culture of tracheal aspirate specimen (semiquantitative: 0–1, −2, or 3+)	
	Pathogenic bacteria cultured ⩽1 or no growth	0
	Pathogenic bacteria cultured >1+	1
	Plus same pathogenic bacteria on Gram stain >1+	2

NOTE. ARDS, acute respiratory distress syndrome; PaO_2:FiO_2, ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen.

A score of more than 6 is diagnostic of pneumonia

Clinical Infectious Diseases 2010;51(S1):S131–S135

Modified CPIS

CLINICAL PULMONARY INFECTION SCORE CALCULATION*†

Temperature (°C)
- > or equal to 36.5 and < or equal to 38.4 = 0 point
- > or equal to 38.5 and < or equal to 38.9 = 1 point
- > or equal to 39 and < or equal to 36 = 2 points

Blood leukocytes, mm^3
- > or equal to 4,000 and < or equal to 11,000 = 0 point
- < 4,000 or > 11,000 = 1 point + band forms > equal to 50% = add 1 point

Tracheal secretions
- Absence of tracheal secretions = 0 point
- Presence of nonpurulent tracheal secretions = 1 point
- Presence of purulent tracheal secretions = 2 points

Oxygenation: $Pa_{O_2}/F_{I_{O_2}}$, mm Hg
- > 240 or ARDS (ARDS defined as $Pa_{O_2}/F_{I_{O_2}}$, or equal to 200, pulmonary arterial wedge pressure
- < or equal to 18 mm Hg and acute bilateral infiltrates) = 0 point
- < or equal to 240 and no ARDS = 2 points

Pulmonary radiography
- No infiltrate = 0 point
- Diffuse (or patchy) infiltrate = 1 point
- Localized infiltrate = 2 points

Progression of pulmonary infiltrate
- No radiographic progression = 0 point
- Radiographic progression (after CHF and ARDS excluded) = 2 points

Culture of tracheal aspirate
- Pathogenic bacteria‡ cultured in rare or light quantity or no growth = 0 point
- Pathogenic bacteria cultured in moderate or heavy quantity = 1 point
- Same pathogenic bacteria seen on Gram stain, add 1 point

Definition of abbreviations: ARDS = acute respiratory distress syndrome; CHF = congestive heart failure; $Pa_{O_2}/F_{I_{O_2}}$ = ratio of arterial oxygen pressure to fraction of inspired oxygen.

* Modified from Pugin and coworkers (8).

† CPIS at baseline was assessed on the basis of the first five variables, i.e., temperature, blood leukocyte count, tracheal secretions, oxygenation, and character of pulmonary infiltrate. CPIS at 72 h was calculated based on all seven variables and took into consideration the progression of the infiltrate and culture results of the tracheal aspirate. A score > 6 at baseline or at 72 h was considered suggestive of pneumonia.

‡ Predominant organism in the culture.

Modified CPIS score often
- De-emphasize culture or
- Emphasize on dynamic changes in radiographs

Am J Respir Crit Care Med Vol 162. pp 505–511, 2000
Internet address: www.atsjournals.org

CPIS - limitations

- Validation studies showed poor correlation with autopsy findings:
  - sensitivity of 46%; specificity of 60% [6]
  - Sensitivity 72%; Specificity 85%, and an overall accuracy of 79% [7]
  - Sensitivity 77%; Specificity of 42% [8]

6. Tejerina E, Esteban A, Fernandez-Segoviano P, et al. Accuracy of clinical definitions of ventilator-associated pneumonia: comparison with autopsy findings. J Crit Care. 2010;25:62-68
7. Papazian L, Thomas P, Garbe L, et al. Bronchoscopic or blind sampling techniques for the diagnosis of ventilator-associated pneumonia. Am J Respir Crit Care Med 1995; 152: 1982-1991.
8. Fabregas N, Ewig S, Torres A, et al. Clinical diagnosis of ventilator associated pneumonia revisited: comparative validation using immediate post-mortem lung biopsies. Thorax 1999; 54:867-873

CPIS – limitations
Inter-observer variability

Intensive Care Med (2004) 30:217–224
DOI 10.1007/s00134-003-2018-2

ORIGINAL

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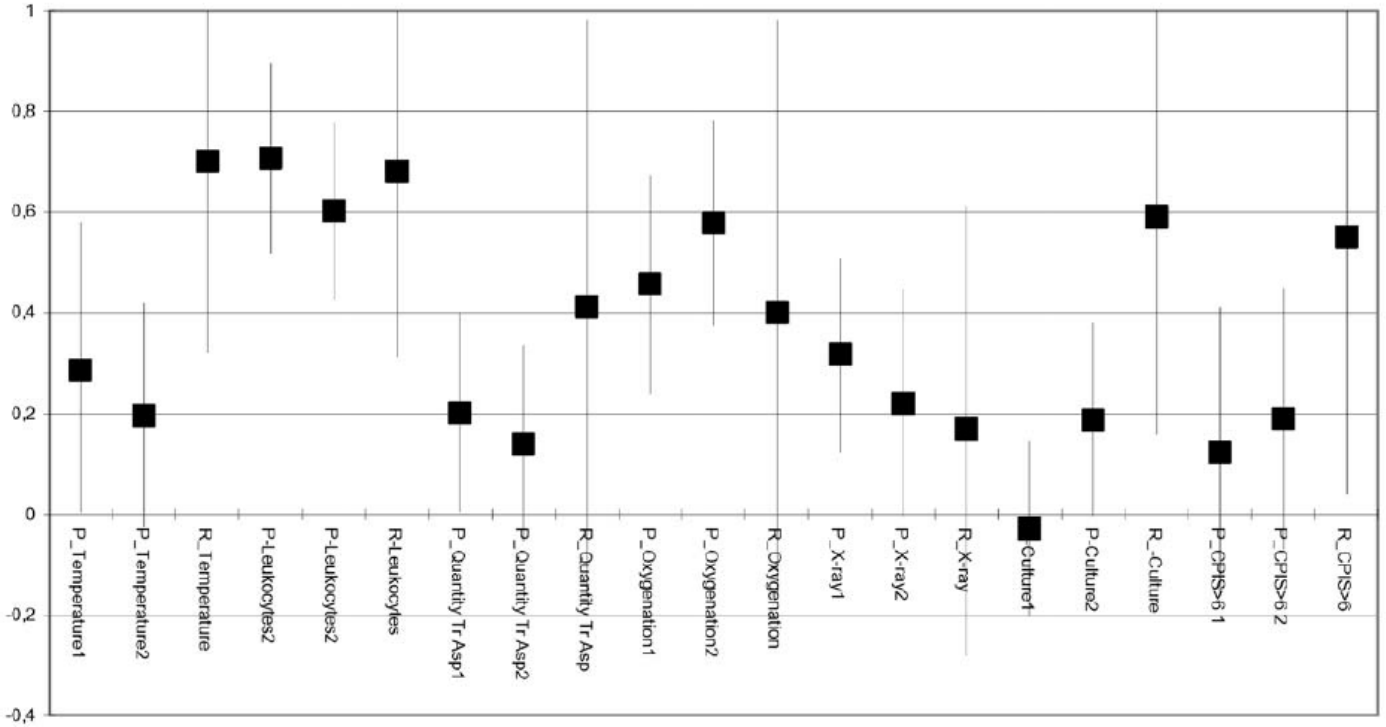
Clinical pulmonary infection score for ventilator-associated pneumonia: accuracy and inter-observer variability



Overall

- the level of inter-rater agreement for the prospectively calculated CPIS at the threshold of 6 was extremely poor (K=0.16)
- The level of discordance indicates that 2 different physicians examining the same patient are highly unlikely to agree about the actual CPIS calculation
- This point alone suggests that the CPIS can not be used to standardize practice

AJIC major articles

CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting

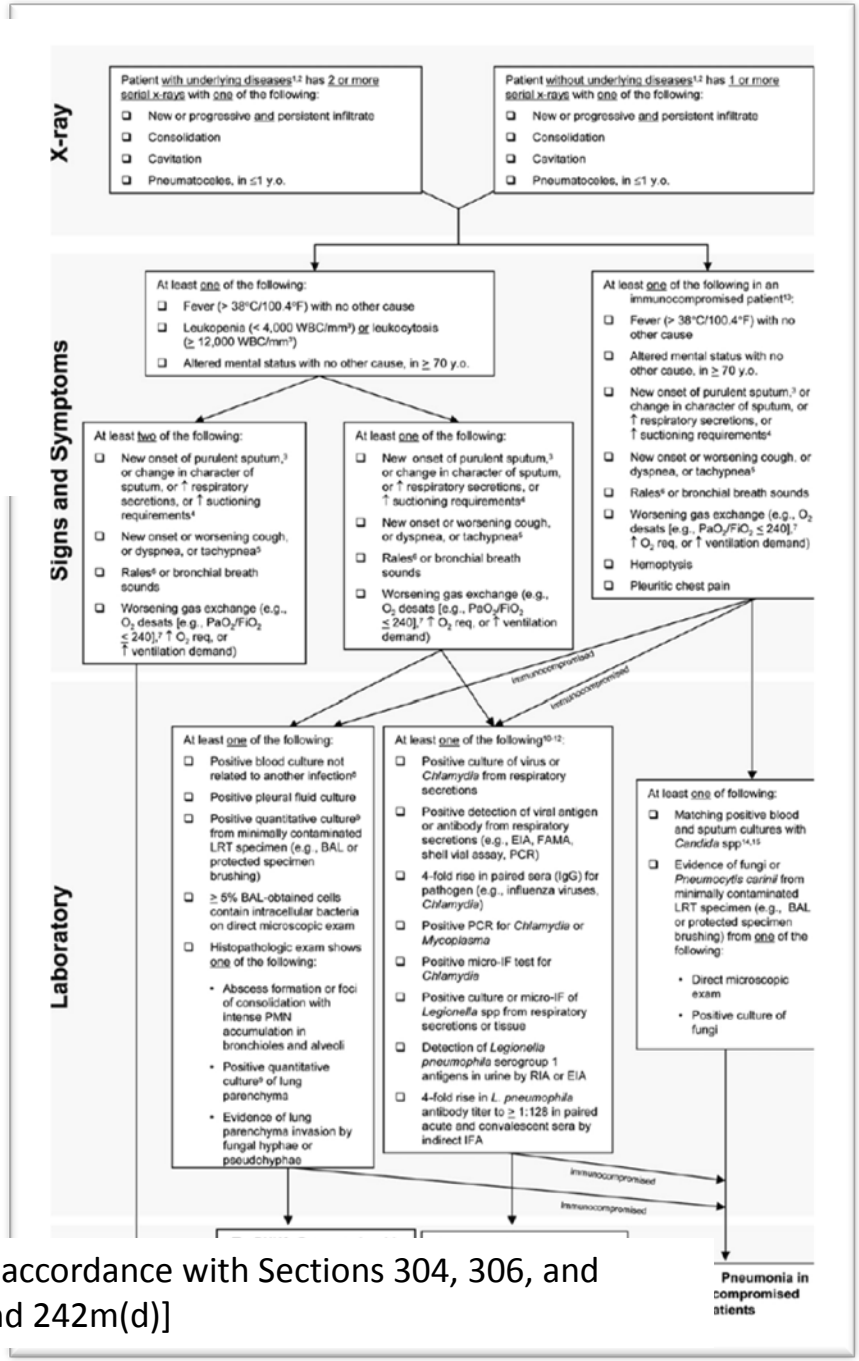
Teresa C. Horan, MPH, Mary Andrus, RN, BA, CIC, and Margaret A. Dudeck, MPH
Atlanta, Georgia

Am J Infect Control 2008;36:309-32.

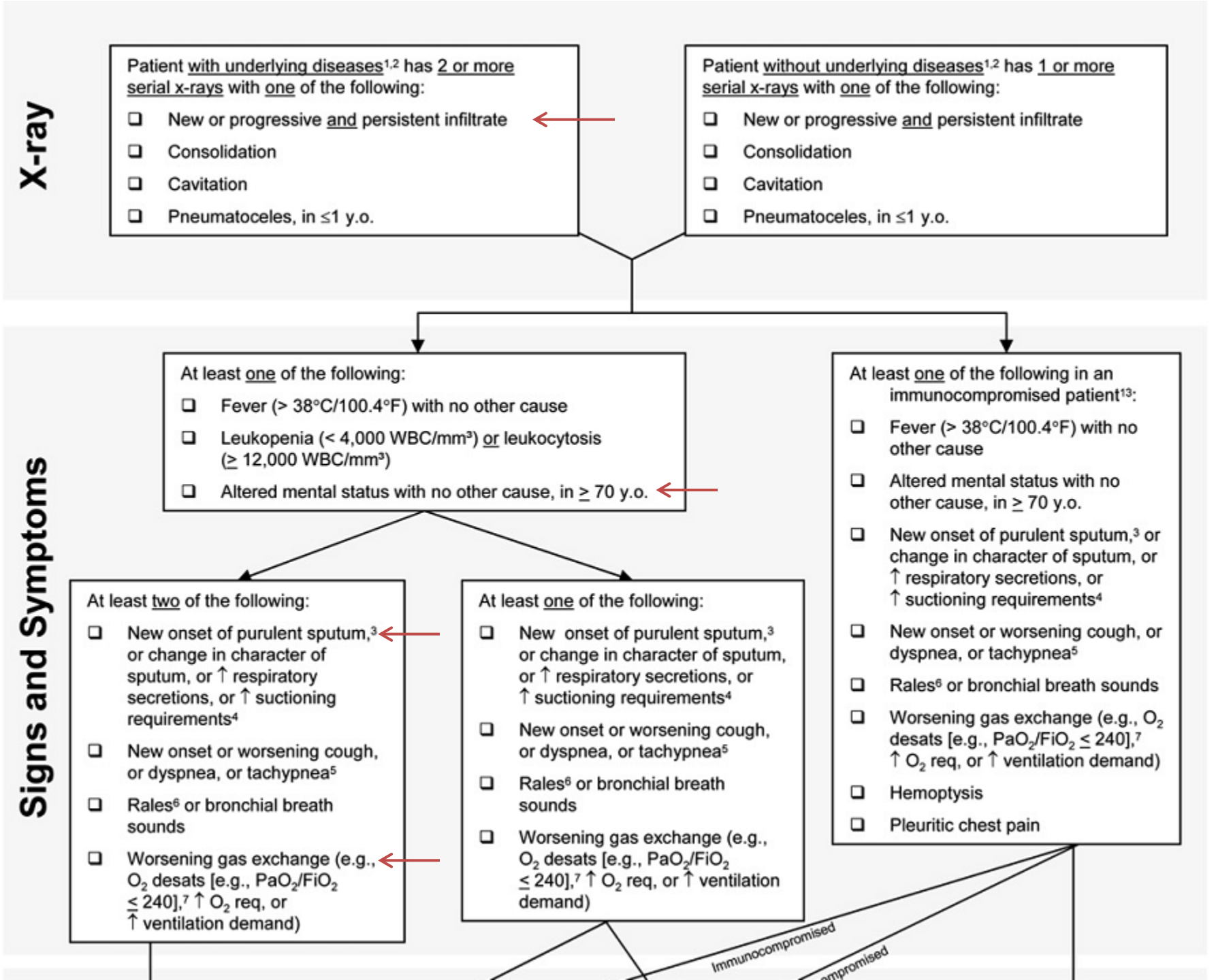
Aim

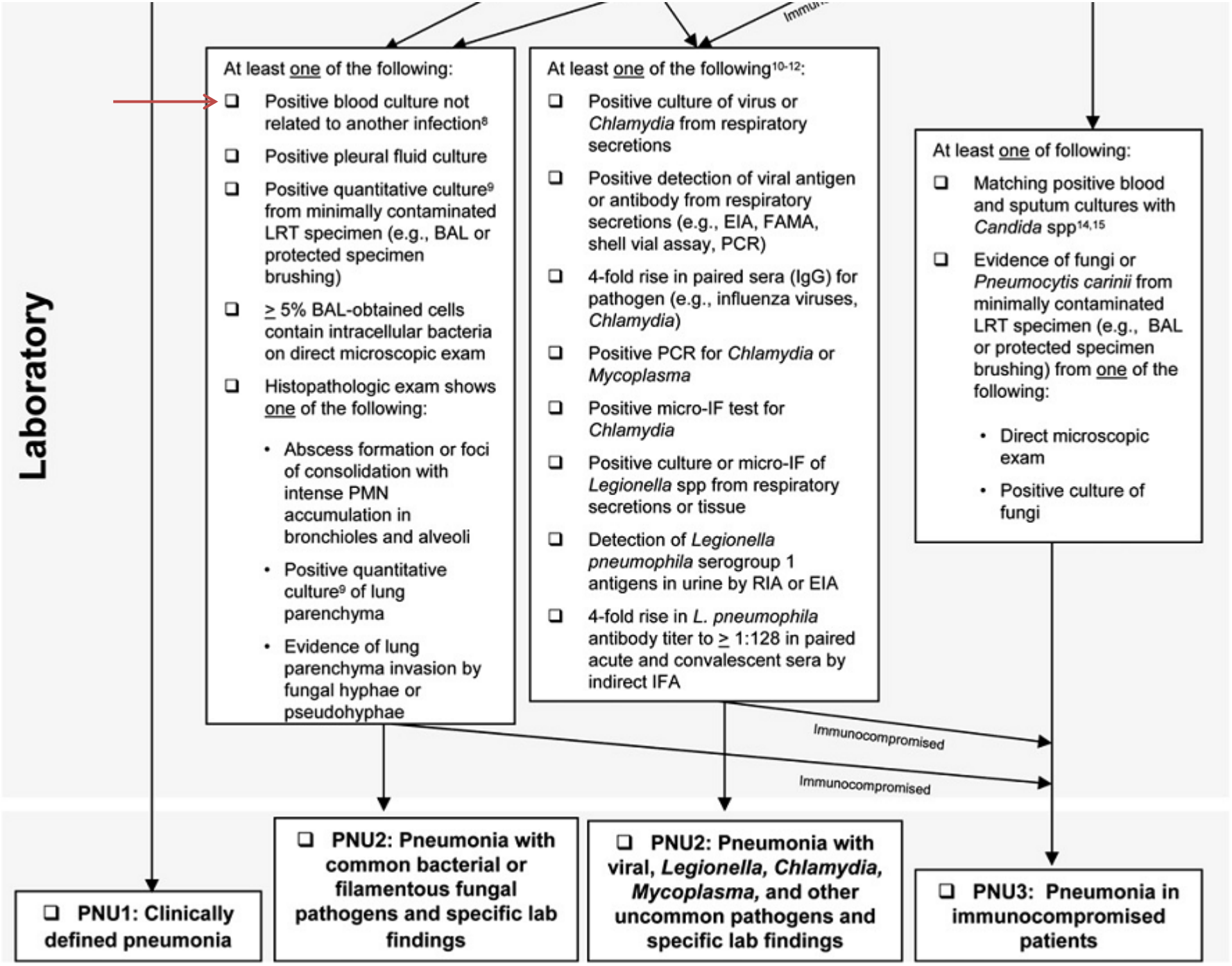
- Estimation of the magnitude of HAIs
- Monitoring of HAI trends
- Facilitation of interfacility and intrafacility comparisons with risk-adjusted data that can be used for local quality improvement activities
- Assistance to facilities in developing surveillance and analysis methods that permit timely recognition of patient safety problems and prompt intervention with appropriate measures.

(Am J Infect Control 2009;37:783-805.)



Identity of all NHSN facilities is kept confidential by the CDC in accordance with Sections 304, 306, and 308(d) of the Public Health Service Act [42 USC 242b, 242k, and 242m(d)]


X-ray
Patient with underlying diseases[1,2] has 2 or more serial x-rays with one of the following:
❑ New or progressive and persistent infiltrate
❑ Consolidation
❑ Cavitation
❑ Pneumatoceles, in ≤1 y.o.
Patient without underlying diseases[1,2] has 1 or more serial x-rays with one of the following:
❑ New or progressive and persistent infiltrate
❑ Consolidation
❑ Cavitation
❑ Pneumatoceles, in ≤1 y.o.
Signs and Symptoms
At least one of the following:
❑ Fever (> 38°C/100.4°F) with no other cause
❑ Leukopenia (< 4,000 WBC/mm³) or leukocytosis (≥ 12,000 WBC/mm³)
❑ Altered mental status with no other cause, in ≥ 70 y.o.
At least one of the following in an immunocompromised patient[13]:
❑ Fever (> 38°C/100.4°F) with no other cause
❑ Altered mental status with no other cause, in ≥ 70 y.o.
❑ New onset of purulent sputum,[3] or change in character of sputum, or ↑ respiratory secretions, or ↑ suctioning requirements[4]
❑ New onset or worsening cough, or dyspnea, or tachypnea[5]
❑ Rales[6] or bronchial breath sounds
❑ Worsening gas exchange (e.g., O_2 desats [e.g., $PaO_2/FiO_2 \leq 240$],[7] ↑ O_2 req, or ↑ ventilation demand)
❑ Hemoptysis
❑ Pleuritic chest pain
At least two of the following:
❑ New onset of purulent sputum,[3] or change in character of sputum, or ↑ respiratory secretions, or ↑ suctioning requirements[4]
❑ New onset or worsening cough, or dyspnea, or tachypnea[5]
❑ Rales[6] or bronchial breath sounds
❑ Worsening gas exchange (e.g., O_2 desats [e.g., $PaO_2/FiO_2 \leq 240$],[7] ↑ O_2 req, or ↑ ventilation demand)
At least one of the following:
❑ New onset of purulent sputum,[3] or change in character of sputum, or ↑ respiratory secretions, or ↑ suctioning requirements[4]
❑ New onset or worsening cough, or dyspnea, or tachypnea[5]
❑ Rales[6] or bronchial breath sounds
❑ Worsening gas exchange (e.g., O_2 desats [e.g., $PaO_2/FiO_2 \leq 240$],[7] ↑ O_2 req, or ↑ ventilation demand)
Immunocompromised


Laboratory
At least one of the following:
❑ Positive blood culture not related to another infection[8]
❑ Positive pleural fluid culture
❑ Positive quantitative culture[9] from minimally contaminated LRT specimen (e.g., BAL or protected specimen brushing)
❑ ≥ 5% BAL-obtained cells contain intracellular bacteria on direct microscopic exam
❑ Histopathologic exam shows one of the following:
• Abscess formation or foci of consolidation with intense PMN accumulation in bronchioles and alveoli
• Positive quantitative culture[9] of lung parenchyma
• Evidence of lung parenchyma invasion by fungal hyphae or pseudohyphae
At least one of the following[10-12]:
❑ Positive culture of virus or *Chlamydia* from respiratory secretions
❑ Positive detection of viral antigen or antibody from respiratory secretions (e.g., EIA, FAMA, shell vial assay, PCR)
❑ 4-fold rise in paired sera (IgG) for pathogen (e.g., influenza viruses, *Chlamydia*)
❑ Positive PCR for *Chlamydia* or *Mycoplasma*
❑ Positive micro-IF test for *Chlamydia*
❑ Positive culture or micro-IF of *Legionella* spp from respiratory secretions or tissue
❑ Detection of *Legionella pneumophila* serogroup 1 antigens in urine by RIA or EIA
❑ 4-fold rise in *L. pneumophila* antibody titer to ≥ 1:128 in paired acute and convalescent sera by indirect IFA
At least one of following:
❑ Matching positive blood and sputum cultures with *Candida* spp[14,15]
❑ Evidence of fungi or *Pneumocytis carinii* from minimally contaminated LRT specimen (e.g., BAL or protected specimen brushing) from one of the following:
• Direct microscopic exam
• Positive culture of fungi
Immunocompromised
Immunocompromised
❑ PNU1: Clinically defined pneumonia
❑ PNU2: Pneumonia with common bacterial or filamentous fungal pathogens and specific lab findings
❑ PNU2: Pneumonia with viral, *Legionella, Chlamydia, Mycoplasma,* and other uncommon pathogens and specific lab findings
❑ PNU3: Pneumonia in immunocompromised patients

Drawbacks of the 2008 NHSN criteria

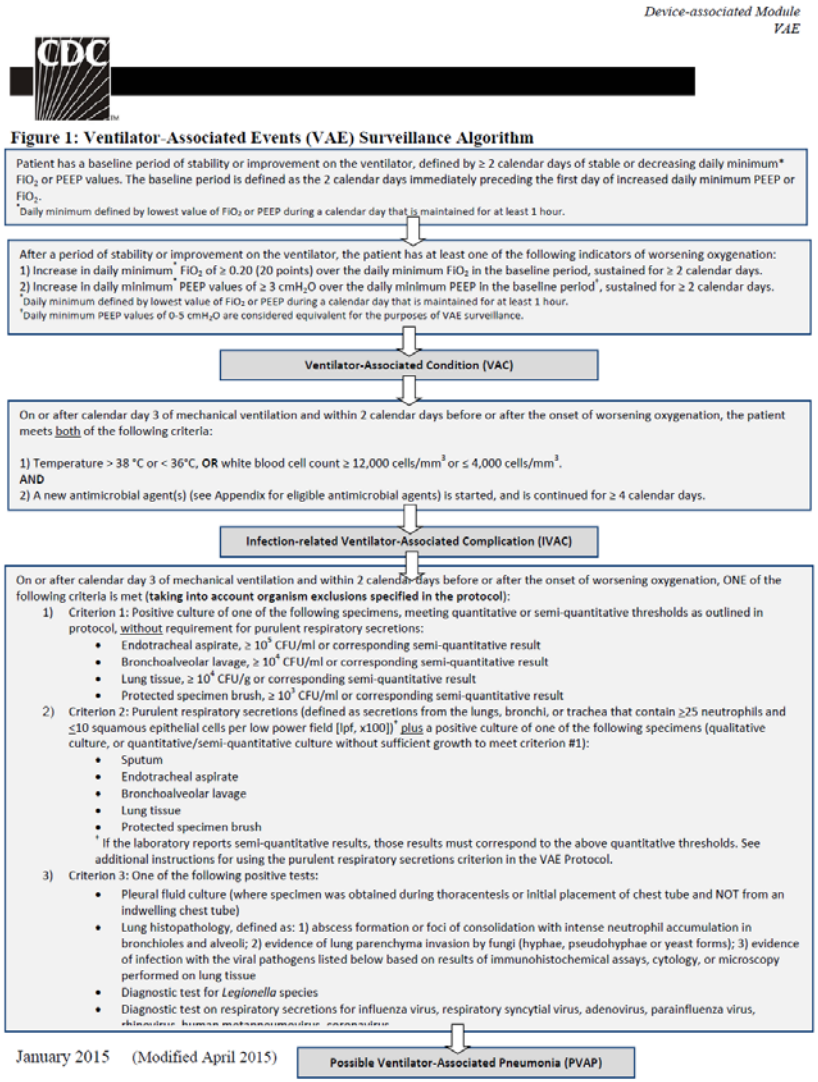
1. Poor correlation with histological findings
2. Inconsistent correlation with patients' outcomes
3. Hospitals' VAP rates can vary markedly
4. Some criterion are subjective and nonspecific

Moving away from VAP

Ventilator-Associated Event (VAE)

For use in adult locations only

- Broadens the focus: from pneumonia alone to complications of mechanical ventilation in general
- Use quantitative criteria to make surveillance
  - Objective
  - Reproducible
  - Integration with IT systems



Device-associated Module
VAE

Figure 1: Ventilator-Associated Events (VAE) Surveillance 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 that is 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 cmH_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 during a calendar day that is maintained for at least 1 hour.
†Daily minimum PEEP values of 0-5 cmH_2O are considered equivalent for the purposes of VAE surveillance.

Ventilator-Associated Condition (VAC)

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 criteria:

1) Temperature > 38 °C or < 36°C, **OR** white blood cell count ≥ 12,000 cells/mm^3 or ≤ 4,000 cells/mm^3.
AND
2) A new antimicrobial agent(s) (see Appendix for eligible antimicrobial agents) is started, and is continued for ≥ 4 calendar days.

Infection-related Ventilator-Associated Complication (IVAC)

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 (**taking into account organism exclusions specified in the protocol**):

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 a positive culture of one of the following specimens (qualitative culture, or quantitative/semi-quantitative culture without sufficient growth to meet criterion #1):
   - Sputum
   - Endotracheal aspirate
   - Bronchoalveolar lavage
   - Lung tissue
   - Protected specimen brush

   * If the laboratory reports semi-quantitative results, those results must correspond to the above quantitative thresholds. See additional instructions for using the purulent respiratory secretions criterion in the VAE Protocol.
3) Criterion 3: One of the following positive tests:
   - Pleural fluid culture (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

January 2015 (Modified April 2015)

Possible Ventilator-Associated Pneumonia (PVAP)

The first Tier
Ventilator-associated conditions [VAC]

- Flag episodes of nosocomial respiratory deterioration
- Based on sustained increases in **ventilator settings**

Figure 2: Ventilator-Associated Condition (VAC)

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 that is maintained for at least 1 hour.

AND

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 cmH_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 during a calendar day that is maintained for at least 1 hour.

†Daily minimum PEEP values of 0-5 cmH_2O are considered equivalent for the purposes of VAE surveillance.

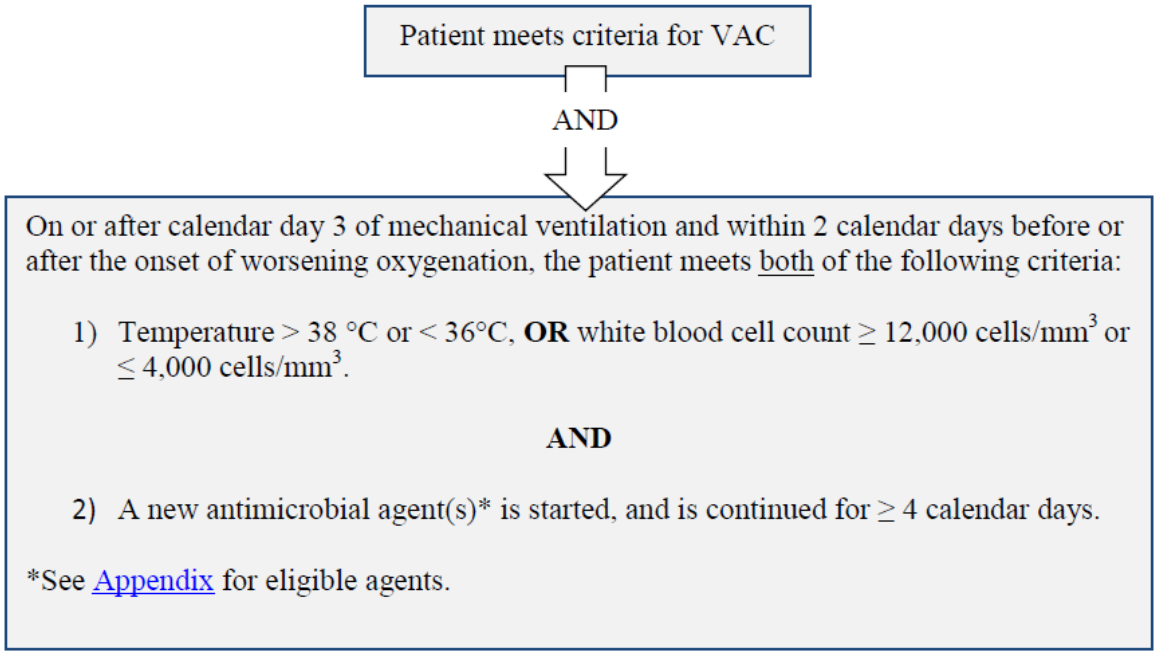
Antimicrobial Agent
AMIKACIN
AMPHOTERICIN B
AMPHOTERICIN B LIPOSOMAL
AMPICILLIN
AMPICILLIN/SULBACTAM
ANIDULAFUNGIN
AZITHROMYCIN
AZTREONAM
CASPOFUNGIN
CEFAZOLIN
CEFEPIME
CEFOTAXIME
CEFOTETAN
CEFOXITIN
CEFTAROLINE
CEFTAZIDIME
CEFTIZOXIME
CEFTRIAXONE
CEFUROXIME
CIPROFLOXACIN
CLARITHROMYCIN
CLINDAMYCIN
COLISTIMETHATE
DORIPENEM
DOXYCYCLINE
ERTAPENEM
FLUCONAZOLE
FOSFOMYCIN
GEMIFLOXACIN
GENTAMICIN
IMIPENEM/CILASTATIN
ITRACONAZOLE
LEVOFLOXACIN
LINEZOLID
MEROPENEM
METRONIDAZOLE
MICAFUNGIN
MINOCYCLINE
MOXIFLOXACIN
NAFCILLIN
OSELTAMIVIR
OXACILLIN
PENICILLIN G
PIPERACILLIN
PIPERACILLIN/TAZOBACTAM
POLYMYXIN B
POSACONAZOLE
QUINUPRISTIN/DALFOPRISTIN
RIFAMPIN
SULFAMETHOXAZOLE/TRIMETHOPRIM
SULFISOXAZOLE
TEDIZOLID
TELAVANCIN
TELITHROMYCIN
TETRACYCLINE
TICARCILLIN/CLAVULANATE
TIGECYCLINE
TOBRAMYCIN
VANCOMYIN, intravenous only
VORICONAZOLE
ZANAMIVIR

The Second Tier

Infection-related ventilator-associated complications [IVAC]

- Identify a subset of VAC that may be infection related
- On the basis of concurrent abnormalities in **temperature** or **WBC** and **new antibiotic starts**

Figure 3: Infection-related Ventilator-Associated Complication (IVAC)



The Third Tier VAP

- Possible pneumonia
  - either purulent sputum
    or
  - positive quantitative / semi-quantitative culture

- Probable pneumonia
  - Purulent sputum, and
  - Neutrophils on direct microscopy, and
  - Positive quantitative or semi-quantitative culture
    or
  - confirmation of respiratory pathogens by other means e.g PCR, UAT, histology

Figure 4: Possible Ventilator-Associated Pneumonia (PVAP)

Patient meets criteria for VAC and IVAC

AND

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 (taking into account organism exclusions specified in the protocol*):

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, $\geq 10^5$ CFU/ml or corresponding semi-quantitative result
   - Bronchoalveolar lavage, $\geq 10^4$ CFU/ml or corresponding semi-quantitative result
   - Lung tissue, $\geq 10^4$ CFU/g or corresponding semi-quantitative result
   - Protected specimen brush, $\geq 10^3$ CFU/ml or corresponding semi-quantitative result
2) Criterion 2: Purulent respiratory secretions (defined as secretions from the lungs, bronchi, or trachea that contain $\geq$25 neutrophils and $\leq$10 squamous epithelial cells per low power field [lpf, x100])† plus a positive culture of one of the following specimens (qualitative culture, or quantitative/semi-quantitative culture without sufficient growth to meet criterion #1):
   - Sputum
   - Endotracheal aspirate
   - Bronchoalveolar lavage
   - Lung tissue
   - Protected specimen brush

   † If the laboratory reports semi-quantitative results, those results must correspond to the quantitative thresholds. See additional instructions for using the purulent respiratory secretions criterion in the VAE Protocol.
3) Criterion 3: One of the following positive tests:
   - Pleural fluid culture (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

*Excludes the following: Normal respiratory/oral flora, mixed respiratory/oral flora or equivalent; *Candida* species or yeast not otherwise specified; coagulase-negative *Staphylococcus* species; *Enterococcus* species. Also excludes the following community-associated respiratory pathogens: *Blastomyces, Histoplasma, Coccidioides, Paracoccidioides, Cryptococcus and Pneumocystis.*

Important absence of radiographic criteria

- This omission does not represent a denial of the central role that radiographs play in routine clinical care
- but rather reflects the recognition that they are counter-productive in surveillance definitions because they introduce substantial complexity and subjectivity without increasing accuracy

Advantage of VAE

- Broaden the focus
  - from pneumonia alone to all important complications of mechanical ventilation
  - Non-VAP VACs are attributable to
    - Pulmonary edema
    - Atelectasis
    - Acute respiratory distress syndrome

    Meaningful: as these events are also potentially actionable

- More objective
  - Surveillance definitions based on changes in ventilator settings

- The inclusion of an antibiotic criterion
  - will provide hospitals with a routine, widely reportable benchmark for the prescribing of antibiotics in ICU

What is the basis of the change?

OPEN ACCESS Freely available online

PLoS one

Multicenter Evaluation of a Novel Surveillance Paradigm for Complications of Mechanical Ventilation

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Abstract

Background: Ventilator-associated pneumonia (VAP) surveillance is time consuming, subjective, inaccurate, and inconsistently predicts outcomes. Shifting surveillance from pneumonia in particular to complications in general might circumvent the VAP definition's subjectivity and inaccuracy, facilitate electronic assessment, make interfacility comparisons more meaningful, and encourage broader prevention strategies. We therefore evaluated a novel surveillance paradigm for ventilator-associated complications (VAC) defined by sustained increases in patients' ventilator settings after a period of stable or decreasing support.

Methods: We assessed 600 mechanically ventilated medical and surgical patients from three hospitals. Each hospital contributed 100 randomly selected patients ventilated 2–7 days and 100 patients ventilated >7 days. All patients were independently assessed for VAP and for VAC. We compared incidence-density, duration of mechanical ventilation, intensive care and hospital lengths of stay, hospital mortality, and time required for surveillance for VAP and for VAC. A subset of patients with VAP and VAC were independently reviewed by a physician to determine possible etiology.

Results: Of 597 evaluable patients, 9.3% had VAP (8.8 per 1,000 ventilator days) and 23% had VAC (21.2 per 1,000 ventilator days). Compared to matched controls, both VAP and VAC prolonged days to extubation (5.8, 95% CI 4.2–8.0 and 6.0, 95% CI 5.1–7.1 respectively), days to intensive care discharge (5.7, 95% CI 4.2–7.7 and 5.0, 95% CI 4.1–5.9), and days to hospital discharge (4.7, 95% CI 2.6–7.5 and 3.0, 95% CI 2.1–4.0). VAC was associated with increased mortality (OR 2.0, 95% CI 1.3–3.2) but VAP was not (OR 1.1, 95% CI 0.5–2.4). VAC assessment was faster (mean 1.8 versus 39 minutes per patient). Both VAP and VAC events were predominantly attributable to pneumonia, pulmonary edema, ARDS, and atelectasis.

Conclusions: Screening ventilator settings for VAC captures a similar set of complications to traditional VAP surveillance but is faster, more objective, and a superior predictor of outcomes.

Retrospectively evaluated 600 medical & surgical patients in 3 hospitals

Results

Matched control for VAC cases

Matched control for VAP cases

Table 3. Results of linear and logistic regression models comparing patient outcomes for ventilator-associated complication or ventilator-associated pneumonia relative to matched patients without ventilator-associated complications or ventilator-associated pneumonia respectively.

	VAC Positive (95% CI)	VAC Negative (95% CI)	P	VAP Positive (95% CI)	VAP Negative (95% CI)	P
Patients matched	127	329		51	188	
Age (mean)	56.5	58.8	NS	60.4	58.0	NS
Male	56%	57%	NS	61%	56%	NS
Comorbidities						
Coronary artery disease	19%	20%	NS	10%	14%	NS
Cerebrovascular disease	9%	14%	NS	16%	16%	NS
Congestive heart failure	31%	32%	NS	18%	28%	NS
Chronic obstructive lung disease	31%	32%	NS	31%	29%	NS
Rheumatologic disease	4%	4%	NS	2%	3%	NS
Liver disease	17%	17%	NS	6%	15%	NS
Diabetes	24%	24%	NS	14%	26%	NS
Renal insufficiency	57%	42%	NS	39%	37%	NS
Cancer	49%	41%	NS	39%	36%	NS
Charlson index (mean)	2.7	2.7	NS	2.9	2.9	NS
Duration of ventilation (days)	14.7 (13.2–16.4)	9.0 (8.2–9.9)	<.001	16.9 (14.2–20.2)	11.0 (9.5–12.8)	<.001
ICU length of stay (days)	17.6 (15.7–19.6)	13.0 (11.9–14.3)	<.001	20.9 (17.7–24.7)	14.9 (13.1–17.1)	<.001
Hospital length of stay (days)	25.4 (22.7–28.4)	23.4 (21.5–25.4)	.14	30.5 (15.6–36.4)	26.8 (24.0–30.0)	.16
Days from event to extubation*	9.7 (8.4–11.2)	3.7 (3.3–4.1)	<.001	10.3 (7.9–13.4)	4.5 (3.7–5.4)	<.001
Days from event to ICU discharge*	11.8 (10.3–13.5)	6.8 (6.2–7.6)	<.001	13.2 (10.7–16.4)	7.5 (6.5–8.7)	<.001
Days from event to hospital discharge*	16.4 (14.2–18.8)	13.4 (12.1–14.8)	.01	19.7 (16.0–24.3)	15.0 (13.4–16.8)	.02
Hospital mortality (odds ratio)	2.0 (1.3–3.2)	–	.003	1.1 (0.51–2.4)	–	.78

*Date of event in cases defined as the ventilator day on which VAC or VAP began. Date of event in controls defined as the ventilator day on which the matched case patient developed VAC or VAP.
Abbreviations:
VAC – ventilator associated complications; VAP – ventilator associated pneumonia; ICU – intensive care unit.
Model adjusted for age, sex, hospital, unit type, and Charlson comorbidity index.
doi:10.1371/journal.pone.0018062.t003

Both VAC and VAP are significantly prolonged duration as compared to controls

Only VAC associated with increased hospital mortality

Authors' concluding remark on VAC

- Robust
  - 1.8 minutes per patient versus 39 minutes per patient (2008 NHSN VAP)
- Better predictors of mortality
- Less inter-individual variation
  - Ventilated ≤ 7 days
    - VAP rate varied from 0 to 4%
    - VAC rate varied from 7 to 9%
  - Similar findings also seen in patients ventilated > 7 days

Ventilator-Associated Events: Prevalence, Outcome, and Relationship With Ventilator-Associated Pneumonia

Lila Bouadma, MD, PhD[1–3]; Romain Sonneville, MD[3]; Maité Garrouste-Orgeas, MD, PhD[1,4]; Michael Darmon, MD, PhD[5,6]; Bertrand Souweine, MD, PhD[7]; Guillaume Voiriot, MD[2,3]; Hatem Kallel, MD[8]; Carole Schwebel, MD, PhD[9]; Dany Goldgran-Toledano, MD[10]; Anne-Sylvie Dumenil, MD[11]; Laurent Argaud, MD, PhD[12]; Stéphane Ruckly, MSc[13]; Samir Jamali, MD[14]; Benjamin Planquette, MD[15]; Christophe Adrie, MD, PhD[16]; Jean-Christophe Lucet, MD, PhD[1,2,17]; Elie Azoulay, MD, PhD[2,18]; Jean-François Timsit, MD, PhD[1–3]; on behalf of the OUTCOMEREA Study Group

Objectives: Centers for Disease Control and Prevention built up new surveillance paradigms for the patients on mechanical ventilation and the ventilator-associated events, comprising ventilator-associated conditions and infection-related ventilator-associated complications. We assess 1) the current epidemiology of ventilator-associated event, 2) the relationship between ventilator-associated event and ventilator-associated pneumonia, and 3) the impact of ventilator-associated event on antimicrobials consumption and mechanical ventilation duration.

Design: Inception cohort study from the longitudinal prospective French multicenter OUTCOMEREA database (1996-2012).

Patients: Patients on mechanical ventilation for greater than or equal to 5 consecutive days were classified as to the presence of a ventilator-associated event episode, using slightly modified Centers for Disease Control and Prevention definitions.

Intervention: None.

DOI: 10.1097/CCM.0000000000001091

Critical Care Medicine 2015

- French study – OUTCOMEREA database
- Surveyed 3028 ICU patients with MV ≥ 5 days

Results

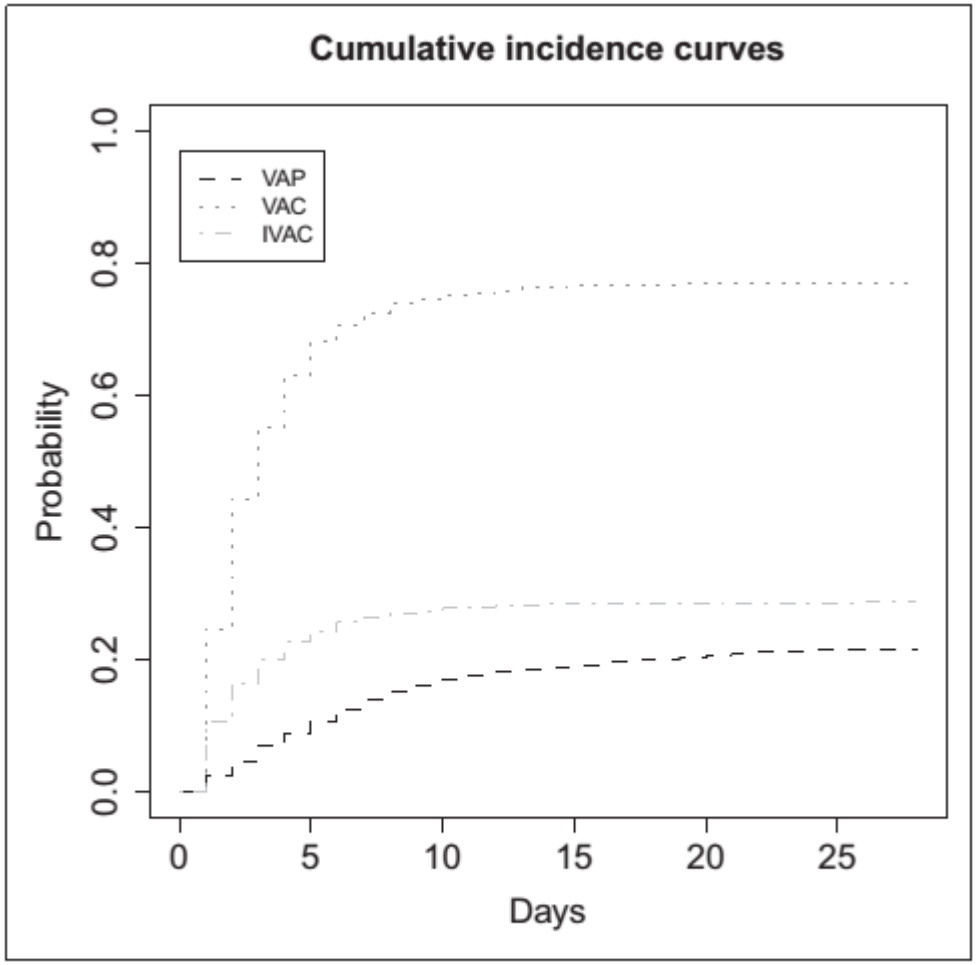

Figure 2. Daily incidence rates for ventilator-associated pneumonia (VAP), ventilator-associated conditions (VAC), and infection-related ventilator-associated complications (IVAC).

- VAEs common
  - VAC 77%
  - IVAC 29%
- Correlation of Prevalence
  - VAC vs VAP $r^2 = 0.67$ ($p<0.0001$)
  - IVAC vs VAP $r^2 = 0.82$ ($p<0.0001$)

Conditions associated with VAE

TABLE 3. Causes of Ventilator-Associated Events

Variables[a]	Ventilator-Associated Condition ($n = 2,331$)	Infection-Related Ventilator-Associated Complication ($n = 869$)
Number of etiologies per patient		
0	818 (35.1)	189 (21.78)
1	726 (31.2)	260 (29.9)
2	445 (19.1)	213 (24.5)
3	214 (9.2)	124 (14.3)
≥ 4	128 (5.5)	83 (9.6)
Nosocomial infections	637 (27.3)	381 (43.8)
Ventilator-associated pneumonia	339 (14.5)	240 (27.6)
Tracheobronchitis	23 (1)	12 (1.4)
Bloodstream infection	173 (7.4)	95 (10.9)
Catheter-related infection	81 (3.5)	44 (5.1)
Urinary infection	102 (4.4)	42 (4.8)
Sinusitis	5 (0.2)	4 (0.5)
Viral infection	10 (0.4)	8 (0.9)
Surgical site infections	41 (1.8)	30 (3.5)
Iatrogenic adverse events	322 (13.8)	137 (15.8)
Pneumothorax	37 (1.6)	23 (2.6)
Failure of planned extubation	11 (0.5)	1 (0.1)
Accidental extubation	21 (0.9)	9 (1)
Self-extubation	71 (3)	19 (2.2)
Venous puncture accident	14 (0.6)	9 (1)
Atelectasis	52 (2.2)	20 (2.3)
Peripheral thrombosis	36 (1.5)	18 (2.1)
Pulmonary embolism	9 (0.4)	1 (0.1)
Myocardial infarction	10 (0.4)	4 (0.5)
Cardiac arrest	43 (1.8)	24 (2.8)
Cardioversion	29 (1.2)	17 (2)
Gastrointestinal bleeding	26 (1.1)	11 (1.3)
Acute mesenteric infarction	5 (0.2)	4 (0.5)
Intestinal pseudo-obstruction	2 (0.1)	0
Transport	387 (16.6)	186 (21.4)
Fluid resuscitation	123 (5.3)	58 (6.7)

[a]Expressed as number (%).

- Multiple etiologies or no etiology is common
- IVAC episodes
  - Only 43.8% related to nosocomial infections
  - 15.8% related to iatrogenic adverse events

Nosocomial infection and iatrogenic adverse events were predefined by the steering committee of the OUTCOMEREA group when the database was started in 1997

Reviewed each episode of VAE to identify episodes associated with nosocomial infections and iatrogenic adverse events within 2 calendar days before or after the onset of worsening oxygenation

Correlation with outcome and **antimicrobial usage**

- Median number of days alive without antimicrobials at 28 days
  - Patients with no episode of VAC: 24 days (95% CI: 2 – 26)
  - ≥ 1 episode of VAC: 17 days (95% CI: 4 - 23] ($p < 0.05$)
  - ≥ 1 episode of IVAC: 10 days (95% CI 4 - 23) ($P = 0.05$)
- The median number of days alive without MV at day 28:
  - patients with no episode of VAC: 24 days (95% CI: 0 - 26)
  - ≥ 1 episode of VAC: 14 days (95% CI 0 -23) ($p < 0.05$)
  - ≥ 1 episode of IVAC: 5 days (95% CI 0 - 18) ($P = 0.05$)

VAE clearly associate with poor outcome

- Good correlation with number of antibiotic-days (within each ICU):
  - **VAC: R^2 =0.987 (p<0.0001)**
  - **IVAC R^2 = 0.99 (p<0.0001)**

VAE may be useful as Quality indicator / ASP

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Major article

Surveillance versus clinical adjudication: Differences persist with new ventilator-associated event definition

Kathleen M. McMullen MPH, CIC[a,*], Anthony F. Boyer MD[b], Noah Schoenberg MD[b], Hilary M. Babcock MD, MPH[c], Scott T. Micek PharmD[d], Marin H. Kollef MD[b]

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Analysed 1209 patients in medical & surgical ICU

IP – **Retrospective** surveillance using an automated algorithm with manual chart review by Infection prevention (IP) control strategy

Prospective manual surveillance by pulmonary physicians working with ICU critical care team

Clinician surveillance	IP VAE	IP no VAE	Total
Clin VAE	56	11	67
Clin no VAE	13	1,129	1,142
Total	69	1,140	1,209

K = 0.81, *P* = 0.4

Good agreement between study teams

Awareness of the limitations of the surveillance definition needed for optimal use of data

Reasons for disagreement

- VAE called retrospectively only:
  - **Died on the second calendar day** of the worsening oxygenation
    - Prospective: imminent mortality, not secondary to a new VAE
  - **Extubated on day 2** of worsening oxygenation
    - Prospectively: extubation process, not a new event
- VAE called prospectively only:
  - **Died on calendar day 1** of worsening oxygenation.
    - Hence not meeting the ≥ 2 days of worsening ventilator status criterion
  - **On airway pressure release ventilation (APRV)**

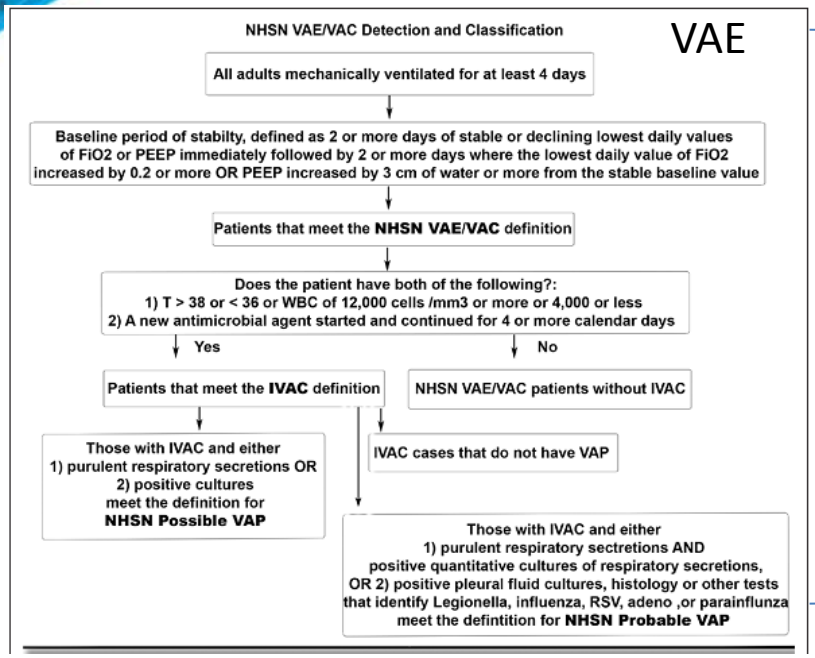
Prevalence and Test Characteristics of National Health Safety Network Ventilator-Associated Events

Craig M. Lilly, MD[1,2,3,4]; Karen E. Landry, BS[5]; Rahul N. Sood, MD[1];
Cheryl H. Dunnington, RN, MS[5,6]; Richard T. Ellison III, MD[1,5,7]; Peter H. Bagley, MD[1,5];
Stephen P. Baker, MScPH[1,2,4,8,9,10]; Shawn Cody, RN, MSN/MBA[5,6]; Richard S. Irwin, MD[1,8];
for the UMass Memorial Critical Care Operations Group

- 2 academic medical centre
- 8400 patients

Design: Prospective cohort study.
Setting: Two inpatient campuses of an academic medical center.
Patients: Eight thousand four hundred eight mechanically ventilated adults discharged from an ICU.
Interventions: None.
Measurements and Main Results: The National Health Safety Network ventilator-associated event/ventilator-associated condition constructs detected less than a third of ventilator-associated pneumonia cases with a sensitivity of 0.325 and a positive predictive value of 0.07. Most National Health Safety Network ventilator-associated event/ventilator-associated condition cases (93%) did not have ventilator-associated pneumonia or other hospital-acquired complications; 71% met the definition for acute respiratory distress syndrome. Similarly, most patients with National Health Safety Network probable ventilator-associated pneumonia did not have ventilator-associated pneumonia because radiographic criteria were not met. National Health Safety Network ventilator-associated event/ventilator-associated condition rates were reduced 93% by an unsophisticated manipulation of ventilator management protocols.
Conclusions: The National Health Safety Network ventilator-associated event/ventilator-associated condition constructs failed to detect many patients who had ventilator-associated pneumonia, detected many cases that did not have a hospital complication, and were susceptible to manipulation. National Health Safety Network ventilator-associated event/ventilator-associated condition surveillance did not perform as well as ventilator-associated pneumonia surveillance and had several undesirable characteristics. (*Crit Care Med* 2014; 42:2019–2028)

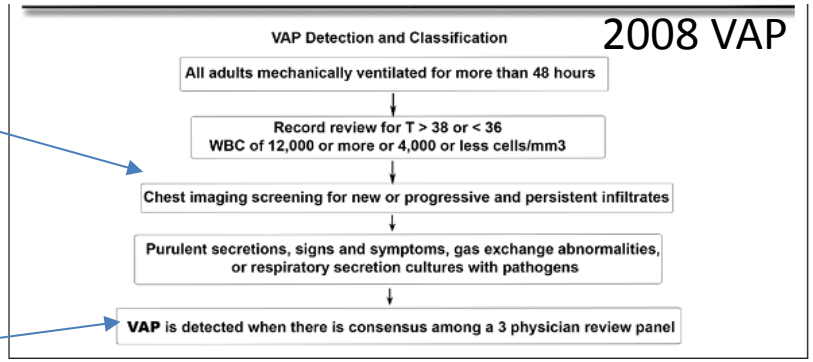
Methods



Electronic protocol

Daily CXR screened for new or progressive and persistent infiltrates, consolidation, or cavitation - by Independent intensive care specialist

1 ICO (Infectious Disease Specialist) plus 2 Pulmonary Medicine physicians



Results

- The VAE have sensitivity of 0.325 and PPV of 0.07 in detecting VAP
- Most patients with probable VAP did not have VAP because radiographic criteria were not met

Results

TABLE 3. Outcomes by Group

Characteristic	Mechanically Ventilated	National Health Safety Network Ventilator-Associated Event/Ventilator-Associated Condition	Infection-Related Ventilator Condition	Ventilator-Associated Pneumonia
Actual hospital mortality (%)	1,921 (23.8)	158 (42.0)[a]	143 (42.7)[a]	23 (28.4)
Predicted hospital mortality (SD)	2,231 (0.26)	125 (0.25)	111 (0.25)	23 (0.21)
O/E hospital mortality ratio	0.86	1.26	1.29	0.98
In-hospital mortality, odds ratio (95% CI)[b]	Reference	1.84 (0.95–3.6)	1.32 (0.66–2.6)	1.03 (0.61–1.7)
Actual ventilator days (95% CI)	4.8 (4.98–4.62)	14.8 (16.6–13.2)[a]	14.5 (15.8–13.1)[a]	17.6 (20.5–14.8)[a]
Predicted ventilator days (95% CI)[c]	4.0 (4.01–3.98)	4.7 (4.82–4.53)	4.7 (4.84–4.54)	4.5 (4.81–4.21)
O/E ventilator days (95% CI)	1.1 (1.17–1.09)	3.3 (3.68–3.01)	3.3 (3.63–2.93)	4.2 (4.93–3.4)
Actual hospital LOS (95% CI)	15.1 (15.2–15.1)	25.3 (26.9–23.6)[a]	25.1 (26.9–23.3)[a]	31.1 (35.2–27.1)[e]
Predicted hospital LOS (95% CI)[d]	12.3 (12.4–12.2)	13.7 (14.3–13.2)	13.7 (14.2–13.1)	13.7 (14.5–12.8)
O/E hospital LOS (95% CI)	1.3 (1.36–1.28)	2.0 (2.2–1.89)	2.0 (2.22–1.86)	2.45 (2.83–2.08)

O/E = observed/expected, LOS = length of stay.

[a] $p < 0.001$ compared to mechanically ventilated patients without ventilator-associated pneumonia (VAP) or ventilator-associated condition (VAC).

[b] Adjusted for Acute Physiology and Chronic Health Evaluation IV score and type of ICU.

[c] Among 5,804 mechanically ventilated, 281 VAC, 249 infection-related ventilator condition (IVAC), and 57 VAP patients had valid predictions.

[d] Among 8,408 mechanically ventilated, 374 VAC, 333 IVAC, and 81 VAP patients had valid predictions. Data from all patients are included in this tabulation; statistical analyses excluded patients in more than one category as detailed in the *Statistical Analyses* section.

[e] $p < 0.05$ compared to those without VAP in the National Health Safety Network ventilator-associated event/ventilator-associated condition and IVAC groups.

Crude mortality

- The NHSN VAE/VAC and IVAC groups had significantly higher crude mortality rates than all mechanically ventilated patients than those with VAP
- After adjustment for acuity and type of ICU, the difference were no longer statistically significant

Time Required for surveillance

- VAP surveillance: 1152 person hours for 5448 patients (12.6 min /episode)
- NHSN VAE/VAC surveillance: 621 hours for 2857 episodes (12.4 min/episode)

Prevalence and Test Characteristics of National Health Safety Network Ventilator-Associated Events

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for the UMass Memorial Critical Care Operations Group

VAP is still the GOLD STANDARD

- VAE/VAC construct will **miss Probable VAP**:
  - Because they did not meet the requirement of stable baseline mechanical ventilator setting
  - Because it does not use chest radiograph

    (which is the "state of the art of diagnosing life-threatening chest infections")

- VAP - clinically accepted and publicly reported entity that is widely regarded as a complication of hospitalization

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VAE/VAC ≠ Nosocomial

- Most VAE/VAC cases did not have evidence of any hospitalized-acquired complications

- >70% due to consequence of having their ventilator settings increase, met the definition of ARDS. The ARDS defining illness was nearly always their presenting illness rather than being caused by hospitalization or mechanical ventilation

TABLE 4. Risk Factors for Respiratory Failure of Those Meeting the National Health Safety Network Ventilator-Associated Event/ Ventilator-Associated Condition Definition

Condition	*n* (%)
National Health Safety Network ventilator-associated event/ventilator-associated condition	387 (100)
Ventilator-associated pneumonia	27 (7.0)
Risk factors for respiratory failure	
ARDS	181 (46.8)
Acute kidney injury and ARDS	77 (19.9)
Acute kidney injury	20 (5.2)
ARDS and volume overload	18 (4.7)
Acute kidney injury, ARDS, and volume overload	6 (1.6)
Volume overload	2 (0.5)
Acute kidney injury and volume overload	2 (0.5)
Other	54 (14.0)

ARDS = acute respiratory distress syndrome.

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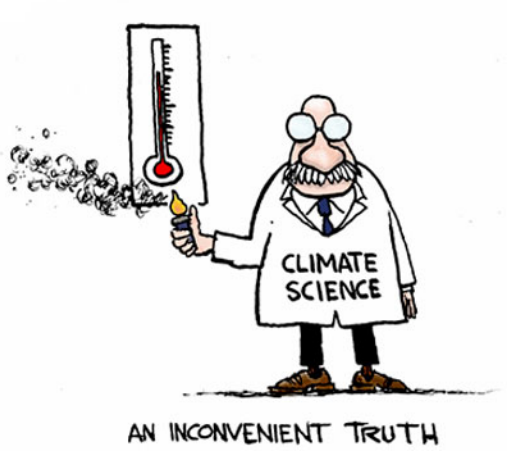
Ease of data manipulation



- Modelled the effects of **simple algorithm changes to respiratory therapy protocols** and assessed the ability of an automated system to detect NHSN VAE/VAC

- **93% NHSN VAE/VAC cases escaped detection**

  (because they did not meet the requirement for a stable or improving baseline period)

Final Thoughts

- Which one is better?
  - CPIS or VAE
- Clinical protocol or surveillance protocol, or both?
- Can VAP/VAE become a performance indicator?


Thank you