VAP Prevention Strategies

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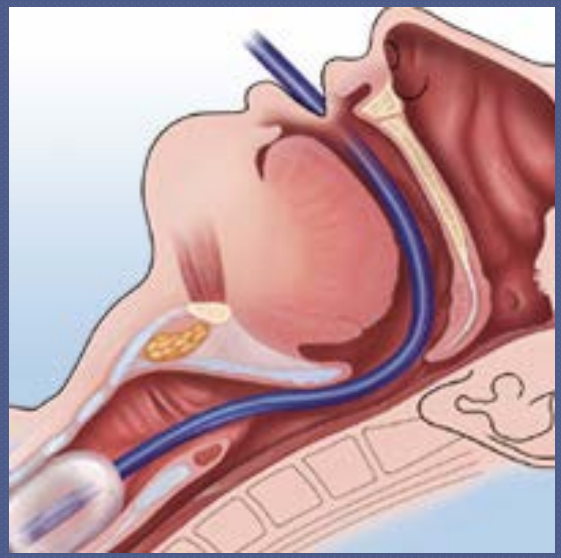
Symposium on Prevention of Healthcare-associated Infections in Hospitals and Community Institutions

18th January, 2019

VAP: what are we dealing with?

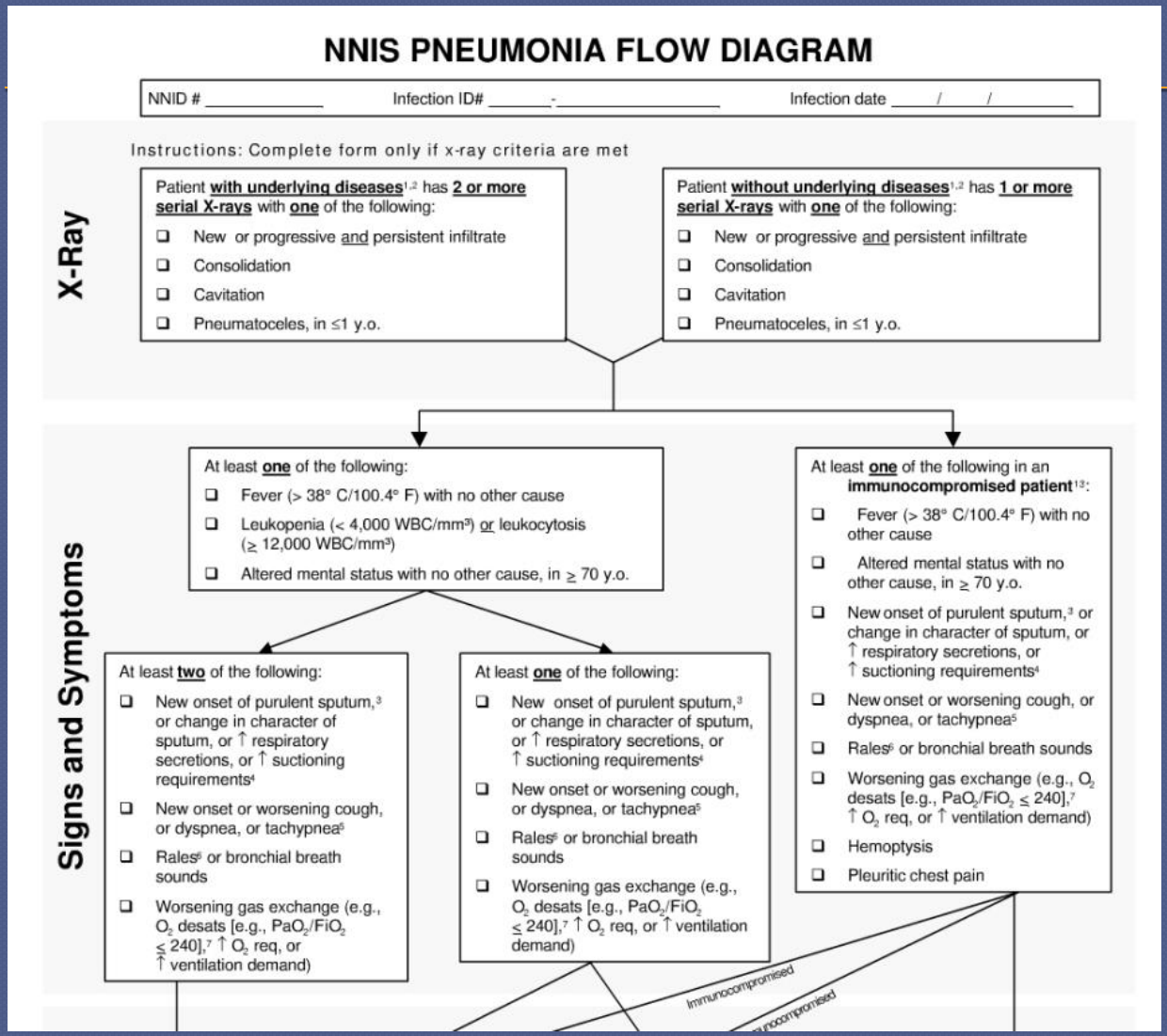
- **Major mechanisms**:
  1. Microaspiration (of materials from oropharyngeal cavities, sinuses, gastro-intestinal tract)
  2. Biofilm formation
  3. Inhalation
  4. Bacteraemia
  5. haematogenous spread



- Crude mortality: 70%
- Attributable mortality: 2 – 13%
- Higher mean hospitalization cost

Melsen WG, et al. Lancet Infect Dis. 2013
Van Vught LA, et al. JAMA. 2016
Jaillette E, Girault C, Brunin G, et al. ICM 2017

The CDC/NHSN PNU1 criteria



NNIS PNEUMONIA FLOW DIAGRAM

NNID # _____ Infection ID# _____-_____ Infection date ____/____/_____

Instructions: Complete form only if x-ray criteria are met

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 **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)

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- ❑ 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 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

Immunocompromised

PNU1

PNU2 = PNU1 + definite laboratory findings

PNU3: For immunocompromised patients only, = a slightly different set of clinical critieria + positive microbiological criteria

CDC/NHSN since 2002

TABLE 1] The Diagnostic Requirements for the Six Published Sets of Criteria

Published Criteria	Systemic Criteria	Chest Criteria	Chest Radiography Criteria	Microbiologic Criteria
New criteria CDC/NHSN[17] **VAE**	- Inflammatory response (fever or WBC>12,000/mm³ or <4,000/mm³) - Or new antimicrobial agent is started for ≥4 d → Infection-related ventilator-associated complication	After a period of stability or improvement on the ventilator (≥2 calendar days of stable or decreasing F_{IO_2} or PEEP): - Minimum daily F_{IO_2} increase ≥0.20 remain 2 d - Or minimum daily PEEP values increase ≥3 cm H_2O remain 2 d → Ventilator-associated condition	...	Microbiologic quantitative positive, or histologic positive, or positive for *Legionella*, influenza virus, RSV, adenovirus, or parainfluenza And Gram-stain evidence ≥25 neutrophils/lpf and ≤10 epithelial cells/lpf → Probable VAP
CDC/NHSN PNU1[12]	At least one criterion: - Temperature>38°C - WBC>12,000/mm³ or <4,000/mm³ - For patient >70 y old: altered mental status with no other cause	At least two criteria: - New purulent sputum or change in character - Cough, dyspnea, or tachypnea - Auscultation suggestive - Worsening gas exchange (desaturation, increasing F_{IO_2} or ventilation requirements)	Two or more radiographs with at least one criterion: - New or progressive and persistent infiltrate - Consolidation - Cavitation	...
HELICS[16]	At least one criteria: - WBC>12,000/mm³ - Temperature >38°C	At least one criteria (2 if qualitative aspirate culture or if culture is negative): - New purulent sputum or change in character - Cough, dyspnea, or tachypnea - Auscultation suggestive - Worsening gas exchange (desaturation, increasing F_{IO_2} or ventilation requirements)	Image suggestive of pneumonia (two or more required for patients with underlying cardiac or pulmonary disease)	...
CPIS[13] (A score >6 is suggestive of VAP)	Fever: - 38.5-38.9: 1 - ≥39 or <36.5: 2 WBC: - <4,000/mm³ or >11,000/mm³: 2	- Secretions but not purulent: 1 - Purulent secretions: 2 - Pao_2/F_{IO_2}<240 without ARDS: 2	Diffuse infiltrate: 1 Localized infiltrate: 2 Progressive infiltrate (without cardiac disease or ARDS): +2	Positive: 1
CHEST[15]	At least two criteria: - Temperature >38°C - WBC>12.000/mm³ or <4.000/mm³ - Purulent secretions	...	New or progressive consolidation	...

Ego A, et al. CHEST 2015

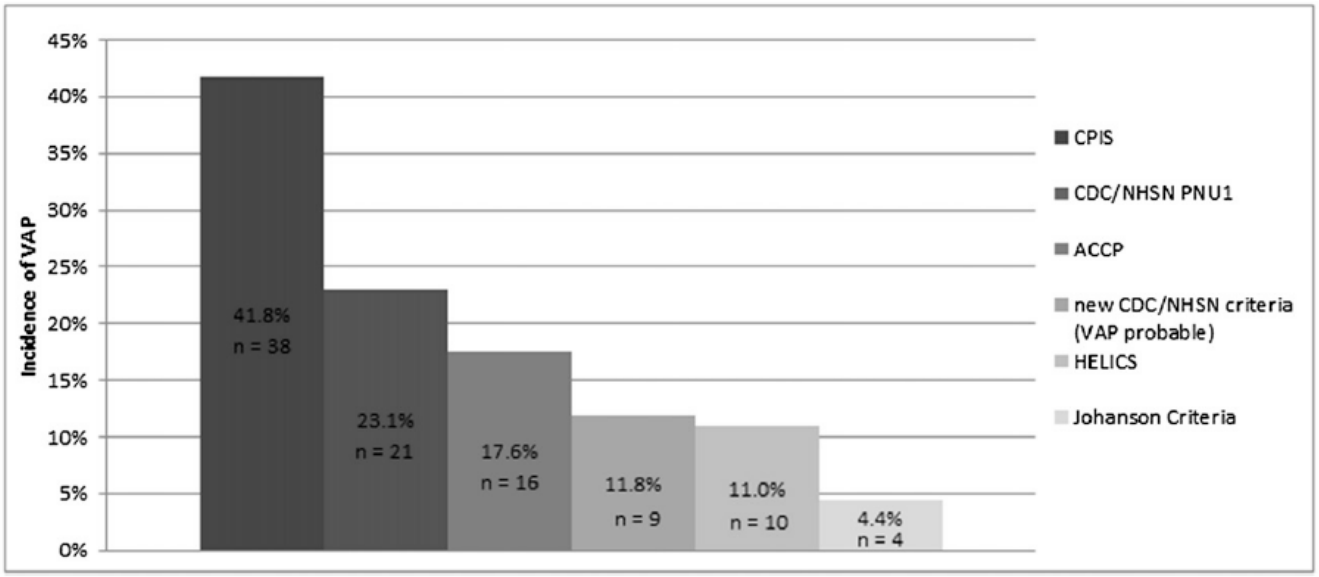


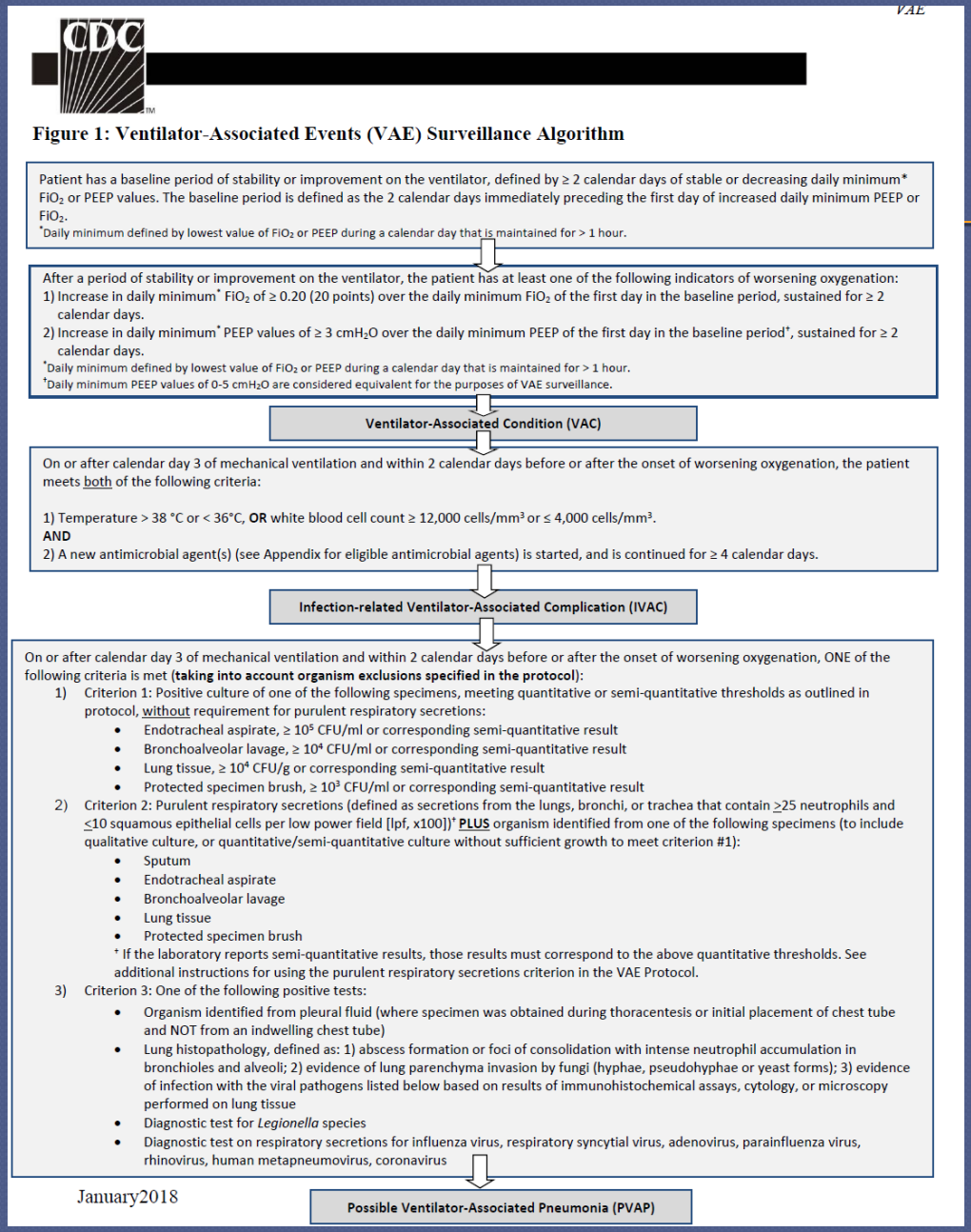
Figure 3 – *Incidence of VAP according to the published algorithms. CDC/NHSN PNU1 = US Centers for Disease Control and Prevention/National Healthcare Safety Network clinically defined pneumonia; ACCP = American College of Chest Physicians; CPIS = Clinical Pulmonary Infection Score; HELICS = Hospital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

TABLE 4] Agreement Between Published Criteria[a]

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.
[a]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).

Ego A, et al. Chest 2015



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 > 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 of the first day 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 of the first day 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 > 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** 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

   † 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:
   - 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

January2018

Possible Ventilator-Associated Pneumonia (PVAP)

Ventilator-associated events (VAE) Surveillance Algorithm

- Three categories of VAE:
  1. VAC: Ventilator-associated condition
  2. IVAC: Infection-related ventilator-associated complication
  3. PVAP: Possible ventilator-associated pneumonia

- Meet Criterion 1: if growth is reported as moderate or heavy
- Meet Criterion 2: if WBC is 4+ and epithelial cells are rare, occasional, few, 1+ or 2+, or <=10 squamous epithelial cells per lfp (x100)

From Clinical Microbiology Procedures Handbook 3rd ed (CMPH)

CDC/NHSN, since Jan 2013

Relationship within VAE and between VAP and VAE

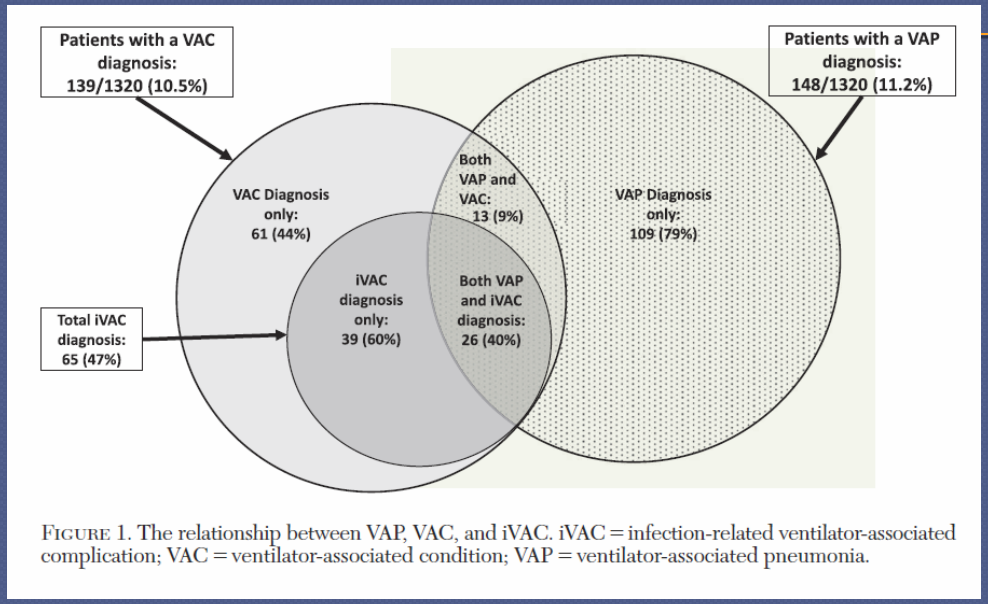


FIGURE 1. The relationship between VAP, VAC, and iVAC. iVAC = infection-related ventilator-associated complication; VAC = ventilator-associated condition; VAP = ventilator-associated pneumonia.

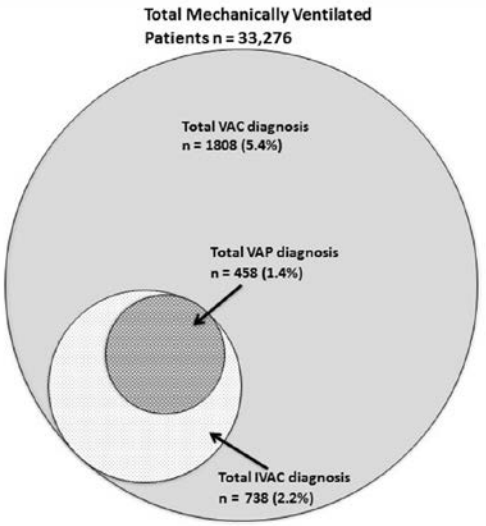


Fig. 2. Diagram summarizing cumulative number of patients that met VAC, iVAC, and both possible- and probable-VAP criteria from the published studies summarized in Table 2.

Table 3—*Relationship Between VAP, VAC, and iVAC*

Condition as Compared With VAP	VAP as the Comparison Standard (n = 148): Presence of Both VAP and VAC or iVAC	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %
VAC (n = 139)	39 of 148 (26.4%)	26	91	28	91
iVAC (n = 65)	26 of 148 (17.6%)	18	97	40	90

See Table 1 legend for expansion of abbreviations.

Spalding MC, et al. Crit Care Clin 2017
Muscedere J, et al. Chest 2013

Pros and Cons of VAE as a quality metric

Table 2. Pros and Cons of Ventilator-Associated Events as a Quality Metric

Pros	Cons
VAE definitions are objective, reproducible, electronically computable, and amenable to automation.	VAE is an unfamiliar entity to most clinicians (no gestalt sense as to what it means).
First tier of the VAE framework is conceptually very simple to define and explain (change in PEEP or F_{IO_2}).	The second and third tiers of the VAE framework (IVAC and PVAP) are complicated to explain and automate.
VAEs strongly and consistently associated with increased mortality.	VAE surveillance misses many traditionally defined VAPs.
VAE definitions expand the focus of surveillance and prevention to include multiple causes of deterioration in ventilated patients, not just pneumonia.	Positive predictive value of VAE for VAP is low.
There is mounting evidence that VAEs can be prevented and that preventing VAEs is associated with less time to extubation and other objective benefits.	Ventilator settings are poor and indirect measures of respiratory physiology.
Best practices to prevent VAEs highly aligned with best practices in critical care.	Sometimes raising ventilator settings can be good for patients.
VAEs provide a tangible focus for root cause analyses to explore local factors that may be modifiable to improve outcomes for ventilated patients.	Some VAEs may better reflect the natural history of severe illness rather than potentially preventable complications.
VAE surveillance and prevention encourages cross-collaboration between multiple disciplines (physicians, nurses, infection control, respiratory therapy, pharmacy, physical therapy, etc).	VAE surveillance requires infection preventionists to grapple with new sources of data (ventilator settings) and practices of care (ventilator management, sedation management, fluid management) that are unfamiliar to them.
	VAE detection can be averted by manipulating ventilator settings in trivial ways.
	Extent of VAE preventability unknown. It is unlikely that *all* VAEs can be avoided.

VAE = ventilator-associated event
VAP = ventilator-associated pneumonia
IVAC = infection-related ventilator-associated complication
PVAP = possible ventilator-associated pneumonia

Klompas M and Berra L. Resp Care 2016

Adoption of VAP and/or VAE surveillance in HK ICUs

Surveillance methods	Jul 2017 (N=15)	Oct 2018 (N=13)
VAP only	8	6
VAE only	2	0
Both Yes	2	4
Both No	3	4
Total	**15**	**14**
Either VAP or VAE	12/15 (80.0%)	10/14 (71.4%)

Future: ?VAE for all before end of 2019 (after CIS update)

Changes in Prevalence of Health Care – Associated Infections in U.S. Hospitals

A one-day random sample of patients, a total of 12,299 patients in 199 US hospitals were surveyed in 2015, as compared with 11,282 patients in 183 hospitals in 2011.

Table 4. Percentages of All Surveyed Patients with Specific Types of Health Care–Associated Infection, 2011 vs. 2015 Survey.*

Type of Infection	2011 Survey			2015 Survey			P Value†
	No. of Patients with Infection	No. of Infections	Percentage of Patients with Infection (95% CI)	No. of Patients with Infection	No. of Infections	Percentage of Patients with Infection (95% CI)	
Pneumonia	110	110	0.98 (0.81–1.20)	110	110	0.89 (0.74–1.10)	0.52
Ventilator-associated pneumonia	43	43	0.38 (0.28–0.51)	39	39	0.32 (0.23–0.43)	0.41
Other pneumonia	67	67	0.59 (0.47–0.75)	71	71	0.58 (0.46–0.73)	0.87
Gastrointestinal infection	86	86	0.76 (0.62–0.94)	91	91	0.74 (0.60–0.91)	0.84
Clostridium difficile infection‡	61	61	0.54 (0.42–0.69)	66	66	0.54 (0.42–0.68)	0.97
Other gastrointestinal infection	25	25	0.22 (0.15–0.33)	25	25	0.20 (0.14–0.30)	0.76
Surgical-site infection	109	110	0.97 (0.80–1.20)	69	69	0.56 (0.44–0.71)	<0.001
Deep incisional or organ-space infection	77	77	0.68 (0.55–0.85)	54	54	0.44 (0.34–0.57)	0.01
Superficial incisional infection	33	33	0.29 (0.21–0.41)	15	15	0.12 (0.07–0.20)	0.004
Bloodstream infection	50	50	0.44 (0.34–0.58)	51	52	0.41 (0.31–0.55)	0.74
Central catheter–associated bloodstream infection	42	42	0.37 (0.27–0.50)	37	38	0.30 (0.22–0.42)	0.35
Other primary bloodstream infection	8	8	0.07 (0.03–0.14)	14	14	0.11 (0.07–0.19)	0.29
Urinary tract infection	65	65	0.58 (0.45–0.73)	39	39	0.32 (0.23–0.43)	0.003
Catheter-associated urinary tract infection	44	44	0.39 (0.29–0.52)	24	24	0.20 (0.13–0.29)	0.005
Other urinary tract infection	21	21	0.19 (0.12–0.29)	15	15	0.12 (0.07–0.20)	0.21
Other infection§	78	83	0.69 (0.55–0.86)	61	66	0.50 (0.39–0.64)	0.05
Any infection	452	504	4.0 (3.7–4.4)	394	427	3.2 (2.9–3.5)	<0.001

* A total of 11,282 patients were included in the 2011 survey, and 12,299 in the 2015 survey; these values are the denominators for the percentages of patients with infection. Patients could have more than one health care–associated infection.
† P values were calculated by a mid-P exact test.
‡ *Clostridium difficile* is now known as *Clostridioides difficile*.
§ Other infections in the 2011 survey included the following: ear, eye, nose, and throat infections (28 infections); lower respiratory tract infection (20); skin and soft-tissue infections (16); cardiovascular infection (6); bone and joint infections (5); central nervous system infection (4); reproductive tract infection (3); and systemic infection (1). Other infections in the 2015 survey included the following: skin and soft-tissue infections (22 infections); ear, eye, nose, and throat infections (21); lower respiratory tract infection (18); bone and joint infections (2); central nervous system infection (1); cardiovascular infection (1); and reproductive tract infection (1).

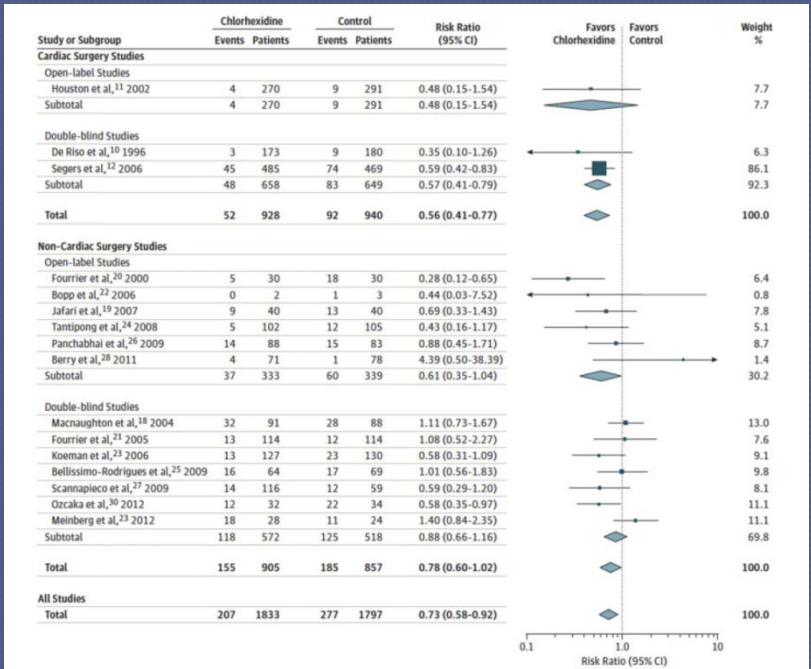
Magill SS, O'Leary E, Janelle SJ, et al, for the Emerging Infections Program Hospital Prevalence Survey Team, NEJM Nov 2018

VAP Prevention strategies – Right or wrong?

Common VAP prevention strategies	Right or wrong?
Spontaneous awakening and breathing trials	So far yes
Head-of-bed elevation	So far yes
Thromboembolism prophylaxis	So far yes, though not directly related to VAP
Selective digestive decontamination	Lowers VAP and mortality rates, Controversial, seldom practiced, will increase resistant organisms
Subglottic secretion drainage	Uncertain
Probiotics	Uncertain
Cuff material: Polyurethrane	Uncertain
Cuff shape: Conical, tapered cuff	Uncertain
Protocolized weaning	Uncertain
Oral care with chlorhexidine	Potentially harmful
Stress ulcer prophylaxis	Potentially harmful
Lateral Trendelenberg positioning	Lowers microbiologically confirmed VAP, but patient cannot tolerate

Oral care with chlorhexidine

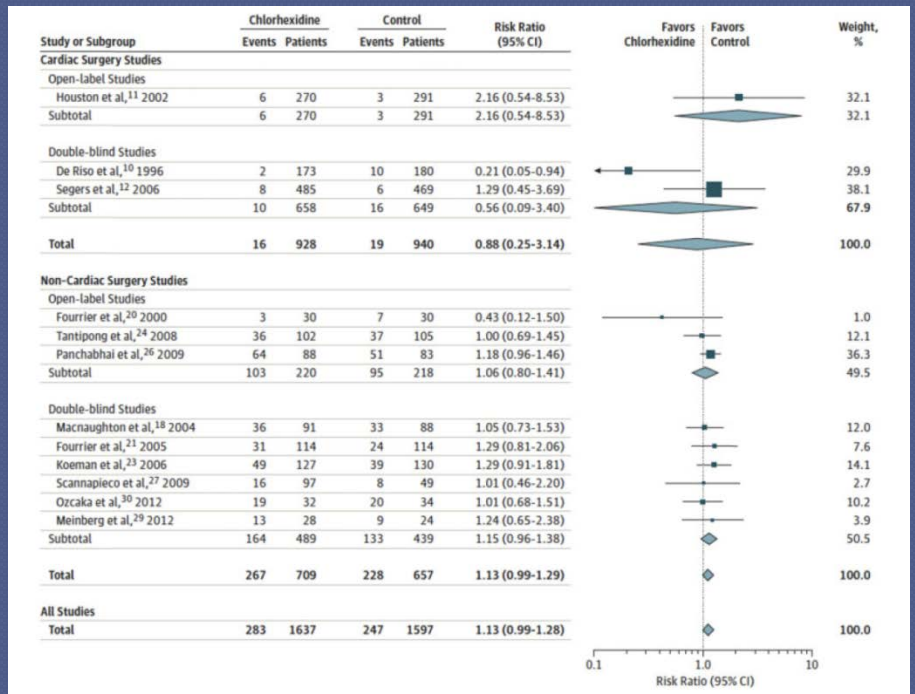
VAP



Study or Subgroup	Chlorhexidine Events	Chlorhexidine Patients	Control Events	Control Patients	Risk Ratio (95% CI)	Weight %
Cardiac Surgery Studies						
Open-label Studies						
Houston et al,[11] 2002	4	270	9	291	0.48 (0.15-1.54)	7.7
Subtotal	4	270	9	291	0.48 (0.15-1.54)	7.7
Double-blind Studies						
De Riso et al,[10] 1996	3	173	9	180	0.35 (0.10-1.26)	6.3
Segers et al,[12] 2006	45	485	74	469	0.59 (0.42-0.83)	86.1
Subtotal	48	658	83	649	0.57 (0.41-0.79)	92.3
Total	**52**	**928**	**92**	**940**	**0.56 (0.41-0.77)**	**100.0**
Non-Cardiac Surgery Studies						
Open-label Studies						
Fourrier et al,[20] 2000	5	30	18	30	0.28 (0.12-0.65)	6.4
Bopp et al,[22] 2006	0	2	1	3	0.44 (0.03-7.52)	0.8
Jafari et al,[19] 2007	9	40	13	40	0.69 (0.33-1.43)	7.8
Tantipong et al,[24] 2008	5	102	12	105	0.43 (0.16-1.17)	5.1
Panchabhai et al,[26] 2009	14	88	15	83	0.88 (0.45-1.71)	8.7
Berry et al,[28] 2011	4	71	1	78	4.39 (0.50-38.39)	1.4
Subtotal	37	333	60	339	0.61 (0.35-1.04)	30.2
Double-blind Studies						
Macnaughton et al,[18] 2004	32	91	28	88	1.11 (0.73-1.67)	13.0
Fourrier et al,[21] 2005	13	114	12	114	1.08 (0.52-2.27)	7.6
Koeman et al,[23] 2006	13	127	23	130	0.58 (0.31-1.09)	9.1
Bellissimo-Rodrigues et al,[25] 2009	16	64	17	69	1.01 (0.56-1.83)	9.8
Scannapieco et al,[27] 2009	14	116	12	59	0.59 (0.29-1.20)	8.1
Ozcaka et al,[30] 2012	12	32	22	34	0.58 (0.35-0.97)	11.1
Meinberg et al,[23] 2012	18	28	11	24	1.40 (0.84-2.35)	11.1
Subtotal	118	572	125	518	0.88 (0.66-1.16)	69.8
Total	**155**	**905**	**185**	**857**	**0.78 (0.60-1.02)**	**100.0**
All Studies						
Total	**207**	**1833**	**277**	**1797**	**0.73 (0.58-0.92)**	**100.0**

Fig. 1 Impact of chlorhexidine versus comparators on nosocomial pneumonia in cardiac surgery patients and ventilator-associated pneumonia in noncardiac surgery patients. Reproduced with permission from Klompas et al. JAMA Internal Medicine 2014;174(5):751–761. Copyright © 2014 American Medical Association. All rights reserved.[49]

Mortality rates



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Open-label Studies						
Fourrier et al,[20] 2000	3	30	7	30	0.43 (0.12-1.50)	1.0
Tantipong et al,[24] 2008	36	102	37	105	1.00 (0.69-1.45)	12.1
Panchabhai et al,[26] 2009	64	88	51	83	1.18 (0.96-1.46)	36.3
Subtotal	103	220	95	218	1.06 (0.80-1.41)	49.5
Double-blind Studies						
Macnaughton et al,[18] 2004	36	91	33	88	1.05 (0.73-1.53)	12.0
Fourrier et al,[21] 2005	31	114	24	114	1.29 (0.81-2.06)	7.6
Koeman et al,[23] 2006	49	127	39	130	1.29 (0.91-1.81)	14.1
Scannapieco et al,[27] 2009	16	97	8	49	1.01 (0.46-2.20)	2.7
Ozcaka et al,[30] 2012	19	32	20	34	1.01 (0.68-1.51)	10.2
Meinberg et al,[29] 2012	13	28	9	24	1.24 (0.65-2.38)	3.9
Subtotal	164	489	133	439	1.15 (0.96-1.38)	50.5
Total	**267**	**709**	**228**	**657**	**1.13 (0.99-1.29)**	**100.0**
All Studies						
Total	**283**	**1637**	**247**	**1597**	**1.13 (0.99-1.28)**	**100.0**

Fig. 2 Impact of chlorhexidine versus comparators on mortality. Reproduced with permission from Klompas et al. JAMA Internal Medicine 2014;174(5):751–761. Copyright © 2014 American Medical Association. All rights reserved.[49]

A possible signal that oral chlorhexidine may increase mortality rates

Klompas M. Semin Respir Crit Care Med 2017

Effects of chlorhexidine gluconate oral care on hospital mortality: a hospital-wide, observational cohort study

- Single-center, retrospective, hospital-wide, observational cohort study, adult hospitalized patients (2012-2014)
- Low-level exposure to chlorhexidine oral care (≤ 300 mg) was associated with increased risk of death The adjusted number of patients needed to be exposed to result in one additional fatality case was 47.1 (95% CI 45.2-49.1)

Patient types	Odds ratio (OR) of death
lower risk of death	5.50 (95% CI 4.51-6.71)
minor/moderate risk	2.33 (95% CI 1.96-2.78)
major risk	1.13 (95% CI 0.90-1.41) - non-significant
Overall	**2.61; 95% confidence interval (CI) 2.32-2.92**

Deschepper M, Waegeman W, Eeckloo K, Vogelaers D, Blot S. Intensive Care Med 2018

Stress ulcer prophylaxis

- No difference in GI bleed requiring endoscopic intervention (N=70862, retrospective, 0.6 vs 0.5%) or 30-d mortality rates, but higher rates of HAP (Sasabuchi Y et al. 2016)
- No difference in GIB and IVAC (N=214, RCT, Selvanderan et al 2016)
- More VAP in pantoprazole group (N=91, RCT, also no difference after combing data with other RCT (N=713, meta-analysis) (Alhazzani et al 2017)

Pantoprazole in Patients at Risk for Gastrointestinal Bleeding in the ICU

- European, multicenter, parallel-group, blinded trial
- Randomly assigned adults who had been admitted to the ICU for an acute condition (i.e., an unplanned admission) and who were at risk for gastrointestinal bleeding to receive 40 mg of intravenous pantoprazole (a proton-pump inhibitor) or placebo daily during the ICU stay.
- Primary outcome: death by 90 days after randomization.
- Results:
  - 3298 patients (1645 pantoprazole and 1653 placebo)
  - Data on the primary outcome were available for 3282 patients (99.5%).

Mette Krag, M.D., Søren Marker, Anders Perner, et al, for the SUP-ICU trial group. NEJM 2018

Table 2. Primary and Secondary Outcome Measures.

Outcomes	Pantoprazole	Placebo	Relative Risk (95% CI)*	P Value†
Primary outcome: death by day 90 — no./total no. (%)	510/1642 (31.1)	499/1640 (30.4)	1.02 (0.91–1.13)	0.76
Secondary outcomes				
One or more clinically important events — no./total no. (%)‡	360/1644 (21.9)	372/1647 (22.6)	0.96 (0.83–1.11)	—
One or more episodes of clinically important gastrointestinal bleeding — no./total no. (%)	41/1644 (2.5)	69/1647 (4.2)	0.58 (0.40–0.86)	—
One or more infectious adverse events — no./total no. (%)§	276/1644 (16.8)	279/1647 (16.9)	0.99 (0.84–1.16)	—
Severe adverse reaction — no./total no. (%)¶	0/1644 (0)	0/1647 (0)	—	—
Median percentage of days alive without the use of life support (IQR)‖	92 (60–97)	92 (65–97)	—	—

* Confidence intervals were not adjusted for the comparisons of multiple secondary outcomes.

† Logistic-regression analyses were adjusted for the stratification variables (site and hematologic cancer). The results of the unadjusted outcome analyses and the fully adjusted analyses are presented in Tables S4 and S6 in the Supplementary Appendix. Secondary outcomes are presented without P values because of the lack of adjustment for multiple comparisons.

‡ Clinically important events included clinically important gastrointestinal bleeding, pneumonia, *Clostridium difficile* infection, and myocardial ischemia.

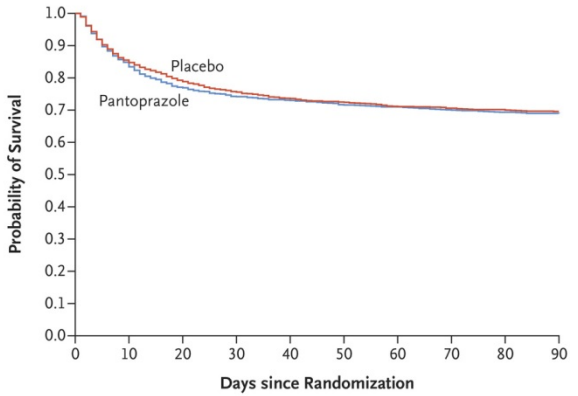
§ Infectious adverse events included pneumonia and *C. difficile* infection.

¶ Severe adverse reactions were defined as anaphylactic reactions, agranulocytosis, pancytopenia, acute hepatic failure, the Stevens–Johnson syndrome, toxic epidermal necrolysis, interstitial nephritis, and angioedema related to the intervention (as judged by the treating clinicians and investigators).[14] Specific events that were adjudicated as not to being related to pantoprazole or placebo, including the reasoning behind each adjudication, are described in Table S11 in the Supplementary Appendix.

‖ The percentage of days alive without the use of life support was calculated as the number of days without the use of invasive or noninvasive mechanical ventilation, infusion of vasopressor or inotropic agents, or any form of renal-replacement therapy, divided by the number of days alive within the 90-day follow-up period.

Mette Krag, M.D., Søren Marker, Anders Perner, et al, for the SUP-ICU trial group. NEJM 2018

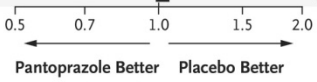
A Time to Death



No. at Risk				
Placebo	1647	1243	1167	1141
Pantoprazole	1643	1219	1163	1133

B Relative Risk of the Primary Outcome

Subgroup	Pantoprazole	Placebo	Relative Risk (95% CI)	P Value for Heterogeneity
	no. of events/no. of patients in subgroup			
Shock at randomization				0.92
Yes	413/1251	395/1210	1.01 (0.90–1.13)	
No	97/391	104/430	1.02 (0.80–1.31)	
Mechanical ventilation at randomization				0.74
Yes	399/1272	400/1310	1.03 (0.91–1.16)	
No	111/370	99/330	0.98 (0.77–1.25)	
Coagulopathy at randomization				0.54
Yes	135/352	118/299	0.95 (0.77–1.17)	
No	375/1290	381/1341	1.03 (0.91–1.16)	
History of liver disease				0.69
Yes	20/44	25/48	0.93 (0.60–1.44)	
No	490/1598	474/1592	1.02 (0.92–1.14)	
Type of ICU admission				0.38
Medical	361/1045	328/994	1.04 (0.92–1.18)	
Surgical	149/597	171/646	0.94 (0.78–1.14)	
SAPS II score >53				0.05
Yes	272/579	229/558	1.13 (0.99–1.30)	
No	205/929	231/967	0.92 (0.78–1.09)	
All patients	510/1642	499/1640	1.02 (0.91–1.13)	

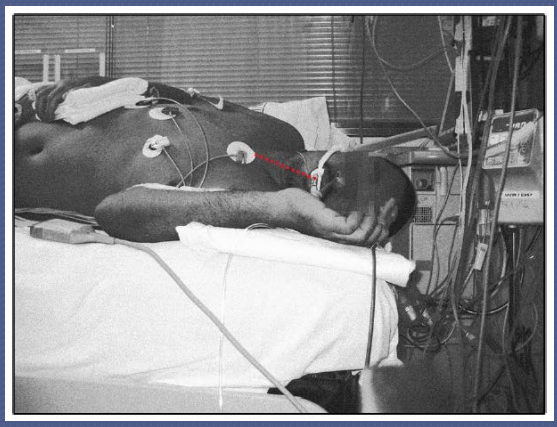


Mette Krag, M.D., Søren Marker, Anders Perner, et al, for the SUP-ICU trial group. NEJM 2018

The Gravity-VAP Trial

Only one randomised study with a non–intention-to-treat protocol of 86 MV patients, comparing the supine and semi-recumbent positions, in which the VAP rates were 34% and 8%, respectively. Subsequent studies were not able to reproduce these results, and found that a 45° position was difficult to maintain, and the mean angle achievable was only 28°.

VS



- In human beings, the trachea/ETT axis is below the horizontal in the lateral Trendelenburg position (ie lying lateral, at 5°-10° below the horizontal).
- The Gravity VAP-Trial, an international randomised controlled trial (RCT) aiming at enrolment of 800 patients
- to compare the efficacy and safety of the two body positions, namely
  - the lateral Trendelenburg position (LTP) versus
  - the semi-recumbent positions (SRP), in reducing the incidence of VAP.

Gianluigi Li Bassi (Barcelona, Spain) and Mauro Panigada (Milan, Italy). Results were first presented at in Milan at LIVES 2016, the annual congress of ESICM.

Drakulovic MB, et al. Lancet 1999
Li Bassi G, Panigada M, Ranzani OT, et al, for the Gravity-VAP Network. ICM 2017

Results of the Gravity-VAP Trial (stopped at second interim analysis)

	Semirecumbent ($n = 201$)	Lateral Trendelenburg ($n = 194$)	Relative risk or risk difference (95% CI)	*P* value
Main outcome				
Incidence of microbiologically confirmed VAP, no. (%)	8 (4.0)	1 (0.5)	0.13 (0.02–1.03)[a]	0.04
Microbiologically confirmed VAP per 1000 ventilator days, no. (95% CI)	7.19 (3.60–14.37)	0.88 (0.12–6.25)	0.12 (0.01–0.91)	0.02
Secondary outcome				
Incidence of early microbiologically confirmed VAP, no. (%)[c]	6 (3.0)	1 (0.5)	0.17 (0.02–1.42)	0.12
Incidence of late microbiologically confirmed VAP, no. (%)	2 (1.0)	0	NA	0.45
Incidence of clinically suspected VAP, no. (%)	21 (10.5)	18 (9.3)	0.89 (0.49–1.62)	0.74
Clinically suspected VAP per 1000 ventilator days, no. (95% CI)	19.55 (12.75–30.00)	17.09 (10.77–27.13)	0.87 (0.44–1.72)	0.68
Median duration of MV (IQR) (days)	4 (2–9)	5 (2–9)	0 (−1.00 to 1.00)[b]	0.73
Median duration of ICU stay (IQR) (days)	8 (4–16)	7 (4–13)	0 (−1.00 to 1.00)[b]	0.98
Median duration of hospital stay (IQR) (days)	16 (9–30)	15 (8–28)	−2.00 (−5.00 to 1.00)[b]	0.24
ICU mortality, no. (%)	48 (23.9%)	59 (30.4%)	1.27 (0.92–1.76)	0.17
Hospital mortality, no. (%)	63 (31.3%)	72 (37.1%)	1.18 (0.90–1.56)	0.24
28-day mortality, no. (%)	53 (26.4%)	60 (30.9%)	1.17 (0.86–1.60)	0.32

Stopped due to low incidence of VAP, lack of benefit in secondary outcomes, and occurrence adverse events

Li Bassi G, Panigada M, Ranzani OT, et al, for the Gravity-VAP Network. ICM 2017

	Semirecumbent ($n = 201$)	Lateral Trendelenburg ($n = 194$)	p value
New pressure ulcer	21 (10.5%)	21 (10.8%)	>0.99
Displacement of endotracheal tube, no. (%)	13 (6.5%)	11 (5.7%)	0.83
Loss of intravascular access, no. (%)	2 (1.0%)	5 (2.6%)	0.28
Displacement of drainage tube, no (%)	1 (0.5%)	0 (0%)	>0.99
Severe obstruction of endotracheal tube, no. (%)	1 (0.5%)	2 (1.0%)	0.62
Vomiting, no. (%)	5 (2.5%)	16 (8.3%)	0.01
Displacement of nasogastric tube, no. (%)	2 (1.0%)	7 (3.6%)	0.10

Serious adverse events in lateral Trendelenburg position

Time of occurrence after enrollment (days)	Patient comorbidities	Report of the event	Association with the intervention	Outcome
1	Hepatic fibrosis and cirrhosis Diabetes Renal failure	Oxygen desaturation during positioning	Definitely	Required prompt intervention to prevent further damage
2	Asthma Hepatic fibrosis and cirrhosis Diabetes Valvular heart disease	Severe hemodynamic impairment, shortly after positioning	Definitely	Required prompt intervention to prevent further damage
3	Liver transplant	Endotracheal extubation	Definitely	Required prompt intervention to prevent further damage
0	Arterial hypertension Cardiac arrhythmia	Sustained bradycardia, shortly after positioning	Definitely	Required prompt intervention to prevent further damage
12	Kyphoscoliosis Restrictive pulmonary disease	Neurological damage of the left brachial plexus	Possible	Permanent damage
8	End-stage liver failure	Intracerebral hemorrhage	Possible	Fatal

In a population at low risk of VAP, LTP caused a reduction in microbiologically confirmed VAP, but the results are inconclusive because of the lack of other clinical benefits, increased safety risks, and challenges in nursing compliance.

Li Bassi G, Panigada M, Ranzani OT, et al, for the Gravity-VAP Network. ICM 2017

Decontamination Strategies and Bloodstream Infections With Antibiotic-Resistant Microorganisms in Ventilated Patients - A Randomized Clinical Trial

- Question: Is use of chlorhexidine 2% mouthwash, selective oropharyngeal decontamination (SOD), or selective digestive tract decontamination (SDD) associated with reduced risk of bloodstream infections due to multidrug-resistant gram-negative bacteria among ventilated patients in intensive care units (ICUs) with moderate to high prevalence of antibiotic resistance?
- Findings: In this randomized trial of 8665 patients, the use of chlorhexidine 1% mouthwash, SOD, or SDD was not associated with significant differences in ICU-acquired bloodstream infections with multidrug-resistant gram-negative bacteria (adjusted hazard ratios, 1.13, 0.89, and 0.70, respectively), compared with a baseline period of chlorhexidine body washing and a hand hygiene improvement program.
- Meaning: Among ventilated patients in ICUs with moderate to high prevalence of antibiotic resistance, use of chlorhexidine 1% mouthwash, SOD, or SDD was not associated with a significant difference in bloodstream infections with multidrug-resistant gram-negative bacteria compared with standard care.

Wittekamp BH, Plantinga NL, Cooper BS, et al. JAMA, 27 Nov, 2018

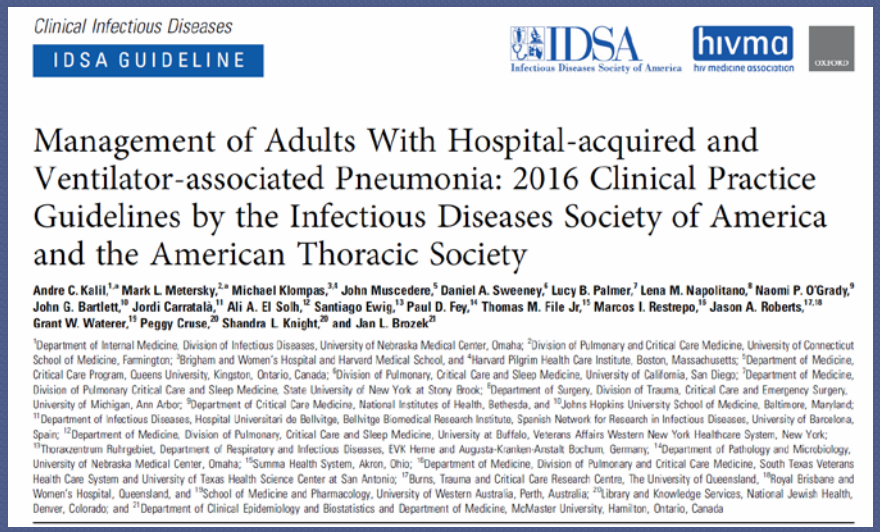
Effect of Protocolized Weaning With Early Extubation to Noninvasive Ventilation vs Invasive Weaning on Time to Liberation From Mechanical Ventilation Among Patients With Respiratory Failure
The Breathe Randomized Clinical Trial

- Question In adults in whom weaning from invasive mechanical ventilation is difficult, does early extubation using a protocolized noninvasive weaning regimen reduce the time to liberation from ventilation compared with protocolized invasive weaning?
- Findings In this randomized clinical trial that included 364 adults, the median time to liberation from ventilation for patients randomized to noninvasive weaning vs invasive weaning was 4.3 days vs 4.5 days, a difference that was not statistically significant.
- Meaning Protocolized weaning with early extubation to noninvasive ventilation compared with invasive weaning did not significantly shorten time to liberation from all forms of mechanical ventilation.

Perkins GD, Mistry D, Gates S, et al, for the Breathe Collaborators. JAMA, 13 Nov 2018

Latest guidelines

American



Clinical Infectious Diseases

IDSA GUIDELINE

IDSA Infectious Diseases Society of America · hivma hiv medicine association

Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society

Andre C. Kalil,[1,a] Mark L. Metersky,[2,a] Michael Klompas,[3,4] John Muscedere,[5] Daniel A. Sweeney,[6] Lucy B. Palmer,[7] Lena M. Napolitano,[8] Naomi P. O'Grady,[9] John G. Bartlett,[10] Jordi Carratalà,[11] Ali A. El Solh,[12] Santiago Ewig,[13] Paul D. Fey,[14] Thomas M. File Jr,[15] Marcos I. Restrepo,[16] Jason A. Roberts,[17,18] Grant W. Waterer,[19] Peggy Cruse,[20] Shandra L. Knight,[20] and Jan L. Brozek[21]

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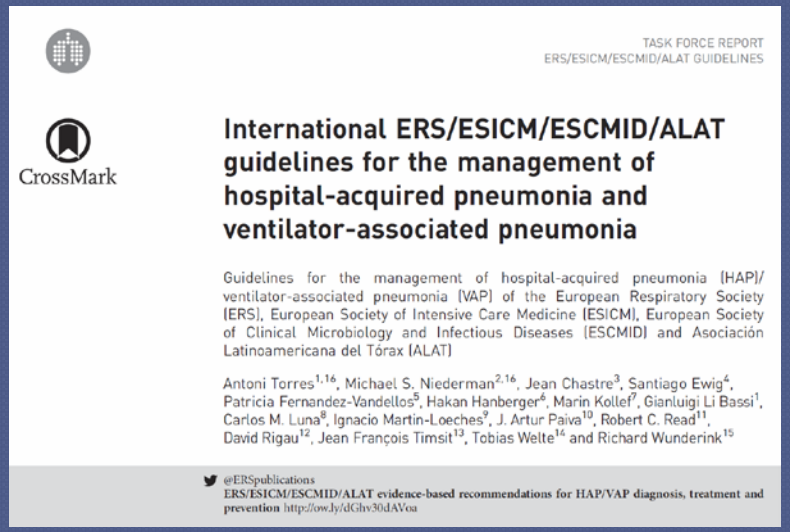
IDSA/ATS Guideline 2016
Last guideline: 2005

HK CHP Guideline: Nov 2018
Last guideline: 2010

European



TASK FORCE REPORT
ERS/ESICM/ESCMID/ALAT GUIDELINES

CrossMark

International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia

Guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT)

Antoni Torres[1,16], Michael S. Niederman[2,16], Jean Chastre[3], Santiago Ewig[4], Patricia Fernandez-Vandellos[5], Hakan Hanberger[6], Marin Kollef[7], Gianluigi Li Bassi[1], Carlos M. Luna[8], Ignacio Martin-Loeches[9], J. Artur Paiva[10], Robert C. Read[11], David Rigau[12], Jean François Timsit[13], Tobias Welte[14] and Richard Wunderink[15]

@ERSpublications
ERS/ESICM/ESCMID/ALAT evidence-based recommendations for HAP/VAP diagnosis, treatment and prevention http://ow.ly/dGhv30dAVoa

ERS/ESICM/ESCMID/ALAT
Guidelines 2017
Last guideline: 2009

Differences between ERS and IDSA/ATS guidelines

- Local microbiology differs
- No interest in VAC by ERS
- ERS endorses quantitative cultures
- ERS with higher threshold for using empiric MRSA therapy
- ERS prefers linezolid to vancomycin
- Duration of therapy longer for resistance in ERS guideline
- ERS with less focus on combination therapy and broad spectrum. IDSA/ATS with 95% coverage goal
- ERS not as enthusiastic about PCT for duration of treatment
- ERS endorses SOD

Ref: Niederman M. Autumn Resp Seminar 2018 HK

Conclusion

- VAP >>>> VAE, more objective, but what are we measuring
- First, do no harm? Which interventions are definitely beneficial?
- Guidelines: differences seen

The future is ??

Thank you!

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