International Symposium on Immunotherapy of Severe Infections
May 16th - 17th 2024, Kalamata, Greece

Session: Immune therapy for hospital-acquired infections

Epidemiology & Outcomes of Hospital-acquired pneumonia

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Declaration:

Speaker/moderator is MSD sponsored symposia

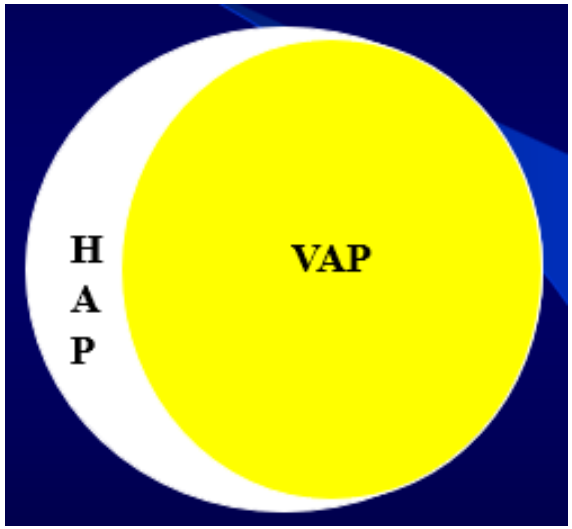
Hospital-acquired pneumonia (HAP): pneumonia arising ≥ 48 hours after admission and which was not incubating at the time of admission

Ventilator-associated pneumonia (VAP): pneumonia arising ≥ 48 hours after endotracheal intubation and initiation of mechanical ventilation which was not incubating at the time of intubation.

Hospital-acquired pneumonia (HAP): pneumonia arising ≥ 48 hours after admission and which was not incubating at the time of admission

Non-ventilated HAP (nv-HAP):
in the ward or the ICU (ICU-AP)

Ventilated HAP (v-HAP):
onset in non-intubated patients that due to deterioration subsequently needs intubation



VAP onset after >48 h of intubation

HAP = Nosocomial pneumonia

The definitions of HAP are not homogeneous (and thus, may alter the incidences reported)

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ERS/ESICM/ESCMID/ALAT 2017:
HAP is an infection of the pulmonary parenchyma caused by pathogens that are present in hospital settings. Nosocomial pneumonia develops in patients admitted to the hospital for >48 h and usually the incubation period is at least 2 days. Among nosocomial pneumonias, VAP develops in ICU patients who have been mechanically ventilated for at least 48 h.

Torres et al. European Respiratory Journal 2017 50: 1700582

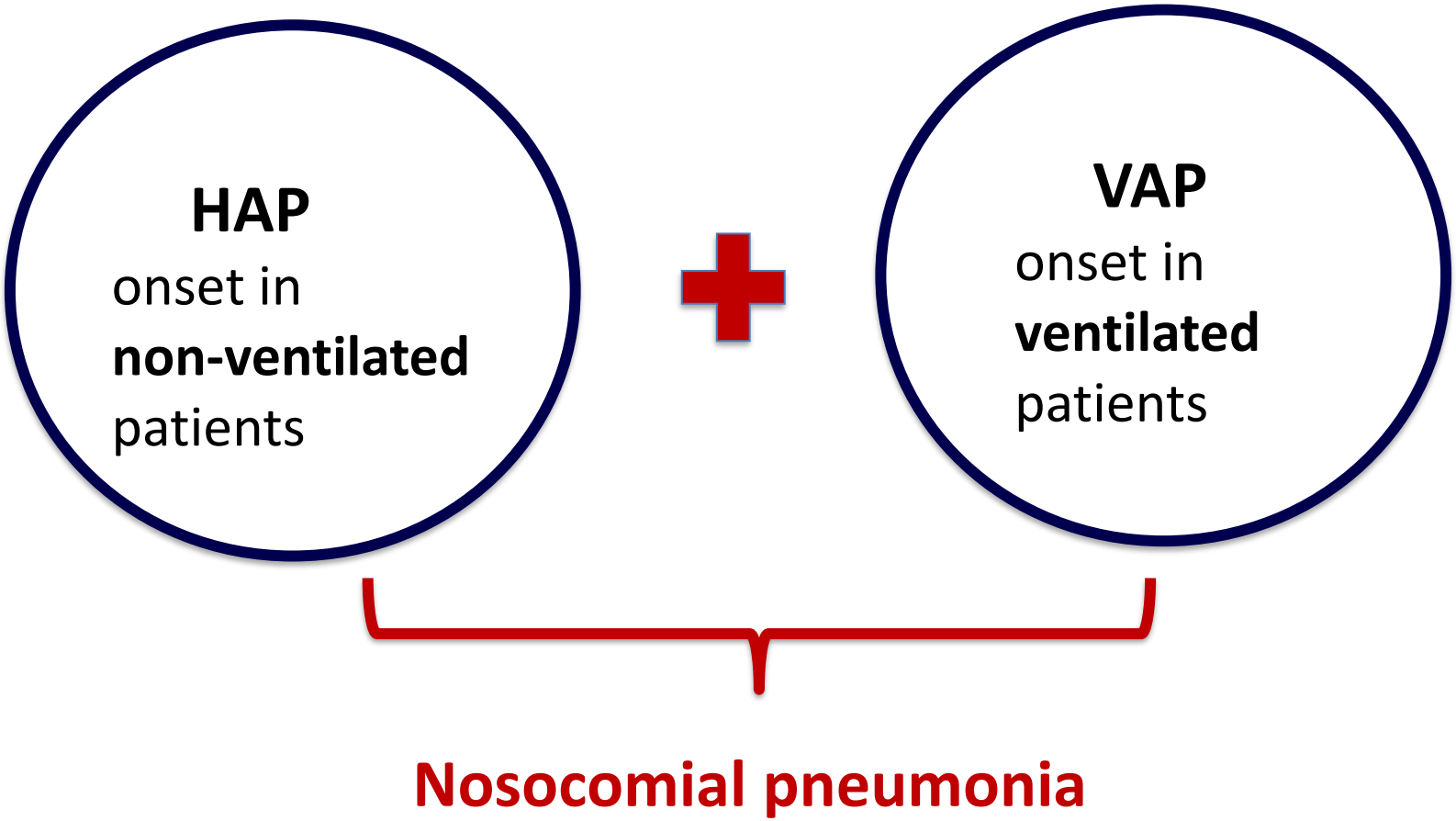
The definitions of HAP are not homogeneous (and thus, may alter the incidences reported)

ATS/IDSA 2016:

'In this 2016 guideline, the term "hospital-acquired pneumonia" **(HAP) denotes an episode of pneumonia not associated with mechanical ventilation.** Thus, patients with HAP and ventilator-associated pneumonia (VAP) belong to 2 distinct groups.'

Management of Adults With HAP/VAP

Clin Infect Dis. 2016; 63:e61-e111


HAP
onset in
non-ventilated
patients
VAP
onset in
ventilated
patients
Nosocomial pneumonia

Epidemiology

Risk factors for HAP/VAP

- ✓ **Patient-related:** prolonged hospital length of stay, prolonged MV duration, prolonged sedation, comorbidities, prior use of antibiotics & septic shock, underlying pathology (e.g., TBI), presence of ARDS
- ✓ **Procedure-related:** inadequate hand hygiene or inappropriate care of respiratory support devices
- ✓ **Intervention-related:** immunosuppressants & prolonged/inappropriate antibiotic treatment, ECMO

Zaragoza et al. Critical Care (2020) 24:383

Risk factors for VAP in TBI

- Alcohol
- Drug abuse
- Energy of trauma
- Young age
- Chest trauma
- H2-receptor antagonist intake
- No antibiotic prophylaxis.

Robba et al. Chest 2020; 158(6):2292-2303

HAP/VAP Epidemiology

- Marked differences in the epidemiology between countries
- Between different types of ICU
- Variations due to:

  -differences in the definition used

  - diagnostic difficulties/subjective criteria

  - different diagnostic methods used

HAP Epidemiology

- HAP: No 2 Nosocomial Infection
- HAP incidence varies significantly: **5-20 cases/1000 hospital admissions**
- Artificial airway: 21-fold of pneumonia risk
- VAP accounts for 1/3 of HAP overall & 80% of HAP in the ICU
- **VAP 1-18.5 episodes/1000 ventilator-days**

Torres et al. European Respiratory Journal 2017 50: 1700582; Clin Infect Dis 2016;63:e63-e11; Bonnel et al. Clin Infect Diseases 2019; 68(1):511; Koulenti et al. Crit Care Med 2009; 37(8): 2360-8

Incidence density variability

- **USA:** 1-2.5 episodes/1000 ventilator-days (vd)
- **Europe:** 8.9 episodes/1000 vd
- **Asia-lower income:** 18.5 episodes/1000 vd ventilator-days
- **Asia-upper/middle income:** 15.2 episodes/vd episodes/1000 ventilator-days
- **Asia-high income:** 9.0 episodes/1000 vd

Zaragosa et al. Crit Care 2020; 24:383; Bonnel et al. Clin Infect Diseases 2019; 68(1):511

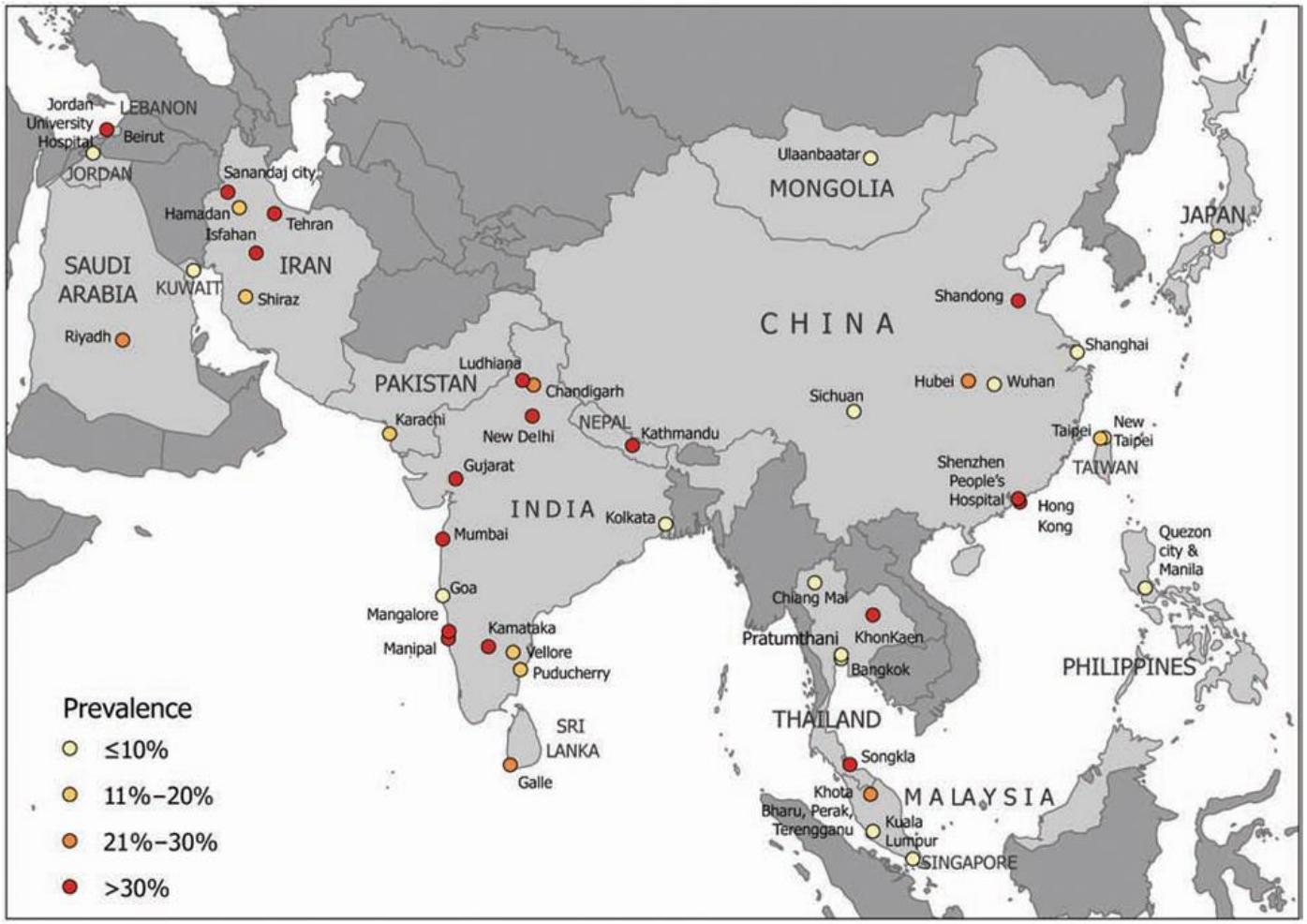
Clinical Infectious Diseases

REVIEW ARTICLE

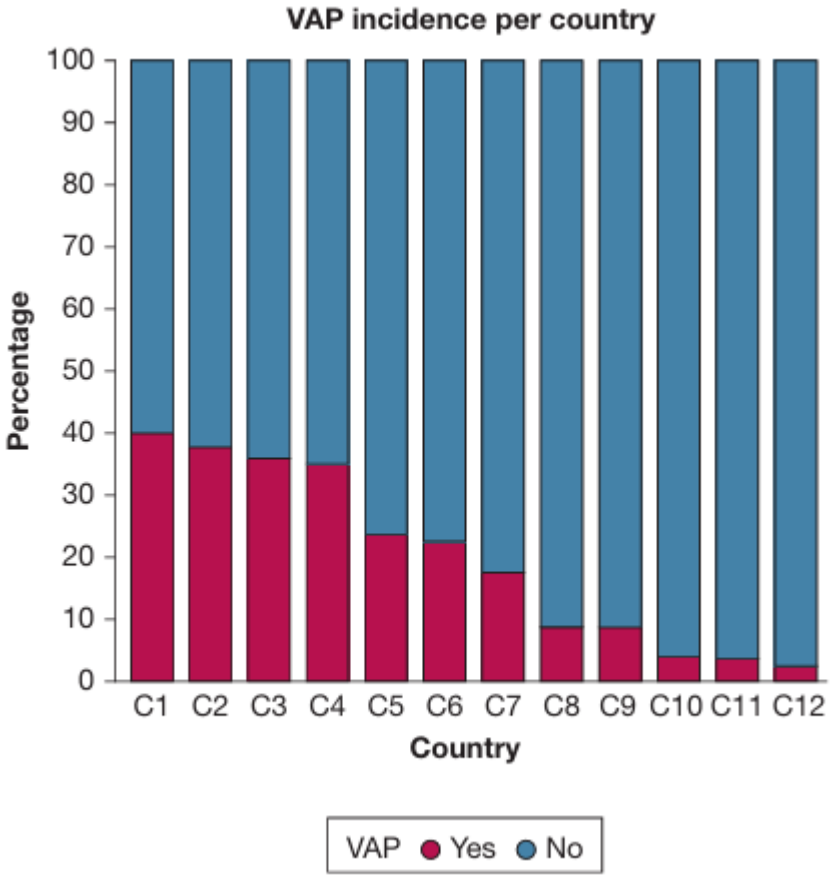
CID 2019:68 (1 February)

A Systematic Review and Meta-analysis of Ventilator-associated Pneumonia in Adults in Asia: An Analysis of National Income Level on Incidence and Etiology

Ana Bonell,[1] Ryan Azarrafiy,[2] Vu Thi Lan Huong,[1] Thanh Le Viet,[1] Vu Dinh Phu,[3] Vu Quoc Dat,[4] Heiman Wertheim,[5,6] H. Rogier van Doorn,[1] Sonia Lewycka,[1] and Behzad Nadjm[1]



CENTER-TBI STUDY: Collaborative European **NeuroTrauma Effectiveness Research in Traumatic Brain Injury** data set: large, multicenter, prospective, observational study including patients with TBI admitted to European ICUs



962 patients:
196 **(20.4%)** developed a VAP at a median interval of 5 days [IQR 3-7] after intubation

Marked variability in VAP incidence between the countries

Robba et al. Chest 2020; 158(6):2292-2303

Galerneau *et al. Critical Care (2023) 27:359*
https://doi.org/10.1186/s13054-023-04631-2

RESEARCH **Open Access**

Non-ventilator-associated ICU-acquired pneumonia (NV-ICU-AP) in patients with acute exacerbation of COPD: From the French OUTCOMEREA cohort

Louis-Marie Galerneau[1,2*], Sébastien Bailly[2], Nicolas Terzi[1,2], Stéphane Ruckly[3], Maité Garrouste-Orgeas[4], Johanna Oziel[5], Vivien Hong Tuan Ha[6], Marc Gainnier[7], Shidasp Siami[8], Claire Dupuis[9], Jean-Marie Forel[10], Anaïs Dartevel[1], Julien Dessajan[11], Christophe Adrie[12], Dany Goldgran-Toledano[13], Virginie Laurent[14], Laurent Argaud[15], Jean Reignier[16], Jean-Louis Pepin[2], Michael Darmon[17], Jean-François Timsit[11] and OUTCOME R. E. A. network

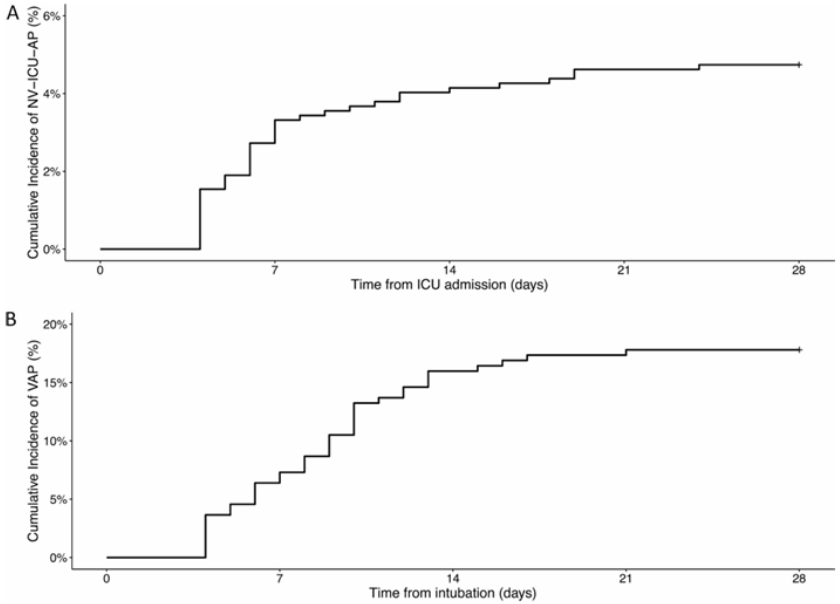


Fig. 2 Cumulative incidences of non-ventilator-associated ICU-acquired pneumonia and ventilator-associated pneumonia in patients admitted in ICU for a severe acute exacerbation of COPD. **A** Cumulative incidence of non-ventilator-associated ICU-acquired pneumonia from ICU admission in patients admitted to an ICU for a severe acute exacerbation of COPD. **B** Cumulative incidence of ventilator-associated pneumonia from intubation in ICU for a severe acute exacerbation of COPD (n = 219). *ICU* intensive care unit, *NV-ICU-AP* non-ventilator-associated intensive care unit acquired pneumonia, *VAP* ventilator-associated pneumonia

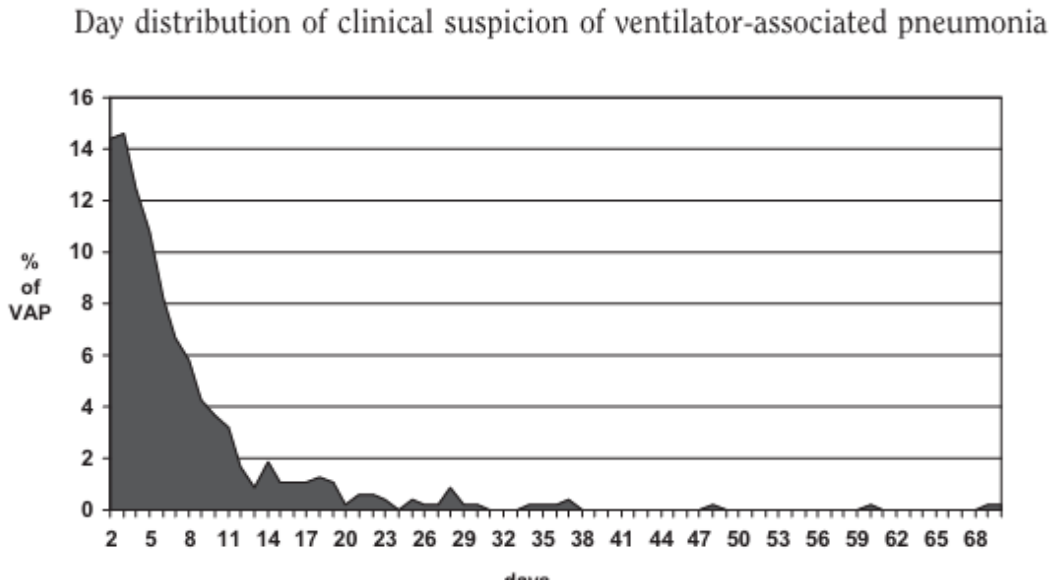
Of the 844 COPD exacerbations managed in ICUs without immediate IMV, NV-ICU-AP occurred in 42 patients (5%) with **an incidence density of 10.8 per 1,000 patient-days**

Lower risk of NV-ICU-AP if:

- **prescription of antibiotics at ICU admission (sHR, 0.45 [0.23; 0.86], p = 0.02) &**
- **no decrease in consciousness (sHR, 0.35 [0.16; 0.76]; p < 0.01)**

Risk of VAP development

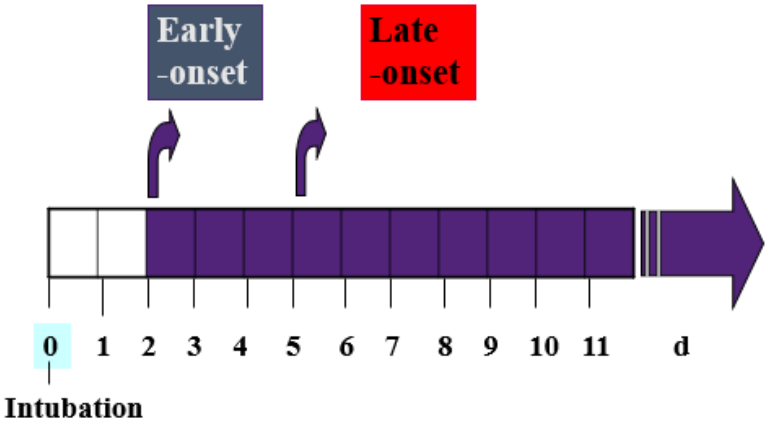
Estimated risk of **VAP 3% per day during the first 5 days on MV**, **2% per day from day 5-10** & **1% per day for the remaining days** *(although incidence seems decreasing, probably due to more stringent application prevention measures)*



Cook et al. Ann Intern Med 1998; 129: 433–40; Koulenti et al. Crit Care Med 2009; 37(8): 2360-8; Torres et al. European Respiratory Journal 2017 50: 1700582; Figure from: Koulenti et al. Crit Care Med 2009; 37(8): 2360-8;

Etiology

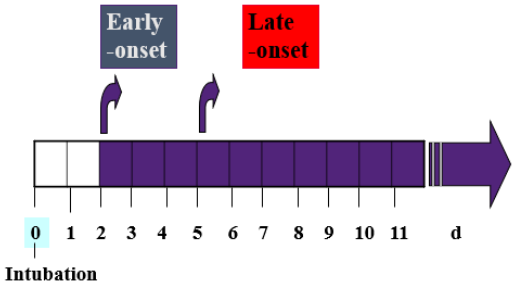
Early- & Late-onset VAP



Etiology

Early-onset VAP	Late-onset VAP
• *Streptococcus pneumoniae*	• *Pseudomonas aeruginosa*
• *Hemophilus influenza*	• *Acinetobacter baumannii*
• Methicillin-sensitive *Staphylococcus aureus* (MSSA)	• Methicillin-resistant *Staphylococcus aureus* (MRSA)
• *Enterobacteriaceae*	• *Enterobacteriaceae*
Antibiotic-sensitive pathogens more likely*	***Antibiotic-resistant pathogens more likely***

Early- & Late-onset VAP



Early vs. Late VAP

Early vs late VAP - concept from 1980's

-Threshold varies: within 4- 7days of admission

-Community like pattern associated with early onset pneumonia

-Nosocomial pattern associated with late onset pneumonia

Subsequent studies

-Nil significant differences in pathogen patterns

-Differ in the definition of time zero and RF for MDR

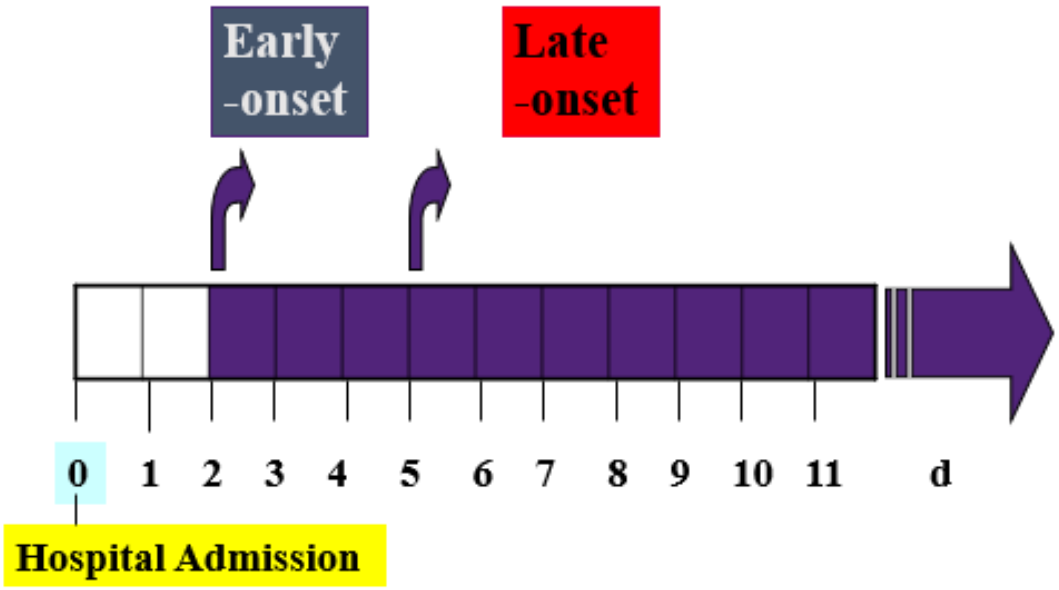
-Time zero: time of hospital admission **not** intubation

-Presence of RF for MDR takes precedence over timing of onset

->5+ days of hospitalisation: at risk for MDR

MORE IMPORTANT FOR ETIOLOGY

Early- & Late-onset Nosocomial pneumonia



ATS/IDSA Guidelines 2016

Risk Factors (RF) for MDR VAP

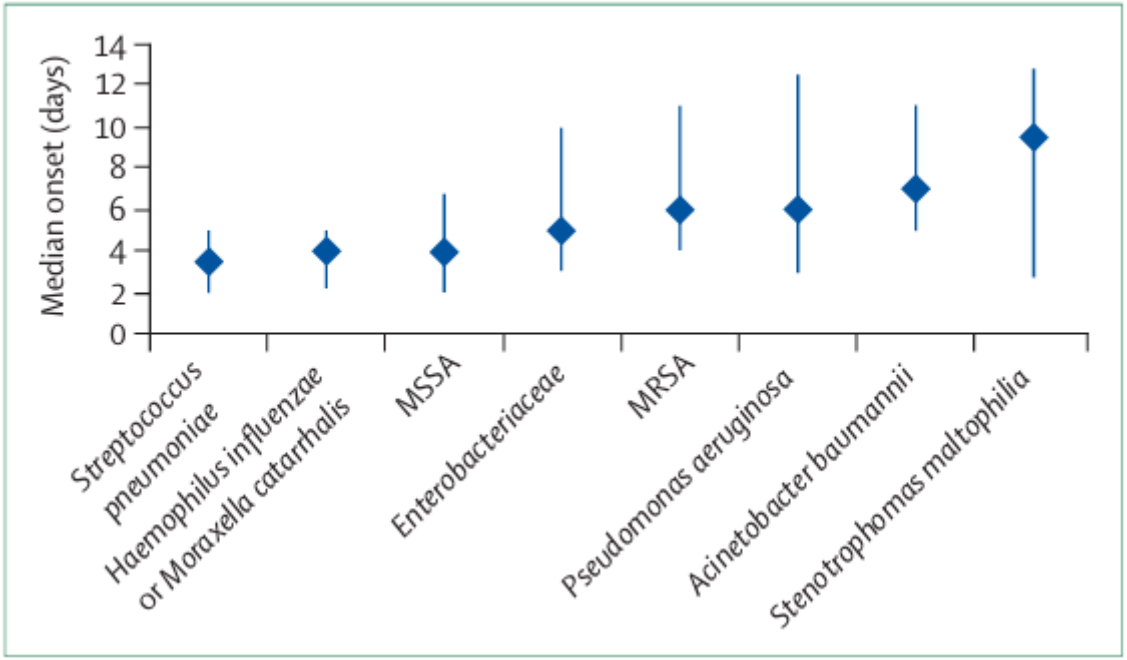
- Prior IV antibiotics previous 90 d (**OR 12.3**)
- Septic shock at onset of VAP (OR 2.01)
- ARDS preceding VAP (OR 3.1)
- **5+** days of hospitalisation prior to VAP
- Acute RRT prior to VAP onset (OR 2.5)

RF for MDR HAP, MRSA HAP/VAP, MDR Pseudomonas HAP/VAP

- Prior IV antibiotics previous 90 d
- Underlying clinical conditions may influence microbiology
  - -sepsis
  - - ARDS
  - -coma: ↓ risk of MDR VAP (OR 0.21)
- Systemic steroids: a RF in one study, not replicated
- Other potential RFs not consistently associated with MDR :
  Reintubation, tracheostomy, diabetes, chronic respiratory failure, immunosuppression

Clin Infect Dis. 2016; 63:e61-e111

Correlation between median onset of VAP & etiology



Jordi Rello, Thiago Lisboa, Despoina Koulenti **Lancet Respir Med 2014**

Etiology of HAP

Etiology may vary by:	
•Hospital	•Department
•Type of ICU	•Patient population
•Exposure to antibiotics	•Time (changes over time)

Need for timely local surveillance data of microbial flora and resistance patterns

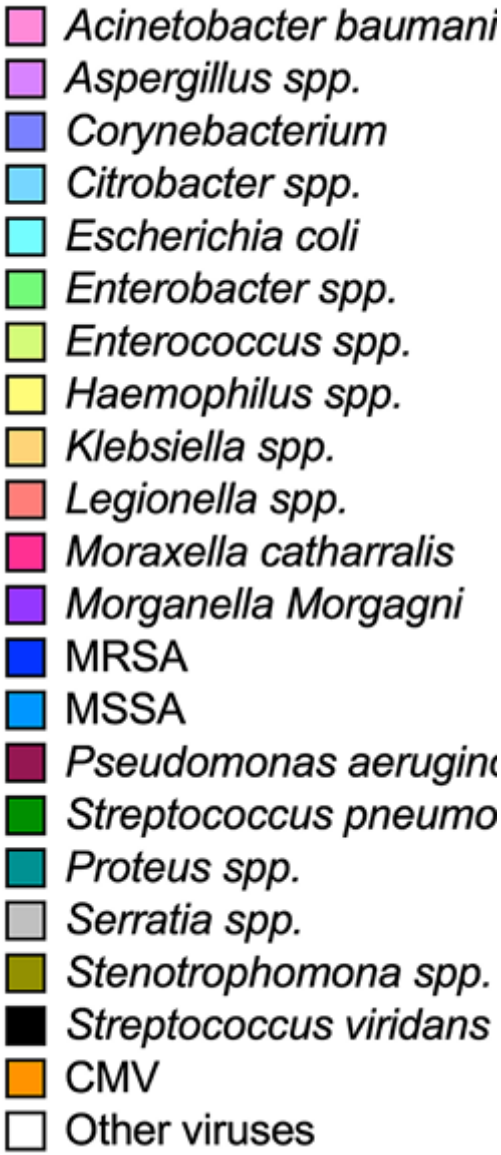
European Network for ICU-Related Respiratory Infections (ENIRRIs): a multinational, prospective, cohort study of nosocomial LRTI

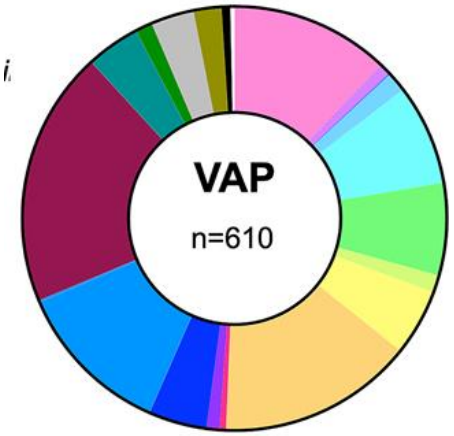
Ignacio Martin-Loeches[1,37*], Luis Felipe Reyes[2,3,4], Saad Nseir[5], Otavio Ranzani[6], Pedro Povoa[7], Emili Diaz[8], Marcus J. Schultz[9,10,40], Alejandro H. Rodríguez[11], Cristian C. Serrano-Mayorga[2,3], Gennaro De Pascale[12], Paolo Navalesi[13,20], Mauro Panigada[14], Luis Miguel Coelho[7], Szymon Skoczynski[15], Mariano Esperatti[16], Andrea Cortegiani[17], Stefano Aliberti[15,18,19], Anselmo Caricato[20], Helmut J. F. Salzer[21,22,34], Adrian Ceccato[6], Rok Civljak[23], Paolo Maurizio Soave[24], Charles-Edouard Luyt[25], Pervin Korkmaz Ekren[26], Fernando Rios[27], Joan Ramon Masclans[28,38,39], Judith Marin[38], Silvia Iglesias-Moles[29], Stefano Nava[30,35,36], Davide Chiumello[31], Lieuwe D. Bos[9], Antoni Artigas[8], Filipe Froes[32], David Grimaldi[33], Fabio Silvio Taccone[33], Massimo Antonelli[12] and Antoni Torres[6*] on behalf of the European Network for ICU-Related Respiratory Infections (ENIRRIs) European Respiratory Society-Clinical Research Collaboration Investigators

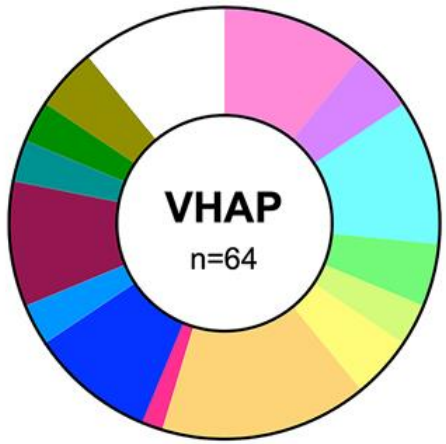
Intensive Care Med (2023) 49:1212–1222

1060 patients with LRTI:

- **VAT**: 160 (15.1%)
- **VAP:** 556 (52.5%)
- **ICU-HAP**: 98 (9.2%)
- **HAP**: 152 (14.3%)
- **vHAP**: 94 (8.9%)







Patients with vHAP & HAP had a lower prevalence of *P.aeruginosa, Klebsiella spp.,* & MRSA vs. VAP (and vs. nvHAP & vs. VAT) other groups

Patients with vHAP yielded lower microbiological confirmation: 41.5% vs 75.4% in VAP

Loeches et al. Intensive Care Med 2023; 49:1212-22

Review > Curr Opin Crit Care. 2018 Oct;24(5):332-338. doi: 10.1097/MCC.0000000000000526.

Microbial cause of ICU-acquired pneumonia: hospital-acquired pneumonia versus ventilator-associated pneumonia

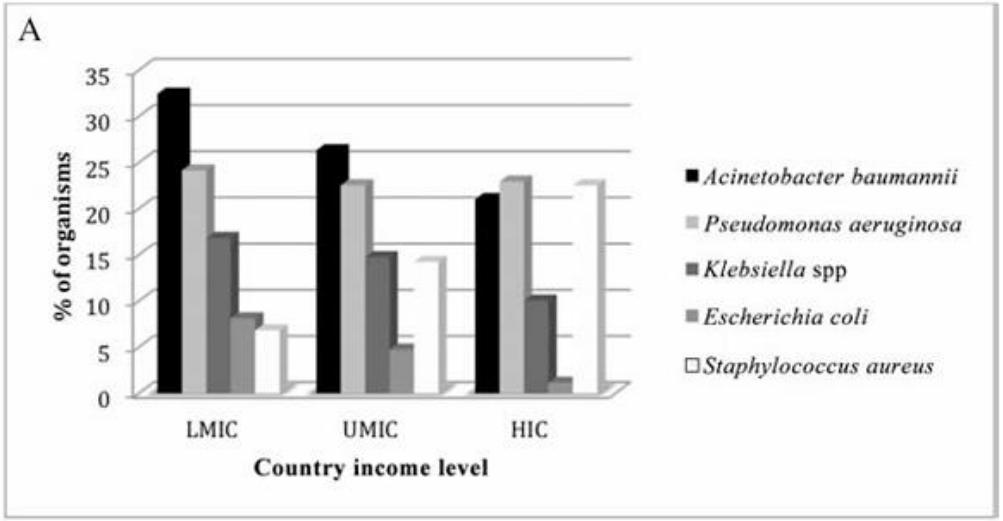
Charles-Edouard Luyt [1 2], Guillaume Hékimian [1 2], Despoina Koulenti [3 4], Jean Chastre [1 2]

Table 2. Most common etiological pathogens grouped by type of pneumonia, as documented in a prospective obs[vHAP]nal study that enrolled patients from 27 ICUs in nine European countries

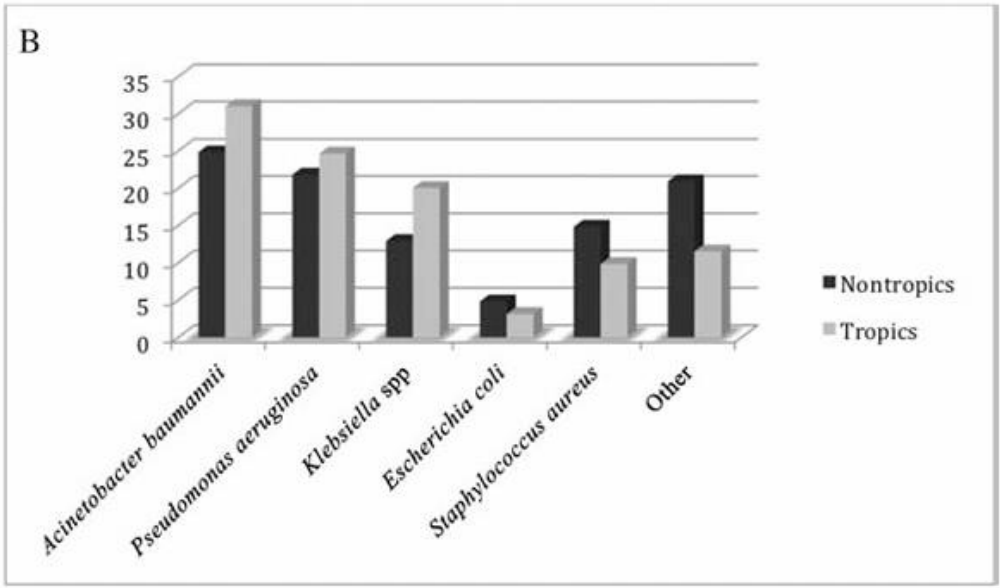
Causative pathogen	Very-early VAP[a] (*n* = 138)	VAP[b] (*n* = 465)	HAP[c] (*n* = 224)
Unknown, *n* (%)	59 (42.8)	109 (23.4)	84 (37.5)
Other, *n* (%)	31 (22.5)	69 (14.8)	20 (8.9)
Staphylococcus aureus, *n* (%)	26 (18.8)	116 (24.9)	44 (19.6)
MRSA, *n* (%)	10 (7.2)	52 (11.2)	30 (13.4)
MSSA, *n* (%)	16 (11.6)	64 (13.8)	14 (6.3)
P. aeruginosa, *n* (%)	16 (11.6)	81 (17.4)	36 (16.1)
Acinetobacter spp., *n* (%)	8 (5.8)	72 (15.5)	30 (13.4)
Enterobacteriaceae, *n* (%)	29 (21)	153 (32.9)	70 (31.3)
Polymicrobial infection, *n* (%)	25 (18.1)	114 (24.5)	46 (20.5)

ASIA

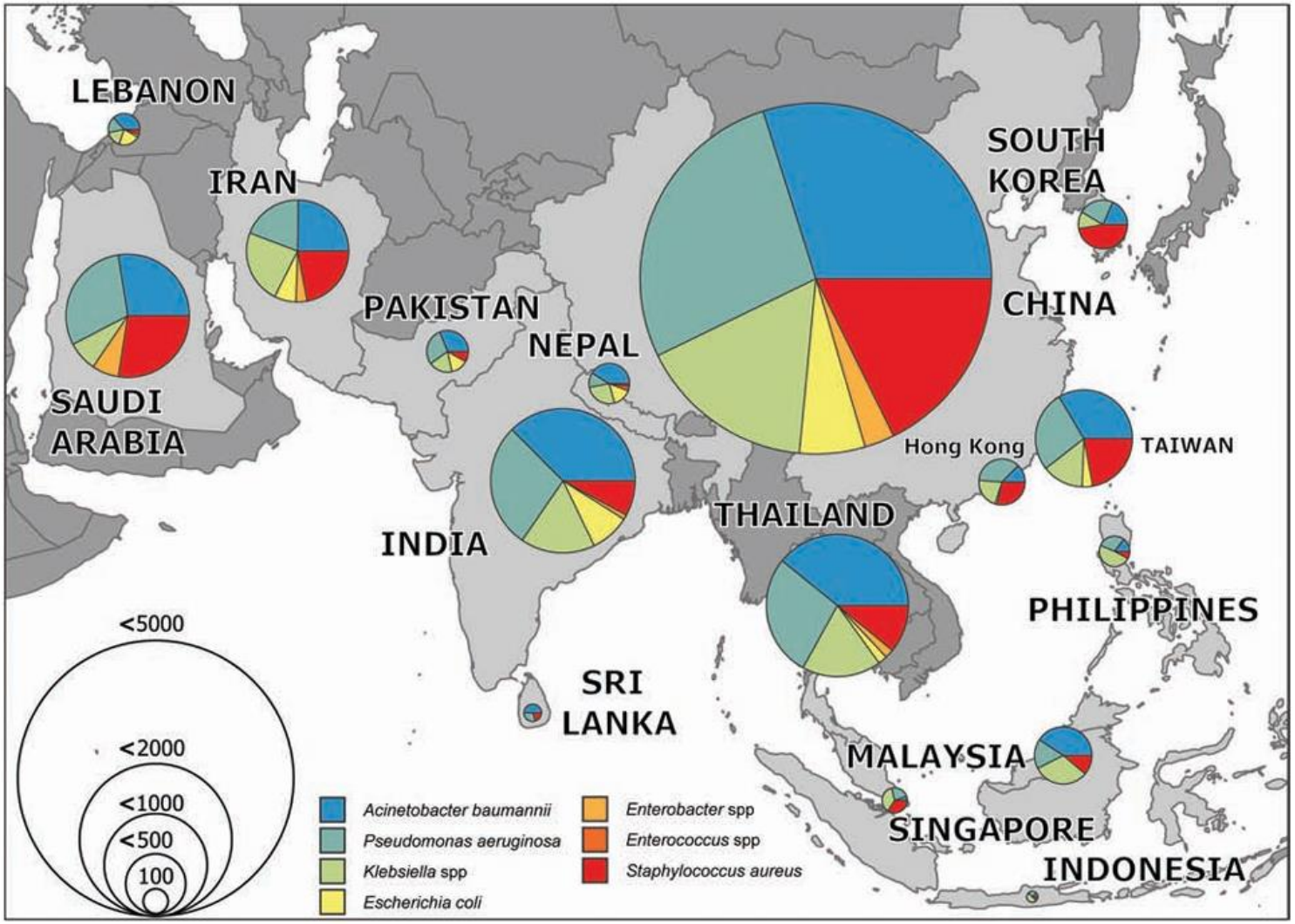
A, Pooled microbiology results of ventilator-associated pneumonia (VAP) etiology by country income level.



B, Pooled microbiology results of VAP etiology by geographic area (tropical vs nontropical). A



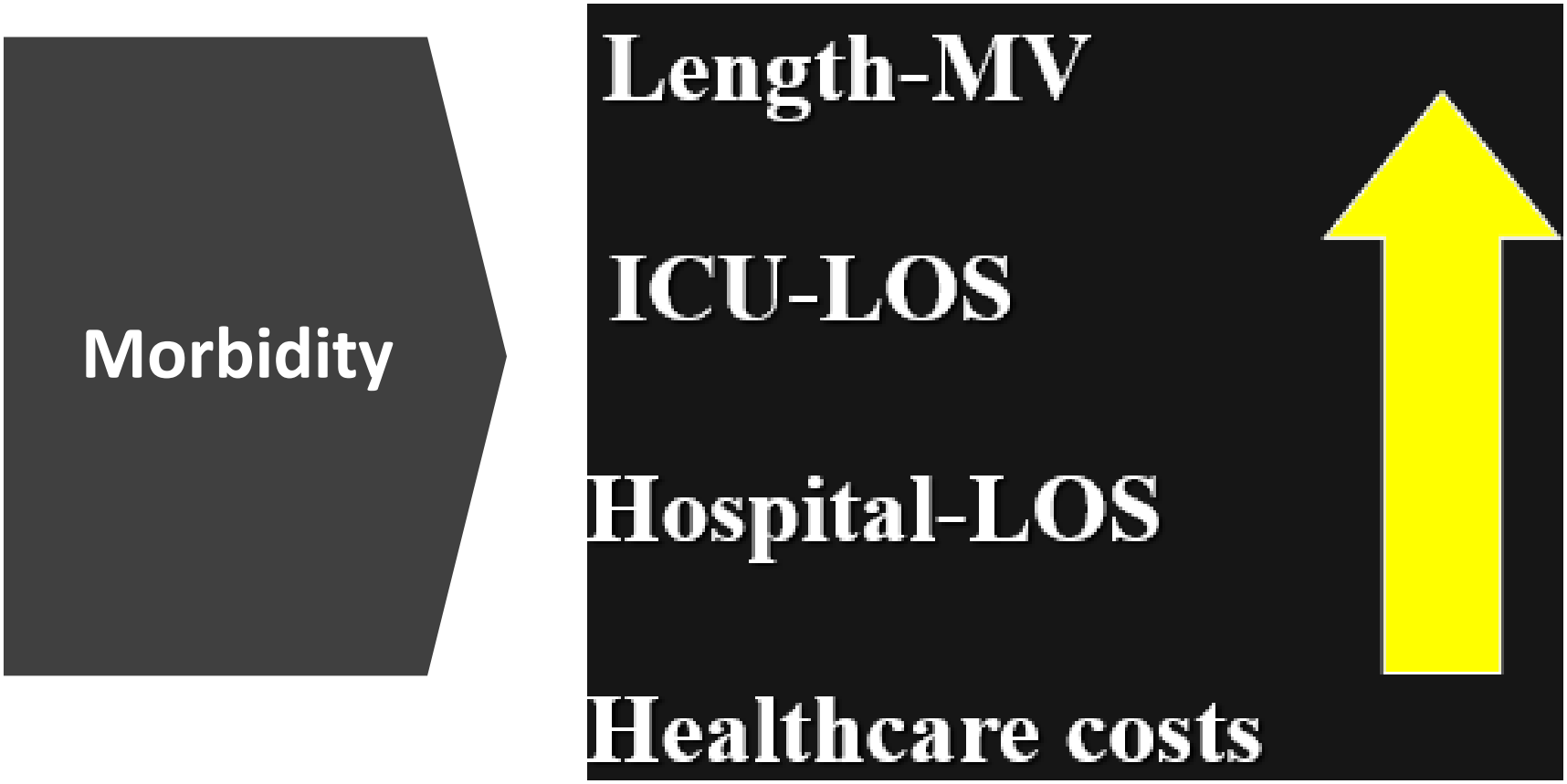
Mapped pooled microbiology results by country VAP etiology



Organisms are color coded, and the size of the pie chart reflects the total number of isolates identified per country.

Source: http://naturalearthdata.com.

Morbidity & Mortality



Torres et al. European Respiratory Journal 2017 50: 1700582; Clin Infect Dis 2016;63:e63-e11; Bonnel et al. Clin Infect Diseases 2019; 68(1):511; Koulenti et al. Crit Care Med 2009; 37(8): 2360-8

Mortality

Mortality 20-70%

Attributable mortality???

European Network for ICU-Related Respiratory Infections (ENIRRIs): a multinational, prospective, cohort study of nosocomial LRTI

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Table 4 Systemic complications upon diagnosis and clinical outcomes stratified the study groups

Complications at ICU admission	VAT n = 160	VAP n = 556	ICU-HAP n = 98	VHAP n = 94	HAP n = 152	All cohort n = 1060
Acute kidney injury	23 (14.4)	106 (19.1)	12 (12.2)	16 (17)	22 (14.5)	179 (16.9)
ARDS	20 (12.5)	116 (20.9)	16 (16.3)	32 (34)	45 (29.6)	229 (21.6)
Septic shock	19 (11.9)	148 (26.6)	22 (22.5)	38 (40.4)	31 (20.4)	258 (24.3)
Multiple organ failure	14 (8.8)	60 (10.8)	6 (6.1)	16 (17)	8 (5.3)	104 (9.8)
Clinical cure, n (%)	96 (60)	331 (59.5)	62 (63.3)	45 (47.9)	85 (55.9)	619 (58.4)
Treatment failure, n (%)	52 (32.5)	184 (33.1)	22 (22.5)	44 (46.8)	52 (34.2)	354 (33.4)
ICU mortality, n (%)	48 (30)	176 (31.7)	16 (16.3)	38 (40.3)	48 (31.6)	326 (30.8)
Hospital mortality, n (%)	59 (36.9)	210 (37.8)	24 (24.5)	47 (50)	57 (37.5)	397 (37.5)
28-days mortality, n (%)	51 (31.8)	143 (25.7)	14 (14.3)	39 (41.5)	44 (28.9)	291 (27.4)
ICU LOS, median (IQR)	20.5 (11.5–30)	25 (15–41)	20 (11–35)	12 (6–27)	12 (6–19.5)	20 (11–35)
Hospital LOS, median (IQR)	31 (19–57)	44 (24–70)	38 (28–72)	34.5 (20–61)	34 (21–54.5)	38 (22–65)

ARDS acute respiratory distress syndrome, *ICU* intensive care unit, *LOS* lenght of stay, *VAP* ventilator-associated pneumonia, *VAT* ventilator-associated tracheobronchitis, *VHAP* ventilated hospital-acquired pneumonia

Presence of nos ocomial pneumonia significantly prolonged mean MV length (10.3 days, p < .05) and mean ICU-LOS (12.2 days, p < .05) in ICU survivors

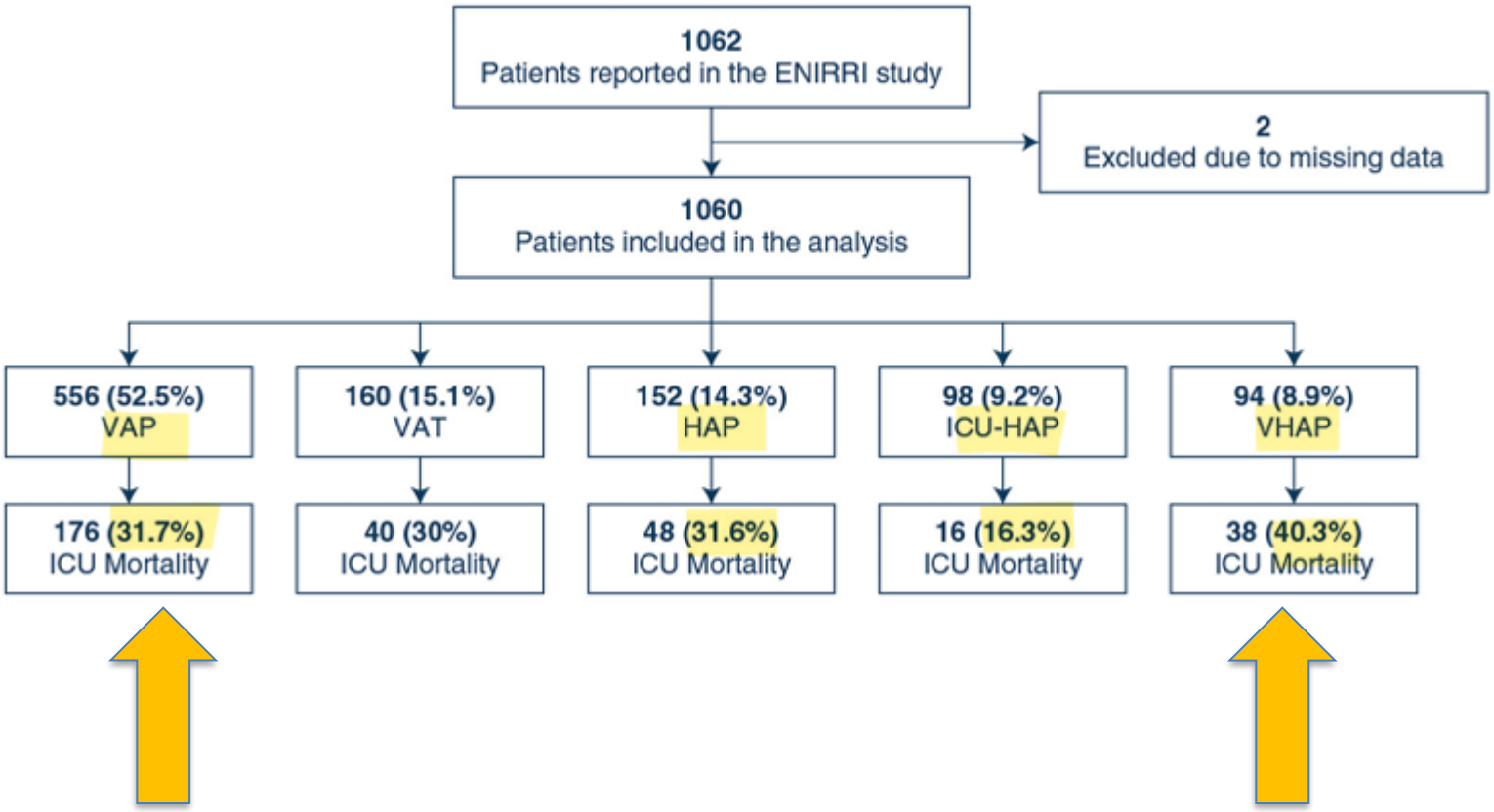
	Overall n=2436	Without Pneumo n=1347	HAP vHAP n=224	VAP n=465	VE-VAP n=138	CAP n=262
* MV-length, (d) Mean, (SD)	12.4 (14.4)	8.6 (9.4)	16.8 (18.9)	21.5 (20.6)	13.1 (11.8)	14.8 (20.0)
*ICU-LOS , (d) Mean, (SD)	17.8 (17.0)	13.4 (13.0)	22.2 (19.7)	28.8 (22.0)	18.9 (16.3)	18.2 (21.8)
Mortality, n (%)	839 (34.4)	425 (31.6)	91 (40.6)	165 (35.5)	56 (40.6)	102 (38.9)
Pneumonia's contribution to death, n (%) Direct cause Contributing Not Related No answer	_____	_____	25 (27.5) 46 (50.5) 16 (17.6) 4 (4.4)	24 (14.6) 71 (43.3) 64 (39.0) 5 (5.0)	12 (21.4) 20 (35.7) 24 (42.9) 0 (0.0)	44 (43.1) 41 (40.2) 16(15.7) 2 (2.0)

* ICU survivors

Koulenti et al. Crit Care Med 2009; 37(8): 2360-8

Intensive Care Med (2023) 49:1212–1222

Comparison of mortality



Comparison of mortality

vHAP

	Overall n=2436	Without Pneumo n=1347	HAP n=224	VAP n=465	VE-VAP n=138	CAP n=262
* MV-length, (d) Mean, (SD)	12.4 (14.4)	8.6 (9.4)	16.8 (18.9)	21.5 (20.6)	13.1 (11.8)	14.8 (20.0)
*ICU-LOS , (d) Mean, (SD)	17.8 (17.0)	13.4 (13.0)	22.2 (19.7)	28.8 (22.0)	18.9 (16.3)	18.2 (21.8)
Mortality, n (%)	839 (34.4)	425 (31.6)	91 (40.6)	165 (35.5)	56 (40.6)	102 (38.9)
Pneumonia's contribution to death, n (%) Direct cause Contributing Not Related No answer	———	———	25 (2) 46 (5) 16 (1) 4 (4.4)	24 .6) 71 .3) 64 .0) 5 (5.0)	12 (21.4) 20 (35.7) 24 (42.9) 0 (0.0)	44 (43.1) 41 (40.2) 16(15.7) 2 (2.0)

* ICU survivors

Koulenti et al. Crit Care Med 2009; 37(8): 2360-8

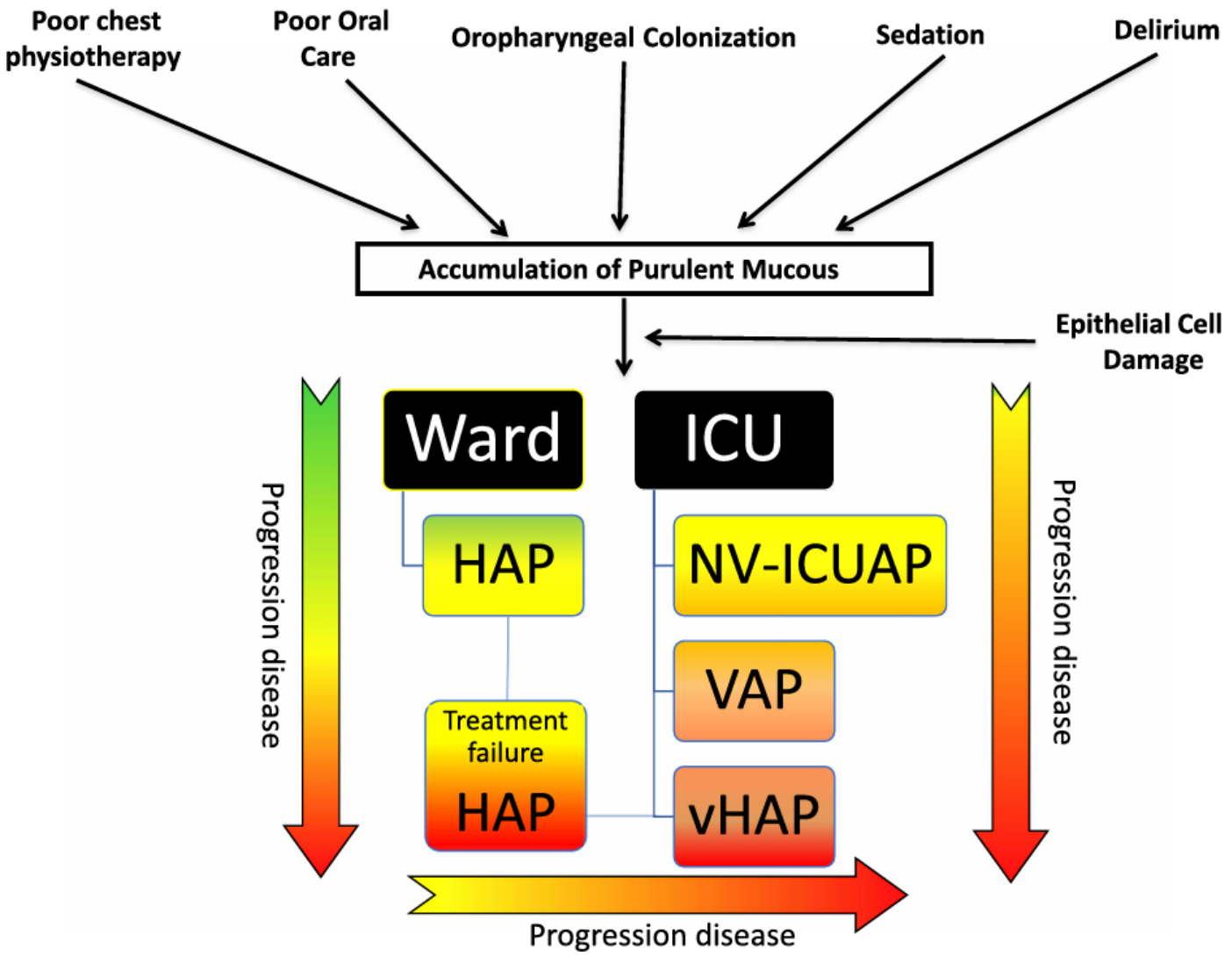


Figure from: Zaragosa et al. Crit Care 2020; 24:383

Meta-Analysis > Lancet Infect Dis. 2013 Aug;13(8):665-71. doi: 10.1016/S1473-3099(13)70081-1.
Epub 2013 Apr 25.

Attributable mortality of ventilator-associated pneumonia: a meta-analysis of individual patient data from randomised prevention studies

Wilhelmina G Melsen [1], Maroeska M Rovers, Rolf H H Groenwold, Dennis C J J Bergmans, Christophe Camus, Torsten T Bauer, Ernst W Hanisch, Bengt Klarin, Mirelle Koeman, Wolfgang A Krueger, Jean-Claude Lacherade, Leonardo Lorente, Ziad A Memish, Lee E Morrow, Giuseppe Nardi, Christianne A van Nieuwenhoven, Grant E O'Keefe, George Nakos, Frank A Scannapieco, Philippe Seguin, Thomas Staudinger, Arzu Topeli, Miquel Ferrer, Marc J M Bonten

6284 individual patient's data from 24 trials of VAP

Estimated attributable mortality of VAP: 13%

Large differences between subgroups of patients, with attributable mortality rates:

- **36%** in patients with an intermediate severity of illness (ie, APACHE 20–29).
- **69%** in surgical patients
- **close to zero**

  in trauma,

  low severity of illness (ie, APACHE <20 or SAPS 2 <35)

  high severity (APACHE scores> 30 or SAPS 2 score >58)

Attributable mortality mainly due to longer ICU stay

Incidence, Risk Factors, and Effects on Outcome of Ventilator-Associated Pneumonia in Patients With Traumatic Brain Injury

Analysis of a Large, Multicenter, Prospective, Observational Longitudinal Study

Check for updat

CHEST 2020; 158(6):2292-2303

*Chiara Robba, PhD; Paola Rebora, PhD; Erika Banzato, MSc; Eveline J. A. Wiegers, MSc; Nino Stocchetti, MD; David K. Menon, PhD; and Giuseppe Citerio, MD; on behalf of the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury Participants and Investigators**

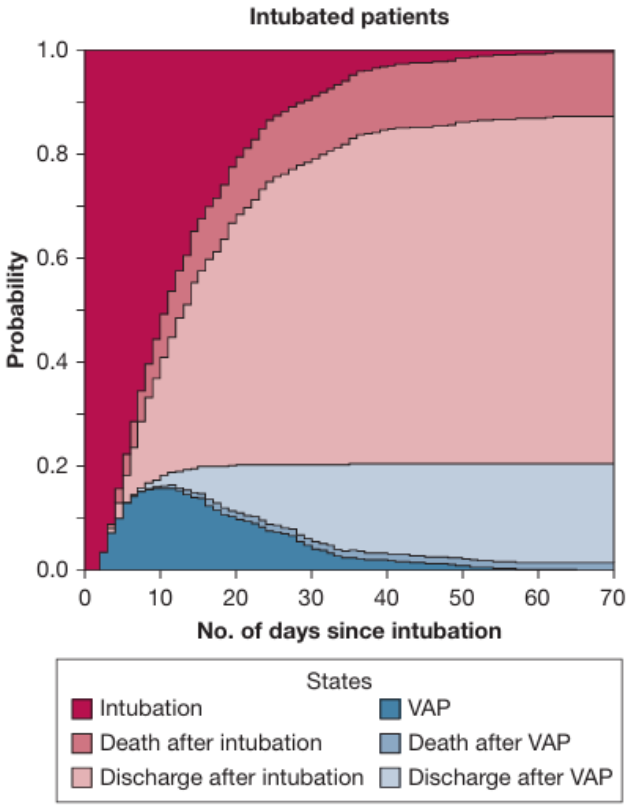


Figure 2 – *Overall transition probabilities of patients who had undergone intubation. The x-axis indicates the time since intubation, and the y-axis indicates the probability of being in one of the possible states. In*

Patients with VAP had longer:

- MV duration: **15** [10-22] d vs **8** [5-14] d; P < .001
- ICU LOS: **20** [14-29] d vs **13** [8-21] d; P < .001

Attributable Mortality of Ventilator-associated Pneumonia Among Patients with COVID-19

Charles-Hervé Vacheron[1,2,3], Alain Lepape[1,2,3], Anne Savey[2,3,4], Anaïs Machut[3], Jean Francois Timsit[5], Sylvie Comparot[6], Gaelle Courno[7], Philippe Vanhems[2,8], Verena Landel[9], Thierry Lavigne[10], Sebastien Bailly[11], Francois Bettega[11], Delphine Maucort-Boulch[12,13,14], Arnaud Friggeri[1,2,3], and the REA-REZO Study Group

Am J Respir Crit Care Med Vol 206, Iss 2, pp 161–169, Jul 15, 2022

REA-REZO surveillance network

3 groups of medical ICU patients:

- control pre-pandemic (2016-2019)
- pandemic COVID-19
- pandemic nonCOVID-19

Primary outcome:

- attributable mortality
- attributable fraction related to VAP

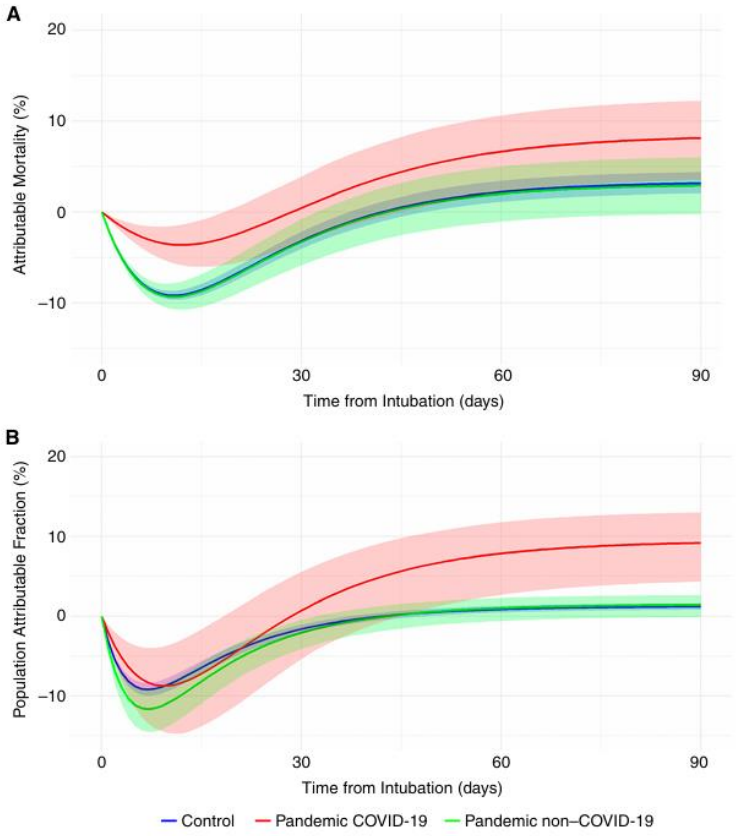


Figure 1. Attributable mortality and attributable fraction of mortality related to ventilator-associated pneumonia over time among the control, pandemic coronavirus disease (COVID-19), and pandemic non–COVID-19 groups.

VAP-attributable mortality higher in COVID-19 patients

>9% of overall mortality related to VAP at D90 (attributable fraction)

A Comparison of the Mortality Risk Associated With Ventilator-Acquired Bacterial Pneumonia and Nonventilator ICU-Acquired Bacterial Pneumonia*

Ibn Saied, Wafa MD[1–3]; Mourvillier, Bruno MD[1,4]; Cohen, Yves MD[5,6]; Ruckly, Stephane MSc[1,7]; Reignier, Jean MD, PhD[8]; Marcotte, Guillaume MD[9]; Siami, Shidasp MD, PhD[10]; Bouadma, Lila MD, PhD[1,4]; Darmon, Michael MD, PhD[11,12]; de Montmollin, Etienne MD[13]; Argaud, Laurent MD, PhD[14]; Kallel, Hatem MD[15]; Garrouste-Orgeas, Maité MD[1,16,17]; Soufir, Lilia MD[16,17]; Schwebel, Carole MD, PhD[18]; Souweine, Bertrand MD, PhD[19]; Glodgran-Toledano, Dany MD[20]; Papazian, Laurent MD, PhD[21]; Timsit, Jean-François MD, PhD[1,4,7]

Critical Care Medicine 47(3):p 345-352, March 2019.

- ❑ 14,212 patients admitted to the ICUs for >48 hours
- ❑ 15% developed VAP
- ❑ 2% developed ICU-HAP
- ❑ **When adjusted on prognostic variables, both VAP & ICU-HAP were associated with increased 30-day mortality:**

VAP: HR 1.38 (1.24–1.52); $p < 0.0001$

ICU-HAP: HR 1.82 (1.35–2.45); $p < 0.0001$

Galerneau *et al. Critical Care (2023) 27:359*
https://doi.org/10.1186/s13054-023-04631-2

RESEARCH **Open Access**

Non-ventilator-associated ICU-acquired pneumonia (NV-ICU-AP) in patients with acute exacerbation of COPD: From the French OUTCOMEREA cohort

Louis-Marie Galerneau[1,2*], Sébastien Bailly[2], Nicolas Terzi[1,2], Stéphane Ruckly[3], Maité Garrouste-Orgeas[4], Johanna Oziel[5], Vivien Hong Tuan Ha[6], Marc Gainnier[7], Shidasp Siami[8], Claire Dupuis[9], Jean-Marie Forel[10], Anaïs Dartevel[1], Julien Dessajan[11], Christophe Adrie[12], Dany Goldgran-Toledano[13], Virginie Laurent[14], Laurent Argaud[15], Jean Reignier[16], Jean-Louis Pepin[2], Michael Darmon[17], Jean-François Timsit[11] and OUTCOME R. E. A. network

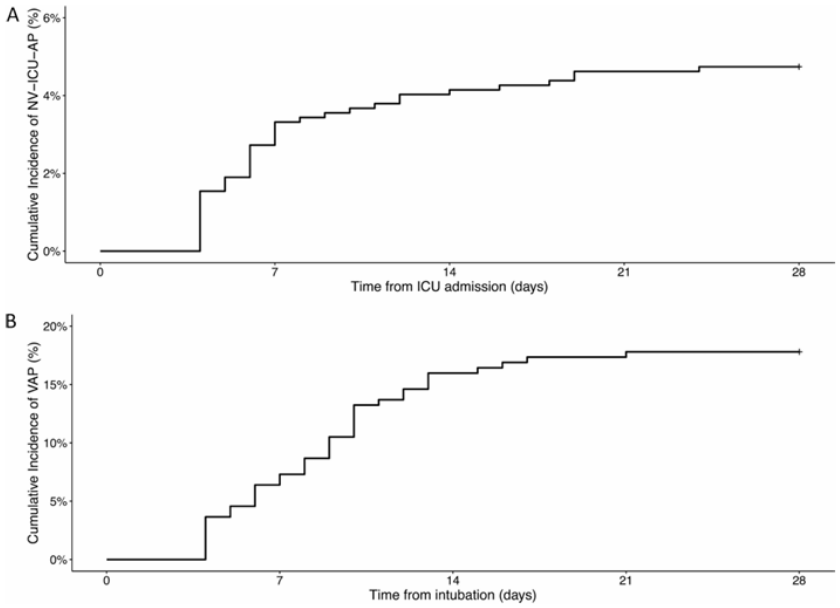


Fig. 2 Cumulative incidences of non-ventilator-associated ICU-acquired pneumonia and ventilator-associated pneumonia in patients admitted in ICU for a severe acute exacerbation of COPD. **A** Cumulative incidence of non-ventilator-associated ICU-acquired pneumonia from ICU admission in patients admitted to an ICU for a severe acute exacerbation of COPD. **B** Cumulative incidence of ventilator-associated pneumonia from intubation in ICU for a severe acute exacerbation of COPD (n = 219). *ICU* intensive care unit, *NV-ICU-AP* non-ventilator-associated intensive care unit acquired pneumonia, *VAP* ventilator-associated pneumonia

NV-ICU-AP associated with:

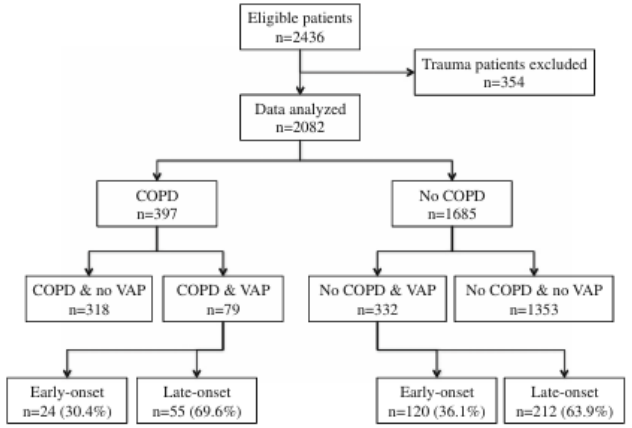
- Increased 28-day mortality (HR = 3.03 [1.36; 6.73]; p < 0.01)
- Increased risk of intubation (csHR, 5.00 [2.54; 9.85]; p < 0.01)
- 10-day increase in ICU length of stay (p < 0.01).

Eur J Clin Microbiol Infect Dis (2015) 34:2403–2411
DOI 10.1007/s10096-015-2495-6

ORIGINAL ARTICLE

COPD patients with ventilator-associated pneumonia: implications for management

D. Koulenti[1,2] · S. Blot[2,3] · J. M. Dulhunty[2,4] · L. Papazian[5] · I. Martin-Loeches[6,7,14] · G. Dimopoulos[1] · C. Brun-Buisson[8] · M. Nauwynck[9] · C. Putensen[10] · J. Sole-Violan[11] · A. Armaganidis[1] · J. Rello[12,13,14] · and the EU-VAP/CAP Study Group



COPD patients are not more predisposed to VAP than other ICU patients, but **if COPD patients develop VAP, they have a worse outcome [odds ratio (OR) 2.28; 95 % confidence interval (CI) 1.35–3.87]**

Incidence, Risk Factors, and Effects on Outcome of Ventilator-Associated Pneumonia in Patients With Traumatic Brain Injury

Analysis of a Large, Multicenter, Prospective, Observational Longitudinal Study

Chiara Robba, PhD; Paola Rebora, PhD; Erika Banzato, MSc; Eveline J. A. Wiegers, MSc; Nino Stocchetti, MD; David K. Menon, PhD; and Giuseppe Citerio, MD; on behalf of the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury Participants and Investigators[*]

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CHEST 2020; 158(6):2292-2303

- Overall mortality at 6 months: 22%
- VAP **was not** associated with increased mortality or worse neurological outcome.

Attributable Mortality of Ventilator-associated Pneumonia

Replicating Findings, Revisiting Methods

Johan Steen[1,2,3,4], Stijn Vansteelandt[4,5], Liesbet De Bus[1], Pieter Depuydt[1,3], Bram Gadeyne[1], Dominique D. Benoit[1,3], and Johan Decruyenaere[1,3]

Ann Am Thorac Soc Vol 18, No 5, pp 830–837, May 2021

Abstract

Rationale: Estimating the impact of ventilator-associated pneumonia (VAP) from routinely collected intensive care unit (ICU) data is methodologically challenging.

Objectives: We aim to replicate earlier findings of limited VAP-attributable ICU mortality in an independent cohort. By refining statistical analyses, we gradually tackle different sources of bias.

Methods: Records of 2,720 adult patients admitted to Ghent University Hospital ICUs (2013–2017) and receiving mechanical ventilation within 48 hours after admission were extracted from linked Intensive Care Information System and Computer-based Surveillance and Alerting of Nosocomial Infections, Antimicrobial Resistance, and Antibiotic Consumption in the ICU databases. The VAP-attributable fraction of ICU mortality was estimated using a competing risk analysis that is restricted to VAP-free patients (approach 1), accounts for VAP onset by treating it as either a competing (approach 2) or censoring event (approach 3), or additionally adjusts for time-dependent confounding via inverse probability weighting (approach 4).

Results: A total of 210 patients (7.7%) acquired VAP. Based on benchmark approach 4, we estimated that (compared with current preventive measures) hypothetical eradication of VAP would lead to a relative ICU mortality reduction of 1.7% (95% confidence interval, −1.3 to 4.6) by Day 10 and of 3.6% (95% confidence interval, 0.7 to 6.5) by Day 60. Approaches 1–3 produced estimates ranging from −0.7% to 2.5% by Day 10 and from 5.2% to 5.5% by Day 60.

Conclusions: In line with previous studies using appropriate methodology, we found limited VAP-attributable ICU mortality given current state-of-the-art VAP prevention measures. Our study illustrates that inappropriate accounting of the time dependency of exposure and confounding of its effects may misleadingly suggest protective effects of early-onset VAP and systematically overestimate attributable mortality.

Keywords: hospital mortality; survival analysis; confounding factors (epidemiology); causality; ventilator-associated pneumonia

Take home message

- The heterogeneity in HAP definition contributes to the wide range of reported incidence.
- There is plenty of evidence that HAP increases morbidity, however regarding attributable mortality the data are more controversial.
- Ventilated HAP is quite different than non-ventilated HAP -there is accumulating evidence that vHAP might carry the worst prognosis than all HAP types.