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

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BACKGROUND: Ventilator-associated pneumonia (VAP) is a frequent complication of prolonged invasive ventilation. Because VAP is largely preventable, its incidence has been used as an index of quality of care in the ICU. However, the incidence of VAP varies according to which criteria are used to identify it. We compared the incidence of VAP obtained with different sets of criteria.

METHODS: We collected data from all adult patients admitted to our 35-bed ICU over a 7-month period who had no pulmonary infection on admission or within the first 48 h and who required mechanical ventilation for > 48 h. To diagnose VAP, we applied six published sets of criteria and 89 combinations of criteria for hypoxemia, inflammatory response, purulence of tracheal secretions, chest radiography findings, and microbiologic findings of varying levels of severity. The variables used in each diagnostic algorithm were assessed daily.

RESULTS: Of 1,824 patients admitted to the ICU during the study period, 91 were eligible for inclusion. The incidence of VAP ranged from 4% to 42% when using the six published sets of criteria and from 0% to 44% when using the 89 combinations. The delay before diagnosis of VAP increased from 4 to 8 days with increasingly stringent criteria, and mortality increased from 50% to 80%.

CONCLUSIONS: Applying different diagnostic criteria to the same patient population can result in wide variation in the incidence of VAP. The use of different criteria can also influence the time of diagnosis and the associated mortality rate. CHEST 2015; 147(2):347-355

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ABBREVIATIONS: APACHE = Acute Physiology and Chronic Health Evaluation; CDC/NHSN = US Centers for Disease Control and Prevention/National Healthcare Safety Network; CDC/NHSN PNU1 = US Centers for Disease Control and Prevention/National Healthcare Safety Network clinically defined pneumonia; CHEST = American College of Chest Physicians; CPIS = Clinical Pulmonary Infection Score; CRP = C-reactive protein; HELICS = Hospital in Europe Link for Infection Control through Surveillance; MV = mechanical ventilation; PEEP = positive-end expiratory pressure; VAP = ventilator-associated pneumonia

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Ventilator-associated pneumonia (VAP) is a common complication in patients in the ICU and is associated with increased mortality,[1,2] prolonged duration of mechanical ventilation (MV) and length of stay, and increased costs.[3,4] Institutions are encouraged to use preventive measures, including careful hand washing, oral care, and decontamination; high-volume low-pressure balloon cuffs; elevation of the head of the patient's bed; early feeding; avoidance of sedative agents; and early weaning from MV.[5]

The reported incidence of VAP varies considerably among studies, ranging from 5% to 67%.[1,3,6] A survey of US trauma centers showed that the incidence of VAP was markedly higher than those reported by the National Healthcare Safety Network and varied considerably among centers.[7] However, the criteria used to diagnose VAP also vary widely, as shown by the large number of published diagnostic algorithms, and this may impact the reported incidence of VAP.[8-11] It is, therefore, difficult to compare the incidence of VAP among hospitals. Even with strict criteria, the interpretation of some factors, such as the radiographs or the aspect of tracheal secretions, can be very subjective.

Therefore, we evaluated how the use of different criteria may lead to different apparent incidences of VAP. This effect may have important implications for clinical trials, hospital management, and quality control.

Materials and Methods

This study was conducted in the Erasme University Hospital, 35-bed, medical-surgical ICU, which admits 3,000 to 3,500 patients per year. The nurse-to-bed ratio varies between 2:4 and 2:6, and respiratory physiotherapists are on-site 24/7. The study was approved by the institution's Ethics Committee (reference P2013/076), which waived the need for informed consent in view of the purely observational nature of the study.

We prospectively screened all adult patients (> 18 years old) treated with invasive MV for more than 48 h between January 1, 2012, and July 31, 2012. Patients with a diagnosis of respiratory tract infection and/or pneumonia on admission or within the first 48 h of MV were not included. We collected epidemiologic data on admission. During invasive MV, we collected respiratory data (mode of MV, positive end-expiratory pressure [PEEP], Pao_2, Fio_2), WBC count including differential, C-reactive protein (CRP) level, temperature, the degree of purulence of tracheal secretions and microbiology data from tracheal aspirates or BAL, when performed. Chest radiography was conducted on a daily basis. We recorded durations of MV, lengths of ICU and hospital stays, and ICU and hospital mortality rates.

We applied six sets of published criteria: US Centers for Disease Control and Prevention/National Healthcare Safety Network clinically defined pneumonia (CDC/NHSN PNU1) 2008,[12] the Clinical Pulmonary Infection Score (CPIS),[13] Johanson's criteria,[14] American College of Chest Physicians (CHEST),[15] Hospital in Europe Link for Infection Control through Surveillance (HELICS),[16] and the new definition (probable VAP) from US Centers for Disease Control and Prevention/National Healthcare Safety Network (CDC/NHSN)[17] (Table 1). We also combined criteria for oxygenation, host response, purulence of tracheal aspirates, and chest radiography and microbiologic findings that have been used in previous diagnostic algorithms (Fig 1, Table 2) to create 89 sets, varying in number of criteria (two to five) and in the thresholds required.

We selected the worst values of the day for each variable, except for the application of the new definition from CDC/NHSN,[17] which requires the minimum daily Fio_2 or PEEP. All the variables used for the different diagnostic algorithms were assessed daily during MV.

Statistical Analysis

Normality of distribution was checked by the Shapiro-Wilk test. Variables that were not normally distributed are expressed as median (with 25th-75th percentiles). We used Cohen κ to evaluate the agreement between algorithms. All statistical analyses were performed using IBM SPSS 21.0 (IBM). A P value $< .05$ was considered statistically significant.

Results

Among the 1,824 admissions between January 1 and July 31, 2012, 144 patients required invasive MV for more than 48 h. Of these patients, 53 had a diagnosis of respiratory infection on admission or within the first 48 h of MV, and 91 patients were eligible for analysis (Fig 2). The characteristics of these patients are shown in Table 3: The population was severely ill, as indicated by a median APACHE (Acute Physiology and Chronic Health Evaluation) II score of 25.

Using the published criteria, the incidence of VAP ranged from 4% with Johanson's criteria to 42% with the CPIS (Fig 3), with poor agreement between the scores (Table 4). Using the 89 combined sets of criteria, the incidence of VAP decreased from 44% to 0% when applying combinations of increasing stringency (Fig 4, e-Table 1). The least stringent set of criteria included just two factors of low level severity (increase in Fio_2 by at least 0.15 or in PEEP values by at least 2 cm H_2O, and increase in CRP values by at least 50 mg/L from one day to the next), whereas the most stringent set included five criteria with much higher levels of severity required (increase in Fio_2 values by at least 0.30 or in PEEP values by at least 5 cm H_2O for at least two calendar days; increase in CRP value by at least 50 mg/L or temperature at 38°C or above; purulent tracheal secretions; positive microbiology; and new or progressive and persistent infiltrate/consolidation on chest radiography). Mortality was greatest in patients in whom VAP was diagnosed using

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]	- 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	…

(Continued)

TABLE 1] *(continued)*

Published Criteria	Systemic Criteria	Chest Criteria	Chest Radiography Criteria	Microbiologic Criteria
Johanson's criteria[14]	- Temperature > 38.5°C - WBC > 12,000/mm³	Purulent secretions	New or progressive consolidation	...

CDC/NHSN = US Centers for Disease Control and Prevention/National Healthcare Safety Network; CDC/NHSN PNU1 = US Centers for Disease Control and Prevention/National Healthcare Safety Network clinically defined pneumonia; CHEST = American College of Chest Physicians; CPIS = Clinical Pulmonary Infection Score; HELICS = Hospital in Europe Link for Infection Control through Surveillance; lpf = low-power field; PEEP = positive-end expiratory pressure; RSV = respiratory syncytial virus; VAP = ventilator-associated pneumonia.

the most stringent set of criteria (Fig 4A). The diagnosis of VAP took longer to establish when applying more stringent compared with less stringent criteria (Fig 4B). There was a slight increase in the duration of MV in patients in whom VAP was diagnosed using the most stringent sets of criteria compared with less stringent sets (Fig 4C).

Discussion

The aim of the present study was to demonstrate that the incidence of VAP can vary widely according to the criteria chosen to diagnose it, and we, therefore, deliberately chose not to define our rate of VAP. Indeed, the estimated incidence of VAP varied from 4% to 42% depending on which of the six published diagnostic algorithms was used. We also illustrated that, by selecting specific, stringent criteria, we could manipulate the incidence of VAP to zero. As expected, stringent and thus more specific sets of criteria selected patients with higher mortality rates than did less stringent sets.

Our results are consistent with previous studies on this issue. Minei et al[8] showed that the incidences of VAP using the CDC/NHSN PNU1 criteria, Johanson's criteria, and clinician's opinion were 48%, 4%, and 17%, respectively. Skrupky et al[9] showed poor agreement between the CDC/NHSN PNU1 criteria and the CHEST criteria ($\kappa = 0.26$). Tejerina et al[10] compared eight sets of criteria and showed a decrease in the incidence of VAP and improved specificity by applying more rigorous sets of criteria. Similarly, Klompas et al[11] showed a lower incidence of VAP when using the more stringent of 32 sets of criteria.

Our study confirms these observations but with the added advantage of using a very large number of criteria with a larger range of stringent combinations, thus enabling us to achieve a virtual zero VAP rate. The relevance of surveillance of VAP as a marker of quality of care can thus be questioned, because the subjectivity and inconsistencies of the criteria used to diagnose VAP make it possible to manipulate its true incidence. Even studies using microbiologic criteria to diagnose VAP have shown differences in diagnostic rates depending on which technique is used to collect the sample.[19,20] Thus, studies on VAP surveillance should also be interpreted with caution.

The strengths of our study include the prospective inclusion of consecutive patients, and so it was representative of the entire patient population admitted to a large multidisciplinary ICU during the study period.

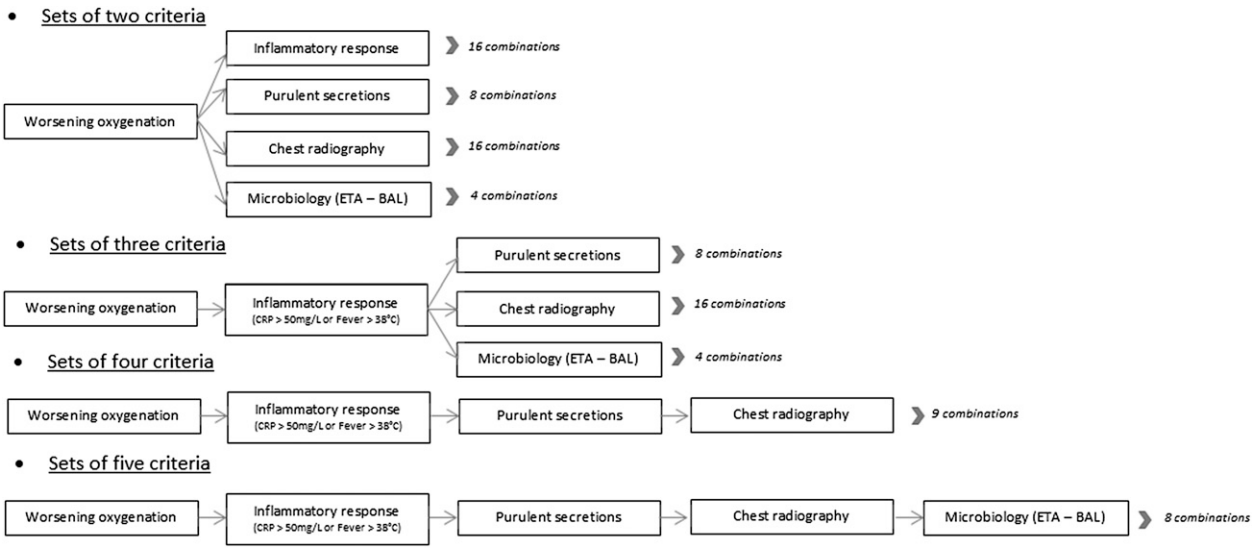

Figure 1 – *Construction of the 89 sets of criteria. See also e-Table 1. CRP = C-reactive protein; ETA = endotracheal aspirate.*

The population studied was severely ill, with a median APACHE score of 25 and a 50% hospital mortality rate. We did not attempt to evaluate the quality of care in our institution, as this was not the purpose of the study.

TABLE 2] Criteria Used to Build the 89 Sets

Worsening oxygenation
PEEP > 2 cm H_2O or FIO_2 > 0.15
PEEP > 5 cm H_2O or FIO_2 > 0.30
PEEP > 2 cm H_2O or FIO_2 > 0.15 for two successive days
PEEP > 5 cm H_2O or FIO_2 > 0.30 for two successive days
Inflammatory response
Leukopenia < 4,000 mm^3 or leukocytosis > 12,000/mm^3
CRP > 50 mg/L
Neutrophils > 7,700/mm^3
Pyrexia > 38°C
Tracheal aspirates
Purulent
Type 5 ETA[a] (< 25 leukocytes, > 10 epithelial cells per field)
Chest radiography
Diffuse infiltrates
Consolidation
Worsening infiltrates
Microbiology (qualitative culture)
ETA positive
BAL positive

CRP = C-reactive protein; ETA = endotracheal aspirate. See Table 1 legend for expansion of other abbreviation.
[a]Bartlett classification.[18]

The single-center nature of our study could be seen as a weakness but also a strength, as it limits the variability in care that can occur across different centers. The number of patients was relatively limited, but sufficient to demonstrate clear differences in incidence rates and outcomes with different criteria. We may have underestimated slightly the incidence of VAP according to the US Centers for Disease Control and Prevention definition,[12] which allows for diagnosis of VAP for up to 48 h after extubation, but this would not have impacted our main findings. The impossibility of obtaining a definitive diagnosis based on pathologic evaluation is an obvious limitation of all studies on this topic.

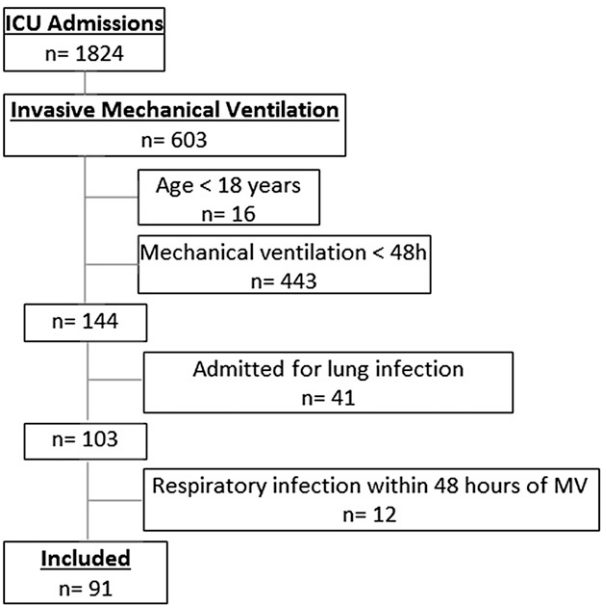

Figure 2 – *Population flowchart. MV = mechanical ventilation.*

TABLE 3] Population Characteristics

Characteristic	Patients (N = 91)
Male patient	52 (57.1)
Age, median (IQR), y	59 (51-69)
Type of patient	
Surgical	50 (54.9)
Neurosurgery	22 (24.2)
Cardiovascular	9 (9.9)
Transplant	8 (8.8)
Lung	3 (3.3)
Digestive	7 (7.7)
Polytrauma	4 (4.4)
Medical	41 (45.1)
Cardiovascular	22 (24.2)
Digestive	6 (6.6)
Lung disease	5 (5.5)
Neurologic disease	3 (3.3)
Urology	2 (2.2)
Others	3 (3.3)
APACHE II score, median (IQR)	25 (21-30.5)
ECMO	15 (16.5)
VV	12 (13.2)
VA	2 (2.2)
Comorbidities	
Chronic lung disease	15 (16.5)
Diabetes mellitus	11 (12.1)
Transplant	10 (11)
Chronic renal failure	5 (5.5)
Liver disease	4 (4.4)
Autoimmune disease	4 (4.4)
HIV	1 (1.1)
Smoker	33 (36.3)
Outcome	
Hospital length of stay, median (IQR), d	25 (8-14)
ICU length of stay, median (IQR), d	13 (7-22)
Duration of ventilation, median (IQR), d	5 (3-8)
Hospital mortality	45 (49.5)
ICU mortality	38 (41.8)
Mortality during mechanical ventilation	32 (35.2)

Data given as No. (%) unless otherwise indicated.
APACHE = Acute Physiology and Chronic Health Evaluation; ECMO = extracorporeal membrane oxygenation; IQR = interquartile range; VA = venoarterial; VV = venovenous.

These observations challenge the use of VAP as a marker of quality of care, at least if the criteria used are left to the individual's choice. Even if the criteria are well defined, there may still be interobserver variability, but we did not specifically study this phenomenon.

In conclusion, the diagnosis of VAP is highly variable depending on the criteria selected to identify it. VAP may even "disappear" totally if stringent criteria are used.

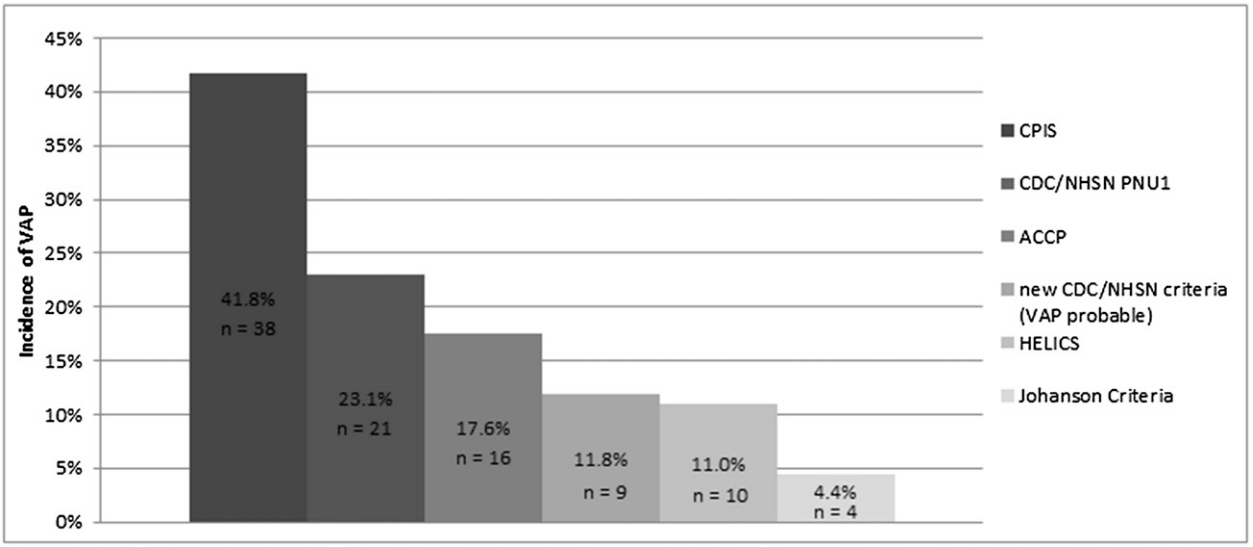

Figure 3 – *Incidence of VAP according to the published algorithms. CDC/NHSN PNU1 = US Centers for Disease Control and Prevention/National Healthcare Safety Network clinically defined pneumonia; ACCP = American College of Chest Physicians; CPIS = Clinical Pulmonary Infection Score; HELICS = Hospital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

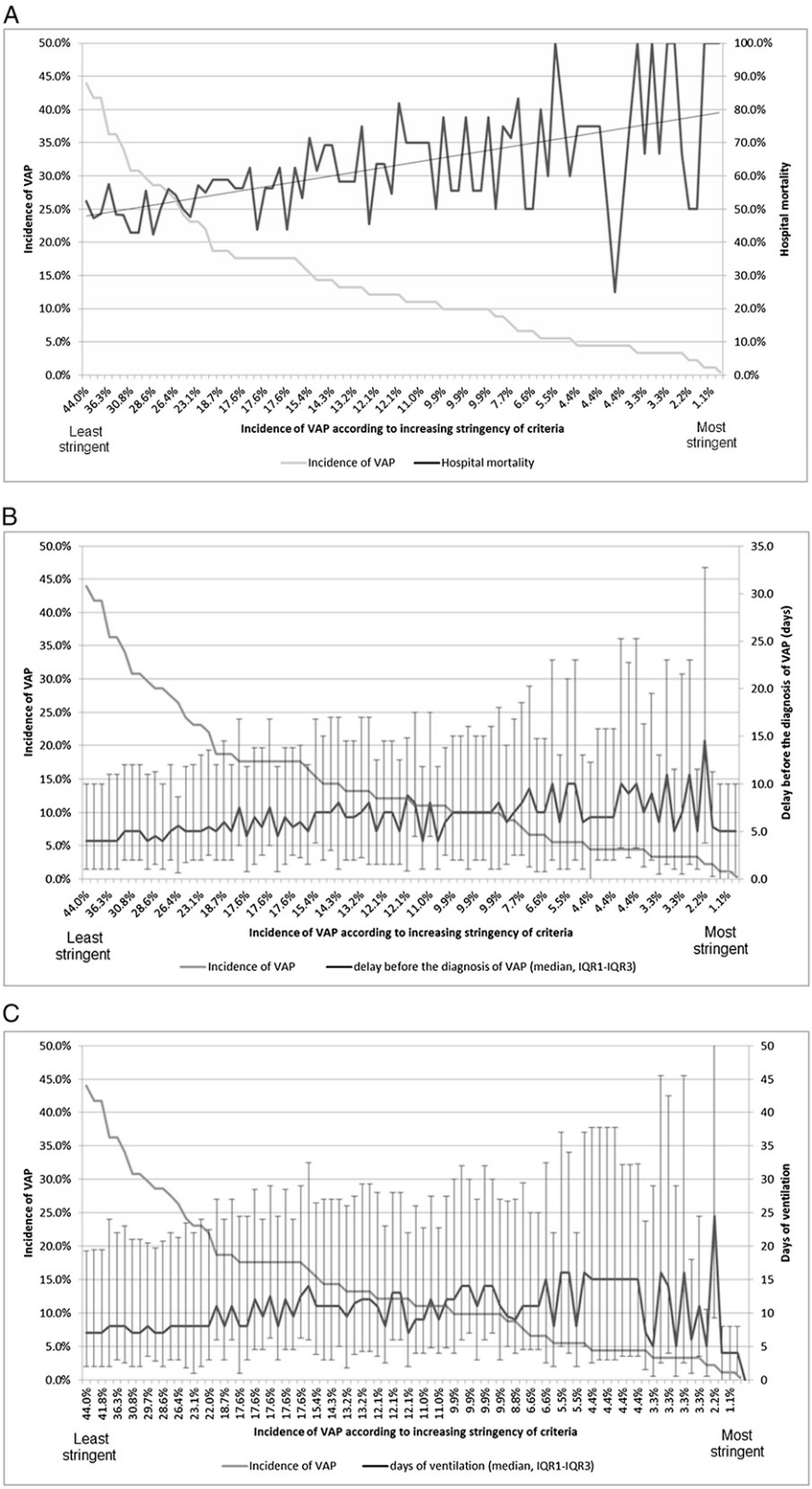

Figure 4 – *A, Incidence of VAP according to the 89 sets of criteria used and hospital mortality. B, Delay before the diagnosis of VAP according to the incidence of VAP. C, Duration of MV according to the incidence of VAP. IQR = interquartile range. See Figure 2 and 3 legends for expansion of other abbreviations.*

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Author contributions: A. E. is the guarantor of the manuscript and takes responsibility for the integrity of the data and the accuracy of the data analysis. A. E. drafted the manuscript, collected data, and served as principal author; A. E. and J.-C. P. contributed to data analysis; J.-C. P. and J.-L. V. contributed to revising the manuscript; and A. E., J.-C. P., and J.-L. V. contributed to the study design and all approved the final version of the manuscript.

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Additional information: The e-Table can be found in the Supplemental Materials section of the online article.

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