

Ventilator-associated Events Surveillance in a Trauma Intensive Care Unit: A Prospective Study of Incidence, Predictive Values, Sensitivity, Specificity, Accuracy, and Concordance with Ventilator-associated Pneumonia

Kulbeer Kaur¹, Kajal Jain², Manisha Biswal³, Surinder Kaur Dayal⁴

ABSTRACT

Introduction: The Centre of Disease Control and Prevention (CDC) introduced a new definition of ventilator-associated events (VAEs) in 2013 in place of longstanding ventilator-associated pneumonia (VAP) definition. Three entities under VAE, ventilator-associated condition (VAC), infection-related ventilator-associated complication (IVAC), and possible ventilator-associated pneumonia (PVAP), were introduced.

Objectives: To assess the incidence of all VAEs in a tertiary care trauma ICU and to find the predictive value of VAE and sensitivity of VAE definitions for VAP.

Design: Cohort prospective study at trauma intensive care unit (ICU) of PGIMER, Chandigarh, from July 2018 till June 2019.

Method: Patients admitted in trauma ICU were checked for VAP and VAE criteria defined by CDC.

Results: Four hundred and sixty five patients were observed. Around 378 patients were included in the study with 4046 patient days and 3031 mechanical ventilation (MV) days. Incidence rate of PVAP, IVAC, VAC, and VAP was 2.97, 6.60, 10.23, and 9.24 per 1000 ventilator days, respectively. Sensitivity, specificity, positive predictive value, and negative predictive value (NPV) of diagnosing VAP were 0.61, 0.97, 0.68, and 0.97 for VAC; 0.80, 0.97, 0.57, and 0.99 for IVAC; and 0.78, 0.94, 0.25, and 0.9 for PVAP, respectively. Kendall's W test showed that there was very poor concordance between VAP and VAE.

Keywords: Infection-related ventilator-associated complication, Possible ventilator-associated pneumonia, Ventilator-associated condition, Ventilator-associated events, Ventilator-associated pneumonia.

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INTRODUCTION

The Centre of Disease Control and Prevention (CDC) introduced a new definition of ventilator-associated events (VAEs) in 2013 in place of the earlier definition of ventilator-associated pneumonia (VAP). The three tiers included under VAE were ventilator-associated condition (VAC), infection-related ventilator-associated complication (IVAC), and possible ventilator-associated pneumonia (PVAP). This was done to simplify surveillance, increase objectivity, and broaden prevention efforts.

Trauma patients are at high risk of VAP as compared to non-trauma patients.¹⁻⁴ Magill et al. analyzed data reported from U.S. healthcare facilities for VAEs that occurred in 2014.⁴ They found substantial variability in VAE incidence and in the proportions of VAE characterized as infection-related, and ventilator utilization within and among location types. It therefore becomes a critical issue to work on a surveillance definition closely related to the clinical pneumonia. Apart from accuracy, other important factors are sensitivity, specificity, and predictive values of the surveillance tests. Piriypatsom et al. evaluated infection-related VAE algorithm for VAP in their surveillance in a trauma population at Massachusetts. They reported that IVAC criteria had poor sensitivity and positive predictive value (PPV) for the diagnosis of VAP according to the 2008 CDC/NHSN definition.⁵

In India, the adoption of VAE surveillance is still limited. There are no published studies on the same. One of the reasons of limited work on VAE is the uncertainty about possible overlap with the VAP

¹Medical Microbiology, Infection Control, Nursing, Post Graduate Institute of Medical Education and Research, Chandigarh, India

²Anesthesia and ICU, Post Graduate Institute of Medical Education and Research, Chandigarh, India

³Medical Microbiology, Infection Control, Scrubtyphus, Post Graduate Institute of Medical Education and Research, Chandigarh, India

⁴Nursing, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Corresponding Author: Kajal Jain, Anesthesia and ICU, Post Graduate Institute of Medical Education and Research, Chandigarh, India, Phone: 1722756500, e-mail: kajalteji@gmail.com

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definition. It is important to determine the impact of VAP episodes missed by VAE surveillance and vice versa. The objective of the present study is to determine the incidence of all VAEs and VAP in a tertiary care trauma intensive care unit (ICU) and to determine the predictive values, sensitivity, specificity, and accuracy of VAE definitions for detection of VAP.

METHODS

Design

A prospective study was done at the Trauma ICU of PGIMER, Chandigarh from July 2018 till June 2019.

Inclusion and Exclusion Criteria

All the patients who were admitted in the Trauma ICU and mechanically ventilated for more than two days were recruited in the study. The patients who were not mechanically ventilated or mechanically ventilated for less than 2 days or organ donors were excluded from the surveillance.

Data Collection

The data collection forms were made and finalized by the study group. One dedicated infection control nursing officer visited the ICU every day at same time of the day for data collection. The denominator data were collected for all the patients present at the Trauma ICU. The patients were prospectively followed up for the development of VAP (NHSN definition) and VAEs (Flowchart 1 and Table 1) based on criteria defined by CDC. Daily monitoring of positive-end expiratory pressure (PEEP), fraction of inspired oxygen (FiO₂), fever, total leukocyte count, mental status deterioration, increase in volume and change in character of secretions, tachypnea, bronchial breath sounds, worsening gas exchange, and progressive or new infiltrates/consolidation/cavitation, along with new antibiotics and positive microbiology cultures. All the patients who fit into the criteria of VAP and VAE were recognized and discussed with the study group and included in numerator data.

Statistical Analysis

Kendall's coefficient of concordance was calculated using the Statistical Package for Social Sciences software version 20 to find the agreement between VAE (VAC, IVAC, and PVAP) and VAP. MEDCALC statistical software was used to calculate the PPV, NPV, sensitivity, specificity, and accuracy of the VAE (VAC, IVAC, and PVAP) for the diagnosis of VAP.

RESULTS

Five hundred and nine admissions were enrolled over a period of 1 year in the Trauma ICU. One hundred and thirty-one patients were excluded from the study. Three hundred and seventy-eight patients who were mechanically ventilated for more than two days were recruited as study population for surveillance of VAP and VAE. The majority of patients were male (76.2%) and around 70% of the patients were less than 40 years of age without any co-morbidity. Most of them (73.3%) were received after average 2–3 days stay in emergency unit and 50% of the patients were intubated either in emergency or outside PGIMER (Table 2). The total patient days in the study were 4046 and mechanical ventilation days were 3031. The MV utilization ratio was 0.75. Out of total study population 40 (10.6%) patients developed VAE and/or VAP-NHSN (Table 3). The incidence of VAC ranged from 0 to 24 in 12 months with a peak in April (20), while that of VAP ranged from 0 to 18.96 with a peak in March (9.48) (Fig. 1). The mortality was 21.4% overall, 66.7% in patients who developed VAP and 73.4% in those with VAC (Table 2).

The sensitivity, specificity, PPV, NPV, and accuracy of VAEs for VAP-NHSN diagnosis is shown in Table 4. In this study population, the agreement (Kendall's coefficient for concordance) between VAP and VAC (0.005), VAP and IVAC (0.095), and VAP and PVAP (0.374) was poor.

Most common pathogens isolated as a cause for VAP and IVAC in the patients included *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterobacter* spp., and *Staphylococcus aureus* (Table 5).

DISCUSSION

VAE surveillance has not been widely adopted beyond the United States. One of the reasons may be that there exists uncertainty about the overlap between VAP and VAE, thereby with implications of the same on clinical utility. We sought to determine the accuracy of VAC for the diagnosis of VAP and vice versa in a setting of trauma ICU in our tertiary care hospital in India.

As previous studies have also reported,^{6,7} we found a higher incidence of VAC compared to VAP (10.2 vs 9.2 per 1000 MV days). However, the incidence of VAP was more than IVAC (6.6/1000 MV days) and much higher than PVAP (2.97/1000 MV days). Here was therefore a poor concordance of VAP with VAC (0.005), IVAC (0.095), and PVAP (0.374) in our patients. The PPV of VAC and IVAC for VAP-NHSN was 67.9 and 57.1%, respectively, while that of PVAP for VAP was only 25%. The sensitivity of VAC and IVAC for VAP-NHSN was 61.3 and 80.0%, respectively.

Table 6 lists the previous studies conducted to compare VAP and VAE in different study populations. The results of these studies also show poor relation between both definitions. V-associated event surveillance did not accurately detect cases of traditionally defined VAP in ICUs.

As the study was conducted in trauma intensive care, the majority of the cohort comprised severe head injury. In such patient profile, it may be worth noting that certain trauma-related factors like depressed consciousness, loss of protective reflexes, reduced muscle strength, and delayed presentation may contribute to higher infectivity and mortality.

COMPARISON OF CHALLENGES FACED DURING VAP AND VAE SURVEILLANCE

To meet VAP definition, subjective criteria [amount of endotracheal (ET) secretions, change in character of ET secretions, progressive/new and persistent X-ray changes] are applied, which for some patients, clinicians and surveillance team might find difficult to agree on. Ventilator-associated event is more objective, easy to use, and has less chances of disagreement on case definition. However, there is a strict definition for window period in VAE which sometimes excludes some cases if the definition criteria meet \pm few days of that period. For example, if a tracheal aspirate (TA) culture has come positive 1–4 days before worsening PEEP/FiO₂, clinicians sometimes do not repeat the TA for surveillance purposes. Our study found a low concordance found between VAP and VAE (including VAC, IVAC, and PVAP). It is possible that the new VAE definitions are missing out on the patients who would fit into VAP criteria.

Klompas and Berra¹¹ found that a screening ventilator setting for VAC captures a similar set of complications to traditional VAP

Flowchart 1: Ventilator-associated Events (VAE) Surveillance Algorithm

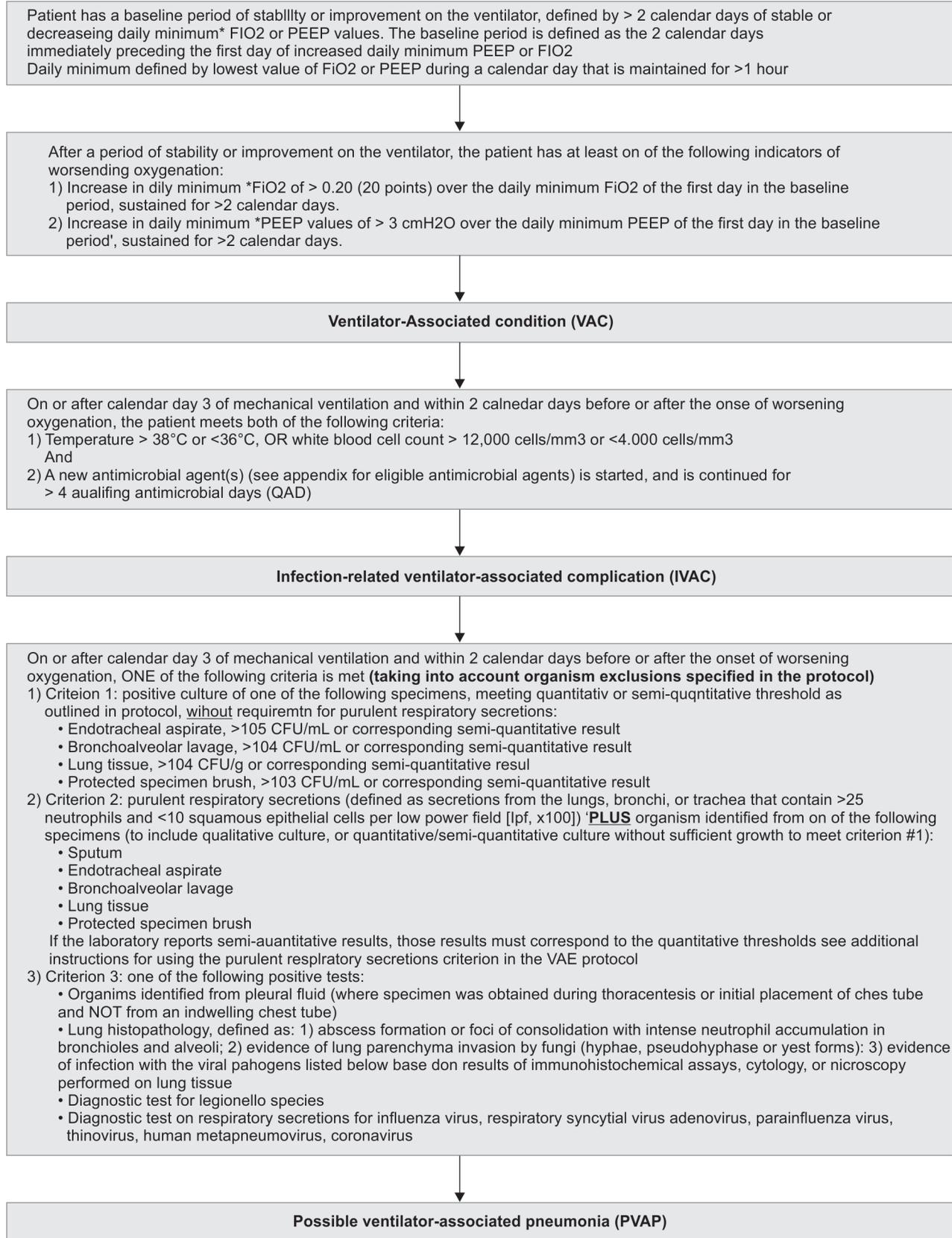


Table 1: VAP_ PNEU1 criteria (CDC)

For ANY PATIENT, at least **one** of the following:

- Fever (>38.0°C or >100.4°F)
- Leukopenia ($\leq 4,000$ WBC/mm) or leukocytosis (>12,000 WBC/mm³)
- For adults >70 years old, altered mental status with no other recognized cause

And at least **two** of the following:

- New onset of purulent sputum or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements
- New onset or worsening cough, or dyspnea, or tachypnea
- Rales or bronchial breath sounds
- Worsening gas exchange (for example: O₂ desaturations (for example: PaO₂/FiO₂ <240), increased oxygen requirements, or increased ventilator demand)

Two or more serial chest imaging test results with at least one of the following:

New and persistent
or
Progressive and persistent

- Infiltrate
- Consolidation
- Cavitation
- Pneumatoceles, in infants ≤ 1 -year-old

Table 2: Demographic data of study participants

	Categories	Number (%)
Admission units	Neurosurgery	264 (69.8)
	Orthopedics	43 (11.4)
	Others	71 (18.8)
Gender	Male	288 (76.2)
	Female	90 (23.8)
Age (years)	<18	84 (22.2)
	19–40	183 (48.4)
	41–60	76 (20.1)
	>61	22 (5.8)
	No data	13 (3.4)
Previous unit	Emergency	277 (73.3)
	Ward	76 (20.1)
	No data	25 (6.6)
Intubation	Before ICU admission	189 (50)
	Intubated inside ICU	189 (50)
End status	Expired	81 (21.4)
	LAMA*	10 (2.6)
	Transferred to another unit	287 (76)
Trauma with head injury	Yes	231(61.1)
	No	84 (22.2)
	No data	63 (16.7)
Co-morbidity**	Present	27 (7.1)
	Not present	181(47.9)
	No data	170 (45)

*Left against medical advice

**Diabetes mellitus, hypertension, asthma, alcoholism, coronary artery disease, hypothyroidism, and cerebrovascular accident

Table 3: Incidence of VAP and VAE in trauma ICU from July 2018 till June 2019

Entity	Number (%) (N = 378)	Incidence per 1,000 MV days (MV days = 3031)
VAP	28 (7.41)	9.24
VAC/VAE	31 (8.20)	10.23
IVAC	20 (5.29)	6.60
PVAP	9 (2.38)	2.97
VAP but no VAE	9 (2.38)	2.97
VAC but no VAP	12 (3.17)	3.96
IVAC but no VAP	4 (1.06)	1.32
PVAP but no VAP	2 (0.53)	0.66
Both VAC and VAP	19 (5.02)	6.26

surveillance but is faster, more objective, and superior predictor of outcomes. Klompas and Berra also analyzed pros and cons of VAE. They added that VAE surveillance has the potential to catalyze better care and to help hospitals track outcomes in ventilated patients more rigorously and more efficiently. On the con side, the complete VAE definition set with sub-tiers is complicated, neither sensitive nor specific for VAP, non-physiological compared with other ICU metrics, susceptible to gaming, and may bring about changes in clinician behavior that could paradoxically end up harming patients.

Yu et al.¹² studied 71 patients with VAP and coined a new term called “gradual VAP.” They added that “it is challenging for the clinician to make a diagnosis of pneumonia without chest imaging, leading to the fact that the IVAC definition is mainly used in surveillance. Thus, it is a challenge to determine the timing of the initiation of antibiotic treatment. Gradual VAP is a novel concept that might be a better bridge to link VAT and VAP than IVAC.”

LIMITATION OF THE STUDY AND FUTURE AREAS OF WORK

There are many extraneous variables that may have affected the incidence of VAP and VAC. First, the majority of patients in trauma ICU reach ICU after an average 2–3 days stay in emergency. Some of the patients even get initial first aid or sometimes get endotracheal intubation done at the local hospitals. The condition in which the initial intubation done and the care taken post intubation affects the chest status of patients. Second, patients in trauma ICU sometimes have conditions like fracture of ribs, hypoventilation, pneumothorax, aspiration, etc. These patients have higher chances of deteriorating post ventilation. So, it would be worthwhile to conduct studies to evaluate the role of these factors in this patient population in the future.

CONCLUSION

As a surveillance definition, VAC, IVAC, and PVAP have poor concordance with VAP-NHSN. Many extraneous factors as mentioned in the limitations in the study might have contribution to the change in trends. More studies are needed to study the role of pre ICU intervention factors in this population.

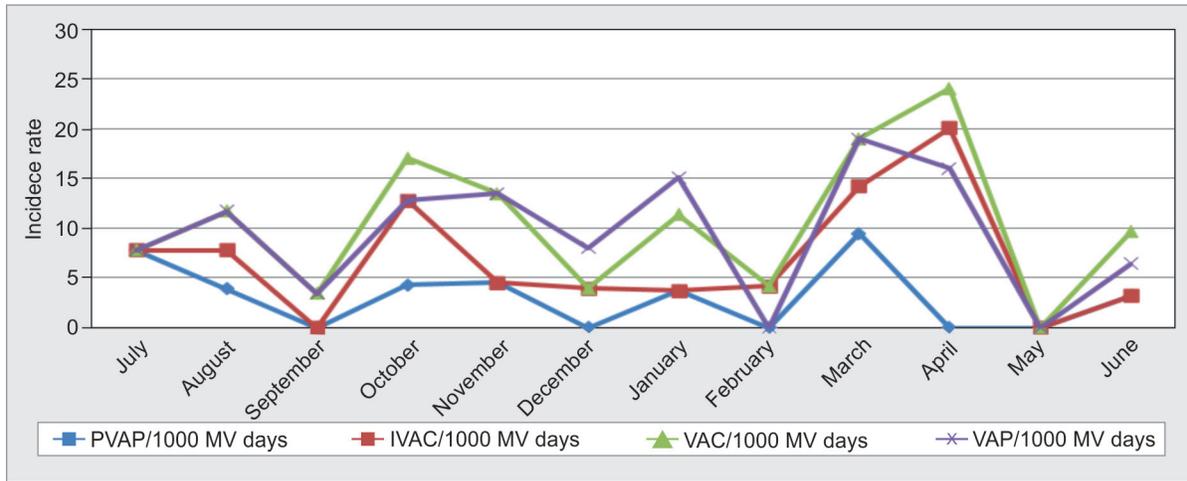


Fig. 1: Incidence rate of VAC, IVAC, PVAP and VAP from July 2018 to June 2019

Table 4: Test characteristics of VACs for the diagnosis of VAP

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
VAC for VAP	61.3% (42.2–78.2)	97.4% (95.1–98.8)	67.9% (51.1–81.0)	96.6% (94.8–97.8)	94.4% (91.6–96.5)
IVAC for VAP	80.0% (56.3–94.3)	96.7% (94.2–98.3)	57.1% (42.4–70.8)	98.9% (97.3–99.5)	95.8% (93.2–97.6)
PVAP for VAP	77.8% (40.0–97.2%)	94.31% (91.4–96.4)	25.0% (16.2–36.5)	99.4% (98.1–99.8)	93.9% (91.0–96.1)

Table 5: Antibiogram of pathogens found during VAP and IVAC surveillance in Trauma ICU from July 2018 to June 2019

Pathogens	No. of patients	Antibiotics													
		AMK	MINO	CIPRO	CEFOTAX	IMI	PIP	CEFOSULB/ CSL	CEFTAZ/ CTZ	DOXY	MERO	ERTA	COL	CEFEP	
<i>Acinetobacter baumannii</i>	10	0	3	0		0	0	1	0	0	0		5	0	
<i>Klebsiella pneumoniae</i>	7	4	1	2		1	1	2			2	1	3	1	
<i>Escherichia coli</i>	3	2	1	0	0	1	1	1	0	0	1	0	3	0	
<i>Pseudomonas aeruginosa</i>	2	2		2		2		2	2		2		2	2	
<i>Enterobacter Spp.</i>	2	2	1	2	0	0	0	0	0	0	0	0		1	
Methicillin resistant <i>staphylococcus aureus</i>	2			0											

Pathogens	No. of patients	Antibiotics											
		TIG	GENT	TETRA	LEVO	CHL	VANCO	TEICO	SAM	LNZ	CLIND	OXA	ERYTHRO
<i>Acinetobacter baumannii</i>	10	4	0	2	1				1				
<i>Klebsiella pneumoniae</i>	7	1											
<i>Escherichia coli</i>	3	2											
<i>Pseudomonas aeruginosa</i>	2				2								
<i>Enterobacter Spp.</i>	2												

Methicillin resistant <i>staphylococcus aureus</i>	2	2	2	1	1	0	0
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AMK, amikacin; MINO, minocycline; CIPRO, ciprofloxacin; CEFOTAX, cefotaxime; IMI, imipenem; PIP, piperacillin; CEFOSULB, cefoperazone-sulbactam; CEFTAZ, ceftazidime; DOXY, doxycycline; MERO, meropenem; ERTA, ertapenem; COL, colistin; CEFEP, cefepime; TIG, tigecycline; GENT, gentamicin; CSL, cefoperazone-sulbactam TETRA, tetracycline; LEVO, levofloxacin, CHL, chloramphenicol; VANCO, vancomycin; TEICO, teicoplanin; SAM, ampicillin-sulbactam; LNZ, linezolid, CLIND, clindamycin; OXA, oxacillin; ERYTHRO, erythromycin

Table 6: List of previous studies conducted to compare VAP and VAE in different study populations

Author, country	Study setting	Incidence of VAP/ VAE	Sensitivity (%) of VAE to detect VAP	Specificity (%)	PPV (%)	NPV (%)	Conclusion
Piriyapatsom et al., ⁵ Massachusetts, USA	Retrospective, single-center, trauma subjects, IVAC compared to VAP	IVAC or VAP 35.6 VAP 29.6% Both 8.3%	IVAC 28.12	91.45	58.06	75.14	IVAC criteria had a low accuracy for identifying VAP-NHSN in subjects with high-risk trauma
Klouwenberg et al., ⁶ Netherlands	Prospective cohort study in two Dutch academic medical centers	VAC 10/1000 MV days IVAC 4.2 VAE-VAP 32. VAP 8.0/100 MV days	VAC 33% IVAC 17%				Noted much poorer concordance between the novel VAE algorithm and VAP. The incidence rate of VAC, IVAC, VAE-VAP, and VAP in the present study was comparable (10.23, 6.60, 6.26, and 9.24, respectively). Poor concordance noted between VAP and VAE in the present study too
Fan et al., ⁷ Wuhan, China	Meta-analysis of 18 studies	VAC 10.23 IVAC 6.6 Possible VAP 2.97 VAP-NHSN 9.24/1,000 MV days	VAE <50%	>80%	<50%	>80%	VAE surveillance missed many cases of VAP, and the population characteristics identified by the two surveillance paradigms differed
Boyer et al., ⁸ St Louis, Missouri	Prospectively surveyed 1,209 patients ventilated for 2 calendar days at medical surgical ICU	VACs 5.5% (7/1,000 MV days) IVAC 3.6/1,000 MV days VAP 10.0/1,000 MV days	VAC 25.9%				VAC criteria captured a minority of VAP episodes
Meagher et al., ⁹ USA	Retrospective study, adult trauma patients (2012–2017)	VAE 8.1% VAP 7.4% and Both 4.1% of patients					The proportions of individual entities were found to be comparable to the present study for VAC (8.2%), VAP (7.41%), and VAE + VAP (5.02%)
Younan et al., ¹⁰ China	Retrospective study, trauma patients	“New” VAP 6.6% “Old” VAP 30.9% Both 5.8%					The concordance between new and old definitions was poor (kappa 0.22), similar to the present study

ORCID

Kulbeer Kaur  <https://orcid.org/0000-0002-6502-6530>

Kajal Jain  <https://orcid.org/0000-0003-3077-8326>

Manisha Biswal  <https://orcid.org/0000-0003-2016-3678>

Surinder Kaur Dayal  <https://orcid.org/0000-0002-8810-524X>

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