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Ventilator-associated pneumonia surveillance using two methods

Thomas H. Craven^{1,2,4*}, Gosha Wojcik², Jodie McCoubrey³, Odette Brooks⁴, Esther Grant⁵,
Sean Keating², Jacqui Reilly³, Ian F. Laurenson⁴, Kallirroi Kefala^{1,2,4} and Timothy S. Walsh^{1,2,4**}

¹ Centre for Inflammation Research, University of Edinburgh, Edinburgh, UK.

² Edinburgh Critical Care Research Group, University of Edinburgh, Edinburgh, UK.

³ Health Protection Scotland, Glasgow, UK.

⁴ Clinical Microbiology, NHS Lothian Infection Service, Royal Infirmary of Edinburgh, Edinburgh, UK.

⁵ Western General Hospital, Edinburgh, UK.

* Corresponding author: Thomas.craven@ed.ac.uk

** Alternate author: Timothy.Walsh@ed.ac.uk

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Declarations of interest: none

Abstract

Background

Ventilator-associated pneumonia surveillance is used as a quality indicator due to concerns that some cases may be preventable and may contribute to mortality. Various surveillance criteria exist for the purposes of national reporting, but a large scale direct comparison has not been conducted.

Methods

A prospective cohort study applied two routinely used surveillance criteria for ventilator-associated pneumonia from the European Centre for Disease Control and the American Centers for Disease Control to all patients admitted to two large general intensive care units. Diagnostic rates and concordance amongst diagnostic events were compared.

Findings

713 at-risk patients were identified during the study period. The European surveillance algorithm returned a rate of 4.6 cases of ventilator-associated pneumonia per 1,000 ventilation days (95% confidence interval 3.1-6.6) and the American surveillance system a rate of 5.4 (3.8-7.5). The concordance between diagnostic events was poor (Cohen's Kappa 0.127 (-0.003 to 0.256))

Conclusions

The algorithms yield similar rates, but the lack of event concordance reveals the absence of inter-algorithm agreement for diagnosing ventilator-associated pneumonia, potentially undermining surveillance as an indicator of care quality.

Keywords

Ventilator-associated pneumonia, Infection surveillance, Mechanical ventilation, Critical care

Introduction

Ventilator associated pneumonia (VAP) refers to inflammation of the lung parenchyma caused by an infectious agent acquired specifically as a result of invasive mechanical ventilation. Throughout the last few decades study investigators have not adopted a fixed set of criteria or a fixed at-risk definition and this has led to an inability to make direct comparisons across study sets. This may account for a wide variety in reported incidence, where rates vary between 4.0% and 28.8% [1–8].

Surveillance and reporting of VAP is often mandated by care quality agencies and remuneration bodies [9] because it is perceived to be a potentially preventable complication which may contribute to morbidity and mortality. However, substantial inter-observer variability has been documented [10] as has a lack of correlation with autopsy findings [11]. Requiring microbiological confirmation adds less strength to the diagnosis than might be expected [12] and commonly used techniques have poor sensitivity and specificity compared to pulmonary biopsy [13,14]. Nonetheless, surveillance has been performed internationally for many years, and if the same method is used, regardless of its weaknesses, it should follow that trends can be observed and benchmarking can occur. Attributable morbidity has been shown to increase when surveillance is suspended, although confusingly not due to increased VAP occurrence [15]. The subjective nature of VAP diagnosis has led to accusations of gaming, undertaken to reduce the locally reported VAP rate; many surveillance rates approach zero, in contrast to the studied rates [16]. Scotland and other European countries use the surveillance methods recommended by the European Centre for Disease Prevention and Control [17] which contain subjective criteria [18].

To address the problem of subjectivity and repeatability, the American Centers for Disease Control and Prevention (CDC) developed a surveillance for Ventilator Associated Events (VAE) with objective and potentially automatable criteria [19]. The CDC algorithm returns a hierarchical diagnosis from

ventilator-associated complication (VAC) to infection related ventilator-associated complication (IVAC), and probable VAP [20]. The aim of this new CDC algorithm is to capture all episodes of deterioration on a ventilator (whatever the cause), facilitate surveillance that can be done objectively, electronically, and reproducibly [9], and is integral to their strategy to reduce ICU acquired infection [21].

The primary aim of this study was to compare the ECDC case definition for VAP with the CDC algorithm for VAP and with clinician suspected VAP (CS VAP). There have been few attempts to directly compare the surveillance algorithms. One UK study compared ECDC and CDC surveillance criteria returning dissimilar VAP rates and did not look specifically at concordance between algorithms [22]. One Serbian study found good concordance between algorithms [23]. We previously reported the initial analysis of the study presented herein, indicating poor concordance amongst individual VAP occurrences [24].

Methods

Setting

A prospective observational cohort study was carried out at two large adult (aged 16 or over) intensive care units located at the Royal Infirmary of Edinburgh and the Western General Hospital, Edinburgh. As a service evaluation ethical approval was not required. The data capture, storage and analysis plans were authorized by the Caldicott guardian.

Data Collection

Data were collated for patients admitted between 1st June 2015 and 31st May 2016 who were admitted for more than two calendar days (where one calendar day was defined as any whole or part period from 0000hrs to 0000hrs). There is no consistent definition of the at-risk population for VAP amongst mechanically ventilated patients. To present comparisons across groups, we defined the at-risk population as those who received at least 2 calendar days of mechanical ventilation.

CDC VAP data: A team of research nurses received training and supervision in the collection of CDC pertinent information for all patients who were admitted for more than two calendar days (CD). CDC VAP was defined according to the CDC algorithm (January 2015, updated April 2015, see supplemental figure 1) which is based on the original publication by the working group [19].

ECDC VAP data: ECDC VAP was defined according ECDC criteria [17]. Routine VAP surveillance data using the ECDC case definition was collected by the ICU acquired infection surveillance team, according to their standard practice. This was a separate team that worked in isolation from the CDC VAP study team. ECDC VAP cases were classified into Pneumonia (PN) 1-5 according to characteristics of microbiological results related to the trigger clinical event (see supplemental table I).

Clinician Suspected VAP (CS VAP) data: Information pertaining to new antibiotic prescriptions for suspected chest infection was also collected by the study team to identify CS VAP. CS VAP was defined as the initiation of a new antibiotic for suspected chest infection in a ventilated patient after 2 CD of mechanical ventilation (MV) which was not a replacement, escalation, or de-escalation for a pre-existing antibiotic prescription. A summary of the three VAP definitions used in the study are shown in table I.

Modification to the CDC Algorithm

Microbiological sampling proceeded as part of routine care but due to subtle differences in the capability of the local microbiology services and the antibiotic uses we modified the CDC surveillance algorithm to ensure it could be delivered. Firstly, we added two commonly used antibiotics, amoxicillin and co-amoxiclav, to the qualifying antibiotic list. Secondly, we modified diagnosis by criterion 2 from purulent respiratory secretions (≥ 25 neutrophils and ≤ 10 squamous epithelial cells per low power field [lpf, x100]) AND identification of organisms NOT meeting the quantitative or semi-quantitative thresholds to:

- For endotracheal aspirates: any mention of purulence and any report of bacterial or fungal culture (discounting commensal organisms specified in the CDC VAE Surveillance protocol e.g. *Candida* spp.).
- For broncho-alveolar lavage: any mention of purulence and positive culture NOT meeting the quantitative threshold.

The modification described here is not among the range of deviation options listed by the CDC but was necessary to accommodate local microbiology reporting practices.

Assessment of Ventilator-associated events

In addition to an assessment of ventilator-associated pneumonia we also performed for surveillance of all hierarchical ventilator associated events as defined by the American CDC (supplemental figure

1, ventilator-associated condition (VAC), infection related ventilator-associated condition (IVAC)).

We calculated the number of events where failure to collect microbiological samples was the cause of failure to progress through the hierarchy. Two intensive care specialists working independently performed an electronic case note review for each VAC/IVAC to determine the underlying cause of deterioration in oxygenation following a period of stability. Choices of True VAP, pulmonary oedema, atelectasis, deterioration in pre-existing condition, inadequate microbiological data to draw further conclusions, and other were permitted.

Analysis

VAP rates were calculated using the total number of ventilation days from the at-risk population and reported on a per patient and per event basis. Details of the statistical test to compare baseline characteristics are shown with the relevant figure. $P < 0.05$ was considered statistically significant. VAP concordance was determined on a per patient basis, presented in a 2x2 table and calculated using Cohen's Kappa (GraphPad online calculator, located at <https://graphpad.com/quickcalcs/kappa1.cfm>). No reference standard was available so positive and negative percent agreements were calculated. (PPA and NPA, analogous to sensitivity to specificity respectively if a perfect reference standard were available)[25].

Results

Summary of enrolled cases

During the period 1st June 2015 and 31st May 2016 1972 patients were admitted. A flow chart describing the breakdown of the admitted population is shown in figure 1. Selected admission characteristics are shown in table II.

Diagnosis of ventilator associated pneumonia

The number of events and the associated VAP rates and proportions detected via the three methods are shown in table III. The two surveillance algorithms returned very similar rates. However, the CS VAP rate was approximately five times that returned by either algorithm, and nearly a quarter of patients who undergo at least two calendar days of mechanical ventilation receive a new antibiotic directed at VAP. The median ($\pm$ IQR) number of calendar days to first diagnosis of event was 5 (4.0-7.0), 6 (3.8-7.0), and 5 (3.0-8.0) for CDC VAP, ECDC VAP, and CS VAP respectively. The baseline characteristics of each VAP cohort and the admission types are summarized in table IV.

Microbiology of VAP

Amongst 35 ECDC VAP identified, 20 (57.1%) were confirmed microbiologically (PN1-4) and 15 (42.9%) were classified as PN5 i.e. there was no supportive microbiological data and VAP was diagnosed clinically.

By definition, for a CDC VAP to be diagnosed, the appropriate respiratory microbiology samples must have been examined at or around the time of sustained deterioration in respiratory function and have met appropriate microbiological thresholds, so all cases have at least one associated microorganism.

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2 There were 150 patients who experienced 160 episodes of CS VAP. Microbiological samples were
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4 sent within five calendar days (2 days before and 2 days after) of the initiation of antibiotics in
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6 34/150 patients and 41/160 (25.6%) occasions. 27/150 patients and 32/160 cases were
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8 microbiologically confirmed. A table of causative organisms is shown in Supplemental table II.
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10 11 12 13 14 Concordance between surveillance methods 15

16 In the absence of a true reference standard for VAP, the CDC surveillance algorithm was compared
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18 to the routinely used ECDC surveillance case definition for VAP. The concordance of at-risk patients
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20 with and without a VAP surveillance diagnosis according to the two surveillance methods is shown in
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22 table V. Positive VAP events from both surveillance algorithms which do not overlap in time remain
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24 concordant in this analysis.
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30 We examined the concordance between CS VAP and each surveillance method (table VI). Due to the
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32 low contemporaneous sampling rate around the initiation of antibiotics we also examined the
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34 concordance between CS VAP where microbiology samples had been sent to the surveillance
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36 definitions (supplemental table III).
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42 Experience of VAE hierarchical diagnosis 43

44 A summary of the incidence of VAEs is shown in table VII. Where a patient experiences more than
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46 one VAE at more than one hierarchical level they are collated into the highest experienced
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48 diagnostic group.
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52 We examined the effect of the strict time window either side of the IVAC day (the first day of the
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54 sustained deterioration in oxygenation) during which positive microbiology samples must be
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1 obtained to diagnose a CDC VAP. Out of 38 IVACs, only 3 (7.9%) would have progressed to CDC VAP
2 had the IVAC window been extended to last for the duration of the trigger antibiotic course.
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7 Of 38 IVACs however, only 19 (50.0%) had appropriate samples taken within the 5-day window,
8 meaning 19 patients could, under no circumstances, progress to CDC VAP. On 13/19 (68.4%) of
9 occasions, the opportunity to take an appropriate sample was missed, and on the remaining six
10 occasions respiratory microbiology was available just prior to the start of the VAE window, making
11 further respiratory sampling redundant. Of the thirteen occasions where sampling was missed,
12 samples were taken after the 5-day window but during the trigger antibiotic course on 8 occasions,
13 three of which were positive.
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26 For each VAC/IVAC a summary of alternative diagnoses is given in Table VIII. The reviewers
27 demonstrated moderate concordance for True VAP diagnosis (see supplemental table IV).
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Discussion

We applied the routinely used VAP surveillance methodology and the CDC VAP algorithm to twelve months' worth of admissions to two large general intensive care units. We found VAP rates that were similar to previously published research and service evaluations [26–31]. We found the surveillance rate of VAP to be very similar between the two surveillance algorithms. We describe the lack of concordance amongst patients who are diagnosed with VAP, regardless of timing of VAP diagnosis. Concordance between the two algorithms has not been examined extensively in the literature since the introduction of the CDC hierarchical approach but at least one study has previously reported good concordance [23]. We previously reported the lack of concordance between individual VAP occurrences where overlap in time was required [24].

At first glance, the similar rates returned by each surveillance algorithm are reassuring and the surveillance output from either system will provide consistent data, if implemented properly. But the lack of concordance highlights a worrying problem with VAP surveillance and a serious problem with VAP research in general. How can VAP rates be used to measure care quality when there is no inter-algorithm agreement on who does and who does not have VAP? If VAP rates established by surveillance do not accurately represent the clinical burden of VAP and incorrectly estimate the clinical problem, clinicians will be reluctant to use the data as means to drive improvement. The lack of an agreed and effective reference standard for VAP has constrained research in the area and using surveillance techniques as a reference standard should not be advocated.

The CS VAP rate was approximately 5 times the VAP rate identified through surveillance, and 21% of patients "at-risk" of VAP received treatment for VAP. Selecting CS VAP as the reference standard for VAP should not be advocated, as it is known that this rate overestimates VAP [32], and clinicians cannot rely on delayed microbiological confirmation or confirmation to guide antibiotic use, which otherwise guides the surveillance algorithms. We found several VAEs did not progress towards CDC

VAP event because of lack of appropriate microbiological sampling and we consider several cases of true VAP to be missed, and this may account for some of the lack of concordance.

In order to make comparisons across diagnostic groups we defined our own at-risk population. The CDC define the at-risk population as those who receive more than 2 calendar days of mechanical ventilation. The ECDC define their at-risk population as the occurrence of invasive ventilation at any point in the preceding 48 hours. We accepted a pragmatic and consistent risk criterion of mechanical ventilation for 2 consecutive calendar days. This practical solution may put the validity of the conclusions at risk, by overestimating the population at risk according to the CDC definition, and underestimating the population at risk according to the ECDC definition. Furthermore, we adapted the microbiological criteria issued by the CDC in order to accommodate local practices. Whilst most of our laboratory reporting was semi-quantitative, local and national practice for respiratory sample handling (especially non broncho-alveolar lavage) yields some qualitative reporting. Relying on qualitative data for some microbiological samples may add a level of subjectivity to an otherwise objective process.

Conclusion

It will be difficult to overcome the uncertainty around the surveillance of VAP without a robust and reproducible reference standard and consensus regarding the definition of the at-risk population. The CDC method offers the theoretical advantages of avoiding subjective chest x-ray interpretation and potential for automaticity, but the results of this study indicate that at present does not offer any advantage in terms of VAP surveillance for the purpose of measuring VAP to drive improvement in Scotland.

Funding

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Figure 1. Flow chart of total admissions for the study period. CD: calendar day, MV: mechanically ventilated.

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ECDC VAP	VAP diagnosed by ECDC surveillance case definition (notably requires chest radiology changes and can include negative cultures, criteria across span of time; purpose - surveillance)
CDC VAP	VAP diagnosed by CDC surveillance criteria (notably requires perturbation in oxygenation after period of stability, qualifying antibiotic prescription, and positive microbiology; criteria across span of time; purpose - surveillance)
CS VAP	Clinician suspected VAP: The initiation of a new antibiotic for suspected chest infection in a ventilated patient after 2 CD of MV which was not a “replacement” for a pre-existing antibiotic prescription (does not mandate radiology or microbiology results; made at a single point in time; purpose - real time empiric management)

Table I - Brief overview of each study VAP definition. CD: Calendar day, MV: Mechanical Ventilation.

	Admitted >2CD	Ventilated >2CD (At-risk cohort)
Number of patients	1 327	713
Number of ventilated CDs (% of admission CDs)	6 870 (62.2)	6 475 (79.2)
Age Median ($\pm$ IQR)	59 (47-70)	59 (47-69)
Male:Female %	61:39	63:37
APACHE II score Median ($\pm$ IQR)	16 (12-21)	18 (13-23)

Table II - Summary of enrolled cases and population at-risk for Ventilator-associated Pneumonia. CD: Calendar day (any part or whole day period from 0000hrs to 0000hrs). APACHE II: Acute physiology and chronic health evaluation. IQR: Interquartile range.

	Number of events	Number of patients	Events per 1000 ventilation days ($\pm$ 95% CI)	Proportion of at- risk patients (% $\pm$ 95% CI)
CDC VAP	30	29	4.6 (3.1-6.6)	4.0 (2.8 – 5.9)
ECDC VAP	35	32	5.4 (3.8-7.5)	4.5 (3.1-6.4)
CS VAP	160	150	24.7 (21.2-28.9)	21.0 (18.1-24.2)

Table III - Rate of Ventilator-associated pneumonia diagnosis and proportion of at-risk patients. CDC VAP: Ventilator-associated pneumonia by CDC surveillance definition. ECDC VAP: Ventilator-associated pneumonia by ECDC surveillance definition. CS VAP: Clinician suspected ventilator-associated pneumonia. CI: Confidence Interval.

	Total at risk cohort	CDC VAP	ECDC VAP	CS VAP	p
Age	59	58.0	49.5	56.0	0.1205 ^a
Median (±IQR)	(47.0-69.0)	(37.0-70.0)	(36.0-63.0)	(44.3-68.0)	
Male:Female	452:261	25:4	27:5	99:51	0.0191 ^b
n (%)	(63.4:36.6)	(86.2:13.8)	(84.4:15.6)	(66.0:34.0)	
Apache score	18	19	17	20	0.2577 ^a
Median (±IQR)	(13-23)	(14.0-23.0)	(13.0-23.3)	(15.0-26.0)	

Table IV - Baseline characteristics of each VAP cohort. ^aKruskal-Wallis test ^bChi-squared test.

Statistical analyses do not include total at risk cohort values. CDC VAP: Ventilator-associated pneumonia by CDC surveillance definition. ECDC VAP: Ventilator-associated pneumonia by ECDC surveillance definition. CS VAP: Clinician suspected ventilator-associated pneumonia. IQR: Inter-quartile range.

		ECDC VAP		
		+	-	
CDC VAP	+	5	24	29
	-	27	657	684
		32	681	
PPA	15.6	Kappa 0.127 (-0.003 to 0.256)		
NPA	92.1			

Table V – Concordance by patient between surveillance algorithms. Kappa: Cohen’s Kappa ($\pm 95\%$ confidence intervals). PPA: Positive percent agreement. NPA: Negative percent agreement. CDC VAP: Ventilator-associated pneumonia by CDC surveillance definition. ECDC VAP: Ventilator-associated pneumonia by ECDC surveillance definition.

	PPA (%)	NPA (%)	Kappa ($\pm$ 95% CI)
CS VAP and ECDC VAP	53.1	80.5	0.122 (0.050 – 0.193)
CS VAP and CDC VAP	58.6	80.6	0.131 (0.059 – 0.202)

Table VI – Concordance amongst patients receiving novel antibiotic courses for suspected ventilator-associated pneumonia or surveillance VAP events. PPA: Positive percent agreement. NPA: Negative percent agreement. CDC VAP: Ventilator-associated pneumonia by CDC surveillance definition. ECDC VAP: Ventilator-associated pneumonia by ECDC surveillance definition. CS VAP: Clinician suspected ventilator-associated pneumonia. CI: Confidence interval.

	Number of events	Number of patients	Events per 1000 ventilation days ($\pm$ 95% CI)	Proportion of at-risk patients (% $\pm$ 95% CI)
VAE	130	124	20.1 (17.0 - 23.8)	17.4 (14.7 - 20.4)
VAC	62	60	9.6 (7.5 - 12.3)	8.4 (6.5 - 10.8)
IVAC	38	38	5.7 (4.3 - 8.1)	5.3 (3.9 - 7.3)
CDC VAP	30	29	4.6 (3.1-6.6)	4.0 (2.8 – 5.9)

Table VII - Incidence of VAEs. VAE: Ventilator associated event. VAC: Ventilator-associated complication. IVAC: Infection related ventilator-associated complication. CDC VAP: Ventilator-associated pneumonia by CDC surveillance definition. CI: Confidence interval.

	Reviewer 1	Reviewer 2
	%	%
True VAP	14.0	15.0
Pulmonary oedema	14.0	10.0
Atelectasis	21.0	17.0
Deterioration of pre-existing condition	27.0	29.0
Inadequate microbiological data to draw further conclusions	14.0	7.0
Other	10.0	22.0

Table VIII – Alternative diagnoses (100 non VAP VAEs were assessed). VAP: Ventilator-associated pneumonia. VAE: Ventilator-associated event.

Criterion	Feature
Radiological	One or, in patients with underlying cardiac or pulmonary disease, two chest x-rays or CT scans with images suggestive of pneumonia.
Systemic. At least one of:	Fever ($>38^{\circ}\text{C}$) Leukopaenia ($<4 \times 10^9/\text{L}$ white cell count) or leukocytosis ($\geq 12 \times 10^9/\text{L}$ white cell count)
Pulmonary. At least one of, or in the absence of supportive microbiological data, at least two of:	New onset of purulent sputum or change in character of sputum. Worsening gas exchange. Cough, or dyspnoea, or tachypnea Suggestive auscultation
An ICU-acquired infection is one that occurs after 48hrs in ICU. For intubation-associated pneumonia, an invasive respiratory device must have been present for at least part of the preceding 48hrs.	
Microbiological category	
PN1	Minimally contaminated lower respiratory tract sample with quantitative culture (10^4 CFU/ml for broncho-alveolar lavage, 10^3 CFU/ml for protected brush samples or distal protected aspirate)
PN2	Non-protected sample (endotracheal aspirate, ETA) with quantitative culture (10^6 CFU/ml)
PN3	Alternative microbiological criteria (e.g. positive blood culture)
PN4	Sputum bacteriology or non-quantitative ETA
PN5	No microbiological documentation

Supplemental Table I - ECDC criteria for ventilator-associated pneumonia. PN = Pneumonia.

Adapted from Pugh et al.[33]

	CDC VAP	ECDC VAP	CS VAP
Organism	n (% of VAP cases)		
No organism	0 (0)	17 (48.5)	129 (80.6)
MSSA	11 (36.7)	6 (17.1)	13 (8.1)
<i>Streptococcus pneumoniae</i>	2 (6.7)	2 (5.7)	3 (1.9)
<i>Enterococcus faecalis</i>	0 (0)	1 (2.9)	0 (0)
<i>Corynebacterium striatum</i>	0 (0)	1 (2.9)	0 (0)
<i>Haemophilus influenzae</i>	5 (16.7)	5 (14.3)	2 (1.3)
<i>Moraxella catarrhalis</i>	1 (3.3)	0 (0)	1 (0.6)
<i>Escherichia coli</i>	3 (10.0)	1 (2.9)	6 (3.8)
<i>Proteus mirabilis</i>	3 (10.0)	0	2 (1.3)
<i>Proteus vulgaris</i>	0 (0)	1 (2.9)	0 (0)
<i>Klebsiella pneumonia</i>	6 (20.0)	0 (0)	0 (0)
<i>Klebsiella oxytoca</i>	2 (6.7)	0 (0)	3 (1.9)
<i>Raoultella ornithinolytica</i>	1 (3.3)	0 (0)	0 (0)
<i>Raoultella planticola</i>	0 (0)	0 (0)	1 (0.6)
<i>Serratia marcescens</i>	1 (3.3)	1 (2.9)	1 (0.6)
<i>Citrobacter koseri</i>	1 (2.5)	0 (0)	2 (1.3)
<i>Morganella morganii</i>	0 (0)	0 (0)	1 (0.6)
<i>Enterobacter aerogenes</i>	1 (3.3)	2 (5.7)	1 (0.6)
<i>Enterobacter cloacae</i>	0 (0)	2 (5.7)	0 (0)
<i>Acinetobacter ursingii</i>	1 (3.3)	1 (2.9)	1 (0.6)
<i>Pseudomonas aeruginosa</i>	1 (3.3)	0 (0)	1 (0.6)
<i>Stenotrophomonas maltophilia</i>	0 (0)	0 (0)	1 (0.6)
Influenza B	1 (3.3)	0 (0)	0 (0)

MSSA: Meticillin sensitive *Staphylococcus aureus*.

Supplemental table II - Microbiology of VAP. Individual VAP events may have had more than one discernible causative organism. Laboratory identifications were by Bruker Maldi-ToF and sensitivity testing by EUCAST methodology. CDC VAP: Ventilator-associated pneumonia by CDC surveillance definition. ECDC VAP: Ventilator-associated pneumonia by ECDC surveillance definition. CS VAP: Clinician suspected ventilator-associated pneumonia.

		ECDC VAP		
		+	-	
CS VAP	+	17	133	150
	-	15	548	563
		32	681	
PPA	53.1	Kappa	0.122 (0.050 – 0.193)	
NPA	80.5			
		CDC VAP		
		+	-	
CS VAP	+	17	133	150
	-	12	551	563
		29	684	
PPA	58.6	Kappa	0.131 (0.059 – 0.202)	
NPA	80.6			
		ECDC VAP		
		+	-	
CS VAPm	+	7	27	34
	-	25	654	679
		32	681	
PPA	21.9	Kappa	0.174 (0.038 – 0.310)	
NPA	96.0			
		CDC VAP		
		+	-	
CS VAPm	+	14	20	34
	-	15	664	679
		29	684	
PPA	48.3	Kappa	0.419 (0.261 – 0.576)	
NPA	97.1			

Supplemental table III – Concordance amongst patients receiving novel antibiotic courses for suspected ventilator-associated pneumonia (CS VAP) or surveillance VAP events. CS VAPm: CS VAP where microbiological samples were sent for analysis with 5 calendar days of the initiation of antibiotics. There is no perfect reference standard amongst the available data so concordance is expressed as positive percent agreement (PPA, analogous to sensitivity if a perfect reference standard were available) and negative percent agreement (NPA, analogous to specificity if a perfect reference standard were available)[25]. Kappa: Cohen's Kappa ($\pm 95\%$ confidence intervals). CDC VAP: Ventilator-associated pneumonia by CDC surveillance

definition. ECDC VAP: Ventilator-associated pneumonia by ECDC surveillance definition. CS
VAP: Clinician suspected ventilator-associated pneumonia.

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		Reviewer 1		
		+	-	
Reviewer 2	+	8	7	15
	-	6	79	85
		14	86	
PPA	57.1	Kappa 0.476 (0.232 - 0.719)		
NPA	91.9			

Supplemental Table IV – Concordance between independent reviewers for True VAP diagnoses. PPA: Positive percent agreement. NPA: Negative percent agreement. Kappa: Cohen’s Kappa.

Supplemental Figure 1 – An overview of hierarchical diagnosis of ventilator-associated events (January 2015, updated April 2015). Adapted from <https://www.cdc.gov/nhsn/acute-care-hospital/vae/index.html>.

figure 1