Is a ventilator-associated pneumonia rate of zero really possible?

Michael Klompas

**Purpose of review**
The increasing number of hospitals reporting ventilator-associated pneumonia (VAP) rates at or close to zero begs the question of whether zero should become the national benchmark for VAP. This article explores the significance of very low VAP rates, reviews differences in surveillance and clinical rates, proposes reasons for their discrepancies, and suggests possible objective alternatives for surveillance.

**Recent findings**
Surveillance rates of VAP are decreasing, whereas clinical diagnoses and antibiotic prescribing remain prevalent. This growing discrepancy reflects the lack of objective and definitive signs to diagnose VAP. External reporting pressures may be encouraging stricter interpretation of subjective signs and other surveillance initiatives that can artifactually lower rates. It is impossible to disentangle the relative contribution of care improvements versus surveillance effects to currently observed low VAP rates.

**Summary**
The increasing mismatch between surveillance rates and clinical diagnoses limits the utility of official VAP rates to estimate disease burden and guide quality improvement. Advocates are advised to consider objective alternatives such as average duration of mechanical ventilation, length of stay, mortality, and antibiotic prescribing. Emerging surveillance definitions that use more objective criteria may better reflect and inform future clinical practice.

**Keywords**
public reporting, quality improvement, surveillance, ventilator-associated pneumonia

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**INTRODUCTION**

Policy and quality initiatives targeting ventilator-associated pneumonia (VAP) continue to blossom. The Joint Commission has proposed making VAP prevention a national patient safety goal. The Centers for Medicare and Medicaid Services are considering making VAP a nonreimbursable event [1]. A few states already require hospitals to report VAP and others are expected to follow [2]. Over 2000 US hospitals have instituted VAP prevention bundles under the auspices of the Institute for Healthcare Improvement’s 100,000 and 5 Million Lives Campaigns [3].

These initiatives appear to be bearing fruit. The literature is now rich with reports of dramatic, sustained decreases in VAP rates attributed to ventilator bundles, including successful statewide initiatives in Rhode Island and Michigan [4–8,9,10]. A number of hospitals have reported VAP rates of zero [11]. Figures from the Centers for Disease Control and Prevention (CDC)’s National Healthcare Safety Network affirm the striking decline in VAP (Fig. 1).

Between 2002 and 2009, the mean VAP rate amongst medical ICUs reporting to CDC dropped from 4.9 to 1.4 events per 1000 ventilator days, and from 9.3 to 3.8 events per 1000 ventilator days in surgical ICUs [12,13]. Remarkably, the 25th percentile VAP rate for most ICU types is now zero [13].

These reports challenge us to consider whether VAP can be eliminated altogether and beg the question of whether a VAP rate of zero ought to be the national benchmark. Notwithstanding these accounts, however, data suggest that clinicians continue to routinely diagnose and treat VAP. VAP rates of zero appear to attest more to the growing divide...
between surveillance and clinical VAP rates than to the feasibility of eliminating VAP. This paper reviews the increasing discrepancy between surveillance and clinical VAP rates, suggests possible reasons, and considers alternative surveillance strategies that may better reflect the clinical burden of disease.

**DISCREPANCIES BETWEEN ‘OFFICIAL’ AND CLINICAL VENTILATOR-ASSOCIATED PNEUMONIA RATES**

Surveillance rates based upon the CDC’s National Healthcare Safety Network definitions for VAP (Table 1) need to be interpreted with caution. The sensitivity and specificity of these definitions have long been questioned. CDC’s own validation studies conducted in the early 1990s found that surveyors missed approximately 32% of VAP cases [14]. The German national nosocomial surveillance system completed a similar validation study of CDC definitions in the early 2000s with almost identical results [15].

More recent studies suggest that surveillance may now be missing even more cases. Intensivists and infection preventionists covering a surgical ICU in Tennessee prospectively and independently surveyed their patients for VAP over a 5-month period using CDC definitions [16]. Amongst 133 patients...
ventilated for more than 48 h, infection preventionists found 11 cases (8.3%) whereas the intensivists found 38 cases (28.5%), a more than three-fold difference.

Comparing CDC surveillance to slightly different surveillance definitions magnifies the discrepancy further. Skrupky et al. [17] prospectively compared CDC VAP rates with American College of Chest Physicians (ACCP) rates. The ACCP definition requires new or progressive consolidation on chest radiographs and at least two of the following: fever, abnormal white blood cell count, and/or purulent secretions [18]. Amongst 2060 patients ventilated for more than 24 h, the infection control team identified 12 cases of VAP using CDC criteria (1.2 cases per 1000 ventilator days), whereas ACCP criteria identified 83 cases (8.5 cases per 1000 ventilator days).

The discrepancy between ‘official’ surveillance rates and purely clinical diagnoses of VAP is even more striking. Koulenti et al. [19], for example, prospectively surveyed pneumonia diagnosis practices in nine European countries. They reported a VAP incidence of 18.3 events per 1000 ventilator days, whereas ACCP criteria identified 83 cases (8.5 cases per 1000 ventilator days).

Table 1. Centers for Disease Control and Prevention National Healthcare Safety Network clinical definition for ventilator-associated pneumonia (PNU1)

<table>
<thead>
<tr>
<th>Two or more serial radiographs with at least one of the following</th>
<th>One of the following</th>
<th>Two of the following</th>
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<tbody>
<tr>
<td>New or progressive and persistent infiltrate</td>
<td>Fever (&gt;38 °C or &gt;100.4 °F)</td>
<td>New onset of purulent sputum or change in character of sputum or increased respiratory secretions or increased suctioning requirements</td>
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<tr>
<td>Consolidation</td>
<td>Leukopenia (&lt;4000 WBC/μl) or leukocytosis (&gt;12 000 WBC/μl)</td>
<td>New onset or worsening cough, or dyspnea, or tachypnea</td>
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<tr>
<td>Cavitation</td>
<td>For adults ≥70 years old, altered mental status with no other recognized cause</td>
<td>Roles or bronchial breath sounds</td>
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<td></td>
<td></td>
<td>Worsening gas exchange (e.g. oxygen desaturations, increased oxygen requirements, or increased ventilator demand)</td>
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WBC, White blood cell.

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Some degree of difference between surveillance definitions and clinical diagnoses of healthcare-associated infections is expected insofar as they are different tools with different purposes. Surveillance definitions are designed to measure population disease burden, compare disease frequencies between different institutions, and assess for changes in disease frequency over time. To serve this role, surveillance definitions are designed to maximize objectivity and positive predictive value, often at the cost of sensitivity. Clinical diagnoses, by contrast, are primarily intended to guide patient management. In critically ill patients small delays in appropriate therapy increase mortality risk, hence clinical management favors sensitivity over specificity (intensivists rate their certainty of pneumonia as ‘high probability’ only 60% of the time) [19]. Nonetheless, the differences between clinical and surveillance rates have become so pronounced as to challenge their utility. There has to be some correspondence between surveillance and clinical definitions if surveillance is to meaningfully reflect and inform clinical practice.
Respiratory infections

WHY THE DISCREPANCY?
Discrepancies in VAP surveillance and diagnoses are due to the inaccuracy and subjectivity of signs used to diagnose VAP. There is poor correspondence between clinical signs and histological pneumonia. Tejerina et al. [22] affirmed this in a retrospective study of 253 autopsies on recently ventilated patients. Two intensivists independently reviewed each patient's records and applied three different definitions of pneumonia: a loose definition (chest radiograph infiltrate and at least two of abnormal temperature, abnormal white blood cell count, and purulent sputum), a rigorous definition (chest radiograph infiltrate and all three of abnormal temperature, abnormal white blood cell count, and purulent sputum), or a clinical pulmonary infection score (CPIS) of greater than six. Overall, 142 of the 253 patients had histological evidence of pneumonia. All three definitions performed poorly: 163 patients fulfilled the loose definition (sensitivity 65%, specificity 36%), 32 patients met the rigorous definition (sensitivity 16%, specificity 91%), and 109 had a CPIS score greater than six (sensitivity 46%, specificity 60%).

Inaccuracy is compounded by subjectivity. The CDC definition requires thoughtful judgment for criteria such as 'worsening gas exchange,' 'change in the character of sputum,' and 'new or progressive and persistent infiltrates.' Not surprisingly, different observers reach different conclusions. In a study of fifty ventilated patients with respiratory deterioration, there was a two-fold difference in VAP rates between three infection control surveyors: 11, 15, or 20 patients were labeled with VAP depending upon the observer. There was consensus on the presence of VAP in only seven patients [23]. Interpretation of chest radiographs is particularly contentious. In an autopsy study by Tejerina et al. [22], the kappa value for agreement between the two intensivists assessing radiographs for pneumonia was 0.47.

The linking of hospitals' VAP rates to their reputation, accreditation, and compensation has created powerful explicit and implicit incentives to lower VAP rates. VAP signs' subjectivity makes surveillance vulnerable to subconscious bias. There is also speculation that patients with some clinical criteria for VAP are being diagnosed with tracheobronchitis or 'sepsis syndrome' instead of VAP and hence excluded from VAP counts [24]. It is impossible to know how much the drop in VAP rates is due to stricter interpretation of subjective clinical signs and shifts to alternative diagnoses versus meaningful improvements in patient care.

Ironically, stricter interpretations of clinical signs and radiographs may be part of hospitals' well intentioned efforts to increase the rigor of VAP surveillance. Other well intentioned efforts to make VAP surveillance ‘more reliable’ can also misleadingly lower VAP rates. Examples include requiring consensus between multiple infection preventionists, seeking endorsement of intensivists before ‘certifying’ cases, inflating the denominator with postoperative patients, requiring positive bronchoalveolar lavage (BAL) cultures to diagnose VAP, and setting quantitative growth thresholds for specimens [25].

Requiring positive BAL cultures is particularly alluring as the test is ostensibly objective and presumed to be accurate. In fact, the primary effect of BAL is to lower event rates. Riaz et al. [26] demonstrated this in a study of 319 consecutive patients clinically suspected of VAP. Case yield dropped progressively depending upon culture criteria from 319 cases (clinical suspicion alone) to 235 cases (any culture positive) to 84 cases (10^5 colony forming units/ml on BAL). There is little evidence that quantitative or qualitative cultures are more accurate than clinical diagnoses. Instead, clinical diagnosis and quantitative culture diagnosis rest on a continuum of sensitivity and specificity – setting quantitative thresholds increases specificity but at substantial cost in sensitivity [22,27]. The exact choice of quantitative threshold is arbitrary; accuracy can be compromised by specimen contamination from the endotracheal tube or oropharynx, sampling the wrong lung segment, prior antibiotic exposure, low inoculum, and operator error [28]. Most importantly, routine BAL for diagnosis has not been shown to improve outcomes compared with endotracheal aspirates alone, and ventilator lengths of stay and mortality tend to be as bad or worse for culture-negative patients as culture-positive patients [16,29–31].

Given the VAP definition's subjectivity and high susceptibility to bias, it seems prudent to focus on concrete outcomes instead of VAP to evaluate new prevention measures and quality improvement initiatives. Duration of mechanical ventilation, hospital length of stay, mortality, and antibiotic dispensing are much more concrete and meaningful metrics [32,33–35].

IS A VENTILATOR-ASSOCIATED PNEUMONIA RATE OF ZERO POSSIBLE?
Enough hospitals have now reported sustained VAP rates of zero to make it clear that zero is possible using the current surveillance definition. The definition's subjectivity, however, makes it impossible to disentangle the relative contributions of improved care versus surveillance artifacts to current low rates. The large differences between official VAP
surveillance figures and independent validations using similar or identical definitions suggest that surveillance artifact is a significant contributor to low official rates. It may well be possible to eliminate VAP but the current surveillance definition is not a reliable indicator.

Recent reports have sounded additional notes of caution around zero VAP rates. Wahl et al. [36] reviewed 105 surgery and trauma patients who underwent BAL within 48 h of intubation. They found that 90% of specimens had some growth and 58% had at least 10⁴ colony forming units/ml. Patients subsequently diagnosed with VAP often grew the same organisms as were present on the initial BAL. On the basis of this, they proposed that many events labeled as VAP are present or incubating on admission and hence are not preventable.

Others have argued that VAP cannot be eliminated because they have had persistent VAP cases despite aggressive use of prevention bundles [6–8]. This argument is unresolved at present, as no organization has yet implemented a truly comprehensive bundle [37]. In addition, the true impact of prevention bundles remains elusive as none to date has been tested prospectively in a randomized, controlled trial. Bundles have only been assessed in before-after studies that are prone to bias and rarely adjust for secular trends in VAP rates [37].

Finally, Sundar et al. [6] warn against comparing large hospitals’ measurable VAP rates with smaller hospitals’ zero VAP rates. They described a community hospital and a referral hospital belonging to a single organization. Both were served by a single group of intensivists, had similar nursing and respiratory therapy staffing patterns, and implemented similar VAP prevention programs. Despite the parallels between the two hospitals, the community hospital had a VAP rate of 0 and the referral center a VAP rate of 2.4 per 1000 ventilator days. The authors suggested that the referral hospital’s measurable VAP rate despite equal attention to VAP prevention underscores the inherent unsuitability of comparing very different institutions. Blot et al. [38] argue that it is unrealistic to suggest that VAP can be eliminated in the most complex ventilated populations. Broad confidence limits around small hospitals’ VAP rates due to small numbers of cases and patients at risk also compromise the validity of comparing small hospitals with larger hospitals.

**OBJECTIVE SURVEILLANCE DEFINITIONS**

New surveillance definitions for VAP that better mirror clinical practice and are less subject to bias are clearly needed. Researchers affiliated with CDC’s Prevention Epicenters have proposed objective modifications to the surveillance definition to decrease subjectivity, increase efficiency, and facilitate the use of electronic data for surveillance. They focused the definition down to its core components (worsening oxygenation, systemic illness, purulent sputum, and new infiltrates) and set quantitative criteria wherever possible (Table 2). Worsening oxygenation was defined as a sustained rise in the daily minimum fraction of inspired oxygen or positive end-expiratory pressure after a period of stable or decreasing settings. Purulent sputum was defined as at least 25 neutrophils per low power field on Gram stain of pulmonary secretions.

This ‘streamlined’ definition was retrospectively compared with standard surveillance amongst

### Table 2. The Prevention Epicenters’ streamlined definition for ventilator-associated pneumonia [39]

<table>
<thead>
<tr>
<th>At least one of the following</th>
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<th>Both of the following</th>
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<td>New or progressive and persistent infiltrate</td>
<td>Fever (≥38 °C or ≥100.4 °F)</td>
<td>≥25 neutrophils per low power field on Gram stain of endotracheal aspirate or bronchoalveolar lavage specimen</td>
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<td>Consolidation</td>
<td>Leukopenia (&lt;4000 WBC/μl) or leukocytosis (&gt;12 000 WBC/μl)</td>
<td>≥2 days of stable or decreasing daily minimum positive end-expiratory pressure followed by a rise in daily minimum positive end-expiratory pressure of ≥2.5 cmH₂O, sustained for ≥2 calendar days OR ≥2 days of stable or decreasing daily minimum fraction of inspired oxygen followed by a rise in daily minimum fraction of inspired oxygen of ≥0.15 points, sustained for ≥2 calendar days</td>
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WBC, White blood cell.
Respiratory infections

600 medical and surgical patients in three academic hospitals. Both the streamlined definition and the conventional definition predicted excess ventilator days equally well but neither was associated with increased mortality. The streamlined definition was faster to apply (mean 3.5 versus 39 min) and more reproducible (kappa 0.79 versus 0.45) [39*].

Notwithstanding improved efficiency and objectivity, the streamlined definition does little to improve the accuracy of VAP diagnosis. Little can be done about this at present, however, given the inherent limitations of all clinical signs for the diagnosis of VAP. Until new diagnostic modalities emerge, we should consider switching the focus of surveillance from pneumonia in particular to complications of mechanical ventilation in general. This substantially simplifies surveillance, provides a more honest description of what can and cannot be discerned at the bedside using surveillance definitions, and shifts the onus of prevention from pneumonia alone to all complications of mechanical ventilation.

Prevention Epicenter researchers proposed a candidate definition for ventilator-associated complications (VAC) solely upon worsening ventilator settings after a period of stability or improvement. The Prevention Epicenters’ proposed definition for VAC is as follows [40*]:

1. At least 2 days of stable or decreasing daily minimum positive end-expiratory pressure followed by a rise in daily minimum positive end-expiratory pressure of at least 2.5 cmH\textsubscript{2}O, sustained for at least 2 calendar days; or

2. At least 2 days of stable or decreasing daily minimum fraction of inspired oxygen followed by a rise in daily minimum fraction of inspired oxygen of at least 0.15 points, sustained for at least 2 calendar days.

Chest radiographs were purposefully excluded from the definition due to their complexity, subjectivity, and lack of specificity. In a retrospective comparison of VAC versus conventional VAP surveillance in three hospitals, there were 8.8 VAPs and 21.2 VACs per 1000 ventilator days. On qualitative analysis, both VAP and VAC were attributable to proportionately similar rates of pneumonia, pulmonary edema, acute respiratory distress syndrome, and atelectasis. Both definitions predicted excess ventilator days, intensive care days, and hospital days equally well but VAC was associated with increased mortality, whereas VAP was not. VAC assessment was faster (mean 1.8 min versus 39 min per patient) [40**].

CONCLUSION

Objective surveillance definitions have the potential to return VAP surveillance to clinical relevance. Current rates reported using the National Healthcare Safety Network definition are uninterpretable given the definition’s subjectivity and surveyors’ susceptibility to external pressures to report low rates. A VAP rate of zero is clearly feasible with the current definition but its significance is unclear. Objective definitions are less prone to bias and, therefore, more likely to be useful tools to monitor quality of care for ventilated patients, identify possible areas for improvement, and assess the impact of prevention initiatives. Further studies are now needed to determine whether objective definitions can fulfill these roles. If ultimately successful, we will be in a better position to assess whether an optimized bundle of prevention measures can indeed eliminate VAP.

Acknowledgements

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Conflicts of interest

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REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

** of special interest

* of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).


Describes the importance of integrating bundle adherence into routine workflows to avoid checklist burnout and rebounding VAP rates.


Follow-up report on the long-term impact of a VAP prevention program in Thailand. Uses a multivariate analysis to suggest that residual cases of VAP may be due to nonmodifiable host factors (such as neurologic disease) and, therefore, VAP rates of zero might not be realistic.
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13. Prospective comparison of 5 months of VAP surveillance by surgical intensivists versus infection preventionists in a surgical ICU using CDC definitions. Intensivists found much higher rates of VAP than infection preventionists.


22. Comparison on how changes in surveillance methodology can artifactually lower observed VAP rates.


