Prevention of VAP: Is Zero Rate Possible?

Stijn Blot, MNSc, PhD\textsuperscript{a}, Thiago Lisboa, MD\textsuperscript{b}, Roser Angles, MD, PhD\textsuperscript{c}, Jordi Rello, MD, PhD\textsuperscript{d,*}

Patients in intensive care units (ICUs) are identified as targets for quality-of-care and patient-safety improvement strategies. Approximately 1.7 errors per patient occur in the ICU daily, and nearly half of these errors were attributable to the physician and nursing staff.\textsuperscript{1} The cost of adverse events in the ICU is substantial, not only because almost 150,000 life-threatening errors occur annually in teaching hospital ICUs\textsuperscript{2} but also because the economic cost of 1 adverse event is approximately $4000.\textsuperscript{3}

Critically ill patients are at high risk for complications because of the complex and invasive nature of critical care treatments and procedures, the severity of their medical conditions, and the use of immunosuppressive drugs. Reports estimate that there were an average of 178 activities per patient per day in the ICU, and the rate for all adverse events was 80.5 per 1000 patient days, but preventable in only 36.2 per 1000 patient days.\textsuperscript{4} The factors that were associated with elevated odds for adverse events were any organ failure, a higher intensity in level of care, and time of exposure.\textsuperscript{4}

Many ICU patients have severe acute and chronic illnesses that may be reversed.\textsuperscript{5,6} This subset of patients is also at a high risk for infection or medical errors that are current targets for quality-improvement strategies.\textsuperscript{7–9}

The World Health Organization defined patient safety as reducing the risk of unnecessary harm associated with health care to an acceptable minimum. An acceptable minimum refers to the collective notions of given current knowledge, resources available, and the context in which care was delivered weighted against the risk of nontreatment or other treatment.\textsuperscript{10}

A safer environment is generated by the prevention of errors and their adverse effects.\textsuperscript{11,12} Acknowledging the potential for errors and creating strategies for reducing errors at every stage of clinical practice are fundamental in the safety-promotion process.\textsuperscript{13,14} Its importance is recognized in the Institute of Medicine report “To Err is Human,”\textsuperscript{15} which provides relevant data regarding quality of care and patient safety in the United States.

Strategies to improve outcomes in ICU patients include safety tools, such as a rapid response team, daily goal sheet, checklists, and the development of care bundles with implementation measures. The most important change, however, is cultural, emphasizing that errors should be considered a failed system rather than a people failure. Harm is often the result of a cascade of broken systems.\textsuperscript{16} A safety program in critical care should provide a practical and goal-oriented...
set of tools to implement a culture of safety to prevent errors and their consequences.\textsuperscript{13}

Shulman and Ost\textsuperscript{17} discussed the connection between patient safety concepts and infection prevention and how measurable interventions impact patient safety and improve the quality of care and patient outcomes. Although lowering the incidence of nosocomial infections would be an important quality-improvement measure and improve patient safety, misleading interpretations of this process may confound concepts, such as safety-related adverse events and unavoidable complications of critical care. Furthermore, an appropriate interpretation of quality-improvement strategies relies on the ability to measure their effects. Unfortunately, the ability to measure and evaluate the effect of interventions related to health care–associated infection prevention, and more specifically ventilator-associated pneumonia (VAP), is severely limited by the lack of diagnostic sensitivity and specificity.

Significant questions and concerns have been raised regarding reporting rates of nosocomial infections: Are all nosocomial infections an adverse event and a medical error? Are all of these infections preventable? Patient safety strategies are clearly able to reduce the risk of infectious complication, but is a zero-infection rate a feasible endpoint for VAP and other nosocomial infections? Are predefined thresholds of VAP rates and other infections an appropriate quality-of-care indicator?

Infection-prevention measures, and specifically VAP prevention, have been proposed as quality-of-care indicators for ICU patients. This article reviews recent evidence regarding ICU safety promotion and the adequacy of this approach.

**INFECTION CONTROL IN THE ICU: THE ROLE OF CARE BUNDLES AND THEIR IMPACT ON PATIENT SAFETY**

Nosocomial infections are the most common complications affecting hospitalized patients and have significant morbidity and mortality.\textsuperscript{18} VAP is the most frequent and costly infectious complication in ICU patients, which has been estimated to cost at least $40,000 per patient as estimated in 3 matched cohort studies.\textsuperscript{19} Currently, infection control is a critical element of patient care and many nosocomial infection episodes are considered potentially preventable. The idea that most infections are unavoidable and some could be preventable has been changed to “all infections are potentially preventable unless proven otherwise.”\textsuperscript{20} Unfortunately, valid data on the proportion of unpreventable episodes in different ICU settings are not available, although it is clear that some types of infection, such as catheter-associated bloodstream infections, are easier to prevent than other infections, such as pneumonia.\textsuperscript{21}

Using a system-approach model to evaluate factors that contribute to infection development might allow for better identification of risk groups and potential interventions for prevention.\textsuperscript{20,22} Jain and colleagues\textsuperscript{23} used this strategy to reduce nosocomial infection rates. A set of 4 interventions were employed to obtain improvement: (1) multidisciplinary rounds; (2) daily reevaluation of the indication for continuing critical care; (3) using care bundles for VAP, urinary tract infection, and catheter-related bloodstream infection; and (4) change in safety culture (although this effect could not be accurately measured). These process interventions resulted in a 58% reduction of VAP incidence, a 48% decrease in catheter-related bloodstream infections, and a 37% reduction in the incidence of urinary tract infections. Although it was not possible to identify the most relevant interventions in this study, the change in the perceptions of safety or culture change appeared to be a key factor for success. Yet, patient safety culture is a complex concept that has been defined as “the product of individual and group values, attitudes, perceptions, competencies, and patterns of behavior that determine the commitment to, and the style and proficiency of, an organization’s health and safety management that include personnel’s safety attitudes, beliefs and knowledge.”\textsuperscript{24} Important aspects were the conditions that facilitate implementation and adherence to the recommended protocols and processes of care; identifying evidenced-based interventions that improve the outcome; selecting the interventions that impact outcomes; developing measures to evaluate reliability; measuring the baseline situation; ensuring that patients received evidence-based interventions; and a combination of reminders and continuing education, augmented with an audit and feedback system.\textsuperscript{25,26}

The factors that are important in this process are awareness of the problem, understanding the pathogenesis, and knowledge of evidence-based guidelines. Lack of knowledge is commonly recognized as a crucial hurdle to adhering to the guidelines. Surveys evaluating the knowledge of ICU nurses about evidence-based guidelines for the prevention of VAP found overall poor test scores, suggesting that low knowledge levels could contribute to limited adherence to infection-prevention guidelines.\textsuperscript{27–29} In addition to basic insights and knowledge, skills, attitudes, and
social and organizational context will determine the level of success in reducing infection rates. Because it is multifactorial the result of many factors, overall adherence to evidence-based interventions is highly variable and often at a disappointing level.\textsuperscript{30} It is clear that a new paradigm of nosocomial infection prevention should be based on a multidisciplinary and evidence-based effort with an agenda focused on patient safety promotion and quality improvement. A cornerstone of this approach is the Institute for Health Improvement (IHI) initiative, which incorporates a limited number of effective interventions into a bundle that is both conceptually simple and feasible.\textsuperscript{31}

Prevention strategies based in care bundles aim to translate the best available evidence into clinical practice by allowing for a more uniform management of patients. By comparison, implementation of individual interventions might improve patient care, but the implementation of several simple measures simultaneously, as a bundle, has a greater likelihood of improving outcome.\textsuperscript{32,33} This approach aims to facilitate the implementation of best practice, ensuring a uniform application of the procedures and therapies to all patients. Catheter-related bloodstream infection and VAP are 2 examples of the successful application of prevention and care bundle in the ICU setting.

**VENTILATOR-ASSOCIATED PNEUMONIA**

VAP is the most common nosocomial infection in ICUs and represents 25% of all ICU infections.\textsuperscript{34,35} VAP cost is reported to be as high as $10 billion per year.\textsuperscript{36} While the attributable mortality of VAP is controversial, it certainly does prolong mechanical ventilation and the length of stay in the ICU.\textsuperscript{36,37} Because of its importance and impact on morbidity in ICU patients, VAP prevention was included in the IHI campaign to save 100,000 lives.\textsuperscript{31} This campaign is expected to save 100,000 lives through the implementation of safety measures, specifically through the use of the ventilator bundle to reduce VAP incidence. The bundle included 4 simple measures (Box 1). Although not all interventions could directly affect VAP pathogenesis (eg, deep vein thrombosis prophylaxis), a significant reduction in VAP incidence was reported in most centers participating in the campaign.\textsuperscript{38–40}

Although several studies described numerous effective interventions for VAP prevention, most of them are not routinely performed. Available evidence suggests that VAP prevention has not translated to clinical practice. What is the cause of this gap between best evidence and practice? In a systematic review,\textsuperscript{41} Collard and colleagues identified the following effective interventions to prevent VAP: a semirecumbent position, use of sucralfate in a low-moderate risk for gastrointestinal bleeding prophylaxis, subglottic secretions drainage, and the use of kinetic beds. However, implementation of these interventions has not been uniform. Causes of medical and nursing staff non-adherence have been assessed,\textsuperscript{42–44} suggesting a need for educational interventions that stimulate adoption of these effective measures.

Salahuddin and colleagues\textsuperscript{45} found a 51% reduction in VAP incidence through an educational program for VAP prevention. The program was a selection of recommended VAP prevention measures, and its benefit was persistent for 12 months. Educational strategies for reinforcement of prevention practices may be effective to reduce VAP rates. Use of care bundles to improve compliance with prevention measures was also studied in VAP. Resar and colleagues\textsuperscript{32} found a reduction of 45% in VAP incidence with the implementation of a care bundle for VAP prevention. Moreover, reduction in VAP incidence was correlated to the degree of adherence to the bundle. Again, it is important to note that successful compliance with infection-control bundles will depend on having sufficient and well-educated staffing in the ICU. Moreover, Crunden and colleagues\textsuperscript{46} found a significant reduction in ICU length of stay (LOS) from 13.7 days to 8.36 days, and a reduction in ventilation duration from 10.8 to 6.1 days. Interestingly, Cocanour and colleagues\textsuperscript{40} demonstrated in trauma patients that isolated implementation of the ventilator bundle was not enough, and VAP rates decreased only when compliance with the ventilator bundle was improved. This finding, however, underscores the need for an approach that goes beyond the sum of the individual items of the VAP bundle, but
also takes into account targeted education, attitudes, and optimizing the organizational context. Additional support is needed to obtain true quality improvement, especially in care aspects that are perceived as unpleasant and difficult, such as oral hygiene in intubated patients.\textsuperscript{44} Further studies should also evaluate other endpoints, such as antibiotic use, that should decline if VAP is being prevented.

Although care-bundle implementation appears to be associated with the successful reduction in VAP rates, there should be a cautious interpretation of their benefit. Misinterpretation of prevention study results and of the pathophysiology of VAP may lead to an erroneous idea that a zero-VAP rate is feasible. Studies on the prevention by care bundles are encouraging. Yet, pathophysiologic aspects of VAP, such as differences between early and late-VAP episodes,\textsuperscript{35,47,48} and risk factors that differ between trauma and medical patients,\textsuperscript{40,49} were not considered in the current version of bundles which limit their ability to prevent all episodes of VAP. In addition, the inaccuracy of VAP diagnoses limits the interpretation of these data, as discussed later. Appropriate staffing levels may be a major influence on the LOS in the ICU, duration of mechanical ventilation, and the development of VAP, presumably because of the maintenance of infection-control standards.\textsuperscript{50–53} Lapses in basic infection-control measures, such as hand washing, are more likely with increased workloads for nurses and increased reliance on less-trained health care personnel to deliver care.\textsuperscript{54,55} Educational reinforcement and opportunities for ICU staff to participate in mandatory training aimed at hospital-acquired pneumonia/ VAP prevention is also important to improve safety and to optimize VAP prevention.\textsuperscript{39,56}

A last important aspect for the implementation of a care bundle is that there be a consensus about which items to include in the bundle. As long as a critical number of staff members remains reluctant to implement some preventive measure, successful implementation and favorable adherence is highly unlikely. Preventive measures that appear to be less labor intensive, for example semirecumbent positioning, or the use of innovative devices, such as endotracheal tubes with an ultrathin\textsuperscript{57} tapered shape cuff,\textsuperscript{58} may be chosen over a strict oral hygiene protocol, which can be perceived as time consuming. Throughout the democratic process to develop a care bundle, the available evidence of the individual preventive measures must remain a major consideration, despite the differences in evidence available for some measures,\textsuperscript{59} as well as ongoing controversies about the efficacy of some prevention efforts.\textsuperscript{60}

### SHOULD VAP BE USED AS A QUALITY INDICATOR FOR SAFETY IN THE ICU?

Initiatives to stop paying hospitals for care made necessary by preventable complications,\textsuperscript{61} including nosocomial infections, may have both desirable and unintended consequences.\textsuperscript{62} Preventable complications, such as vascular-catheter–associated infections, will no longer be reimbursed by Medicare in the United States. Other ICU infections, such as VAP, may follow.\textsuperscript{62} The plan has been criticized for penalizing hospitals that admit frail and other high-risk patients.\textsuperscript{63} In addition, an undesirable effect of the plan might be to encourage institutions to underreport nosocomial infections. Linking accreditation and compensation to the incidence of VAP is problematic because there is a considerable uncertainty in making a VAP diagnosis. Controversies regarding this issue are summarized in Box 2.

Physicians’ ability to diagnose VAP is often poor, and several pulmonary diseases may present with similar clinical signs. Clinical signs of pneumonia (fever, pulmonary infiltrates, and purulent pulmonary secretion) present in ICU patients are caused by VAP in only 30% to 40%.\textsuperscript{64,65} Using a quantitative culture of respiratory samples has been advocated as a measure to improve the accuracy of VAP diagnosis. However, no study to date has demonstrated any effect on reducing antibiotic use, rates of superinfection, or improvement in outcomes associated with such a diagnostic strategy.

In addition, the presence of positive cultures of respiratory secretions is only moderately specific for VAP.\textsuperscript{64,66} In fact, some of these patients may have purulent tracheobronchitis or ventilator-associated tracheobronchitis (VAT), which is defined as the presence of clinical signs or symptoms of infection and purulent sputum and an endotracheal aspirate with a pathogen having moderate to heavy growth on semiquantitative culture or greater than $10^{6}$ organisms/mL on

### Box 2

**Controversies and issues in using VAP as a quality indicator in ICU**

- Poor ability to definitely diagnose VAP
- Absence of a gold standard for VAP diagnosis
- Differences between surveillance and clinical definitions for VAP
- Case-mix variation in different institutions
- Risk of underreporting of VAP episodes because of the pressure of public reporting
quantitative culture, but no new infiltrate on a chest radiograph.\textsuperscript{67,68} VAT may be a precursor to VAP, and antibiotic treatment appears to prevent VAP and improve patient outcomes.

Interpretation of chest infiltrates on chest radiographs is difficult and may be improved with the use of computed tomography (CT) lung scans, but availability of CT scans for these patients may be limited and difficult to carry out. Furthermore, there can still be infiltrates suggestive of VAP that are difficult to confirm or to find consensus among blinded readers, especially in patients with prior diffuse infiltrates, pleural effusions, prior surgery or chest trauma, congestive heart failure, or adult respiratory distress syndrome (ARDS).\textsuperscript{69} In a recent study, the accuracy of diagnostic criteria for VAP compromises reproducibility and makes the comparison of VAP rates among different ICUs impossible to interpret.

A clinical definition of VAP, based on clinical and microbiologic data, would probably be the most reliable approach; however, heterogeneity in evaluation of these criteria represents an important limitation for the interinstitutional benchmarking of quality based on VAP rates. Perhaps a uniform interhospital surveillance system would allow a more accurate comparison of VAP rates.\textsuperscript{72} By doing so, the denominator problem of reporting VAP rates can be overcome. In a medical ICU, the influence of the denominator used to calculate the occurrence rate of VAP was evaluated.\textsuperscript{74} In a cohort of 106 patients with VAP, depending on the denominator used, the occurrence rate changed from 22.8 VAPs per 1000 ICU days (95% confidence interval [CI] 18.7–27.6), to more than 35.7 VAPs per 1000 ventilator days (95% CI 29.2–43.2), to 44.0 VAPs per 1000 ventilator days at risk (95% CI 36.0–53.2). From this information, it is clear that not only uniform definitions but also uniform reporting of surveillance results are of the utmost important.

Moreover, Hurley\textsuperscript{75} described the effect of design factors on VAP incidence reported in prevention studies and found a high variation in control groups in different studies. Almost 30% of control groups, in antimicrobial methods for VAP prevention studies, were classified as having a high outlier incidence of VAP. Additionally, as pointed by Klompas and colleagues,\textsuperscript{76} if VAP rates are used in determining hospitals’ compensation or affect their public reputation, the rate of diagnosis may decline simply because of a shift in the interpretation of subjective criteria, such as a change in secretion character or a worsening gas exchange. Absence of objective and specific diagnostic criteria for VAP compromises reproducibility and makes the comparison of VAP rates among different ICUs impossible to interpret.

Diagnosis is not the only issue of concern for using VAP as quality indicator. Significant differences in surveillance strategies among centers are well described and might constitute a serious confounding factor when comparing data.\textsuperscript{73} Another important limitation is case mix and what adjustment can or should be made. VAP incidence and ability to prevent episodes may be variable in different populations. Patient differences in age, disease severity, origin (eg, traumatic, surgical, or medical), comorbidities, or immunosuppressive status may affect results. Thus, hospitals admitting and caring for high-risk patients would be penalized. Nonetheless, specialized units, such as trauma, neurosurgery, or postsurgical ICUs, handle specific patients with different risk factors for VAP. Comparisons performed among these units would be inappropriate. Case mix is difficult to assess but
is needed to avoid inaccurate comparisons. Indeed, it has been demonstrated that large (academic) centers have higher nosocomial infection rates compared with smaller hospitals (odds ratio [OR] 1.97, 95% CI 2.90–1.33), but once adjusted for dissimilarities in case-mix, the difference was no longer significant (OR 1.31, 95% CI 2.05–0.84).77

An alternative to reporting VAP incidence rates might be to assess the use of risk-reduction measures for VAP as process-quality indicators. Process-quality indicators are likely to be more reliable and cost-effective than the measurement of VAP rates. Comparison of process-improvement measures (eg, compliance with each item in a care bundle for VAP prevention) would be both patient- and center-independent, more cost-effective, and easier to observe than a VAP incidence that may vary according to case mix and individual patient comorbidities and definitions. Uçkay and colleagues73 describe several risk factors that could be used as potential quality indicators (Table 1).

### Table 1

<table>
<thead>
<tr>
<th>Factor Associated</th>
<th>Impact on VAP Prevention</th>
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<tbody>
<tr>
<td>Length of hospitalization33</td>
<td>++</td>
</tr>
<tr>
<td>Existence of surveillance system69</td>
<td>+++</td>
</tr>
<tr>
<td>Feedback surveillance results69</td>
<td>+++</td>
</tr>
<tr>
<td>Education to staff69</td>
<td>+++</td>
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<tr>
<td>Alcohol-based hand rub for hand hygiene69</td>
<td>+++</td>
</tr>
<tr>
<td>Endotracheal suction systems69</td>
<td>++</td>
</tr>
<tr>
<td>Heat and moisture exchangers33,69</td>
<td>+</td>
</tr>
<tr>
<td>Sedation policy33</td>
<td>+</td>
</tr>
<tr>
<td>Weaning protocol33</td>
<td>+</td>
</tr>
<tr>
<td>Short duration of ventilation33,70</td>
<td>+++</td>
</tr>
<tr>
<td>Frequent ventilator circuit changes69</td>
<td>++</td>
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<tr>
<td>Endotracheal tube cuff pressure33,71</td>
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<tr>
<td>Supine head position33,72</td>
<td>+</td>
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<tr>
<td>Subglottic secretion drainage33,73</td>
<td>+++</td>
</tr>
<tr>
<td>Compliance with hand hygiene33,69</td>
<td>+++</td>
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<tr>
<td>Oral hygiene42</td>
<td>+</td>
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<tr>
<td>Stress ulcer prophylaxis20</td>
<td>?</td>
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<tr>
<td>Deep venous thrombosis prophylaxis20</td>
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<tr>
<td>Selective digestive decontamination74,75</td>
<td>?</td>
</tr>
<tr>
<td>Oral decontamination75</td>
<td>?</td>
</tr>
<tr>
<td>Silver-coated endotracheal tube76</td>
<td>++?</td>
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</tbody>
</table>

+, of concern; ++, important; ++++, very important.


### SUMMARY

Quality-of-care and safety improvement should be a priority in intensive care. The prevention of nosocomial infections should be a cornerstone in this process, and significant advances have been made.75,76,78–84 Effective design and implementation requires a multidisciplinary approach, taking into account barriers as well as facilitators. Indeed, design of newer care bundles for VAP prevention based on evidence85 represents a significant step forward. Implementation of care bundles for prevention seems to be an effective way to improve patient safety. However, some nosocomial infections, such as tracheobronchitis and pneumonia, are not always preventable.

### REFERENCES


