Collaborative Strategies for Improving Clinical Resource Utilization: How Pharmacists Can Make a Difference

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ABSTRACT
BACKGROUND: Ventilator-associated pneumonia (VAP) is associated with substantial health care costs that place a significant burden on scarce hospital resources. Preventative measures and appropriate management strategies can be effective in reducing the incidence of VAP and in improving VAP-related resource utilization.

OBJECTIVE: To provide an overview of the economic costs associated with VAP and of strategies that can be used to meet the goals of improving the efficiency of resource utilization without negatively impacting clinical outcomes.

SUMMARY: The substantial costs attributed to VAP are mainly due to the prolonged hospital length of stay (LOS) associated with these patients. Initial appropriate antimicrobial therapy is critical in achieving successful outcomes—including reducing LOS, mechanical ventilation days, and mortality. Initial treatment includes combination therapy when a multidrug-resistant pathogen or Pseudomonas aeruginosa is suspected. Once microbiologic results are available, de-escalation of therapy should be considered to reduce the unnecessary use of antimicrobials without impacting clinical outcomes. VAP prevention programs can also be an effective means to improve resource utilization in hospitals, although it is important to adopt a multidisciplinary team approach for acceptance of such programs and adherence to them.

CONCLUSION: In the current health care environment of increased transparency and accountability, renewed efforts must be made to not only prevent VAP but also to appropriately manage patients with VAP. All health care personnel involved in the management of patients with VAP must take a proactive role in reducing its incidence.


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Introduction
Although largely considered preventable, ventilator-associated pneumonia (VAP) is among the most common nosocomial infections acquired by adults and children in the intensive care unit (ICU), affecting approximately 9% to 27% of patients undergoing mechanical ventilation. With an incidence that can be as high as 10 episodes per 1,000 ventilator-days, VAP is associated with an attributable mortality of 33% to 50%. In addition, the economic burden is substantial due to extended periods of mechanical ventilation, prolonged length of stay (LOS) in the ICU and hospital, overconsumption of antimicrobial agents, and increased health care costs.

Given the economic impact of VAP and that it is generally preventable in most cases, renewed efforts must be made by all health care personnel to implement and adhere to strategies that prevent VAP or minimize the risk of VAP. It is critical for health care professionals and administrators to be aware of strategies that have been proven effective in improving resource utilization and to adopt strategies that can be appropriately implemented at their institutions.

The Clinical and Economic Costs of VAP
A number of studies have evaluated the clinical and economic impact of VAP. The Society for Healthcare Epidemiology of America (SHEA) released guidelines in 2007 on how to make a business case for infection control programs at hospitals. The report included costs attributable to different types of hospital-acquired infections (HAIs), including VAP, catheter-related bloodstream infection, coronary artery graft bypass surgery-associated surgical site infection, and catheter-related urinary tract infection. VAP was found to be associated with the highest attributable costs (an additional $23,000 per episode on average), compared with bloodstream infection ($18,432), surgical site infection ($17,944), and urinary tract infection ($1,257). An episode of VAP was also associated with a mean increase in the LOS by nearly 10 days.

A prospective, cohort study conducted by Warren et al. at a community hospital evaluated the impact of VAP on clinical outcomes and costs. The study included patients from the medical and surgical ICU from 1998 to 1999 and compared outcomes in patients who developed VAP with those who did not develop VAP. A total of 819 patients were included in the analysis, of which 127 had developed VAP. Patients with VAP were found to have a higher APACHE II (Acute Physiology and Chronic Health Evaluation) score, higher rate of congestive heart failure on admission, higher rate of hemodialysis, and longer duration of central venous catheter use and mechanical ventilation (Table 1). When considering patient outcomes, the LOS was significantly longer for patients with VAP—over 20 days longer on average for both ICU LOS and hospital LOS. Total hospital costs for patients with VAP were $48,948 higher. When these costs were adjusted for disease severity, the attributable cost was $11,897 for each case of VAP. Mortality rates were also significantly higher in patients with VAP (50% vs. 34%, P<br>0.001).
Muscedere et al. reviewed the published literature and institutional data to assess the impact of VAP on the Canadian health care system. In this study, the incidence of VAP in Canada was estimated at 10.6 cases per 1,000 ventilator-days, which equated to approximately 4,000 VAP cases each year. VAP increased the mean ICU LOS by 4.3 days per episode and resulted in a total excess cost of CAN $46 million (about $11,500 per VAP case). The attributable mortality was estimated to be 5.8%, or 232 deaths each year. The authors emphasized that eradication of this preventable infection will significantly impact VAP-associated mortality rates and health care resources. The excess ICU LOS reported by Muscedere et al. was much less than what was reported in the Warren study (22 additional days by VAP patients); this difference may be due to differences in the methodology and patient selection of the 2 studies. The Warren study compared all ICU patients (with and without VAP) requiring > 24 hours of mechanical ventilation during a set time period, while the Muscedere analysis was based on 1 matched cohort study (cases included patients requiring > 48 hours mechanical ventilation and developed VAP).

Cost Distribution of VAP
The excess costs associated with VAP can be directly linked to the prolonged LOS. Warren et al. analyzed the cost distribution associated with VAP and determined that room and nursing costs accounted for nearly 50% of the total hospital costs. Pharmacy costs, including antimicrobial therapy, accounted for approximately 20% of the total costs with the remainder of costs attributed to operating room, laboratory, respiration therapy, radiology, and other expenses.

The cost distribution among ICU infected patients with and without VAP was also evaluated in a matched cohort study in Switzerland. The matching procedure identified 97 pairs of mechanically ventilated patients and revealed that the largest proportion of costs (approximately 75%) for patients with and without VAP was related to the costs of the ward (or fixed costs) (Figure 1). These costs also included the expenses related to physicians and nurses. For patients who remained free of any ICU-acquired infection, the total cost was less than one-third of the cost for ICU patients with VAP.

Cost Burden: Impact of Resistance
The increasing prevalence of resistant and multidrug-resistant pathogens can impact the cost of managing patients with VAP. Antimicrobial resistance can increase the risk of inappropriate therapy, which potentially increases mortality rates as well as LOS and duration of mechanical ventilation. In a retrospective, cohort study was conducted to compare the clinical and economic outcomes for patients with early-onset VAP infected with methicillin-resistant S. aureus (MRSA) versus methicillin-susceptible S. aureus (MSSA). A total of 154 patients with S. aureus infections were included (59 patients with MRSA) in the multivariate analysis. MRSA infections were associated with a significant increase in mechanical ventilation days and ICU LOS (Table 2) and an insignificant increase in total LOS (3.8 days more) and total costs ($7,731 higher). These results imply that there is a greater use of resources for managing patients with MRSA-related VAP compared with patients with MSSA-related VAP. Strategies should, therefore, be employed to quickly diagnose patients with VAP caused by MRSA to reduce morbidity and hospital costs.

Clinical Burden: Initial Inappropriate Therapy
Initial inappropriate therapy for VAP is associated with significantly higher mortality rates than initial appropriate therapy. In a retrospective, observational cohort study, the 30-day mortality rates were determined in 76 patients with VAP caused by poten-
appropriate antimicrobial therapy \((n=59)\) within 24 hours of bronchoalveolar lavage sampling had a significantly lower 30-day mortality rate compared with those who received inappropriate therapy \((n=17, 17.2\% \text{ vs. } 50.0\%, P=0.005)\). Due to an increased mortality and shorter hospital LOS of patients with inappropriate antimicrobial therapy, there was no significant difference in total hospital costs between the 2 patient populations.

A meta-analysis conducted by Kuti et al. evaluated the impact of initial inappropriate antibiotic therapy on mortality of VAP patients.\(^{12}\) All studies published from 1966 to December 2006 were included if they met all of the following criteria: (a) observational studies, (b) compared patients receiving appropriate and inappropriate antibiotic therapy, and (c) reported data on incidence of mortality. Appropriate therapy was defined as treatment with at least 1 antibiotic having in vitro activity against the cultured pathogen. A total of 9 studies (813 total patients) met the inclusion criteria. Unadjusted mortality data revealed that inappropriate therapy significantly increased the risk of death in patients with VAP (odds ratio [OR] = 2.34, 95% CI = 1.51-3.63). An adjusted analysis was performed that included only those studies that used an appropriate analytic method to estimate an adjusted effect, adjusted ORs, and CIs. Three studies (323 patients) were included in the adjusted mortality analysis and showed similar results (OR = 3.03, 95% CI = 1.12-8.19). The authors suggest that the data show a clear association between inappropriate therapy and mortality in VAP patients. Clinicians should attempt to adopt protocols that help ensure initial appropriate therapy for these patients.

### Improving Resource Utilization Through Appropriate Antimicrobial Therapy

Ideal therapy for VAP involves appropriate initial therapy while avoiding unnecessary antimicrobial use. These goals have been emphasized in the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guidelines pertaining to management of hospital-acquired pneumonia.\(^{1}\) The ATS/IDSA guidelines recommend early, appropriate antimicrobials in adequate doses while avoiding excessive antimicrobial use through de-escalation of initial therapy and shortening the duration of therapy to the minimum effective period. The guidelines further state that antimicrobial selection and therapeutic adjustment should be based on microbiologic cultures and clinical response of the patient.

Selecting the appropriate initial therapy can be challenging, given the variety of causative pathogens and the difficulty in predicting their susceptibility profile. Because of the importance of appropriate initial antimicrobial therapy for VAP, the ATS/IDSA guidelines recommend initial combination therapy when a multidrug-resistant pathogen or \(P.~aeruginosa\) is suspected.\(^{1}\) However, to limit the excessive use of antimicrobials, the guidelines recommend de-escalation of therapy once microbiologic results are available.

### De-escalation of Therapy

De-escalation of therapy reduces the unnecessary use of antimicrobials and has the potential to decrease the risk of development of resistance without affecting clinical outcomes. How to de-escalate is still controversial; while more research is needed to arrive at the optimal approach, several steps have been outlined on adopting this strategy.\(^{1,13,14}\) The following steps can serve as a useful guide in adopting a strategy of de-escalation. However, adjustments to this model should be made based on the individual patient characteristics and specific conditions at each institution.

**Step 1. Obtain microbiologic samples.** Microbiologic samples should be obtained as soon as VAP is suspected due to the significant time needed to obtain culture and susceptibility results.

**Step 2. Begin empiric antimicrobial therapy.** Therapeutic selection should be based on patient risk factors for MDR pathogens as well as local susceptibility patterns. Patients should be carefully monitored for clinical improvement based on their temperature, white blood cell count, chest X-ray, \(\text{PaO}_2/\text{FiO}_2\), organ function, and hemodynamic parameters.

**Step 3. Evaluate and de-escalate.** Response to appropriate therapy can take 48 to 72 hours, so the selected antimicrobial regimen should not be changed during this time unless progressive deterioration of the patient occurs or initial microbiologic results suggest otherwise. Once culture results and susceptibility profiles are obtained, de-escalation of therapy can be considered.

If the patient shows clinical improvement, it may be possible to narrow (de-escalate) the antimicrobial spectrum based on the microbiologic results. After 7 to 8 days of therapy, the patient should be re-assessed for the need of continued therapy. An exception to short duration of therapy for VAP includes
infections caused by nonfermenting gram-negative pathogens, such as P. aeruginosa or Acinetobacter spp., which may require longer antimicrobial courses (e.g., 15 days or longer).15

If the patient shows no or little sign of clinical improvement, the patient should be re-assessed based on pathogen resistance to therapy, the presence of a complication (such as an abscess), a noninfectious diagnosis, or inadequate tissue penetration of the drug to the site of infection.

Use of Institutional Guidelines in VAP Management and Prevention

The use of VAP management guidelines can be effective in improving appropriate antimicrobial therapy and decreasing resource utilization. Recent evidence-based clinical guidelines by Muscedere et al. incorporate many of the aspects discussed in this review and can serve as an important reference when managing patients with VAP.16

A recent report from Canada assessed the value of de-escalation of therapy once culture results became available.17 All 740 patients included in the study received empiric broad-spectrum therapy and were then stratified depending on if they received targeted therapy based on culture results. Targeted therapy in this study was defined as a narrower spectrum of antimicrobial therapy based on culture and susceptibility results or discontinuation of antibiotics when cultures were negative. For those with positive cultures (n = 412), the clinical progression of infection, multiple organ dysfunction scores, and mortality were not significantly different between the 2 patient populations. However, those who receive targeted therapy (n = 320) had more days alive and off broad-spectrum antimicrobials (14.5 vs. 13.2 days, P = 0.04). Those with negative cultures (n = 327) and treated with targeted therapy (n = 230) had more days alive and off broad-spectrum therapy (15.9 vs. 13.1 days, P < 0.001) and fewer days on mechanical ventilation (9.8 vs. 14.7 days, P = 0.03). The authors concluded that targeted therapy resulted in less antimicrobial use without any clinical compromise.

A report from a university-affiliated teaching hospital in Seattle, Washington, compared outcomes before and after the implementation of VAP management guidelines based on local microbiologic data.18 The guidelines promoted the use of quantitative bronchoscopy for diagnosis and initiated empiric therapy based on local microbiologic findings and resistance patterns. Therapy was then tailored based on culture results, and the duration of therapy was carefully considered based on clinical response. Following implementation of the guidelines, there were significant increases in the rate of tailoring therapy based on culture results and the use of definitive therapy, as well as a decrease in the mean duration of therapy (Table 3). The implementation of the guidelines led to a significant improvement in antimicrobial use practices, although no improvement was observed in the all-cause mortality rate of these patients.

Finally, a university teaching hospital in Kansas reported the effects of implementing evidence-based VAP prevention strategies on the incidence of infection in ventilated trauma patients.19 The VAP prevention protocol was modified to include elevation of the head of the bed, twice-daily chlorhexidine oral cleansing, a once-daily respiratory therapy-driven weaning attempt, and conversion from a nasogastric to an orogastric tube whenever possible. In 2003 (prior to guidelines), there were 1,600 days of ventilator support compared with 703 days of ventilation in 2004 (following guideline implementation). Following implementation of these guidelines, the incidence of VAP decreased from 6.9 per 1,000 ventilator-days to 2.8 per 1,000 ventilator-days. This had a significant impact on resource utilization given that VAP patients had, on average, greater hospital LOS (an additional 25.4 days per episode), greater ventilator days (an additional 11.3 days per episode), and greater hospital charges (an additional $233,000 per episode). This study illustrates the importance of considering improved preventative strategies as an effective means to reduce resource utilization among patients with VAP.

Multidisciplinary Team Model for VAP Prevention

Improving resource utilization when managing patients with VAP will require greater efforts in education of health care personnel, improved early and accurate diagnosis, appropriate empiric therapy, and the use of prevention measures.

The goals of VAP prevention programs are to decrease morbidity and mortality associated with these infections and to reduce hospital costs. Achieving these goals will require implementing tactics that reduce the risk of infection, which can include improved infection control, reduced inappropriate antimicrobial use, and limiting device days. Initially, it may be practical for an institution to focus on implementing a few proven cost-effective strategies.

The Institute for Healthcare Improvement (IHI) 100,000 Lives Campaign recommends a VAP “bundle” that includes 4 components: (a) elevation of head of the bed to between 30 degrees and 45 degrees, (b) daily “sedation vacations” and assessment for readiness to extubate, (c) prophylaxis for peptic ulcer disease, and (d) prophylaxis for deep vein thrombosis.20 Initial reports have shown a dramatic decrease in VAP rates once these tactics were implemented at institutions.21,22

VAP prevention programs require widespread support within the institution for implementation and adherence. Prevention programs should be multidisciplinary and evidence-based and should translate prevention strategies into hospital practice focused on patient safety and quality improvement.23 Dr. Donald

### Table 3: Outcomes Before and After Implementation of VAP Management Guidelines

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Before Period (n = 168)</th>
<th>After Period (n = 216)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy tailored based on culture</td>
<td>61.3%</td>
<td>69.4%</td>
<td>0.034</td>
</tr>
<tr>
<td>Use of appropriate definitive therapy</td>
<td>80.4%</td>
<td>89.4%</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean duration of therapy, days</td>
<td>12.0</td>
<td>10.7</td>
<td>0.001</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>22.6%</td>
<td>21.3%</td>
<td>0.756</td>
</tr>
</tbody>
</table>


VAP = ventilator-associated pneumonia.
Craven, in his guidelines for VAP prevention, suggests that a prevention program be led by a “champion leader” while other core members include administration, nursing, infectious disease and critical care physicians, respiratory therapists, and microbiologists, among others. Although clinical pharmacists are not specifically listed, several reports have described and documented the impact of critical care pharmacists within a multidisciplinary ICU team. Evaluations of clinical pharmacists in the ICU setting have demonstrated the potential for improved patient outcomes and cost savings in critically ill patients, including those with VAP.

One of the greatest barriers to implementing a prevention program is gaining administrative support and funding. However, as previously described, there is a wealth of information available demonstrating the high costs of these infections. This aspect should be emphasized when presenting to the administrators the need for improved prevention programs that will lead to improved clinical outcomes and decreased resource utilization. Today’s environment of increased transparency and accountability at hospitals should also provide incentive to implement strategies that lead to fewer cases of VAP.

Summary

When managing patients with VAP, clinicians must find a balance between (a) initiating appropriate therapy that provides adequate coverage, and (b) avoiding the overuse of antimicrobial agents. This approach will be important in achieving successful clinical outcomes while efficiently using scarce hospital resources. Strategies aimed at reducing hospital LOS will be most effective in improving resource utilization for patients with VAP. However, the greatest reduction in hospital costs will be through the implementation of preventative strategies that effectively reduce the actual number of VAP episodes. A multidisciplinary team approach will be critical in the success of these programs, and clinical pharmacists can play an integral role as part of the critical care team.

REFERENCES