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# Can We Achieve Zero Hospital-Acquired Pneumonia?

*Joana Alves, MD*[1,2]
*Yolanda Peña-López, MD*[3]
*José N. Rojas, MD*[4]
*Magda Campins, PhD, MD*[5]
*Jordi Rello, MD*[6,*]

**Address**
[1]Infectious Diseases Department, Centro Hospitalar São João, Porto, Portugal
[2]Faculty of Medicine of University of Porto, Porto, Portugal
[3]Paediatric Critical Care Department, Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain
[4]Critical Care Department, Fundación Santa Fe de Bogotá, Bogotá, Colombia
[5]Epidemiology Department, Vall d'Hebron Barcelona Campus Hospital, Barcelona, Spain
[*,6]Critical Care Department, Vall d'Hebron Barcelona Hospital Campus & Centro de Investigacion Biomedica en Red (CIBERES), Ps Vall d'Hebron 119, AMI- 14a Planta, 08035, Barcelona, Spain
Email: jrello@crips.es

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## Abstract

*Purpose of Review* Ventilator-associated pneumonia (VAP) is still a common complication in intensive care units, being associated with higher costs, increasing hospital length of stay, duration of mechanical ventilation and use of antimicrobials. Ventilator care bundles are key measures to patient care quality improvement, and their implementation contributes to the reduction in the incidence of VAP. The current review focuses on preventive measures of VAP and a potential concept of zero VAP rate.
*Recent Findings* Several reports have documented a decrease in VAP rate with the implementation of ventilator care bundles. Despite the improvement on VAP incidence, risk factors to VAP are numerous and although some are preventable, it is unachievable to eliminate the majority.
*Summary* VAP is not always preventable and thus unlikely to reach zero rate. Several reports have documented a decrease in the incidence of VAP when a bundle is

implemented. The major restrain to care bundles implementation is adherence; compliance to them is the achieving goal that can be reached by the use of a maximum of five interventions, with a strong effort on multidisciplinary education and continued feedback. Surveillance, prevention, and education remain a priority in critical care in order to minimize VAP.

## Introduction

Nosocomial infections are the most common complication in intensive care units and are associated with increased length of hospital stay and morbidity in hospitalized patients. These patients can be seen as targets to improve quality strategies on patient care and safety. VAP is the most severe infectious complication in mechanically ventilated patients. Preventive strategies have recently been focused on ventilator bundles, which have been associated with a significant reduction in the incidence of VAP in several studies.

According to Centers for Disease Control and Prevention (CDC), there is a striking decline in VAP, and in the USA over 2000 hospitals have instituted VAP prevention bundles. VAP rates in ICUs have decreased from 9.3 to 3.8 events and in Pediatric ICUs from 4.9 to 1.4 events per 1000 ventilator days in the period from 2002 to 2009 [1]. The true incidence of VAP is unclear and varies widely depending on the population. At the same time, surveillance is conditioned by subjective, insensitive and unspecific clinical criteria. In recent years, VAP has been declining, although around 10% of ventilated patients can still develop infection [2–4]. In an effort to improve VAP surveillance and outcome measurement, CDC modified the definition criteria in 2013 and focused on the ventilatory-associated events (VAE) concept [5].

The incidence reduction has raised questions regarding whether it is possible to achieve a VAP zero rate as a global reference point and, therefore, reduce the current daily practice of antimicrobial prescription.

The current review focuses on preventive measures of VAP and their role in the potential concept of zero VAP rate.

# Ventilator-Associated Pneumonia

The American Thoracic Society and Infectious Diseases Society of America published practical guidelines on hospital-acquired infection in 2005 [6]. Ventilator-associated pneumonia (VAP) definition was characterized by the presence of progressive new infiltrate, signs of systemic infection, changes in sputum characteristics, and detection of the causative agent in patients with mechanical ventilation for at least 48 h, to differentiate any new infection from processes that were already present or in progress at the time of intubation.

Ventilated patients are at higher risk of VAP, increased ICU (and hospital) length of stay, duration of mechanical ventilation, and use of antimicrobials. VAP also increases the mortality risk [7], estimated to be 13% according to Melsen et al. [8], with differences depending on patient comorbidities [9, 10] and etiology. *Pseudomonas*, *Acinetobacter*, and methicillin-resistant *Staphylococcus aureus* are associated with increased mortality of VAP [11].

VAP can also be divided into early and late onset. Early VAP, which occurs within the first 96 h of mechanical ventilation, has a better prognosis; whereas late-onset VAP has a higher mortality and is frequently associated with multiresistant bacteria. Despite the newer definitions and recommendations, they are still based on clinical findings and subjective criteria. As examples, diagnosis is dependent on the secretions characteristics and on high inter-observer variability in chest X-ray interpretation. Diagnostic techniques for VAP (broncho-alveolar lavage, brush, or tracheal aspirate) offer a quantitative analysis for interpretation, but a gold standard is lacking [4, 6, 12].

Care bundles for patients undergoing mechanical ventilation were designed to reduce or eliminate VAP: peptic ulcer disease prophylaxis, deep vein thrombosis prophylaxis, elevation of the head of the bed, daily sedation vacation, oral care with chlorhexidine, strict protocols on hand hygiene, selective decontamination of the digestive tract, endotracheal tube cuff pressure control, and continuous removal of subglottic secretions [13–15].

Each preventive measures for VAP and their quality of evidence rating, (high = 1, moderate = II, or low = III), according to the quality of evidence by GRADE—Grading of Recommendations, Assessment, Development and Evaluation, was stratified by Klompas et al. [16] report.

# Interventions

## Strict Hand Hygiene for Airway Management

In hospitals, infections spread mainly through hand transmission. Resident and transient microbial flora colonize the hands and may be transferred on to a port of entry, such as an artificial airway. In a susceptible host, this can cause potentially life-threatening infections.

The relation of hand hygiene and reduction of hospital-acquired infections has been widely established, but compliance among health care workers is poor [17–19]. Hand hygiene is the gold standard of infection control and the most basic and simple measure to prevent health care infections. Interventions to encourage hand hygiene during artificial airway manipulation are of utmost importance and guidance should be promoted in order to achieve high compliance.

## Oral Hygiene With Chlorhexidine

Oral care with chlorhexidine (quality of evidence: II) is an integrated strategy in mechanically ventilated patients care [20] to decrease the oral bacterial load and hence reducing the risk of VAP. Among different studies, the effectiveness of chlorhexidine on VAP outcomes is variable. A recent meta-analysis reported a reduction in the incidence of VAP without further influence on duration of ventilation, ICU stay or mortality [21•]. These studies are heterogeneous on chlorhexidine concentration, frequency, and technique. Recently, Zand et al. [22•], compared 0.12 vs. 2% chlorhexidine concentration and reported greater efficiency on the 2% group, with reversible oral mucosa irritation in both groups. However, higher incidence of oral mucosal lesions is reported with 2% chlorhexidine [23]. Thus, our recommendation is to use 0.12% concentration combining both teeth and tongue brushing.

## Semi-Recumbent Positioning

Regurgitation of the gastric content plays an important role on the pathogenesis of VAP, as it may increase oropharynx colonization. In hospitalized patients, the use of antacids and enteral nutrition not only modifies the gastric flora, but also promotes bacterial growth [24, 25].

Gastric reflux can be reduced by a semi-recumbent position (30–45°) in mechanically ventilated patients with nasogastric tube (quality of evidence: III) [26, 27]. Kollef et al. reported increased pneumonia risk in patients with a supine head position (0°) during the first 24 h of mechanical ventilation [28]; according to Drakulovic et al. [29], besides higher nosocomial pneumonia in supine head position's patients, VAP incidence was decreased more than 75% when ventilated patients were on semi-recumbent position (45°), especially those receiving enteral nutrition. A different study reported unchanged rate of VAP with a maximum of 28° elevation [30]. It is relevant to mention the consequences of semi-recumbent position, as it can reduce the cardiac output, compromising hemodynamic stability, and may not be feasible in selected patients [31]. Despite various studies and recommendations, a systematic review [32] was unable to reach any conclusion, and uncertainty remains regarding the benefits and harms of this position for VAP prevention; however, according to experts, patients receiving enteral nutrition should be at a semi-recumbent positioning [16, 33].

## Subglottic Secretions Drainage

Microaspiration into the lungs occurs after the accumulation of oropharyngeal secretions above the endotracheal cuff [34]. Aspiration of subglottic secretions is another preventive measure to avoid secretions descent (quality of evidence: II). Vallés et al. [35] reported 43.5% reduced pneumonia incidence when using continuous aspiration of subglottic secretions; interestingly, secretions drainage was ineffective for *Pseudomonas aeruginosa*, where the inoculum even increased. Dezfulian et al. [36], only found a positive association for early-onset VAP in patients requiring more than 72 h of mechanical ventilation; Muscedere et al. [37] demonstrated a 50% reduction of VAP with this preventive measure; furthermore, the patients that eventually developed VAP had delayed onset pneumonia. Mortality, mechanical ventilation, and ICU duration were not affected by its implementation [37–39]. It is important to highlight the need for strict "cuff pressure control" to ensure effective drainage.

## Cuff Pressure Control

Cuffed endotracheal tubes seal the trachea, enhance positive pressure ventilation, and prevent aspiration of secretions [34]. Every measure that reduces the leakage of secretions to the lower respiratory tract reduces the risk of VAP. According to previous studies, persistent intra-cuff pressure below 20-cm H2O was independently associated with higher risk of VAP [40], but pressure above 30-cm H2O were associated with tracheal injury [41]. The pressure of the cuff should be monitored in order to maintain a 20–30-cm H2O pressure range and avoid leakage of contaminated secretions around the cuff into the lower respiratory tract (quality of evidence: III).

## Promoting Measures That Safely Avoid or Reduce Ventilation Duration

The presence of an endotracheal tube is a requirement for the development of VAP; it leads to a higher probability of pathogen aspiration to the lower airways. The association between duration of mechanical ventilation and development of VAP is well establish [42–45]. There is a cumulative probability of developing

VAP according to the number of days on mechanical ventilation [46].

Before inserting an endotracheal tube, noninvasive ventilation (NIV) can be used (quality of evidence: I); critically ill patients have improved outcomes with NIV instead of mechanical ventilation [47, 48]. Recently, a new alternative technique has been introduced: humidified high-flow nasal cannula (HHFNC). Sotello [49] and Papazian et al. [50] reviewed the use of HHFNC and reported improved oxygenation in several studies, with higher number of ventilator-free days and lower re-intubation rates.

VAP can also be reduced when decreasing the duration of mechanical ventilation, so protocols aimed at sedation restriction and early ventilator weaning must be implemented (quality of evidence: II) [51, 52]. Regarding sedation, the use of alpha-2 adrenergic receptor agonists instead of benzodiazepines is better in terms of readiness for extubation, reducing ICU length of stay [53, 54].

Whenever feasible, intubation should be avoided without compromising the health of the patient. Strategies to minimize sedation and assessment of readiness to extubate are recommended on a daily basis. This does not apply to patients with consciousness impairment in need of airway protection.

## Selective Decontamination

Since the oropharynx colonization is an independent risk factor of VAP [13], different strategies of decontamination of digestive tract (SDD) have been proposed (quality of evidence: I). The strategy either uses non-absorbable antimicrobial agents (polymyxin, trobamycin, and amphotericin B), often with adjuvant pre-emptive systemic antibiotic within the first 2–4 days of ventilation. Some investigators added vancomycin, whereas others limit the implementation into the oropharynx. This approach is intended to avoid colonization by Gram-negative bacteria, *S. aureus*, and yeasts.

Certainly, some studies have reported a reduction in VAP incidence and mortality using SDD [55–63]. For instance, Smet et al. [55] found a reduction in culture positive Gram-negative bacteria, ranging from 56 to 15% after 14 days of antimicrobial treatment, and reported a 13% reduction in mortality without evidence of emergence of antibiotic-resistant bacteria. However, most of these effects were documented in units with low incidence of multidrug resistance organisms. Moreover, the majority of these reports is short-term and has not evaluated the consequences of using SDD in a long-term basis. As a consequence, selective decontamination remains a highly controversial prevention measure and caution is recommended due to selective pressure exerted on the respiratory microbiome. Usually, SDD is implemented in regions with low risk of multidrug resistant infections, whereas it is commonly avoided in areas of high resistance. Large RCT are ongoing in ICUs with MDRs and these findings would be available in late 2018. In the 2017 International ERS/ESICM/ESCMID/ALAT guidelines, SDD was not recommended [4].

## Tracheostomy

As a measure to prevent complications associated with prolonged intubation (laryngeal injury and tracheal stenosis [64, 65]), early tracheostomy has been suggested (quality of evidence: I). Early tracheostomy has been associated with decreased mechanical ventilation duration and VAP rates [66, 67]. However, this has not been confirmed by three recently meta-analysis [68–70]. As we cannot fully predict which patients will require prolonged mechanical ventilation, the optimal time to perform a tracheostomy is difficult and inconsistent, except for patient with severe brain trauma.

## Short Course of Systemic Antibiotics

A different point of view regarding antimicrobials is their use as prophylaxis in comatose patients after intubation (quality of evidence: NA). A study by Rello et al. [71] identified cardiopulmonary resuscitation and coma as important risk factors for VAP, indicating a role for gastric aspiration in the pathogenesis of VAP within the first 48 h of ventilation; furthermore, the use of antibiotic as prophylaxis reduced the incidence of pneumonia, although no protective effect was demonstrated after 48 h. Vallés et al. [72] reported a reduction in VAP with a single-dose antibiotic, without increasing multidrug resistance. A recent systematic review from Righy et al. [73•] not only confirmed a reduction in the VAP incidence, but also the ICU length of stay.

Despite the efficacy of short course of systemic antimicrobials for VAP prevention in a subset of patients demonstrated by some studies, the emergence of multidrug resistant strains is still a concern. More randomized studies are recommended to evaluate the safety and efficacy of this intervention.

# Ventilator-Associated Respiratory Infections in Children

VAP is the first or second most commonly diagnosed nosocomial infection in the Pediatric Intensive Care Unit (PICU), related to higher mechanical ventilation days and PICU length of stay. Ventilator-associated tracheobronchitis (VAT) has also been independently associated with PICU morbidity and health-resources consumption [74–77]. Furthermore, VAT is a more frequent condition in children than VAP, and it represents a clinically important nosocomial infection in its own right, regardless of whether it progresses to VAP [78].

As in adults, a lack of a precise definition makes that clinical definitions for VAP and VAT may be applied inconsistently, particularly in some pediatric conditions, such as cyanotic heart diseases that make it more difficult to assess the worsening gas exchange. On the other hand, it is difficult to distinguish between colonization and infection in mechanically ventilated children with viral respiratory infection and fever, as viral acute infection and early VAP may coexist.

In recent years, the use of specific care bundles to prevent infections in the intensive care unit has demonstrated its effectiveness. A reduction in pediatric VAP incidence rates, based on standardized surveillance data from PICU in the USA, has been reported from more than 5 cases per 1000 ventilator days in 2007 to near zero in 2012 [79]. No data has been compiled for VAT by the National Health Care Safety Network (NHSN) during this period, but Muszinsky et al. reported rates of 3.9 VAT cases per 1000 ventilator days after implementation of a ventilator bundle in a PICU and zero VAP rates [76]. Wheeler et al. found an increase in ventilator-associated tracheobronchitis coincident with the near-elimination of ventilator-associated pneumonia [77]. In contrast, Peña et al. reported a different impact on VAP and VAT after the implementation of a care bundle to prevent ventilator-associated respiratory infections in children when including prolonged mechanically ventilated patients, diminishing VAP rates, and delaying VAT onset [80••].

It is also important to consider risk factors when referring to ventilator-related infections in the pediatric care unit, such as genetic abnormalities (OR 2.04), steroids (OR 1.87), re-intubation or self-extubation (OR 3.16), prior antibiotic therapy (OR 2.89), and bronchoscopy (OR 4.48) [81]. Enteral feeding as a risk factor in children is inconsistent throughout the literature [82].

### Pediatric Ventilator Bundles

The bundle approach has spread worldwide in adults Intensive Care Units. Preventive strategies have been also introduced to reduce pediatric VAP and, more recently, for VAT [76, 80••]. However, pediatric ventilator care bundles have not been validated. Different tailored ventilator bundles have been used in PICUs [76, 80••, 83–85]. Size-related factors must be considered as a difficulty to introduce some of the measures [86]: subglottic secretion drainage in infants and children needing endotracheal tube < 5 or 5.5 mm or cuffed tubes in low-height infants, are technically unfeasible. And although semi-recumbent position in children is frequently adopted, maintaining 30 to 45° head-of-bed elevation is challenging for infants and newborns.

In another hand, tracheostomy in children is less frequent than in adults, related to previous prolonged mechanical ventilation at home, or performed late following PICU admission, usually surgical [88]. In opposition to adult data, it has been associated with an increased risk of VAP [87]. Moreover, in a recent study including prolonged mechanical ventilated children, some differences in the ventilator care bundle were reported according to the airway device [80••]: VAP among tracheostomized patients decreased by 60% after the introduction of the bundle and 81% after standardization of tracheal stoma care and disinfection of the cannula. In contrast, VAP rates decreased only by 28% in patients ventilated through endotracheal tubes. The fact that the closing of the vocal cords is preserved in most children undergoing tracheostomy and difficulties for maintaining 30° to 45° head-of-bed elevations for infants and newborns, it may explain lower effectiveness of the bundle in VAP rates in this population. In conclusion, pediatric patients with a tracheostomy tube are clearly at an increased risk of ventilator-associated infections, but preventive measures may have a higher impact. Further studies should probably provide more information.

Finally, antibiotic treatment for VAT is more extended than in adult population, but its optimal duration is a controversial issue, being probably antibiotics overused. Tamma et al. demonstrated that a prolonged course of antibiotic for VAT did not protect against progression to VAP compared with short-course therapy (< 7 days) [75].

## Care Bundles in Prevention

Infection control is a critical element of patient care; many hospital-acquired infections are considered potentially preventable. The most important factors in the process of care are the pathogenesis of the disease, knowledge of evidence-based guidelines, and the problem itself as a whole. The concept that nosocomial infections are inevitable has been changing to that they are all potentially preventable. For some device-related infections, such as those related to central venous catheter, intervention programs are usually very successful, compared to programs targeted to VAP, in which several difficult to modify factors play a key role on the development of the infection. Exogenous sources are potentially preventable, but this is not true for many endogenous sources.

These bundle strategies prompt a practical change in patient care, which may lead to an improvement in VAP reduction [15, 89•, 90–93], but as has been previously discussed, the best selection of each bundle should be tailored according to the type of patients and institution. Care bundles have also shown to decrease the health care costs and antimicrobials use, length of ICU stay, and the need of mechanical ventilation therapy [89•].

Effective preventive measures are not always followed, and they cannot be correctly implemented without huge efforts on health care education and training. Several studies [94–96] have reported the association between education and the decrease of VAP. Zack et al. performed an approach to ventilator education, with a 57.6% decrease in VAP rate [97]. Nursing care is essential to ensure good quality of health care delivery. Furthermore, lower patient-to-nurse ratios are associated with better outcomes, such as a decrease of nosocomial infections and on mortality rate [98–101]. Compliance to ventilator care bundles requires continuous education of health care workers and an appropriate ratio of nursing staff. Education programs focused on infection control are highly important, and in order to implement ventilation care bundles worldwide, ICU's health care professions need to be trained through multidisciplinary interventions, and the facilities should be prepared to the needed changes.

Recent guidelines [4, 12] are available, but little is mentioned about ventilator bundles. The worldwide implementation of ventilation bundles is a goal to achieve. The implementation of only five interventions in care bundles to promote higher compliance from health care professionals is recommended (Table 1).

## Ventilator-Associated Pneumonia Rate of Zero

Patients requiring mechanical ventilation will be invariably at risk for VAP. Its incidence is diverse among different studies, but has been decreasing due to safer health care and technological innovations, and more recently due to care

**Table 1. Suggested ventilator care bundle**

| |
|---|
| Hand hygiene |
| Chlorhexidine oral care |
| Semi-recumbent position |
| Endotracheal tube cuff pressure control (enhanced by SSD) |
| Avoid or reduce time of ventilator* |

*SSD* subglottic secretions drainage
*Avoid midazolam. Minimize sedation

**Table 2. Characteristics and VAP Rate of included studies**

| Primary author | Type study (unit/month) | Applied bundles | Outcome measures | VAP rate previous care bundles (episodes/1000 vent. days) | VAP rate after care bundles (episodes/1000 vent. days) | VAP reduc (%) | *p* value | C (%) |
|---|---|---|---|---|---|---|---|---|
| Resar et al. | Prosp. (35/18) | HOB elevation; sedation vacation; peptic ulcer disease prophylaxis; deep vein thrombosis prophylaxis; | Frequency of VAP; | compliance | 6.6 | 2.7 | 59* | |
| 0.001 | 95* | | | | | | | |
| Youngquist et al. | Retros*p* (2/6) | HOB elevation; sedation vacation; peptic ulcer disease prophylaxis; deep vein thrombosis prophylaxis; hand hygiene; oral care. | Frequency of VAP; duration of MV; ICU LOS; ICU mortality | 6.01<br>2.66 | 2.70<br>0 | 55<br>100 | NS<br>NS | 100 |
| Blamoun et al | Retros*p* (1/18) | HOB elevation; hand hygiene; oral care; sedation vacation; early tracheostomy. | Frequency of VAP | 14.1 | 0 | 100 | 0.006 | – |
| Rello et al | Cohort (5/22) | Sedation vacation; hand hygiene; oral care; endotracheal tube cuff pressure monitoring. | Frequency of VAP<br>Duration of MV<br>ICU LOS<br>Compliance | 12.9 | 9.28 | 28 | 0.05 | 30 |
| Ding et al | Cohort (9/84) | HOB elevation; sedation vacation; peptic ulcer disease prophylaxis; deep vein thrombosis prophylaxis; | Incidence of VAP; time onset to VAP; duration of MV; hospital and ICU | 9 | 10.1 | 0 | 0.73 | 97 |

**Table 2.** (Continued)

| Primary author | Type study (unit/month) | Applied bundles | Outcome measures | VAP rate previous care bundles (episodes/1000 vent. days) | VAP rate after care bundles (episodes/1000 vent. days) | VAP reduc (%) | *p* value | C (%) |
|---|---|---|---|---|---|---|---|---|
| | | | length of stay; ICU mortality | | | | | |
| Sulis et al | Retros*p* (-/60) | HOB elevation; sedation vacation; peptic ulcer disease prophylaxis; deep vein thrombosis prophylaxis; hand hygiene; oral care. | Frequency of VAP, all-cause | bacteremia, *C. difficile* infection, and MRSA or VRE colonization or infection | 3.99 | 0 | 100 | |
| 0.001 | – | | | | | | | |
| Okgun et al | QE (1/7) | HOB elevation; sedation vacation; peptic ulcer disease prophylaxis; deep vein thrombosis prophylaxis; hand hygiene; oral care; endotracheal tube cuff pressure monitoring. | Frequency of VAP Compliance | 15.91 | 8.5 | 46.5 | 0.0001 | 89.8 |

*C* compliance, *VAP* ventilator-associated pneumonia, *HOB* head-of-bed, *MV* mechanical ventilation, *LOS* length of stay, *MRSA* methicillin-resistant *Staphylococcus aureus*, *VRE* vancomycin-resistant Enterococcus, *QE* quasi-experimental, *NS* not statistically significant

*Variable according to units

-missing value

**Table 3. Implementation strategies**

| Engage | Educate | Execute | Evaluate |
|---|---|---|---|
| Develop a multidisciplinary team | Provide educational sessions | Standardize care processes | Measure performance |
| Involve local champions | Provide education materials | Create redundancy | Provide feedback to staff |
| Utilize peer networks | | | |

bundles implementation [2, 4, 102]. Since the introduction of ventilator bundles, a drastic reduction of VAP rates has been reported.

Can we reach a zero VAP rate? According to some authors [90–92], we can achieve a zero VAP rate as shown in Table 2, but some caution is advised: all of these studies had almost a 100% bundle compliance, and most of the studies were retrospective and undertaken in limited periods of time, with potential selection bias and incomplete data on outcomes. In the study by Ding et al. [103], no reduction on VAP was observed with a 97% of bundle compliance. Other studies have reported reduced VAP rates [15, 89•, 93] even without high compliance. Further studies are needed with better methodological design, inclusion of all respiratory infections, including VAT, adequate and precise definitions, blinding, and quality assessment. Preclinical-defined outcomes should enclose safety variables, like mortality and efficacy variables, such as time to resolution, overall antibiotic use, mechanical ventilation duration, and length of (ICU) stay.

The major restrain to preventive measures is adherence; care bundles require timely interventions with work changes and a team effort within the facility. In 2013, Rello et al. [93], confirmed the association between compliance and VAP incidence. Adherence is variable and can range from 20 to 100% [104]. Regarding ventilator bundles, Cook et al. [105] reported a 64 and a 30% compliance bundle care in two institutions, with multiple barriers observed: fear of adverse effects, lack of convincing benefit, nurse inconvenience, and cost. Rello et al. [106] reported disagreement with trials and lack of resources as the main reasons to non-adherence.

Risk factors for VAP are multiple and although some are preventable (mechanical ventilation duration, re-intubation, antacids, multiple central venous catheters, tracheostomy); it is probably not feasible to eliminate the majority. From the host (age, gender, comorbidities, malignancy, immunosuppression), to the health care unit (health care facility and professional health worker, local pattern ecology), and the virulence of the pathogen, it is improbable to reach a zero VAP rate.

As an effort to diminish the incidence of VAP, surveillance and prevention remain priorities in intensive care units. This reduction translates into lower morbidity and mortality, less antimicrobial use, shorter length of ICU stay, and a decrease on health care costs. In Table 3, we suggest some strategies for the implementation of ventilator care bundles.

## Conclusions

VAP is associated with worse outcomes (length of stay, ventilation duration, increase of antimicrobial use), and some pathogens, such as *Pseudomonas*, *Acinetobacter*, MRSA may contribute to increase mortality. Although important changes that contributed to VAP reduction have been implemented in recent years, this infection is not always preventable and thus unlikely to reach zero rate. Several reports have documented a decrease in the incidence of VAP when a bundle is implemented. The strategic objective of research should focus on pre-defined clinical and meaningful outcomes improvement, rather than rate modification. Studies should consider both VAP and VAT. The use of a maximum of five interventions is recommended, with a strong effort on multidisciplinary education and continued feedback to sustain efficacy. Patients with tracheostomy and children would require a specific bundle. At bedside, techniques to avoid or reduce the duration of mechanical ventilation, such as the use of HFNC and light sedation, are the cornerstone. An implementation strategy following the 4E rule (Table 3) is strongly recommended.

## Compliance With Ethical Standards

**Conflict of Interest**
The authors declare that they have no competing interests.

**Human and Animal Rights and Informed Consent**
This article does not contain any studies with human or animal subjects performed by any of the authors.

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••Of major importance


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