GUIDE TO INFECTION CONTROL IN THE HEALTHCARE SETTING

Recommendations for The Prevention of Ventilator-Associated Pneumonia

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Topic Outline

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DEFINITION

This document intends to review the available evidence and provide a more international spectrum, including specific recommendations to address situations that are particularly relevant in low- and middle-income countries (LMIC). It highlights practical recommendations in a concise format designed to assist acute-care hospitals in implementing and prioritizing their ventilator-associated pneumonia (VAP) prevention efforts in LMICs as well as in high-income countries. We acknowledge statements and recommendations from several previous guidelines, such as those of the SHEA/IDSA/APIC, Practice Recommendation Strategies to prevent VAPs in acute-care hospitals: 2022 Update.[1] Given that the majority of LMICs continue to rely on the criteria and definition of VAP and have yet to adopt the utilization of Ventilator-Associated Events (VAE), our review concentrates on interventions aimed at reducing VAP.[2] This expert guidance document is sponsored by the International Society of Infectious Diseases.

KEY ISSUES

- VAP rates in the USA, as reported by the CDC National Healthcare Safety Network (NHSN), show a median VAP rate of 1.1 per 1,000 mechanical ventilator (MV)-days in medical-surgical intensive care units (ICUs).[3]
- VAP rates in LMICs exceed those in the USA. The International Nosocomial Infection Control Consortium (INICC) observed consistently higher VAP rates in LMICs over the past two decades. The INICC report from 2002 to 2005 indicated a VAP rate of 24.1/1,000 MV-days,[4] gradually reducing to 11.96 in the report covering data from 2015 to 2020,[2] but still far above CDC/NHSN. Consequently, there is a need to assess strategies to address this critical situation, particularly in LMICs.
- Costs associated with VAP vary globally, with reported costs in the USA, of $9,966,[5] and in Argentina, $2,255, in 2005.[6]
- Regarding the associated length of stay (LOS), pooling 630 ICUs from 2015 to 2020 of 45 LMICs, from Africa, Asia, Eastern Europe, Latin America, and the Middle East, with data from 204,770 patients, 1,480,620 patient days, 637,850 MV-days, and 7,635 VAPs, LOS was as follows: 6.57 days for patients without healthcare-associated infections (HAIs), 22.54 days for those with VAP. Patients with two simultaneous HAIs experienced LOS ranging from 29.13 to 32.01 days, while those with all three types of HAIs (VAP + central line-associated bloodstream infection (CLABSI) + catheter-associated urinary tract infection [CAUTI]) had a LOS of 33.53 days.[2]
- Regarding associated mortality. VAPs have a significant impact on healthcare, leading to increased mortality rates.[2] Pooling 630 ICUs from 2015 to 2020 of 45 LMICs, the mortality rates were as follows: 14.06% for patients without HAI, and 36.89% for those with VAP. Patients with two simultaneous HAIs experienced mortality rates ranging from 38.79% to 43.32%, while those with all three types of HAIs (VAP + CLABSI + CAUTI) had a mortality rate of 46.56%.[2]
- Regarding risk factors for mortality. Studies have documented that VAP is an independent significant risk factor for mortality. In a multicenter, multinational, multicontinental study involving 786 ICUs across 312 hospitals in 147 cities spanning 37 countries between 1998 and

2022, a total of 300,827 patients were followed during 2,167,397 patient-days, resulting in 21,371 HAIs. Multiple logistic regression identified the following mortality risk factors: VAPs (P<.0001), MV-days with a risk increase of 2% per day (P<.0001), mechanical ventilator (MV)-utilization ratio (P<.0001)LOS with a risk increase of 1% per day (P<.0001), CLABSI (P<.0001), CAUTI (P<.0001), medical hospitalization (P<.0001), female sex (P<.0001), and age (P<.0001).[7]

KNOWN FACTS

Risk factors for VAP

- Several authors identified the following as VAP risk factor (RF): Tracheostomy,[8, 9] length of stay (LOS),[10, 11] older age,[12] trauma patients,[13] post-surgical patients,[14] burns patients,[14] longer duration of surgery,[15] history of smoking,[15] low serum albumin concentration,[14] high score on the American Society of Anesthesiologists Physical Status Classification System,[14] APACHE II score >20,[11] acute respiratory distress syndrome,[16] lung injury,[16] chronic obstructive pulmonary disease,[13] upper respiratory tract colonization,[13], sinusitis,[13] PaO2/FiO2 ratio <200mmHg,[11] oropharyngeal colonization,[12] biofilm on the surface and within lumen of the endotracheal tube,[13] duration of mechanical ventilator (MV),[11, 12] frequent change in ventilator circuit,[13] lack of use of heat and moist exchange humidifiers,[13] supine position,[12, 17] frequent reintubation,[13] enteral feeding,[13] multiple central venous line insertions,[9] presence of catheter-related infection,[11] paralytic agents,[13] previous use of broad-spectrum antibiotics,[10, 12] and patients transported out of ICU.[13]
- At LMICs a study was conducted in 743 ICUs of 282 hospitals in 144 cities in 36 Asian, African, European, Latin American, and Middle Eastern countries. Patients admitted to ICUs over 24 years. 289,643 patients were followed during 1,951,405 patient days and acquired 8,236 VAPs. We analyzed 10 independent variables. Multiple logistic regression identified the following independent VAP RFs: longer length of stay (LOS), raising the risk 7% daily (aOR:1.07; 1.07-1.08; p<.0001); mechanical ventilation (MV) utilization ratio (adjusted Odds Ratio [aOR]:1.27; 95% CI, 1.23-1.31; p<.0001); CPAP was associated with the highest risk (aOR:13.38; 11.57-15.48; p<.0001), followed by tracheostomy connected to a MV (aOR:8.31; 7.21-9.58; p<.0001), and endotracheal tube connected to a MV (aOR:6.76; 6.34-7.21; p<.0001); male gender (aOR:1.22; 1.16-1.28; p<.0001); surgical hospitalization (aOR:1.23; 1.17-1.29; p<.0001); public hospital (aOR:1.59; 1.35-1.86; p<.0001); middle-income country (aOR:1.22; 15-1.29; p<.0001); adult-oncology ICU was associated with the highest risk (aOR:4.05; 3.22-5.09; p<.0001), followed by neurologic ICU (aOR:2.48; 1.78-3.45; p<.0001) and respiratory ICU (aOR:2.35; 1.79-3.07; p<.0001). Coronary ICU showed the lowest risk (aOR:0.63; 0.51-0.77; p<.0001).[18]

SUGGESTED PRACTICE

Necessary prerequisites.

Establishments implementing VAP surveillance and prevention should possess the following components:

- Assets for delivering suitable education and training.[1]
- A sufficiently staffed infection prevention program is responsible for identifying patients who meet the surveillance definition for VAP.[1]
- A well-staffed infection prevention professional (IPP), with the potential inclusion of information technology support, is crucial for gathering and computing MV-days as a denominator in VAP rate calculations.[1]
- Effective laboratory support is crucial for the timely processing of specimens and reporting results, adhering to the instructions provided by the supervisor of the surveillance program.[1]

Implementation of VAP prevention strategies

- **Multidimensional approach.** Numerous national, multinational, and multicontinental studies, employing a multidimensional approach, have been conducted, achieving a significant reduction in rates of VAP and mortality. All of them include six components: (a) bundle, (b) education, (c) surveillance of VAP, (d) monitoring compliance with recommendations to prevent VAP, (e) internal reports of VAP rates, and (f) performance feedback.[19]

1. **Bundles:**

- Care "bundles" in infection prevention and safety are simple sets of evidence-based practices that, when implemented collectively, improve the reliability of their delivery and improve patient outcomes.[20]
- Martinez-Reviejo et al. (2023) conducted a systematic review and meta-analysis on the effectiveness of ventilator care bundles in preventing VAP among mechanically ventilated patients. The study, which included 36 studies comprising 116,873 participants, found that implementing care bundles reduced the number of VAP episodes significantly (OR=0.42, 95% CI: 0.33, 0.54). The most commonly utilized components of the ventilator bundle were head-of-bed elevation (n=83,146) and oral care (n=80,787). Moreover, the implementation of care bundles was associated with a decrease in the duration of mechanical ventilation (MD=-0.59, 95% CI: -1.03, -0.15) and hospital length of stay (MD=-1.24, 95% CI: -2.30, -0.18), particularly when educational activities were integrated into the bundle. However, data regarding mortality outcomes were inconclusive. These findings highlight the efficacy of ventilator care bundles in reducing VAP episodes and improving clinical outcomes in adult intensive care units.[21]
- Mastrogianni et al. (2023) conducted a systematic review to assess the impact of care bundles on VAP prevention in adult ICUs. They identified 38 studies meeting their inclusion criteria, focusing on interventions implemented since the introduction of the "Institute for Healthcare Improvement Ventilator Bundle" in December 2004. The most commonly monitored interventions in these care bundles included sedation and weaning protocols, semi-recumbent positioning, oral and hand hygiene, peptic ulcer disease and deep venous thrombosis prophylaxis, subglottic suctioning, and cuff pressure control. Head-of-bed elevation and oral hygiene were among the most widely used interventions. Results showed varying degrees of VAP reduction across studies, with four studies reporting low reductions, 22 studies indicating a decline of over 36% in VAP cases, and ten studies reporting reductions exceeding 65%. Notably, some studies achieved nearly zero VAP rates post-intervention, particularly when implementing the "IHI Ventilator Bundle" alongside optimal endotracheal tube cuff pressure and subglottic suctioning. The findings suggest that multifaceted approaches, including multidisciplinary measures and ongoing education programs, coupled with monitoring bundle compliance, are crucial for achieving significant reductions in VAP incidence.[22]
- Da Rocha Gaspar et al. (2023) conducted a systematic review to examine the impact of evidence-based bundles on preventing VAP in adult and elderly populations. The review focused on articles published between January 2008 and December 2017, retrieved from PubMed, EBSCO, and Scielo databases using the keywords "Bundle" and "Pneumonia". After screening for duplicates and assessing titles and abstracts, 18 articles met the inclusion

criteria. These articles were evaluated based on various criteria including research reference, study type, patient characteristics, interventions performed, bundle items investigated, and outcomes. Results revealed that four bundle items were consistently present across all studies, with 61% of the articles considering seven to eight bundle items. Key bundle components included daily evaluation of sedation interruption, assessment for extubation readiness, head-of-bed elevation at 30 degrees, cuff pressure monitoring, coagulation prophylaxis, and oral hygiene. One study highlighted increased mortality in mechanically ventilated patients when oral hygiene and stress ulcer prophylaxis were omitted. Head-of-bed elevation at 30 degrees was universally reported in all studies. Overall, the research indicated that implementing bundle items was associated with a reduction in VAP incidence among adults and the elderly. Additionally, several studies underscored the importance of team education in reducing ventilator-related events.[23]

- Alfano et al. (2024) conducted a quality improvement project aimed at reducing the incidence of VAP through nursing education. The project targeted registered nurses in a 14-bed neuro trauma surgical burn ICU at a level 1 trauma center. A total of 146 patients were enrolled in this quasi-experimental study. Data collected before and after the nursing education intervention showed promising outcomes. Ventilator days decreased from 17.45 days to 13.42 days (P=.085), and ICU length of stay reduced from 24.77 days to 17.62 days (P=.035). Additionally, patient laboratory data indicated improvements in white blood cell values (P<.001), decreased oxygen requirements (P<.001), and fewer patients meeting VAP diagnostic criteria (P=.073). Although there were no statistically significant changes in nurses' knowledge or oral care bundle compliance, the positive patient outcomes following the education intervention underscored the importance of continued education for nursing staff in reducing hospital stays and associated costs related to VAP.[24].
- The INICC (2024) utilizes a bundle as part of its approach to reducing VAP rates and was effective in Africa, Asia, Latin America, Eastern Europe, and the Middle East, resulting in a VAP rate reduction. It implemented a multidimensional approach and an 8-component bundle in 374 ICUs across 35 low and middle-income countries (LMICs) from Latin America, Asia, Eastern Europe, and the Middle-East, to reduce VAP rates in ICUs. The VAP rate per 1000 mechanical ventilator (MV)-days was measured at baseline and during intervention at the 2nd month, 3rd month, 4–15 month, 16–27 month, and 28–39 month periods. 174,987 patients, during 1,201,592 patient days, used 463,592 MV-days. VAP per 1000 MV-days rates decreased from 28.46 at baseline to 17.58 at the 2nd month (RR=0.61; 95% CI=0.58-0.65; P<.001); 13.97 at the 3rd month (RR=0.49; 95% CI= 0.46-0.52; P<.001); 14.44 at the 4-15 month (RR=0.51; 95% CI=0.48-0.53; P<.001); 11.40 at the 16-27 month (RR=0.41; 95% CI=0.38-0.42; P<.001), and to 9.68 at the 28-39 month (RR=0.34; 95% CI=0.32-0.36; P<.001). The multilevel Poisson regression model showed a continuous significant decrease in incidence rate ratios, reaching 0.39 (p<.0001) during the 28th to 39th months after implementation of the intervention. This intervention resulted in a significant VAP rate reduction of 66% which was maintained throughout the 39 months.[19]

2. **Education.**

HCPs, patients, and caregivers participating in the care of a MV should receive training and demonstrate competence, commensurate with their roles, in understanding the recommendations to prevent VAP.[25]

3. **Surveillance of VAP.**

- **VAP.** Employ uniform surveillance methods and definitions to facilitate the comparison of data with benchmark standards. As the one published by the CDC/NHSN.[26]
- **Outcome measures.** Calculate the VAP rate using CDC/NHSN definitions by dividing the number of VAPs in each unit by the total number of MV-days in each unit, then multiply the result by 1,000 to express the measure as the number of VAPs/1,000 MV-days.[26]
- **Risk adjustment:** Stratify VAP rates based on the type of patient-care unit and provide comparisons using both historical data, CDC/NHSN data,[3] and the INICC data.[2]
- **Device utilization ratio (DUR)** can be monitored longitudinally to identify any variations, allowing for comparisons at both hospital and unit levels, and serving as a surrogate for assessing patient exposure risk. The DUR, a CDC/NHSN,[3] and INICC measure,[2] considers facility- and location-level factors influencing device use, calculated as the observed device-days divided by observed patient-days.

4. **Internal reporting of VAP rates.**

- These measures are crafted to enhance internal hospital quality improvement initiatives, and it is important to convey these measures to senior hospital leadership, nursing leadership, and clinicians engaged in the care of patients at risk for VAP.
- When providing internal reporting as a benchmark, compare the VAP rates of the given hospital against data from the CDC/NHSN,[3] and the INICC.[2]

5. **Monitoring compliance with recommendations to prevent VAP.**

- Assess compliance with MV connection and maintenance guidelines by employing a documented insertion paper or online checklist across all hospital settings, assigning knowledgeable HCP to this task.[19]
- This checklist could be a paper form or an online form. Documenting compliance using the checklist ensures adherence to proper procedural steps, and identifies and addresses any gaps, with the IHI offering an MV checklist as an example.[27]
- Document MV connection procedures, encompassing all relevant measures.
- Calculate compliance by dividing the compliance of each particular recommendation by the total number of MV connections, then multiply by 100 for a percentage expression. As one example, evaluate compliance with the documentation of daily assessments for the necessity of continuing MV access by measuring the percentage of patients with an MV where daily assessment documentation is present.
- Jalal et al. (2022) conducted an observational cross-sectional study in the ICUs of selected hospitals in eastern Saudi Arabia to assess the performance of medical professionals (MPs) in preventing VAP. Out of 152 MPs surveyed, 40.8% demonstrated adequate knowledge, while 7.9% had inadequate knowledge regarding VAP prevention. Physicians obtained the highest mean score (12.9 +/- 2.2), followed by nurses (11.3 +/- 1.6), respiratory therapists (RTs) (9.8 +/- 2.2), and interns (8.6 +/- 2.1). Overall, 52.6% of MPs exhibited satisfactory performance. Key findings included the majority of MPs adhering to hand hygiene practices before patient and ventilator contact, and the use of personal protective equipment in the ICU. However, only 47.4% of MPs regularly changed patient positions, and 77.6% followed sterile techniques during airway suctioning. Significant associations were found between MPs' performance and factors such as age, designation, professional experience, management of

chronic obstructive pulmonary disease conditions, and attendance of training sessions. The study concluded that while some MPs demonstrated satisfactory performance in VAP prevention, there is a need for enhanced training on clinical guidelines to further improve healthcare quality and reduce VAP rates in ICUs.[28]

6. **Performance feedback.**

- For the performance feedback, IPPs present charts, showcasing data related to attending HCPs' monthly degree of compliance with infection prevention practices.[19]
- The infection control tool plays a crucial role, enabling HCPs to identify areas for improvement in cases of low degree of compliance with infection prevention practices. Leveraging the "observer effects" on HCPs' behavior, this method's strength lay in influencing their practices to enhance efficiency.[29]
- This approach aimed to shape behaviors for more effective implementation.[30]

Main approaches

- **Avoid intubation and prevent reintubation**.[1] (Quality of Evidence HIGH).
  - Use high-flow nasal oxygen or noninvasive positive pressure ventilation as appropriate whenever safe and feasible.[31]
- **Minimize sedation**.[32] (Quality of Evidence MODERATE)
  - Avoid benzodiazepines in favor of other agents.[32]
  - Use a protocol to minimize sedation.[33]
  - Implement a ventilator liberation protocol.[34]
- **Maintain and improve physical conditioning**.[35] (Quality of Evidence MODERATE)
  - Initiating exercise and mobilization programs at an early stage could potentially decrease the duration of MV, shorten the LOS in the ICU, decrease the incidence of VAP, and enhance the likelihood of patients returning to independent function.
- **Elevate the head of the bed to 30–45°**.[36] (Quality of Evidence LOW)
- **Provide oral care with toothbrushing but without chlorhexidine**.[37] (Quality of Evidence MODERATE)
- **Provide early enteral vs. parenteral nutrition**.[38] (Quality of Evidence HIGH)
- **Change the ventilator circuit only if visibly soiled or malfunctioning** (or per manufacturers' instructions).[39] (Quality of Evidence HIGH)

Supplementary interventions

Other supplementary interventions encompass interventions linked with reduced rates of VAP, shortened periods of MV ventilation, reduced LOS, and/or decreased mortality, albeit with associated risks. These additional methods, yet their impact on objective outcomes remain unclear due to insufficient data. Hospitals might contemplate integrating additional approaches if their VAP rates persist despite achieving high compliance with the main approaches.

- Use selective oral or digestive decontamination in countries and ICUs with a low prevalence of antibiotic-resistant organisms.[40] (Quality of Evidence HIGH)
- Utilize endotracheal tubes with subglottic secretion drainage ports for patients expected to require >48–72 hours of MV.[41] (Quality of Evidence MODERATE)
- Consider early tracheostomy.[42] (Quality of Evidence MODERATE)
- Consider post-pyloric rather than gastric feeding for patients with gastric intolerance or at high risk for aspiration.[43] (Quality of Evidence MODERATE)

Not Advisable Interventions to Prevent VAP

- Ultrathin polyurethane endotracheal tube cuffs.[44] (Quality of Evidence MODERATE)
- Tapered endotracheal tube cuffs.[45] (Quality of Evidence MODERATE)
- Kinetic beds.[46] (Quality of Evidence MODERATE)
- Prone positioning.[47] (Quality of Evidence MODERATE)
- Chlorhexidine bathing.[48] (Quality of Evidence MODERATE)
- Stress-ulcer prophylaxis.[49] (Quality of Evidence MODERATE)
- Monitoring residual gastric volumes.[50] (Quality of Evidence MODERATE)

- Early parenteral nutrition.[51] (Quality of Evidence MODERATE)
- Automated control of endotracheal tube cuff pressure.[52] (Quality of Evidence MODERATE)
- Frequent cuff-pressure monitoring.[53] (Quality of Evidence MODERATE)
    - Naghibi and Karimi (2023) conducted a double-blind, randomized clinical trial exploring the impact of inspiratory pressure on VAP. A total of 120 MV patients were divided into two groups: control (pressure level 20) and intervention (pressure level 30). Results revealed no significant difference in demographic data and disease severity between groups. However, the intervention group exhibited a notably lower average Clinical Pulmonary Infection Score (P=.02) and Sequential Organ Failure Assessment score (p=.016) compared to the control group. These findings suggest that higher pressure levels may reduce VAP incidence and organ failure. Further research with a larger and more diverse population is recommended.[54]
- Oral care with chlorhexidine.[55] (Quality of Evidence MODERATE)
    - Vieira et al. (2022) examined the role of oral chlorhexidine in VAP prevention bundles, considering recent studies questioning its safety and efficacy. Despite its potential benefits, meta-analyses of double-blind randomized trials found no association between oral chlorhexidine and lower VAP rates. Conversely, a significant increase in mortality was reported, suggesting potential harm. Concerns arise regarding chlorhexidine's cytotoxicity and adverse effects on organic sectors. While it may still hold benefits in specific contexts, robust evidence supporting its routine application for all MV patients is lacking. Therefore, until further studies provide clarity, adherence to the principle of non-maleficence is prudent.[56]
    - Emami Zeydi et al. (2023) conducted a systematic review and meta-analysis to evaluate the effect of oral care with povidone-iodine (PI) in preventing VAP among adult patients admitted to ICUs. The study included four studies in the meta-analysis. While three studies suggested a decrease in VAP incidence with PI compared to placebo, the difference was not statistically significant (RR= 0.61, 95% CI: 0.25 to 1.47, Z=1.10, P=.27, I2:71.5%). One study comparing PI with chlorhexidine found no significant difference in VAP rates (RR= 1.50, 95% CI: 0.46 to 4.87, Z=0.67, P=.50, I2:0). Although two studies indicated a decrease in ICU length of stay with PI use compared to placebo, the effect was not statistically significant (WMD: -0.35, 95% CI: -3.90 to 3.20, Z=0.19, P=.85, I2:0). Additionally, three studies showed that PI had almost no effect on mortality rate compared to placebo (RR= 1.05, 95% CI: 0.66 to 1.53, Z=0.8, P=.27, I2:29.0%). The authors concluded that more rigorously designed randomized clinical trials and further evidence are needed to determine the effectiveness of PI in preventing VAP among adult ICU patients.[57]
- Probiotics.[58] (Quality of Evidence MODERATE)
    - In their 2022 study published in Nutrients, Cheema et al. conducted a systematic review and meta-analysis to assess the efficacy of probiotics in preventing VAP Their analysis of 18 randomized controlled trials (RCTs) involving 4893 patients revealed that probiotics may decrease the incidence of VAP (RR 0.68, 95% CI: 0.55-0.84; low certainty). However, subgroup and sensitivity analyses showed no significant effect in double-blind studies or those with a low risk of bias in randomization. The authors concluded that while probiotics may offer some benefit in reducing VAP incidence,

caution is warranted due to the low quality of evidence. They advocate for further large-scale, high-quality RCTs to establish conclusive evidence on the use of probiotics in preventing VAP.[59]

- Sun, Y. C., et al. (2022) conducted a meta-analysis on the role of probiotics in preventing VAP in critically ill patients undergoing MV. Their systematic review included 23 trials involving 5543 patients. The analysis revealed a significant decrease in the risk of VAP with probiotic treatment, with a combined RR (RR) of 0.67 (95% CI: 0.56, 0.81) across all studies, and 0.69 for adults and 0.55 for neonates/children. The positive effects observed in adult studies were further supported by trial sequential analysis (TSA) and subgroup analyses. Notably, a 31% decrease in VAP risk was noted in adults receiving prophylactic probiotics. However, no significant differences were found in mortality rates or other complications between probiotic and placebo groups. The study suggests the potential of probiotics as a preventive measure for VAP in both adults and neonates/children undergoing mechanical ventilation, but calls for further large-scale, high-quality randomized controlled trials (RCTs) to validate their efficacy and safety, especially in neonatal and pediatric populations and for long-term outcomes.[60]
    - Han et al. (2024) conducted an overview of systematic reviews and meta-analyses examining the role of probiotics in preventing ventilator-associated pneumonia (VAP). Thirteen studies were analyzed, revealing generally low methodological quality due to the absence of registered protocols and exclusion criteria lists. Reporting quality was inadequate, with deficiencies in reporting registration protocols, search strategies, and additional analyses. According to GRADE, 36.17% of outcomes were of moderate quality, 42.55% were of low quality, and 21.28% were of very low quality. Despite suggesting a potential reduction in VAP incidence with probiotics, caution is advised due to the current evidence's poor quality.[61]

Interventions Pending Resolution

- **Closed endotracheal suctioning systems.[62]**
    - Sanaie et al. (2022) conducted a systematic review and meta-analysis comparing closed tracheal suction systems (CTSS) versus open tracheal suction systems (OTSS) in preventing VAP in adult patients receiving MV. A comprehensive literature search yielded 59 publications, of which 10 were eligible for meta-analysis. Results indicated a significant increase in the incidence of VAP with OTSS compared to CTSS, with OTSS increasing VAP incidence by 57% (OR 1.57, 95% CI 1.063-2.32, p=.02). The study concludes that CTSS can significantly reduce VAP development compared to OTSS. However, the routine use of CTSS as a standard VAP prevention measure for all patients is not warranted, considering individual patient factors and cost implications. The authors highlight the need for high-quality trials with larger sample sizes to further evaluate these findings. This systematic review and meta-analysis offer valuable insights for healthcare practitioners in selecting appropriate suctioning systems for ventilated patients.[63]

- Silver-coated endotracheal tubes.[64] (Quality of Evidence MODERATE)
    - In a recent randomized clinical trial by Tincu et al. (2022), the efficacy of noble metal-alloy endotracheal tubes (ETTs) in preventing VAP was investigated. ETTs are recognized as a significant risk factor for VAP due to their role as a reservoir for infectious microorganisms. While previous studies have shown a reduction in biofilm formation with silver-coated ETTs, the effectiveness of noble metal-alloy ETTs remained uncertain. The study aimed to assess the efficacy of noble metal-alloy ETTs, specifically coated Bactiguard Infection Protection ETTs, compared to standard non-coated ETTs in patients requiring at least 48 hours of MV due to drug intoxication-induced coma. This randomized controlled trial involved 180 patients, with 97 in the intervention group and 83 in the control group. Results showed a significant reduction in VAP incidence in the intervention group (27.83% vs. 43.16%, P=.03) and a lower VAP ratio per 1000 ventilation days (51.26/1000 vs. 83.38/1000, P=.01) compared to the control group. Although there was no significant difference in the mean duration of MV between the two groups, the noble metal-alloy ETTs demonstrated a promising trend toward reducing ventilation days and ICU stay. This study underscores the potential of noble metal-alloy ETTs in reducing the incidence of VAP and associated complications in MV patients.[65]
    - Damas et al. (2022) conducted a multi-center, randomized, double-blind study to assess the efficacy of noble metal coating on endotracheal tubes (ETT) in preventing VAP among MV patients in ICUs. The study enrolled 323 patients from nine ICUs across four hospital sites in Belgium, with 168 patients receiving noble metal alloy (NMA)-coated ETTs and 155 patients receiving non-coated ETTs. While VAP incidence was lower in the NMA-coated group (6.5%) compared to the control group (11.6%), this difference was not statistically significant (p=.11). However, a Cox proportional hazards regression analysis revealed a delayed occurrence of VAP in the NMA-coated group (HR 0.41, 95% CI 0.19-0.88, p=.02). Additionally, the NMA-coated group showed a trend towards reduced antibiotic usage (58.8% vs. 65.4%, p=.06) and similar rates of tracheal colonization compared to the control group (30.2% vs. 33.9%, p=.57). These findings suggest the potential benefits of noble metal coating in VAP prevention, warranting further investigation in large-scale studies.[66]

SUGGESTED PRACTICE IN UNDER-RESOURCED SETTINGS

- **Education:** It was observed that there is a lack of sufficient education; therefore, an effort should be made to reverse it.
    - In a study by Lkubati et al. (2023), HCWs' understanding of VAP prevention in Hodeida, Yemen, was assessed. VAP, a common ICU infection, was targeted due to its impact on hospital stays, costs, and mortality rates. The research aimed to gauge HCWs' grasp of VAP prevention guidelines and their correlation with demographics.

Between April and July 2017, 140 HCWs from public and private hospitals in Hodeida received questionnaires. Among the 120 respondents (20 physicians, 20 anesthesia technicians, and 80 nurses), the mean knowledge score was low (41 +/- 18). Notably, anesthesia technicians scored highest, followed by physicians and nurses. Males outperformed females. Previous education on VAP correlated with better knowledge. Continuous training is crucial for improving HCWs' ability to prevent VAP.[67]

- In their 2022 study, Getahun et al. explored the knowledge of intensive care nurses regarding ventilator-associated pneumonia (VAP) prevention in Northwest Ethiopia referral hospitals in 2021. VAP, a common nosocomial infection among critically ill patients on intubation and MV, requires adherence to evidence-based guidelines, which may be hindered by nurses' lack of understanding. Their multicenter cross-sectional study, conducted from April to July 2021, included all intensive care nurses in the area. With a response rate of 95.77%, data analysis revealed a mean knowledge score of 10.1 +/- 2.41 out of 20 questions, with 48.04% demonstrating good knowledge and 51.96% showing poor knowledge of VAP prevention. Higher academic qualifications and completion of ICU training were significantly associated with better knowledge. The study emphasizes the urgent need for enhanced training and educational efforts among intensive care nurses to improve VAP prevention practices.[68]

- **Bundle approach:**
    - In a NICU in Egypt, a study showed a significant reduction in VAP rate from 36.4 to 23.0 VAPs per 1,000 MV-days (RR= 0.565, 95% CI= 0.408-0.782, p=0.0006) by applying a bundle consisting of the following seven components: (1) Head-of-bed elevation of 30-45 degrees, (2) Reinforcement of hand hygiene practice, (3) Sterile suction and handling of respiratory equipment, (4) Strict adherence to the unit protocol for intubation, re-intubation, and endotracheal tube suction, (5) Changing ventilator circuit if visibly soiled or mechanically malfunctioning, (6) Proper timed mouth care with normal saline and suction of oro-pharyngeal secretion, (7) Daily evaluation for readiness for extubation to nasal continuous airway pressure (NCPAP) at morning round, along with sedation vacation for sedated patients.[69]
    - According to eleven research studies implemented by INICC, a bundle with the following eight components, [70-80] was effective in significantly reducing the rates of VAP in LMICs:
        1. Optimize hand hygiene compliance;[70-80]
        2. Assess readiness to extubate daily in patients without contraindications;[70-80]
        3. Maintain cuff pressure and volume at the minimal occlusive settings to prevent clinically significant air leaks around the endotracheal tube, typically 20 cm of water;[70-80]
        4. Minimize the duration of MV;[70-80]
        5. Minimize the duration of the ICU stay;[70-80]
        6. Elevate the head of the bed to 30–45°;[70-80]
        7. Provide oral care with toothbrushing but without chlorhexidine;[70-80]
        8. Prevent condensation from reaching the patient.[70-80]

- **Multidimensional Approach**: Numerous national, multinational, and multicontinental studies, employing a multidimensional approach, have been conducted in LMICs, achieving a significant reduction in rates of VAP and mortality. All of them include six components: (a) bundle, (b) education, (c) surveillance of VAP, (d) monitoring compliance with recommendations to prevent VAP, (e) internal reports of VAP rates, and (f) performance feedback. The following 11 studies were conducted applying this specific intervention:
    1. Conducted in two Argentinean hospitals in 2006, the study demonstrated a significant reduction in the VAP rate following the intervention (51.28 vs 35.50 episodes of VAP per 1000 MV-days, respectively, RR= 0.69, 95% CI: 0.49-0.98, P ≤ .003).[70]
    2. Conducted in pediatric ICUs of five LMICs in 2012, the study showed a significant reduction in the VAP rate following the intervention (11.7 per 1,000 MV-days vs 8.1 per 1,000 MV-days [RR= 0.69; 95% CI, 0.5-0.96; P=.02]).[71]
    3. Conducted in neonatal ICUs in 10 LMICs in 2012, the study demonstrated a significant reduction in the VAP rate following the intervention (17.8 vs 12.0 cases per 1,000 MV-days during phase 2 [RR= 0.67; 95% CI, 0.50-0.91]).[72]
    4. Conducted in Shanghai in 2012, the study revealed a significant reduction in the VAP rate following the intervention (24.1 per 1000 vs 5.7 per 1000 MV-days [RR= 0.31; 95% CI, 0.16-0.36; P=.0001]).[73]

5. Conducted in Cuba in 2013, the study demonstrated a significant reduction in the VAP rate following the intervention (52.63 per 1000 MV days vs 15.32 per 1000 MV-days [RR= 0.3; 95% CI, 0.12-0.7; P, 0.003]).[74]
6. Conducted in 11 adult ICUs from 10 cities in Turkey in 2013, the study revealed a significant reduction in the VAP rate following the intervention (31.14 per 1,000 MV-days vs 16.82 per 1,000 MV-days [RR= 0.54; 95% CI, 0.42-0.7; P, 0.0001]).[75]
7. Conducted in 21 adult ICUs from 10 cities in India in 2013, the study demonstrated a significant reduction in the VAP rate following the intervention (17.43/1000 MV-days vs 10.81 [RR 0.62, 95% CI 0.5-0.78, P=.0001]).[76]
8. Conducted in 22 hospitals in 14 cities in Saudi Arabia in 2018, the study revealed a significant reduction in the VAP rate following the intervention (7.84 VAPs vs 4.74 VAPs per 1000 MV-days [incidence density rate 0.61; 95% CI 0.5-0.7; P<.001]).[77]
9. Conducted ICUs of two hospitals in Kuwait in 2018, the study demonstrated a significant reduction in the VAP rate following the intervention (7.0 vs 3.0 VAPs per 1000 MV-days). The VAP rate was reduced by 57.1% (incidence-density ratio = 0.51; 95% CI= 0.28-0.93; p=.042).[78]
10. Conducted in 14 ICUs in 11 hospitals in 5 cities within Argentina in 2018, the study revealed a significant reduction in the VAP rate following the intervention (19.9 vs 9.4 VAPs per 1,000 MV-days [incidence density rate, 0.48; 95% CI, 0.3-0.7; P<.001]).[79]
11. Conducted in 374 ICUs across 35 LMICs from Latin America, Asia, Eastern Europe, and the Middle East in 2024, the study demonstrated a significant reduction in the VAP rate following the intervention (28.46 vs 9.68 at the 28-39 month [RR= 0.34; 95% CI= 0.32-0.36; P<.001]).[80]

SUMMARY

The empirical evidence delineated in this review incontrovertibly establishes that VAP rates in LMICs persist at a magnitude exceeding tenfold that observed in high-income countries. The review systematically presents scientific insights regarding the efficacy of diverse interventions across all settings, distinguishing between proven effective measures, those demonstrated to be ineffective, and the prescription of supplementary measures specifically advocated for adoption in LMICs.

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