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ISID Guideline

Preventing ventilator-associated pneumonia: A position paper of the International Society for Infectious Diseases, 2024 update

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ABSTRACT

Objectives: This review by a panel of experts convened by the International Society for Infectious Diseases aims to consolidate current recommendations for preventing ventilator-associated pneumonia (VAP). It provides insights into VAP rates, the attributable extra length of stay, costs, mortality, and risk factors in high-income and low- and middle-income countries (LMICs).
Methods: A comprehensive review of existing recommendations and evidence-based strategies for preventing VAP was conducted. The expert panel analyzed data on VAP incidence, associated healthcare burdens, and risk factors across different economic settings to formulate applicable preventive measures.
Results: The review identifies significant differences in VAP rates, healthcare costs, extra length of hospital stay, and mortality between high-income and LMICs. Evidence-based strategies for preventing VAP were highlighted, demonstrating their effectiveness across different healthcare settings.
Conclusion: The recommendations and insights provided in this position paper aim to guide healthcare professionals in effectively preventing VAP. The adoption of evidence-based preventive strategies can potentially reduce VAP rates, and associated costs, and improve patient outcomes in both high-income and LMICs.

Introduction

This document examines existing evidence and offers an international perspective with focused suggestions for addressing critical issues in high-income and low- and middle-income countries (LMICs). It provides concise, actionable recommendations to prevent ventilator-associated pneumonia (VAP). We acknowledge statements and recommendations from previous guidelines, such as those of the SHEA/IDSA/APIC [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, our review concentrates on interventions aimed at reducing VAP. The International Society of Infectious Diseases sponsors this expert guidance document.

VAP rates in the USA, as reported by the CDC National Healthcare Safety Network (NHSN), show a median VAP rate of 1.1/1000 mechanical ventilator (MV)-days in medical-surgical intensive care units (ICUs) [2]. The International Nosocomial Infection Control Consortium (INICC) observed consistently higher VAP rates in LMICs over the past two decades. The INICC report 2002-2005 indicated a VAP rate of 24.1/1000 MV-days, gradually reducing to 11.96 in the report 2015-2020 [3], but still far above CDC/NHSN. Consequently, strategies must be assessed to address this critical situation, particularly in LMICs. VAP is the second most common healthcare-associated infection (HAI) in pediatric ICUs. It affects critically ill children due to their underdeveloped immune systems and prolonged MV [1].

Costs associated with VAP vary globally, with reported costs in the USA of $9966 [4], and in Spain EUR 20,965.28 [5]. Pooling data from 630 ICUs from 2015 to 2020 across 45 LMICs in Africa, Asia, Eastern Europe, Latin America, and the Middle East, including 204,770 patients, 1480,620 patient days, 637,850 MV-days, and 7635 VAP cases. For patients without HAIs, the length of stay (LOS)

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was 6.57 days, and mortality rates were 14.06%, and for those with VAP, LOS was 22.54 days, and mortality was 36.89% [3].

VAP is a major ICU concern, responsible for over half of antibiotic use in mechanically ventilated patients. The rise of antimicrobial-resistant (AMR) pathogens complicates treatment, making it essential to understand local resistance patterns to guide effective therapy. Continuous surveillance of AMR helps refine antibiotic selection, reduce misuse, and improve patient outcomes [1]. A study covering 204 countries estimates the burden of AMR from 1990 to 2021. The results highlight 4.71 million AMR-associated deaths in 2021, with methicillin-resistant *Staphylococcus aureus* and Gram-negative carbapenem resistance causing significant mortality increases. The highest mortality was found in South Asia and Latin America. Antimicrobial stewardship is crucial to reducing the inappropriate use of antibiotics, which drives multidrug-resistant organisms. Interventions such as infection prevention, antibiotic stewardship, and vaccination are critical [6].

Studies have documented that VAP is an independent significant risk factor for mortality. In a multicenter, multinational, multicontinental study involving 786 ICUs in 147 cities spanning 37 countries between 1998 and 2022, a total of 300,827 patients were followed during 2167,397 patient days, resulting in 21,371 HAIs. Multiple logistic regression identified the following mortality risk factors: VAP ($P < 0.0001$), MV-days with a risk increase of 2% per day ($P < 0.0001$), LOS with a risk increase of 1% per day ($P < 0.0001$), female sex ($P < 0.0001$), and age ($P < 0.0001$) [7].

Several authors identified the following as VAP risk factors: tracheostomy, LOS, older age, trauma patients, postsurgical patients, burn patients, longer duration of surgery, history of smoking, low serum albumin concentration, high score on the American Society of Anesthesiologists Physical Status Classification System, APACHE II score >20, acute respiratory distress syndrome, lung injury, chronic obstructive pulmonary disease, upper respiratory tract colonization, sinusitis, PaO2/FiO2 ratio<200 mmHg, oropharyngeal colonization, biofilm on the surface and within the lumen of the endotracheal tube (ETT), duration of MV, frequent change in the ventilator circuit, lack of use of heat and moisture exchange humidifiers, supine position, frequent reintubation, enteral feeding, multiple central venous line insertions, presence of catheter-related infection, paralytic agents, previous use of broad-spectrum antibiotics, and patients transported out of the ICU [1].

Methods

The International Society of Infectious Diseases (ISID) recruited five subject-matter experts in VAP prevention to edit the ISID guidelines. Each expert conducted a comprehensive search of PubMed and Embase (January 2014 to June 2024). The experts first reviewed the abstracts of the articles identified and then proceeded with full-text reviews. Relevant references were incorporated into the review. Recommendations resulting from this process were classified based on the quality of evidence (QoE) and the balance between the desirable and potential undesirable effects of various interventions. The experts reached a consensus regarding the literature findings, recommendations, the QoE supporting these recommendations, and their classification into the following categories [1]: Necessary prerequisites [2], Implementation of VAP prevention strategies [3], Before insertion [4], At insertion [5], After insertion [6], Supplementary interventions [7], Not advisable interventions to prevent VAP [8], Interventions pending resolution, and [9] Suggested practice in under-resourced settings. After reaching a consensus, the experts reviewed the draft manuscript and approved the document and its recommendations. All panel members adhered to ISID policies on conflict-of-interest disclosure.

Suggested practice

(1) **Necessary prerequisites.**

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

b) Assets for delivering suitable education and training. Structured education and training programs focused on infection prevention and VAP-specific strategies must be provided. They should target all relevant staff, ensuring proficiency in proper MV practices and infection control protocols. Training should include regular workshops, hands-on simulations, and competency assessments to maintain adherence to guidelines. Additionally, the content should be tailored to the facility's patient population and local antimicrobial resistance patterns, with ongoing updates to reflect current best practices [1].

c) A sufficiently staffed infection prevention program is responsible for identifying patients who meet the surveillance definition for VAP. An adequately staffed infection prevention professionals (IPP) team is crucial for monitoring and identifying patients at risk for VAP using standardized definitions, such as those from the CDC/NHSN. Their duties include conducting audits, reviewing clinical data, and ensuring accurate VAP case reporting. They collaborate with ICU staff to implement timely interventions and update prevention protocols based on surveillance data and antimicrobial resistance trends [1].

d) A well-staffed IPP, with the potential inclusion of information technology support, is crucial for gathering and computing MV-days as a denominator in VAP rate calculations. A dedicated IPP team is essential for accurately tracking MV days, a key metric in calculating VAP rates. IPPs should work closely with IT departments to streamline data collection and ensure precise tracking of MV-days. Integrating IT systems enables efficient and accurate computation, facilitating real-time monitoring of VAP rates and allowing for timely interventions and adjustments in infection control strategies [1].

e) 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].

f) Providing epidemiological bulletins to doctors is essential for effective empirical therapy, particularly for patients at risk of VAP. Access to localized infection data, such as VAP incidence and antimicrobial resistance patterns, enables doctors to make informed decisions, tailor treatments, reduce inappropriate antibiotic use, and improve patient outcomes, especially in ICUs [1].

(2) **Implementation of VAP prevention strategies**

a) **Multidimensional approach:**

1. Numerous national, multinational, and multicontinental studies employing a multidimensional approach have been conducted, achieving significant reductions in rates of VAP and mortality. All of these studies incorporate six components: (a) bundle, (b) education, (c) surveillance, (d) monitoring compliance with VAP prevention recommendations, (e) internal reporting of VAP rates, and (f) performance feedback [8–15].

b) **Bundles:**

i) Care "bundles" in infection prevention and safety are simple sets of evidence-based practices that, when im-

plemented collectively, improve the reliability of their delivery and enhance patient outcomes [16].

ii) According to 11 research studies implemented by INICC, a multidimensional approach with six steps, including an eight-component bundle, significantly reduced VAP rates in LMICs. The components included [1] Hand hygiene compliance [2], daily readiness assessment for extubation in patients without contraindications [3], maintaining cuff pressure at minimal occlusive settings (typically 20 cm of water) [4], minimizing the duration of MV [5], minimizing the ICU stay [6], elevating the head of the bed to 30°-45° [7], providing oral care with toothbrushing, and [8] preventing condensation from reaching the patient. This approach was implemented in 374 ICUs across 35 LMICs in Latin America, Asia, Eastern Europe, and the Middle East. Monitoring 174,987 patients over 1201,592 patient days, utilizing 463,592 MV-days, VAP rates per 1000 MV-days decreased significantly from baseline 28.46 to 17.58 at the 2nd month (RR = 0.61; 95% CI = 0.58-0.65; $P < 0.001$), 13.97 at the 3rd month (RR = 0.49; 95% CI = 0.46-0.52; $P < 0.001$), 14.44 at 4-15 months (RR = 0.51; 95% CI = 0.48-0.53; $P < 0.001$), 11.40 at 16-27 months (RR = 0.41; 95% CI = 0.38-0.42; $P < 0.001$), and 9.68 at 28-39 months (RR = 0.34; 95% CI = 0.32-0.36; $P < 0.001$). A multilevel Poisson regression model showed a continuous significant decrease in incidence rate ratios, reaching 0.39 ($P < 0.0001$) during the 28th to 39th months after the intervention was implemented, resulting in a significant and sustained reduction in VAP rates by 66% over 39 months. See Table 1 [8–15].

iii) A meta-analysis on the effectiveness of ventilator care bundles in preventing VAP included 36 studies. It found that implementing care bundles significantly reduced the number of VAP episodes. The most commonly utilized components of the ventilator bundle were head-of-bed elevation and oral care [17].

iv) Da Rocha Gaspar et al. conducted a systematic review to examine the impact of evidence-based bundles on preventing VAP in adult and elderly populations. Eighteen articles met the inclusion criteria. 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 [1] daily evaluation of sedation interruption [2], assessment for extubation readiness [3], head-of-bed elevation at 30° [4], cuff pressure monitoring [5], prophylaxis for coagulation disorders, and [6] oral hygiene. Head-of-bed elevation at 30° was universally reported in all studies. Overall, the research indicated that implementing bundle items was associated with a reduction in VAP incidence [18].

v) In a NICU in Egypt, a study demonstrated a significant reduction in VAP rate from 36.4 to 23.0 VAPs per 1000 MV-days (RR = 0.56, 95% CI = 0.40-0.78, $P = 0.0006$) by implementing a bundle consisting of the following seven components [1]: Head-of-bed elevation of 30°-45° [2], Hhand hygiene practices [3], Sterile suction and handling of respiratory equipment [4], Adherence to the unit protocol for intubation, re-intubation, and ETT suction [5], Changing ventilator circuit if visibly soiled or mechanically malfunctioning [6], Proper timed mouth care with normal saline and suction of oropharyngeal secretions [7], Daily evaluation for readiness for extubation to nasal continuous airway pressure during morning rounds, along with sedation vacation for sedated patients [19].

c) **Education:**

i) Healthcare providers (HCPs), and patients involved in managing MV patients should receive training and demonstrate competence according to their roles. This training should ensure understanding and proficiency in implementing recommendations to prevent VAP [1].

ii) Alfano et al. conducted a quality improvement project aimed at reducing the incidence of VAP through nursing education. The project targeted registered nurses. MV-days decreased from 17.45 to 13.42 days ($P = 0.085$), and ICU LOS reduced from 24.77 to 17.62 days ($P = 0.035$). Additionally, patient laboratory data indicated improvements in white blood cell values ($P < 0.001$), decreased oxygen requirements ($P < 0.001$), and a trend toward fewer patients meeting VAP diagnostic criteria ($P = 0.073$) [20].

iii) A study explored the knowledge of ICU nurses regarding VAP prevention in Ethiopian referral hospitals. 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 [21].

d) **Surveillance of VAP:**

i) Employ uniform surveillance methods and definitions, such as those published by the CDC/NHSN, to facilitate the comparison of data with benchmark standards [1].

ii) The VAP rate is calculated using CDC/NHSN definitions by dividing the number of VAPs by the total MV-days in each unit and multiplying by 1000 to express the measure as VAPs per 1000 MV-days [1].

iii) Stratify VAP rates based on the type of patient-care unit and provide comparisons using historical data, CDC/NHSN data [2], and the INICC international data [3].

iv) Device utilization ratio can be longitudinally monitored to detect variations, enabling comparisons at hospital and unit levels, and serving as a surrogate for assessing patient exposure risk. The DUR, a CDC/NHSN [2], and INICC measure [3], considers facility and location-level factors influencing MV use, calculated as the observed MV-days divided by observed patient days.

e) **Internal reporting of VAP rates:**

i) These measures are designed to bolster internal hospital quality improvement initiatives, emphasizing the importance of communicating them to senior leadership and clinicians involved in caring for 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 [2], and the INICC international data [3].

f) **Monitoring compliance with recommendations to prevent VAP:**

i) Assess compliance with MV connection and maintenance guidelines by implementing a documented insertion paper or online checklist across all hospital settings and assigning knowledgeable HCPs to oversee this task [1].

ii) The checklist ensures compliance with procedural steps for MV connection and maintenance, identifying and addressing any gaps. An example is the MV checklist provided by the IHI [1].

iii) Document MV connection procedures comprehensively, covering all relevant measures. Calculate compliance by dividing the number of times each specific recommenda-

Table 1
Impact of a multidimensional approach on VAP rates in low- and middle-income countries.

Setting	Number of ICUs	Study period	ICU type	Baseline VAP rate[a]	Intervention VAP rate[a]	RR; 95% CI; *P*-value	Ref.
35 LMICs	374	1998-2022	AICU	28.46	9.68	RR = 0.34; 95% CI = 0.32-0.36; $P < 0.001$	V. D. Rosenthal *et al.*, "Assessing the impact of a multidimensional approach and an 8-component bundle in reducing incidences of ventilator-associated pneumonia across 35 countries in Latin America, Asia, the Middle East, and Eastern Europe," *J Crit Care,* vol. 80, p. 154500, Apr 2024, doi: 10.1016/j.jcrc.2023.154500.
Saudi Arabia	37	2016-2017	AICU	7.84	4.74	RR = 0.61; 95% CI 0.5-0.7; $P < 0.001$	H. M. Al-Abdely *et al.*, "Impact of the International Nosocomial Infection Control Consortium (INICC)'s multidimensional approach on rates of ventilator-associated pneumonia in intensive care units in 22 hospitals of 14 cities of the Kingdom of Saudi Arabia," *J Infect Public Health,* vol. 11, no. 5, pp. 677-684, Sep-Oct 2018, doi: 10.1016/j.jiph.2018.06.002.
India	21	2004-2011	AICU	17.43	10.81	RR = 0.62, 95% CI 0.5-0.78, $P = 0.0001$	Y. Mehta *et al.*, "Effectiveness of a multidimensional approach for prevention of ventilator-associated pneumonia in 21 adult intensive-care units from 10 cities in India: findings of the International Nosocomial Infection Control Consortium (INICC)," *Epidemiol Infect,* vol. 141, no. 12, pp. 2483-91, Dec 2013, doi: 10.1017/S0950268813000381.
10 LMICs	15	2003-2010	NICU	17.8	12.0	RR = 0.67; 95% CI, 0.50-0.91; $P < 0.001$	V. D. Rosenthal *et al.*, "Findings of the International Nosocomial Infection Control Consortium (INICC), Part II: Impact of a multidimensional strategy to reduce ventilator-associated pneumonia in neonatal intensive care units in 10 developing countries," *Infect Control Hosp Epidemiol,* vol. 33, no. 7, pp. 704-10, Jul 2012, doi: 10.1086/666342.
Argentina	14	2014-2017	AICU	19.9	9.4	RR = 0.48; 95% CI, 0.3-0.7; $P < 0.001$	V. D. Rosenthal *et al.*, "Impact of the International Nosocomial Infection Control Consortium's multidimensional approach on rates of ventilator-associated pneumonia in 14 intensive care units in 11 hospitals of 5 cities within Argentina," *Am J Infect Control,* vol. 46, no. 6, pp. 674-679, Jun 2018, doi: 10.1016/j.ajic.2017.11.021.
Turkey	11	2003-2009	AICU	31.14	16.82	RR = 0.54; 95% CI, 0.42-0.7; *P*, 0.0001	H. Leblebicioglu *et al.*, "Effectiveness of a multidimensional approach for prevention of ventilator-associated pneumonia in 11 adult intensive care units from 10 cities of Turkey: findings of the International Nosocomial Infection Control Consortium (INICC)," *Infection,* vol. 41, no. 2, pp. 447-56, Apr 2013, doi: 10.1007/s15010-013-0407-1.
5 LMICs	8	2003-2010	PICU	11.7	8.1	RR = 0.69; 95% CI, 0.5-0.96; $P = 0.02$	V. D. Rosenthal *et al.*, "Effectiveness of a multidimensional approach to reduce ventilator-associated pneumonia in pediatric intensive care units of 5 developing countries: International Nosocomial Infection Control Consortium findings," *Am J Infect Control,* vol. 40, no. 6, pp. 497-501, Aug 2012, doi: 10.1016/j.ajic.2011.08.005.
Argentina	4	2001-2002	AICU	51.28	35.50	RR = 0.69, 95% CI: 0.49-0.98, $P \leq 0.003$	V. D. Rosenthal, S. Guzman, and C. Crnich, "Impact of an infection control program on rates of ventilator-associated pneumonia in intensive care units in 2 Argentinean hospitals," *Am J Infect Control,* vol. 34, no. 2, pp. 58-63, Mar 2006, doi: 10.1016/j.ajic.2005.11.002.
China	3	2005-2009	AICU	24.1	5.7	RR = 0.31; 95% CI, 0.16-0.36; $P = 0.0001$	L. Tao, B. Hu, V. D. Rosenthal, Y. Zhang, X. Gao, and L. He, "Impact of a multidimensional approach on ventilator-associated pneumonia rates in a hospital of Shanghai: findings of the International Nosocomial Infection Control Consortium," *J Crit Care,* vol. 27, no. 5, pp. 440-6, Oct 2012, doi: 10.1016/j.jcrc.2011.12.018.
Kuwait	3	2014-2015	AICU	7.0	3.0	RR = 0.51; 95% CI = 0.28-0.93; $P = 0.042$	H. H. Al-Mousa *et al.*, "Impact of the International Nosocomial Infection Control Consortium (INICC) multidimensional approach on rates of ventilator-associated pneumonia in intensive care units of two hospitals in Kuwait," *J Infect Prev,* vol. 19, no. 4, pp. 168-176, Jul 2018, doi: 10.1177/1757177418759745.
Cuba	1	2007-2010	AICU	52.63	15.32	RR = 0.3; 95% CI, 0.12-0.7; *P*, 0.003	H. Guanche-Garcell, C. Morales-Perez, and V. D. Rosenthal, "Effectiveness of a multidimensional approach for the prevention of ventilator-associated pneumonia in an adult intensive care unit in Cuba: findings of the International Nosocomial Infection Control Consortium (INICC)," *J Infect Public Health,* vol. 6, no. 2, pp. 98-107, Apr 2013, doi: 10.1016/j.jiph.2012.11.009.

AICU, adult intensive care unit; CI, confidence interval; ICU, intensive care unit; LMICs, low- and middle-income country; NICU, neonatal intensive care unit; PICU, pediatric intensive care unit; Ref, reference; RR, relative risk; VAP, ventilator-associated pneumonia.
[a] VAPs per 1000 mechanical ventilator days.

tion is followed by the total number of MV connections, then multiply by 100 to express the compliance rate as a percentage.

iv) An observational cross-sectional study in ICUs of selected hospitals in Saudi Arabia to evaluate HCPs' performance in preventing VAP was conducted. Among 152 HCPs surveyed, 40.8% demonstrated adequate knowledge, while 7.9% had inadequate knowledge regarding VAP prevention. Physicians achieved 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 HCPs exhibited satisfactory performance. The study highlighted that most HCPs adhered to hand hygiene practices before patient and ventilator contact and used personal protective equipment in the ICU. However, only 47.4% of HCPs regularly changed patient positions, and 77.6% followed sterile techniques during airway suctioning [22].

g) **Performance feedback:**
   i) For performance feedback, IPPs present charts displaying data on attending HCPs' monthly compliance with infection prevention practices [8–15].
   ii) The infection control tool plays a crucial role by enabling HCPs to identify areas for improvement in cases of low compliance with infection prevention practices. Leveraging the "observer effect" on HCPs' behavior, this method's strength lies in influencing their practices to enhance efficiency [23].

(3) **Main approaches**
a) **Avoid intubation and prevent reintubation** [1]. (QoE HIGH). Use high-flow nasal oxygen or noninvasive positive pressure ventilation as appropriate whenever safe and feasible [1].
b) **Minimize sedation** [1]. (QoE MODERATE). Avoid benzodiazepines in favor of other agents [1]. Use a protocol to minimize sedation [1]. Implement a ventilator liberation protocol [1].
c) **Maintain and improve physical conditioning** [1]. (QoE MODERATE)
d) 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.
e) **Elevate the head of the bed to 30°-45°** [1]. (QoE LOW)
f) **Provide oral care with toothbrushing but without chlorhexidine (CHG)** [1]. (QoE MODERATE)
g) **Provide early enteral vs parenteral nutrition** [1]. (QoE HIGH)
h) **Change the ventilator circuit only if visibly soiled or malfunctioning** (or per manufacturers' instructions) [24]. (QoE HIGH)
i) **Use continuous cuff pressure control**
   i) A meta-analysis aimed to evaluate the effectiveness of continuous cuff pressure control (CCPC) in preventing VAP, as micro-aspiration of subglottic secretions is the primary cause of VAP. The study included 11 randomized controlled trials (RCTs) with 2092 intubated adult patients. Results showed that CCPC reduced the risk of VAP (OR 0.51), while secondary outcomes revealed no significant differences in mortality but a decrease in the duration of MV and ICU stay. However, the evidence was rated as "very low" [25].
   ii) A study evaluated the impact of CCCP vs intermittent control cuff pressure (ICCP) for preventing VAP in critically ill patients. A meta-analysis of 14 RCTs (2080 patients) revealed that CCCP significantly reduced VAP incidence compared to ICCP (RR = 0.52, 95% CI = 0.37-0.74, $P < 0.001$) despite considerable heterogeneity ($I^2 = 71\%$). Subgroup analysis showed an even greater reduction in VAP when CCCP was combined with subglottic secretion drainage (SSD) (RR = 0.39, 95% CI = 0.29-0.52, $P < 0.001$). CCCP also decreased the duration of mechanical ventilation (MD = –2.42 days, 95% CI = –4.71 to 0.12, $P = 0.04$), although no significant differences were found in LOS or mortality. The results suggest that CCCP, particularly in combination with SSD, is effective in reducing VAP and stabilizing cuff pressure [26].

(4) **Supplementary interventions**
a) Other supplementary interventions include strategies associated with reduced rates of VAP, shortened durations of MV, decreased LOS, and/or lower mortality rates. Hospitals may consider integrating these approaches if their VAP rates persist despite achieving high compliance with primary prevention strategies.
b) Use selective oral or digestive decontamination in settings with a low prevalence of AMR organisms [1]. (QoE HIGH)
c) Utilize endotracheal tube (ETTs) with subglottic secretion drainage (SSD) ports for patients expected to require >48-72 hours of MV [1]. (QoE MODERATE)
d) Consider early tracheostomy [1]. (QoE MODERATE)
e) Consider postpyloric rather than gastric feeding for patients with gastric intolerance or at high risk for aspiration [1]. (QoE MODERATE)

(5) **Not advisable interventions to prevent VAP**
a) **Ultrathin polyurethane ETT cuffs** [1]. (QoE MODERATE)
b) **Tapered ETT cuffs** [1]. (QoE MODERATE)
c) **Kinetic beds** [1]. (QoE MODERATE)
d) **Prone positioning** [1]. (QoE MODERATE)
e) **CHG bathing** [1]. (QoE MODERATE)
f) **Stress-ulcer prophylaxis** [1]. (QoE MODERATE)
g) **Monitoring residual gastric volumes** [1]. (QoE MODERATE)
h) **Early parenteral nutrition** [1]. (QoE MODERATE)
i) **Automated control of ETT cuff pressure** [27]. (QoE MODERATE)
j) **Oral care with CHG** [28]. (QoE MODERATE)
   i) A study evaluated the effects of selective digestive decontamination (SDD), selective oropharyngeal decontamination (SOD), and topical CHG on mortality in ICU patients through a network meta-analysis of RCTs. SDD significantly reduced mortality (OR = 0.73; 95% CI = 0.64-0.84), while SOD also showed a reduction in mortality (OR = 0.85; 95% CI = 0.74-0.97). In contrast, CHG was linked to an increased risk of mortality (OR = 1.25; 95% CI = 1.05-1.50). Both SDD and SOD were superior to CHG in reducing mortality, though the distinction between SDD and SOD was less clear. The review emphasized that CHG, commonly used in ICUs, might be associated with increased mortality, suggesting caution in its widespread use for infection prevention in ICUs [29].
   ii) A cohort study investigated the impact of CHG oral care on mortality in a general hospitalized population. The study included 82,274 adult patients, of which 11,133 (14%) received CHG. Low-level exposure to CHG (≤300 mg) was associated with an increased risk of death (OR = 2.61; 95% CI = 2.32-2.92). The risk was higher among patients with a lower risk of death: OR = 5.50 (95% CI = 4.51-6.71) in those with minor/moderate risk, OR = 2.33 (95% CI = 1.96-2.78) in those with major risk, and no significant increase in those with extreme risk (OR = 1.13; 95% CI = 0.90-1.41). Similar patterns were observed for high-level exposure (>300 mg). Notably, no harmful effects were seen in ventilated or nonventilated ICU patients, but an increased risk of death was found in non-ICU patients who were not mechanically ventilated. The number needed to expose one additional fatality was 47.1 (95% CI = 45.2-49.1). The study suggests caution in the widespread use of CHG oral care without proven benefit [30].
   iii) A study examines the consequences of discontinuing the use of CHG in oral care protocols within ICU settings. While CHG has long been a standard practice for preventing VAP, the authors present evidence suggesting that its routine use may not offer substantial benefits and could be linked to increased mortality. The findings prompt a reconsideration of CHG use in ICUs and advocate for a more holistic approach to oral care, emphasizing the importance of comprehensive regimens that extend beyond the application of antiseptic solutions alone.

This shift calls for reevaluating oral care strategies in ICU settings, ensuring they prioritize patient safety and overall well-being [31].

iv) A meta-analysis included 10 RCTs that assessed the effectiveness of CHG in preventing VAP in mechanically ventilated patients. The outcomes included VAP incidence, all-cause mortality, duration of MV, and LOS. The results showed that oral application of CHG significantly reduced VAP incidence (RR = 0.73, 95% CI = 0.55-0.97) without increasing all-cause mortality (RR = 1.13, 95% CI = 0.96-1.32). While CHG effectively reduced VAP, the evidence on its impact on mortality was inconclusive [32].

k) **Probiotics** [33]. (QoE MODERATE)

i) A meta-analysis to assess the efficacy of probiotics in preventing VAP, including 18 RCTs, 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 QoE [34].

ii) A meta-analysis on the role of probiotics in preventing VAP in critically ill patients undergoing MV included 23 trials. The analysis revealed a significant decrease in the risk of VAP with probiotic treatment, with a combined RR = 0.67 (95% CI = 0.56-0.81) across all studies 0.69 for adults, and 0.55 for neonates/children. Notably, a 31% decrease in VAP risk was noted in adults receiving prophylactic probiotics. The study suggests the potential of probiotics as a preventive measure for VAP [35].

iii) A meta-analysis examining the role of probiotics in preventing VAP included 13 studies, 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 "poor quality" of current evidence [36].

(6) **Interventions pending resolution**

a) **Closed endotracheal suctioning systems** [1]

i) A meta-analysis compared closed tracheal suction systems (CTSS) vs open tracheal suction systems (OTSS) in preventing VAP in adult patients, included 10 studies. Results indicated a significant increase in the incidence of VAP with OTSS compared to CTSS, increasing VAP incidence by 57% (OR = 1.57, 95% CI = 1.063-2.32, $P = 0.02$). The study concludes that CTSS can significantly reduce VAP risk [37].

b) **Silver-coated ETTs** [1]. (QoE MODERATE)

i) In an RCT, the efficacy of noble metal-alloy ETTs in preventing VAP was investigated. The study aimed to assess the efficacy of noble metal-alloy ETTs, specifically coated Bactiguard Infection Protection ETTs, compared to standard noncoated ETTs in patients requiring at least 48 hours of MV. This RCT involved 180 patients. Results showed a significant reduction in VAP rate (51.26/1000 vs 83.38/1000, $P = 0.01$) compared to the control group [38].

ii) Damas et al. conducted an RCT to assess the efficacy of noble metal coating on ETT in preventing VAP. The study enrolled 323 patients from nine ICUs in Belgium. 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, $P = 0.02$). These findings suggest the potential benefits of noble metal coating in VAP prevention, warranting further investigation in large-scale studies [39].

iii) It is important to highlight that silver-coated ETTs are limited to certain regions and are not yet widespread globally.

(7) **Suggested practice in under-resourced settings**

a) **Practices that in LMICs demonstrated being risk factors for VAP:**

i) In LMICs, a study was conducted across 743 ICUs spanning 144 cities in 36 Asian, African, European, Latin American, and Middle Eastern countries. Over 24 years, 289,643 patients were followed during 1951,405 patient days, and 8236 cases of VAP were identified. Multiple logistic regression identified several independent risk factors for VAP. Based on this research, it is recommended to reduce LOS, which increases the risk of VAP by 7% per day of hospitalization (aOR = 1.07; 95% CI = 1.07-1.08; $P < 0.0001$); reduce the utilization ratio of MV (aOR = 1.27; 95% CI = 1.23-1.31; $P < 0.0001$); reduce the use of continuous positive airway pressure, which was associated with the highest risk (aOR = 13.38; 95% CI = 11.57-15.48; $P < 0.0001$); and improve the quality of healthcare at public hospitals, as admission to a public hospital significantly increased the risk (aOR = 1.59; 95% CI = 1.35-1.86; $P < 0.0001$) [40].

Summary

The empirical evidence outlined in this review establishes that VAP rates in LMICs exceed those in high-income countries. The review presents scientific insights regarding the efficacy of various interventions across all settings, distinguishing between measures proven effective and those shown to be ineffective and recommending additional measures specifically advocated for adoption in LMICs.

Declarations of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Ethical approval

Done.

Author contributions

All authors contributed equally to this scientific review paper. They jointly undertook the tasks of conceptualization, literature review, data analysis, and interpretation, drafting of the initial manuscript, critical review, and editing, supervision, and final approval of the manuscript.

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