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## Strategies to prevent ventilator-associated pneumonia in critically ill mechanically ventilated patients: a SIAARTI consensus statement

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### Abstract

#### Background

Ventilator-associated pneumonia (VAP) remains a major complication in mechanically ventilated critically ill patients. Although several preventive strategies have been proposed

and incorporated into international guidelines, emerging evidence and evolving epidemiology warrant updated statements. The Italian Society of Anaesthesia, Analgesia, Resuscitation and Intensive Care (SIAARTI) developed an expert consensus statement to provide pragmatic guidance for VAP prevention.

## Methods

This consensus statement was developed in accordance with SIAARTI methodology for consensus-based documents. A multidisciplinary panel of 10 experts was appointed and identified key items through a modified Delphi process. Consensus was defined as  $\geq 75\%$  agreement within the same Likert scale range. A structured literature search was conducted. Statements and supporting rationales were drafted by multidisciplinary subgroups and subjected to blinded voting. External peer review was performed prior to final approval.

## Results

Of ten proposed items, four achieved consensus in agreement and were included in the final document. Individual statements address: (1) subglottic secretion drainage, (2) endotracheal cuff pressure control, (3) chlorhexidine for oral hygiene, and (4) selective digestive decontamination (SDD). Subglottic secretions drainage and appropriate cuff pressure control are supported as preventive measures, while routine chlorhexidine use is not recommended outside selected cardiac surgery populations, and SDD was demonstrated effective to reduce VAP and mortality in low multidrug-resistant (MDR) settings.

## Conclusions

This consensus statement provide updated, pragmatic guidance for VAP prevention. Implementation should consider local epidemiology, particularly MDR prevalence, and patient-specific risk profiles.

## Keywords

Ventilator-associated pneumonia, mechanical ventilation, sepsis, critical care, intensive care, bundles, prevention

## Background

Ventilator-associated pneumonia (VAP) is one of the most frequent pulmonary infections occurring in  $\approx 50\%$  of critically ill mechanically ventilated patients admitted to the intensive care unit (ICU) with low respiratory tract infections (1). This condition has been associated with increased morbidity, prolonged ICU and hospital length of stay, and higher risk of mortality (1–3), thereby challenging patients, physicians, and health care systems. Therefore, the identification of effective, evidence-based, strategies for the prevention of VAP has been recognised as a priority within the critical care research agenda, with the aim of improving patient care (4). At the same time, the promotion of these strategies through continuous educational initiatives has been acknowledged as essential to ensuring high-quality patient care.

From a pathophysiological standpoint, the interplay between several pathways has been involved in the development of VAP, whose large-scale epidemiological evaluation has led to the identification of multiple non-modifiable and modifiable risk factors. Among non-modifiable risk factors (1–3), patient frailty — both intrinsic (e.g. comorbidities) and acquired (e.g. endotracheal intubation) — plays a pivotal role, although these conditions are not amenable to specific interventions. In contrast, a thorough understanding of modifiable risk factors (e.g. aspiration) is essential to guide the investigation and implementation of preventive targeted interventions aimed at reducing the burden of VAP, thereby improving patient outcomes and optimising resource utilisation.

In recent years, robust evidence has supported the implementation of several preventive strategies, which have been advocated by international guidelines published more than a decade ago (2,3). Consequently, an update of these guidelines in light of more recent findings is warranted. In this context, a systematic approach that takes into account the specific characteristics of critically ill patients and the resources available across different hospital settings appears particularly appropriate. For this reason, the Executive Council of the Italian Society of Anaesthesia, Analgesia, Resuscitation and Intensive Care (SIAARTI) supported the development of this Good Clinical Practice (GCP) statements for the prevention of VAP.

The SIAARTI consensus statement for the prevention of VAP aim to provide anaesthetists–intensivists and other healthcare professionals involved in the care of

patients at risk of developing this condition with pragmatic and up-to-date guidance at the bedside.

## Methods

This consensus document was developed in accordance with SIAARTI methodology for consensus-based documents. A brief description of this process was briefly reported as follow. First, the SIAARTI Executive Council identified and declared VAP prevention as priority topic. The methodological conduct was coordinated by an anaesthetist–intensivist with expertise in research methodology (AC), while a multidisciplinary panel of experts in this topic was appointed by the SIAARTI Executive Council. The panel consisted of ten members, that were selected by curriculum vitae and professional competencies. As consensus-based document, the relevant clinical questions for this document were not designed on PICO framework. Nonetheless, the methodological pathway was based on principles of rapid review of the literature and the modified Delphi method (5,6).

During the initial scoping workshop, held virtually, the panel discussed the key issues and research questions addressed in this document. All proposed items emerging from the discussion were collected and rationalised into a single list by the panel coordinator. All experts were asked to express their views on the priority of the proposed items via an online form. Blinded voting was expressed using an ordinal Likert scale (minimum score 1 = completely disagree; maximum score 9 = completely agree). The rating scale was divided into three sections:

- 1–3: rejection/disagreement (“no priority”);
- 4–6: uncertainty;
- 7–9: agreement/support (“priority”).

Consensus was considered achieved when at least 75% of experts (excluding the methodologist and the literature search specialists) assigned a score within the same interquartile range (1–3, 4–6, or 7–9). This approach ensured that the content was derived from the collective judgment of the panel and reflected the highest-priority. After completion of the vote round, all items underwent a final collegial review by the coordinator, the panellists and the methodologist. During this phase, a limited number of items that had not reached the predefined agreement threshold were further discussed because of their perceived clinical relevance and potential importance for patient

management, leading to the inclusion of items 6 and 9 (eTable 1) in the final document. Conversely, although Item 10 achieved 100% agreement, it was not included in the final document because the interventions addressed by this item are considered part of the standard of care for critically ill patients at risk of respiratory failure, irrespective of their potential impact on VAP prevention.

The approved items were subsequently shared with the two literature search specialists, who conducted a systematic search of PubMed. Inclusion/exclusion process was described by using a PRISMA flow chart (Appendix 1 and eFigure 1). Search strategy was restricted original articles, case series, case reports, narrative reviews, systematic reviews, meta-analyses, position papers, and guidelines. Articles not published in English were excluded.

Panel members were divided into multidisciplinary working subgroups according to their expertise, professional role, competencies and career stage. Each subgroup was assigned one item, and tasked with drafting statements and supporting rationales. Of note, each panel member was given the opportunity to propose relevant reference articles. The outputs produced by the subgroups were shared with the panel coordinator and the SIAARTI Clinical Research Office. The full list of individual statements was subjected to blinded voting to allow all experts to express their level of agreement. The same voting scale for items evaluation was applied.

- 1–3: rejection/disagreement (“disagreement”);
- 4–6: uncertainty;
- 7–9: agreement/support (“agreement”).

All statements and rationales achieved consensus regarding appropriateness (IQR 7–9) in the first online voting round.

The draft was submitted for revision to two independent reviewers, who are recognised experts in anaesthesia and intensive care (RV and CAV). The comments were analysed and discussed collectively by the panel, and were incorporated into the final version of the document. The final manuscript was prepared, reviewed by all panel members, and external reviewers (three experts in methodology and in the specific subject area), before dissemination through SIAARTI website dissemination and scientific publication. The development process of these statements was conducted in full autonomy and editorial

independence. No direct or indirect funding was received from pharmaceutical companies or other entities with commercial interests. Panel members contributed on a voluntary basis and in accordance with their scientific, clinical and methodological expertise. The final document reflects exclusively the opinion of the expert panel, based on the review of the available literature and a structured consensus process.

## Statements

The literature search was completed on 9 July 2024. Of the 10 items evaluated, only 4 achieved agreement in the first round (eTable 1). Following collegial discussion of the results, the panel agreed to include items 1, 2, 9 and 10, and to exclude the remaining items from the present document (eTable 2). All feedback received by external reviewer consisted exclusively of minor revisions, primarily related to formal aspects and wording, rather than substantive content. This document reports the final version of the 4 items, that were approved by all panel members in the current form (Table 1).

## ITEM 1 - ROLE OF SUBGLOTTIC SECRETION DRAINAGE IN THE PREVENTION OF VAP

### *Statements*

- 1.1 The use of endotracheal tubes (ETTs) equipped with a dedicated lumen for subglottic secretion drainage can be considered as part of a preventive strategies for VAP, particularly in patients expected to require invasive mechanical ventilation for more than 48–72 hours.**
- 1.2 Available evidence does not allow a statement on any specific suctioning modality (continuous vs intermittent; manual vs automated) for the prevention of microaspiration.**

### *Rationale*

The accumulation of oropharyngeal and gastric secretions in the subglottic space — namely the area between the vocal cords and the cranial portion of the endotracheal tube (ETT) cuff — represents a critical factor in the pathogenesis of VAP (7). Despite strict control of cuff pressure, the use of advanced materials and designs of the cuff aimed at

optimised tracheal sealing (e.g. tapered and conically shaped polyurethane cuffs), microaspiration of both oropharyngeal and gastric secretions remains frequent. This phenomenon can be documented by measuring pepsin and salivary amylase levels in tracheal secretions of mechanically ventilated patients (8). Approximately 30 years ago, ETTs equipped with a suction port above the cuff for subglottic secretion clearance were introduced into clinical practice. Over time, these devices have undergone significant technological improvements in terms of materials and suction performance. Their effectiveness in removing a subglottic secretions is well established, and a considerable body of literature supports their use as an effective strategy for mitigating the incidence of VAP (9). Nevertheless, the large-scale application of these systems in daily clinical practice remains debated, and further technological improvements are expected to occur over the next years.

### Evidence Summary

The main randomised controlled trial in this area demonstrated the efficacy of manual subglottic secretion suctioning, performed by nursing staff every 1–2 hours, who drained up to 50 mL per day (hazard ratio [HR] 3.3; 95% CI 1.66–6.67;  $p = 0.001$ ) (10). In recent years, automated intermittent and continuous suction systems have been introduced into clinical practice. Although highly effective in secretion clearance, Berra et al (11) documented an association with suction-related injury to the tracheal mucosa in preclinical model, particularly in the presence of excessive negative pressures in a preclinical model. The use of tracheostomy cannulas equipped with subglottic suction cannal may also represent a valuable option, particularly in patients expected to require prolonged artificial airway placement (12). Notably, although these systems have been reported effective to reduce the incidence of VAP, major clinical trials have not consistently demonstrated improvements in more objective clinical outcomes, such as ventilator-associated events (VAE), duration of mechanical ventilation, ICU length of stay, or mortality (13). However, the lack of benefit on these outcomes is not unexpected, as the specific clinical impact of VAP on patient-related clinical outcomes appears of difficult within the complex trajectory of critically ill patients. Taking all these considerations into account, current international guidelines suggest the use of ETTs equipped with subglottic suction as an additional preventive measure particularly in patients expected to require intubation for more than 48–72 hours (7,13)

### ITEM 2 – ENDOTRACHEAL CUFF PRESSURE CONTROL

## *Statements*

**2.1 Endotracheal cuff pressure monitoring is indicated to reduce the risk of VAP.**

**2.2 Cuff pressure should be kept consistently between 20 and 30 cm H<sub>2</sub> O.**

**2.3 Manual cuff pressure adjustment remains the reference method. There is currently insufficient evidence to support a specific monitoring frequency or routine use of continuous automated systems.**

## *Rationale*

Microaspiration of supraglottic secretions represents the main pathogenic mechanism leading to VAP, thereby maintaining adequate endotracheal cuff pressure is essential to prevent this phenomenon (14). Accordingly, endotracheal cuff pressure should be sufficiently high to prevent air leaks and ensure adequate ventilation, while simultaneously limiting the progression of secretions from the oropharynx (14,15). However, cuff pressure should not be excessively elevated, as this may cause tracheal mucosal ischaemia and increase the risk of tracheomalacia and tracheal stenosis (14,15). Although cuff pressure fluctuates over time, evidence is insufficient to recommend a specific monitoring frequency or devices. Clinical practice varies widely, ranging from sporadic checks to continuous monitoring (15,16).

## *Evidence summary*

Cuff pressure below 20 cm H<sub>2</sub> O has been reported to increase the risk of developing VAP up to fourfold compared with higher pressure values (14,15). An early study suggested that continuous cuff pressure monitoring systems were associated with a significant reduction in the risk of VAP and microaspiration (14). In this setting, a randomised crossover study comparing automated continuous cuff pressure control with periodic manual measurements showed no different incidence of microaspiration events, although continuous systems resulted in more stable pressure values (15–17). Furthermore, available evidence has not demonstrated differences in ventilator-associated events (VAE), antibiotic use, duration of mechanical ventilation, or mortality when comparing manual cuff pressure measurement (three times daily) with continuous automated systems (17,18). Indeed, a recent meta-analysis suggested that continuous cuff pressure control may be associated with a reduction in VAP incidence; however, the certainty of evidence was very low, largely burdened by high heterogeneity among the included studies (19).

### ITEM 3 – ROLE OF CHLORHEXIDINE IN ORAL HYGIENE

#### *Statements*

**3.1 Routine use of chlorhexidine for oral hygiene in mechanically ventilated patients is not recommended for the prevention of ventilator-associated pneumonia (VAP). However, in post-operative cardiac surgery patients admitted to intensive care, the use of chlorhexidine may be taken into account for reducing the risk of the individual clinical context.**

#### *Rationale*

Oral hygiene plays a key role in preventing bacterial colonisation of the oropharynx, which may contribute to microaspiration and subsequent development of VAP. Chlorhexidine, as a broad-spectrum antiseptic agent, has been widely investigated as part of oral care bundles in mechanically ventilated patients. However, the available evidence remains inconsistent, particularly outside the cardiac surgery population. Concerns regarding safety, including a potential association with increased mortality in certain populations, warrant a cautious approach.

#### *Evidence Summary*

The use of chlorhexidine for oral hygiene remains a highly debated topic because of supported by conflictual evidence. Some reports (20–22) suggest that adding an antiseptic oral rinse after tooth brushing, or incorporating it into a comprehensive oral care protocol, may help reduce the risk of VAP. Certain data indicate that applying chlorhexidine gluconate mouthwash twice daily, within two hours of tooth brushing, may lower VAP rates (23), with the strongest evidence observed in patients undergoing cardiac surgery (24). A Cochrane review by Zhao et al. found that effective oral hygiene, including the use of chlorhexidine mouthwash or gel, reduced VAP incidence in critically ill patients from 26% to 18% (RR 0.67; 95% CI 0.47–0.97;  $p = 0.03$ ;  $I^2 = 66\%$ ). However, no significant impact was observed on mortality, duration of mechanical ventilation, or ICU length of stay (25). Conversely, another meta-analysis reported that chlorhexidine use for oral hygiene in patient populations outside cardiac surgery ICUs may be associated with an increased risk of mortality ( $p = 0.01$ ;  $I^2 = 0\%$ ) (26). Furthermore, a recent network meta-analysis

conducted by an Italian research group found no differences in any of the evaluated outcomes — including VAP, mortality, duration of mechanical ventilation, or ICU length of stay — between chlorhexidine and no-chlorhexidine groups, nor among different chlorhexidine dosages (27). European guidelines do not provide a recommendation regarding the use of chlorhexidine for oral hygiene in mechanically ventilated patients, owing to insufficient safety data and a lack of clear evidence of efficacy (3). Similarly, the Society for Healthcare Epidemiology of America advises against the routine use of oral chlorhexidine due to concerns about increased mortality (13). The recent meta-analysis by De Cassai et al. (27) aligns with these statements, further reinforcing the position against routine use. At present, routine administration of chlorhexidine cannot be recommended. Further research is needed to clarify its potential risks and benefits, including optimal dosage, frequency, and mode of application in critically ill patients.

#### ITEM 4 – ROLE OF SELECTIVE DIGESTIVE DECONTAMINATION (SDD)

##### *Statements*

**4.1 Current evidence supports the use of SDD to reduce the risk of VAP and hospital mortality in patients expected to require mechanical ventilation for more than 48 hours. However, most of the evidence comes from geographical areas with a low prevalence of multidrug-resistant (MDR) organisms.**

##### *Rationale*

Selective digestive decontamination is an infection prevention strategy consisting of the administration of non-absorbable topical antibiotics and antifungals (e.g. colistin, tobramycin, amphotericin B or nystatin) to the oropharyngeal mucosa and gastrointestinal tract, with or without a short course of systemic broad-spectrum antibiotics (typically a third-generation cephalosporin). The primary objective is to prevent VAP caused by Gram-negative bacteria and to limit excessive secondary overgrowth of yeasts from the upper gastrointestinal tract. While several studies have demonstrated reductions in VAP incidence and hospital mortality with SDD, most of the available evidence derives from geographical areas with relatively low MDR prevalence. The applicability of these findings to high-resistance settings remains uncertain.

##### *Evidence Summary*

Current Infectious Diseases Society of America guidelines on VAP prevention support the use of SDD in ICUs with a low prevalence of multidrug-resistant (MDR) organisms, while advising against its use in settings with a high prevalence of MDR pathogens (high-quality evidence) (13). A 2022 meta-analysis (28) including 32 randomised controlled trials (24,389 patients) demonstrated a reduction in hospital mortality (RR 0.91; 95% CrI 0.82–0.99) and VAP incidence (RR 0.44; 95% CrI 0.36–0.54) in patients receiving SDD compared with standard care. Notably, the mortality reduction was observed primarily in SDD protocols that included a short course of systemic antibiotics (RR 0.84; 95% CrI 0.74–0.94), whereas protocols using only non-absorbable oral and/or enteral antibiotics did not demonstrate mortality benefit (RR 1.01; 95% CrI 0.91–1.11). The same meta-analysis did not show a significant association between SDD use and increased MDR incidence. However, the available evidence on antimicrobial resistance remains limited, and the possibility that large-scale use of broad-spectrum antibiotics may promote MDR development cannot be definitively excluded. Importantly, most included studies were conducted in settings with relatively low baseline MDR prevalence. Therefore, the generalisability of these findings to countries with higher MDR rates (such as Italy) is uncertain.

A randomised controlled trial conducted in 13 ICUs across six European countries with  $\geq 5\%$  prevalence of ESBL-producing Enterobacterales bacteraemia did not demonstrate reductions in bloodstream infections (HR 0.70; 95% CI 0.43–1.14) or mortality (HR 1.03; 95% CI 0.80–1.32) with SDD compared with standard care (29).

Although some studies conducted in areas with moderate-to-high MDR prevalence have not demonstrated further increases in resistance associated with SDD (30,31), these findings require confirmation through more rigorous and larger-scale investigations. Furthermore, microbiota analyses suggest that SDD may affect not only potential Gram-negative pathogens but the overall intestinal microbiota composition, raising additional considerations regarding long-term ecological impact (32).

## Conclusions

Ventilator-associated pneumonia remains a major challenge in mechanically ventilated critically ill patients. This SIAARTI consensus statement provide updated, consensus-based guidance on four key preventive strategies, that complement current international recommendations. As reinforced by recent evidence (33,34), subglottic secretion drainage

and appropriate cuff pressure control should be considered core components of VAP prevention, although the optimal modalities for achieving these objectives remain a matter of debate (35). Routine chlorhexidine use for oral hygiene is not supported by solid evidence (36), outside selected cardiac surgery populations. Conversely, selective digestive decontamination may reduce VAP and mortality in low-MDR settings, although its impact in high-resistance environments remains uncertain and is likely to have a neutral effect on patient outcomes (37,38).

Effective prevention requires integration of evidence-based interventions with local epidemiology, organisational support, and ongoing education. Continuous reassessment of preventive strategies is essential to ensure patient safety and high-quality ICU care.

#### List of abbreviations

#### Declarations

- Ethics approval and consent to participate declarations: not applicable
- Consent for publication: not applicable
- Availability of data and materials: not applicable
- Competing interests: Andrea Cortegiani is the Editor-in-Chief of the Journal of Anesthesia Analgesia and Critical Care (JAACC). Daniela Pasero is an Associate Editor for the Journal of Anesthesia Analgesia and Critical Care (JAACC). The other authors declare that they have no competing interests.
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All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.
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**Table 1. Items and statements**

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|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>ITEM 1 - ROLE OF SUBGLOTTIC SECRETION DRAINAGE IN THE PREVENTION OF VAP</b>                                                                                                                                                                                                          |
| 1.1 The use of endotracheal tubes (ETTs) equipped with a dedicated lumen for subglottic secretion drainage <b>can be considered</b> as part of a preventive strategies for VAP, particularly in patients expected to require invasive mechanical ventilation for more than 48–72 hours. |
| 1.2 Available evidence does not allow a recommendation in favour of any specific suctioning modality (continuous vs intermittent; manual vs automated) for the prevention of microaspiration.                                                                                           |
| <b>ITEM 2 – ENDOTRACHEAL CUFF PRESSURE CONTROL</b>                                                                                                                                                                                                                                      |
| <b>2.1</b> Endotracheal cuff pressure monitoring is indicated to reduce the risk of VAP                                                                                                                                                                                                 |
| <b>2.2</b> Cuff pressure <b>should be kept consistently between 20 and 30 cm H<sub>2</sub>O</b> .                                                                                                                                                                                       |
| <b>2.3</b> Manual cuff pressure adjustment remains the reference method. There is currently insufficient evidence to recommend a specific monitoring frequency or to support routine use of continuous automated systems.                                                               |

**ITEM 3 – ROLE OF CHLORHEXIDINE IN ORAL HYGIENE**

3.1 Routine use of chlorhexidine for oral hygiene in mechanically ventilated patients is not recommended for the prevention of ventilator-associated pneumonia (VAP). However, in post-operative cardiac surgery patients admitted to intensive care, the use of chlorhexidine may be taken into account for reducing the risk of the individual clinical context.

**ITEM 4 - ROLE OF SELECTIVE DIGESTIVE DECONTAMINATION (SDD)**

4.1 Current evidence supports the use of SDD to reduce the risk of VAP and hospital mortality in patients expected to require mechanical ventilation for more than 48 hours. However, most of the evidence comes from geographical areas with a low prevalence of multidrug-resistant (MDR) organisms.