







SHEA/IDSA/APIC Practice Recommendation

Strategies to prevent ventilator-associated pneumonia, ventilator-associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 Update

Michael Klompas MD, MPH^{1,2} , Richard Branson MSc, RRT³ , Kelly Cawcutt MD, MS⁴ , Matthew Crist MD⁵ , Eric C. Eichenwald MD^{6,7}, Linda R. Greene RN, MPS, CIC⁸, Grace Lee MD⁹, Lisa L. Maragakis MD, MPH¹⁰, Krista Powell MD, MPH⁵ , Gregory P. Priebe MD¹¹ , Kathleen Speck MPH¹², Deborah S. Yokoe MD, MPH¹³ and Sean M. Berenholtz MD, MHS^{12,14,15}

¹Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts, ²Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, ³Department of Surgery, University of Cincinnati Medicine, Cincinnati, Ohio, ⁴Department of Medicine, University of Nebraska Medical Center, Omaha, Nebraska, ⁵Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, ⁶Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, ⁷Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, ⁸Highland Hospital, University of Rochester, Rochester, New York, ⁹Stanford University School of Medicine, Palo Alto, California, ¹⁰Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, ¹¹Department of Anesthesiology, Critical Care and Pain Medicine; Department of Pediatrics, Boston Children's Hospital, Boston, Massachusetts; and Harvard Medical School, Boston, Massachusetts, ¹²Department of Anesthesiology and Critical Care Medicine, The Johns Hopkins University School of Medicine, Baltimore, Maryland, ¹³Department of Medicine, University of California San Francisco, San Francisco, California, ¹⁴Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland and ¹⁵Department of Health Policy & Management, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland

Abstract

The purpose of this document is to highlight practical recommendations to assist acute care hospitals to prioritize and implement strategies to prevent ventilator-associated pneumonia (VAP), ventilator-associated events (VAE), and non-ventilator hospital-acquired pneumonia (NV-HAP) in adults, children, and neonates. This document updates the *Strategies to Prevent Ventilator-Associated Pneumonia in Acute Care Hospitals* published in 2014. This expert guidance document is sponsored by the Society for Healthcare Epidemiology (SHEA), and is the product of a collaborative effort led by SHEA, the Infectious Diseases Society of America, the American Hospital Association, the Association for Professionals in Infection Control and Epidemiology, and The Joint Commission, with major contributions from representatives of a number of organizations and societies with content expertise.

(Received 21 March 2022; accepted 21 March 2022)

Purpose

The purpose of this document is to highlight practical recommendations to assist acute-care hospitals to prioritize and implement strategies to prevent ventilator-associated pneumonia (VAP), ventilator-associated events (VAEs), and nonventilator hospital-acquired pneumonia (NV-HAP) in adults, children, and neonates. This document updates the *Strategies to Prevent Ventilator-Associated Pneumonia in Acute-Care Hospitals* published in 2014.¹ This expert guidance document is sponsored by the Society for Healthcare Epidemiology (SHEA); it is the product of a collaborative effort led by SHEA, the Infectious Diseases Society of America, the Association for Professionals in Infection Control

and Epidemiology, the American Hospital Association, and The Joint Commission, with major contributions from representatives of a number of organizations and societies with content expertise.

Summary of major changes

This section lists major changes from the *Strategies to Prevent Ventilator-Associated Pneumonia in Acute-Care Hospitals: 2014 Update*¹ including recommendations that have been added, removed, or altered. Recommendations are categorized as “essential practices” that should be adopted by all acute-care hospitals (in 2014 these were “basic practices,” renamed to highlight their importance as foundational for hospitals’ healthcare-associated infection (HAI) prevention programs) or as “additional approaches” that can be considered for use in locations and/or populations within hospitals when these HAIs are not controlled after implementation of essential practices (in 2014 these were “special approaches”). See Tables 2, 3, and 4 for a complete summary of the recommendations contained in this document.

Author for correspondence: Michael Klompas, E-mail: mklompas@bwh.harvard.edu

Cite this article: Klompas M, et al. (2022). Strategies to prevent ventilator-associated pneumonia, ventilator-associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 Update. *Infection Control & Hospital Epidemiology*, <https://doi.org/10.1017/ice.2022.88>

© The Author(s), 2022. Published by Cambridge University Press on behalf of The Society for Healthcare Epidemiology of America. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted re-use, distribution and reproduction, provided the original article is properly cited.

Essential practices

- Added a recommendation for high flow nasal oxygen or non-invasive positive pressure ventilation as options to avoid intubation, minimize duration of intubation, and prevent reintubations
- Added a recommendation for spontaneous awakening trials or sedation protocols as effective strategies to minimize sedation in adults
- Reclassified endotracheal tubes with subglottic secretion drainage from an Essential Practice to an Additional Approach
- Added a recommendation for daily toothbrushing
- Added a recommendation to use caffeine therapy to facilitate extubation in preterm neonates

Additional approaches

- Reclassified endotracheal tubes with subglottic secretion drainage as an additional approach rather than an essential practice for adults and older children
- Added a recommendation to consider early tracheostomy
- Added a recommendation to consider postpyloric rather than gastric feeding in patients at high risk for aspiration

Not recommended

- Oral care with chlorhexidine
- Probiotics
- Ultrathin polyurethane endotracheal tube cuffs
- Tapered endotracheal tube cuffs
- Automated control of endotracheal cuff pressures
- Frequent endotracheal cuff pressure monitoring

New

- Section on prevention of nonventilator hospital-acquired pneumonia (NV-HAP)

Intended use

This document was developed following the process outlined in the *Handbook for SHEA-Sponsored Guidelines and Expert Guidance Documents*.² No guideline or expert guidance document can anticipate all clinical situations, and this document is not meant to be a substitute for individual clinical judgment by qualified professionals. This document is based on a synthesis of evidence, theoretical rationales, current practices, practical considerations, writing-group consensus, and consideration of potential harm, where applicable.

Methods

SHEA recruited 2 subject-matter experts in the prevention of VAP, VAE, and NV-HAP to lead a panel of members representing the Compendium partnering organizations: SHEA, the Infectious Diseases Society of America (IDSA), the Association for Professionals in Infection Control and Epidemiology (APIC), the American Hospital Association (AHA), and The Joint Commission, as well as representation by the Centers for Disease Control and Prevention (CDC).

SHEA utilized a consultant medical librarian, who worked with each panel to develop a comprehensive search strategy for PubMed and Embase (January 2012–July 2019; updated to August 2021). Articles' abstracts were reviewed by panel members in a double-blind fashion using the abstract management software

Covidence (Melbourne, Australia), and potentially relevant articles were reviewed as full text. The Compendium Lead Authors subsequently voted to update the literature findings, and the librarian reran the search to include articles published through August 2021. Panel members reviewed the abstracts of these articles via Covidence and incorporated relevant references.

Recommendations resulting from this literature review process were classified based on the quality of evidence and the balance between desirable and potentially undesirable effects of various interventions (see Table 1). Panel members met via video conference to discuss literature findings; recommendations; quality of evidence for these recommendations; and classification as essential practices, additional approaches, or unresolved issues. Panel members reviewed and approved the document and its recommendations.

The Compendium Expert Panel, made up of members with broad healthcare epidemiology and infection prevention expertise, reviewed the draft manuscript after consensus had been reached by writing panel members.

Following review and approval by the Expert Panel, the 5 partnering organizations, stakeholder organizations, and the CDC reviewed the document. Prior to dissemination, the guidance document was reviewed and approved by the SHEA Guidelines Committee, the IDSA Standards and Practice Guidelines Committee, and the Boards of SHEA, IDSA, APIC, AHA, and The Joint Commission.

All panel members complied with SHEA and IDSA policies on conflict-of-interest disclosure.

Section 1: Rationale and statements of concern

1. Hospitalized patients are at high risk for pneumonia and other pulmonary complications, particularly patients on mechanical ventilation.
 - a. Hospital-acquired pneumonia is the most common nosocomial infection.³ It affects ~1 in 100 patients overall and up to 1 in 10 patients on invasive mechanical ventilation.^{3,4} The true incidence of nosocomial pneumonia is difficult to discern, however, because diagnostic criteria vary widely, correlate poorly with histology, are often subjective, and are applied differently by different surveyors.^{5–8}
 - b. Many hospitals have reported dramatic decreases in VAP rates over the past 20 years, but the extent to which these declines reflect better care versus stricter application of subjective surveillance criteria remains unclear.^{9,10} Clinical surveys suggest that 5%–10% of ventilated patients continue to be treated for VAP,^{11–14} and an independent audit conducted by the Centers for Medicare and Medicaid Services reported that VAP rates were stable between 2005 and 2013.¹⁵
 - c. Patients on mechanical ventilation are at risk for a variety of serious complications in addition to pneumonia. Examples include acute respiratory distress syndrome, fluid overload, atelectasis, pneumothorax, barotrauma, and pulmonary embolism. The CDC created VAE definitions to better capture the breadth of serious complications associated with mechanical ventilation.¹⁶ Approximately 5%–10% of mechanically ventilated patients develop VAEs.^{17–24}
 - d. The coronavirus disease 2019 (COVID-19) pandemic has been associated with an increase in the incidence of nosocomial pneumonia due to hospital-acquired severe acute respiratory coronavirus virus 2 (SARS-CoV-2) infections and hospital-acquired bacterial superinfections in patients

admitted with COVID-19 pneumonia.^{25–27} Differentiating superinfection from underlying COVID-19 pneumonia and COVID-19–related ARDS is challenging due to considerable overlap in clinical signs.

2. VAP, VAE, and NV-HAP are detrimental to patients and increase costs.
 - a. The attributable mortality of VAP is estimated to be ~10% but varies considerably by type and severity of underlying illness.^{28–32}
 - b. VAP and VAE extend duration of invasive mechanical ventilation, prolong intensive care unit (ICU) and hospital length of stay, and increase mortality risk.^{18,21–23,31,33,34} They are also associated with greater use of antimicrobials and higher costs.^{19,33} Patients with VAEs are ~50% more likely to die compared to similar patients with VAP.³⁵ NV-HAP is associated with a doubling of the length of time until discharge and substantially higher mortality rates compared to similar patients without NV-HAP.^{36,37}

Section 2: Background on detection of VAP, VAE, and NV-HAP

1. Despite pneumonia's clinical importance, our ability to conduct accurate pneumonia surveillance is very limited.
 - a. Pneumonia is usually defined by clinical, radiographic, and microbiological criteria. These signs are neither sensitive nor specific relative to histopathology.^{6,38–40} In addition, the signs and symptoms used to diagnose pneumonia are subjective, which leads to substantial interobserver variability.^{8,12,13,41–43} Administrative data are similarly inaccurate.^{11,44–47} Improvements in VAP rates do not reliably correlate with improvements in outcomes.^{48,49}
 - i. The weaknesses of traditional pneumonia surveillance definitions limit their utility for measuring the impact of care improvement programs and for benchmarking quality of care between different healthcare facilities.^{50–53}
 2. CDC's VAE framework:
 - a. The CDC created VAE definitions to try to overcome the subjectivity, complexity, and limited focus of traditional VAP surveillance definitions.¹⁶ VAE definitions were designed to capture a range of severe complications of mechanical ventilation while being objective, reproducible, and amenable to automation.
 - b. VAEs are triggered by sustained increases in ventilator settings after a period of stable or decreasing ventilator settings.
 - c. There are 3 nested tiers of VAEs in adults: ventilator-associated conditions (VACs), infection-related ventilator-associated complications (IVACs), and possible VAP (PVAP). Similar subcategories for pediatric patients are being evaluated but have not yet been adopted by the CDC.^{54,55}
 - i. In adults, VAEs and VACs are synonymous and are defined as an increase in the daily minimum positive end expiratory pressure (PEEP) of ≥ 3 cm H₂O sustained for ≥ 2 calendar days after ≥ 2 days of stable or decreasing daily minimum PEEP, or an increase in the fraction of inspired oxygen (FiO₂) of ≥ 20 points sustained for ≥ 2 days after ≥ 2 days of stable or decreasing daily minimum FiO₂ levels.⁵⁶
 - ii. IVAC is defined as a VAC with concurrent indications of possible infection, namely an abnormal temperature (<36 or $>38^{\circ}\text{C}$) or white blood cell count ($\leq 4,000$ or $\geq 12,000$ cells/mm³), and 1 or more new antibiotic starts that continue for ≥ 4 days, all beginning within 2 days before or 2 days after VAC onset.⁵⁶
 - iii. PVAP is defined as an IVAC with indications that infection might be localized to the lungs. It requires respiratory secretion cultures positive for potentially pathogenic organisms, positive cultures from pleural fluid, positive assays for respiratory viruses or *Legionella*, or suggestive histopathology concurrent with the IVAC. The culture criterion can be fulfilled via quantitative cultures above various thresholds that vary depending upon specimen type or through positive cultures with any amount of growth if there is concurrent Gram-stain evidence of purulence.⁵⁶
 - d. In children and neonates, a pediatric VAE (PedVAE) is defined as an increase in the daily minimum mean airway pressure of ≥ 4 cm H₂O sustained for ≥ 2 calendar days after ≥ 2 days of stable or decreasing daily minimum mean airway pressure, or an increase in FiO₂ of ≥ 25 points sustained for ≥ 2 days after ≥ 2 days of stable or decreasing daily minimum FiO₂s.⁵⁴
 - e. There are 2 subcategories of VAEs in adults: infection-related ventilator-associated complications (IVAC) and possible VAP (PVAP). Similar subcategories for pediatric patients are being evaluated but have not yet been adopted by the CDC.^{55,57}
 - f. VAE is not synonymous with VAP. Only ~25%–33% of VAEs are due to pneumonia, and many mild pneumonias do not meet the VAE thresholds for increased ventilator settings.³⁵
 - g. Qualitative studies suggest that most VAEs in adults and children are caused by pneumonia, fluid overload, atelectasis, and/or ARDS.^{17,19,22,58–63}
 - h. Potential risk factors for VAE include sedatives (especially benzodiazepines and propofol),^{64–67} opioids,⁶⁴ positive fluid balance,^{60,63,64,66,68–71} mandatory modes of mechanical ventilation with high tidal volumes and/or high inspiratory driving pressures,^{60,64,69,72} blood transfusions,^{63,68,73} oral care with chlorhexidine,⁷⁴ stress ulcer prophylaxis,⁷⁵ patient transport,⁷⁶ gastric retention,⁶⁶ reintubation,⁶⁸ and neuromuscular blockade.^{63,64,69} Dexmedetomidine, spontaneous awakening and breathing trials, and conservative fluid management may be protective.^{21,65,75,77,78}
 - i. A growing body of literature demonstrates the preventability of VAEs.^{21,77–83} The best-studied interventions to date that have been associated with lower VAE rates in interventional trials include spontaneous awakening trials, spontaneous breathing trials, and conservative fluid management.^{21,77–79,81,82}
3. Recommended surveillance strategies:
 - a. The CDC recommends that hospitals conduct surveillance for VAE in lieu of VAP using CDC definitions and surveillance protocols.⁵⁶
 - b. VAE definitions are amenable to partial or complete automation using electronic data.^{22,84–87} Facilities seeking to automate VAE detection should work with their information technology personnel and/or electronic health record vendor(s).
 - c. Alternatively, infection preventionists should work with their critical care, respiratory therapy, and/or information technology staff to develop efficient means to gather and aggregate ventilator data (daily minimum PEEP and daily minimum FiO₂) from all patients ventilated for ≥ 4 days.

- i. Temperature, white blood cell count, and antibiotic exposure data are only needed for the subset of patients with VAEs to determine whether they fulfill IVAC criteria. Pulmonary-specimen Gram stains and microbiology test results are only required for the subset of patients who meet IVAC criteria to determine whether they fulfill PVAP criteria.
- ii. Organizing daily ventilator data into 'line lists' for every patient with 1 row of data per patient per calendar day facilitates VAE detection by allowing the surveyor to vertically scan daily ventilator settings to look for sustained increases that cross the threshold for VAE.⁸⁸ Surveyors can also enter their data into the CDC online VAE calculators to assist with case identification (adult VAE: <http://www.cdc.gov/nhsn/VAE-calculator/index.html>; pediatric VAE (PedVAE): <https://www.cdc.gov/nhsn/pedvae-calculator/index.html>).
- d. The CDC has not yet developed NV-HAP surveillance definitions. The CDC is exploring the feasibility, reliability, and significance of low-burden reporting options that utilize readily available electronic data.^{36,89}

Section 3: Background on prevention of VAP, VAE, and NV-HAP

Framework for evaluating and prioritizing interventions

1. The subjectivity and lack of specificity of diagnosing pneumonia complicate the interpretation of VAP and NV-HAP prevention studies.⁹⁰ Subjectivity makes it possible that decreases in observed pneumonia rates are due to stricter interpretation of subjective diagnostic criteria rather than true decreases in disease. Lack of specificity makes it possible that lower pneumonia rates are due to less colonization or decreases in conditions that mimic the presentation of pneumonia without corresponding decreases in true pneumonia cases.
2. VAE criteria are more objective and hence less susceptible to these sources of bias, but the literature on VAE prevention is still relatively sparse.
3. Given the limitations of the pneumonia prevention literature and the relative paucity of VAE prevention literature, we prioritize pneumonia prevention strategies associated with improvements in objective outcomes such as duration of mechanical ventilation, ICU or hospital length of stay, mortality, VAEs, antibiotic utilization, and/or costs in randomized controlled trials. In addition, the potential benefits of different interventions are balanced against their feasibility, costs, and potential harms.

Section 4: Recommended strategies to prevent VAP, VAE, and NV-HAP

Recommendations are classified as either: 1) essential practices that improve objective outcomes such as duration of mechanical ventilation, length of stay, mortality, VAEs, antibiotic utilization, and/or costs with little risk of harm that should be adopted by all hospitals. We also recommend interventions that are outcome-neutral but cost saving. Or 2) additional approaches that improve objective outcomes (including VAE) but carry some risk of harm, and interventions that lower VAP or NV-HAP rates, but where insufficient data exist to determine their impact on objective outcomes. Hospitals can consider adopting additional approaches if their VAE, VAP, or NV-HAP rates do not improve despite high performance rates of essential practices. Interventions that do not

Table 1. Quality of Evidence^a

Category	Definition
HIGH	Highly confident that the true effect lies close to that of the estimated size and direction of the effect. Evidence is rated as "HIGH" quality when there are a wide range of studies with no major limitations, there is little variation between studies, and the summary estimate has a narrow confidence interval.
MODERATE	The true effect is likely to be close to the estimated size and direction of the effect, but there is a possibility that it is substantially different. Evidence is rated as "MODERATE" quality when there are only a few studies and some have limitations but not major flaws, there is some variation between studies, or the confidence interval of the summary estimate is wide.
LOW	The true effect may be substantially different from the estimated size and direction of the effect. Evidence is rated as "LOW" quality when supporting studies have major flaws, there is important variation between studies, the confidence interval of the summary estimate is very wide, or there are no rigorous studies.

^aBased on the CDC Healthcare Infection Control Practices Advisory Committee (HICPAC)

"Update to the Centers for Disease Control and Prevention and the Healthcare Infection Control Practices Advisory Committee Recommendations Categorization Scheme for Infection Control and Prevention Guideline Recommendations" (October 2019), the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE),³⁸⁶ and the Canadian Task Force on Preventive Health Care.³⁸⁷

improve VAE, VAP, or NV-HAP rates nor objective outcomes are not recommended. The quality of evidence rating scheme is summarized in Table 1. Recommended strategies are summarized in Table 2 for adults, Table 3 neonates, and Table 4 for pediatric patients.

Essential practices for preventing VAP and/or VAEs in adult patients

Interventions with little risk of harm that are associated with decreases in duration of mechanical ventilation, length of stay, mortality, antibiotic utilization, and/or costs.

Avoid intubation and reintubation if possible

1. **Use high-flow nasal oxygen or non-invasive positive pressure ventilation (NIPPV) as appropriate whenever safe and feasible** (Quality of Evidence: HIGH).
 - a. High-flow nasal oxygen may help avert intubation in patients with hypoxemic respiratory failure and prevent reintubation after extubation of critically ill patients and postoperative patients compared to conventional oxygen therapy.⁹¹⁻⁹⁴ High-flow nasal oxygen has also been associated with a trend toward less nosocomial pneumonia in patients with hypoxemic respiratory failure.⁹⁵
 - b. NIPPV is associated with lower rates of intubation, reintubation, VAP, and mortality compared to conventional oxygen therapy in patients with acute hypercapnic or hypoxemic respiratory failure.⁹⁶⁻¹⁰⁰ Use caution when considering NIPPV to manage patients with impaired consciousness, acute lung injury, acute respiratory distress syndrome, severe hypoxemia, severe acidemia, or when continuing NIPPV for patients whose dyspnea or gas exchange fails to rapidly respond to NIPPV. Helmet ventilation may be associated with better outcomes than face-mask ventilation.^{99,101}

Table 2. Summary of Recommendations to Prevent VAP and/or VAE in Adult Patients

Category	Rationale	Intervention	Quality of Evidence
Essential practices	Good evidence that the intervention decreases the average duration of mechanical ventilation, length of stay, mortality, and /or costs. Benefits likely outweigh risks.	Avoid intubation and prevent reintubation • Use high-flow nasal oxygen or noninvasive positive pressure ventilation (NIPPV) as appropriate whenever safe and feasible ^{91–93,96,99}	HIGH
		Minimize sedation ^{105,106} • Avoid benzodiazepines in favor of other agents ¹⁰⁶ • Use a protocol to minimize sedation ¹¹⁰ • Implement a ventilator liberation protocol ¹¹³	MODERATE
		Maintain and improve physical conditioning ^{113,120–123}	MODERATE
		Elevate the head of the bed to 30–45° ^{125,388–390}	LOW ^a
		Provide oral care with toothbrushing but <i>without</i> chlorhexidine ^{126,127}	MODERATE
		Provide early enteral vs. parenteral nutrition ¹³¹	HIGH
		Change the ventilator circuit only if visibly soiled or malfunctioning (or per manufacturers' instructions) ^{391–394}	HIGH
		Additional approaches	Good evidence that the intervention improves outcomes in some populations, but may confer some risk in others.
Utilize endotracheal tubes with subglottic secretion drainage ports for patients expected to require >48–72 hours of mechanical ventilation ³⁹⁵	MODERATE		
May lower VAP rates but insufficient data to determine impact on duration of mechanical ventilation, length of stay, or mortality.	Consider early tracheostomy ¹⁴⁴		MODERATE
Consider postpyloric rather than gastric feeding for patients with gastric intolerance or at high risk for aspiration ^{131,147}	MODERATE		
Generally not recommended	Inconsistently associated with lower VAP rates and no impact or negative impact on duration of mechanical ventilation, length of stay, or mortality.	Oral care with chlorhexidine ^{75,128–130,150}	MODERATE
		Probiotics ^{153–156}	MODERATE
		Ultrathin polyurethane endotracheal tube cuffs ^{165–167}	MODERATE
		Tapered endotracheal tube cuffs ¹⁶⁹	MODERATE
		Automated control of endotracheal tube cuff pressure ^{170,171,174,175}	MODERATE
		Frequent cuff-pressure monitoring ¹⁷⁶	MODERATE
		Silver-coated endotracheal tubes ¹⁷⁸	MODERATE
		Kinetic beds ¹⁸⁰	MODERATE
		Prone positioning ^{181,183,a}	MODERATE
		Chlorhexidine bathing ^{184–186,a}	MODERATE
	No impact on VAP rates, average duration of mechanical ventilation, length of stay, or mortality. ^a	Stress-ulcer prophylaxis ^{190,191,193}	MODERATE
		Monitoring residual gastric volumes ¹⁹⁴	MODERATE
		Early parenteral nutrition ¹⁹⁵	MODERATE
No recommendation	No impact on VAP rates or other patient outcomes, unclear impact on costs.	Closed endotracheal suctioning systems ^{197–199}	MODERATE

Note. VAP, ventilator-associated pneumonia.

^aMay be indicated for reasons other than VAP prevention.

- c. High-flow nasal oxygen and NIPPV appear to be similar in their capacity to prevent intubation, reintubation, and postextubation respiratory failure. Some meta-analyses suggest that high-flow nasal cannula may reduce ICU and hospital length of stay compared to NIPPV, while others do not.^{92,102}
 - d. Combining high-flow nasal oxygen with NIPPV immediately after extubation may further decrease the risk of reintubation in patients at high risk for extubation failure compared to using high-flow nasal oxygen alone.¹⁰³
2. **Placing nonintubated patients with COVID-19 acute hypoxic respiratory failure in the prone position may lower the risk of intubation compared to standard care** (Quality of Evidence: MODERATE).¹⁰⁴

Minimize sedation

 1. **Minimize sedation of ventilated patients whenever possible** (Quality of Evidence: HIGH).^{105,106}

2. Preferentially use multimodal strategies and medications other than benzodiazepines to manage agitation (Quality of Evidence: HIGH).¹⁰⁶

- a. Examples include analgesics for pain, reassurance for anxiety, and antipsychotics, dexmedetomidine, and/or propofol for agitation.¹⁰⁶ Dexmedetomidine and propofol are associated with shorter duration of mechanical ventilation and ICU length of stay compared to benzodiazepines.¹⁰⁷ A randomized trial of light sedation with dexmedetomidine versus propofol found no difference in ventilator-free days or mortality.¹⁰⁸ Dexmedetomidine may decrease need for intubation in patients on noninvasive ventilation.¹⁰⁹

3. Utilize a protocol to minimize sedation (Quality of Evidence: HIGH).¹¹⁰

- a. Potential strategies to minimize sedation include nurse-driven protocols for targeted light sedation and daily sedative interruptions (ie, spontaneous awakening trials) for patients without contraindications.^{106,110}
- b. A meta-analysis of 6 randomized trials reported that protocols to minimize sedation were associated with significantly shorter ICU length of stay compared to managing patients without protocols.¹¹⁰ There was no significant association between the use of protocols to minimize sedation and duration of mechanical ventilation or short-term mortality. There was insufficient evidence to recommend one protocol over another.
- c. A small, single-center, randomized trial¹¹¹ suggested that patients managed with no sedation (but morphine as needed) versus propofol or midazolam may be extubated sooner and have shorter ICU length of stay, but a subsequent multicenter randomized trial of no sedation versus light sedation with daily sedative interruptions reported no difference in ventilator-free days, ICU-free days, or 90-day mortality.¹¹²

4. Implement a ventilator liberation protocol (Quality of Evidence: HIGH)¹¹³

- a. Assess readiness to extubate daily in patients without contraindications (i.e., conduct spontaneous breathing trials).^{114–117}
- b. Ventilator liberation protocols are associated with extubating patients an average of 1 day earlier compared to managing patients without a protocol.¹¹³
- c. Protocols to minimize sedation, mobilize patients, and liberate them from mechanical ventilation may be synergistic.^{118,119}

Maintain and improve physical conditioning

1. Provide early exercise and mobilization (Quality of Evidence: MODERATE).

- a. Early exercise and mobilization programs may shorten duration of mechanical ventilation, reduce ICU length of stay, lower VAP rates, and increase the rate of return to independent function.^{113,120–123} There is no consistent association between early mobilization and hospital length of stay or mortality.
- b. Financial modeling suggests that early mobility programs may be cost saving.^{119,124}

Elevate the head of the bed

1. Elevate the head of the bed to 30–45° (Quality of Evidence: LOW).

- a. A meta-analysis of 8 randomized trials reported that elevating the head of the bed was associated with a significant reduction in VAP rates but no difference in duration of mechanical ventilation or mortality.¹²⁵ The data on outcomes other than VAP, however, were sparse (combined sample size <500 patients); thus, the impact on these outcomes is uncertain. Given the simplicity, ubiquity, minimal risk, lack of cost, and potential benefit of this intervention, we nonetheless classify it as an essential practice while we await further data.

Provide oral care with toothbrushing but without chlorhexidine

1. Provide daily oral care with toothbrushing but without chlorhexidine (Quality of Evidence: MODERATE).

- a. Daily toothbrushing is associated with significantly lower VAP rates, shorter duration of mechanical ventilation, and shorter ICU length of stay.^{126,127}
- b. Meta-analyses of randomized trials and observational studies allow for the possibility that oral care with chlorhexidine may increase mortality rates.^{75,128–130} This is further discussed below.

Provide early enteral rather than parenteral nutrition

1. Provide early enteral rather than parenteral nutrition (Quality of Evidence: HIGH).

- a. Early enteral nutrition is associated with a lower risk of nosocomial pneumonia, shorter ICU length of stay, and shorter hospital length of stay compared to early parenteral nutrition.¹³¹

Maintain ventilator circuits

1. Change the ventilator circuit only if visibly soiled or malfunctioning (Quality of Evidence: HIGH).

- a. Changing the ventilator circuit as needed rather than on a fixed schedule has no impact on VAP rates or patient outcomes but decreases costs.¹³²
- b. Follow manufacturers' instructions for use if they differ from this recommendation.
- c. Follow CDC/Healthcare Infection Control Practices Advisory Committee guidelines and manufacturers' instructions for use of sterilization and disinfection of respiratory care equipment.¹³³

Additional approaches for preventing VAP and/or VAEs in adult patients

Additional approaches are interventions associated with lower VAP rates that may also decrease VAE rates, duration of mechanical ventilation, length of stay, and/or mortality but carry some risk of harm. Additional approaches also include interventions that are associated with lower VAP rates, but insufficient data exist to determine their impact on objective outcomes. Hospitals can consider adopting additional approaches if their VAP or VAE rates do not improve despite high performance rates with essential practices.

The following interventions may decrease duration of mechanical ventilation, length of stay, and/or mortality in some populations but not in others, and they may confer some risk of harm in some populations.

1. Consider using selective decontamination of the oropharynx and digestive tract to decrease microbial burden in ICUs with low prevalence of antibiotic-resistant organisms.^{128,134,135}

Antimicrobial decontamination is not recommended in countries, regions, or ICUs with high prevalence of antibiotic-resistant organisms¹³⁶ (Quality of Evidence: HIGH).

- a. A meta-analysis of 6 cluster randomized trials performed in countries with low levels of antibiotic resistance reported that selective decontamination of the oropharynx with topical antibiotics was associated with a 16% reduction in hospital mortality, and decontamination of the oropharynx and digestive tract with a combination of topical, oral, and parenteral antibiotics was associated with an 18% reduction in hospital mortality.¹³⁵ Selective digestive decontamination was more effective than selective oral decontamination alone (OR, 0.90; 95% CI, 0.82–0.97 for hospital death).¹³⁵ A broader meta-analysis that included a larger but more heterogeneous set of studies had similar findings.¹³⁷
 - i. Oral agents that have been used for digestive decontamination include colistin, tobramycin, and amphotericin B. Parenteral agents include cefotaxime.
 - ii. ICUs that implement this practice should actively monitor its impact on antibiotic utilization, antimicrobial resistance, and *Clostridioides difficile* infections.
 - iii. There is no consensus on what constitutes “low levels of antibiotic resistance,” but an arbitrary threshold that has been used by other guidelines and randomized trials is <5% of bloodstream infections caused by extended-spectrum β -lactamase-producing Enterobacterales.^{136,138}
- b. A cluster randomized trial of selective digestive decontamination (without parenteral antibiotics) versus selective oral decontamination versus oral care with 2% chlorhexidine versus routine care conducted in ICUs with high levels of antibiotic resistance ($\geq 5\%$ of bloodstream infections caused by extended-spectrum β -lactamase-producing Enterobacterales) found no difference between study arms in ICU-acquired bloodstream infections or 28-day mortality rates.¹³⁶ Selective oral and digestive decontamination with antibiotics is therefore not recommended in settings with high baseline levels of antibiotic resistance.

The following interventions may lower VAP rates, but current data are insufficient to determine their impact on duration of mechanical ventilation, length of stay, and mortality.

1. Consider using endotracheal tubes with subglottic secretion drainage ports to minimize pooling of secretions above the endotracheal cuff in patients likely to require >48–72 hours of intubation (Quality of Evidence: MODERATE).

- a. Intermittent and continuous drainage of subglottic secretions has been studied in at least 20 randomized controlled trials. On meta-analysis, the use of endotracheal tubes with subglottic drainage reduced VAP rates by 44%.¹³⁹ There was no association, however, between subglottic secretion drainage and duration of mechanical ventilation, ICU length of stay, or hospital length of stay. One meta-analysis reported a significant impact on mortality but abstracted one large study twice.^{139,140} The effect on mortality was no longer significant after removing the duplicate study (OR, 0.92; 95% CI, 0.83–1.02). One large trial included VAE as an outcome and found no association between subglottic secretion

drainage and VAE rates.¹⁴⁰ Some studies have reported that subglottic secretion drainage is associated with less antibiotic utilization, but others have not.^{140–142}

- b. Reductions in duration of mechanical ventilation with subglottic secretion drainage appear to be limited to patients expected to require >48–72 hours of mechanical ventilation.¹⁴³ Endotracheal tubes with subglottic secretion drainage ports should therefore be reserved for patients likely to require >48–72 hours of intubation. Patients requiring emergency intubation in the hospital and preoperative patients at risk for prolonged mechanical ventilation are reasonable candidates.
 - c. Extubation followed by immediate reintubation to exchange a conventional endotracheal tube for a subglottic secretion drainage endotracheal tube is not recommended.
- 2. Consider early tracheostomy** (Quality of Evidence: MODERATE).
- a. Meta-analysis of 17 randomized trials suggests that early tracheostomy (within 7 days of intubation) may be associated with a 40% decrease in VAP rates, less time on mechanical ventilation, and fewer ICU days but no difference in mortality.¹⁴⁴
 - b. Decision makers should integrate these potential benefits with each patient’s values and preferences when determining whether and when to proceed with tracheostomy.¹⁴⁵
- 3. Consider postpyloric feeding tube placement in patients with gastric feeding intolerance at high risk for aspiration** (Quality of Evidence: MODERATE).
- a. Postpyloric feeding is associated with less aspiration and less pneumonia compared to gastric-tube feeding. Meta-analyses vary in their assessment of whether postpyloric feeding is associated with decreases in ventilator, ICU, and/or hospital length of stay.^{146,147}
 - b. Postpyloric tube placement requires special expertise that is not available in all centers and may incur delay in placement. Postpyloric feeding is considered less physiologic than gastric feeding.¹³¹
 - c. Postpyloric feeding should therefore be reserved for patients with gastric feeding intolerance and for patients at high risk for aspiration as detailed in nutrition society guidelines.^{131,148,149}

Approaches that should not be considered a routine part of VAP and/or VAE prevention in adult patients

The following interventions are inconsistently associated with lower VAP rates and have no impact or negative impact on duration of mechanical ventilation, length of stay, or mortality.

1. Oral care with chlorhexidine (Quality of Evidence: MODERATE)

- a. Oral care with chlorhexidine has been studied in multiple randomized controlled trials.¹⁵⁰ The impact of oral care with chlorhexidine on pneumonia rates is unclear. Meta-analyses report significantly lower VAP rates, but this signal is driven by unblinded studies. There was no association between oral care with chlorhexidine and lower VAP rates when the analysis was restricted to double-blinded studies.¹²⁹ Meta-analyses of both blinded and unblinded studies also show no impact on duration of mechanical ventilation or ICU length of stay.^{129,150} Chlorhexidine’s lack of impact

on VAP, duration of mechanical ventilation, or ICU length of stay was echoed in a large randomized trial of chlorhexidine de-adoption versus usual care.¹⁵¹

- b. Some meta-analyses of randomized trials and some observational studies report an association between oral care with chlorhexidine and higher mortality rates.^{75,128–130} The mortality signal is uncertain, however, because other meta-analyses did not find higher mortality rates, there was no change in mortality observed in a large randomized trial of chlorhexidine de-adoption, and the observational studies may be at risk of residual confounding.^{126,151,152} Nonetheless, given chlorhexidine's lack of clear impact on VAP rates and the possibility of harm, routine oral care with chlorhexidine is not recommended. Oral care including toothbrushing without chlorhexidine, however, is considered an essential practice.
2. **Probiotics** (Quality of Evidence: MODERATE)
 - a. Multiple meta-analyses of randomized controlled trials have reported a possible association between probiotics and lower VAP rates, but these analyses have included many studies at high risk of bias due to lack of blinding.^{153–156} There is no association between probiotics and VAP when restricting the analysis to double-blinded studies.¹⁵⁵ This finding was mirrored in a large, rigorous, multicenter, randomized trial conducted after the most recent meta-analysis.¹⁵⁷ Neither this trial nor the meta-analyses found a significant impact on ICU length of stay, hospital length of stay, or mortality.
 - b. Probiotics should not be used in patients with compromised immune systems or gastrointestinal diseases that increase the risk of gut translocation. Multiple cases of fungemia or bacteremia have been reported in patients administered probiotics as have cases of aerosol transmission of probiotics within ICUs.^{158–164}
 3. **Ultrathin polyurethane endotracheal tube cuffs** (Quality of Evidence: MODERATE)
 - a. Ultrathin polyurethane cuffs seal more uniformly against the tracheal wall and may therefore allow fewer secretions to seep around the cuff and into the lungs. Two small randomized trials^{165,166} reported lower VAP rates but a larger, more rigorous study found no difference in VAP rates, duration of endotracheal intubation, or ICU length of stay.¹⁶⁷ Similarly, there were no significant associations between polyurethane cuffs and VAP rates, duration of mechanical ventilation, ICU length of stay, or mortality on meta-analysis.¹⁶⁸
 4. **Tapered endotracheal tube cuffs** (Quality of Evidence: MODERATE)
 - a. A meta-analysis of 5 randomized trials of tapered versus conical endotracheal tube cuffs found no differences in VAP rates, duration of mechanical ventilation, ICU length of stay, hospital length of stay or mortality.¹⁶⁹
 5. **Automated control of endotracheal-tube cuff pressure** (Quality of Evidence: MODERATE)
 - a. Automated control of endotracheal-tube cuff pressure was associated with lower VAP rates in 2 small trials but this signal has not been borne out in other trials.^{170–174} Indeed, 2 large, multicenter, randomized trials of automated cuff-pressure regulation versus thrice-daily manual cuff-pressure assessments found no difference between arms in VAP, VAE, antibiotic utilization, duration of mechanical ventilation, ICU length of stay, or mortality.^{174,175}
 6. **Frequent endotracheal-tube cuff-pressure monitoring** (Quality of Evidence: MODERATE)
 - a. A single-center prospective trial found no advantage to more frequent versus less frequent cuff-pressure monitoring.¹⁷⁶ At least 1 laboratory investigation suggests that manual measurement of cuff pressure is associated with loss of cuff pressure and potential leakage of fluid around the cuff.¹⁷⁷
 7. **Silver-coated endotracheal tubes** (Quality of Evidence: MODERATE)
 - a. A large, multicenter, randomized controlled trial found that silver-coated endotracheal tubes reduced VAP rates by 36%. However, the organisms associated with VAP included nonpathogenic colonizers, and there was no impact on mean duration of mechanical ventilation, hospital length of stay, or mortality.^{178,179}
 8. **Kinetic beds** (continuous lateral rotational therapy and oscillation therapy) (Quality of Evidence: MODERATE)
 - a. A meta-analysis of 15 randomized controlled trials found a significant decrease in VAP rates but no impact on duration of mechanical ventilation or mortality.¹⁸⁰ The meta-analysis researchers warned that the observed reduction in VAP rates might be artifactual given weaknesses in contributing studies' design and execution.
 9. **Prone positioning** (Quality of Evidence: MODERATE)
 - a. Prone positioning is associated with lower mortality rates among patients with moderate-to-severe ARDS, but this signal appears to be independent of VAP. Prone positioning may be indicated for reasons other than VAP prevention.^{181–183}
 10. **Chlorhexidine bathing** (Quality of Evidence: MODERATE)
 - a. Observational studies have suggested that chlorhexidine bathing may reduce the risk of VAP, but this finding has not been borne out in randomized trials.^{184–186} Chlorhexidine bathing is, however, beneficial in preventing other healthcare-associated infections.¹⁸⁷
- Approaches that definitively are not recommended for VAP or VAE prevention*
- Good-quality evidence suggests that the following interventions neither lower VAP/VAE rates nor decrease duration of mechanical ventilation, length of stay, or mortality.
1. **Stress-ulcer prophylaxis** (Quality of Evidence: MODERATE)
 - a. Stress-ulcer prophylaxis lowers the risk of gastrointestinal bleeding, but a meta-analyses of randomized trials suggested no impact on nosocomial pneumonia, length of stay, or mortality.^{188–192} A large, multicenter randomized trial of pantoprazole versus placebo in ICU patients reported no difference in pneumonia rates or mortality rates.¹⁹³
 - b. Stress-ulcer prophylaxis may be indicated for reasons other than VAP prevention.
 2. **Monitoring residual gastric volumes** (Quality of Evidence: MODERATE)
 - a. Monitoring patients for regurgitation and vomiting alone is as effective as monitoring patients for regurgitation, vomiting, and residual gastric volumes with regard to VAP rates, duration of mechanical ventilation, and mortality.¹⁹⁴

3. **Early versus late parenteral nutrition** (Quality of Evidence: MODERATE)
- Early parenteral nutrition (within 48 hours of ICU admission) is associated with increased mortality and nosocomial infections compared to late parenteral nutrition (initiated on or after ICU day 8).¹⁹⁵

Approaches that are neither recommended nor discouraged for VAP prevention in adult patients

These interventions have no impact on VAP rates or patient outcomes and have unclear impact on costs.

1. **Closed endotracheal tube suctioning systems** (Quality of Evidence: MODERATE)
- Meta-analyses have found no difference in VAP rates, duration of mechanical ventilation, ICU length of stay or mortality between patients randomized to open versus closed endotracheal suctioning systems.^{196–198} A crossover trial in 4 ICUs found no difference between open versus closed systems in patient-to-patient transmissions of gram-negative pathogens.¹⁹⁹ Different trials have reached different conclusions regarding cost.^{197,200,201}

Preventing VAP and/or VAEs in neonatal patients

1. Framework for evaluating and prioritizing interventions:
- Very few studies in neonates have evaluated the impact of VAP or VAE prevention interventions on duration of mechanical ventilation, length of stay, or mortality; therefore, we evaluated potential interventions on the basis of safety, feasibility, and potential impact on VAP and PedVAE rates. Interventions that lower VAP or PedVAE rates and confer minimal risks of harm are classified as essential practices. Interventions with unproven but potential impact on VAP or PedVAE rates and minimal risk of harm are classified as additional approaches. Hospitals can consider additional approaches if their VAP or PedVAE rates do not improve despite high performance rates for essential practices. Interventions with unknown benefits, known risks of harm, or unknown risks of harm are not recommended.

Special considerations in preterm neonates

- Clinical signs used to diagnose VAP and VAE in adults have limited utility in preterm neonates. Fever rarely occurs in preterm neonates because they are prone to hypothermia and are therefore often thermoregulated with heated incubators or radiant warmers. Worsening gas exchange or apnea can be caused by significant nonpulmonary illnesses, including sepsis and necrotizing enterocolitis. New or progressive infiltrates in ventilated preterm neonates often indicate progression of chronic lung disease rather than new infection.
- Adult VAE definitions are not suitable for neonates because they do not reflect standard ventilator management practices for this population. The CDC recently published VAE definitions for children and neonates, denoted PedVAE, based on sustained increases in daily minimum mean airway pressure and/or FiO₂ but data on the incidence, causes, and preventability of PedVAE in preterm infants are sparse.^{54,55,63,202}

- Pooled mean VAP rates for neonates reported to CDC's National Healthcare Safety Network (NHSN) in 2011 ranged from 0.2 to 1.8 infections per 1,000 ventilator days.²⁰³ Whether these rates are broadly representative of all neonatal units remains unknown, however, because many hospitals do not perform VAP surveillance for neonates (especially those born preterm) in light of the limitations of VAP definitions. VAP rates in NICUs are no longer reported to the NHSN.

Essential practices for preterm neonates

These interventions confer minimal risk of harm and may lower VAP and/or PedVAE rates.

Avoid intubation

- Avoid intubation if possible** (Quality of Evidence: HIGH).
 - Nasal continuous positive airway pressure (CPAP) ventilation (with or without nasal intermittent mechanical ventilation) and high-flow oxygen via nasal cannula are viable alternatives to intubation in most preterm infants, but success rates are greatest for those delivered at >28 weeks gestation.^{204–208}
 - Many premature neonates (especially those with a gestational age >28 weeks) can be successfully supported with noninvasive positive pressure ventilation in the delivery room and subsequently in the NICU.

Minimize duration of mechanical ventilation

- Manage patients without sedation whenever possible**^{209,210} (Quality of Evidence: LOW).
- Use caffeine therapy for apnea of prematurity within 72 hours after birth to facilitate extubation**²¹¹ (Quality of Evidence: HIGH).
- Assess readiness to extubate daily** (Quality of Evidence: LOW).
- Take steps to minimize unplanned extubations and reintubations**^{212,213} (Quality of Evidence: LOW).
 - Use nasal CPAP or nasal NIPPV in the postextubation period to help prevent the need for reintubation.²¹⁴
- Provide regular oral care with sterile water (extrapolated from practice in infants and children, no data in preterm neonates)** (Quality of Evidence: LOW).
- Change the ventilator circuit only if visibly soiled or malfunctioning or per manufacturers' instructions for use (extrapolated from studies in adults and children, no data in preterm neonates)** (Quality of Evidence: LOW).

Additional approaches for preterm neonates

These interventions have minimal risks of harm, but their impact on VAE and VAP rates is unknown.

- Lateral recumbent positioning**²¹⁵ (Quality of Evidence: LOW)
- Reverse Trendelenburg positioning** (Quality of Evidence: LOW)
- Closed/in-line suctioning**^{216,217} (Quality of Evidence: LOW)
- Oral care with maternal colostrum**²¹⁸ (Quality of Evidence: MODERATE)

Table 3. Summary of Recommendations to Prevent VAP and/or VAE in Preterm Neonates

Category	Rationale	Intervention	Quality of Evidence
Essential practices	May lower VAP and/or PedVAE rates and have minimal risks of harm. Benefits likely outweigh potential risks.	Use non-invasive positive pressure ventilation in selected populations ^{62,205,206}	HIGH
		Minimize the duration of mechanical ventilation	HIGH
		Use caffeine therapy to facilitate extubation ^{396,397}	HIGH
		Assess readiness to extubate daily	LOW
		Manage patients without sedation whenever possible ^{209,210}	LOW
		Avoid unplanned extubations and reintubations ²¹²	LOW
		Avoid reintubation by using nasal CPAP, non-invasive positive pressure ventilation (NIPPV), or high flow nasal cannula in the post-extubation period ³⁹⁶	HIGH
		Provide regular oral care with sterile water	LOW
Additional approaches	Unknown impact on VAP and VAE rates but risk of harm likely minimal. Reasonable to consider implementing if rates remain elevated despite essential practices.	Change the ventilator circuit only if visibly soiled or malfunctioning ²⁵⁹ (or per manufacturer's instructions)	LOW
		Lateral recumbent positioning ²¹⁵	LOW
		Reverse Trendelenberg positioning	LOW
		Closed/in-line suctioning systems ^{216,217}	LOW
Generally not recommended	Unknown impact on VAP rates and inadequate data on risks.	Oral care with maternal colostrum ²¹⁸	MODERATE
		Regular oral care with an antiseptic or Biotene ²¹⁹	LOW
	May be harmful. Risk-benefit balance does not favor intervention, unless specifically indicated for reasons other than VAP prevention	Histamine-2 receptor antagonists ^{220,221}	MODERATE
		Prophylactic broad-spectrum antibiotics ^{222–225}	MODERATE
		Daily spontaneous breathing trials ^{398,399}	LOW
		Daily sedative interruptions	LOW
		Prophylactic probiotics or synbiotics ^{228,229}	LOW
	Not recommended because appropriate products are not available or approved for use in this population.	Endotracheal tubes with subglottic secretion drainage ports	NA
		Silver-coated endotracheal tubes	NA

Note. CPAP, continuous positive airway pressure; VAP, ventilator-associated pneumonia.

Approaches that are generally not recommended for preterm neonates

This intervention has inadequate data on risks and unknown impact on VAP rates in preterm neonates.

- Regular oral care with an antiseptic or Biotene²¹⁹** (Quality of Evidence: LOW).
 - Data are insufficient regarding the impact of altering neonatal microflora and whether oral antiseptics are absorbed across the oral mucosa of preterm neonates.

These interventions may be harmful to preterm neonates:

- Histamine H2-receptor antagonists** (Quality of Evidence: MODERATE)
 - H2-receptor antagonists may increase the risk of nosocomial infection and mortality in preterm neonates.^{220,221}
- Prophylactic broad-spectrum antibiotics** (Quality of Evidence: MODERATE)
 - Prophylactic broad-spectrum antibiotics are associated with increased risk of necrotizing enterocolitis, prolonged length of stay, and death in premature infants.^{222–225}

- Spontaneous breathing trials** (Quality of Evidence: LOW)
 - Ventilating preterm neonates with prolonged continuous positive airway pressure alone increases the risk of extubation failure.^{226,227}

Approaches that are not applicable to preterm neonates

- Daily interruption of sedation** (Quality of Evidence: LOW)
 - Sedation is not routinely used for neonates on mechanical ventilation.
- Prophylactic probiotics and synbiotics** (Quality of Evidence: LOW)
 - Currently, no products have been approved by the FDA for preterm neonates. Limited data suggest that these may benefit some patients, but multiple cases of *Lactobacillus* bacteremia have been reported in infants and children following probiotic therapy.^{228–232}
- Endotracheal tubes equipped with subglottic secretion drains.** (Quality of Evidence: NA).
 - Products sized for neonates are not commercially available.
- Silver coated endotracheal tubes. Products sized for neonates are not commercially available** (Quality of Evidence: NA).

Preventing VAP and/or PedVAE in pediatric patients outside the neonatal period

1. Framework for evaluating and prioritizing interventions:

- a. Diagnosing VAP is as challenging in term infants and children, as it is in adults and preterm neonates. The CDC recently published definitions for pediatric ventilator-associated events, denoted PedVAE, predicated on detecting patients with sustained increases in mean airway pressure or FiO₂ after a period of stability or improvement.⁵⁴
- b. Risk factors for VAE and VAP in infants and children are similar to those of adults.^{233–237} The majority of PedVAEs are not infection related; thus, there are additional risk factors for PedVAE beyond those for VAP alone. Neuromuscular blockade, sedative type, blood transfusions, positive fluid balance, and acute kidney injury have been associated with PedVAE.^{63,69,238,239}
- c. In general, most VAP prevention interventions recommended for adults are presumed to be applicable to older infants and children. Some interventions recommended for adults, however, are not available for infants and small children. For example, the smallest available endotracheal tube equipped with subglottic secretion drainage ports is size 6.0 and therefore is not an option for children under 10 years of age. Similarly, the smallest available silver-coated endotracheal tube is size 6.0.

Essential practices for pediatric patients

The following interventions confer minimal risk of harm, and some data suggest that they may lower VAP rates, PedVAE rates, and/or duration of mechanical ventilation.

Avoid intubation if possible

1. **Use noninvasive positive pressure ventilation (NIPPV) or high flow oxygen by nasal cannula whenever safe and feasible** (Quality of Evidence: MODERATE).
 - a. Risks of NIPPV in pediatric patients mirror those for adults with the added issue that pediatric patients often need sedation to tolerate NIPPV.^{240,241}
 - b. CPAP may be superior to high flow oxygen by nasal cannula to avoid intubation in infants with bronchiolitis.²⁴²

Minimize duration of mechanical ventilation

1. **Assess readiness to extubate daily in patients without contraindications**^{243–247} (Quality of Evidence: MODERATE).
 - a. Randomized controlled trials suggest that daily spontaneous breathing trials can decrease mean duration of ventilation and PICU length of stay in postoperative cardiac surgery patients.^{245,248} There is no consensus on the most effective technique for spontaneous breathing trials in pediatric patients.^{243,246}
2. **Take steps to minimize unplanned extubations and reintubations**^{249,250} (Quality of Evidence: LOW)
 - a. A multicenter, quality-improvement initiative tested a bundle of measures to reduce unplanned extubations.²⁵⁰ The bundle included standardized anatomic reference points and securement methods, protocols for high-risk situations, and multidisciplinary apparent-cause analyses. The bundle

was associated with significant reductions in unplanned extubations and episodes of cardiovascular collapse.

3. **Avoid fluid overload** (Quality of Evidence: MODERATE).
 - a. Meta-analysis of the association between fluid balance and outcomes in critically ill children suggests that fluid overload is associated with increased risk for prolonged mechanical ventilation (>48 hours).²⁵¹
 - b. Interventional studies on fluid management in critically ill children are sparse. One of the few available studies assessed infants at risk for acute kidney injury and fluid overload following cardiac surgery. These infants were randomized to peritoneal dialysis versus furosemide; those randomized to peritoneal dialysis were less likely to develop fluid overload and less likely to have prolonged ventilator use.²⁵² The generalizability of these findings to other populations is unknown.
 - c. The Pediatric Surviving Sepsis Campaign and the Pediatric Acute Lung Injury Consensus Conference recommend limiting fluid intake, starting diuretics, and/or early renal replacement therapy for children with ARDS and for children in the postresuscitation phase of sepsis.^{253,254}

Provide regular oral care

1. **Provide regular oral care** (Quality of Evidence: LOW).
 - a. Four before-and-after studies of VAP bundles that emphasized oral care reported significant decreases in VAP rates following bundle implementation.^{234,255–257}
 - b. The American Dental Association recommends beginning oral hygiene a few days after birth in term infants. Wipe the gums with a gauze pad after each feeding to remove plaque and residual formula that could harm erupting teeth.
 - c. For children aged <3 years, the ADA recommends brushing children's teeth as soon as they begin to come into the mouth using fluoride toothpaste in an amount no more than a smear the size of a grain of rice.²⁵⁸ A pea-sized amount of fluoride toothpaste is recommended for children aged 3–6 years.²⁵⁸
 - d. After oral hygiene, rinse and suction the mouth. Keep the oral mucosa and lips clean, moist, and intact using sponge-tipped applicators dipped in non-alcohol, non-peroxide mouth rinse.²⁵⁵

Elevate the head of the bed

1. **Elevate the head of the bed unless medically contraindicated** (Quality of Evidence: LOW).
 - a. Three before-and-after studies of VAP bundles that included head of bed elevation reported lower VAP rates.^{234,256,257}
 - b. Many hospital cribs do not have inbuilt angle-measuring devices. Alternative measuring devices are required in these circumstances.

Maintain ventilator circuits

1. **Change ventilator circuits only when visibly soiled or malfunctioning or per manufacturers' instructions** (Quality of Evidence: MODERATE).
 - a. A meta-analysis of 6 studies reported no difference in VAP rates or mortality with 3-day versus 7-day circuit changes.²⁵⁹ Circuit changes are therefore recommended only when the circuit is soiled or malfunctioning to minimize costs.^{260,261}
 - b. Follow manufacturers' instructions for use if they differ from this recommendation.

Table 4. Summary of Recommendations to Prevent VAP and/or PedVAE in Pediatric Patients

Category	Rationale	Intervention	Quality of Evidence
Essential practices	Interventions with minimal risk of harm and some data that they may lower VAP rates, PedVAE rates, and/or duration of mechanical ventilation.	Avoid intubation if possible. Use non-invasive positive pressure ventilation for selected populations ^{240–242}	MODERATE
		Assess readiness to extubate daily in patients without contraindications ^{244–248}	MODERATE
		Take steps to minimize unplanned extubations and reintubations ²⁴⁹	LOW
		Avoid fluid overload ^{251,253,254}	MODERATE
		Provide regular oral care (i.e., toothbrushing or gauze if no teeth) ^{234,256,257}	LOW
		Elevate the head of the bed unless medically contraindicated ²³⁴	LOW
		Change ventilator circuits only if visibly soiled or malfunctioning ²⁵⁹ (or per manufacturer's instructions)	MODERATE
		Prevent condensate from reaching the patient ^{234,266}	LOW
		Use cuffed endotracheal tubes ^{262–264}	LOW
		Maintain cuff pressure and volume at the minimal occlusive settings	LOW
Additional approaches	Risk of harm likely minimal with some evidence of benefit in adult patients, but data in pediatric populations are limited. Reasonable to consider implementing if rates remain elevated despite essential practices.	Suction oral secretions before each position change	LOW
		Interrupt sedation daily ²⁶⁷	MODERATE
		Utilize endotracheal tubes with subglottic secretion drainage ports for older pediatric patients expected to require >48 or 72 hours of mechanical ventilation ³⁹⁵	LOW
Generally not recommended	Unknown impact on VAP rates and inadequate data on risks.	Consider early tracheostomy ^{268–270}	LOW
		Prolonged systemic antimicrobial therapy for ventilator-associated tracheitis ²⁷²	LOW
		Selective oropharyngeal or digestive decontamination ²⁷⁴	LOW
	No impact on VAP rates. ^a	Prophylactic probiotics ¹⁶³	LOW
		Oral care with antiseptics such as chlorhexidine ^{280,284,285}	MODERATE
Lowers VAP rates in adults but no impact on duration of mechanical ventilation, length of stay, or mortality.	Stress-ulcer prophylaxis ^{286–288}	LOW	
	Silver-coated endotracheal tubes	LOW	
No recommendation	Limited data on pediatric patients, no impact on VAP rates or outcomes in adults, unclear impact on costs	Closed or in-line suctioning ²⁹³	LOW

Note. VAP, ventilator-associated pneumonia

^aMay be indicated for reasons other than VAP prevention.

2. Remove condensate from the ventilator circuit frequently (Quality of Evidence: LOW).

- a. Avoid draining the condensate toward the patient.²³⁴

Endotracheal tube selection and management

1. Use cuffed endotracheal tubes (Quality of Evidence: LOW).

- a. Pediatric intensivists have historically favored uncuffed tubes due to concern that cuffs may induce subglottic stenosis in pediatric airways. Cuffing has proven safe, however, and may decrease the risk of microaspiration.^{262,263} Cuffed tubes are now recommended for term newborns and children.²⁶⁴

2. Maintain cuff pressure and volume at the minimal occlusive settings to prevent clinically significant air leaks around the endotracheal tube, typically 20–25 cm H₂O.^{171,262,265} This “minimal leak” approach is associated with lower rates of post-extubation stridor²⁶⁵ (Quality of Evidence: LOW).

- a. The potential merits of automated manometers for VAP prevention have not been studied in pediatric patients.

3. Suction oral secretions before each position change (Quality of Evidence: LOW).²⁶⁶

Additional approaches to preventing VAP and VAE in pediatric patients

The following interventions are associated with minimal risks of harm and some evidence of benefit in adult patients, but data in pediatric populations are limited.

1. Minimize sedation (Quality of Evidence: MODERATE).

- a. Daily sedative interruptions decreased duration of mechanical ventilation and ICU length of stay without increases in adverse event rates in 1 small, randomized trial.²⁶⁷
- b. There is nonetheless concern that sedative interruptions will increase the frequency of unplanned extubations and reintubations in younger patients, so this practice may be safest in older pediatric patients.

2. **Use endotracheal tubes with subglottic secretion drainage ports** (Quality of Evidence: LOW).
 - a. This intervention has not been studied in children and is only feasible for children aged ≥ 10 years because the smallest available endotracheal tube with subglottic secretion drainage ports is size 6.0.
3. **Consider early tracheostomy** (Quality of Evidence: LOW).
 - a. A small, single-center, retrospective cohort study reported that early tracheostomy (< 10 days) was associated with lower VAP rates and shorter ICU length of stay compared with late tracheostomy.²⁶⁸
 - b. A propensity-matched analysis of the timing of tracheostomy among children with severe traumatic brain injury reported an association between early tracheostomy and lower pneumonia rates, shorter ICU length of stay, and shorter hospital length of stay.²⁶⁹
 - c. A meta-analysis of retrospective cohort studies reported that early tracheostomy was associated with lower mortality rates, fewer ventilator days, and shorter ICU length of stay.²⁷⁰
 - d. Tracheostomy complications are more frequent in children versus adults.²⁷¹

Approaches that are generally not recommended for VAE and VAE prevention in pediatric patients

The following interventions have unknown impact on VAP and PedVAE rates and/or have inadequate data on risks.

1. **Prolonged systemic antimicrobial therapy for ventilator-associated tracheitis** (Quality of Evidence: LOW)
 - a. One retrospective study found that prolonged antibiotics for ventilator-associated tracheitis did not protect against VAP but did increase the prevalence of multidrug-resistant organisms.²⁷² Whether, when, and how long to treat ventilator-associated tracheitis to prevent VAP in children remains unresolved.²⁷³
2. **Selective oropharyngeal or digestive decontamination** (Quality of Evidence: LOW)
 - a. A meta-analysis of 4 randomized trials in critically ill children published between 1991 and 2001 reported that selective digestive decontamination using a combination of oral and parenteral antibiotics may be associated with a decrease in pneumonia rates but no change in mortality.²⁷⁴ Trials were small, and the long-term impact on antibiotic resistance was not assessed.
3. **Prophylactic probiotics** (Quality of Evidence: LOW)
 - a. Probiotics should be considered with caution due to sparse data on impact in children, lack of clear benefit in adults, and case reports of *Lactobacillus* bacteremia associated with probiotic therapy in pediatric patients, including those not known to be immunocompromised.^{157,163,230–232,275–278}

No impact on VAP rates for pediatric patients

These interventions may be indicated for reasons other than VAP prophylaxis.

1. **Oral care with chlorhexidine** (Quality of Evidence: MODERATE)
 - a. Chlorhexidine appears to be safe for developing teeth,²⁷⁹ but randomized controlled trials have found no difference in VAP rates, length of stay, or mortality in infants and children.^{280–285}

2. **Stress-ulcer prophylaxis** (Quality of Evidence: LOW)
 - a. Two small studies found no impact on VAP rates.^{286,287} A larger, multicenter, cohort study and a meta-analysis reported that acid-suppressive medications were associated with higher VAP rates.^{288,289}

Lowers VAP rates but no impact on duration of mechanical ventilation, length of stay, or mortality

1. **Silver-coated endotracheal tubes** (Quality of Evidence: LOW)
 - a. These tubes have not been studied in children and are only feasible for children aged ≥ 10 years since the smallest available size is 6.0.

No recommendation

These interventions have limited data from pediatric studies, no impact on VAP rates or outcomes in adults, and unclear impact on costs.

1. **Closed/in-line suctioning** (Quality of Evidence: LOW)
 - a. Closed suctioning may be associated with fewer transient decreases in oxygenation and increases in heart rate and blood pressure compared to open suctioning, but the clinical significance of these findings is unclear.^{290–292}
 - b. An observational study of open versus closed suctioning in children did not find any difference in VAP rates, length of stay, or mortality, but the significance of these findings are unclear given the lack of blinding and randomization.²⁹³

Recommendations to prevent NV-HAP

Little robust data exist on interventions to prevent NV-HAP. Most studies are nonrandomized, and many do not report the impact on objective outcomes such as length of stay, mortality, or antibiotic utilization. We classify potential prevention strategies into (1) practices supported by interventional studies suggesting lower NV-HAP rates, (2) practices with insufficient data of benefit or harm, and (3) practices that are not recommended, with evidence of futility or possible harm.

Interventions that may lower NV-HAP rates with little risk of harm

Provide regular oral care

1. Oral care is the most commonly studied strategy to prevent NV-HAP. Before-and-after series suggest a possible benefit.^{294–297} Two large, cluster randomized trials conducted in nursing homes did not show a benefit, but their generalizability to acute-care hospitals is unknown.^{298,299} Most randomized trials in acute-care hospitals have focused on ICU patients, most of whom were on mechanical ventilation, making it difficult to discern their effect on NV-HAP.^{300,301}
 - a. Uncertainty remains regarding the most effective protocols, including types of staff involved (eg, dentistry professionals versus nondentistry professionals), frequency of oral care, whether to include an antiseptic, and if so, what type of antiseptic to use (eg, chlorhexidine gluconate, sodium bicarbonate, hydrogen peroxide, cetylpyridinium chloride, povidone-iodine).
 - b. Notwithstanding the gaps in current evidence, we recommend toothbrushing daily given its benefits for oral health and the possible positive impact on objective outcomes observed in before-and-after studies in nonventilated patients and meta-analyses of randomized trials in ventilated patients.^{126,127,294–297}

Diagnose and manage dysphagia

1. Early diagnosis and treatment of dysphagia may prevent NV-HAP, especially among neurologically impaired post-stroke patients.^{302–304}
2. Potential approaches to diagnose dysphagia include nurse-administered risk assessment tools, bedside functional evaluations of swallowing, video fluoroscopic study, and fiberoptic endoscopic examination.
3. Potential options to manage dysphagia include changes in method of pill administration, adjustments in consistencies of liquids and solids, supervision or assistance with meals, use of straws, and elevation of the head of bed while eating.

Provide early mobilization

1. Data for early mobilization to prevent NV-HAP among hospitalized patients are sparse.^{304,305} One quasi-experiment found that bundling mobilization with other interventions reduced NV-HAP, attributable mortality, and antibiotic utilization, but the relative contribution of mobilization to these benefits is unclear.³⁰⁵ A randomized trial of engaging families to provide turning plus passive mobilization to post-stroke patients versus turning by nursing staff alone reported a significant decrease in pneumonia rates but did not report impact on length of stay or mortality.³⁰⁶ A nonrandomized controlled trial reported that mobilizing patients in 2 geriatric and respiratory wards was associated with a significant decrease in pneumonia rates compared to usual care in matched wards, although falls were significantly more frequent in the intervention group than in the control group and data were not provided on length of stay or mortality.³⁰⁷ In a quasi-experimental study, intensified postoperative physical therapy for elderly patients undergoing hip fracture surgery was associated with less pneumonia and shorter length of stay compared to historical controls.³⁰⁸
2. Additional trials are needed to better quantify the possible benefits versus fall-related harms of mobility programs. Implementation strategies are needed to increase the feasibility, frequency, and safety of mobilizing acute-care patients. In the meantime, early mobilization of patients should take into the account the risk of falls.

Implement multimodal interventions to prevent viral infections

1. Approximately 20%–40% of NV-HAP is attributable to viral pathogens, and the ongoing coronavirus disease 2019 (COVID-19) pandemic has highlighted the risk and morbidity of within-hospital transmission of respiratory viruses.^{25,309–311}
2. Possible strategies to prevent nosocomial viral transmission include symptom screening of patients and healthcare workers, surveillance testing of all admitted patients, transmission-based precautions for patients with suspected and confirmed respiratory viral infections, universal masking when respiratory virus transmission rates are high in the hospital or in the community, assuring adequate ventilation, and vaccination of healthcare personnel and patients.^{312,313}

Bundles

1. Multiple observational studies have reported lower NV-HAP rates after implementing prevention bundles.^{305,314,315} Effective bundles have included heterogeneous combinations of oral hygiene, bed positioning, dysphagia diagnosis and management, mobilizing patients, nasal hygiene, sedation restrictions, incentive spirometry, education for physicians and

nurses, and/or electronic order-set bundles. One small randomized trial of usual care versus a bundle comprising dysphagia screening, oral care with chlorhexidine, placing the bed in the reverse Trendelenburg position, and vaccination against influenza and pneumococcus reported no difference in NV-HAP rates, length of stay, or mortality but did report a lower 1-year risk of readmission for respiratory infection.³¹⁶

2. The respective contribution of each bundle component, the extent to which bundle components are synergistic versus additive, and the most effective combination of interventions to include in bundles remains unknown.

Interventions with insufficient data to determine impact on NV-HAP

Bed positioning

1. Elevating the head of the bed is recommended to prevent VAP and VAE despite sparse evidence because some studies suggest benefit, it is simple, economical, and associated with minimal risk of harm in ventilated patients. Even fewer data, however, are available to inform whether and to what extent this applies to NV-HAP.
2. One randomized trial among critically ill patients with tetanus in Vietnam found that semirecumbent position was associated with no difference in pneumonia rates but more frequent complications including the need for tracheostomy.³¹⁷ The generalizability of these findings to nontetanus patients in other settings is unknown.

Stress-ulcer prophylaxis

1. Observational studies suggest an association between stress-ulcer prophylaxis and risk for NV-HAP but we are not aware of any randomized trials assessing the impact of acid-suppressing medications on NV-HAP outside the ICU setting.³¹⁸

Approaches not generally recommended for routine NV-HAP prevention

Systemic antibiotic prophylaxis

1. Randomized trials of prophylactic antibiotics in acute stroke patients show no impact on pneumonia rates, functional outcome, or mortality.³¹⁹

Section 5: Performance measures

Monitoring and reporting

1. Regular monitoring and internal reporting of patient outcomes and adherence rates to recommended prevention strategies (“process measures”) are important quality improvement strategies.
2. Both outcome and process-measure reporting are likely beneficial: improving outcomes is the primary goal of care improvement programs but process of care surveillance can help identify specific processes to target for improvement.
3. Report outcome measures to key organizational stakeholders including frontline care providers, service leaders (medical, nursing, respiratory therapy), and senior hospital administrators. Reporting these data back to providers and leaders has been associated with improvements in both performance rates and outcomes.^{320–325}
4. Report process measures internally only. External reporting of process measure data is not appropriate given substantial

variability in the ways different organizations define, collect, analyze, and present process measure data.

Process measures

1. Process-measure definitions and measurement strategies vary widely.
2. For organizations that collect and report process measures:
 - a. Clearly define measures including data sources, inclusion and exclusion criteria, frequency of monitoring, and numerator and denominator criteria.
 - b. Develop a formal system to document compliance.
 - i. Compliance can be measured via direct observations or via audits of patient charts, bedside checklists, and/or electronic medical records. Periodically validate the accuracy of paper and/or electronic documentation.
 - c. Perform assessments regularly.
 - i. The optimal frequency of assessments (eg, once daily, twice daily, or weekly) is not known but can likely be adjusted based on compliance rates and unit size.
 - ii. An analysis of a large collaborative quality improvement effort suggests that the following approach can be used to determine the frequency of process measure assessments.³²⁶
 1. Start by measuring processes daily. If compliance is consistently high for a given process, then decrease the frequency of measures (ie, once every 2–3 days or once per week, and if compliance continues to be high, then decrease to once per month). If compliance is low or variable, then continue with daily measurements.
 2. For units with at least 30 ventilator days per month, measuring compliance on 7 consecutive days per month provides accurate performance estimates
 3. For units with <30 ventilator days per month, daily data collection is required to achieve accurate performance estimates.
 - d. There is no consensus on how best to define adherence to different process measures and definitions for measuring adherence vary widely.
 - i. Several published studies provide examples of how process measures were defined.^{118,325,327–329} These approaches can be used as starting points to come up with local strategies to define adherence.

Prevention bundles

1. Prevention bundles are widespread in critical care and have been associated with decreases in VAP, VAE, NV-HAP, and in some cases, length of stay and mortality.
2. A meta-analysis of 13 observational studies in adults found that implementation of ventilator bundles was associated with a 10% decrease in mortality, less time to extubation, and shorter length of stay.³³⁰ All the studies included in this analysis, however, were before-and-after or time-series analyses. It is therefore difficult to discern the extent to which lower VAP rates and better outcomes were due to prevention bundles versus changes in patient mix or unrelated changes in care.³³¹ Observational analyses of pediatric bundles have reported significant decreases in VAP rates, but few data are available on other outcomes.³³²
3. Prevention bundles have only been tested in 1 randomized trial. Researchers in Brazil randomized 188 ICUs to a multifaceted intervention including checklists for the prevention of VAP,

daily goal assessments, and clinician prompts. There were no significant differences between intervention versus control units in VAP rates or mortality rates.³²⁹ These results should be interpreted with caution, however, given that baseline adherence with some process measures was already high (eg, head of bed elevation), adherence with other measures did not improve (eg, light sedation, low tidal volume ventilation), and the intervention period may have been too brief to achieve significant changes.³³³

4. There is no consensus on which processes to include in VAP/VAE prevention bundles. Bundles vary widely among different centers.^{330,334}
5. Ventilator bundle components potentially associated with lower mortality rates include staff education, performance feedback, and in adults, elevating the head of the bed, minimizing sedation, and assessing readiness for extubation.^{110,113,330,335} Additional promising strategies include conservative fluid management, low tidal volume ventilation, and early mobility.^{77,119,336}
6. Compliance can be reported for each process measure individually and/or as ‘all or none’ compliance with a bundle of process measures. For ‘all or none’ compliance, credit is given only if all components have been accomplished and documented; if any components were not performed and/or were not documented, no credit is given.

Outcome measures

1. Conduct surveillance for all VAEs including VAC, IVAC, and PVAP in adult ICUs.^{54,337} Report PedVAE rates in pediatric and neonatal ICUs. Report location-stratified rates for all events included in VAE and PedVAE algorithms. Report standardized infection ratios (SIRs) for all events included in VAE algorithms.⁵⁴
 1. VAE and PedVAE incidence density.
 - i. Numerator: total number of VAEs (including VAC+IVAC+PVAP) or PedVAEs
 - ii. Denominator: total ventilator days
 - iii. Multiply by 1,000 and express as VAEs or PedVAEs per 1,000 ventilator days
 2. IVAC incidence density (adults)
 - i. Numerator: total number of IVACs and PVAPs
 - ii. Denominator: total ventilator days
 - iii. Multiply by 1,000 and express as the IVAC rate per 1,000 ventilator days
 3. PVAP incidence density (adults)
 - i. PVAP rate
 - ii. Numerator: total number of PVAPs
 - iii. Denominator: total ventilator days
 - iv. Multiply by 1,000 and express as the overall PVAP rate per 1,000 ventilator days
 4. Total VAE SIR (adults)
 - i. Numerator: total number of VAEs, including VAC, IVAC, and PVAP
 - ii. Denominator: total number of predicted VAEs
 5. IVAC plus SIR (adults)
 - i. Numerator: total number of IVACs (including PVAPs)
 - ii. Denominator: total number of predicted IVACs (including PVAPs)
 6. Note that the combined outcome of IVAC including PVAPs is sometimes referred to as “IVAC-plus.”

External reporting

1. VAE is a potentially appropriate metric for public reporting, interfacility comparison, and pay-for-performance programs. Better data on the responsiveness of VAE to quality-improvement programs are necessary, however, before recommending VAEs for interfacility comparisons or pay-for-performance programs. Suitable risk adjustment strategies are also needed.
2. PVAP is not suitable for external reporting because substantial variability in clinical and laboratory practices in the acquisition, processing, and interpretation of culture data preclude meaningful comparisons of PVAP rates between institutions.
3. VAP rates generated using former NHSN surveillance definitions are not appropriate for external reporting in light of their considerable subjectivity.
4. Hospitals in states that have mandatory reporting laws must collect and report data as required by their state. Pennsylvania and South Carolina are currently the only 2 states that require hospitals to report VAEs. Local and state health departments can provide specific information on public reporting requirements.

Section 6: Implementation of VAP, VAE, and NV-HAP prevention strategies

Prevention of VAP, VAE, and NV-HAP requires implementing best practices to reduce the risk of infection and nurturing a culture that supports implementation. Accountability is an essential principle for preventing healthcare-associated infections. It provides the necessary translational link between science and implementation. Without clear accountability, scientifically based implementation strategies will be used in an inconsistent and fragmented way, decreasing their effectiveness in preventing HAIs. Accountability begins with the chief executive officer and other senior leaders who must make preventing healthcare-associated infections an organizational priority. Senior leadership is accountable for providing adequate resources for effective implementation of a healthcare-associated infection prevention program. These resources include necessary personnel (clinical and nonclinical), education, and equipment.

Engagement, education, execution, and evaluation are common attributes of successful care improvement programs.^{321,338} These attributes are elaborated below.

Engage

Develop a multidisciplinary team

1. Multidisciplinary teams set goals, define each step in the implementation process, and monitor progress in reaching goals.^{79,83,234,339–341} Programs developed by team consensus are more effective and increase guideline adherence.^{234,339,342} Multidisciplinary teams include representatives from all disciplines that care for ventilated patients, including, at a minimum, unit directors, physicians, nurses, and respiratory therapists. Other partners that can strengthen the team include infection preventionists, pharmacists, nutritionists, physical therapists, occupational therapists, family members, and patient advocates.^{77,83,325,343–347}

Involve local champions

1. Identify local champions, including formal (eg, medical director, nursing director, charge nurses, director of respiratory

therapy) and informal leaders (eg, engaged frontline staff).^{321,325,328,340,343–345,348,349}

2. Local champions are important to success because they engage stakeholders, educate peers, encourage ongoing improvement, and increase buy-in and ownership by both staff and administrators.^{234,321,325,342,346,348,350}
3. Local champions should know their hospital's interests and needs and should be able to shape strategies to match local unit culture, monitor progress, and facilitate necessary changes during implementation.^{320,351–353} Early and continual communication between local champions and frontline staff allows providers to ask questions, resolve concerns, prepare for action, and sustain improvements.^{320,350,352}

Utilize peer networks

1. Horizontal networking of peers across hospitals can promote and increase compliance with evidence-based best practices. Voluntary peer networks encourage collaboration, analysis of performance, accountability, and commitment to specific goals.^{77,79,325,327,345,354,355} Comparing progress and benchmarks between ICUs can help units better understand their local strengths and weaknesses, learn from best practices, brainstorm solutions to common problems, and promulgate local successes.^{77,79,327,336,345,353}

Educate

Provide education sessions

1. The introduction of evidence-based practices in the clinical setting should be supported by active and multifaceted education programs.^{77,330,356}
2. Education sessions help summarize evidence, explain new processes, set expectations, and encourage staff to adopt recommended practices.^{320,327,357,358}
3. Education sessions can include workshops, hands-on training, conferences, slide presentations, and/or interactive discussions; employing multiple teaching modalities can help meet diverse learning styles.^{327,341,350,359,360} Both local champions and topic experts (eg, infection preventionists) can lead staff education.^{234,351,355,361}
4. Education sessions must be informative and relevant for the learner; therefore it is important to have multidisciplinary educational programs customized for different levels of training and different specialties.^{81,321,322,339}
5. Ongoing staff education helps maintain high levels of compliance with recommended practices.^{323,345,347,359,362}
6. Implementation of experiential learning strategies (simulation models, play activities, knowledge and attitude competencies, role-playing and feedback) may improve bundle adherence.³⁴¹
7. Educating patients and family members may help them better engage with and support the medical team's plan of care.^{336,363}

Provide educational materials

1. Provide educational materials to staff that summarize the evidence, support self-study, and remind staff about new practices.³⁶⁴
2. Examples of educational materials include smartphone applications, interactive websites, pocket cards, brochures, posters, fact sheets, daily guides, guideline summaries, flow sheets and 1-page bulletins.^{234,323,325,345,362–366}

Execute

Standardize care processes

1. Standardize care processes through the implementation of guidelines, bundles, protocols or pathways. Standardization helps establish new care processes as “normal behaviors” for staff.^{77,79,81,83,320,347,349,353,358}
2. Interventions to improve adherence with best practices in the ICU that include protocols with or without education are associated with the greatest improvements in processes of critical care.³⁶⁷
3. Daily multidisciplinary rounds are widely recommended.^{368,369} Rounds should follow a structured format and include discussion about the patients’ goals for the day, consideration of what resources and actions are necessary to achieve these goals, and identification of potential barriers and/or safety issues.^{322,325,344,363,370,371}

Create redundancy

1. Build redundancy or independent checks into care delivery processes to increase the likelihood that best practices are followed.^{320,321,347,363,367,372}
2. Redundancy includes reminders about best practice and can take the form of posters, bulletins, pens, stamps, pocket cards, 1-page signs, daily goal lists in patient rooms, checklists, and preprinted order sets, text messages, and screensavers on clinical computers.^{81,321,323,351,355,366,372–378}
3. Engage family members to assist with preventive care as appropriate and/or to discuss prevention practices with the care team daily. This provides an external prompt for the performance of best practices and can help increase patient acceptance of practices such as oral care, mobilization, and delirium prevention.^{325,363}
4. The combination of education and reminders significantly improves process of care performance rates.³⁵⁷

Evaluate

Measure performance

1. Measure performance using frequent formal and informal audits of clinical practice.^{77,81,83,321,327,363,379}
2. Measuring process and outcome measures enhances awareness, establishes expectations, creates urgency, and rewards changes in behavior.^{320,360–362}
3. Evaluating performance provides an ongoing, real-time image of actual implementation rates. Areas of poor compliance can be rapidly identified and rectified.^{321,341,346,351,358,374,379,380} If compliance remains poor in one area, the improvement team should walk the process with staff to gain additional insights into barriers to implementation.^{321,341,346,351,352}
4. Analyze all or a representative sample of VAEs for etiology and preventability. Pneumonia, pulmonary edema, acute respiratory distress syndrome, and atelectasis are the precipitants for most VAEs.^{17,19,22,58,60,61} Use these analyses to select and refine prevention strategies that address the most frequent and preventable causes of VAEs in the specific unit of interest.^{83,351}

Provide feedback to staff

1. Provide regular feedback on process and/or outcome data to staff.^{77,79,320,322,355,360,372,375} Feedback can be provided via dashboards, wall displays, or during meetings.^{81,234,320,351,358,364,365}

2. Providing feedback helps staff appreciate how their efforts to improve are affecting performance rates and patients’ outcomes. This helps maintain staff motivation and can boost adherence to new processes.^{79,321,327,351,381}
3. Feedback is also important for future efforts because feedback helps pinpoint new areas for improvement and marks successful transitions to new standards of care.^{320,321,351,379,381}

Barriers and facilitators for adoption

Qualitative studies have identified several common barriers and facilitators to the implementation of VAE/VAP prevention programs.

1. Barriers related to staff workload and time (ie, competing priorities, data collection burden, not enough time), staff turnover, and lack of leadership support can impede implementation progress.^{382,383}
2. Barriers may also include a unit culture that does not prioritize preventive care and lack of a structured interdisciplinary approach to minimizing sedation and facilitating liberation from mechanical ventilation.³⁷⁸
3. Facilitators for bundle adherence include ‘reflective motivation’ (ie, VAE and VAP are perceived as serious and common problems among ICU patients; providers consider prevention measures useful to lower VAE or VAP rates and improve patients’ outcomes). Reflective motivation can be achieved through increasing knowledge and understanding or through eliciting positive (or negative) feelings about adopting new practices.³⁸³
4. Goddard et al,³⁸⁴ using a Theoretical Domains Framework of behavior change, found that the social influences domain (local champions, ICU leadership, engagement between providers and family members) and behavioral regulation domain (feedback and having a unit protocol) may act as barriers or facilitators to early rehabilitation.

Positive examples and resources

Many successful improvement programs have been published and provide additional insights into practical strategies to engage multidisciplinary teams, educate key stakeholders, implement multifaceted interventions, and achieve significant reductions in VAE, VAP, and/or NV-HAP.^{77,83,305,325,341,345,358,367} In addition, The Society of Critical Care Medicine’s (SCCM) ICU Liberation initiative offers numerous tools and resources to assist hospitals with implementing bundles designed to improve patient outcomes and reduce the risk of long-term consequences of critical illness.^{369,385}

Acknowledgments. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Conflicts of interest. The following disclosures are a reflection of what has been reported to SHEA. To provide thorough transparency, SHEA requires full disclosure of all relationships, regardless of relevancy to the guideline topic. Such relationships as potential conflicts of interest are evaluated in a review process that includes assessment by the SHEA Conflict of Interest Committee and may include the Board of Trustees and Editor of Infection Control and Hospital Epidemiology. The assessment of disclosed relationships for possible conflicts of interest has been based on the relative weight of the financial relationship (i.e., monetary amount) and the relevance of the relationship (ie, the degree to which an association might reasonably be interpreted by an independent observer as related to the topic or recommendation of consideration).

M.K. has received grant funding from CDC and AHRQ plus royalties from UpToDate, Inc. R.B. has served as an advisor/consultant for Pfizer, Mallinckrodt, Ventec Life Systems, Vyair and Zoll Medical. K.A.C. has received honoraria from Becton Dickinson, CloroxPro, and Elsevier. L.R.G. has received honoraria from Premier Inc, Care Fusion, Infection Control Today, and Advanced Sterilization Products. All other authors report no conflicts of interest.

References

- Klompas M, Branson R, Eichenwald EC, *et al*. Strategies to prevent ventilator-associated pneumonia in acute-care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;35:915–936.
- The Society for Healthcare Epidemiology of America (SHEA) handbook for SHEA-sponsored guidelines and expert guidance documents, 2021. SHEA website. <https://shea-online.org/wp-content/uploads/2022/02/2022-Handbook-Update-Approved-Posted.pdf>. Accessed August 2021.
- Magill SS, O'Leary E, Janelle SJ, *et al*. Changes in prevalence of healthcare-associated infections in US hospitals. *N Engl J Med* 2018;379:1732–1744.
- Walter J, Haller S, Quinten C, *et al*. Healthcare-associated pneumonia in acute-care hospitals in European Union/European Economic Area countries: an analysis of data from a point prevalence survey, 2011 to 2012. *Euro Surveill* 2018;23:1700843.
- Ego A, Preiser JC, Vincent JL. Impact of diagnostic criteria on the incidence of ventilator-associated pneumonia. *Chest* 2015;147:347–355.
- Tejerina E, Esteban A, Fernandez-Segoviano P, *et al*. Accuracy of clinical definitions of ventilator-associated pneumonia: comparison with autopsy findings. *J Crit Care* 2010;25:62–68.
- Kerlin MP, Trick WE, Anderson DJ, *et al*. Interrater reliability of surveillance for ventilator-associated events and pneumonia. *Infect Control Hosp Epidemiol* 2017;38:172–178.
- Stevens JP, Kachniarz B, Wright SB, *et al*. When policy gets it right: variability in US hospitals' diagnosis of ventilator-associated pneumonia. *Crit Care Med* 2014;42:497–503.
- Dudeck MA, Horan TC, Peterson KD, *et al*. National Healthcare Safety Network (NHSN) report, data summary for 2010, device-associated module. *Am J Infect Control* 2011;39:798–816.
- Klompas M. Eight initiatives that misleadingly lower ventilator-associated pneumonia rates. *Am J Infect Control* 2012;40:408–410.
- Thomas BW, Maxwell RA, Dart BW, *et al*. Errors in administrative-reported ventilator-associated pneumonia rates: are never events really so? *Am Surg* 2011;77:998–1002.
- Skrupky LP, McConnell K, Dallas J, Kollef MH. A comparison of ventilator-associated pneumonia rates as identified according to the National Healthcare Safety Network and American College of Chest Physicians criteria. *Crit Care Med* 2012;40:281–284.
- Novosel TJ, Hodge LA, Weireter LJ, *et al*. Ventilator-associated pneumonia: depends on your definition. *Am Surg* 2012;78:851–854.
- Vincent JL, Sakr Y, Singer M, *et al*. Prevalence and outcomes of infection among patients in intensive care units in 2017. *JAMA* 2020;323:1478–1487.
- Metersky ML, Wang Y, Klompas M, Eckenrode S, Bakullari A, Eldridge N. Trend in ventilator-associated pneumonia rates between 2005 and 2013. *JAMA* 2016;316:2427–2429.
- Magill SS, Klompas M, Balk R, *et al*. Developing a new, national approach to surveillance for ventilator-associated events. *Crit Care Med* 2013;41:2467–2475.
- Klompas M, Khan Y, Kleinman K, *et al*. Multicenter evaluation of a novel surveillance paradigm for complications of mechanical ventilation. *PLoS One* 2011;6:e18062.
- Klompas M, Magill S, Robicsek A, *et al*. Objective surveillance definitions for ventilator-associated pneumonia. *Crit Care Med* 2012;40:3154–3161.
- Hayashi Y, Morisawa K, Klompas M, *et al*. Toward improved surveillance: the impact of ventilator-associated complications on length of stay and antibiotic use in patients in intensive care units. *Clin Infect Dis* 2013;56:471–477.
- Prospero E, Illuminati D, Marigliano A, *et al*. Learning from Galileo: ventilator-associated pneumonia surveillance. *Am J Respir Crit Care Med* 2012;186:1308–1309.
- Muscudere J, Sinuff T, Heyland D, *et al*. The clinical impact and preventability of ventilator-associated conditions in critically ill mechanically ventilated patients. *Chest* 2013;144:1453–1460.
- Klein Klouwenberg PM, van Mourik MS, Ong DS, *et al*. Electronic implementation of a novel surveillance paradigm for ventilator-associated events: feasibility and validation. *Am J Respir Crit Care Med* 2014;189:947–955.
- Klompas M, Kleinman K, Murphy MV. Descriptive epidemiology and attributable morbidity of ventilator-associated events. *Infect Control Hosp Epidemiol* 2014;35:502–510.
- Magill SS, Li Q, Gross C, Dudeck M, Allen-Bridson K, Edwards JR. Incidence and characteristics of ventilator-associated events reported to the National Healthcare Safety Network in 2014. *Crit Care Med* 2016;44:2154–2162.
- Klompas M, Baker MA, Rhee C, *et al*. A SARS-CoV-2 cluster in an acute-care hospital. *Ann Intern Med* 2021;174:794–802.
- Russell CD, Fairfield CJ, Drake TM, *et al*. Coinfections, secondary infections, and antimicrobial use in patients hospitalised with COVID-19 during the first pandemic wave from the ISARIC WHO CCP-UK study: a multicentre, prospective cohort study. *Lancet Microbe* 2021;2:e354–e365.
- Lumley SF, Constantinides B, Sanderson N, *et al*. Epidemiological data and genome sequencing reveals that nosocomial transmission of SARS-CoV-2 is underestimated and mostly mediated by a small number of highly infectious individuals. *J Infect* 2021;83:473–482.
- Nguile-Makao M, Zahar JR, Francais A, *et al*. Attributable mortality of ventilator-associated pneumonia: respective impact of main characteristics at ICU admission and VAP onset using conditional logistic regression and multistate models. *Intensive Care Med* 2010;36:781–789.
- Bekaert M, Timsit JF, Vansteelandt S, *et al*. Attributable mortality of ventilator associated pneumonia: a reappraisal using causal analysis. *Am J Respir Crit Care Med* 2011;184:1133–1139.
- Melsen WG, Rovers MM, Koeman M, Bonten MJ. Estimating the attributable mortality of ventilator-associated pneumonia from randomized prevention studies. *Crit Care Med* 2011;39:2736–2742.
- Melsen WG, Rovers MM, Groenwold RH, *et al*. Attributable mortality of ventilator-associated pneumonia: a meta-analysis of individual patient data from randomised prevention studies. *Lancet Infect Dis* 2013;13:665–671.
- Steen J, Vansteelandt S, De Bus L, *et al*. Attributable mortality of ventilator-associated pneumonia. Replicating findings, revisiting methods. *Ann Am Thorac Soc* 2021;18:830–837.
- Safdar N, Dezfoulian C, Collard HR, Saint S. Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. *Crit Care Med* 2005;33:2184–2193.
- Zhu S, Wang W, Kang Y, *et al*. Clinical outcomes and risk factors for mortality from ventilator-associated events: a registry-based cohort study among 30,830 intensive care unit patients. *Infect Control Hosp Epidemiol* 2022;43:48–55.
- Fan Y, Gao F, Wu Y, Zhang J, Zhu M, Xiong L. Does ventilator-associated event surveillance detect ventilator-associated pneumonia in intensive care units? A systematic review and meta-analysis. *Crit Care* 2016;20:338.
- Ji W, McKenna C, Ochoa A, *et al*. Development and assessment of objective surveillance definitions for nonventilator hospital-acquired pneumonia. *JAMA Netw Open* 2019;2:e1913674.
- Zilberberg MD, Nathanson BH, Puzniak LA, Shorr AF. Descriptive epidemiology and outcomes of nonventilated hospital-acquired, ventilated hospital-acquired, and ventilator-associated bacterial pneumonia in the United States, 2012–2019. *Crit Care Med* 2022;50:460–468.
- Kirtland SH, Corley DE, Winterbauer RH, *et al*. The diagnosis of ventilator-associated pneumonia: a comparison of histologic, microbiologic, and clinical criteria. *Chest* 1997;112:445–457.
- Klompas M. Does this patient have ventilator-associated pneumonia? *JAMA* 2007;297:1583–1593.

40. Wunderink RG, Woldenberg LS, Zeiss J, Day CM, Ciemins J, Lacher DA. The radiologic diagnosis of autopsy-proven ventilator-associated pneumonia. *Chest* 1992;101:458–463.
41. Schurink CA, Van Nieuwenhoven CA, Jacobs JA, *et al.* Clinical pulmonary infection score for ventilator-associated pneumonia: accuracy and inter-observer variability. *Intensive Care Med* 2004;30:217–224.
42. Klompas M. Interobserver variability in ventilator-associated pneumonia surveillance. *Am J Infect Control* 2010;38:237–239.
43. Klein Klouwenberg PM, Ong DS, Bos LD, *et al.* Interobserver agreement of centers for disease control and prevention criteria for classifying infections in critically ill patients. *Crit Care Med* 2013;41:2373–2378.
44. Sherman ER, Heydon KH, St John KH, *et al.* Administrative data fail to accurately identify cases of healthcare-associated infection. *Infect Control Hosp Epidemiol* 2006;27:332–337.
45. Stevenson KB, Khan Y, Dickman J, *et al.* Administrative coding data, compared with CDC/NHSN criteria, are poor indicators of healthcare-associated infections. *Am J Infect Control* 2008;36:155–164.
46. Drees M, Hausman S, Rogers A, Freeman L, Frosch K, Wroten K. Underestimating the impact of ventilator-associated pneumonia by use of surveillance data. *Infect Control Hosp Epidemiol* 2010;31:650–652.
47. van Mourik MS, van Duijn PJ, Moons KG, Bonten MJ, Lee GM. Accuracy of administrative data for surveillance of healthcare-associated infections: a systematic review. *BMJ Open* 2015;5:e008424.
48. Klompas M. The paradox of ventilator-associated pneumonia prevention measures. *Crit Care* 2009;13:315.
49. Bonten MJ. Healthcare epidemiology: ventilator-associated pneumonia: preventing the inevitable. *Clin Infect Dis* 2011;52:115–121.
50. Klompas M, Platt R. Ventilator-associated pneumonia—the wrong quality measure for benchmarking. *Ann Intern Med* 2007;147:803–805.
51. van Saene HK, Silvestri L, de la Cal MA, Baines P. The emperor's new clothes: the fairy tale continues. *J Crit Care* 2009;24:149–152.
52. Uckay I, Ahmed QA, Sax H, Pittet D. Ventilator-associated pneumonia as a quality indicator for patient safety? *Clin Infect Dis* 2008;46:557–563.
53. Blot S, Lisboa T, Angles R, Rello J. Prevention of VAP: is zero rate possible? *Clin Chest Med* 2011;32:591–599.
54. Pediatric ventilator-associated events (PedVAE), 2021. Centers for Disease Control and Prevention website. <https://www.cdc.gov/nhsn/psc/pedvae/index.html>. Published June 3, 2021. Accessed March 31, 2022.
55. Cocoros NM, Priebe GP, Logan LK, *et al.* A pediatric approach to ventilator-associated events surveillance. *Infect Control Hosp Epidemiol* 2017;38:327–333.
56. Ventilator-Associated event protocol. Centers for Disease Control and Prevention website. <http://www.cdc.gov/nhsn/acute-care-hospital/vae/index.html>. Published March 25, 2014. Accessed March 31, 2022.
57. Karandikar MV, Coffin SE, Priebe GP, *et al.* Variability in antimicrobial use in pediatric ventilator-associated events. *Infect Control Hosp Epidemiol* 2019;40:32–39.
58. Boyer AF, Schoenberg N, Babcock H, McMullen KM, Micek ST, Kollef MH. A prospective evaluation of ventilator-associated conditions and infection-related ventilator-associated conditions. *Chest* 2015;147:68–81.
59. Whiting J, Edriss H, Nugent K. Frequency and etiology of ventilator-associated events in the medical intensive care unit. *Am J Med Sci* 2015;350:453–457.
60. Nakahashi S, Yamada T, Ogura T, Nakajima K, Suzuki K, Imai H. Association of patient care with ventilator-associated conditions in critically ill patients: risk factor analysis. *PLoS One* 2016;11:e0153060.
61. Chao WC, Chang WL, Wu CL, Chan MC. Using Objective fluid balance data to identify pulmonary edema in subjects with ventilator-associated events. *Respir Care* 2018;63:1413–1420.
62. Ramirez-Estrada S, Lagunes L, Pena-Lopez Y, *et al.* Assessing predictive accuracy for outcomes of ventilator-associated events in an international cohort: the EUVAE study. *Intensive Care Med* 2018;44:1212–1220.
63. Cocoros NM, Priebe G, Gray JE, *et al.* Factors associated with pediatric ventilator-associated conditions in six US hospitals: a nested case-control study. *Pediatr Crit Care Med* 2017;18:e536–e545.
64. Lewis SC, Li L, Murphy MV, Klompas M. Risk factors for ventilator-associated events: a case-control multivariable analysis. *Crit Care Med* 2014;42:1839–1848.
65. Klompas M, Li L, Szumita P, Kleinman K, Murphy MV. Associations between different sedatives and ventilator-associated events, length of stay, and mortality in patients who were mechanically ventilated. *Chest* 2016;149:1373–1379.
66. Liu J, Zhang S, Chen J, *et al.* Risk factors for ventilator-associated events: A prospective cohort study. *Am J Infect Control* 2019;47:744–749.
67. Rello J, Ramirez-Estrada S, Romero A, *et al.* Factors associated with ventilator-associated events: an international multicenter prospective cohort study. *Eur J Clin Microbiol Infect Dis* 2019;38:1693–1699.
68. He S, Wu F, Wu X, *et al.* Ventilator-associated events after cardiac surgery: evidence from 1,709 patients. *J Thorac Dis* 2018;10:776–783.
69. Guess R, Vaewpanich J, Coss-Bu JA, *et al.* Risk factors for ventilator-associated events in a PICU. *Pediatr Crit Care Med* 2018;19:e7–e13.
70. Sim JK, Oh JY, Min KH, *et al.* Clinical significance of ventilator-associated event. *J Crit Care* 2016;35:19–23.
71. Wang W, Zhu S, He Q, *et al.* Fluid balance and ventilator-associated events among patients admitted to ICUs in China: a nested case-control study. *Crit Care Med* 2022;50:307–316.
72. Ogbu OC, Martin GS, Sevransky JE, Murphy DJ. High tidal volumes are independently associated with development of a ventilator-associated condition in the ICU. *Am J Respir Crit Care Med* 2015;191:A3117.
73. Wang W, He Q, Zhu S, *et al.* Association between blood transfusion and ventilator-associated events: a nested case-control study. *Infect Control Hosp Epidemiol* 2021. doi: 10.1017/ice.2021.178.
74. Harris BD, Thomas GA, Greene MH, Spiers SS, Talbot TR. Ventilator bundle compliance and risk of ventilator-associated events. *Infect Control Hosp Epidemiol* 2018;39:637–643.
75. Klompas M, Li L, Kleinman K, Szumita PM, Massaro AF. Associations between ventilator bundle components and outcomes. *JAMA Intern Med* 2016;176:1277–1283.
76. Bouadma L, Sonnevill R, Garrouste-Orgeas M, *et al.* Ventilator-associated events: prevalence, outcome, and relationship with ventilator-associated pneumonia. *Crit Care Med* 2015;43:1798–1806.
77. Klompas M, Anderson D, Trick W, *et al.* The preventability of ventilator-associated events. The CDC Prevention Epicenters Wake Up and Breathe Collaborative. *Am J Respir Crit Care Med* 2015;191:292–301.
78. Mekontso Dessap A, Katsahian S, Roche-Campo F, *et al.* Ventilator-associated pneumonia during weaning from mechanical ventilation: role of fluid management. *Chest* 2014;146:58–65.
79. Rawat N, Yang T, Ali KJ, *et al.* Two-State collaborative study of a multifaceted intervention to decrease ventilator-associated events. *Crit Care Med* 2017;45:1208–1215.
80. Anand T, Ponce S, Pakula A, Norville C, Kallish D, Martin M, *et al.* Results from a quality improvement project to decrease infection-related ventilator events in trauma patients at a community teaching hospital. *Am Surg* 2018;84:1701–1704.
81. Chumpia MM, Ganz DA, Chang ET, de Peralta SS. Reducing the rare event: lessons from the implementation of a ventilator bundle. *BMJ Open* 2019;8:e000426.
82. Augustus Oglesby HJ, Cataldo SH, Pedro MJ. Automated near real-time ventilator data feedback reduces incidence of ventilator-associated events: a retrospective observational study. *Crit Care Explor* 2021;3:e0379.
83. Seaver J, Grant K, Lunn J, Sandor P, Moran P, Shapiro DS. A multidisciplinary approach to reducing ventilator-associated events in a busy urban hospital. *Am J Infect Control* 2020;48:828–830.
84. Shenoy ES, Rosenthal ES, Shao YP, *et al.* Real-time, automated detection of ventilator-associated events: avoiding missed detections, misclassifications, and false detections due to human error. *Infect Control Hosp Epidemiol* 2018;39:826–833.
85. Stevens JP, Silva G, Gillis J, *et al.* Automated surveillance for ventilator-associated events. *Chest* 2014;146:1612–1618.
86. Hebert C, Flaherty J, Smyer J, Ding J, Mangino JE. Development and validation of an automated ventilator-associated event electronic surveillance system: a report of a successful implementation. *Am J Infect Control* 2018;46:316–321.
87. Nuckchady D, Heckman MG, Diehl NN, *et al.* Assessment of an automated surveillance system for detection of initial ventilator-associated events. *Am J Infect Control* 2015;43:1119–1121.

88. Klompas M. Ventilator-associated events surveillance: a patient safety opportunity. *Curr Opin Crit Care* 2013;19:424–431.
89. Wolfensberger A, Jakob W, Faes Hesse M, *et al*. Development and validation of a semi-automated surveillance system-lowering the fruit for non-ventilator-associated hospital-acquired pneumonia (nvHAP) prevention. *Clin Microbiol Infect* 2019;25:1428e7–e13.
90. Klompas M. Prevention of intensive care unit-acquired pneumonia. *Semin Resp Crit Care Med* 2019;40:548–557.
91. Rochweg B, Granton D, Wang DX, *et al*. High flow nasal cannula compared with conventional oxygen therapy for acute hypoxemic respiratory failure: a systematic review and meta-analysis. *Intensive care medicine*. 2019;45:563–572.
92. Granton D, Chaudhuri D, Wang D, *et al*. High-flow nasal cannula compared with conventional oxygen therapy or noninvasive ventilation immediately postextubation: a systematic review and meta-analysis. *Crit Care Med* 2020;48:e1129–11e36.
93. Chaudhuri D, Granton D, Wang DX, *et al*. High-flow nasal cannula in the immediate postoperative period: a systematic review and meta-analysis. *Chest* 2020;158:1934–1946.
94. Yasuda H, Okano H, Mayumi T, *et al*. Post-extubation oxygenation strategies in acute respiratory failure: a systematic review and network meta-analysis. *Crit Care (London)* 2021;25:135.
95. Frat JP, Thille AW, Mercat A, *et al*. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med* 2015; 372:2185–2196.
96. Osadnik CR, Tee VS, Carson-Chahhoud KV, Picot J, Wedzicha JA, Smith BJ. Non-invasive ventilation for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2017;7:CD004104.
97. Xu XP, Zhang XC, Hu SL, *et al*. Noninvasive ventilation in acute hypoxemic nonhypercapnic respiratory failure: a systematic review and meta-analysis. *Crit Care Med* 2017;45:e727–e733.
98. David-Joao PG, Guedes MH, Rea-Neto A, Chaiben VBO, Baena CP. Noninvasive ventilation in acute hypoxemic respiratory failure: a systematic review and meta-analysis. *J Crit Care* 2019;49:84–91.
99. Ferreyro BL, Angriman F, Munshi L, *et al*. Association of noninvasive oxygenation strategies with all-cause mortality in adults with acute hypoxemic respiratory failure: a systematic review and meta-analysis. *JAMA* 2020;324:57–67.
100. Vaschetto R, Pecere A, Perkins GD, *et al*. Effects of early extubation followed by noninvasive ventilation versus standard extubation on the duration of invasive mechanical ventilation in hypoxemic non-hypercapnic patients: a systematic review and individual patient data meta-analysis of randomized controlled trials. *Crit Care (London)* 2021;25:189.
101. Grieco DL, Menga LS, Cesarano M, *et al*. Effect of helmet noninvasive ventilation vs high-flow nasal oxygen on days free of respiratory support in patients with COVID-19 and moderate to severe hypoxemic respiratory failure: the HENIVOT randomized clinical trial. *JAMA* 2021;325:1731–1743.
102. Sang L, Nong L, Zheng Y, *et al*. Effect of high-flow nasal cannula versus conventional oxygen therapy and non-invasive ventilation for preventing reintubation: a Bayesian network meta-analysis and systematic review. *J Thorac Dis* 2020;12:3725–3736.
103. Thille AW, Muller G, Gacouin A, *et al*. Effect of postextubation high-flow nasal oxygen with noninvasive ventilation vs high-flow nasal oxygen alone on reintubation among patients at high risk of extubation failure: a randomized clinical trial. *JAMA* 2019;322:1465–1475.
104. Ehrmann S, Li J, Ibarra-Estrada M, *et al*. Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial. *Lancet Respir Med* 2021;9: 1387–1395.
105. Shehabi Y, Bellomo R, Kadiman S, *et al*. Sedation intensity in the first 48 hours of mechanical ventilation and 180-day mortality: a multinational prospective longitudinal cohort study. *Crit Care Med* 2018;46:850–859.
106. Devlin JW, Skrobik Y, Gelinas C, *et al*. Executive summary: clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit Care Med* 2018;46:1532–1548.
107. Fraser GL, Devlin JW, Worby CP, *et al*. Benzodiazepine versus nonbenzodiazepine-based sedation for mechanically ventilated, critically ill adults: a systematic review and meta-analysis of randomized trials. *Crit Care Med* 2013;41:S30–S38.
108. Hughes CG, Mailloux PT, Devlin JW, *et al*. Dexmedetomidine or propofol for sedation in mechanically ventilated adults with sepsis. *N Engl J Med* 2021;384:1424–1436.
109. Lewis K, Pitcaru J, Chaudhuri D, *et al*. Safety and efficacy of dexmedetomidine in acutely ill adults requiring noninvasive ventilation: a systematic review and meta-analysis of randomized trials. *Chest* 2021; 159:2274–2288.
110. Ouellette DR, Patel S, Girard TD, *et al*. Liberation from mechanical ventilation in critically ill adults: an official American College of Chest Physicians/American Thoracic Society clinical practice guideline: inspiratory pressure augmentation during spontaneous breathing trials, protocols minimizing sedation, and noninvasive ventilation immediately after extubation. *Chest* 2017;151:166–180.
111. Strom T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. *Lancet* 2010;375:475–480.
112. Olsen HT, Nedergaard HK, Strom T, *et al*. Nonsedation or light sedation in critically ill, mechanically ventilated patients. *N Engl J Med* 2020; 382:1103–1111.
113. Girard TD, Alhazzani W, Kress JP, *et al*. An official American Thoracic Society/American College of Chest Physicians clinical practice guideline: liberation from mechanical ventilation in critically ill adults. Rehabilitation protocols, ventilator liberation protocols, and cuff leak tests. *Am J Resp Crit Care Med* 2017;195:120–133.
114. Ely EW, Baker AM, Dunagan DP, *et al*. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. *N Engl J Med* 1996;335:1864–1869.
115. Kollef MH, Shapiro SD, Silver P, *et al*. A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. *Crit Care Med* 1997;25:567–574.
116. Marelich GP, Murin S, Battistella F, Inciardi J, Vierra T, Roby M. Protocol weaning of mechanical ventilation in medical and surgical patients by respiratory care practitioners and nurses: effect on weaning time and incidence of ventilator-associated pneumonia. *Chest* 2000;118:459–467.
117. Lellouche F, Mancebo J, Jolliet P, *et al*. A multicenter randomized trial of computer-driven protocolized weaning from mechanical ventilation. *Am J Respir Crit Care Med* 2006;174:894–900.
118. Girard TD, Kress JP, Fuchs BD, *et al*. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (awakening and breathing controlled trial): a randomised controlled trial. *Lancet* 2008;371:126–134.
119. Hsieh SJ, Otusanya O, Gershengorn HB, *et al*. Staged implementation of awakening and breathing, coordination, delirium monitoring and management, and early mobilization bundle improves patient outcomes and reduces hospital costs. *Crit Care Med* 2019;47:885–893.
120. Zhang L, Hu W, Cai Z, *et al*. Early mobilization of critically ill patients in the intensive care unit: a systematic review and meta-analysis. *PLoS One* 2019;14:e0223185.
121. Waldauf P, Jiroutkova K, Krajcova A, Puthuchery Z, Duska F. Effects of Rehabilitation interventions on clinical outcomes in critically ill patients: systematic review and meta-analysis of randomized controlled trials. *Crit Care Med* 2020;48:1055–1065.
122. Wang J, Ren D, Liu Y, Wang Y, Zhang B, Xiao Q. Effects of early mobilization on the prognosis of critically ill patients: a systematic review and meta-analysis. *Int J Nurs Stud* 2020;110:103708.
123. Zang K, Chen B, Wang M, *et al*. The effect of early mobilization in critically ill patients: A meta-analysis. *Nurs Crit Care* 2020;25:360–367.
124. Lord RK, Mayhew CR, Korupolu R, *et al*. ICU early physical rehabilitation programs: financial modeling of cost savings. *Crit Care Med* 2013;41: 717–724.
125. Wang L, Li X, Yang Z, Tang X, Yuan Q, Deng L, *et al*. Semirecumbent position versus supine position for the prevention of ventilator-associated pneumonia in adults requiring mechanical ventilation. *Cochrane Database Syst Rev* 2016:CD009946.

126. Zhao T, Wu X, Zhang Q, Li C, Worthington HV, Hua F. Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database Syst Rev* 2020;12:CD008367.
127. Sozkes S, Sozkes S. Use of toothbrushing in conjunction with chlorhexidine for preventing ventilator-associated pneumonia: a random-effect meta-analysis of randomized controlled trials. *Int J Dent Hyg* 2021. doi: 10.1111/idh.12560.
128. Price R, MacLennan G, Glen J. Selective digestive or oropharyngeal decontamination and topical oropharyngeal chlorhexidine for prevention of death in general intensive care: systematic review and network meta-analysis. *BMJ* 2014;348:g2197.
129. Klompas M, Speck K, Howell MD, Greene LR, Berenholtz SM. Reappraisal of routine oral care with chlorhexidine gluconate for patients receiving mechanical ventilation: systematic review and meta-analysis. *JAMA Intern Med* 2014;174:751–761.
130. Deschepper M, Waegeman W, Eeckloo K, Vogelaers D, Blot S. Effects of chlorhexidine gluconate oral care on hospital mortality: a hospital-wide, observational cohort study. *Intensive Care Med* 2018;44:1017–1026.
131. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr* 2019;38:48–79.
132. Han J, Liu Y. Effect of ventilator circuit changes on ventilator-associated pneumonia: a systematic review and meta-analysis. *Respir Care* 2010; 55:467–474.
133. Rutala WA, Weber DJ, and the Healthcare Infection Control Practices Advisory Committee (HICPAC). Guideline for disinfection and sterilization in healthcare facilities, 2008. Updated May 2019. Centers for Disease Control and Prevention, 2019.
134. Bos LD, Stips C, Schouten LR, et al. Selective decontamination of the digestive tract halves the prevalence of ventilator-associated pneumonia compared to selective oral decontamination. *Intensive Care Med* 2017; 43:1535–1537.
135. Plantinga NL, de Smet A, Oostdijk EAN, et al. Selective digestive and oropharyngeal decontamination in medical and surgical ICU patients: individual patient data meta-analysis. *Clin Microbiol Infect* 2018;24: 505–513.
136. Wittekamp BH, Plantinga NL, Cooper BS, et al. Decontamination strategies and bloodstream infections with antibiotic-resistant microorganisms in ventilated patients: a randomized clinical trial. *JAMA* 2018; 320:2087–2098.
137. Minozzi S, Pifferi S, Brazzi L, Pecoraro V, Montrucchio G, D'Amico R. Topical antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving mechanical ventilation. *Cochrane Database Syst Rev* 2021;1:CD000022.
138. Torres A, Niederman MS, Chastre J, et al. International ERS/ESICM/ ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: Guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociacion Latinoamericana del Torax (ALAT). *Eur Respir J* 2017;50.
139. Pozuelo-Carrascosa DP, Herraiz-Adillo A, Alvarez-Bueno C, Anon JM, Martinez-Vizcaino V, Caverro-Redondo I. Subglottic secretion drainage for preventing ventilator-associated pneumonia: an overview of systematic reviews and an updated meta-analysis. *Eur Respir Rev* 2020;29.
140. Damas P, Frippiat F, Ancion A, et al. Prevention of ventilator-associated pneumonia and ventilator-associated conditions: a randomized controlled trial with subglottic secretion suctioning. *Crit Care Med* 2015;43: 22–30.
141. Bouza E, Perez MJ, Munoz P, Rincon C, Barrio JM, Hortal J. Continuous aspiration of subglottic secretions in the prevention of ventilator-associated pneumonia in the postoperative period of major heart surgery. *Chest* 2008;134:938–946.
142. Lacherade JC, De Jonghe B, Guezennec P, et al. Intermittent subglottic secretion drainage and ventilator-associated pneumonia: a multicenter trial. *Am J Respir Crit Care Med* 2010;182:910–917.
143. Frost SA, Azeem A, Alexandrou E, et al. Subglottic secretion drainage for preventing ventilator associated pneumonia: a meta-analysis. *Aust Crit Care* 2013;26:180–188.
144. Chorath K, Hoang A, Rajasekaran K, Moreira A. Association of early vs late tracheostomy placement with pneumonia and ventilator days in critically ill patients: a meta-analysis. *JAMA Otolaryngol Head Neck Surg* 2021;147:450–459.
145. Ferguson ND. Tracheostomy for ventilated patients—not when, but in whom? *Crit Care Med* 2005;33:2695–2696.
146. Alkhawaja S, Martin C, Butler RJ, Gwadry-Sridhar F. Postpyloric versus gastric tube feeding for preventing pneumonia and improving nutritional outcomes in critically ill adults. *Cochrane Database Syst Rev* 2015: CD008875.
147. Liu Y, Wang Y, Zhang B, Wang J, Sun L, Xiao Q. Gastric-tube versus postpyloric feeding in critical patients: a systematic review and meta-analysis of pulmonary aspiration- and nutrition-related outcomes. *Eur J Clin Nutr* 2021;75:1337–1348.
148. McClave SA, DeMeo MT, DeLegge MH, et al. North American Summit on Aspiration in the Critically Ill Patient: consensus statement. *J Parenter Enteral Nutr* 2002;26:S80–S85.
149. Taylor BE, McClave SA, Martindale RG, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN). *Crit Care Med* 2016;44:390–438.
150. Hua F, Xie H, Worthington HV, Furness S, Zhang Q, Li C. Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database Syst Rev* 2016;10:CD008367.
151. Dale CM, Rose L, Carbone S, et al. Effect of oral chlorhexidine de-adoption and implementation of an oral care bundle on mortality for mechanically ventilated patients in the intensive care unit (CHORAL): a multi-center stepped-wedge cluster-randomized controlled trial. *Intensive Care Med* 2021;47:1295–1302.
152. Lee S, Lighvan NL, McCredie V, et al. Chlorhexidine-related mortality rate in critically ill subjects in intensive care units: a systematic review and meta-analysis. *Respir Care* 2019;64:337–349.
153. Ji T, Zhu X, Shang F, Zhang X. Preventive effect of probiotics on ventilator-associated pneumonia: a meta-analysis of 2,428 patients. *Ann Pharmacother* 2021;55:949–962.
154. Batra P, Soni KD, Mathur P. Efficacy of probiotics in the prevention of VAP in critically ill ICU patients: an updated systematic review and meta-analysis of randomized control trials. *J Intensive Care* 2020;8:81.
155. Su M, Jia Y, Li Y, Zhou D, Jia J. Probiotics for the prevention of ventilator-associated pneumonia: a meta-analysis of randomized controlled trials. *Respir Care* 2020;65:673–685.
156. Zhao J, Li LQ, Chen CY, Zhang GS, Cui W, Tian BP. Do probiotics help prevent ventilator-associated pneumonia in critically ill patients? A systematic review with meta-analysis. *ERJ Open Res* 2021;7: 00302–2020.
157. Johnstone J, Meade M, Lauzier F, et al. Effect of probiotics on incident ventilator-associated pneumonia in critically ill patients: a randomized clinical trial. *JAMA* 2021;326:1024–1033.
158. Lherm T, Monet C, Nougier B, et al. Seven cases of fungemia with *Saccharomyces boulardii* in critically ill patients. *Intensive Care Med* 2002;28:797–801.
159. Munoz P, Bouza E, Cuenca-Estrella M, et al. *Saccharomyces cerevisiae* fungemia: an emerging infectious disease. *Clin Infect Dis* 2005;40:1625–1634.
160. Salminen MK, Rautelin H, Tynkkynen S, et al. *Lactobacillus* bacteremia, clinical significance, and patient outcome, with special focus on probiotic *L. rhamnosus* GG. *Clin Infect Dis* 2004;38:62–69.
161. Cassone M, Serra P, Mondello F, et al. Outbreak of *Saccharomyces cerevisiae* subtype *boulardii* fungemia in patients neighboring those treated with a probiotic preparation of the organism. *J Clin Microbiol* 2003;41:5340–5343.
162. Graf C, Gavazzi G. *Saccharomyces cerevisiae* fungemia in an immunocompromised patient not treated with *Saccharomyces boulardii* preparation. *J Infect* 2007;54:310–311.

163. Yelin I, Flett KB, Merakou C, *et al*. Genomic and epidemiological evidence of bacterial transmission from probiotic capsule to blood in ICU patients. *Nat Med* 2019;25:1728–1732.
164. Kara I, Yildirim F, Ozgen O, *et al*. *Saccharomyces cerevisiae* fungemia after probiotic treatment in an intensive care unit patient. *J Mycol Med* 2018;28:218–21.
165. Lorente L, Lecuona M, Jimenez A, Mora ML, Sierra A. Influence of an endotracheal tube with polyurethane cuff and subglottic secretion drainage on pneumonia. *Am J Respir Crit Care Med* 2007;176:1079–1083.
166. Poelaert J, Depuydt P, De Wolf A, Van de Velde S, Herck I, Blot S. Polyurethane cuffed endotracheal tubes to prevent early postoperative pneumonia after cardiac surgery: a pilot study. *J Thorac Cardiovasc Surg* 2008;135:771–776.
167. Philippart F, Gaudry S, Quinquis L, *et al*. Randomized intubation with polyurethane or conical cuffs to prevent pneumonia in ventilated patients. *Am J Respir Crit Care Med* 2015;191:637–645.
168. Saito M, Maruyama K, Mihara T, Hoshijima H, Hirabayashi G, Andoh T. Comparison of polyurethane tracheal tube cuffs and conventional polyvinyl chloride tube cuff for prevention of ventilator-associated pneumonia: a systematic review with meta-analysis. *Medicine (Baltimore)* 2021;100:e24906.
169. Maertens B, Blot K, Blot S. Prevention of ventilator-associated and early postoperative pneumonia through tapered endotracheal tube cuffs: a systematic review and meta-analysis of randomized controlled trials. *Crit Care Med* 2018;46:316–323.
170. Valencia M, Ferrer M, Farre R, *et al*. Automatic control of tracheal tube cuff pressure in ventilated patients in semirecumbent position: a randomized trial. *Crit Care Med* 2007;35:1543–1549.
171. Nseir S, Zerimech F, Fournier C, *et al*. Continuous control of tracheal cuff pressure and microaspiration of gastric contents in critically ill patients. *Am J Respir Crit Care Med* 2011;184:1041–1047.
172. Sevidi MS, Demirgan S, Erkalp K, *et al*. Continuous endotracheal tube cuff pressure control decreases incidence of ventilator-associated pneumonia in patients with traumatic brain injury. *J Invest Surg* 2022;35:525–530.
173. Dauvergne JE, Geffray AL, Asehnoune K, Rozec B, Lakhil K. Automatic regulation of the endotracheal tube cuff pressure with a portable elastomeric device. A randomised controlled study. *Anaesth Crit Care Pain Med* 2020;39:435–441.
174. Dat VQ, Yen LM, Loan HT, *et al*. Effectiveness of continuous endotracheal cuff pressure control for the prevention of ventilator associated respiratory infections: an open-label randomised, controlled trial. *Clin Infect Dis* 2021. doi: 10.1093/cid/ciab724.
175. Marjanovic N, Boisson M, Asehnoune K, *et al*. Continuous pneumatic regulation of tracheal cuff pressure to decrease ventilator-associated pneumonia in trauma patients who were mechanically ventilated: the AGATE multicenter randomized controlled study. *Chest* 2021;160:499–508.
176. Letvin A, Kremer P, Silver PC, Samih N, Reed-Watts P, Kollef MH. Frequent versus infrequent monitoring of endotracheal tube cuff pressures. *Respir Care* 2018;63:495–501.
177. Aepli N, Lindauer B, Steurer MP, Weiss M, Dullenkopf A. Endotracheal tube cuff pressure changes during manual cuff pressure control manoeuvres: an in-vitro assessment. *Acta Anaesthesiol Scand* 2019;63:55–60.
178. Kollef MH, Afessa B, Anzueto A, *et al*. Silver-coated endotracheal tubes and incidence of ventilator-associated pneumonia: the NASCENT randomized trial. *JAMA* 2008;300:805–813.
179. Klompas M. Silver-coated endotracheal tubes and patient outcomes in ventilator-associated pneumonia. *JAMA* 2008;300:2605.
180. Delaney A, Gray H, Laupland KB, Zuege DJ. Kinetic bed therapy to prevent nosocomial pneumonia in mechanically ventilated patients: a systematic review and meta-analysis. *Crit Care* 2006;10:R70.
181. Ayzac L, Girard R, Baboi L, *et al*. Ventilator-associated pneumonia in ARDS patients: the impact of prone positioning. A secondary analysis of the PROSEVA trial. *Intensive Care Med* 2016;42:871–878.
182. Dupont H, Depuydt P, Abroug F. Prone position acute respiratory distress syndrome patients: less prone to ventilator associated pneumonia? *Intensive Care Med* 2016;42:937–939.
183. Munshi L, Del Sorbo L, Adhikari NKJ, *et al*. Prone position for acute respiratory distress syndrome. a systematic review and meta-analysis. *Ann Am Thorac Soc* 2017;14:S280–S288.
184. Boonyasiri A, Thaisiam P, Permpikul C, *et al*. Effectiveness of chlorhexidine wipes for the prevention of multidrug-resistant bacterial colonization and hospital-acquired infections in intensive care unit patients: a randomized trial in Thailand. *Infect Control Hosp Epidemiol* 2016;37:245–253.
185. Pallotto C, Fiorio M, De Angelis V, *et al*. Daily bathing with 4% chlorhexidine gluconate in intensive care settings: a randomized controlled trial. *Clin Microbiol Infect* 2019;25:705–710.
186. Swan JT, Ashton CM, Bui LN, *et al*. Effect of chlorhexidine bathing every other day on prevention of hospital-acquired infections in the surgical ICU: a single-center, randomized controlled trial. *Crit Care Med* 2016;44:1822–1132.
187. Frost SA, Hou YC, Lombardo L, *et al*. Evidence for the effectiveness of chlorhexidine bathing and healthcare-associated infections among adult intensive care patients: a trial sequential meta-analysis. *BMC Infect Dis* 2018;18:679.
188. Barbateskovic M, Marker S, Granholm A, *et al*. Stress ulcer prophylaxis with proton pump inhibitors or histamin-2 receptor antagonists in adult intensive care patients: a systematic review with meta-analysis and trial sequential analysis. *Intensive Care Med* 2019;45:143–158.
189. Reynolds PM, MacLaren R. Re-evaluating the utility of stress ulcer prophylaxis in the critically ill patient: a clinical scenario-based meta-analysis. *Pharmacotherapy* 2019;39:408–420.
190. Marik PE, Vasu T, Hirani A, Pachinburavan M. Stress ulcer prophylaxis in the new millennium: a systematic review and meta-analysis. *Critical Care Med* 2010;38:2222–2228.
191. Alhazzani W, Alenezi F, Jaeschke RZ, Moayyedi P, Cook DJ. Proton pump inhibitors versus histamine 2 receptor antagonists for stress ulcer prophylaxis in critically ill patients: a systematic review and meta-analysis. *Crit Care Med* 2013;41:693–705.
192. Deliwala SS, Hamid K, Goyal H, *et al*. Proton pump inhibitors versus histamine-2-receptor antagonists for stress ulcer prophylaxis in critically ill patients: a meta-analysis and trial sequential analysis. *J Clin Gastroenterol* 2022;56:204–217.
193. Krag M, Marker S, Perner A, *et al*. Pantoprazole in patients at risk for gastrointestinal bleeding in the ICU. *N Engl J Med* 2018;379:2199–2208.
194. Reignier J, Mercier E, Le Gouge A, *et al*. Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. *JAMA* 2013;309:249–256.
195. Casaer MP, Mesotten D, Hermans G, *et al*. Early versus late parenteral nutrition in critically ill adults. *N Engl J Med* 2011;365:506–517.
196. Vonberg RP, Eckmanns T, Welte T, Gastmeier P. Impact of the suctioning system (open vs. closed) on the incidence of ventilation-associated pneumonia: meta-analysis of randomized controlled trials. *Intensive Care Med* 2006;32:1329–1335.
197. Jongerden IP, Rovers MM, Grypdonck MH, Bonten MJ. Open and closed endotracheal suction systems in mechanically ventilated intensive care patients: a meta-analysis. *Crit Care Med* 2007;35:260–270.
198. Siempos IL, Vardakas KZ, Falagas ME. Closed tracheal suction systems for prevention of ventilator-associated pneumonia. *Br J Anaesth* 2008;100:299–306.
199. Jongerden IP, Buiting AG, Leverstein-van Hall MA, *et al*. Effect of open and closed endotracheal suctioning on cross-transmission with gram-negative bacteria: a prospective crossover study. *Crit Care Med* 2011;39:1313–1321.
200. Lorente L, Lecuona M, Jimenez A, Mora ML, Sierra A. Tracheal suction by closed system without daily change versus open system. *Intensive Care Med* 2006;32:538–544.
201. Maggiore SM. Endotracheal suctioning, ventilator-associated pneumonia, and costs: open or closed issue? *Intensive Care Med* 2006;32:485–487.
202. Cocoros NM, Kleinman K, Priebe GP, *et al*. Ventilator-associated events in neonates and children—a new paradigm. *Crit Care Med* 2016;44:14–22.

203. Dudeck MA, Horan T, Peterson KD, *et al.* National Healthcare Safety Network (NHSN) report, data summary for 2011, device-associated module. Centers for Disease Control and Prevention website. <http://www.cdc.gov/nhsn/PDFs/dataStat/NHSN-Report-2011-Data-Summary.pdf>. Updated April 1, 2013. Accessed March 31, 2022.
204. Bhandari V, Finer NN, Ehrenkranz RA, *et al.* Synchronized nasal intermittent positive-pressure ventilation and neonatal outcomes. *Pediatrics* 2009;124:517–526.
205. Finer NN, Carlo WA, Walsh MC, *et al.* Early CPAP versus surfactant in extremely preterm infants. *N Engl J Med* 2010;362:1970–1979.
206. Bhandari V. Nasal intermittent positive pressure ventilation in the newborn: review of literature and evidence-based guidelines. *J Perinatol* 2010;30:505–512.
207. Wilkinson D, Andersen C, O'Donnell CP, De Paoli AG, Manley BJ. High-flow nasal cannula for respiratory support in preterm infants. *Cochrane Database Syst Rev* 2016;2:CD006405.
208. Hong H, Li XX, Li J, Zhang ZQ. High-flow nasal cannula versus nasal continuous positive airway pressure for respiratory support in preterm infants: a meta-analysis of randomized controlled trials. *J Matern Fetal Neonatal Med* 2021;34:259–266.
209. Hamid MH, Malik MA, Masood J, Zia A, Ahmad TM. Ventilator-associated pneumonia in children. *J Coll Phys Surg Pakistan* 2012;22:155–158.
210. Ng E, Taddio A, Ohlsson A. Intravenous midazolam infusion for sedation of infants in the neonatal intensive care unit. *Cochrane Database Syst Rev* 2012;6:CD002052.
211. Murner-Lavanchy IM, Doyle LW, Schmidt B, *et al.* Neurobehavioral outcomes 11 years after neonatal caffeine therapy for apnea of prematurity. *Pediatrics* 2018;141.
212. Veldman A, Trautshold T, Weiss K, Fischer D, Bauer K. Characteristics and outcome of unplanned extubation in ventilated preterm and term newborns on a neonatal intensive care unit. *Paediatr Anaesth* 2006;16:968–973.
213. Merkel L, Beers K, Lewis MM, Stauffer J, Mjuscic DJ, Kresch MJ. Reducing unplanned extubations in the NICU. *Pediatrics* 2014;133:e1367–e1372.
214. Ramaswamy VV, Bandyopadhyay T, Nanda D, *et al.* Efficacy of noninvasive respiratory support modes as postextubation respiratory support in preterm neonates: a systematic review and network meta-analysis. *Pediatr Pulmonol* 2020;55:2924–2939.
215. Aly H, Badawy M, El-Kholy A, Nabil R, Mohamed A. Randomized, controlled trial on tracheal colonization of ventilated infants: can gravity prevent ventilator-associated pneumonia? *Pediatrics* 2008;122:770–774.
216. Taylor JE, Hawley G, Flenady V, Woodgate PG. Tracheal suctioning without disconnection in intubated ventilated neonates. *Cochrane Database Syst Rev* 2011:CD003065.
217. van Veenendaal MB, Miedema M, de Jongh FH, van der Lee JH, Frerichs I, van Kaam AH. Effect of closed endotracheal suction in high-frequency ventilated premature infants measured with electrical impedance tomography. *Intensive Care Med* 2009;35:2130–2134.
218. Ma A, Yang J, Li Y, Zhang X, Kang Y. Oropharyngeal colostrum therapy reduces the incidence of ventilator-associated pneumonia in very low birth weight infants: a systematic review and meta-analysis. *Pediatr Res* 2021;89:54–62.
219. Stefanescu BM, Hetu C, Slaughter JC, O'Shea TM, Shetty AK. A pilot study of Biotene OralBalance gel for oral care in mechanically ventilated preterm neonates. *Contemp Clin Trials* 2013;35:33–39.
220. Terrin G, Passariello A, De Curtis M, *et al.* Ranitidine is associated with infections, necrotizing enterocolitis, and fatal outcome in newborns. *Pediatrics* 2012;129:e40–e45.
221. Guillet R, Stoll BJ, Cotten CM, *et al.* Association of H2-blocker therapy and higher incidence of necrotizing enterocolitis in very low birth weight infants. *Pediatrics* 2006;117:e137–e142.
222. Kuppala VS, Meinen-Derr J, Morrow AL, Schibler KR. Prolonged initial empirical antibiotic treatment is associated with adverse outcomes in premature infants. *J Pediatr* 2011;159:720–725.
223. Alexander VN, Northrup V, Bizzarro MJ. Antibiotic exposure in the newborn intensive care unit and the risk of necrotizing enterocolitis. *J Pediatr* 2011;159:392–397.
224. Shah P, Nathan E, Doherty D, Patole S. Prolonged exposure to antibiotics and its associations in extremely preterm neonates—the Western Australian experience. *J Matern Fetal Neonat Med* 2013;26:1710–1714.
225. Weintraub AS, Ferrara L, Deluca L, *et al.* Antenatal antibiotic exposure in preterm infants with necrotizing enterocolitis. *J Perinatol* 2012;32:705–709.
226. Teixeira RF, Carvalho ACA, de Araujo RD, Veloso FCS, Kassab SB, Medeiros AMC. Spontaneous breathing trials in preterm infants: systematic review and meta-analysis. *Respir Care* 2021;66:129–137.
227. Shalish W, Kanbar L, Kovacs L, *et al.* Assessment of extubation readiness using spontaneous breathing trials in extremely preterm neonates. *JAMA Pediatr* 2020;174:178–185.
228. Rojas MA, Lozano JM, Rojas MX, *et al.* Prophylactic probiotics to prevent death and nosocomial infection in preterm infants. *Pediatrics* 2012;130:e1113–e1120.
229. Manzoni P, Mostert M, Leonessa ML, *et al.* Oral supplementation with *Lactobacillus casei* subspecies *rhamnosus* prevents enteric colonization by *Candida* species in preterm neonates: a randomized study. *Clin Infect Dis* 2006;42:1735–1742.
230. De Groote MA, Frank DN, Dowell E, Glode MP, Pace NR. *Lactobacillus rhamnosus* GG bacteremia associated with probiotic use in a child with short gut syndrome. *Pediatr Infect Dis J* 2005;24:278–280.
231. Kunz AN, Noel JM, Fairchok MP. Two cases of *Lactobacillus* bacteremia during probiotic treatment of short gut syndrome. *J Pediatr Gastroenterol Nutr* 2004;38:457–458.
232. Land MH, Rouster-Stevens K, Woods CR, Cannon ML, Cnota J, Shetty AK. *Lactobacillus* sepsis associated with probiotic therapy. *Pediatrics* 2005;115:178–181.
233. Foglia E, Meier MD, Elward A. Ventilator-associated pneumonia in neonatal and pediatric intensive care unit patients. *Clin Microbiol Rev* 2007;20:409–425.
234. Bigham MT, Amato R, Bondurant P, *et al.* Ventilator-associated pneumonia in the pediatric intensive care unit: characterizing the problem and implementing a sustainable solution. *J Pediatr* 2009;154:582–587.
235. Taira BR, Fenton KE, Lee TK, *et al.* Ventilator-associated pneumonia in pediatric trauma patients. *Pediatr Crit Care Med* 2009;10:491–494.
236. Gautam A, Ganu SS, Tegg OJ, Andresen DN, Wilkins BH, Schell DN. Ventilator-associated pneumonia in a tertiary paediatric intensive care unit: a 1-year prospective observational study. *Crit Care Resusc* 2012;14:283–289.
237. Awasthi S, Tahazzul M, Ambast A, Govil YC, Jain A. Longer duration of mechanical ventilation was found to be associated with ventilator-associated pneumonia in children aged 1 month to 12 years in India. *J Clin Epidemiol* 2013;66:62–66.
238. Vaewpanich J, Akcan-Arikan A, Coss-Bu JA, Kennedy CE, Starke JR, Thammasitboon S. Fluid overload and kidney injury score as a predictor for ventilator-associated events. *Front Pediatr* 2019;7:204.
239. Pena-Lopez Y, Ramirez-Estrada S, Serrano-Megias M, *et al.* Short-acting sedative-analgesic drugs protect against development of ventilator-associated events in children: secondary analysis of the EUVAE study. *Respir Care* 2021;66:798–805.
240. Javouhey E, Barats A, Richard N, Stamm D, Floret D. Noninvasive ventilation as primary ventilatory support for infants with severe bronchiolitis. *Intensive Care Med* 2008;34:1608–1614.
241. Yanez LJ, Yunge M, Emilfork M, *et al.* A prospective, randomized, controlled trial of noninvasive ventilation in pediatric acute respiratory failure. *Pediatr Crit Care Med* 2008;9:484–489.
242. Milesi C, Essouri S, Pouyau R, *et al.* High flow nasal cannula (HFNC) versus nasal continuous positive airway pressure (nCPAP) for the initial respiratory management of acute viral bronchiolitis in young infants: a multicenter randomized controlled trial (TRAMONTANE study). *Intensive Care Med* 2017;43:209–216.

243. Ferguson LP, Walsh BK, Munhall D, Arnold JH. A spontaneous breathing trial with pressure support overestimates readiness for extubation in children. *Pediatr Crit Care Med* 2011;12:e330–5.
244. Randolph AG, Wypij D, Venkataraman ST, *et al*. Effect of mechanical ventilator weaning protocols on respiratory outcomes in infants and children: a randomized controlled trial. *JAMA* 2002;288:2561–2568.
245. Foronda FK, Troster EJ, Farias JA, *et al*. The impact of daily evaluation and spontaneous breathing test on the duration of pediatric mechanical ventilation: a randomized controlled trial. *Crit Care Med* 2011;39:2526–2533.
246. Newth CJ, Hotz JC, Khemani RG. Ventilator liberation in the pediatric ICU. *Respir Care* 2020;65:1601–1610.
247. Faustino EV, Gedeit R, Schwarz AJ, *et al*. Accuracy of an extubation readiness test in predicting successful extubation in children with acute respiratory failure from lower respiratory tract disease. *Crit Care Med* 2017;45:94–102.
248. Ferreira FV, Sugo EK, Aragon DC, Carmona F, Carlotti A. Spontaneous breathing trial for prediction of extubation success in pediatric patients following congenital heart surgery: a randomized controlled trial. *Pediatr Crit Care Med* 2019;20:940–946.
249. Lucas da Silva PS, de Carvalho WB. Unplanned extubation in pediatric critically ill patients: a systematic review and best practice recommendations. *Pediatr Crit Care Med* 2010;11:287–294.
250. Klugman D, Melton K, Maynard PO, *et al*. Assessment of an unplanned extubation bundle to reduce unplanned extubations in critically ill neonates, infants, and children. *JAMA Pediatr* 2020;174:e200268.
251. Alobaidi R, Morgan C, Basu RK, *et al*. Association between fluid balance and outcomes in critically ill children: a systematic review and meta-analysis. *JAMA Pediatr* 2018;172:257–268.
252. Kwiatkowski DM, Goldstein SL, Cooper DS, Nelson DP, Morales DL, Krawczeski CD. Peritoneal dialysis vs furosemide for prevention of fluid overload in infants after cardiac surgery: a randomized clinical trial. *JAMA Pediatr* 2017;171:357–364.
253. Weiss SL, Peters MJ, Alhazzani W, *et al*. Surviving Sepsis Campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. *Pediatr Crit Care Med* 2020;21:e52–e106.
254. Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: consensus recommendations from the Pediatric Acute Lung Injury Consensus Conference. *Pediatr Crit Care Med* 2015;16:428–439.
255. Curley MA, Schwalenstocker E, Deshpande JK, *et al*. Tailoring the Institute for Health Care Improvement 100,000 Lives campaign to pediatric settings: the example of ventilator-associated pneumonia. *Pediatr Clin N Am* 2006;53:1231–1251.
256. De Cristofano A, Peuchot V, Canepari A, Franco V, Perez A, Eulmesekian P. Implementation of a ventilator-associated pneumonia prevention bundle in a single PICU. *Pediatr Crit Care Med* 2016;17:451–456.
257. McBeth CL, Montes RS, Powne A, North SE, Natale JE. Interprofessional approach to the sustained reduction in ventilator-associated pneumonia in a pediatric intensive care unit. *Crit Care Nurse* 2018;38:36–45.
258. American Dental Association. Fluoride toothpaste use for young children. *J Am Dent Assoc* 2014;145:190–191.
259. Abiramalatha T, Ramaswamy VV, Thanigainathan S, Pullattayil AK, Kirubakaran R. Frequency of ventilator circuit changes to prevent ventilator-associated pneumonia in neonates and children—a systematic review and meta-analysis. *Pediatr Pulmonol* 2021;56:1357–1365.
260. Samransamruajkit R, Jirapaiboonsuk S, Siritantiwat S, *et al*. Effect of frequency of ventilator circuit changes (3 vs 7 days) on the rate of ventilator-associated pneumonia in PICU. *J Crit Care* 2010;25:56–61.
261. Hsieh TC, Hsia SH, Wu CT, Lin TY, Chang CC, Wong KS. Frequency of ventilator-associated pneumonia with 3-day versus 7-day ventilator circuit changes. *Pediatr Neonatol* 2010;51:37–43.
262. Gopalareddy V, He Z, Soundar S, *et al*. Assessment of the prevalence of microaspiration by gastric pepsin in the airway of ventilated children. *Acta Paediatr* 2008;97:55–60.
263. Weiss M, Dullenkopf A, Fischer JE, Keller C, Gerber AC. Prospective randomized controlled multi-centre trial of cuffed or uncuffed endotracheal tubes in small children. *Br J Anaesthesia* 2009;103:867–873.
264. Topjian AA, Raymond TT, Atkins D, *et al*. Part 4: Pediatric basic and advanced life support: 2020 American Heart Association Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2020;142:S469–S523.
265. Schneider J, Mulale U, Yamout S, Pollard S, Silver P. Impact of monitoring endotracheal tube cuff leak pressure on postextubation stridor in children. *J Crit Care* 2016;36:173–177.
266. Tsai HH, Lin FC, Chang SC. Intermittent suction of oral secretions before each positional change may reduce ventilator-associated pneumonia: a pilot study. *Am J Med Sci* 2008;336:397–401.
267. Gupta K, Gupta VK, Jayashree M, Singhi S. Randomized controlled trial of interrupted versus continuous sedative infusions in ventilated children. *Pediatr Crit Care Med* 2012;13:131–135.
268. Pizza A, Picconi E, Piastra M, Genovese O, Biasucci DG, Conti G. Early versus late tracheostomy in pediatric intensive care unit: does it matter? A 6-year experience. *Minerva Anestesiol* 2017;83:836–43.
269. McLaughlin C, Darcy D, Park C, *et al*. Timing of tracheostomy placement among children with severe traumatic brain injury: a propensity-matched analysis. *J Trauma Acute Care Surg* 2019;87:818–26.
270. Alkhatib AA, Younis M, Jamshidi N, *et al*. Timing of tracheostomy in pediatric patients: a systematic review and meta-analysis. *Crit Care Med* 2020;48:233–240.
271. Watters KF. Tracheostomy in infants and children. *Respir Care* 2017;62:799–825.
272. Tamma PD, Turnbull AE, Milstone AM, Lehmann CU, Sydnor ER, Cosgrove SE. Ventilator-associated tracheitis in children: does antibiotic duration matter? *Clin Infect Dis* 2011;52:1324–1331.
273. Willson DF, Hoot M, Khemani R, *et al*. Pediatric ventilator-associated infections: the ventilator-associated infection study. *Pediatr Crit Care Med* 2017;18:e24–e34.
274. Petros A, Silvestri L, Booth R, Taylor N, van Saene H. Selective decontamination of the digestive tract in critically ill children: systematic review and meta-analysis. *Pediatr Crit Care Med* 2013;14:89–97.
275. Siempos II, Ntaidou TK, Falagas ME. Impact of the administration of probiotics on the incidence of ventilator-associated pneumonia: a meta-analysis of randomized controlled trials. *Crit Care Med* 2010;38:954–962.
276. Liu KX, Zhu YG, Zhang J, *et al*. Probiotics' effects on the incidence of nosocomial pneumonia in critically ill patients: a systematic review and meta-analysis. *Crit Care* 2012;16:R109.
277. Petrof EO, Dhaliwal R, Manzanares W, Johnstone J, Cook D, Heyland DK. Probiotics in the critically ill: a systematic review of the randomized trial evidence. *Crit Care Med* 2012;40:3290–3302.
278. Barraud D, Bollaert PE, Gibot S. Impact of the administration of probiotics on mortality in critically ill adult patients: a meta-analysis of randomized controlled trials. *Chest* 2013;143:646–655.
279. Wan AK, Seow WK, Purdie DM, Bird PS, Walsh LJ, Tudehope DI. The effects of chlorhexidine gel on *Streptococcus mutans* infection in 10-month-old infants: a longitudinal, placebo-controlled, double-blind trial. *Pediatr Dent* 2003;25:215–222.
280. Jacomo AD, Carmona F, Matsuno AK, Manso PH, Carlotti AP. Effect of oral hygiene with 0.12% chlorhexidine gluconate on the incidence of nosocomial pneumonia in children undergoing cardiac surgery. *Infect Control Hosp Epidemiol* 2011;32:591–596.
281. Kusahara DM, Friedlander LT, Peterlini MA, Pedreira ML. Oral care and oropharyngeal and tracheal colonization by gram-negative pathogens in children. *Nurs Crit Care* 2012;17:115–122.
282. Kusahara DM, Peterlini MA, Pedreira ML. Oral care with 0.12% chlorhexidine for the prevention of ventilator-associated pneumonia in critically ill children: randomised, controlled and double-blind trial. *Int J Nurs Stud* 2012;49:1354–1363.
283. Pedreira ML, Kusahara DM, de Carvalho WB, Nunez SC, Peterlini MA. Oral care interventions and oropharyngeal colonization in children receiving mechanical ventilation. *Am J Crit Care* 2009;18:319–328.
284. Sebastian MR, Lodha R, Kapil A, Kabra SK. Oral mucosal decontamination with chlorhexidine for the prevention of ventilator-associated

- pneumonia in children—a randomized, controlled trial. *Pediatr Crit Care Med* 2012;13:e305–e310.
285. Karakaya Z, Duyu M, Yersel MN. Oral mucosal mouthwash with chlorhexidine does not reduce the incidence of ventilator-associated pneumonia in critically ill children: a randomised controlled trial. *Aust Crit Care* 2021. doi: 10.1016/j.aucc.2021.06.011.
 286. Yildizdas D, Yapicioglu H, Yilmaz HL. Occurrence of ventilator-associated pneumonia in mechanically ventilated pediatric intensive care patients during stress ulcer prophylaxis with sucralfate, ranitidine, and omeprazole. *J Crit Care* 2002;17:240–245.
 287. Lopriore E, Markhorst DG, Gemke RJ. Ventilator-associated pneumonia and upper airway colonisation with gram-negative bacilli: the role of stress ulcer prophylaxis in children. *Intensive Care Med* 2002;28:763–767.
 288. Albert BD, Zurakowski D, Bechara LJ, et al. Enteral nutrition and acid-suppressive therapy in the PICU: impact on the risk of ventilator-associated pneumonia. *Pediatr Crit Care Med* 2016;17:924–929.
 289. Yao DWJ, Ong C, Eales NM, Sultana R, Wong JJ, Lee JH. Reassessing the use of proton pump inhibitors and histamine-2 antagonists in critically ill children: a systematic review and meta-analysis. *J Pediatr* 2021;228:164–176.
 290. Evans J, Syddall S, Butt W, Kinney S. Comparison of open and closed suction on safety, efficacy and nursing time in a paediatric intensive care unit. *Aust Crit Care* 2014;27:70–74.
 291. Taheri P, Asgari N, Mohammadzadeh M, Golchin M. The effect of open and closed endotracheal tube suctioning system on respiratory parameters of infants undergoing mechanical ventilation. *Iran J Nurs Midwife Res* 2012;17:26–29.
 292. Tume LN, Baines PB, Guerrero R, et al. Pilot study comparing closed versus open tracheal suctioning in postoperative neonates and infants with complex congenital heart disease. *Pediatr Crit Care Med* 2017;18:647–654.
 293. Morrow BM, Mowzer R, Pitcher R, Argent AC. Investigation into the effect of closed-system suctioning on the frequency of pediatric ventilator-associated pneumonia in a developing country. *Pediatr Crit Care Med* 2012;13:e25–e32.
 294. Chick A, Wynne A. Introducing an oral care assessment tool with advanced cleaning products into a high-risk clinical setting. *Br J Nurs* 2020;29:290–296.
 295. Warren C, Medei MK, Wood B, Schutte D. A nurse-driven oral care protocol to reduce hospital-acquired pneumonia. *Am J Nurs* 2019;119:44–51.
 296. Munro S, Haile-Mariam A, Greenwell C, Demirci S, Farooqi O, Vasudeva S. Implementation and dissemination of a department of veterans affairs oral care initiative to prevent hospital-acquired pneumonia among non-ventilated patients. *Nurs Admin Qtrly* 2018;42:363–372.
 297. Baker D, Quinn B, Ewan V, Giuliano KK. Sustaining quality improvement: long-term reduction of nonventilator hospital-acquired pneumonia. *J Nurs Care Qual* 2019;34:223–229.
 298. Juthani-Mehta M, Van Ness PH, McGloin J, et al. A cluster-randomized controlled trial of a multicomponent intervention protocol for pneumonia prevention among nursing home elders. *Clin Infect Dis* 2015;60:849–57.
 299. Zimmerman S, Sloane PD, Ward K, et al. Effectiveness of a mouth care program provided by nursing home staff vs standard care on reducing pneumonia incidence: a cluster randomized trial. *JAMA Netw Open* 2020;3:e204321.
 300. Kaneoka A, Pisejna JM, Miloro KV, Lo M, Saito H, Riquelme LF, et al. Prevention of healthcare-associated pneumonia with oral care in individuals without mechanical ventilation: a systematic review and meta-analysis of randomized controlled trials. *Infect Control Hosp Epidemiol* 2015;36:899–906.
 301. Satheeshkumar PS, Papatheodorou S, Sonis S. Enhanced oral hygiene interventions as a risk mitigation strategy for the prevention of non-ventilator-associated pneumonia: a systematic review and meta-analysis. *Br Dent J* 2020;228:615–622.
 302. Cipra EJ. Implementation of a risk assessment tool to reduce aspiration pneumonia in nonstroke patients. *Clin Nurse Spec* 2019;33:279–283.
 303. Mitchell BG, Russo PL, Cheng AC, et al. Strategies to reduce non-ventilator-associated hospital-acquired pneumonia: a systematic review. *Infect Dis Health* 2019;24:229–239.
 304. Passaro L, Harbarth S, Landelle C. Prevention of hospital-acquired pneumonia in nonventilated adult patients: a narrative review. *Antimicrob Resist Infect Control* 2016;5:43.
 305. Lacerna CC, Patey D, Block L, et al. A successful program preventing nonventilator hospital-acquired pneumonia in a large hospital system. *Infect Control Hosp Epidemiol* 2020;41:547–552.
 306. Cuesy PG, Sotomayor PL, Pina JO. Reduction in the incidence of poststroke nosocomial pneumonia by using the “turn-mob” program. *J Stroke Cerebrovasc Dis* 2010;19:23–28.
 307. Stolbrink M, McGowan L, Saman H, et al. The early mobility bundle: a simple enhancement of therapy which may reduce incidence of hospital-acquired pneumonia and length of hospital stay. *J Hosp Infect* 2014;88:34–39.
 308. Stahl A, Westerdahl E. Postoperative physical therapy to prevent hospital-acquired pneumonia in patients over 80 years undergoing hip fracture surgery—a quasi-experimental study. *Clin Interv Aging* 2020;15:1821–1829.
 309. Ambrosch A, Rockmann F, Klawonn F, Lampl B. Effect of a strict hygiene bundle for the prevention of nosocomial transmission of SARS-CoV-2 in the hospital: a practical approach from the field. *J Infect Public Health* 2020;13:1862–1867.
 310. Abbas M, Robalo Nunes T, Martischang R, et al. Nosocomial transmission and outbreaks of coronavirus disease 2019: the need to protect both patients and healthcare workers. *Antimicrob Resist Infect Control* 2021;10:7.
 311. Pagani L, Thomas Y, Huttner B, et al. Transmission and effect of multiple clusters of seasonal influenza in a Swiss geriatric hospital. *J Am Geriatr Soc* 2015;63:739–744.
 312. Klompas M, Milton DK, Rhee C, Baker MA, Leekha S. Current insights into respiratory virus transmission and potential implications for infection control programs: a narrative review. *Ann Intern Med* 2021;174:1710–1718.
 313. Klompas M. New Insights into the prevention of hospital-acquired pneumonia/ventilator-associated pneumonia caused by viruses. *Semin Respir Crit Care Med* 2022;42.
 314. Kazaure HS, Martin M, Yoon JK, Wren SM. Long-term results of a post-operative pneumonia prevention program for the inpatient surgical ward. *JAMA Surg* 2014;149:914–918.
 315. de Assis MCS, Macedo ABT, Martins C, et al. The impact of a bundle to prevent hospital-acquired pneumonia in a cohort of nonventilated patients on enteral nutrition. *Infect Control Hosp Epidemiol* 2021;42:100–102.
 316. Rosario BH, Shafi H, Yii ACA, et al. Evaluation of multicomponent interventions for prevention of nosocomial pneumonia in older adults: a randomized, controlled trial. *Eur Geriatr Med* 2021;12:1045–1055.
 317. Loan HT, Parry J, Nga NT, et al. Semirecumbent body position fails to prevent healthcare-associated pneumonia in Vietnamese patients with severe tetanus. *Trans R Soc Trop Med Hyg* 2012;106:90–97.
 318. Herzig SJ, Howell MD, Ngo LH, Marcantonio ER. Acid-suppressive medication use and the risk for hospital-acquired pneumonia. *JAMA* 2009;301:2120–2128.
 319. Vermeij JD, Westendorp WF, Dippel DW, van de Beek D, Nederkoorn PJ. Antibiotic therapy for preventing infections in people with acute stroke. *Cochrane Database Syst Rev* 2018;1:CD008530.
 320. Hatler CW, Mast D, Corderella J, et al. Using evidence and process improvement strategies to enhance healthcare outcomes for the critically ill: a pilot project. *Am J Crit Care* 2006;15:549–555.
 321. Pronovost PJ, Berenholtz SM, Needham DM. Translating evidence into practice: a model for large scale knowledge translation. *BMJ* 2008;337:a1714.
 322. Krinsky WS, Mroz IB, McIlwaine JK, et al. A model for increasing patient safety in the intensive care unit: increasing the implementation rates of proven safety measures. *Qual Saf Health Care* 2009;18:74–80.

323. Hawe CS, Ellis KS, Cairns CJ, Longmate A. Reduction of ventilator-associated pneumonia: active versus passive guideline implementation. *Intensive Care Med* 2009;35:1180–1186.
324. Rello J, Lode H, Cornaglia G, Masterton R. A European care bundle for prevention of ventilator-associated pneumonia. *Intensive Care Med* 2010;36:773–780.
325. Berenholtz SM, Pham JC, Thompson DA, *et al*. Collaborative cohort study of an intervention to reduce ventilator-associated pneumonia in the intensive care unit. *Infect Control Hosp Epidemiol* 2011;32:305–314.
326. Diehl A, Yang T, Speck K, *et al*. Evaluating the accuracy of sampling strategies for estimation of compliance rate for ventilator-associated pneumonia process measures. *Infect Control Hosp Epidemiol* 2016;37:1037–1043.
327. Alvarez-Lerma F, Palomar-Martinez M, Sanchez-Garcia M, *et al*. Prevention of ventilator-associated pneumonia: the multimodal approach of the Spanish ICU “Pneumonia Zero” Program. *Crit Care Med* 2018;46:181–188.
328. Bloos F, Muller S, Harz A, *et al*. Effects of staff training on the care of mechanically ventilated patients: a prospective cohort study. *Br J Anaesth* 2009;103:232–237.
329. Checklist ICU Investigators. Effect of a quality improvement intervention with daily round checklists, goal setting, and clinician prompting on mortality of critically ill patients: a randomized clinical trial. *JAMA* 2016;315:1480–1490.
330. Pileggi C, Mascaro V, Bianco A, Nobile CGA, Pavia M. Ventilator bundle and its effects on mortality among ICU patients: a meta-analysis. *Crit Care Med* 2018;46:1167–1174.
331. Klompas M, Kalil AC. Rethinking ventilator bundles. *Crit Care Med* 2018;46:1201–1203.
332. de Neef M, Bakker L, Dijkstra S, Raymakers-Janssen P, Vileito A, Ista E. Effectiveness of a ventilator care bundle to prevent ventilator-associated pneumonia at the PICU: a systematic review and meta-analysis. *Pediatr Crit Care Med* 2019;20:474–480.
333. Nunez RM, Perdomo HA, Chavez IC. Quality improvement intervention and mortality of critically ill patients. *JAMA* 2016;316:879.
334. Klompas M. Ventilator-associated pneumonia: is zero possible? *Clin Infect Dis* 2010;51:1123–1126.
335. Stephens RJ, Dettmer MR, Roberts BW, *et al*. Practice patterns and outcomes associated with early sedation depth in mechanically ventilated patients: a systematic review and meta-analysis. *Crit Care Med* 2018;46:471–479.
336. Pun BT, Balas MC, Barnes-Daly MA, *et al*. Caring for critically ill patients with the ABCDEF bundle: results of the ICU Liberation Collaborative in over 15,000 adults. *Crit Care Med* 2019;47:3–14.
337. Ventilator-associated event (VAE) 2021. Centers for Disease Control and Prevention website. https://www.cdc.gov/nhsn/PDFs/pscManual/10-VAE_FINAL.pdf. Accessed June 17, 2021.
338. Goutier JM, Holzmueller CG, Edwards KC, Klompas M, Speck K, Berenholtz SM. Strategies to enhance adoption of ventilator-associated pneumonia prevention interventions: a systematic literature review. *Infect Control Hosp Epidemiol* 2014;35:998–1004.
339. Aragon D, Sole ML. Implementing best practice strategies to prevent infection in the ICU. *Crit Care Nurs Clin N Am* 2006;18:441–152.
340. Burns SM, Earven S, Fisher C, Lewis R, Merrell P, Schubart JR, *et al*. Implementation of an institutional program to improve clinical and financial outcomes of mechanically ventilated patients: one-year outcomes and lessons learned. *Crit Care Med* 2003;31:2752–2763.
341. Michelangelo H, Angriman F, Pizarro R, *et al*. Implementation of an experiential learning strategy to reduce the risk of ventilator-associated pneumonia in critically ill adult patients. *J Intensive Care Soc* 2020;21:320–326.
342. Brierley J, Highe L, Hines S, Dixon G. Reducing VAP by instituting a care bundle using improvement methodology in a UK paediatric intensive care unit. *Eur J Pediatr* 2012;171:323–330.
343. Weireter LJ Jr, Collins JN, Britt RC, Reed SF, Novosel TJ, Britt LD. Impact of a monitored program of care on incidence of ventilator-associated pneumonia: results of a longterm performance-improvement project. *J Am Coll Surg* 2009;208:700–704.
344. Johnson V, Mangram A, Mitchell C, Lorenzo M, Howard D, Dunn E. Is there a benefit to multidisciplinary rounds in an open trauma intensive care unit regarding ventilator-associated pneumonia? *Am Surg* 2009;75:1171–1174.
345. Rello J, Afonso E, Lisboa T, *et al*. A care bundle approach for prevention of ventilator-associated pneumonia. *Clin Microbiol Infect* 2013;19:363–369.
346. Khan R, Al-Dorzi HM, Al-Attas K, *et al*. The impact of implementing multifaceted interventions on the prevention of ventilator-associated pneumonia. *Am J Infect Control* 2016;44:320–326.
347. Lim KP, Kuo SW, Ko WJ, *et al*. Efficacy of ventilator-associated pneumonia care bundle for prevention of ventilator-associated pneumonia in the surgical intensive care units of a medical center. *J Microbiol Immunol Infect* 2015;48:316–321.
348. Heimes J, Braxton C, Nazir N, *et al*. Implementation and enforcement of ventilator-associated pneumonia prevention strategies in trauma patients. *Surg Infect (Larchmt)* 2011;12:99–103.
349. Danckers M, Grosu H, Jean R, *et al*. Nurse-driven, protocol-directed weaning from mechanical ventilation improves clinical outcomes and is well accepted by intensive care unit physicians. *J Crit Care* 2013;28:433–441.
350. Craven DE. Preventing ventilator-associated pneumonia in adults: sowing seeds of change. *Chest* 2006;130:251–260.
351. Miller K, Briody C, Casey D, *et al*. Using the comprehensive unit-based safety program model for sustained reduction in hospital infections. *Am J Infect Control* 2016;44:969–976.
352. Robinson C, Hoze M, Hevener S, Nichols AA. Development of an RN champion model to improve the outcomes of ventilator-associated pneumonia patients in the intensive care unit. *J Nurs Adm* 2018;48:79–84.
353. Khan RM, Al-Juaid M, Al-Mutairi H, *et al*. Implementing the comprehensive unit-based safety program model to improve the management of mechanically ventilated patients in Saudi Arabia. *Am J Infect Control* 2019;47:51–58.
354. Mangino JE, Peyrani P, Ford KD, *et al*. Development and implementation of a performance improvement project in adult intensive care units: overview of the Improving Medicine Through Pathway Assessment of Critical Therapy in Hospital-Acquired Pneumonia (IMPACT-HAP) Study. *Crit Care* 2011;15:R38.
355. Scales DC, Dainty K, Hales B, *et al*. A multifaceted intervention for quality improvement in a network of intensive care units: a cluster randomized trial. *JAMA* 2011;305:363–372.
356. Jansson M, Kaariainen M, Kyngas H. Effectiveness of educational programmes in preventing ventilator-associated pneumonia: a systematic review. *J Hosp Infect* 2013;84:206–214.
357. Grimshaw J, Eccles M, Thomas R, *et al*. Toward evidence-based quality improvement. Evidence (and its limitations) of the effectiveness of guideline dissemination and implementation strategies 1966–1998. *J Gen Intern Med* 2006;21 suppl 2:S14–S20.
358. Talbot TR, Carr D, Lee Parmley C, *et al*. Sustained reduction of ventilator-associated pneumonia rates using real-time course correction with a ventilator bundle compliance dashboard. *Infect Control Hosp Epidemiol* 2015;36:1261–1267.
359. Bouadma L, Mourvillier B, Deiler V, *et al*. Changes in knowledge, beliefs, and perceptions throughout a multifaceted behavioral program aimed at preventing ventilator-associated pneumonia. *Intensive Care Med* 2010;36:1341–1347.
360. Rosenthal VD, Dese J, Maurizi DM, *et al*. Impact of the International Nosocomial Infection Control Consortium (INICC)’s multidimensional approach on rates of central line-associated bloodstream infection in 14 intensive care units in 11 hospitals of 5 cities in Argentina. *Infect Control Hosp Epidemiol* 2018;39:445–451.
361. Al-Abdely HM, Khidir Mohammed Y, Rosenthal VD, *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* 2018;11:677–684.
362. Parisi M, Gerovasili V, Dimopoulos S, *et al*. Use of ventilator bundle and staff education to decrease ventilator-associated pneumonia in intensive care patients. *Crit Care Nurse* 2016;36:e1–e7.
363. Kellie SP, Scott MJ, Cavallazzi R, *et al*. Procedural and educational interventions to reduce ventilator-associated pneumonia rate and

- central-line-associated bloodstream infection rate. *J Intensive Care Med* 2014;29:165–174.
364. Bassi GL, Ferrer M, Saucedo LM, Torres A. Do guidelines change outcomes in ventilator-associated pneumonia? *Curr Opin Infect Dis* 2010;23:171–177.
365. Berenholtz S, Pronovost PJ. Barriers to translating evidence into practice. *Curr Opin Crit Care* 2003;9:321–325.
366. Lyerla F. Design and implementation of a nursing clinical decision support system to promote guideline adherence. *Comput Inform Nurs* 2008;26:227–233.
367. Sinuff T, Muscedere J, Cook DJ, *et al.* Implementation of clinical practice guidelines for ventilator-associated pneumonia: a multicenter prospective study. *Crit Care Med* 2013;41:15–23.
368. Weled BJ, Adzhigirey LA, Hodgman TM, *et al.* Critical care delivery: the importance of process of care and icu structure to improved outcomes: an update from the American College of Critical Care Medicine Task Force on Models of Critical Care. *Crit Care Med* 2015;43:1520–1525.
369. Balas MC, Weinhouse GL, Denehy L, *et al.* Interpreting and implementing the 2018 pain, agitation/sedation, delirium, immobility, and sleep disruption clinical practice guideline. *Crit Care Med* 2018;46:1464–1470.
370. Kim MM, Barnato AE, Angus DC, Fleisher LA, Kahn JM. The effect of multidisciplinary care teams on intensive care unit mortality. *Arch Intern Med* 2010;170:369–376.
371. Stone ME Jr, Snetman D, O'Neill A, *et al.* Daily multidisciplinary rounds to implement the ventilator bundle decreases ventilator-associated pneumonia in trauma patients: but does it affect outcome? *Surg Infect* 2011;12:373–378.
372. Youngquist P, Carroll M, Farber M, *et al.* Implementing a ventilator bundle in a community hospital. *Joint Comm J Qual Patient Saf* 2007;33:219–225.
373. Sinuff T, Muscedere J, Cook D, Dodek P, Heyland D. Ventilator-associated pneumonia: Improving outcomes through guideline implementation. *J Crit Care* 2008;23:118–125.
374. Omrane R, Eid J, Perreault MM, *et al.* Impact of a protocol for prevention of ventilator-associated pneumonia. *Ann Pharmacother* 2007;41:1390–1396.
375. Zaydfudim V, Dossett LA, Starmer JM, *et al.* Implementation of a real-time compliance dashboard to help reduce SICU ventilator-associated pneumonia with the ventilator bundle. *Arch Surg* 2009;144:656–662.
376. Winters BD, Gurses AP, Lehmann H, Sexton JB, Rampersad CJ, Pronovost PJ. Clinical review: checklists—translating evidence into practice. *Crit Care (London)* 2009;13:210.
377. Teixeira PG, Inaba K, Dubose J, *et al.* Measurable outcomes of quality improvement using a daily quality rounds checklist: two-year prospective analysis of sustainability in a surgical intensive care unit. *J Trauma Acute Care Surg* 2013;75:717–721.
378. Ladbroke E, Bouchoucha SL, Hutchinson A. Lessons learned from a rapid implementation of a ventilator-associated pneumonia prevention bundle. *J Infect Prev* 2019;20:274–280.
379. Westwell S. Implementing a ventilator care bundle in an adult intensive care unit. *Nurs Crit Care* 2008;13:203–207.
380. Eom JS, Lee MS, Chun HK, *et al.* The impact of a ventilator bundle on preventing ventilator-associated pneumonia: a multicenter study. *Am J Infect Control* 2014;42:34–37.
381. Pinto A, Burnett S, Benn J, *et al.* Improving reliability of clinical care practices for ventilated patients in the context of a patient safety improvement initiative. *J Eval Clin Pract* 2011;17:180–187.
382. Ali KJ, Farley DO, Speck K, Catanzaro M, Wicker KG, Berenholtz SM. Measurement of implementation components and contextual factors in a two-state healthcare quality initiative to reduce ventilator-associated pneumonia. *Infect Control Hosp Epidemiol* 2014;35 suppl 3:S116–S123.
383. Wolfensberger A, Meier MT, Clack L, Schreiber PW, Sax H. Preventing ventilator-associated pneumonia—a mixed-method study to find behavioral leverage for better protocol adherence. *Infect Control Hosp Epidemiol* 2018;39:1222–1229.
384. Goddard SL, Lorencatto F, Koo E, *et al.* Barriers and facilitators to early rehabilitation in mechanically ventilated patients—a theory-driven interview study. *J Intensive Care* 2018;6:4.
385. The Society of Critical Care Medicine's ICU Liberation Bundle 2021 Society of Critical Care Medicine website. <https://www.sccm.org/Clinical-Resources/ICULiberation-Home>. Accessed May 25, 2021.
386. Guyatt GH, Oxman AD, Vist GE, *et al.* GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–926.
387. Canadian Task Force on Preventive Health Care website. <http://canadiantaskforce.ca/methods/grade/>. Accessed December 31, 2021.
388. Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogue S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. *Lancet* 1999;354:1851–1858.
389. van Nieuwenhoven CA, Vandenbroucke-Grauls C, van Tiel FH, *et al.* Feasibility and effects of the semirecumbent position to prevent ventilator-associated pneumonia: a randomized study. *Crit Care Med* 2006;34:396–402.
390. Keeley L. Reducing the risk of ventilator-acquired pneumonia through head of bed elevation. *Nurs Crit Care* 2007;12:287–294.
391. Dreyfuss D, Djedaini K, Weber P, *et al.* Prospective study of nosocomial pneumonia and of patient and circuit colonization during mechanical ventilation with circuit changes every 48 hours versus no change. *Am Rev Respir Dis* 1991;143(4 pt 1):738–743.
392. Kollef MH, Shapiro SD, Fraser VJ, *et al.* Mechanical ventilation with or without 7-day circuit changes: a randomized controlled trial. *Ann Intern Med* 1995;123:168–174.
393. Long MN, Wickstrom G, Grimes A, Benton CF, Belcher B, Stamm AM. Prospective, randomized study of ventilator-associated pneumonia in patients with one versus three ventilator circuit changes per week. *Infect Control Hosp Epidemiol* 1996;17:14–19.
394. Lorente L, Lecuona M, Galvan R, Ramos MJ, Mora ML, Sierra A. Periodically changing ventilator circuits is not necessary to prevent ventilator-associated pneumonia when a heat and moisture exchanger is used. *Infect Control Hosp Epidemiol* 2004;25:1077–1082.
395. Muscedere J, Rewa O, McKechnie K, Jiang X, Laporta D, Heyland DK. Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: a systematic review and meta-analysis. *Crit Care Med* 2011;39:1985–1991.
396. Ferguson KN, Roberts CT, Manley BJ, Davis PG. Interventions to improve rates of successful extubation in preterm infants: a systematic review and meta-analysis. *JAMA Pediatr* 2017;171:165–174.
397. Rosenthal VD, Rodriguez-Calderon ME, Rodriguez-Ferrer M, *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* 2012;33:704–710.
398. Kaczmarek J, Kamlin CO, Morley CJ, Davis PG, Sant'anna GM. Variability of respiratory parameters and extubation readiness in ventilated neonates. *Arch Dis Child Fetal Neonat Ed* 2013;98:F70–F73.
399. Kamlin CO, Davis PG, Argus B, Mills B, Morley CJ. A trial of spontaneous breathing to determine the readiness for extubation in very low birth weight infants: a prospective evaluation. *Arch Dis Child Fetal Neonat Ed* 2008;93:F305–F306.