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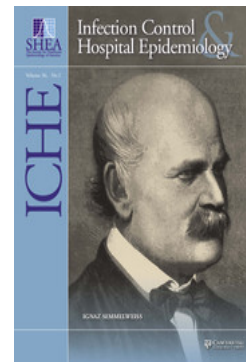
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Strategies to Prevent Ventilator-Associated Pneumonia in Acute Care Hospitals: 2014 Update

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PURPOSE

Previously published guidelines are available that provide comprehensive recommendations for detecting and preventing healthcare-associated infections (HAIs). The intent of this document is to highlight practical recommendations in a concise format to assist acute care hospitals in implementing and prioritizing strategies to prevent ventilator-associated pneumonia (VAP) and other ventilator-associated events (VAEs) and to improve outcomes for mechanically ventilated adults, children, and neonates. This document updates “Strategies to Prevent Ventilator-Associated Pneumonia in Acute Care Hospitals,” published in 2008.¹ This expert guidance document is sponsored by the Society for Healthcare Epidemiology of America (SHEA) and is the product of a collaborative effort led by SHEA, the Infectious Diseases Society of America (IDSA), the American Hospital Association (AHA), the Association for Professionals in Infection Control and Epidemiology (APIC), and The Joint Commission, with major contributions from representatives of a number of organizations and societies with content expertise. The list of endorsing and supporting organizations is presented in the introduction to the 2014 updates.²

SECTION 1: RATIONALE AND STATEMENT OF CONCERNS

- I. Patients on mechanical ventilation are at high risk for VAP and other complications
 - A. The true incidence of VAP is difficult to determine since

surveillance definitions are subjective and nonspecific. Historically, 10%–20% of ventilated patients have developed VAP. More recent reports suggest much lower rates, but it is unclear to what extent these lower rates reflect better care versus stricter application of subjective surveillance criteria.^{3,4} Notwithstanding surveillance rates that hover near zero, clinical surveys suggest that 5%–15% of ventilated patients still develop nosocomial pneumonias.^{5–9}

- B. Patients on mechanical ventilation are at risk for a variety of serious complications in addition to pneumonia. These include acute respiratory distress syndrome, pneumothorax, pulmonary embolism, lobar atelectasis, and pulmonary edema. The Centers for Disease Control and Prevention (CDC) released new surveillance definitions for VAE designed to make surveillance more objective and to expand surveillance from VAP alone to include additional serious complications of mechanical ventilation (see section 2). VAE definitions include criteria for ventilator-associated conditions (VACs), infection-related ventilator-associated complications (IVACs), possible pneumonia, and probable pneumonia. Approximately 5%–10% of mechanically ventilated patients develop VAEs.^{10–16}
- II. VAP and other complications of mechanical ventilation are detrimental to patients and increase costs
 - A. The attributable mortality of VAP is estimated to be approximately 10% but varies considerably for different kinds of patients.^{17–20}

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- B. Both VAP and VAC extend patients' duration of mechanical ventilation, increase intensive care and hospital length of stay, and increase mortality risk.^{11,14-16,20,21} They are also associated with increased use of antimicrobials.¹²
- C. VAP increases direct medical costs.²¹ Excess costs attributable to VAC have not been quantified.

SECTION 2: BACKGROUND—STRATEGIES TO DETECT VAP AND OTHER VAES

I. Despite VAP's clinical importance, our ability to conduct accurate VAP surveillance is very limited.

A. VAP is usually defined by clinical, radiographic, and microbiological criteria. These signs are neither sensitive nor specific relative to histopathology.²²⁻²⁵ These criteria are also very subjective, leading to substantial interobserver variability.^{8,9,26-29} Administrative data are similarly inaccurate.^{7,30-32} Improvements in VAP rates do not reliably correlate with improvements in outcomes.^{33,34}

1. The weaknesses of traditional VAP surveillance definitions limit their utility for measuring the impact of care improvement programs and for benchmarking quality of care between different healthcare facilities.³⁵⁻³⁸

II. CDC's VAE framework

A. The CDC convened representatives from critical and respiratory care, infectious diseases, healthcare epidemiology, and infection prevention professional societies in 2011–2012 to develop a new approach to surveillance for mechanically ventilated patients in an attempt to overcome some of the limitations of traditional VAP surveillance definitions.³⁹

1. The working group recommended the following:
 - a. Developing new definitions based on objective, quantitative criteria to increase the reliability, reproducibility, comparability, and efficiency of surveillance.
 - b. Broadening the focus of surveillance from pneumonia alone to complications of mechanical ventilation in general. This simultaneously sidesteps VAP definitions' poor specificity and emphasizes the importance of preventing all complications of mechanical ventilation, not just pneumonia.
2. The CDC and the working group utilized emerging research on objective surveillance definitions to develop VAE definitions for adults.^{10-13,40,41}
 - a. Objective definitions predicated on sustained increases in ventilator settings after a period of stability detect a range of clinically significant events, including VAP, pulmonary edema, acute respiratory distress syndrome, and atelectasis.^{10,12} They consistently predict poor patient outcomes, including prolonged mechanical ventilation, increased length of stay in both the intensive care

unit (ICU) and the hospital, and increased hospital mortality.¹⁰⁻¹³ Early data suggest that VACs may be preventable.^{14,42} Surveillance using these definitions is efficient and potentially automatable.^{10,11,15}

b. The VAE surveillance framework includes 3 definition tiers. These definitions are briefly summarized below, but readers are advised to consult the CDC's surveillance protocol for comprehensive details.⁴³

i. VACs

- (a) VAC is defined by greater than or equal to 2 days of stable or decreasing daily minimum positive end expiratory pressure (PEEP) or daily minimum fraction of inspired oxygen (F_{iO_2}) followed by an increase in daily minimum PEEP greater than or equal to 3 cm of H_2O or daily minimum F_{iO_2} greater than or equal to 0.20 points sustained for greater than or equal to 2 calendar days.

ii. IVACs

- (a) IVAC is triggered by the presence of possible infection indicators concurrent with VAC onset, namely, an abnormal temperature (below 36°C or above 38°C) or white blood cell count (less than or equal to 4,000 or greater than or equal to 12,000 cells/mm³) and 1 or more new antibiotic starts that continue for greater than or equal to 4 days.

iii. Possible VAP and probable VAP

- (a) Possible VAP is defined as Gram stain evidence of purulent pulmonary secretions or a pathogenic pulmonary culture in a patient with IVAC. Probable VAP is defined as Gram stain evidence of purulence plus quantitative or semiquantitative growth of a pathogenic organism beyond specified thresholds. Probable VAP can also be triggered by positive tests for respiratory viruses, *Legionella* species, pleural fluid cultures, and suggestive histopathology with or without an abnormal Gram stain result.

iv. VAC and IVAC were developed to be appropriate for public reporting; however, further evidence is needed of their preventability and comparability between institutions before recommending their adoption for public reporting or benchmarking.

v. Possible and probable VAP were developed for healthcare facilities to use for internal quality improvement purposes only. They are not suitable for public reporting or benchmarking because clinicians and hospitals vary widely in when and how they acquire and process pulmonary specimens from ventilated patients.

- vi. VAE definitions were designed for adult patients. More data are needed to inform whether and how VAE can be adapted for surveillance in children and neonates.

III. Recommended surveillance strategies

- A. Hospitals are advised to conduct active surveillance for VAE, using CDC definitions and surveillance protocols.⁴³ The CDC's VAE module requires surveillance for all definition tiers (VAC, IVAC, possible VAP, and probable VAP).
 - 1. 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 Fro₂) from all patients ventilated for greater than or equal to 4 days. Temperature, white blood cell count, and antibiotic exposure data are needed only for the subset of patients who fulfill VAC criteria to determine if they fulfill IVAC criteria. Pulmonary specimen Gram stains and microbiology test results are required only for the subset of patients who meet IVAC criteria to determine if they fulfill possible or probable VAP criteria.
 - 2. Organizing daily ventilator data into "line lists" for every patient, with 1 row of data per patient per calendar day, facilitates VAC detection by allowing the surveyor to vertically scan daily ventilator settings to look for sustained increases that cross the threshold for VAC.⁴⁴ Surveyors can also enter raw data into the CDC's online "VAE calculator" to assist with case identification (<http://www.cdc.gov/nhsn/VAE-calculator/index.html>).
 - a. The VAE definitions are amenable to partial or complete automation using electronic data. Facilities seeking to automate VAE detection should work with their information technology personnel and/or electronic health record vendor(s).

SECTION 3: BACKGROUND—STRATEGIES TO PREVENT VAP AND OTHER VAES

- I. Framework for evaluating and prioritizing interventions
 - A. Although VAE is now the CDC's recommended surveillance metric for ventilated patients, almost all of the existing literature on VAP prevention is based on traditional VAP definitions rather than VAE definitions. There are no data at present on the impact of traditional VAP prevention strategies on "probable pneumonias" (the closest proxy for VAP in the VAE framework), and there are very little data regarding their impact on VAC and IVAC.^{14,45} Of note, VAC and IVAC intentionally flag more than just pneumonia; hence, interventions directed solely against pneumonia may not be sufficient to reduce VAE rates.
 - B. VAC may be a surveillance marker for nosocomial acute

lung injury. Qualitative analyses suggest that most VACs are due to pneumonia, pulmonary edema, atelectasis, and acute respiratory distress syndrome.^{10,12,15} Interventions that target these complications in particular and interventions designed to shorten the duration of mechanical ventilation in general may therefore be effective strategies to lower VAE rates. These could include minimizing the use of sedatives, paired daily spontaneous awakening and breathing trials, early mobility, endotracheal tubes with subglottic secretion drainage ports, low tidal volume ventilation, intermittent recruitment maneuvers, conservative fluid management, and restrictive transfusion thresholds.⁴⁶⁻⁵⁴ Studies evaluating the impact of these and other interventions on VAE rates are needed.

- C. Until studies of the best strategies to prevent all VAEs are published, the existing VAP prevention literature is the best available guide to improving outcomes for ventilated patients. Given the uncertainty surrounding the accuracy and reproducibility of VAP diagnoses, however, we prioritize VAP interventions that have been shown to improve objective outcomes, such as duration of mechanical ventilation, intensive care or hospital length of stay, mortality, and/or costs in randomized controlled trials. In addition, the potential benefits of different interventions are balanced against their feasibility, costs, and potential harm. Recent reviews using this framework informed our recommendations.^{33,34,55,56}

SECTION 4: RECOMMENDATIONS FOR PREVENTION OF VAP AND OTHER VAES

Interventions that improve objective outcomes with little risk of harm are classified as basic practices that are suitable for all hospitals. We also recommend interventions that are outcome neutral but cost saving. Interventions that improve objective outcomes but carry some risk of harm and interventions that lower VAP rates but for which insufficient data exist to determine their impact on objective outcomes are classified as special approaches. Hospitals can consider adopting special approaches if their VAE rates do not improve despite high performance rates on basic practices. Interventions that improve neither VAP 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, in Table 3 for preterm neonates, and in Table 4 for infants and children.

Adult Patients

- I. Basic practices to prevent VAP and other VAEs in adult patients: interventions with little risk of harm that decrease duration of mechanical ventilation, length of stay, mortality, and/or costs

TABLE 1. Grading of the Quality of Evidence

Grade	Definition
I. 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 is a wide range of studies with no major limitations, there is little variation between studies, and the summary estimate has a narrow confidence interval.
II. 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.
III. 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, only expert consensus.

NOTE. Based on Grades of Recommendation, Assessment, Development, and Evaluation (GRADE)²³⁹ and the Canadian Task Force on Preventive Health Care.²⁴⁰

A. Avoid intubation if possible

1. Use noninvasive positive pressure ventilation (NIPPV) whenever feasible (quality of evidence: I).
 - a. NIPPV can be beneficial for patients with acute hypercarbic or hypoxemic respiratory failure secondary to chronic obstructive pulmonary disease or cardiogenic congestive heart failure.⁵⁷⁻⁵⁹ NIPPV for these indications may decrease VAP risk, shorten the duration of mechanical ventilation, decrease length of stay, and lower mortality rates compared with invasive ventilation. Use caution when considering NIPPV to manage impaired consciousness, acute lung injury, acute respiratory distress syndrome, severe hypoxemia, and severe acidemia or when continuing NIPPV for patients whose dyspnea or gas exchange fails to rapidly respond to NIPPV. Use of NIPPV for these indications may delay intubation and increase harm, including death.^{59,60}

B. Minimize sedation

1. Manage ventilated patients without sedatives whenever possible (quality of evidence: II).⁴⁶
 - a. Preferentially use agents and strategies other than benzodiazepines to manage agitation, such as analgesics for patients in pain, reassurance, antipsychotics, dexmedetomidine, and propofol.⁶¹
2. Interrupt sedation once a day (spontaneous awakening trials) for patients without contraindications (quality of evidence: I).^{62,63}
 - a. Two randomized controlled trials found that daily sedative interruptions decreased net sedative exposures and reduced the average duration of mechanical ventilation by 2–4 days.^{48,62} A third trial found no impact on duration of mechanical ventilation but used substantially higher doses of benzodiazepines compared with the first 2 trials and observed an increase in sedative use in the sedation-interruption group.⁶⁴ These factors may have

mitigated the potential benefits of sedative interruption in this trial.⁶⁵

3. Assess readiness to extubate once a day (spontaneous breathing trials) in patients without contraindications (quality of evidence: I).^{47,66-68}
 - a. Daily spontaneous breathing trials are associated with extubation 1–2 days earlier compared with usual care.^{47,69}
4. Pair spontaneous breathing trials with spontaneous awakening trials (quality of evidence: I).⁴⁸
 - a. Patients are more likely to pass a spontaneous breathing trial and be extubated if they are maximally awake at the time of the breathing trial.

C. Maintain and improve physical conditioning

1. Provide early exercise and mobilization (quality of evidence: II).
 - a. Early exercise and mobilization speed extubation, decrease length of stay, and increase the rate of return to independent function.^{49,70-77}
 - b. Financial modeling suggests that early mobility programs may be cost saving.⁷⁸

D. Minimize pooling of secretions above the endotracheal tube cuff

1. Provide endotracheal tubes with subglottic secretion drainage ports for patients likely to require greater than 48 or 72 hours of intubation (quality of evidence: II).
 - a. Intermittent and continuous drainage of subglottic secretions has been studied in 13 randomized controlled trials. On meta-analysis, the use of endotracheal tubes with subglottic drainage reduced VAP rates by 55%, mean duration of mechanical ventilation by 1.1 days, and intensive care length of stay by 1.5 days.⁵⁰ There was no impact on hospital length of stay or mortality. One study found that subglottic secretion drainage was associated with less antibiotic utilization, while a second did not.^{79,80}
 - b. Endotracheal tubes with subglottic secretion drainage may be cost saving.^{81,82}

- c. Reductions in duration of mechanical ventilation with subglottic secretion drainage appear to be limited to patients expected to require greater than 48–72 hours of mechanical ventilation.⁸³ Endotracheal tubes with subglottic secretion drainage ports are therefore recommended only as a basic practice for patients likely to require greater than 48–72 hours of intubation. Identifying these patients in advance can be very difficult. Patients requiring emergency intubation in the hospital and preoperative patients at risk for prolonged mechanical ventilation are reasonable candidates.
 - d. Extubating patients to place a subglottic secretion drainage endotracheal tube is not recommended.
- E. Elevate the head of the bed
1. Elevate the head of the bed to 30°–45° (quality of evidence: III).
 - a. Elevating the head of the bed has been evaluated in only 3 randomized controlled trials enrolling 337 patients altogether.^{84–86} One trial reported a 76% decrease in VAP rates, whereas the other 2 found no difference in VAP rates. Of note, the larger of the 2 negative studies achieved minimal difference in head-of-bed elevation between the intervention and control groups, thereby limiting this study's capacity to evaluate the effect of head-of-bed elevation on VAP or other outcomes.⁸⁵ Nonetheless, a meta-analysis pooling these 3 studies did find a significant impact on VAP.⁸⁷ In addition, enteral feeding in the supine position substantially increases the risk of developing VAP.⁸⁴
 - b. There are insufficient data at present to determine the impact of head-of-bed elevation on duration of mechanical ventilation or mortality, but given the simplicity, ubiquity, minimal risk, lack of cost, and potential benefit of this intervention we classify it as a basic practice while we await further data.
- F. Maintain ventilator circuits
1. Change the ventilator circuit only if visibly soiled or malfunctioning (quality of evidence: I).
 - 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.^{88–91}
 2. Follow CDC/Healthcare Infection Control Practices Advisory Committee guidelines for sterilization and disinfection of respiratory care equipment (quality of evidence: II).⁹²
- II. Special approaches
- A. Interventions that decrease duration of mechanical ventilation, length of stay, and/or mortality but for which insufficient data on possible risks are available
1. Use selective decontamination of the oropharynx to decrease the microbial burden of the aerodigestive tract (quality of evidence: I).^{93–98}
 - a. Selective decontamination of the oropharynx with topical antibiotics or of the oropharynx and digestive tract with a combination of topic, oral, and parenteral antibiotics decreased mortality rates by 14% and 17%, respectively, in a large cluster randomized trial conducted in the Netherlands.⁹⁵
 - b. This strategy has not yet been adopted by North American centers, however, due to fear that it might increase the risk of antibiotic-resistant infections, including *Clostridium difficile* infections, especially in centers with high baseline rates of antimicrobial-resistant organisms. Most studies to date do not indicate an elevated short-term risk for antimicrobial resistance, but long-term studies are lacking.^{99,100} Hospitals with high baseline rates of antibiotic resistance are advised to await the results of long-term studies of digestive decontamination in high-resistance environments before routinely adopting this strategy.
- B. Interventions that may lower VAP rates but for which there are insufficient data at present to determine their impact on duration of mechanical ventilation, length of stay, and mortality
1. Perform oral care with chlorhexidine (quality of evidence: II).
 - a. Oral care with chlorhexidine has been studied in at least 16 randomized controlled trials and 9 meta-analyses to date.^{98,101–108} The benefits of oral care with chlorhexidine appear to be most pronounced in preventing postoperative respiratory tract infections in cardiac-surgery patients.^{108–110} The data for non-cardiac-surgery patients are more equivocal. Meta-analyses suggest that oral care with chlorhexidine can reduce pneumonia rates in this population by 10%–30%; however, there is no apparent impact on average duration of mechanical ventilation, intensive care length of stay, or mortality.^{98,101,102,108}
 - b. Routine oral care without chlorhexidine may be indicated for reasons other than VAP prevention.
 2. Administer prophylactic probiotics (quality of evidence: II).
 - a. Four meta-analyses of randomized controlled trials have found an association between probiotics and lower VAP rates.^{111–114} Three of the meta-analyses reported on length of stay and mortality. Two found a positive impact on intensive care length of stay, while the third did not.^{111,112,114} None detected a significant impact on mortality rates. Probiotics should not be used in patients with compromised immune systems or gastrointestinal diseases that increase the risk of gut translocation. There are multiple case reports of fungemia or bacteremia in patients administered probiotics and case reports of aerosol transmission of probiotics within ICUs.^{115–119}

TABLE 2. Summary of Recommendations for Preventing Ventilator-Associated Pneumonia (VAP) in Adult Patients

Recommendation	Rationale	Intervention	Quality of evidence
Basic practices	Good evidence that the intervention decreases the average duration of mechanical ventilation, length of stay, mortality, and/or costs; benefits likely outweigh risks	Use noninvasive positive pressure ventilation in selected populations ^{57,58}	High
		Manage patients without sedation whenever possible ^{46,61}	Moderate
		Interrupt sedation daily ⁶²	High
		Assess readiness to extubate daily ^{47,66-68}	High
		Perform spontaneous breathing trials with sedatives turned off ⁴⁸	High
		Facilitate early mobility ^{49,70-75,78}	Moderate
		Utilize endotracheal tubes with subglottic secretion drainage ports for patients expected to require greater than 48 or 72 hours of mechanical ventilation ⁵⁰	Moderate
		Change the ventilator circuit only if visibly soiled or malfunctioning ⁸⁸⁻⁹¹	High
		Elevate the head of the bed to 30°–45° ^{68,86}	Low ^a
Special approaches	Good evidence that the intervention improves outcomes but insufficient data available on possible risks	Selective oral or digestive decontamination ⁹³⁻⁹⁶	High ^b
		Regular oral care with chlorhexidine ^{98,101-104}	Moderate
		Prophylactic probiotics ¹¹¹⁻¹¹⁴	Moderate
		Ultrathin polyurethane endotracheal tube cuffs ^{120,121}	Low
		Automated control of endotracheal tube cuff pressure ^{122,123}	Low
		Saline instillation before tracheal suctioning ¹²⁴	Low
Generally not recommended	Lowers VAP rates but ample data suggest no impact on duration of mechanical ventilation, length of stay, or mortality	Silver-coated endotracheal tubes ¹²⁷	Moderate
		Kinetic beds ¹²⁸	Moderate
		Prone positioning ^{87,129-134,c}	Moderate
	No impact on VAP rates, average duration of mechanical ventilation, length of stay, or mortality ^c	Stress ulcer prophylaxis ^{135,136}	Moderate
		Early tracheotomy ¹³⁷	High
		Monitoring residual gastric volumes ¹³⁸ Early parenteral nutrition ¹³⁹	Moderate Moderate
No recommendation	No impact on VAP rates or other patient outcomes, unclear impact on costs	Closed/in-line endotracheal suctioning ¹⁴¹⁻¹⁴³	Moderate

^a There are very little data on head-of-bed elevation, but it is classified as a basic practice because of its simplicity, ubiquity, low cost, and potential benefit.

^b There are abundant data on the benefits of digestive decontamination but insufficient data on the long-term impact of this strategy on antimicrobial resistance rates.

^c May be indicated for reasons other than VAP prevention.

3. Use ultrathin polyurethane endotracheal tube cuffs (quality of evidence: III).
 - 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 studies reported lower VAP rates but were underpowered to assess other outcomes.^{120,121}
4. Provide automated control of endotracheal tube cuff

pressure (quality of evidence: III).

- a. Automated control of endotracheal tube cuff pressure led to lower VAP rates in one trial but not in another.^{122,123} Neither trial detected an impact on duration of mechanical ventilation, length of stay, or mortality.
5. Instill saline before tracheal suctioning (quality of evidence: III).

- a. One randomized trial in oncology patients found that saline instillation before tracheal suctioning lowered the rate of microbiologically confirmed VAP but had no impact on clinical VAP rates or patient outcomes.¹²⁴
- 6. Provide mechanical tooth brushing (quality of evidence: III).
 - a. One small randomized controlled trial suggested that tooth brushing can lower VAP rates, but a meta-analysis of 4 trials did not detect a significant impact on VAP risk, duration of mechanical ventilation, intensive care length of stay, or mortality.^{125,126}
- III. Approaches that are generally not recommended for routine VAP prevention
 - A. Generally not recommended for VAP prevention: interventions that may lower VAP rates but good-quality evidence suggests no impact on duration of mechanical ventilation, length of stay, or mortality
 - 1. Silver-coated endotracheal tubes (quality of evidence: II).
 - a. A large, multicenter randomized controlled trial found that silver-coated endotracheal tubes reduced VAP rates by 36% but found no impact on mean duration of mechanical ventilation, hospital length of stay, or mortality.¹²⁷
 - 2. Kinetic beds (continuous lateral rotational therapy and oscillation therapy; quality of evidence: II).
 - 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.¹²⁸ The meta-analysis authors warned that the observed reduction in VAP rates might be artifactual given weaknesses in contributing studies' design and execution.
 - 3. Prone positioning (quality of evidence: II).
 - a. Placing patients in the prone position is controversial. Most meta-analyses suggest a borderline effect on VAP rates and no impact on objective outcomes, except among patients with severe acute respiratory distress syndrome.^{87,129-134}
 - B. Definitely not recommended for VAP prevention: interventions with good-quality evidence suggesting that they neither lower VAP rates nor decrease duration of mechanical ventilation, length of stay, or mortality.
 - 1. Stress ulcer prophylaxis (quality of evidence: II).
 - a. Stress ulcer prophylaxis lowers the risk of gastrointestinal bleeding, but meta-analyses suggest that there is no impact on nosocomial pneumonia rates, length of stay, or mortality.^{135,136} Effects may differ in patients receiving enteral nutrition: gastrointestinal bleeding is less likely, and stress ulcer prophylaxis may increase the risk of nosocomial pneumonia and mortality.¹³⁵
 - b. Stress ulcer prophylaxis may be indicated for reasons other than VAP prevention.
 - 2. Early tracheotomy (quality of evidence: I).
 - a. Early versus late tracheotomy had no impact on VAP rates, duration of mechanical ventilation, or mortality risk on meta-analysis of 7 randomized controlled trials.¹³⁷
 - 3. Monitoring residual gastric volumes (quality of evidence: II).
 - 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.¹³⁸
 - 4. Early parenteral nutrition (quality of evidence: II).
 - a. Initiation of parenteral nutrition in critically ill patients within 48 hours of ICU admission is associated with an increased risk of nosocomial infections and mortality compared with initiating parenteral nutrition on or after 8 days.¹³⁹
- IV. Approaches that are neither recommended nor discouraged
 - A. Interventions with no impact on VAP rates or patient outcomes and unclear impact on costs
 - 1. Closed endotracheal tube suctioning systems (quality of evidence: II).
 - a. Meta-analyses have found no difference in VAP rates, duration of mechanical ventilation, intensive care length of stay, or mortality between patients randomized to open versus closed endotracheal suctioning systems.¹⁴⁰⁻¹⁴² A crossover trial in 4 ICUs found no difference between open versus closed systems in patient-to-patient transmissions of gram-negative pathogens.¹⁴³ Different trials have reached different conclusions regarding cost.^{141,144,145}

Neonatal Patients

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

Specific considerations in preterm neonates. Clinical signs used to diagnose VAP in adults have limited utility in preterm neonates. Fever rarely occurs in preterm neonates, since they are prone to hypothermia and are therefore often thermoregulated with incubators or radiant heaters. Worsening gas exchange or apnea can be caused by significant nonpulmon-

TABLE 3. Summary of Recommendations for Preventing Ventilator-Associated Pneumonia (VAP) in Preterm Neonates

Recommendation	Rationale	Intervention	Quality of evidence
Basic practices	May lower VAP rates and minimal risks of harm; benefits likely outweigh potential risks	Use noninvasive positive pressure ventilation in selected populations ^{148,149}	High
		Minimize the duration of mechanical ventilation	High
		Assess readiness to extubate daily	Low
		Manage patients without sedation whenever possible ^{150,151}	Low
		Avoid unplanned extubation ¹⁵²	Low
		Provide regular oral care with sterile water	Low
		Minimize breaks in the ventilator circuit	Low
		Change the ventilator circuit only if visibly soiled or malfunctioning ²⁴¹	Low
Special approaches	Unknown impact on VAP rates, but risk of harm likely minimal; reasonable to consider implementing if rates remain elevated despite basic practices	Lateral recumbent positioning ¹⁵⁵	Low
		Reverse Trendelenburg positioning	Low
		Closed/in-line suctioning systems ^{156,157}	Low
Generally not recommended	Unknown impact on VAP rates and inadequate data on risks	Regular oral care with antiseptics	Low
		Histamine 2 receptor antagonists ^{158,159}	Moderate
		Prophylactic broad-spectrum antibiotics ¹⁶⁰⁻¹⁶³	Moderate
		Daily spontaneous breathing trials ^{165,166}	Low
		Daily sedative interruptions	Low
		Not recommended because appropriate products are not available or approved for use in this population	Prophylactic probiotics or synbiotics ^{167,168}
Endotracheal tubes with subglottic secretion drainage ports	NA		
Silver-coated endotracheal tubes	NA		

NOTE. NA, none available.

ary illnesses, including sepsis and necrotizing enterocolitis. New or progressive infiltrates often indicate progression of chronic lung disease rather than new infection.

Pooled mean VAP rates for neonates reported to the CDC's National Healthcare Safety Network (NHSN) vary from 0.2 to 1.8 infections per 1,000 ventilator days.¹⁴⁶ It is not known whether these rates are broadly representative of all neonatal units, however, since many hospitals do not perform VAP surveillance for neonates in light of the limitations of VAP definitions.

The CDC has not yet developed VAE definitions for neonates. Adult VAE definitions are not suitable for neonates, as they do not reflect standard ventilator management practices for this population.

I. Basic practices for preterm neonates: interventions with minimal risk of harm that may lower VAP rates

A. Avoid intubation if possible

1. Consider nasal continuous positive airway pressure ventilation with or without nasal intermittent mechanical ventilation as an alternative to intubation (quality of evidence: I).¹⁴⁷⁻¹⁴⁹

- a. Many premature neonates can be successfully supported with NIPPV.

B. Minimize the duration of mechanical ventilation

1. Manage patients without sedation whenever possible (quality of evidence: III).^{150,151}
2. Assess readiness to extubate daily (quality of evidence: III).
3. Avoid unplanned extubations and reintubations (quality of evidence: III).¹⁵²
4. Provide regular oral care with sterile water (extrapolated from studies in adults, no data in preterm neonates; quality of evidence: III).
5. Minimize breaks in the ventilator circuit (extrapolated from studies in adults, no data in preterm neonates; quality of evidence: III).
6. Change the ventilator circuit only if visibly soiled or malfunctioning (extrapolated from studies in adults and children, no data in preterm neonates; quality of evidence: III).^{153,154}

II. Special approaches for preterm neonates

- A. Interventions with minimal risks of harm but unknown

impact on VAP rates

1. Lateral recumbent positioning (quality of evidence: III).¹⁵⁵
2. Reverse Trendelenburg positioning (quality of evidence: III).
3. Closed/in-line suctioning (quality of evidence: III).^{156,157}

III. Generally not recommended

A. Inadequate data on risks and unknown impact on VAP rates in preterm neonates

1. Regular oral care with antiseptic (quality of evidence: III).
 - a. There are insufficient data on the impact of altering neonatal microflora and whether oral antiseptics are absorbed across the oral mucosa of preterm neonates.

B. May be harmful to preterm neonates

1. Histamine H2-receptor antagonists may increase the risk of nosocomial infection and mortality in preterm neonates (quality of evidence: II).^{158,159}
2. Prophylactic broad-spectrum antibiotics are associated with increased risk of necrotizing enterocolitis, prolonged length of stay, and death in premature infants (quality of evidence: II).¹⁶⁰⁻¹⁶³
3. Spontaneous breathing trials (quality of evidence: III).
 - a. Ventilating preterm neonates with prolonged continuous positive airway pressure alone increases the risk of extubation failure.¹⁶⁴⁻¹⁶⁶

C. Not applicable to preterm neonates

1. Daily interruption of sedation (quality of evidence: III).
 - a. Sedation is not routinely required for neonates on mechanical ventilation.
 - b. There are no data on the impact of interrupting sedatives when sedation is used.
2. Prophylactic probiotics and synbiotics (quality of evidence: III).
 - a. There are currently no products approved by the US Food and Drug Administration for preterm neonates. Limited data suggest that these may benefit some patients, but there are also multiple case reports of *Lactobacillus* bacteremia in infants and children following probiotic therapy.¹⁶⁷⁻¹⁷¹
3. Endotracheal tubes equipped with subglottic secretion drains; suitably sized products are not commercially available (quality of evidence: none available).
4. Silver-coated endotracheal tubes; suitably sized products are not commercially available (quality of evidence: none available).

Pediatric Patients

Framework for evaluating and prioritizing interventions. Diagnosing VAP is as challenging in term infants and children

as in preterm neonates and adults. The CDC has convened a working group to consider whether modified VAE definitions might be suitable for infants and children.

Risk factors for VAP in infants and children are similar to those of adults.¹⁷²⁻¹⁷⁶ Once they develop teeth, children's oral flora are similar to those of adults.^{177,178}

In general, most VAP prevention interventions recommended for adults are presumed to be applicable to infants and children. Some interventions recommended for adults, however, are not available for infants and small children. For example, some specialized endotracheal tubes are available only in larger sizes.

I. Basic practices for pediatric patients: interventions with minimal risk of harm and some data that they lower VAP rates

A. Avoid intubation if possible

1. Use NIPPV in selected populations whenever feasible (quality of evidence: II).
 - a. Risks of NIPPV in pediatric patients mirror those for adults listed above in section I.A.1.A, with the added issue that pediatric patients often need sedation to tolerate NIPPV.^{179,180}

B. Minimize the duration of mechanical ventilation

1. Assess readiness to extubate daily in patients without contraindications (quality of evidence: II).¹⁸¹⁻¹⁸³
 - a. A randomized controlled trial in Brazil reported that daily spontaneous breathing trials decreased the mean duration of ventilation.¹⁸³ There is no consensus on the most effective technique for spontaneous breathing trials in pediatric patients.^{181,184}
2. Avoid unplanned extubations and reintubations (quality of evidence: III).¹⁸⁵

C. Provide regular oral care

1. Provide regular oral care (quality of evidence: III).
 - a. Two before-after studies of VAP bundles that emphasized oral care found decreases in VAP rates.^{173,186}
 - b. The American Dental Association recommends beginning oral hygiene a few days after birth.¹⁸⁷ Wipe the gums with a gauze pad after each feeding to remove plaque and residual formula that could harm erupting teeth. When teeth erupt, brush them gently twice a day with a child's size toothbrush and water. Fluoride toothpaste is recommended from 2 years of age onward. After oral hygiene, rinse and suction the mouth. Keep the oral mucosa and lips clean, moist, and intact using sponge-tipped applicators dipped in nonalcohol, nonperoxide mouth rinse.¹⁸⁶

D. Elevate the head of the bed

1. Elevate the head of the bed unless medically contraindicated (quality of evidence: III).
 - a. One before-after study of a VAP bundle that in-

TABLE 4. Summary of Recommendations for Preventing Ventilator-Associated Pneumonia (VAP) in Pediatric Patients

Recommendation	Rationale	Intervention	Quality of evidence
Basic practices	Some data that the intervention lowers VAP rates and minimal risks of harm; potential benefits likely outweigh potential risks	Use noninvasive positive pressure ventilation for selected populations ^{179,180}	Moderate
		Assess readiness to extubate daily using spontaneous breathing trials in patients without contraindications ^{182,183}	Moderate
		Avoid unplanned extubations ¹⁸⁵	Low
		Provide regular oral care (ie, toothbrushing or gauze if no teeth) ¹⁷³	Low
		Elevate the head of the bed to 30°–45° ¹⁷³	Low
		Change ventilator circuits only if visibly soiled or malfunctioning ¹⁷²	Moderate
		Use cuffed endotracheal tubes ^{189,190}	Low
		Prevent condensate from reaching the patient ^{173,188}	Low
Special approaches	Unknown impact on VAP rates, but risk of harm likely minimal; reasonable to consider implementing if rates remain elevated despite basic practices	Interrupt sedation daily ¹⁹²	Moderate
		Prophylactic probiotics	Low
		Utilize endotracheal tubes with subglottic secretion drainage ports for older pediatric patients expected to require greater than 48 or 72 hours of mechanical ventilation ⁵⁰	Low
Generally not recommended	Unknown impact on VAP rates and inadequate data on risks	Systemic antimicrobial therapy for ventilator-associated tracheobronchitis	Low
		Selective oropharyngeal or digestive decontamination	Low
	No impact on VAP rates ^a	Oral care with antiseptics, such as chlorhexidine ^{193,195}	Moderate
		Stress ulcer prophylaxis ^{199,200}	Low
		Early tracheotomy	Low
	Lowers VAP rates in adults, but no impact on duration of mechanical ventilation, length of stay, or mortality	Thromboembolism prophylaxis	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/in-line suctioning ²⁰¹	Low

^a May, however, be indicated for reasons other than VAP prevention.

cluded head-of-bed elevation observed a decrease in VAP rates.¹⁷³

- b. Many hospital cribs do not have inbuilt angle-measuring devices. Alternative measuring devices are required in these circumstances.

E. Maintain ventilator circuits

1. Change ventilator circuits only when visibly soiled or malfunctioning (quality of evidence: II).
 - a. One randomized trial and 1 observational study found no difference in VAP rates or mortality with 3-day versus 7-day circuit changes. Circuit changes are therefore recommended only when the circuit is soiled or malfunctioning, to minimize costs.^{153,154}
2. Remove condensate from the ventilator circuit fre-

quently (quality of evidence: III).

- a. Avoid draining the condensate toward the patient.¹⁷³
 3. Suction oral secretions before each position change (quality of evidence: III).¹⁸⁸
- #### F. Endotracheal tube selection and maintenance
1. Use cuffed endotracheal tubes (quality of evidence: III).
 - a. Pediatric intensivists have historically favored uncuffed tubes due to concern that cuffs may induce subglottic stenosis in pediatric airways. Cuffing has been proven safe, however, and may decrease the risk of microaspiration.^{189,190} Cuffed tubes are now used routinely for term newborns and children.¹⁹¹
 2. Maintain cuff pressure and volume at the minimal

occlusive settings to prevent clinically significant air leaks around the endotracheal tube, typically 20 cm of water (quality of evidence: III).^{123,189}

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

II. Special approaches for pediatric patients

A. Interventions with evidence of benefit in adult patients and minimal risks of harm but limited data in pediatric populations

1. Interrupt sedation once a day (quality of evidence: II).
 - a. Daily sedative interruptions decreased duration of mechanical ventilation and intensive care length of stay without increases in adverse event rates in 1 small randomized controlled trial.¹⁹²
 - 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. More data are needed.
2. Administer prophylactic probiotics (quality of evidence: III).
 - a. This recommendation is inferred from adult data but should be considered with caution due to sparse safety data in pediatric patients and case reports of *Lactobacillus* bacteremia associated with probiotic therapy, including cases in children without known immunodeficiency.^{111-114,169-171}
3. Use endotracheal tubes with subglottic secretion drainage ports (quality of evidence: III).
 - a. This intervention is feasible only for children aged greater than or equal to 10 years since the smallest available endotracheal tube with subglottic secretion drainage ports is size 6.0.

III. Generally not recommended for pediatric patients

A. Unknown impact on VAP rates and/or inadequate data on risks

1. Systemic antimicrobial therapy for ventilator-associated tracheobronchitis (quality of evidence: III).
 - a. One retrospective study found that prolonged antibiotics for tracheobronchitis did not protect against VAP but did increase the prevalence of multidrug-resistant organisms.¹⁹³
2. Selective oropharyngeal or digestive decontamination (quality of evidence: III).
 - a. See comments in section on adults.

B. No impact on VAP rates (these interventions may, however, be indicated for reasons other than VAP prophylaxis)

1. Oral care with chlorhexidine (quality of evidence: II).
 - a. Chlorhexidine appears to be safe for developing teeth,¹⁹⁴ but randomized controlled trials have found no difference in VAP rates, length of stay, or mortality in infants and children.^{193,195-198}

2. Stress ulcer prophylaxis (quality of evidence: III).

- a. Two small studies found no impact on VAP rates.^{199,200}

3. Early tracheotomy (quality of evidence: III).

4. Thromboembolism prophylaxis (quality of evidence: III).

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

1. Silver-coated endotracheal tubes (quality of evidence: III).

IV. No recommendation: limited data from pediatric studies, no impact on VAP rates or outcomes in adults, unclear impact on costs

A. Closed/in-line suctioning

1. 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 (quality of evidence: III).²⁰¹

SECTION 5: PERFORMANCE MEASURES

I. Internal reporting

- A. Regular monitoring and internal reporting of patient outcomes and adherence rates to recommended prevention strategies (“process measures”) are important quality improvement strategies.
- B. Both outcome and process measure reporting are likely beneficial: improving outcomes is the primary goal of care improvement programs, but analyzing performance rates for key processes of care may help identify specific processes to target for improvement.
- C. Report process and outcome measures to key organizational stakeholders, including frontline care providers, respiratory therapy directors, nursing and medical leaders, and senior hospital administrators. Feeding these data back to providers and leaders has been associated with improvements in both performance rates and outcomes.²⁰²⁻²⁰⁷
- D. Report process measures internally only. External reporting of process measure data is not appropriate at this time given substantial variability in the ways different organizations define, collect, analyze, and present process measure data.
- E. There are insufficient data at present to guide the definition and implementation of process measures for the prevention of VAP in neonatal and pediatric units.

II. Process measures

- A. Process measure definitions and measurement strategies vary widely
 1. For organizations that collect and report process measures, clearly define measures, including data sources, inclusion and exclusion criteria, frequency of monitoring, and numerator and denominator criteria.
 2. Develop a formal system to document compliance.

- a. Compliance can be measured via direct observations or via audits of patient charts, bedside paperwork, and/or electronic medical records. Periodically validate the accuracy of paper and/or electronic documentation.
 3. Perform assessments regularly.
 - a. The optimal frequency of assessments (eg, once daily, twice daily, or weekly) is not known, but the frequency can likely be adjusted on the basis of compliance rates (eg, as compliance improves, less frequent observations may be sufficient).
 - B. Prevention bundles
 1. Consider combining a core set of critical process measures together into a bundle to enhance care. Bundling care processes facilitates implementation by providing a clear, tangible set of expectations to follow. In addition, some care processes may be synergistic.
 2. There is no consensus on which care processes to include in a VAP prevention bundle. There is substantial heterogeneity in different hospitals' ventilator bundles.²⁰⁸
 3. Evidence on the impact of bundles is limited. Many prevention bundles have been associated with variable reductions in VAP rates. A smaller subset has been associated with improvements in objective outcomes.²⁰⁹⁻²¹⁴ To date, however, prevention bundles have been tested only in observational before-after and time-series analyses rather than in randomized controlled trials. It is therefore difficult to disentangle the extent to which lower VAP rates and better outcomes are due to prevention bundles versus secular trends in severity of illness, advances in medical care, and ascertainment biases.
 4. 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.^{212,215}
 - III. Approaches to defining process measures
 - A. There is no consensus on how best to define adherence to different process measures. Examples of how different organizations have defined selected process measures are summarized below. These examples are primarily drawn from multicenter quality improvement initiatives.
 1. Optimize hand hygiene
 - a. Readers are referred to the Compendium article "Strategies to Prevent Healthcare-Associated Infections through Hand Hygiene"²¹⁶ for a comprehensive discussion of this topic.
 2. Minimize sedation
 - a. Perform spontaneous awakening trials daily.
 - i. Definitions
 - (a) Girard et al⁴⁸ defined this as the percentage of sedative-days (ventilator-days during which sedatives are administered) on which sedative and analgesic continuous infusions were interrupted or where at least 1 scheduled dose of an intermittently prescribed sedative or analgesic was withheld.
 - (b) Berenholtz et al²⁰⁷ defined this as the percentage of ventilator-days on which patients prescribed any sedative medications were able to follow commands at least once during the course of the day.
 - b. Inclusion criteria: all patients on mechanical ventilation being treated with 1 or more of the following drugs: lorazepam, midazolam, propofol, fentanyl, morphine, meperidine, hydromorphone, or dexmedetomidine.²⁰⁷
 - c. Exclusion criteria: patients receiving a sedative infusion for active seizures or alcohol withdrawal, escalating sedative doses due to ongoing agitation, neuromuscular blockade, evidence of active myocardial ischemia within the previous 24 hours, evidence of increased intracranial pressure.^{48,207}
3. Expedite extubation
 - A. Perform spontaneous breathing trials daily
 - a. Definitions
 - i. Percentage of ventilator-days on which patients received a trial of spontaneous ventilation. A trial of spontaneous breathing is defined as a period of time where ventilatory support is removed. This can be done by allowing the patient to
 - (a) Breathe through a T-tube circuit
 - (b) Breathe through a ventilator circuit using "flow triggering" with continuous positive airway pressure of 0–5 cm of water and/or pressure support ventilation with 5–8 cm of water.^{48,207,217}
 - ii. The initial spontaneous breathing trial should last at least 30 minutes.
 - b. Inclusion criteria: all patients on mechanical ventilation.
 - c. Exclusion criteria: oxygen saturation less than 88%, F_{iO_2} greater than 50%, PEEP greater than 8 cm of water, lack of spontaneous breathing effort for greater than or equal to 5 minutes, agitation, active myocardial ischemia, significant vasopressor requirement, increased intracranial pressure, moribund state with death likely imminent.⁴⁸
4. Minimize the risk of aspiration
 - a. Elevate the head of the bed
 - i. Definitions
 - (a) Berenholtz et al²⁰⁷ defined this as the per-

centage of ventilator-days on which the head of the bed is elevated 30°–45°.

- (b) Bloos et al²¹³ had access to continuous electronic monitoring of their beds' backrest elevation angles. They therefore defined head-of-bed elevation compliance as the mean daily backrest elevation angle.
- (c) Sinuff et al²¹⁴ tracked concordance with head-of-bed elevation to 45°. They defined concordance as the sum of days on which the head of the bed was elevated plus the days on which head-of-bed elevation was contraindicated divided by total ventilator-days. They encouraged providers to consider elevating the head of the bed as much as possible when elevation to 45° was not possible.
 - ii. Inclusion criteria: all patients on mechanical ventilation.
 - iii. Exclusion criteria: patients with hemodynamic instability, undergoing resuscitation, unstable spine or not cleared, pelvic instability or fractures, prone position, intra-aortic balloon pump in femoral vessels, and obesity procedures.²¹⁴

IV. Outcome measures

- A. Conduct surveillance for all VAEs, including VAC, IVAC, possible VAP, and probable VAP in adult ICUs. Report rates for all events included in the algorithm. VAE definitions are not currently available for pediatric and neonatal patients; hence, these units should continue to use traditional NHSN VAP definitions.
 - 1. VAE incidence density
 - a. Numerator: total number of VACs, including IVACs, possible VAPs, and probable VAPs.
 - b. Denominator: total ventilator-days.
 - c. Multiply by 1,000 and express as VAEs per 1,000 ventilator-days.
 - d. Note that the total VAE rate is synonymous with the total VAC rate.
 - 2. IVAC incidence density
 - a. Numerator: total number of IVACs, including possible VAPs and probable VAPs.
 - b. Denominator: total ventilator-days.
 - c. Multiply by 1,000 and express as the IVAC rate per 1,000 ventilator-days.
 - 3. VAP incidence density
 - a. Organizations can consider calculating both their total VAP rate (sum of possible and probable VAPs) and their probable VAP rate for internal monitoring purposes. The former metric is presumed to be more sensitive, the latter more specific.
 - b. Total VAP rate
 - i. Numerator: total number of all possible and probable VAPs.
 - ii. Denominator: total ventilator-days.

- iii. Multiply by 1,000 and express as the overall VAP rate per 1,000 ventilator-days.

- c. Probable VAP rate
 - i. Numerator: total number of all probable VAP events.
 - ii. Denominator: total ventilator-days.
 - iii. Multiply by 1,000 and express as the probable VAP rate per 1,000 ventilator-days.

V. External reporting

- A. VAC and IVAC are potentially appropriate metrics for public reporting, interfacility comparison, and pay-for-performance programs. Better data on their responsiveness to quality improvement programs are necessary, however, before recommending them for interfacility comparisons or pay-for-performance programs. Suitable risk-adjustment strategies are also needed.
- B. Possible and probable VAP are not suitable for external reporting at this time since substantial variability in clinical and laboratory practices in the acquisition, processing, and interpretation of culture data preclude meaningful comparisons of VAP rates between institutions.
- C. VAP rates generated using NHSN's former surveillance definitions are not appropriate for external reporting in light of their considerable subjectivity.
- D. Hospitals in states that have mandatory reporting laws must collect and report data as required by their state. Local and state health departments can provide specific information on public reporting requirements.

SECTION 6: IMPLEMENTATION STRATEGIES

Accountability is an essential principle for preventing HAIs. 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 provide the imperative for HAI prevention, thereby making HAI prevention an organizational priority. Senior leadership is accountable for providing adequate resources needed for effective implementation of an HAI prevention program. These resources include necessary personnel (clinical and nonclinical), education, and equipment (Table 5).

Engagement, education, execution, and evaluation are further common attributes of successful care improvement programs.²⁰³ These attributes are elaborated below.

I. Engage

- A. Develop a multidisciplinary team
 - 1. Multidisciplinary teams set goals, define each step in the implementation process, and monitor progress in

TABLE 5. Fundamental Elements of Accountability for Healthcare-Associated Infection Prevention

Senior management is responsible for ensuring that the healthcare system supports an infection prevention and control (IPC) program that effectively prevents healthcare-associated infections (HAIs) and the transmission of epidemiologically important pathogens
Senior management is accountable for ensuring that an adequate number of trained personnel are assigned to the IPC program and adequate staffing of other departments that play a key role in HAI prevention (eg, environmental services)
Senior management is accountable for ensuring that healthcare personnel, including licensed and nonlicensed personnel, are adequately trained and competent to perform their job responsibilities
Direct healthcare providers (such as physicians, nurses, aides, and therapists) and ancillary personnel (such as environmental service and equipment processing personnel) are responsible for ensuring that appropriate IPC practices are used at all times (including hand hygiene, standard and isolation precautions, and cleaning and disinfection of equipment and the environment)
Senior and unit leaders are responsible for holding personnel accountable for their actions
IPC leadership is responsible for ensuring that an active program to identify HAIs is implemented, that HAI data are analyzed and regularly provided to those who can use the information to improve the quality of care (eg, unit staff, clinicians, and hospital administrators), and that evidence-based practices are incorporated into the program
Senior and unit leaders are accountable for ensuring that appropriate training and educational programs to prevent HAIs are developed and provided to personnel, patients, and families
Personnel from the IPC program, the laboratory, and information technology departments are responsible for ensuring that systems are in place to support the surveillance program

reaching goals.^{173,218,219} Programs developed by team consensus are more effective and increase guideline adherence.^{173,218,220} 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 who can strengthen the team include infection preventionists, pharmacists, nutritionists, physical therapists, occupational therapists, family members, and patient advocates.^{207,219,221,222}

B. Involve local champions

1. Identify local champions, including formal (eg, medical director, nursing director, charge nurses, director of respiratory therapy) and informal (eg, engaged frontline staff) leaders.^{207,213,219,221-223}
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.^{173,203,207,220,223,224}
3. Local champions should know their hospital's interests and needs, be able to shape strategies to match local unit culture, monitor progress, and facilitate necessary changes during implementation.²⁰² Early and continual communication between local champions and frontline staff allows providers to ask questions, resolve concerns, prepare for action, and sustain improvements.^{202,224}

C. 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.^{207,225-227} 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.²²⁷

II. Educate

A. Provide education sessions

1. Education sessions help summarize evidence, explain new processes, set expectations, and encourage staff to adopt recommended practices.^{202,228} Education sessions can include workshops, hands-on trainings, conferences, slide presentations, and/or interactive discussions; employing multiple teaching modalities can help meet diverse learning styles.^{224,229,230} Both local champions and topic experts (eg, infection preventionists) can lead staff education.^{173,226}
2. Education sessions must be informative and relevant for the learner; therefore, it is important to have multidisciplinary educational programs customized for different specialties.^{203,204,218}
3. Ongoing staff education helps maintain high levels of compliance with recommended practices.^{205,230}
4. Educating patients and family members may help them better engage with and support the medical team's plan of care.

B. Provide educational materials

1. Provide educational materials to staff that summarize the evidence, support self-study, and remind staff about new practices.²³¹ Examples of educational materials include pocket cards, brochures, posters, fact sheets, daily guides, guideline summaries, flow sheets and 1-page bulletins.^{173,205,207,227,229,232}

III. Execute

A. 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.²⁰²

2. Daily multidisciplinary rounds are widely advocated; these 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.^{204,207,222}
- B. Create redundancy
1. Build redundancy or independent checks into care-delivery processes to remind staff about new practices.^{202,203,212} Redundancy can take the form of posters, bulletins, pens, stamps, pocket cards, 1-page signs, daily goals in patient rooms, checklists and preprinted order sets, text messages, and screen savers on clinical computers.^{203,205,212,226,232-235} Encourage family members to ask the care team if patients are receiving evidence-based therapies for VAP prevention.²⁰⁷
 2. The combination of both education and reminders significantly improves processes of care.^{228,236}
- IV. Evaluate
- A. Measure performance
1. Measure performance using frequent formal and informal audits of clinical practice.^{203,237}
 2. Measuring process and outcome measures enhances awareness, establishes expectations, creates urgency, and rewards changes in behavior.²⁰²
 3. Evaluating performance provides an ongoing, real-time image of actual implementation rates.²³⁴
 4. Areas of poor compliance can be rapidly identified and rectified.^{203,237} If compliance remains poor in one area, the improvement team should walk the process with staff to gain additional insights into barriers to implementation.²⁰³
 5. Analyze all or a representative sample of VACs for etiology and preventability. Pneumonia, pulmonary edema, acute respiratory distress syndrome, and atelectasis are typical etiologies for VACs.^{10,12,15} Use your analyses to select and refine prevention strategies that address the most frequent and preventable causes of VACs in your clinical setting.
- B. Provide feedback to staff
1. Provide regular feedback on process and/or outcome data to staff.^{202,204,212,226,235} Feedback can be provided via wall displays or during meetings.^{173,202,229,231}
 2. Providing feedback helps staff appreciate how their efforts to improve are impacting performance rates and patients' outcomes. This helps maintain staff motivation and can boost adherence to new processes.^{203,238}
 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.^{202,203,237,238}

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REFERENCES

1. Coffin SE, Klompas M, Classen D, et al. Strategies to prevent ventilator-associated pneumonia in acute care hospitals. *Infect Control Hosp Epidemiol* 2008;29(suppl 1):S31–S40.
2. Yokoe DS, Andersen DJ, Berenholtz SM, et al. Introduction to “A Compendium of Strategies to Prevent Healthcare-Associated Infections in Acute Care Hospitals: 2014 Updates.” *Infect Control Hosp Epidemiol* 2014;35(5):455–459.
3. 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(10):798–816.
4. Klompas M. Eight initiatives that misleadingly lower ventilator-associated pneumonia rates. *Am J Infect Control* 2012;40(5):408–410.
5. Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. *JAMA* 2009;302(21):2323–2329.
6. Magill SS, Hellinger W, Cohen J, et al. Prevalence of healthcare-associated infections in acute care hospitals in Jacksonville, Florida. *Infect Control Hosp Epidemiol* 2012;33(3):283–291.
7. 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(8):998–1002.
8. 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(1):281–284.
9. Novosel TJ, Hodge LA, Weireter LJ, et al. Ventilator-associated pneumonia: depends on your definition. *Am Surg* 2012;78(8):851–854.
10. Klompas M, Khan Y, Kleinman K, et al. Multicenter evaluation of a novel surveillance paradigm for complications of mechanical ventilation. *PLoS ONE* 2011;6(3):e18062.
11. Klompas M, Magill S, Robicsek A, et al. Objective surveillance definitions for ventilator-associated pneumonia. *Crit Care Med* 2012;40(12):3154–3161.
12. 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(4):471–477.

13. Prospero E, Illuminati D, Marigliano A, et al. Learning from Galileo: ventilator-associated pneumonia surveillance. *Am J Respir Crit Care Med* 2012;186(12):1308–1309.
14. Muscedere 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(5):1453–1460.
15. 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(8):947–955.
16. Klompas M, Kleinman K, Murphy MV. Descriptive epidemiology and attributable morbidity of ventilator-associated events. *Infect Control Hosp Epidemiol* 2014;35(5):502–510.
17. 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 multi-state models. *Intensive Care Med* 2010;36(5):781–789.
18. 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(10):1133–1139.
19. 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(12):2736–2742.
20. 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(8):665–671.
21. Safdar N, Dezfulian C, Collard HR, Saint S. Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. *Crit Care Med* 2005;33(10):2184–2193.
22. 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(2):445–457.
23. Klompas M. Does this patient have ventilator-associated pneumonia? *JAMA* 2007;297(14):1583–1593.
24. Wunderink RG, Woldenberg LS, Zeiss J, Day CM, Ciemins J, Lacher DA. The radiologic diagnosis of autopsy-proven ventilator-associated pneumonia. *Chest* 1992;101(2):458–463.
25. 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(1):62–68.
26. 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(2):217–224.
27. Klompas M. Interobserver variability in ventilator-associated pneumonia surveillance. *Am J Infect Control* 2010;38(3):237–239.
28. 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(10):2373–2378.
29. Stevens JP, Kachniarz B, Wright SB, et al. When policy gets it right: variability in U.S. hospitals' diagnosis of ventilator-associated pneumonia. *Crit Care Med* 2014;42(3):497–503.
30. 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(4):332–337.
31. Stevenson KB, Khan Y, Dickman J, et al. Administrative coding data, compared with CDC/NHSN criteria, are poor indicators of health care-associated infections. *Am J Infect Control* 2008;36(3):155–164.
32. 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(6):650–652.
33. Klompas M. The paradox of ventilator-associated pneumonia prevention measures. *Crit Care* 2009;13(5):315.
34. Bonten MJ. Ventilator-associated pneumonia: preventing the inevitable. *Clin Infect Dis* 2011;52(1):115–121.
35. Klompas M, Platt R. Ventilator-associated pneumonia—the wrong quality measure for benchmarking. *Ann Intern Med* 2007;147(11):803–805.
36. 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(1):149–152.
37. Uckay I, Ahmed QA, Sax H, Pittet D. Ventilator-associated pneumonia as a quality indicator for patient safety? *Clin Infect Dis* 2008;46(4):557–563.
38. Blot S, Lisboa T, Angles R, Rello J. Prevention of VAP: is zero rate possible? *Clin Chest Med* 2011;32(3):591–599.
39. Magill SS, Klompas M, Balk R, et al. Developing a new, national approach to surveillance for ventilator-associated events. *Crit Care Med* 2013;41(11):2467–2475.
40. Klompas M, Kleinman K, Platt R. Development of an algorithm for surveillance of ventilator-associated pneumonia with electronic data and comparison of algorithm results with clinician diagnoses. *Infect Control Hosp Epidemiol* 2008;29(1):31–37.
41. Klompas M, Kleinman K, Khan Y, et al. Rapid and reproducible surveillance for ventilator-associated pneumonia. *Clin Infect Dis* 2012;54:370–377.
42. Dessap AM, Katsahian S, Roche-Campo F, et al. Ventilator-associated pneumonia during weaning from mechanical ventilation: role of fluid management. *Chest*. doi:10.1378/chest.13-2564. Electronically published March 20, 2014.
43. Centers for Disease Control and Prevention (CDC). *Ventilator-Associated Event Protocol*. Atlanta: CDC, 2014. <http://www.cdc.gov/nhsn/acute-care-hospital/vae/index.html>. Accessed March 25, 2014.
44. Klompas M. Ventilator-associated events surveillance: a patient safety opportunity. *Curr Opin Crit Care* 2013;19(5):424–431.
45. Lewis SC, Li L, Murphy MV, Klompas M. Risk factors for ventilator-associated events: a case-control multivariable analysis. *Crit Care Med*. doi:10.1097/CCM.0000000000000338. Electronically published April 18, 2014.
46. Strom T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. *Lancet* 2010;375(9713):475–480.
47. 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(25):1864–1869.
48. 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(9607):126–134.
49. Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009; 373(9678):1874–1882.
 50. 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(8):1985–1991.
 51. Determann RM, Royakkers A, Wolthuis EK, et al. Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without acute lung injury: a preventive randomized controlled trial. *Crit Care* 2010;14(1):R1.
 52. Futier E, Constantin J-M, Paugam-Burtz C, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. *N Engl J Med* 2013;369(5):428–437.
 53. Wiedemann HP, Wheeler AP, Bernard GR, et al. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med* 2006;354(24):2564–2575.
 54. Hebert PC, Wells G, Blajchman MA, et al; Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. *N Engl J Med* 1999;340(6):409–417.
 55. Klompas M. Prevention of ventilator-associated pneumonia. *Expert Rev Anti Infect Ther* 2010;8(7):791–800.
 56. Bouadma L, Wolff M, Lucet JC. Ventilator-associated pneumonia and its prevention. *Curr Opin Infect Dis* 2012;25(4): 395–404.
 57. Hess DR. Noninvasive positive-pressure ventilation and ventilator-associated pneumonia. *Respir Care* 2005;50(7):924–929.
 58. Burns KE, Adhikari NK, Keenan SP, Meade MO. Noninvasive positive pressure ventilation as a weaning strategy for intubated adults with respiratory failure. *Cochrane Database Syst Rev* 2010(8):CD004127.
 59. Carron M, Freo U, BaHammam AS, et al. Complications of non-invasive ventilation techniques: a comprehensive qualitative review of randomized trials. *Br J Anaesth* 2013;110(6): 896–914.
 60. Aboussouan LS, Ricaurte B. Noninvasive positive pressure ventilation: increasing use in acute care. *Cleve Clin J Med* 2010; 77(5):307–316.
 61. Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* 2013;41(1): 263–306.
 62. Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med* 2000;342(20):1471–1477.
 63. Schweickert WD, Gehlbach BK, Pohlman AS, Hall JB, Kress JP. Daily interruption of sedative infusions and complications of critical illness in mechanically ventilated patients. *Crit Care Med* 2004;32(6):1272–1276.
 64. Mehta S, Burry L, Cook D, et al. Daily sedation interruption in mechanically ventilated critically ill patients cared for with a sedation protocol. *JAMA* 2012;308(19):1985–1992.
 65. Kress JP, Hall JB. The changing landscape of ICU sedation. *JAMA* 2012;308(19):2030–2031.
 66. 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(4):567–574.
 67. 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(2):459–467.
 68. 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(8): 894–900.
 69. Esteban A, Frutos F, Tobin MJ, et al; Spanish Lung Failure Collaborative Group. A comparison of four methods of weaning patients from mechanical ventilation. *N Engl J Med* 1995; 332(6):345–350.
 70. Hopkins RO, Spuhler VJ, Thomsen GE. Transforming ICU culture to facilitate early mobility. *Crit Care Clin* 2007;23(1): 81–96.
 71. Morris PE, Goad A, Thompson C, et al. Early intensive care unit mobility therapy in the treatment of acute respiratory failure. *Crit Care Med* 2008;36(8):2238–2243.
 72. Bailey P, Thomsen GE, Spuhler VJ, et al. Early activity is feasible and safe in respiratory failure patients. *Crit Care Med* 2007; 35(1):139–145.
 73. Morris PE, Griffin L, Berry M, et al. Receiving early mobility during an intensive care unit admission is a predictor of improved outcomes in acute respiratory failure. *Am J Med Sci* 2011;341(5):373–377.
 74. Burtin C, Clerckx B, Robbeets C, et al. Early exercise in critically ill patients enhances short-term functional recovery. *Crit Care Med* 2009;37(9):2499–2505.
 75. Needham DM, Korupolu R, Zanni JM, et al. Early physical medicine and rehabilitation for patients with acute respiratory failure: a quality improvement project. *Arch Phys Med Rehabil* 2010;91(4):536–542.
 76. Titsworth WL, Hester J, Correia T, et al. The effect of increased mobility on morbidity in the neurointensive care unit. *J Neurosurg* 2012;116(6):1379–1388.
 77. Balas MC, Vasilevskis EE, Olsen KM, et al. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Crit Care Med* 2014;42(5):1024–1036.
 78. Lord RK, Mayhew CR, Korupolu R, et al. ICU early physical rehabilitation programs: financial modeling of cost savings. *Crit Care Med* 2013;41(3):717–724.
 79. 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(5):938–946.
 80. 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(7):910–917.
 81. Shorr AF, O'Malley PG. Continuous subglottic suctioning for the prevention of ventilator-associated pneumonia: potential economic implications. *Chest* 2001;119(1):228–235.
 82. Hallais C, Merle V, Guitard PG, et al. Is continuous subglottic suctioning cost-effective for the prevention of ventilator-

- associated pneumonia? *Infect Control Hosp Epidemiol* 2011; 32(2):131–135.
83. Frost SA, Azeem A, Alexandrou E, et al. Subglottic secretion drainage for preventing ventilator associated pneumonia: a meta-analysis. *Aust Crit Care* 2013;26(4):180–188.
 84. 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(9193):1851–1858.
 85. 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(2):396–402.
 86. Keeley L. Reducing the risk of ventilator-acquired pneumonia through head of bed elevation. *Nurs Crit Care* 2007;12(6):287–294.
 87. Alexiou VG, Ierodiakonou V, Dimopoulos G, Falagas ME. Impact of patient position on the incidence of ventilator-associated pneumonia: a meta-analysis of randomized controlled trials. *J Crit Care* 2009;24(4):515–522.
 88. 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.
 89. 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(3):168–174.
 90. 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(1):14–19.
 91. 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(12):1077–1082.
 92. Rutala WA, Weber DJ; Healthcare Infection Control Practices Advisory Committee. Guideline for *Disinfection and Sterilization in Healthcare Facilities, 2008*. http://www.cdc.gov/hicpac/Disinfection_Sterilization/acknowledg.html. Accessed April 1, 2014.
 93. Krueger WA, Lenhart FP, Neeser G, et al. Influence of combined intravenous and topical antibiotic prophylaxis on the incidence of infections, organ dysfunctions, and mortality in critically ill surgical patients: a prospective, stratified, randomized, double-blind, placebo-controlled clinical trial. *Am J Respir Crit Care Med* 2002;166(8):1029–1037.
 94. de Jonge E, Schultz MJ, Spanjaard L, et al. Effects of selective decontamination of digestive tract on mortality and acquisition of resistant bacteria in intensive care: a randomised controlled trial. *Lancet* 2003;362(9389):1011–1016.
 95. de Smet AM, Kluytmans JA, Cooper BS, et al. Decontamination of the digestive tract and oropharynx in ICU patients. *N Engl J Med* 2009;360(1):20–31.
 96. Liberati A, D'Amico R, Pifferi S, Torri V, Brazzi L, Parmelli E. Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care. *Cochrane Database Syst Rev* 2009(4):CD000022.
 97. de Smet AM, Kluytmans JA, Blok HE, et al. Selective digestive tract decontamination and selective oropharyngeal decontamination and antibiotic resistance in patients in intensive-care units: an open-label, clustered group-randomised, crossover study. *Lancet Infect Dis* 2011;11(5):372–380.
 98. Chan EY, Ruest A, Meade MO, Cook DJ. Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis. *BMJ* 2007;334(7599):889.
 99. Daneman N, Sarwar S, Fowler RA, Cuthbertson BH. Effect of selective decontamination on antimicrobial resistance in intensive care units: a systematic review and meta-analysis. *Lancet Infect Dis* 2013;13(4):328–341.
 100. van der Meer JW, Vandenbroucke-Grauls CM. Resistance to selective decontamination: the jury is still out. *Lancet Infect Dis* 2013;13(4):282–283.
 101. Chlebicki MP, Safdar N. Topical chlorhexidine for prevention of ventilator-associated pneumonia: a meta-analysis. *Crit Care Med* 2007;35(2):595–602.
 102. Pileggi C, Bianco A, Flotta D, Nobile CG, Pavia M. Prevention of ventilator-associated pneumonia, mortality and all intensive care unit acquired infections by topically applied antimicrobial or antiseptic agents: a meta-analysis of randomized controlled trials in intensive care units. *Crit Care* 2011;15(3):R155.
 103. Labeau SO, Van de Vyver K, Brusselaers N, Vogelaers D, Blot SI. Prevention of ventilator-associated pneumonia with oral antiseptics: a systematic review and meta-analysis. *Lancet Infect Dis* 2011;11(11):845–854.
 104. Tantipong H, Morkchareonpong C, Jaiyindee S, Thamlikitkul V. Randomized controlled trial and meta-analysis of oral decontamination with 2% chlorhexidine solution for the prevention of ventilator-associated pneumonia. *Infect Control Hosp Epidemiol* 2008;29(2):131–136.
 105. Li J, Xie D, Li A, Yue J. Oral topical decontamination for preventing ventilator-associated pneumonia: a systematic review and meta-analysis of randomized controlled trials. *J Hosp Infect* 2013;84(4):283–293.
 106. Shi Z, Xie H, Wang P, et al. Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database Syst Rev* 2013;8:CD008367.
 107. Silvestri L, Weir I, Gregori D, et al. Effectiveness of oral chlorhexidine on nosocomial pneumonia, causative microorganisms and mortality in critically ill patients: a systematic review and meta-analysis. *Minerva Anestesiol*. Electronically published November 21, 2013.
 108. 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(5):751–761.
 109. DeRiso AJ 2nd, Ladowski JS, Dillon TA, Justice JW, Peterson AC. Chlorhexidine gluconate 0.12% oral rinse reduces the incidence of total nosocomial respiratory infection and nonprophylactic systemic antibiotic use in patients undergoing heart surgery. *Chest* 1996;109(6):1556–1561.
 110. Segers P, Speekenbrink RG, Ubbink DT, van Ogtrop ML, de Mol BA. Prevention of nosocomial infection in cardiac surgery by decontamination of the nasopharynx and oropharynx with chlorhexidine gluconate: a randomized controlled trial. *JAMA* 2006;296(20):2460–2466.
 111. 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(3):954–962.
112. 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(3):R109.
 113. 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(12):3290–3302.
 114. 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(3):646–655.
 115. Lherm T, Monet C, Nougere B, et al. Seven cases of fungemia with *Saccharomyces boulardii* in critically ill patients. *Intensive Care Med* 2002;28(6):797–801.
 116. Munoz P, Bouza E, Cuenca-Estrella M, et al. *Saccharomyces cerevisiae* fungemia: an emerging infectious disease. *Clin Infect Dis* 2005;40(11):1625–1634.
 117. Salminen MK, Rautelin H, Tynkynen S, et al. *Lactobacillus* bacteremia, clinical significance, and patient outcome, with special focus on probiotic *L. rhamnosus* GG. *Clin Infect Dis* 2004;38(1):62–69.
 118. 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(11):5340–5343.
 119. Graf C, Gavazzi G. *Saccharomyces cerevisiae* fungemia in an immunocompromised patient not treated with *Saccharomyces boulardii* preparation. *J Infect* 2007;54(3):310–311.
 120. 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(11):1079–1083.
 121. 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(4):771–776.
 122. Valencia M, Ferrer M, Farre R, et al. Automatic control of tracheal tube cuff pressure in ventilated patients in semi-recumbent position: a randomized trial. *Crit Care Med* 2007;35(6):1543–1549.
 123. 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(9):1041–1047.
 124. Caruso P, Denari S, Ruiz SA, Demarzo SE, Deheinzelin D. Saline instillation before tracheal suctioning decreases the incidence of ventilator-associated pneumonia. *Crit Care Med* 2009;37(1):32–38.
 125. Yao LY, Chang CK, Maa SH, Wang C, Chen CC. Brushing teeth with purified water to reduce ventilator-associated pneumonia. *J Nurs Res* 2011;19(4):289–297.
 126. Alhazzani W, Smith O, Muscedere J, Medd J, Cook D. Toothbrushing for critically ill mechanically ventilated patients: a systematic review and meta-analysis of randomized trials evaluating ventilator-associated pneumonia. *Crit Care Med* 2013;41(2):646–655.
 127. 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(7):805–813.
 128. 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(3):R70.
 129. Sud S, Sud M, Friedrich JO, Adhikari NK. Effect of mechanical ventilation in the prone position on clinical outcomes in patients with acute hypoxemic respiratory failure: a systematic review and meta-analysis. *Can Med Assoc J* 2008;178(9):1153–1161.
 130. Alsaghir AH, Martin CM. Effect of prone positioning in patients with acute respiratory distress syndrome: a meta-analysis. *Crit Care Med* 2008;36(2):603–609.
 131. Abroug F, Ouanes-Besbes L, Elatrous S, Brochard L. The effect of prone positioning in acute respiratory distress syndrome or acute lung injury: a meta-analysis. Areas of uncertainty and recommendations for research. *Intensive Care Med* 2008;34(6):1002–1011.
 132. Kopterides P, Siempos II, Armaganidis A. Prone positioning in hypoxemic respiratory failure: meta-analysis of randomized controlled trials. *J Crit Care* 2009;24(1):89–100.
 133. Abroug F, Ouanes-Besbes L, Dachraoui F, Ouanes I, Brochard L. An updated study-level meta-analysis of randomised controlled trials on proning in ARDS and acute lung injury. *Crit Care* 2011;15(1):R6.
 134. Guerin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 2013;368(23):2159–2168.
 135. Marik PE, Vasu T, Hirani A, Pachinburavan M. Stress ulcer prophylaxis in the new millennium: a systematic review and meta-analysis. *Crit Care Med* 2010;38(11):2222–2228.
 136. 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(3):693–705.
 137. Wang F, Wu Y, Bo L, et al. The timing of tracheotomy in critically ill patients undergoing mechanical ventilation: a systematic review and meta-analysis of randomized controlled trials. *Chest* 2011;140(6):1456–1465.
 138. 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(3):249–256.
 139. Casaer MP, Mesotten D, Hermans G, et al. Early versus late parenteral nutrition in critically ill adults. *N Engl J Med* 2011;365(6):506–517.
 140. 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(9):1329–1335.
 141. 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(1):260–270.
 142. Siempos II, Vardakas KZ, Falagas ME. Closed tracheal suction systems for prevention of ventilator-associated pneumonia. *Br J Anaesth* 2008;100(3):299–306.

143. 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(6):1313–1321.
144. 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(4):538–544.
145. Maggiore SM. Endotracheal suctioning, ventilator-associated pneumonia, and costs: open or closed issue? *Intensive Care Med* 2006;32(4):485–487.
146. Dudeck MA, Horan T, Peterson KD, et al. *National Healthcare Safety Network (NHSN) Report, Data Summary for 2011, Device-Associated Module*. Atlanta: Centers for Disease Control and Prevention, 2013. <http://www.cdc.gov/nhsn/PDFs/dataStat/NHSN-Report-2011-Data-Summary.pdf>. Accessed April 1, 2014.
147. Bhandari V, Finer NN, Ehrenkranz RA, et al. Synchronized nasal intermittent positive-pressure ventilation and neonatal outcomes. *Pediatrics* 2009;124(2):517–526.
148. Finer NN, Carlo WA, Walsh MC, et al. Early CPAP versus surfactant in extremely preterm infants. *N Engl J Med* 2010;362(21):1970–1979.
149. Bhandari V. Nasal intermittent positive pressure ventilation in the newborn: review of literature and evidence-based guidelines. *J Perinatol* 2010;30(8):505–512.
150. Hamid MH, Malik MA, Masood J, Zia A, Ahmad TM. Ventilator-associated pneumonia in children. *J Coll Physicians Surg Pak* 2012;22(3):155–158.
151. 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.
152. Veldman A, Trautschold 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(9):968–973.
153. 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(1):56–61.
154. 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(1):37–43.
155. 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(4):770–774.
156. Taylor JE, Hawley G, Flenady V, Woodgate PG. Tracheal suctioning without disconnection in intubated ventilated neonates. *Cochrane Database Syst Rev* 2011(12):CD003065.
157. 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(12):2130–2134.
158. Terrin G, Passariello A, De Curtis M, et al. Ranitidine is associated with infections, necrotizing enterocolitis, and fatal outcome in newborns. *Pediatrics* 2012;129(1):e40–e45.
159. 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(2):e137–e142.
160. Kuppala VS, Meinzen-Derr J, Morrow AL, Schibler KR. Prolonged initial empirical antibiotic treatment is associated with adverse outcomes in premature infants. *J Pediatr* 2011;159(5):720–725.
161. Alexander VN, Northrup V, Bizzarro MJ. Antibiotic exposure in the newborn intensive care unit and the risk of necrotizing enterocolitis. *J Pediatr* 2011;159(3):392–397.
162. 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 Neonatal Med* 2013;26(17):1710–1714.
163. Weintraub AS, Ferrara L, Deluca L, et al. Antenatal antibiotic exposure in preterm infants with necrotizing enterocolitis. *J Perinatol* 2012;32(9):705–709.
164. Davis PG, Henderson-Smart DJ. Extubation from low-rate intermittent positive airways pressure versus extubation after a trial of endotracheal continuous positive airways pressure in intubated preterm infants. *Cochrane Database Syst Rev* 2001(4):CD001078.
165. 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 Neonatal Ed* 2013;98(1):F70–F73.
166. 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 Neonatal Ed* 2008;93(4):F305–F306.
167. Rojas MA, Lozano JM, Rojas MX, et al. Prophylactic probiotics to prevent death and nosocomial infection in preterm infants. *Pediatrics* 2012;130(5):e1113–e1120.
168. 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(12):1735–1742.
169. 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(3):278–280.
170. Kunz AN, Noel JM, Fairchok MP. Two cases of *Lactobacillus* bacteremia during probiotic treatment of short gut syndrome. *J Pediatr Gastroenterol Nutr* 2004;38(4):457–458.
171. Land MH, Rouster-Stevens K, Woods CR, Cannon ML, Cnota J, Shetty AK. *Lactobacillus* sepsis associated with probiotic therapy. *Pediatrics* 2005;115(1):178–181.
172. Foglia E, Meier MD, Elward A. Ventilator-associated pneumonia in neonatal and pediatric intensive care unit patients. *Clin Microbiol Rev* 2007;20(3):409–425.
173. 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(4):582e2–587e2.
174. Taira BR, Fenton KE, Lee TK, et al. Ventilator-associated pneumonia in pediatric trauma patients. *Pediatr Crit Care Med* 2009;10(4):491–494.
175. 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(4):283–289.

176. 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(1):62–66.
177. Liljemark WF, Bloomquist C. Human oral microbial ecology and dental caries and periodontal diseases. *Crit Rev Oral Biol Med* 1996;7(2):180–198.
178. Kononen E. Development of oral bacterial flora in young children. *Ann Med* 2000;32(2):107–112.
179. Javouhey E, Barats A, Richard N, Stamm D, Floret D. Non-invasive ventilation as primary ventilatory support for infants with severe bronchiolitis. *Intensive Care Med* 2008;34(9):1608–1614.
180. 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(5):484–489.
181. 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(6):e330–e335.
182. 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(20):2561–2568.
183. 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(11):2526–2533.
184. Newth CJ, Venkataraman S, Willson DF, et al. Weaning and extubation readiness in pediatric patients. *Pediatr Crit Care Med* 2009;10(1):1–11.
185. 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(2):287–294.
186. 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 North Am* 2006;53(6):1231–1251.
187. American Dental Association. Your child's growing smile. *J Am Dent Assoc* 2012;143(1):88.
188. 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(5):397–401.
189. Gopalarreddy 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(1):55–60.
190. 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 Anaesth* 2009;103(6):867–873.
191. Kleinman ME, de Caen AR, Chameides L, et al. Part 10: pediatric basic and advanced life support: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Circulation* 2010;122(16 suppl 2):S466–S515.
192. 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(2):131–135.
193. 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(5):e305–e310.
194. 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(3):215–222.
195. 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(6):591–596.
196. 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(3):115–122.
197. 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(11):1354–1363.
198. 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(4):319–328.
199. 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(4):240–245.
200. 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(6):763–767.
201. 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(1):e25–e32.
202. 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(6):549–555.
203. Pronovost PJ, Berenholtz SM, Needham DM. Translating evidence into practice: a model for large scale knowledge translation. *BMJ* 2008;337:a1714.
204. 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(1):74–80.
205. Hawe CS, Ellis KS, Cairns CJ, Longmate A. Reduction of ventilator-associated pneumonia: active versus passive guideline implementation. *Intensive Care Med* 2009;35(7):1180–1186.
206. Rello J, Lode H, Cornaglia G, Masterton R. A European care bundle for prevention of ventilator-associated pneumonia. *Intensive Care Med* 2010;36(5):773–780.
207. 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(4):305–314.
208. Klompas M. Ventilator-associated pneumonia: is zero possible? *Clin Infect Dis* 2010;51(10):1123–1126.
 209. Crunden E, Boyce C, Woodman H, Bray B. An evaluation of the impact of the ventilator care bundle. *Nurs Crit Care* 2005;10(5):242–246.
 210. Burger CD, Resar RK. “Ventilator bundle” approach to prevention of ventilator-associated pneumonia. *Mayo Clin Proc* 2006;81(6):849–850.
 211. Apisarnthanarak A, Pinitchai U, Thongphubeth K, et al. Effectiveness of an educational program to reduce ventilator-associated pneumonia in a tertiary care center in Thailand: a 4-year study. *Clin Infect Dis* 2007;45(6):704–711.
 212. Youngquist P, Carroll M, Farber M, et al. Implementing a ventilator bundle in a community hospital. *Jt Comm J Qual Patient Saf* 2007;33(4):219–225.
 213. 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(2):232–237.
 214. 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(1):15–23.
 215. Resar R, Pronovost P, Haraden C, Simmonds T, Rainey T, Nolan T. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. *Jt Comm J Qual Patient Saf* 2005;31(5):243–248.
 216. Ellingson K, Haas JP, Aiello AE, et al. Strategies to prevent healthcare-associated infections through hand hygiene. *Infect Control Hosp Epidemiol* 35(8):937–960 (in this issue).
 217. Boles JM, Bion J, Connors A, et al. Weaning from mechanical ventilation. *Eur Respir J* 2007;29(5):1033–1056.
 218. Aragon D, Sole ML. Implementing best practice strategies to prevent infection in the ICU. *Crit Care Nurs Clin North Am* 2006;18(4):441–452.
 219. Burns SM, Earven S, Fisher C, 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(12):2752–2763.
 220. 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(2):323–330.
 221. 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(5):700–704.
 222. 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(12):1171–1174.
 223. 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(2):99–103.
 224. Craven DE. Preventing ventilator-associated pneumonia in adults: sowing seeds of change. *Chest* 2006;130(1):251–260.
 225. 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(1):R38.
 226. 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(4):363–372.
 227. Rello J, Afonso E, Lisboa T, et al. A care bundle approach for prevention of ventilator-associated pneumonia. *Clin Microbiol Infect* 2013;19(4):363–369.
 228. 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.
 229. Berenholtz S, Pronovost PJ. Barriers to translating evidence into practice. *Curr Opin Crit Care* 2003;9(4):321–325.
 230. 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(8):1341–1347.
 231. Bassi GL, Ferrer M, Saucedo LM, Torres A. Do guidelines change outcomes in ventilator-associated pneumonia? *Curr Opin Infect Dis* 2010;23(2):171–177.
 232. Lyerla F. Design and implementation of a nursing clinical decision support system to promote guideline adherence. *Comput Inform Nurs* 2008;26(4):227–233.
 233. Sinuff T, Muscedere J, Cook D, Dodek P, Heyland D. Ventilator-associated pneumonia: improving outcomes through guideline implementation. *J Crit Care* 2008;23(1):118–125.
 234. Omrane R, Eid J, Perreault MM, et al. Impact of a protocol for prevention of ventilator-associated pneumonia. *Ann Pharmacother* 2007;41(9):1390–1396.
 235. 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(7):656–662.
 236. Salahuddin N, Zafar A, Sukhyani L, et al. Reducing ventilator-associated pneumonia rates through a staff education programme. *J Hosp Infect* 2004;57(3):223–227.
 237. Westwell S. Implementing a ventilator care bundle in an adult intensive care unit. *Nurs Crit Care* 2008;13(4):203–207.
 238. 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(1):180–187.
 239. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336(7650):924–926.
 240. GRADE. Canadian Task Force on Preventive Health Care website. <http://canadiantaskforce.ca/methods/grade/>. Accessed December 31, 2013.
 241. 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(7):704–710.