

Prevention of Ventilator-Associated Pneumonia: An Evidence-Based Systematic Review

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Background: Ventilator-associated pneumonia is a common cause of morbidity in critically ill patients. Interventions beneficial to the prevention of ventilator-associated pneumonia would therefore have a significant impact on the care of these patients.

Purpose: To perform a literature review and synthesis of methods for prevention of ventilator-associated pneumonia.

Data Sources: MEDLINE (1966–2001), the Cochrane Library, and bibliographies of retrieved articles.

Study Selection: Studies were required to be prospective and controlled in design and to evaluate clinically important or surrogate outcomes. Surrogate outcomes were required to have a direct link to clinically important outcomes supported by the literature.

Data Extraction: Data on patients, definitions, study design, and outcomes were abstracted and graded by using preestablished criteria.

Data Synthesis: The preventive practices with the strongest

supportive evidence were semi-recumbent positioning, sucralfate instead of H₂-antagonists for stress ulcer prophylaxis, and selective digestive tract decontamination. Aspiration of subglottic secretions and oscillating beds may be useful in select populations. There is no evidence to support specific methods of enteral feeding or increased frequency of ventilator circuitry changes.

Conclusions: After evaluation of potential benefits and risks, the authors recommend considering several specific interventions to reduce the incidence of ventilator-associated pneumonia: semi-recumbent positioning in all eligible patients, sucralfate rather than H₂-antagonists in patients at low to moderate risk for gastrointestinal tract bleeding, and aspiration of subglottic secretions and oscillating beds in select patient populations. Selective digestive tract decontamination is not recommended because routine use may increase antimicrobial resistance.

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Ventilator-associated pneumonia is a common and highly morbid condition in critically ill patients (1). Epidemiologic investigations have shown cumulative incidence rates of 10% to 25% (1–3), crude mortality rates of 10% to 40% (3), and attributable mortality rates of 5% to 27% (4, 5). Hospital length of stay and cost are both increased in patients who develop ventilator-associated pneumonia (5, 6).

Organisms causing ventilator-associated pneumonia generally fall into two groups: those causing early-onset ventilator-associated pneumonia (<4 days of mechanical ventilation) and those causing late-onset ventilator-associated pneumonia (≥4 days of mechanical ventilation) (2, 3). Early-onset organisms are typically antibiotic-susceptible community-acquired bacteria, while late-onset organisms are commonly antibiotic-resistant nosocomial organisms. Colonization of the oropharynx and the stomach with potentially pathogenic organisms precedes the development of ventilator-associated pneumonia in most patients (2). The pathogenesis of ventilator-associated pneumonia probably involves microaspiration of oropharyngeal or gastric secretions contaminated with these organisms (3).

The most widely studied preventive strategies have focused on the prevention of oropharyngeal or gastric colonization and the prevention of aspiration of contaminated oropharyngeal or gastric secretions (3, 6–11). This evidence-based systematic review aims to identify interventions for the prevention of ventilator-associated pneumonia, critically evaluate their efficacy and adverse effects, and recommend an approach to their use. Portions of this ar-

ticle are based on an extensive scientific review of preventive practices for ventilator-associated pneumonia prepared for the Agency for Healthcare Research and Quality (12).

METHODS

Search Strategy

We identified articles by performing a systematic search of MEDLINE and the Cochrane Library and by hand searching bibliographies of retrieved articles. We began the literature review by searching MEDLINE for relevant English-language articles published from 1966 to 2001, using a combination of keywords (for example, *pneumon**, *ventilat**, *prevent**). For the Cochrane Library, we searched both the Database of Systematic Reviews and the Database of Abstracts of Reviews of Effectiveness (DARE) using the terms *pneumonia*, *ventilator*, *ventilator associated pneumonia*, and *nosocomial pneumonia*. To identify additional relevant articles, additional targeted searches were performed with the following keywords and title words: *semi-recumbent patient positioning*, *stress ulcer prophylaxis*, *sucralfate*, *aspiration of subglottic secretions*, *continuous oscillation*, *selective digestive tract decontamination*, *ventilator circuit changes*, *heated humidifiers*, *heat and moisture exchangers*, *enteral feeding*, *metoclopramide*, and *acidification*.

Inclusion and Exclusion Criteria

Study design and outcomes were assessed for each retrieved study (Table 1). For inclusion in this review, studies were required to have at least a level 3 study design (randomized, controlled trial or observational-cohort controlled trial) and a level 2 outcome (clinically important or

surrogate outcome). Meta-analyses and systematic reviews were assigned the level of the best study included, followed by "A."

Grading of Preventive Strategies

Each preventive strategy was graded from I to IV on the basis of the strength of the studies supporting its use. A rating of I indicated evidence from a meta-analysis or systematic review of randomized, controlled trials with clinically important outcomes (study design 1A, outcomes 1A); a rating of IIa indicated evidence from a randomized, controlled trial with clinically important outcomes (study design 1, outcomes 1); a rating of IIb indicated evidence from a randomized, controlled trial with surrogate outcomes (study design 1, outcomes 2); a rating of III indicated evidence from a nonrandomized controlled trial with clinically important or surrogate outcomes (study design 2, outcomes 1 or 2); and a rating of IV indicated evidence from a controlled observational study with clinically important or surrogate outcomes (study design 3, outcomes 1 or 2).

RESULTS

The computerized literature search found 433 articles, which we reviewed for study design and relevance. Additional studies were identified from bibliographic review of relevant articles. For ease of presentation, articles were grouped by individual preventive practice or by general preventive approach. This review discusses semi-recumbent positioning, stress ulcer prophylaxis, aspiration of subglottic secretions, oscillating beds, selective digestive tract decontamination, ventilator circuit management strategies, and methods of enteral feeding. **Appendix Tables 1 through 7** (available at www.annals.org) describe the included articles that examined each of these practices.

There are no standardized criteria for the diagnosis of ventilator-associated pneumonia, but typically three or more of the following are required: fever, leukocytosis, purulent secretions, and an infiltrate on chest radiography. Such criteria result in good sensitivity but poor specificity. Stricter definitions require a microbiological diagnosis as well, either by endotracheal aspirate, protected-specimen brush, or quantitative bronchoalveolar lavage. All studies included in this review required clinical and radiographic evidence of pneumonia. However, the lack of uniform diagnostic criteria makes it difficult to compare the results of individual studies, and we did not combine studies into meta-analyses.

Semi-Recumbent Patient Positioning

Background and Practice Description

Positioning of critically ill patients may affect the incidence of ventilator-associated pneumonia. Supine patient positioning has been shown to be independently associated with the development of ventilator-associated pneumonia, possibly because of an increased risk for gastroesophageal

Table 1. Study Design and Outcomes Rating Scale*

Level	Description
Study design	
1	Randomized, controlled trials (includes pseudo-randomization, such as alternate allocation)
2	Nonrandomized controlled trials (must be prospective, with predefined entry criteria and outcomes)
3	Observational studies with controls (includes interrupted time series, cohort studies, case-control studies)
4	Observational studies without controls (includes cohort studies without controls, case series)
Outcomes	
1	Clinically important outcomes
2	Surrogate or intermediate outcomes
3	Other outcomes relevant to decreasing risk for ventilator-associated pneumonia
4	No outcomes relevant to decreasing risk for ventilator-associated pneumonia

* Studies must have had at least a level 3 study design and a level 2 outcome to be included in this review. Meta-analyses were assigned the level of the best study included, followed by "A."

reflux and aspiration (13). Semi-recumbent positioning (defined as elevation of the head of the bed to 45 degrees) may decrease the risk for ventilator-associated pneumonia.

Summary of the Evidence

Three trials have evaluated the efficacy of semi-recumbent positioning (14–16). Two measured gastroesophageal reflux and aspiration events (surrogate outcomes) (15, 16), and one measured the incidence of ventilator-associated pneumonia (14). Both of the former studies reported a decreased frequency of gastroesophageal reflux and aspiration with semi-recumbent positioning (15, 16). The third trial found a statistically significant reduction in ventilator-associated pneumonia (14). There was no difference in mortality.

Potential for Harm and Cost

No adverse effects were observed in patients randomly assigned to semi-recumbent positioning (14). Patients were excluded if they had undergone abdominal or neurologic surgery within 7 days, had shock refractory to vasoactive therapy, or had had previous endotracheal intubation within 30 days. The cost of semi-recumbent positioning is negligible.

Conclusions and Recommendations

Semi-recumbent patient positioning is a low-cost, low-risk approach to preventing ventilator-associated pneumonia, and all three trials suggested that it is effective (grade IIa) (14–16). Semi-recumbent patient positioning should be considered in all eligible patients. Of importance, only one trial has looked at the clinical outcome of ventilator-associated pneumonia (14). These findings should be confirmed by additional randomized clinical trials.

Stress Ulcer Prophylaxis

Background and Practice Description

Gastric colonization by potentially pathogenic organisms increases with decreasing gastric acidity (17). Medications that alter the gastric pH, such as H₂-antagonists and antacids, may increase organism counts and increase the risk for ventilator-associated pneumonia (18). Sucralfate, an alternative prophylactic agent that does not affect gastric pH, may not increase this risk.

Summary of the Evidence

Seven meta-analyses of more than 20 randomized trials have addressed the risk for ventilator-associated pneumonia associated with various methods of stress ulcer prophylaxis (18–24). Four of the seven meta-analyses reported a significantly decreased incidence of ventilator-associated pneumonia with sucralfate therapy compared with H₂-antagonists (19–22), and three reported a statistically significant mortality benefit with sucralfate (18, 22, 23). Three meta-analyses found similar but nonsignificant trends in reduction of rates of ventilator-associated pneumonia in patients given sucralfate (18, 23, 24).

Potential for Harm and Cost

Gastrointestinal bleeding in critically ill patients is associated with significant morbidity and mortality (25). Stress ulcer prophylaxis is therefore of importance in these patients. Sucralfate therapy was associated with a statistically significant increased risk for clinically important gastrointestinal bleeding compared with H₂-antagonists in a recent randomized, controlled trial of 1200 mechanically ventilated patients (26). Although the results of several meta-analyses addressing this issue have been discordant (18, 19), such striking results from a recent large randomized trial are notable.

A few studies have evaluated the cost-effectiveness of stress ulcer prophylaxis (27, 28). The cost per episode of gastrointestinal bleeding prevented in high-risk patients is estimated to be several thousand dollars higher with H₂-antagonists than with sucralfate (27). No reliable data exist comparing overall costs from actual clinical trials.

Conclusions and Recommendations

Stress ulcer prophylaxis with any agent may increase the risk for ventilator-associated pneumonia (18). Therefore, sucralfate may decrease risk when compared with H₂-antagonists but not when compared with placebo. The data comparing stress ulcer prophylaxis with sucralfate and H₂-antagonists suggest a decreased incidence of ventilator-associated pneumonia with sucralfate (grade I). Clinicians must weight the benefit of sucralfate in limiting the development of ventilator-associated pneumonia against a potential decrease in protection against gastrointestinal bleeding compared with H₂-antagonists. Use of sucralfate in patients at low to moderate risk for gastrointestinal bleed-

ing (that is, those with no coagulopathy or need for prolonged mechanical ventilation) is a reasonable approach (29).

Aspiration of Subglottic Secretions

Background and Practice Description

The accumulation of contaminated oropharyngeal secretions above the endotracheal tube cuff may contribute to the risk for aspiration (3). Removal of these pooled secretions through suctioning of the subglottic region, a practice termed *aspiration of subglottic secretions*, may reduce the risk for aspiration and ventilator-associated pneumonia. Aspiration of subglottic secretions requires the use of specially designed endotracheal tubes containing a separate dorsal lumen that opens into the subglottic region.

Summary of the Evidence

Three randomized, controlled trials have examined aspiration of subglottic secretions (30–32). One found a statistically significant decrease in the incidence of ventilator-associated pneumonia with aspiration of subglottic secretions (30), while a second study showed a trend favoring aspiration of subglottic secretions (31). The third trial, limited to post-cardiac surgery patients, found no difference (32). All three trials reported a statistically significant delay in the time to development of ventilator-associated pneumonia. No difference in mortality was observed (30–32).

Potential for Harm and Cost

No adverse events were reported with aspiration of subglottic secretions in more than 150 patients (32). Specialized endotracheal tubes cost approximately 25% more than standard endotracheal tubes (for example, \$15 per Hi-Lo Evac endotracheal tube, Mallinckrodt, Inc., St. Louis, Missouri) (30).

Conclusions and Recommendations

Aspiration of subglottic secretions is a promising new strategy for the prevention of ventilator-associated pneumonia but cannot be recommended for general use because of the mixed results in the literature (grade IIa). It may be most effective in patients requiring prolonged (>3 days) mechanical ventilation (30, 31). Further study of this approach is warranted.

Oscillating Beds

Background and Practice Descriptions

Immobility in critically ill patients may lead to atelectasis and impaired clearance of bronchopulmonary secretions, thereby potentially increasing the risk for ventilator-associated pneumonia. Continuous rotational movement of critically ill patients on specialized kinetic beds may help prevent ventilator-associated pneumonia.

Summary of the Evidence

A meta-analysis of six randomized, controlled trials of oscillating beds found a statistically significant reduction in the risk for pneumonia (33). However, five of these studies were limited to surgical patients or those with neurologic impairment. The sixth study, which included primarily medical patients, found no significant benefit (34). A recent randomized, controlled trial of medical and surgical patients not included in the meta-analysis also found no benefit to oscillating beds (35).

Potential for Harm and Cost

Inadvertent disconnection of intravenous catheters, pressure ulceration, and an episode of ventricular ectopy were reported as complications of oscillation (34). Conscious patients tolerated oscillating beds poorly. The cost of specialized beds capable of continuous oscillation (for example, Roto Rest Delta bed, Kinetic Concepts, Inc., San Antonio, Texas) is approximately \$200 per day.

Conclusions and Recommendations

Although oscillating beds have no apparent benefit in general populations of medical patients, there is reasonably good evidence that this practice may be effective in surgical patients or patients with neurologic problems (grade I). Use of oscillating beds in these select patient populations should therefore be considered.

Selective Digestive Tract Decontamination

Background and Practice Description

There has been substantial interest in using topical antibiotics to sterilize the oropharynx and stomach in mechanically ventilated patients (a process termed *selective digestive tract decontamination*), with the goal of decreasing the pathogenicity of aspirated secretions and reducing the incidence of ventilator-associated pneumonia. Most studies use a combination of topical polymixin, aminoglycoside, and amphotericin. Many studies also include a short course (usually 3 days) of intravenous antimicrobial therapy. Studies of parenteral antibiotics alone have generally failed to show a benefit (36), although recent studies in patients with severe burns or coma have suggested a decreased incidence (37, 38). Concern over the development of antibiotic resistance has limited widespread investigation of parenteral prophylaxis alone (8).

Summary of the Evidence

Seven meta-analyses of more than 40 randomized, controlled trials of selective digestive tract decontamination have been published in the past decade (39–45). All seven meta-analyses reported a significant reduction in the risk for ventilator-associated pneumonia with the use of selective digestive tract decontamination (39–45). Four reported a significant reduction in mortality (39–41, 43); four separately analyzed trials that used combined topical and systemic antibiotics and those that used topical anti-

otics alone (39, 40, 43, 44). While both approaches prevented ventilator-associated pneumonia, no mortality benefit occurred with topical prophylaxis alone (39, 40, 43, 44).

Subgroup analyses have yielded conflicting results. A recent meta-analysis showed an increased benefit in surgical compared with medical patients (39), while another showed no difference according to type of patient (surgical or medical) or severity of illness (that is, Acute Physiology and Chronic Health Evaluation [APACHE] score) (40). The reason for discordance among these meta-analyses probably stems from differences in inclusion criteria, definitions of outcome measures, and analytic methods.

Potential for Harm and Cost

The primary risk associated with selective digestive tract decontamination is the development of antibiotic resistance (46–48). The impact of selective digestive tract decontamination on the emergence of resistant organisms is currently unknown. Several trials found that this procedure significantly decreases overall cost of antibiotics per patient (by 37% to 42%) (49–51) and hospital costs (by 20%) (51, 52).

Conclusions and Recommendations

Selective digestive tract decontamination seems to reduce the incidence of ventilator-associated pneumonia (grade I) and, when a combined topical and intravenous regimen is used, may reduce intensive care unit–related mortality (grade I) (53). A recent review of 32 studies of selective digestive tract decontamination found an inverse relationship between methodologic quality and benefit, suggesting that the findings of meta-analyses may be overly optimistic (54). Regardless of its likely efficacy, selective digestive tract decontamination cannot be recommended because of serious concern regarding its long-term effects on antibiotic resistance patterns. Future research should clearly focus on this critical issue.

Ventilator Circuit Management Strategies

Background and Practice Descriptions

Methods of ventilator circuit management may affect rates of ventilator-associated pneumonia in several ways. Elimination of contaminated equipment and improved methods of combating colonization of circuit equipment could decrease rates of ventilator-associated pneumonia. Alternatively, decreased manipulation may also reduce incidence. To address these questions, frequent ventilator circuit changes have been compared with less frequent changes, standard daily changes in heat and moisture exchangers have been compared with changes every 5 days, and standard heater-humidifier units (which require heated water for humidification) have been compared with heat and moisture exchanger filters (which have intrinsic humidification properties).

Summary of the Evidence

Four randomized trials of less frequent changes in ventilator circuitry have been published (55–58), and their results have recently been summarized (59). There was no significant difference in the rate of ventilator-associated pneumonia in any of these studies (55–58).

One trial has addressed the effect of less frequent changes in heat and moisture exchangers on the development of ventilator-associated pneumonia (60). Patients were randomly assigned to changes in heat and moisture exchangers daily or every fifth day. No significant difference in the rate of ventilator-associated pneumonia was observed (60).

Five randomized, controlled trials have compared the efficacy of heat and moisture exchangers and heater-humidifiers, as well as their effects on risk for ventilator-associated pneumonia. The results of these trials have recently been summarized (61). Only the largest of these five trials found a statistically significant reduction in the risk for ventilator-associated pneumonia with the use of heat and moisture exchangers (62). There was no effect on mortality (61).

Potential for Harm and Cost

No adverse effects of less frequent changes in ventilator circuits or heat and moisture exchangers were reported. Two trials reported increased rates of endotracheal tube occlusion with the use of heat and moisture exchangers (61). Less frequent equipment changes would be expected to decrease health care costs. Cost savings of \$6 per day per patient were reported when heat and moisture exchangers were used instead of heater-humidifiers (62).

Conclusions and Recommendations

Less frequent changes in ventilator circuits and heat and moisture exchangers do not lead to increased development of ventilator-associated pneumonia (grade I and grade IIa, respectively). Less frequent circuit and humidifier changes are less costly and should therefore be considered in all mechanically ventilated patients. Given the discordance between the largest randomized trial comparing heat and moisture exchangers with heater-humidifiers and the four smaller trials, a meta-analysis would help to determine whether heat and moisture exchangers are associated with lower rates of ventilator-associated pneumonia.

Methods of Enteral Feeding**Background and Practice Description**

Critically ill patients receiving enteral feedings often have substantial gastric volume, which may increase their risk for gastroesophageal reflux, aspiration, and ventilator-associated pneumonia. Small-intestinal feeding or the use of motility agents, such as metoclopramide, may therefore protect patients against ventilator-associated pneumonia (63, 64). Gastric colonization by potentially pathogenic

organisms has been shown to increase with decreasing gastric acidity (17). Acidification of enteral feedings may protect patients against ventilator-associated pneumonia by decreasing the concentration of potentially pathogenic organisms aspirated with each aspiration event (65). Intermittent enteral feeding may likewise increase gastric acidity and reduce the incidence of ventilator-associated pneumonia (66).

Summary of the Evidence

Four recent randomized, controlled trials have evaluated methods of enteral feeding aimed at preventing ventilator-associated pneumonia, each addressing one of the four issues mentioned earlier: small-intestinal feeding, the use of metoclopramide, acidification of feeding, and intermittent feeding (63–66). No difference was found in incidence of ventilator-associated pneumonia or mortality with any of these interventions (63–66).

Potential for Harm and Cost

No adverse events were reported with small-intestinal feedings or metoclopramide (63, 64). Patients receiving acidified feedings had higher incidence of acidemia and gastrointestinal bleeding (65). Intermittent enteral feeding led to more episodes of increased gastric residual volume and lower daily volumes of feeding (66).

Conclusions and Recommendations

In the limited number of studies to date, no method of enteral feeding has been shown to significantly affect the incidence of ventilator-associated pneumonia. The use of small-intestinal feeding, metoclopramide, acidification of feeding, or intermittent feeding is not recommended (grade IIa). Further investigation of small-intestinal and intermittent feeding is warranted because only one study has addressed each approach. Any further investigation of metoclopramide or acidification of feedings should proceed cautiously, however, since both of these methods are associated with potentially serious adverse effects (64, 65).

SUMMARY OF RECOMMENDATIONS

Table 2 provides a summary of the practices discussed in this paper, as well as recommendations for their use. To decrease the incidence of ventilator-associated pneumonia in critically ill patients, physicians should consider the following interventions: 1) semi-recumbent positioning of all eligible patients (grade IIa); 2) sucralfate instead of H₂-antagonists for stress ulcer prophylaxis in patients at low to moderate risk for gastrointestinal bleeding (grade I); 3) aspiration of subglottic secretions in patients likely to require more than 3 days of mechanical ventilation (grade IIa); 4) and oscillating beds in surgical or neurologic patients (grade I).

Although several articles have described the impact of

Table 2. Recommendations for Strategies To Prevent Ventilator-Associated Pneumonia*

Preventive Practice (Reference)	Results	Grade	Recommendations
Semi-recumbent positioning (14–16)	Reduced incidence of VAP	Ila	Consider in all patients who can tolerate head elevation. Additional trials warranted.
Sucralfate for stress ulcer prophylaxis (18–24, 26)	Reduced incidence of VAP	I	Consider in patients at low or moderate risk for gastrointestinal bleeding (i.e., no coagulopathy or prolonged ventilation). Additional trials warranted.
Aspiration of subglottic secretions (30–32)	Mixed	Ila	Consider in patients requiring prolonged (>3 days) mechanical ventilation. Additional trials warranted.
Oscillating bed (33–35)	Mixed	I	Consider in surgical and neurologic patients.
Selective digestive tract decontamination (39–45)	Reduced incidence of VAP	I	Appears effective, but widespread use cannot be recommended given concern for emergence of antibiotic resistance. Additional study of this issue warranted.
Decreased frequency of ventilator circuit changes (55–58)	No effect	I	Consider less frequent circuitry changes.
Decreased frequency of heat and moisture exchanger changes (60)	No benefit	Ila	Consider less frequent exchanger changes. Additional trials warranted.
Heat and moisture exchanger vs. heater-humidifier (61)	Mixed	I	No recommendation. Additional trials warranted.
Small-intestinal feeding (63)	No benefit	Ila	Not recommended. Additional trials warranted.
Metoclopramide (64)	No benefit	Ila	Not recommended.
Acidification of enteral feeding (65)	No benefit	Ila	Not recommended.
Intermittent enteral feeding (66)	No benefit	Ila	Not recommended. Additional trials warranted.

* Each preventive strategy is graded on the basis of the strength of the studies supporting its use. Grading is on a scale of I to IV. I = evidence from a meta-analysis of randomized, controlled trials with clinical outcomes (study design 1A, outcomes 1A); Ila = evidence from a randomized, controlled trial with clinical outcomes (study design 1, outcomes 1); IIb = evidence from a randomized, controlled trial with surrogate outcomes (study design 1, outcomes 2); III = evidence from a nonrandomized controlled trial with clinical or surrogate outcomes (study design 2, outcomes 1 or 2); IV = evidence from a controlled observational study with clinical or surrogate outcomes (study design 3, outcomes 1 or 2). VAP = ventilator-associated pneumonia.

preventive programs on ventilator-associated pneumonia (67–69), no randomized, controlled study has evaluated the effects of combining the preventive practices discussed here. Whether the preventive benefits of these practices would be additive is therefore unknown. Only through continued clinical investigation will we determine the best ways to prevent ventilator-associated pneumonia, thereby reducing morbidity and mortality in critically ill patients.

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References

1. Ibrahim EH, Tracy L, Hill C, Fraser VJ, Kollef MH. The occurrence of ventilator-associated pneumonia in a community hospital: risk factors and clinical outcomes. *Chest*. 2001;120:555-61. [PMID: 11502658]
2. George DL, Falk PS, Wunderink RG, Leeper KV Jr, Meduri GU, Steere EL, et al. Epidemiology of ventilator-acquired pneumonia based on protected bronchoscopic sampling. *Am J Respir Crit Care Med*. 1998;158:1839-47. [PMID: 9847276]
3. Craven DE, Steger KA. Nosocomial pneumonia in mechanically ventilated adult patients: epidemiology and prevention in 1996. *Semin Respir Infect*. 1996; 11:32-53. [PMID: 8885061]
4. Fagon JY, Chastre J, Hance AJ, Montravers P, Novara A, Gibert C. Nosocomial pneumonia in ventilated patients: a cohort study evaluating attributable mortality and hospital stay. *Am J Med*. 1993;94:281-8. [PMID: 8452152]
5. Heyland DK, Cook DJ, Griffith L, Keenan SP, Brun-Buisson C. The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient. The Canadian Critical Trials Group. *Am J Respir Crit Care Med*. 1999;159:1249-56. [PMID: 10194173]
6. Thompson R. Prevention of nosocomial pneumonia. *Med Clin North Am*. 1994;78:1185-98. [PMID: 8078375]
7. Bassin AS, Niederman MS. Prevention of ventilator-associated pneumonia. An attainable goal? *Clin Chest Med*. 1995;16:195-208. [PMID: 7768091]
8. Kollef MH. The prevention of ventilator-associated pneumonia. *N Engl J Med*. 1999;340:627-34. [PMID: 10029648]
9. Guidelines for prevention of nosocomial pneumonia. Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 1997;46(RR-1):1-79. [PMID: 9036304]
10. Stoutenbeek CP, van Saene HK. Nonantibiotic measures in the prevention of ventilator-associated pneumonia. *Semin Respir Infect*. 1997;12:294-9. [PMID: 9436956]

11. Livingston DH. Prevention of ventilator-associated pneumonia. *Am J Surg*. 2000;179:12S-17S. [PMID: 10896634]
12. Collard HR, Saint S. Preventive Practices for Ventilator-Associated Pneumonia. In: Shojania KG, Duncan BW, McDonald KM, Wachter RM, eds. *Making Health Care Safer: A Critical Analysis of Patient Safety Practices*. Evidence Report/Technology Assessment No. 43. AHRQ Publication no. 01-E058. Rockville, MD: Agency for Healthcare Research and Quality; 2001.
13. Kollef MH. Ventilator-associated pneumonia. A multivariate analysis. *JAMA*. 1993;270:1965-70. [PMID: 8411554]
14. Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogué S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. *Lancet*. 1999;354:1851-8. [PMID: 10584721]
15. Orozco-Levi M, Torres A, Ferrer M, Piera C, el-Ebiary M, de la Bellacasa JP, et al. Semirecumbent position protects from pulmonary aspiration but not completely from gastroesophageal reflux in mechanically ventilated patients. *Am J Respir Crit Care Med*. 1995;152:1387-90. [PMID: 7551400]
16. Torres A, Serra-Batllés J, Ros E, Piera C, Puig de la Bellacasa J, Cobos A, et al. Pulmonary aspiration of gastric contents in patients receiving mechanical ventilation: the effect of body position. *Ann Intern Med*. 1992;116:540-3. [PMID: 1543307]
17. Donowitz LG, Page MC, Mileur BL, Guenther SH. Alteration of normal gastric flora in critical care patients receiving antacid and cimetidine therapy. *Infect Control*. 1986;7:23-6. [PMID: 3633241]
18. Cook DJ, Reeve BK, Guyatt GH, Heyland DK, Griffith LE, Buckingham L, et al. Stress ulcer prophylaxis in critically ill patients. Resolving discordant meta-analyses. *JAMA*. 1996;275:308-14. [PMID: 8544272]
19. Messori A, Trippoli S, Vaiani M, Gorini M, Corrado A. Bleeding and pneumonia in intensive care patients given ranitidine and sucralfate for prevention of stress ulcer: meta-analysis of randomised controlled trials. *BMJ*. 2000;321:1103-6. [PMID: 11061729]
20. Tryba M, Cook DJ. Gastric alkalinization, pneumonia, and systemic infections: the controversy. *Scand J Gastroenterol Suppl*. 1995;210:53-9. [PMID: 8578208]
21. Cook DJ. Stress ulcer prophylaxis: gastrointestinal bleeding and nosocomial pneumonia. Best evidence synthesis. *Scand J Gastroenterol Suppl*. 1995;210:48-52. [PMID: 8578207]
22. Tryba M. Sucralfate versus antacids or H₂-antagonists for stress ulcer prophylaxis: a meta-analysis on efficacy and pneumonia rate. *Crit Care Med*. 1991;19:942-9. [PMID: 1675976]
23. Tryba M. Prophylaxis of stress ulcer bleeding. A meta-analysis. *J Clin Gastroenterol*. 1991;13 Suppl 2:S44-55. [PMID: 1832181]
24. Cook DJ, Laine LA, Guyatt GH, Raffin TA. Nosocomial pneumonia and the role of gastric pH. A meta-analysis. *Chest*. 1991;100:7-13. [PMID: 1676361]
25. Cook DJ, Fuller HD, Guyatt GH, Marshall JC, Leasa D, Hall R, et al. Risk factors for gastrointestinal bleeding in critically ill patients. Canadian Critical Care Trials Group. *N Engl J Med*. 1994;330:377-81. [PMID: 8284001]
26. Cook D, Guyatt G, Marshall J, Leasa D, Fuller H, Hall R, et al. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. Canadian Critical Care Trials Group. *N Engl J Med*. 1998;338:791-7. [PMID: 9504939]
27. Ben-Menachem T, McCarthy BD, Fogel R, Schiffman RM, Patel RV, Zarowitz BJ, et al. Prophylaxis for stress-related gastrointestinal hemorrhage: a cost effectiveness analysis. *Crit Care Med*. 1996;24:338-45. [PMID: 8605811]
28. Erstad BL, Camamo JM, Miller MJ, Webber AM, Fortune J. Impacting cost and appropriateness of stress ulcer prophylaxis at a university medical center. *Crit Care Med*. 1997;25:1678-84. [PMID: 9377882]
29. Saint S, Mathay MA. Risk reduction in the intensive care unit. *Am J Med*. 1998;105:515-23. [PMID: 9870839]
30. Mahul P, Auboyer C, Jospe R, Ros A, Guerin C, el Khouri Z, et al. Prevention of nosocomial pneumonia in intubated patients: respective role of mechanical subglottic secretions drainage and stress ulcer prophylaxis. *Intensive Care Med*. 1992;18:20-5. [PMID: 1578042]
31. Vallés J, Artigas A, Rello J, Bonsoms N, Fontanals D, Blanch L, et al. Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia. *Ann Intern Med*. 1995;122:179-86. [PMID: 7810935]
32. Kollef MH, Skubas NJ, Sundt TM. A randomized clinical trial of continuous aspiration of subglottic secretions in cardiac surgery patients. *Chest*. 1999;116:1339-46. [PMID: 10559097]
33. Choi SC, Nelson LD. Kinetic therapy in critically ill patients: combined results based on meta-analysis. *J Crit Care*. 1992;7:57-62.
34. Sumner WR, Curry P, Haponik EF, Nelson S, Elston R. Continuous mechanical turning of intensive care unit patients shortens length of stay in some diagnosis-related groups. *J Crit Care*. 1989;4:45-53.
35. Traver GA, Tyler ML, Hudson LD, Sherrill DL, Quan SF. Continuous oscillation: outcome in critically ill patients. *J Crit Care*. 1995;10:97-103. [PMID: 7496451]
36. Lode H, Höffken G, Kemmerich B, Schaberg T. Systemic and endotracheal antibiotic prophylaxis of nosocomial pneumonia in ICU. *Intensive Care Med*. 1992;18 Suppl 1:S24-7. [PMID: 1640029]
37. Kimura A, Mochizuki T, Nishizawa K, Mashiko K, Yamamoto Y, Otsuka T. Trimethoprim-sulfamethoxazole for the prevention of methicillin-resistant *Staphylococcus aureus* pneumonia in severely burned patients. *J Trauma*. 1998;45:383-7. [PMID: 9715201]
38. Sirvent JM, Torres A, El-Ebiary M, Castro P, de Batlle J, Bonet A. Protective effect of intravenously administered cefuroxime against nosocomial pneumonia in patients with structural coma. *Am J Respir Crit Care Med*. 1997;155:1729-34. [PMID: 9154884]
39. Nathens AB, Marshall JC. Selective decontamination of the digestive tract in surgical patients: a systematic review of the evidence. *Arch Surg*. 1999;134:170-6. [PMID: 10025458]
40. D'Amico R, Pifferi S, Leonetti C, Torri V, Tinazzi A, Liberati A. Effectiveness of antibiotic prophylaxis in critically ill adult patients: systematic review of randomised controlled trials. *BMJ*. 1998;316:1275-85. [PMID: 9554897]
41. Hurley JC. Prophylaxis with enteral antibiotics in ventilated patients: selective decontamination or selective cross-infection? *Antimicrob Agents Chemother*. 1995;39:941-7. [PMID: 7786000]
42. Kollef MH. The role of selective digestive tract decontamination on mortality and respiratory tract infections. A meta-analysis. *Chest*. 1994;105:1101-8. [PMID: 8162733]
43. Heyland DK, Cook DJ, Jaeschke R, Griffith L, Lee HN, Guyatt GH. Selective decontamination of the digestive tract. An overview. *Chest*. 1994;105:1221-9. [PMID: 8018162]
44. Meta-analysis of randomised controlled trials of selective decontamination of the digestive tract. Selective Decontamination of the Digestive Tract Trialists' Collaborative Group. *BMJ*. 1993;307:525-32. [PMID: 8400971]
45. Vandebroucke-Grauls CM, Vandebroucke JP. Effect of selective decontamination of the digestive tract on respiratory tract infections and mortality in the intensive care unit. *Lancet*. 1991;338:859-62. [PMID: 1681223]
46. van Saene HK, Stoutenbeek CP, Hart CA. Selective decontamination of the digestive tract (SDD) in intensive care patients: a critical evaluation of the clinical, bacteriological and epidemiological benefits. *J Hosp Infect*. 1991;18:261-77. [PMID: 1682365]
47. Ebner W, Kropec-Hübner A, Daschner FD. Bacterial resistance and overgrowth due to selective decontamination of the digestive tract. *Eur J Clin Microbiol Infect Dis*. 2000;19:243-7. [PMID: 10834811]
48. Bartlett JG. Selective decontamination of the digestive tract and its effect on antimicrobial resistance [Editorial]. *Crit Care Med*. 1995;23:613-5. [PMID: 7712747]
49. Quinio B, Albanèse J, Bues-Charbit M, Viviand X, Martin C. Selective decontamination of the digestive tract in multiple trauma patients. A prospective double-blind, randomized, placebo-controlled study. *Chest*. 1996;109:765-72. [PMID: 8617089]
50. Verwaest C, Verhaegen J, Ferdinand P, Schetz M, Van den Bergh G, Verbist L, et al. Randomized, controlled trial of selective digestive decontamination in 600 mechanically ventilated patients in a multidisciplinary intensive care unit. *Crit Care Med*. 1997;25:63-71. [PMID: 8989178]
51. Sánchez García M, Cambronero Galache JA, López Díaz J, Cerdá Cerdá E, Rubio Blasco J, Gómez Aguinaga MA, et al. Effectiveness and cost of selective decontamination of the digestive tract in critically ill intubated patients. A randomized, double-blind, placebo-controlled, multicenter trial. *Am J Respir Crit Care Med*. 1998;158:908-16. [PMID: 9731025]
52. Silvestri L, Mannucci F, van Saene HK. Selective decontamination of the digestive tract: a life saver. *J Hosp Infect*. 2000;45:185-90. [PMID: 10896796]

53. Pittet D, Eggimann P, Rubinovitch B. Prevention of ventilator-associated pneumonia by oral decontamination: just another SDD study? [Editorial] *Am J Respir Crit Care Med*. 2001;164:338-9. [PMID: 11500329]
54. van Nieuwenhoven CA, Buskens E, van Tiel FH, Bonten MJ. Relationship between methodological trial quality and the effects of selective digestive decontamination on pneumonia and mortality in critically ill patients. *JAMA*. 2001;286:335-40. [PMID: 11466100]
55. Dreyfuss D, Djedaini K, Weber P, Brun P, Lanore JJ, Rahmani J, 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;143:738-43. [PMID: 2008985]
56. Kollef MH, Shapiro SD, Fraser VJ, Silver P, Murphy DM, Trovillion E, et al. Mechanical ventilation with or without 7-day circuit changes. A randomized controlled trial. *Ann Intern Med*. 1995;123:168-74. [PMID: 7598297]
57. Long MN, Wickstrom G, Grimes A, Benton CF, Belcher B, Stamm AM. Prospective, randomized study of ventilator-associated pneumonia in patients with one versus three ventilator circuit changes per week. *Infect Control Hosp Epidemiol*. 1996;17:14-9. [PMID: 8789682]
58. Mermel LA, Eveloff S, Short K, Dempsey J, Parenteau S, Gentile S. The risk of pneumonia associated with the use of heated wire versus conventional ventilator circuits: a prospective trial [Abstract]. 4th Annual Meeting of the Society for Hospital Epidemiology of America, New Orleans, Louisiana, March 1994. Abstract no. M45.
59. Stamm AM. Ventilator-associated pneumonia and frequency of circuit changes. *Am J Infect Control*. 1998;26:71-3. [PMID: 9503116]
60. Davis K Jr, Evans SL, Campbell RS, Johannigman JA, Luchette FA, Porembka DT, et al. Prolonged use of heat and moisture exchangers does not affect device efficiency or frequency rate of nosocomial pneumonia. *Crit Care Med*. 2000;28:1412-8. [PMID: 10834688]
61. Cook D, De Jonghe B, Brochard L, Brun-Buisson C. Influence of airway management on ventilator-associated pneumonia: evidence from randomized trials. *JAMA*. 1998;279:781-7. [PMID: 9508156]
62. Kirton OC, DeHaven B, Morgan J, Morejon O, Civetta J. A prospective, randomized comparison of an in-line heat moisture exchange filter and heated wire humidifiers: rates of ventilator-associated early-onset (community-acquired) or late-onset (hospital-acquired) pneumonia and incidence of endotracheal tube occlusion. *Chest*. 1997;112:1055-9. [PMID: 9377917]
63. Kearns PJ, Chin D, Mueller L, Wallace K, Jensen WA, Kirsch CM. The incidence of ventilator-associated pneumonia and success in nutrient delivery with gastric versus small intestinal feeding: a randomized clinical trial. *Crit Care Med*. 2000;28:1742-6. [PMID: 10890612]
64. Yavagal DR, Karnad DR, Oak JL. Metoclopramide for preventing pneumonia in critically ill patients receiving enteral tube feeding: a randomized controlled trial. *Crit Care Med*. 2000;28:1408-11. [PMID: 10834687]
65. Heyland DK, Cook DJ, Schoenfeld PS, Frietag A, Varon J, Wood G. The effect of acidified enteral feeds on gastric colonization in critically ill patients: results of a multicenter randomized trial. Canadian Critical Care Trials Group. *Crit Care Med*. 1999;27:2399-406. [PMID: 10579255]
66. Bonten MJ, Gaillard CA, van der Hulst R, de Leeuw PW, van der Geest S, Stobberingh EE, et al. Intermittent enteral feeding: the influence on respiratory and digestive tract colonization in mechanically ventilated intensive-care-unit patients. *Am J Respir Crit Care Med*. 1996;154:394-9. [PMID: 8756812]
67. Manangan LP, Banerjee SN, Jarvis WR. Association between implementation of CDC recommendations and ventilator-associated pneumonia at selected US hospitals. *Am J Infect Control*. 2000;28:222-7. [PMID: 10840341]
68. Joiner GA, Salisbury D, Bollin GE. Utilizing quality assurance as a tool for reducing the risk of nosocomial ventilator-associated pneumonia. *Am J Med Qual*. 1996;11:100-3. [PMID: 8704496]
69. Kelleghan SI, Salemi C, Padilla S, McCord M, Mermilliod G, Canola T, et al. An effective continuous quality improvement approach to the prevention of ventilator-associated pneumonia. *Am J Infect Control*. 1993;21:322-30. [PMID: 8122805]

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Appendix Table 1. Summary of Studies of Effect of Semi-Recumbent Positioning on Risk for Ventilator-Associated Pneumonia and Death*

Study, Year (Reference)	Description	Study Design Level/Outcomes Level†	Reduction in Pneumonia for Intervention Compared with Control Group	Reduction in Mortality for Intervention Compared with Control Group
Drakulovic et al., 1999 (14)	Randomized, controlled trial of semi-recumbent patient positioning in 86 mechanically ventilated patients. Primary outcome was VAP.	1/1	OR, 0.16 [0.03–0.67]	OR, 0.57 [CI, 0.18–1.80]
Orozco-Levi et al., 1995 (15)	Two-period crossover trial of semi-recumbent patient positioning in 15 mechanically ventilated patients. Primary outcome was amount of pulmonary aspiration.	3/2	35% reduction in radioactive counting measurement compared with supine positioning‡	NA
Torres et al., 1992 (16)	Randomized two-period crossover trial of semi-recumbent patient positioning in 15 mechanically ventilated patients. Primary outcome was amount of pulmonary aspiration.	3/2	77% reduction in radioactive counting measurement compared with supine positioning§	NA

* Values in square brackets are 95% CIs. NA = not available; OR = odds ratio; VAP = ventilator-associated pneumonia.

† See Table 1 for an explanation of the rating scale.

‡ $P < 0.01$.

§ $P = 0.036$.

*Appendix Table 2. Summary of Studies of Effect of Stress Ulcer Prophylaxis on Risk for Ventilator-Associated Pneumonia and Death**

Study, Year (Reference)	Description	Study Design Level/Outcomes Level†	Pneumonia Point Estimate‡	Mortality Point Estimate‡
Messori et al., 2000 (19)	Meta-analysis of randomized, controlled trials comparing ranitidine with placebo, sucralfate with placebo, and ranitidine with sucralfate for the prevention of pneumonia in critically ill patients.	1A/1A	Sucralfate vs. ranitidine, 0.74 [0.59–0.94]	NR
Cook et al., 1998 (26)	Multicenter randomized, blinded, placebo-controlled trial of sucralfate with ranitidine in 1200 critically ill mechanically ventilated patients. End points were gastrointestinal bleeding, VAP, and death.	1/1	Sucralfate vs. ranitidine, 0.82 [0.60–1.11]	Sucralfate vs. ranitidine, 0.96 [0.73–1.27]
Cook et al., 1996 (18)	Meta-analysis of 27 randomized trials of stress ulcer prophylaxis in critically ill patients. Most patients were mechanically ventilated. End points were gastrointestinal bleeding, pneumonia, and death.	1A/1A	Sucralfate vs. H ₂ -antagonist, 0.77 [0.60–1.01]	Sucralfate vs. H ₂ -antagonist, 0.73 [0.54–0.97]
Tryba and Cook, 1995 (20)	Meta-analysis of 14 randomized trials of stress ulcer prophylaxis in critically ill patients.	1A/1A	Sucralfate vs. H ₂ -antagonist/antacid, 0.67 [0.53–0.84]	NR
Cook, 1995 (21)	Meta-analysis of 6 (outcome, VAP) and 7 (outcome, death) randomized trials of stress ulcer prophylaxis in critically ill patients.	1A/1A	Sucralfate vs. H ₂ -antagonist/antacid, 0.50 [0.21–0.79]	Sucralfate vs. H ₂ -antagonist, 0.71 [0.49–1.04]; sucralfate vs. antacid, 0.70 [0.52–0.94]
Tryba, 1991 (22)	Meta-analysis of 14 randomized trials of stress ulcer prophylaxis in critically ill patients. End points were gastrointestinal bleeding and pneumonia.	1A/1A	Sucralfate vs. H ₂ -antagonist, 0.50 [0.32–0.78]; sucralfate vs. antacid, 0.40 [0.24–0.69]	Sucralfate vs. H ₂ -antagonist/antacid, 0.76 [0.59–0.97]
Tryba, 1991 (23)	Meta-analysis of 9 randomized trials of stress ulcer prophylaxis in critically ill patients.	1A/1A	Sucralfate vs. H ₂ -antagonist/antacid, 0.30 [0.08–1.04]	Sucralfate vs. H ₂ -antagonist/antacid, 0.72§
Cook et al., 1991 (24)	Meta-analysis of 8 randomized trials of stress ulcer prophylaxis in critically ill patients, studying the rate of pneumonia with different drug regimens.	1A/1A	Sucralfate vs. H ₂ -antagonist/antacid, 0.55 [0.28–1.06]	NR

* Values in square brackets are 95% CIs. NR = not reported; VAP = ventilator-associated pneumonia.

† See Table 1 for an explanation of the rating scale.

‡ Point estimates reflect odds ratio/relative risk.

§ $P < 0.05$.

Appendix Table 3. Summary of Studies of Effect of Aspiration of Subglottic Secretions on Risk for Ventilator-Associated Pneumonia and Death*

Study, Year (Reference)	Description	Study Design Level/Outcomes Level†	Pneumonia Point Estimate‡	Mortality Point Estimate‡
Kollef et al., 1999 (32)	Randomized trial of 343 patients undergoing cardiac surgery and requiring mechanical ventilation.	1/1	0.61 [0.27–1.40]	0.86 [0.30–2.42]
Vallés et al., 1995 (31)	Randomized trial of 153 patients requiring prolonged mechanical ventilation.	1/1	0.47 [0.21–1.06]	1.09 [0.72–1.63]
Mahul et al., 1992 (30)	Randomized trial of 145 patients requiring mechanical ventilation for >3 days.	1/1	0.46 [0.23–0.93]	1.14 [0.62–2.07]

* Values in square brackets are 95% CIs.

† See Table 1 for an explanation of the rating scale.

‡ Point estimates reflect relative risk.

Appendix Table 4. Summary of Studies of Effect of Continuous Oscillation on Risk for Ventilator-Associated Pneumonia and Death*

Study, Year (Reference)	Study Description	Study Design Level/Outcomes Level†	Reduction in Pneumonia for Intervention Compared with Control Group‡	Reduction in Mortality for Intervention Compared with Control Group‡
Traver et al., 1995 (35)	Randomized, controlled trial of continuous oscillation in 103 critically ill medical and surgical patients (90% mechanically ventilated). Primary outcomes included pneumonia.	1/1	0.55 [0.19–1.55]	0.79 [0.31–2.02]
Choi and Nelson, 1992 (33)	Meta-analysis of 6 randomized, controlled trials of continuous oscillation in critically ill surgical or stroke patients (most were mechanically ventilated).	1A/1A	0.50§	No significant difference (data not reported)
Summer et al., 1989 (34)	Randomized, controlled trial of continuous oscillation in 86 critically ill medical patients (most were mechanically ventilated). Primary outcomes included pneumonia.	1/1	0.53 [0.12–2.25]	0.91 [0.30–2.73]

* Values in square brackets are 95% CIs.

† See Table 1 for an explanation of the rating scale.

‡ Point estimates reflect odds ratio.

§ $P = 0.002$.

Appendix Table 5. Summary of Studies of Effect of Selective Digestive Tract Decontamination on Risk for Ventilator-Associated Pneumonia and Death*

Study, Year (Reference)	Description	Study Design Level/Outcomes Level†	Pneumonia Point Estimate‡	Mortality Point Estimate‡
Nathens and Marshall, 1999 (39)	Meta-analysis of 21 randomized, controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections. Dual analysis of medical and surgical patients.	1A/1A	Medical patients, 0.45 [0.33–0.62]; surgical patients, 0.19 [0.15–0.26]	Medical patients: overall, 0.91 [0.71–1.18]; topical–IV, 0.75 [0.53–1.06]; topical, 1.14 [0.77–1.68] Surgical patients: overall, 0.70 [0.52–0.93]; topical–IV, 0.60 [0.41–0.88]; topical, 0.86 [0.51–1.45]
D’Amico et al., 1998 (40)	Meta-analysis of 33 randomized, controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections. Dual analysis of topical and systemic antibiotics combined and topical antibiotics alone.	1A/1A	Overall, not reported; topical–IV, 0.35 [0.29–0.41]; topical, 0.56 [0.46–0.68]	Overall, 0.88 [0.78–0.98]; topical–IV, 0.80 [0.69–0.93]; topical, 1.01 [0.84–1.22]
Hurley, 1995 (41)	Meta-analysis of 26 randomized, controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections.	1A/1A	Overall, 0.35 [0.30–0.42]	Overall, 0.86 [0.74–0.99]
Kollef, 1994 (42)	Meta-analysis of 16 randomized, controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections.	1A/1A	Overall, 0.28 [0.21–0.38]	Overall, 0.90 [0.74–1.10]
Heyland et al., 1994 (43)	Meta-analysis of 25 randomized, controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections.	1A/1A	Overall, 0.46 [0.39–0.56]; topical–IV, 0.48 [0.39–0.60]; topical, 0.43 [0.32–0.59]	Overall, 0.87 [0.79–0.97]; topical–IV, 0.81 [0.71–0.95]; topical, 1.00 [0.83–1.19]
Selective Decontamination of the Digestive Tract Trialists’ Collaborative Group, 1993 (44)	Meta-analysis of 22 randomized, controlled trials of antibiotic prophylaxis used to decrease nosocomial respiratory tract infections.	1A/1A	Overall, 0.37 [0.31–0.43]; topical–IV, 0.33 [0.27–0.40]; topical, 0.43 [0.33–0.56]	Overall, 0.90 [0.79–1.04]; topical–IV, 0.80 [0.67–0.97]; topical, 1.07 [0.86–1.32]
Vandenbroucke-Grauls and Vandenbroucke, 1991 (45)	Meta-analysis of 6 randomized, controlled trials of antibiotic prophylaxis used to decrease nosocomial infections.	1A/1A	Overall, 0.12 [0.08–0.19]	Overall, 0.70 [0.45–1.09]

* Values in square brackets are 95% CIs. IV = intravenous.

† See Table 1 for an explanation of the rating scale.

‡ Point estimates reflect odds ratio/relative risk.

Appendix Table 6. Summary of Studies of Effect of Ventilator Circuit Management Strategies on Risk for Ventilator-Associated Pneumonia and Death*

Study, Year (Reference)	Description	Study Design Level/Outcomes Level†	Pneumonia Point Estimate‡	Mortality Point Estimate‡
Decreased frequency of ventilator circuit changes Mermel et al., 1994 (58)	Randomized trial comparing weekly ventilator circuit changes with changes every other day.	1/1	0.29§	NR
Kollef et al., 1995 (56)	Randomized trial comparing weekly with no scheduled ventilator circuit changes	1/1	0.84§	NR
Long et al., 1996 (57)	Randomized trial comparing weekly ventilator circuit changes with changes every other day.	1/1	0.85§	NR
Dreyfuss et al., 1991 (55)	Randomized trial comparing weekly with no scheduled ventilator circuit changes.	1/1	0.91§	NR
Decreased frequency of heat and moisture exchanger changes Davis et al., 2000 (60)	Randomized, controlled trial comparing heat and moisture exchanger changes every 5 days with changes every other day.	1/1	0.83§	NR
Heat and moisture exchanger vs. heater-humidifier Cook et al., 1998 (61)	Systematic review of five published trials comparing heat and moisture exchangers with heater-humidifiers	1A/1A	1 study, 0.41 [0.20–0.86]; 4 studies, 0.34, 0.66, 0.68, 0.86§	1 study, NR; 4 studies, ND

* Values in square brackets are 95% CIs. ND = no difference; NR = not reported.

† See Table 1 for an explanation of the rating scale.

‡ Point estimates reflect relative risk.

§ $P > 0.05$.

Appendix Table 7. Summary of Studies of Effect of Methods of Enteral Feeding on Risk for Ventilator-Associated Pneumonia and Death*

Study, Year (Reference)	Description	Study Design Level/Outcomes Level†	Pneumonia Point Estimate‡	Mortality Point Estimate‡
Small-intestinal feeding Kearns et al., 2000 (63)	Randomized, controlled trial of small-intestinal vs. gastric feeding in 44 mechanically ventilated patients.	1/1	1.46 [0.37–5.78]	0.91 [0.33–2.55]
Metoclopramide Yavagal et al., 2000 (64)	Randomized, controlled trial of metoclopramide in 305 critically ill patients (approximately 50% were mechanically ventilated).	1/1	1.22 [0.72–2.07]	1.05 [0.86–1.30]
Acidification of enteral feeding Heyland et al., 1999 (65)	Randomized, controlled trial of acidified enteral feeding in 95 mechanically ventilated patients.	1/1	0.40 [0.11–1.46]	2.01 [0.90–4.49]
Intermittent enteral feeding Bonten et al., 1996 (66)	Randomized, controlled trial of intermittent vs. continuous enteral feeding in 60 mechanically ventilated patients.	1/1	1.67 [0.44–6.36]	3.50 [0.79–15.5]

* Values in square brackets are 95% CIs.

† See Table 1 for an explanation of the rating scale.

‡ Point estimates reflect relative risk.