



Comprehensive evidence-based clinical practice guidelines for ventilator-associated pneumonia: Prevention[☆]

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Abstract

Background: Ventilator-associated pneumonia (VAP) is an important cause of morbidity and mortality in ventilated critically ill patients.

Purpose: To develop evidence-based guidelines for the prevention of VAP.

Data Sources: MEDLINE, EMBASE, CINAHL, and the Cochrane Database of Systematic Reviews and Register of Controlled Trials.

Study Selection: The authors systematically searched for all relevant randomized, controlled trials and systematic reviews on the topic of prevention of VAP in adults that were published from 1980 to October 1, 2006.

Data Extraction: Independently and in duplicate, the panel scored the internal validity of each trial. Effect size, confidence intervals, and homogeneity of the results were scored using predefined definitions. Scores for the safety, feasibility, and economic issues were assigned based on consensus of the guideline panel.

Levels of Evidence: The following statements were used: recommend, consider, do not recommend, and no recommendation due to insufficient or conflicting evidence.

Data Synthesis: To prevent VAP:

We recommend: that the orotracheal route of intubation should be used for intubation; a new ventilator circuit for each patient; circuit changes if the circuit becomes soiled or damaged, but no scheduled changes; change of heat and moisture exchangers every 5 to 7 days or as clinically indicated; the use of a

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closed endotracheal suctioning system changed for each patient and as clinically indicated; subglottic secretion drainage in patients expected to be mechanically ventilated for more than 72 hours; head of bed elevation to 45° (when impossible, as near to 45° as possible should be considered).

Consider: the use of rotating beds; oral antiseptic rinses.

We do not recommend: use of bacterial filters; the use of iseganan

We make no recommendations regarding: the use of a systematic search for sinusitis; type of airway humidification; timing of tracheostomy; prone positioning; aerosolized antibiotics; intranasal mupirocin; topical and/or intravenous antibiotics.

Conclusion: There are a growing number of evidence-based strategies for VAP prevention, which, if applied in practice, may reduce the incidence of this serious nosocomial infection.

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1. Introduction

Ventilator associated pneumonia (VAP) is a healthcare-associated infection that commonly causes morbidity and mortality in mechanically ventilated patients [1]. For example, VAP is associated with an increased duration of mechanical ventilation, crude death rates of 5% to 65% [2-5], and increased healthcare costs [6-8]. However, VAP is preventable and many practices have been demonstrated to reduce the incidence of VAP and its associated burden of illness [9,10]. Because the body of literature on VAP is extensive and in some cases, conflicting, it has become increasingly difficult for critical care practitioners to assimilate and apply best evidence into clinical practice [11]. The synthesis of large bodies of knowledge into clinical practice guidelines (CPGs) is one method of improving the accessibility and utility of medical literature to clinicians [12]. For the management of critically ill patients, guidelines can improve the processes, outcomes, and costs of critical care [13-16]. The optimal method to implement guidelines is uncertain, but active strategies are superior to passive ones, periodic updates are necessary, and continued efforts to effect behavior change are required [17].

The guidelines committee of the Canadian Critical Care Society and Canadian Critical Care Trials Group developed evidence-based CPGs for the prevention of VAP in 2004 [18]. However, only research evidence published before April 1, 2003, was incorporated into those guidelines. Since then, new randomized controlled trials (RCTs) of strategies to prevent VAP have been published, and updating is necessary [19]. Therefore, the Canadian Critical Care Trials Group commissioned the development of up-to-date and comprehensive evidence-based CPGs for the prevention, diagnosis, and treatment of VAP. Herein, we report on the guidelines for the prevention of VAP. The guidelines for the diagnosis and treatment of VAP are reported in a companion manuscript in this issue [20].

2. Methods

A multispecialty and multidisciplinary panel was created to develop the comprehensive VAP CPGs. This group was

composed of 20 intensivists from university-affiliated and community hospitals, 4 infectious disease specialists, 3 intensive care unit (ICU) nurses, an infection control nurse, an ICU pharmacist, an ICU respiratory therapist, and a representative from the Canadian Patient Safety Institute [21]. Panel members were experts in critical care medicine ($n = 20$), infectious diseases ($n = 5$), VAP ($n = 4$), infection control ($n = 2$), nursing education ($n = 3$), evidence-based medicine ($n = 5$), and guideline development ($n = 5$). The clinical context was Canadian ICUs and the target audience was ICU clinicians.

To identify potentially relevant evidence, we searched 4 bibliographic databases (MEDLINE, EMBASE, CINAHL, and the Cochrane Database of Systematic Reviews and Register of Controlled Trials) from 1980 to October 1, 2006, for RCTs and systematic reviews or meta-analyses that evaluated interventions for the prevention of VAP (see Appendix A for search strategy). There were no language restrictions. We also reviewed personal files and the practice guidelines on this subject previously published by the Centers for Disease Control and Prevention and the American Thoracic Society [22,23].

We only included RCTs and systematic reviews of RCTs meeting predefined criteria. All trials measured the effect of an intervention to prevent VAP on the incidence of VAP in adult critically ill patients. Ventilator associated pneumonia was defined according to the definition used by authors of each trial. The most common definition of VAP was a new or persistent radiographic infiltrate plus fever, leukocytosis, change in the volume or color of sputum, or isolation of a pathogen. If available, histologic evidence of pneumonia was also used. A priori, due to the large number of published RCTs on antibiotic prophylaxis and selective decontamination of the digestive tract, and numerous high-quality systematic reviews, we considered only systematic reviews of RCTs for antibiotic prophylaxis. We excluded the following experimental designs: intervention crossover, before and after, and interrupted time series. We also excluded RCTs of ventilator weaning protocols, noninvasive mechanical ventilation, and nutritional interventions related to the prevention of VAP because guidelines addressing these topics have recently been published [24,25]. We did not include RCTs of stress ulcer prophylaxis

Table 1 Summary of recommendations for VAP prevention

<i>1.0 Physical strategies</i>		
1.1	Route of endotracheal intubation	We <i>recommend</i> that the orotracheal route of intubation should be used when intubation is necessary.
1.2	Systematic search for maxillary sinusitis	We make <i>no recommendation</i> .
1.3	Frequency of ventilator circuit changes	We <i>recommend</i> new circuits for each patient, and changes if the circuits become soiled or damaged, but no scheduled ventilator circuit changes.
1.4	Type of airway humidification	We make <i>no recommendation</i> .
1.5	Frequency of change of airway humidification	We <i>recommend</i> changes of heat and moisture exchangers with each patient, every 5-7 days and as clinically indicated.
1.6	Type of endotracheal suctioning system (open vs closed)	We <i>recommend</i> the use of closed endotracheal suctioning system.
1.7	Frequency of change of endotracheal suctioning system	We <i>recommend</i> closed endotracheal suctioning system be changed for each patient and as clinically indicated.
1.8	Subglottic secretion drainage	We <i>recommend</i> the use of subglottic secretion drainage in patients expected to be mechanically ventilated for > 72 h.
1.9	Timing of tracheostomy	We make <i>no recommendation</i> .
1.10	Bacterial filters	We <i>do not recommend</i> .
<i>2.0 Positional strategies</i>		
2.1	Rotating beds	The use of rotating beds <i>should be considered</i> .
2.2	Semirecumbent positioning	We <i>recommend</i> that the head of the bed be elevated to 45°. Where this is not possible, attempts to raise the head of the bed as much as possible should be <i>considered</i> .
2.3	Prone positioning	We make <i>no recommendation</i> .
<i>3.0 Pharmacological strategies</i>		
3.1a	Prophylactic antibiotics: aerosolized antibiotics	We make <i>no recommendation</i> .
3.1b	Prophylactic antibiotics: nasal antibiotics	We make <i>no recommendation</i> .
3.1c	Prophylactic antibiotics: intravenous antibiotics alone	We make <i>no recommendation</i> .
3.1d	Prophylactic antibiotics: topical/topical plus intravenous Antibiotics	We make <i>no recommendation</i> .
3.2a	Oral antiseptic: chlorhexidine	The use of the oral antiseptic chlorhexidine <i>should be considered</i> .
3.2b	Oral antiseptic: povidone-iodine	The use of the oral antiseptic povidone-iodine <i>should be considered</i> in patients with severe head injury.
3.2c	Oral antiseptic: iseganan	We <i>do not recommend</i> .
3.3	Prevention of maxillary sinusitis	We make <i>no recommendation</i> .

because this strategy is not designed to prevent VAP, although it may indirectly influence the incidence of VAP. We graded trials as level 1 if they demonstrated concealed randomization, blinded outcome adjudication, an intention-to-treat analysis, and an explicit definition of VAP. Trials were graded as level 2 if any one of these characteristics was unfulfilled and as level 3 if allocation was not strictly randomized. Level 3 trials were excluded from inclusion into this guideline.

In duplicate and independently, a pair of panel members critically appraised each trial [26,27] and systematic review [28]. Differences were resolved by consensus or independent adjudication by the chair of the panel. For each trial, we abstracted the outcomes of interest and for each intervention; we summarized the risk differences and calculated a pooled risk difference. For each systematic review, we abstracted number of trials, population, intervention, selection criteria, search strategy, validity assessment, method of pooling

results, homogeneity assessment, VAP definition, pooled event rates, and other outcomes. Panel members read all circulated documents and evidence tables in advance of an in-person panel meeting. By abiding by a specified group process, using levels of evidence and consensus methods, a draft recommendation was generated for each intervention reviewed [29]. At the panel meeting, each member disclosed any potential conflicts of interest [30].

Because of the large size of the panel (29) and the large number of RCTs to appraise, the evidence was first reviewed by a small working group and then by the whole panel. The pair of panel members responsible for critical appraisal of each intervention provided a structured written and oral presentation of the evidence to the working group. The working group members assigned levels of evidence, semiquantitative scores to summarize the evidence, and drafted a recommendation statement. The working group chair (PD) was responsible for ensuring it achieved its

Table 2 Semiquantitative scores for each intervention

Intervention	Effect size ^a	Confidence intervals ^b	Validity ^c	Homogeneity ^d	Safety ^e	Feasibility ^f	Cost ^g
1.1 Route of the endotracheal intubation	3	0	2	0	2	3	3
1.2. Systematic search for maxillary sinusitis	3	2	3	0	1	1	1
1.3 Frequency of ventilator circuit changes	0	0	2	3	3	3	3
1.4 Type of airway humidification	0	0	2	1	2	3	3
1.5 Frequency of change of airway humidification	1	0	2	1	2	3	3
1.6 Type of endotracheal suctioning system (open vs closed)	0	0	2	2	3	3	3
1.7 Frequency of change of endotracheal suctioning system	0	0	2	0	2	3	3
1.8 Subglottic secretion drainage	3	3	2	3	3	2	2
1.9 Timing of tracheotomy	2	0	1	0	2	2	1
1.10 Bacterial filters	1	0	2	0	2	2	2
2.1 Rotating beds	3	3	2	3	2	1	1
2.2 Semirecumbent positioning	3	0	3	0	2	1	2
2.3 Prone positioning	1	0	2	3	1	2	2
3.1.a Prophylactic antibiotics: aerosolized antibiotics	3	3	2	3	1	2	1
3.1.b Prophylactic antibiotics: nasal antibiotics	3	3	3	0	1	2	1
3.1.c Prophylactic antibiotics: intravenous antibiotics alone	3	3	2	0	1	2	1
3.1.d Prophylactic antibiotics: topical/topical plus intravenous antibiotics	3	3	2	0	1	2	1
3.2.a Oral decontamination: chlorhexidine	3	1	3	0	3	3	3
3.2.b Oral decontamination: povidone-iodine	3	3	3	0	3	3	3
3.2.c Oral decontamination: iseganan	2	0	3	0	2	2	2
4.1 Prevention of maxillary sinusitis	3	0	3	0	2	2	2

^a Validity: Internal validity of trial—concealed randomization, blinded outcome, an ITT analysis, and explicit definition of VAP. (Higher score = more features.)

^b Effect size: Magnitude of absolute risk reduction. (Higher score = larger effect size.)

^c Confidence interval around estimate of effect, 95% confidence interval of absolute risk reduction. (Higher score = smaller confidence intervals.)

^d Homogeneity of trial results: Similar direction among trials scored. (Higher score = similar results between trials.)

^e Safety: Probability of harm resulting from intervention. (Higher score = lower chance of harm.)

^f Feasibility: Ease of implementation of the intervention. (Higher score = greater ease of implementation.)

objectives through group process. Once the evidence summaries and recommendations were drafted, they were presented to a plenary session of the whole panel for discussion and modifications until consensus was reached.

For each intervention, we used a predefined semiquantitative scoring system for effect size, confidence intervals around the estimate of effect, validity, and homogeneity of trial results (Appendix B). Similar scores for safety, feasibility, and economic consequences of the interventions were developed based on consensus of the panel members. The language of the draft recommendation for each item was keyed to the level of evidence and the semiquantitative scores. We used the term *recommend* if there were no reservations about endorsing an intervention, and the term *consider* if the evidence supported an intervention but there were minor uncertainties about the benefits, harms, or costs. *No recommendation* was made if evidence regarding an intervention was inadequate or if there were major uncertainties about the benefits, harms, and costs. *Do not recommend* was used if there was no evidence of benefit and

there was potential for harm or increased healthcare costs from the intervention.

After the working group meeting and plenary panel meeting, the evidence summaries and draft recommendations were sent to all panel members to check for accuracy and clarity. The guideline chair (JM) organized the background documents, the evidence summaries, and a table of the evidence scores. In addition, a structured abstract was constructed [31].

After approval by the panel members, the draft guideline document was externally reviewed by the Boards of the Canadian Critical Care Society, the Canadian Critical Care Trials Group, the Canadian Association of Critical Care Nurses, the Canadian Society of Respiratory Therapists, the Canadian Association of Medical Microbiology and Infectious Disease, and the Canadian Thoracic Society. In addition, expert external international reviewers (Dr Andrew Shorr and Dr Christian Bruin-Bruissson) were asked to review the guideline. Each of the external societies and reviewers was asked to assess the guideline for logic,

Table 3 Agreement scores *

Recommendations	Mean (n = 29)	Median (n = 29)	Range
1.1 Route of the endotracheal intubation	8.8	9	5-9
1.2 Systematic search for maxillary sinusitis	8.5	9	5-9
1.3 Frequency of ventilator circuit changes	8.9	9	5-9
1.4 Type of airway humidification	8.4	9	5-9
1.5 Frequency of change of airway humidification	8.5	9	5-9
1.6 Type of endotracheal suctioning system (open vs closed)	8.3	9	5-9
1.7 Frequency of change of endotracheal suctioning system	8.8	9	5-9
1.8 Subglottic secretion drainage	8.4	9	5-9
1.9 Timing of tracheotomy	8.3	9	5-9
1.10 Bacterial filters	8.3	9	3-9
2.1 Rotating beds	8.0	8	5-9
2.2 Semirecumbent positioning	8.0	8	3-9
2.3 Prone positioning	8.3	9	4-9
3.1.a Prophylactic antibiotics: aerosolized antibiotics	8.0	9	3-9
3.1.b Prophylactic antibiotics: nasal antibiotics	7.8	9	3-9
3.1.c Prophylactic antibiotics: intravenous antibiotics alone	8.2	9	3-9
3.1.d Prophylactic antibiotics: topical /topical plus intravenous antibiotics	7.8	9	2-9
3.2.a Oral decontamination: chlorhexidine	7.7	9	1-9
3.2.b Oral decontamination: povidone-iodine	7.7	8	3-9
3.2.c Oral decontamination: isenegan	8.0	9	5-9
4.1 Prevention of maxillary sinusitis	7.9	9	4-9

* Agreement scores based on a Likert scale of 1 to 9 anchored by “disagree completely” at the low end and “agree completely” at the high end.

clarity, and practicality, and to critique the guideline development process. The panel revised the document based on this feedback.

Thereafter, each panel member was asked to score his or her level of agreement with the final recommendation statement for each item. Independently, blinded to each other’s ratings, panel members used a Likert scale from 1 to 9 that was anchored by “disagree completely” at the low end and “agree completely” at the high end. The panel will continuously review VAP literature and update this guideline every 2 years [32]. The funding sources played no role in the selection of RCTs for inclusion into this guideline and had no role in its development, review, reporting, approval, or submission for publication.

3. Results

The final evidence summaries and recommendations for each of the interventions are reported. The results are divided into physical strategies, positional strategies, and pharmacologic strategies, and are summarized in Table 1. The semiquantitative scores for each intervention are reported in Table 2 and the agreement scores are reported in Table 3.

4. Ventilator associated pneumonia: Prevention

4.1. Physical strategies

4.1.1. Route of endotracheal intubation

On the basis of 1 level 2 trial [33], we conclude that orotracheal intubation is associated with a trend toward a reduction in VAP compared to nasotracheal intubation.

Furthermore, this trial and 4 other level 2 trials have found that orotracheal intubation is associated with a decreased incidence of sinusitis and that incidence of VAP is lower in patients who do not develop sinusitis [34-37].

Recommendation: We recommend that the orotracheal route of intubation should be used when intubation is necessary.

4.1.2. Systematic search for maxillary sinusitis

On the basis of only 1 level 2 trial [38], we conclude that, although a systematic search for maxillary sinusitis in patients who are intubated by the nasotracheal route may decrease the incidence of VAP, no evidence supports this practice in patients who are intubated by the orotracheal route.

Recommendation: We make no recommendation.

4.1.3. Frequency of ventilator circuit changes

Based on 2 level 2 trials [39,40], we conclude that the frequency of ventilator circuit changes does not influence the incidence of VAP. Cost considerations favor less frequent changes.

Recommendation: We recommend new circuits for each patient, and changes if the circuits become soiled or damaged, but no scheduled ventilator circuit changes.

4.1.4. Airway humidification: type of humidifier

On the basis of 12 level 2 trials [41-52], we conclude that there is no difference in the incidence of VAP between patients whose airways are humidified using a heat and moisture exchanger and those whose airways are humidified using a heated humidifier.

Recommendation: We make no recommendation.

4.1.5. Airway humidification: frequency of humidifier changes

On the basis of 2 level 2 trials [53,54] that compared daily HME changes to HME changes at 5 or 7 days, we conclude

that less frequent HME changes may be associated with a slightly decreased incidence of VAP. Reduction in the frequency of humidifier changes might be considered as a cost-reduction measure.

Recommendation: We recommend changes of HMEs every 5 to 7 days or as clinically indicated.

4.1.6. Endotracheal suctioning system: closed vs open

On the basis of 6 level 2 trials [55-61], we conclude that the type of suctioning system has no effect on the incidence of VAP. Safety considerations (patient and healthcare worker exposure to aerosolized secretions) favor the use of closed systems.

Recommendation: We recommend the use of closed endotracheal suctioning system.

4.1.7. Endotracheal suctioning system: frequency of change

On the basis of 1 level 2 trial [62], we conclude that scheduled daily changes and unscheduled changes of closed systems have no effect on VAP. Cost considerations favor less frequent changes.

Recommendation: We recommend that closed endotracheal suctioning systems be changed for each patient and as clinically indicated.

4.1.8. Subglottic secretion drainage

Based on 5 level 2 trials [63-68], we conclude that subglottic secretion drainage is associated with a decreased incidence of VAP. The incremental cost of these tubes was considered to be reasonable given the burden of illness associated with VAP. To increase their utility and cost-effectiveness, these tubes should only be placed in patients expected to require prolonged mechanical ventilation. Given the increased availability of these tubes compared to when our first guideline was developed, this recommendation was now considered to be more feasible.

Recommendation: We recommend the use of subglottic secretion drainage in patients expected to be mechanically ventilated for more than 72 hours.

4.1.9. Timing of tracheostomy

Based on 4 level 2 trials [69-72], we conclude that there is no difference in the incidence of VAP between early and late tracheostomy. The methodological limitations of these trials (the unclear definition of VAP [69], numerous crossovers [70]) and the higher cost of an earlier tracheostomy were also noted by the committee [71-73].

Recommendation: We make no recommendation.

4.1.10. Bacterial filters

On the basis of 1 level 2 trial [74], we conclude that the use of bacterial filters does not influence the incidence of VAP. In addition, the use of bacterial filters does not influence ICU length of stay or duration of mechanical

ventilation but is associated with a trend toward an increase in mortality.

Recommendation: We do not recommend the use of bacterial filters.

4.2. Positional strategies

4.2.1. Kinetic bed therapy

Based on 7 level 2 trials [75-81], we conclude that the use of rotating beds is associated with a decreased incidence of VAP. However, feasibility, safety, and cost concerns may be barriers to implementation.

Recommendation: The use of rotating beds should be considered.

4.2.2. Semirecumbent positioning

On the basis of 1 level 1 [82] and 1 level 2 trial [83], we conclude that semirecumbent positioning may be associated with a decreased incidence of VAP. The absence of a treatment effect observed in the trial by van Nieuwenhoven et al [82] may have been due to an inability to achieve the intended elevation of 45°, raising concerns about the feasibility of achieving this degree of semirecumbency. Semirecumbent positioning may be unsafe for some patients.

Recommendation: We recommend that the head of the bed be elevated to 45°. When this is not possible, attempts to raise the head of the bed as near to 45° as possible should be considered.

4.2.3. Prone positioning

Based on 2 level 2 trials [84,85], we conclude that the use of prone positioning may be associated with a reduction in the incidence of VAP. However, feasibility and safety issues may be barriers to implementation.

Recommendation: We make no recommendation.

4.3. Pharmacologic strategies

4.3.1. Prophylactic antibiotics: aerosolized antibiotics

Based on 2 level 2 trials [86,87], we conclude that the use of aerosolized antibiotics may decrease the incidence of VAP. The use of aerosolized antibiotics has no effect on ICU mortality, ICU length of stay, or duration of mechanical ventilation. In addition, the panel considered the potential emergence of resistance to antibiotics in arriving at a recommendation.

Recommendation: We make no recommendation.

4.3.2. Prophylactic antibiotics: nasal antibiotics

Based on 1 level 1 trial [88], we conclude that the use of nasal mupirocin may decrease the incidence of VAP due to methicillin-resistant *Staphylococcus aureus* but has no effect on the overall incidence of VAP. Concerns about the emergence of resistance to antibiotics were raised by the panel.

Recommendation: We make no recommendation.

4.3.3. Prophylactic antibiotics: intravenous antibiotics alone

Based on 1 level 2 trial [89], we conclude that the use of prophylactic intravenous antibiotics alone may decrease the incidence of VAP but has no effect on mortality, ICU or hospital length of stay, or duration of mechanical ventilation. In addition, serious concerns were raised by the panel about the emergence of resistance to antibiotics.

Recommendation: We make *no recommendation*.

4.3.4. Prophylactic antibiotics: topical/topical plus intravenous antibiotics

Based on the most recent systematic review [90], 1 level 1 trial [91], and 1 level 2 trial [92], we conclude that the use of topical or topical plus intravenous antibiotics may decrease the incidence of VAP. However, inconsistent effects on mortality, length of stay (ICU and hospital), and mechanical ventilation were noted. In addition, serious concerns were raised about the emergence of resistance to antibiotics.

Recommendation: We make *no recommendation*.

4.3.5. Oral decontamination: chlorhexidine

Based on 1 level 1 and 2 level 2 trials [93-95], we conclude that the use of the oral antiseptic chlorhexidine may decrease the incidence of VAP. Safety, feasibility, and cost considerations for this intervention are all very favorable.

Recommendation: The use of the oral antiseptic chlorhexidine should be *considered*.

4.3.6. Oral decontamination: povidone-iodine

Based on 1 level 2 trial [96], in patients who have severe head injuries, we conclude that the use of the oral antiseptic povidone-iodine decreases the incidence of VAP in this population. Safety, feasibility, and cost considerations for this intervention are all very favorable. There are insufficient data to make a recommendation in critically ill patients other than those who have severe head injury.

Recommendation: The use of the oral antiseptic povidone-iodine should be *considered* in patients with severe head injury.

4.3.7. Oral decontamination: iseganan

Based on 1 level 2 trial [97], we conclude that the use of the oral antiseptic iseganan has no effect on the incidence of VAP.

Recommendation: We *do not recommend* the use of iseganan.

4.3.8. Prevention of maxillary sinusitis

Based on 1 level 2 trial [98], we conclude that the prevention of maxillary sinusitis by xylometazoline nasal drops followed by budesonide spray decreases the incidence of maxillary sinusitis without decreasing the incidence of VAP.

Recommendation: We make *no recommendation*.

5. Discussion

Ventilator associated pneumonia continues to be a cause of significant morbidity and mortality in critically ill patients [99], and the literature on VAP prevention continues to evolve. To synthesize the growing research evidence on VAP prevention, thereby aiding in knowledge transfer, we developed this CPG. Guidelines require periodic updates to reflect current knowledge [19]; accordingly, the recommendations in this article reflect an update of our prior work [18] after reviewing evidence incorporated in the previous guideline and considering new evidence published between 2003 and October 1, 2006. Important changes in the recommendations based on recent trials and the totality of evidence to date are as follows: no recommendation regarding type of humidification, strengthening the recommendation regarding subglottic secretion drainage, a proviso added to the recommendation about semirecumbent positioning, and new recommendations regarding oral antiseptic agents. We continue to make no recommendation regarding prophylactic antibiotics in view of theoretical concerns about the emergence of resistant bacteria despite the apparent benefit in terms of lower VAP rates. We make no recommendations about interventions for which there was insufficient evidence.

Strengths of this guideline include the detailed, explicit processes used to search, select, and appraise the evidence [100]; use of a multidisciplinary and multispecialty panel; and a balance of university-based and community-based clinicians. To improve the transparency of guideline development and strengthen the evidence upon which they are based, we incorporated only evidence from RCTs or systematic reviews of RCTs [101,102]. The evidence for each intervention was scored on trial validity, effect size, homogeneity, and confidence intervals using quantitative measures (Appendix B). The safety, cost, and feasibility of each intervention were scored similarly based on consensus of the panel members. External reviewers included representatives from nursing, respiratory therapy, respirology, infectious diseases, and critical care. We used a transparent method to grade the evidence and a final score to reflect the panelists' confidential agreement with each final recommendation [103]. By following this process, these guidelines meet the strict proposed quality and methodological criteria proposed in the literature [104-106].

The agreement scores (Table 3) for the recommendations indicate a high level of agreement by the large (n = 29) multidisciplinary and multi-specialty panel. This is a product of the group consensus used to arrive at the recommendations and forms the basis for a multidisciplinary approach to the prevention of VAP that includes representation of all members of ICU care teams.

For areas lacking strong RCT evidence, we avoided making recommendations, thereby highlighting the need for further high-quality research in these areas. In the absence of formal evidence-based recommendations for these select

aspects of VAP prevention, clinicians will need to rely upon judgment and expert opinion to guide clinical practice.

This guideline has several limitations. First, our reliance on high-quality RCT evidence for VAP prevention means that we did not generate recommendations for certain fundamental practices about which observational data exist (eg, hand hygiene). Second, the safety, feasibility, and costs of each intervention were graded qualitatively by the panel using their values and judgment; panels with different compositions and values may generate different recommendations. Our panel was formed predominantly by Canadian members, who work chiefly within the Canadian critical care context. Therefore, although these recommendations were based upon a rigorous and transparent evaluation of the international literature, these recommendations reflect our target audience and practice setting. In keeping with the trend toward one universal system to generate clinical recommendations, we plan to use the recently proposed GRADE approach for our next guideline update [107].

Although there is abundant research evidence that VAP is preventable, at least in part, gaps in our understanding exist, as exemplified by our inability to make recommendations related to some interventions. More research is required in areas in which there is a paucity of high-level research evidence. For example, the long-term impact of VAP prevention practices on the microbial ecology of ICUs and antibiotic resistance patterns needs to be further delineated. In addition, even with high-grade evidence and strong recommendations, the challenge is to apply best research evidence into clinical practice. Prior Canadian studies have demonstrated deficiencies in the adoption of strategies shown to decrease the incidence of VAP, underscoring important opportunities to improve VAP prevention practices [108,109]. Further knowledge translation efforts and original research are required to reduce the morbidity and mortality of VAP in the complex environment of the ICU setting.

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Appendix A. Search Strategies for the Databases

Search Strategy for CINAHL database

Database: CINAHL—Cumulative Index to Nursing & Allied Health Literature <1982 to October Week 1 2006>

Search Strategy:

1. exp Pneumonia/
2. Cross Infection/
3. exp Ventilation, Mechanical/
4. Ventilators, Mechanical/
5. 1 and 2 and (3 or 4)
6. (vap and pneumonia\$).mp. [mp=title, cinahl subject headings, abstract, instrumentation] (79)
7. "ventilator associated pneumonia\$".mp. [mp=title, cinahl subject headings, abstract, instrumentation]
8. "ventilator acquired pneumonia\$".mp. [mp=title, cinahl subject headings, abstract, instrumentation]
9. 5 or 6 or 7 or 8
10. limit 9 to (yr=1980-2006 and journal article)

Search Strategy for MEDLINE database

1. exp PNEUMONIA/
2. Cross Infection/
3. Respiration, Artificial/
4. exp Ventilators, Mechanical/
5. 1 and 2 and (3 or 4)
6. (vap and pneumonia\$).mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
7. "ventilator associated pneumonia\$".mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
8. "ventilator acquired pneumonia\$".mp. [mp=title, original title, abstract, name of substance, mesh subject heading]
9. 5 or 6 or 7 or 8
10. limit 9 to (human and yr=1980-2006 and journal article)

Search Strategy for COCHRANE database

Cochrane Register of Controlled Trials

1. vap.ti.
2. (ventilat\$ and associat\$ and pneumonia\$).ti.
3. (ventilat\$ and acquire\$ and pneumonia\$).ti.
4. 1 or 2 or 3
5. from 4 keep 1-52

Database: EBM Reviews—Cochrane Database of Systematic Reviews <3rd

Quarter 2006> Search Strategy:

1. (vap and pneumonia\$).mp.
2. "ventilator associated pneumonia\$".mp.
3. "ventilator acquired pneumonia\$".mp.
4. 1 or 2
5. from 4 keep 1-9

Search Strategy for Embase database

Database: EMBASE <1980 to 2006 Week 41>
Search Strategy:

1. exp PNEUMONIA/
2. Hospital Infection/
3. exp artificial ventilation/
4. ventilator/
5. 1 and 2 and (3 or 4)
6. (vap and pneumonia\$).mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]
7. "ventilator associated pneumonia\$".mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]
8. "ventilator acquired pneumonia\$".mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]
9. 5 or 6 or 7 or 8
10. limit 9 to (human and yr=1980-2006)
11. limit 10 to (book or editorial or erratum or letter or note)
12. 10 not 11

Appendix B. Definitions of Semi-quantitative Scores

Range of values for score: assign 0, 1, 2, and 3 according to rules below

Treatment effect

For treatment effect need to have RR = relative risk from meta-analysis graph or can be calculated. Relative risk ratio (RRR) = $RR (Relative\ risk) - 1$.

If relative risk (RR) is	then RRR is	Score should be
0.9-1.0	<10%	0
0.8-0.9	10%-20%	1
0.7-0.8	21%-30%	2
<0.7	>30%	3

Example: If RR is 0.95 then $RRR = (RR - 1) = 0.95 - 1.0 = -0.05 = 5\% = \text{score } 0$.

Example: If RR is 0.45 then $RRR = (RR - 1) = 0.45 - 1 = -0.55 = 55\% = \text{score } 3$.

Confidence intervals

Rate according to the *P* value of the treatment effect

If the <i>P</i> value is	Score CI as
>.1	0
0.1-0.051	1
0.05-0.01	2
<.01	3

Validity of included trials

If 10-12 (none of ITT, concealed randomization, blinded missing), then 3+

If 6-9 (one is missing), then 2+

If <6 (more than 1 missing), then 1+

Homogeneity

Based on the interclass correlation (\hat{P}) score derived from the meta-analysis plots. For single studies, homogeneity was scored as 0.

If \hat{P} score is	Score homogeneity as
<10%	3
10%-30%	2
31%-50%	1
>50%	0

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