



# Getting Started Kit: Prevent Ventilator-Associated Pneumonia Bibliography

## ***Safer Healthcare Now!***

We invite you to join the *Safer Healthcare Now!* Campaign (SHN) to help improve the safety of our healthcare system in Canada. *Safer Healthcare Now!* is a campaign to enlist Canadian healthcare organizations in implementing six targeted interventions in patient care. The campaign is supported by the Institute for Healthcare Improvement (IHI) and is patterned after IHI's *100,000 Lives* Campaign. Further details, including materials, contact information and discussions are available at

<http://www.saferhealthcarenow.ca>

These kits, based on those originally developed by IHI for its *100,000 Lives* Campaign, are designed to engage your teams and clinicians in a dynamic approach for quality improvement, and to provide a thorough basis for *getting started*. **Please note that although the SHN kits and the original kits developed by IHI are similar, there are also key differences in the content of the interventions and corresponding measures for some kits.** These differences are clearly noted in the body of the SHN kits themselves, and on the SHN website.

The information in these "Getting Started" kits is based on the current state of knowledge. Consistent with the dynamic nature of this campaign, which continues to evolve, emerging evidence may influence adaptation of the kits in the future. We remain open to working consultatively on updating the content as together we make healthcare safer in Canada.

## **Acknowledgement**

We wish to thank and acknowledge the Institute for Healthcare Improvement (IHI) for their significant support and contributions to the *Safer Healthcare Now!* Campaign.

The references included in this Bibliography are those contained in the bibliography for IHI's 100K Lives Campaign, with additional references identified by SHN.

## **BIBLIOGRAPHY – PREVENT VENTILATOR ASSOCIATED PNEUMONIA**

American Thoracic Society. Guidelines for the management of adults with hospital acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med.* 2005;171(4):388-416.

Updated guidelines from the American Thoracic Society and the Infectious Diseases Society of America. Although these guidelines focus on treatment of established ventilator-associated pneumonia, there is also an up-to-date discussion of modifiable risk factors and a series of recommendations for practices that will reduce the risk; these include use of protocols to improve sedation use and to accelerate weaning and nursing patients in the semi recumbent position.

Attia J, Ray JG, Cook DJ, Douketis J, Ginsberg JS, Geerts WH. Deep vein thrombosis and its prevention in critically ill adults. *Arch Intern Med.* 2001;161:1268-1279.

The authors conducted a systematic review of studies referenced in MEDLINE, EMBASE, abstract databases, and the Cochrane database, to determine the incidence of deep venous thrombosis (DVT) and the efficacy of prophylaxis in critically ill adults, including patients admitted to ICUs and following trauma, neurosurgery, or spinal cord injury. They found that 1) 10-30% of medical and surgical ICU patients develop DVT within the first week of ICU admission and 2) the use of subcutaneous low-dose heparin reduces the rate by 50% compared with no prophylaxis.

Babcock HM, Zack JE, Garrison T, Trovillion E, Jones M, Fraser VJ and Kollef MH . Educational Intervention to Reduce Ventilator-Associated Pneumonia in an Integrated Health System. A Comparison of Effects. *Chest.* 2004;125:2224-2231.

An observational study in 4 hospitals before and after implementation of a 10-page educational self-study modular educational program on best practice for prevention of ventilator-associated pneumonia. Rates of ventilator-associated pneumonia fell overall, but no reduction in rate was seen in the hospital with the lowest rate of module completion amongst respiratory therapists.

Center for disease Control and Prevention. Guidelines for preventing health-care-associated pneumonia, 2003 recommendations of the CDC and the Healthcare Infection Control Practices Advisory Committee. *Respir Care.* 2004;49(8):926-39.

This is an abridged version of the full CDC guidelines (see Tablan et al, below), and includes correction of errata in that report.

Collard HR, Saint S. Chapter 17: Prevention of Ventilator-Associated Pneumonia. IN: Agency for Healthcare Research and Quality. *Making health care safer: a critical analysis of patient safety practices.* <http://www.ahrq.gov/clinic/evrptfiles.htm#ptsafety>. Accessed 19 January 2005.

A detailed literature review, performed by the University of California at San Francisco (UCSF)-Stanford University Evidence-Based Practice Center, of published research on prevention of ventilator-associated pneumonia, sponsored by AHRQ and published in July 2001.

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Cook DJ, Fuller HD, Guyatt GH, Marshall JC, Leasa D, Hall R, Winton TL, Rutledge F, Todd T, Roy P, Lacroix J, Griffith L, Willan A for The Canadian Critical Care Trials Group. Risk factors for gastrointestinal bleeding in critically ill patients. *N Engl J Med.* 1994;330:377-381.

The authors describe a prospective multicenter cohort study evaluating risk factors for the development of stress ulceration among patients admitted to ICUs. They also document the incidence of “clinically important” gastrointestinal (GI) bleeding. Both respiratory failure (odds ratio (OR) 15.6) and coagulopathy (OR 4.3) were associated with clinically important GI bleeding. The authors conclude that prophylaxis against stress ulcers can safely be withheld from critically ill patients unless they have coagulopathy or require mechanical ventilation.

Cook DJ, Guyatt G, Marshall J, Leasa D, Fuller H, Hall R, Peters S, Rutledge F, Griffith L, McLellan A, Wood G and Kirby A for The Canadian Critical Care Trials Group. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. *N Engl J Med.* 1998;338:791-797.

The authors describe a multicenter, randomized, blinded, placebo-controlled trial, comparing sucralfate with the H<sub>2</sub>-receptor antagonist ranitidine for the prevention of upper GI bleeding in 1,200 patients who required mechanical ventilation. Patients receiving ranitidine had a significantly lower rate of clinically important GI bleeding than those treated with sucralfate. There were no significant differences in the rates of ventilator-associated pneumonia, the duration of the stay in the ICU, or mortality.

Cook D, Heyland, Griffith L, Cook R, Marshall J, Pagliarello J for The Canadian Critical Care Trials Group. Risk factors for clinically important upper gastrointestinal bleeding in patients requiring mechanical ventilation. *Crit Care Med.* 1999;27:2812-2817.

This paper describes a randomized controlled trial involving 16 university-affiliated ICUs in Canada. The authors assessed the relative impact of intravenous ranitidine and nasogastric sucralfate on the incidence of clinically important GI bleeding among 1,077 critically ill patients who received mechanical ventilation for at least 48 hours. Prophylaxis with ranitidine but not sucralfate was associated with a reduction in GI bleeding.

Cook DJ, Reeve BK, Guyatt GH, Heyland DK, Griffith LE, Buckingham L and Tryba M. Stress ulcer prophylaxis in critically ill patients: resolving discordant meta-analyses. *JAMA.* 1996;275:308-314.

The authors report a meta-analysis of 63 randomized trials of stress ulcer prophylaxis in critically ill patients. They find “strong evidence” of a reduction in clinically important GI bleeding with H<sub>2</sub>-receptor antagonists. They also find that sucralfate may be as effective in reducing bleeding as pH-altering drugs and is associated with lower rates of pneumonia and mortality. However, they note that the data are insufficient to determine the net effect of sucralfate compared with no prophylaxis.

Craven DE, Steger KA. Nosocomial pneumonia in mechanically ventilated adult patients: epidemiology and prevention in 1996. *Semin Respir Infect.* 1996;11(1):32-53.

Review of the epidemiology and causative factors for ventilator-associated pneumonia, concluding that aspiration of gastric contents is a major risk factor.

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Dellinger RP, Carlet J, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, Keh D, Marshall JC, Parker MM, Ramsay G, Zimmerman J, Vincent JL, Levy M for the Surviving Sepsis Campaign Management Guidelines Committee. Surviving Sepsis Campaign: guidelines for management of severe sepsis and septic shock. *Crit Care Med.* 2004;32(3):858-873.

Clinical practice guideline from the Society of Critical Care Medicine on the care of critically ill patients with sepsis. Includes guidance on stress ulcer prophylaxis and prophylactic anticoagulation. Available at [http://www.sccm.org/professional\\_resources/guidelines/table\\_of\\_contents/Documents/FINAL.pdf](http://www.sccm.org/professional_resources/guidelines/table_of_contents/Documents/FINAL.pdf)

Dezfulian C, Shojania K, Collard HR, Kim HM, Matthay MA, Saint S. Subglottic secretion drainage for preventing ventilator-associated pneumonia: a meta-analysis. *The American Journal of Medicine.* 2005;118:11-18.

A comprehensive, systematic meta-analysis of randomized trials (5) that have compared subglottic secretion drainage with standard endotracheal tube care in mechanically ventilated patients. Studies were identified by a computerized database search, review of bibliographies, and expert consultation. Summary risk ratios or weighted mean differences with 95% confidence intervals were calculated for each outcome using a fixed-effects model.

Dodek P, Keenan S, Cook D, Heyland D, Jacka M, Hand L, Muscedere J, Foster D, Mehta N, Hall R, Brun-Buisson C, for the Canadian Critical Care Trials Group and the Canadian Critical Care Society. Evidence-based clinical practice guideline for the prevention of ventilator-associated pneumonia. *Ann Intern Med.* 2004;141(4):305-313.

A clinical practice guideline written by the Joint Planning Group of the Canadian Critical Care Trials Group and the Canadian Critical Care Society. The guidelines were generated after a systematic search of MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews for all relevant randomized controlled trials that involved mechanically ventilated adults published up until 1 April 2003.

Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogue S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomized trial. *Lancet.* 1999;354(9193):1851-1858.

Randomized controlled trial in 86 mechanically ventilated patients assigned to semi-recumbent or supine body position demonstrating the excess risk of ventilator-associated pneumonia associated with supine position.

Fernandez-Crehuet R, Diaz-Molina C, de Irala J, Martinez-Concha D, Salcedo-Leal I, Masa-Calles J. Nosocomial infection in an intensive-care unit: identification of risk factors. *Infect Control Hosp Epidemiol.* 1997;18:825-830.

The authors describe a cohort study identifying risk factors for nosocomial infection among patients admitted to the ICU of a tertiary-level hospital for at least 24 hours. Two factors were associated with an increased risk of nosocomial infection: head of the bed in a horizontal (<30 degrees) position and use of sedative medication.

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Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*. 2004;126(3 Suppl):338S-400S.

A clinical practice guideline issued as part of the Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy: Evidence-based Guidelines. The recommendations cover patients undergoing surgery, trauma patients, acutely ill medical patients, and patients admitted to the intensive care unit.

Heyland D, Cook DJ, Griffith L, Keenan SP and Brun-Buisson C for The Canadian Critical Care Trials Group. The Attributable Morbidity and Mortality of Ventilator-Associated Pneumonia in the Critically Ill Patient. *Am. J. Respir. Crit. Care Med*. 1999;159:1249-1256.

A prospective, matched cohort study to evaluate the morbidity and mortality attributable to ventilator-associated pneumonia (VAP) in intensive care unit (ICU) patients expected to be ventilated for 48 h. To determine the excess ICU stay and mortality attributable to VAP, patients with VAP were matched to patients who did not develop clinically suspected pneumonia. A sensitivity analyses to examine the effect of different populations, onset of pneumonia, diagnostic criteria, causative organisms, and adequacy of empiric treatment on the outcome of VAP was also conducted.

Holzapfel L, Chastang C, Demingeon G, Bohe J, Piralla B, Coupry A. A randomized study assessing the systematic search for maxillary sinusitis in nasotracheally mechanically ventilated patients. Influence of nosocomial maxillary sinusitis on the occurrence of ventilator associated pneumonia. *Am J Respir Crit Care Med*. 1999;159:695–701.

The objective of this randomized study was to compare the occurrence of nosocomial pneumonia in nasotracheally intubated patients who were randomly allocated either to a systematic search of sinusitis by CT scan (study group) or not (control group). A total of 399 patients were included. In the study group, sinus CT scans were performed in case of fever at Days 4 and 8 and then every 7 d. Criteria for nosocomial sinusitis and pneumonia were defined a priori. Patients with sinusitis received sinus lavage and intravenously administered antibiotics. The authors concluded that the occurrence of VAP in patients undergoing prolonged mechanical ventilation via a nasotracheal intubation could be prevented by the systematic search and treatment of nosocomial sinusitis.

Holzapfel L, Chevret S, Madinier G, Ohen F, Demingeon G, Coupry A, Chaudet M. Influence of long-term oro- or nasotracheal intubation on nosocomial maxillary sinusitis and pneumonia: results of a prospective, randomized, clinical trial. *Crit Care Med*. 1993;Aug;21(8):1132-8.

A randomized, clinical trial was performed in a general adult intensive care unit (ICU) of a non teaching public hospital to compare the occurrence rate of nosocomial maxillary sinusitis and pneumonia in patients who have undergone nasotracheal vs. orotracheal intubation. A total of 300 patients were included. Patients were randomized between nasal and oral endotracheal intubation. Gastric intubation was performed via the same route as endotracheal intubation. Sinus computed tomography (CT) scans were performed every 7 days or earlier in case of fever and/or purulent nasal discharge. Criteria for nosocomial sinusitis and pneumonia were defined a priori.

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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(2):555-561.

Prospective, single-center cohort study over 22 months of the risk factors for and mortality from ventilator-associated pneumonia in a medical and surgical ICU in a 500-bed community hospital.

Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET, Chalfin DB, Masica MF, Bjerke HS, Coplin WM, Crippen DW, Fuchs BD, Kelleher RM, Marik PE, Nasraway SA Jr, Murray MJ, Peruzzi WT, Lumb PD; Task Force of the American College of Critical Care Medicine (ACCM) of the Society of Critical Care Medicine (SCCM), American Society of Health-System Pharmacists (ASHP), American College of Chest Physicians. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med*. 2002;30(1):119-141.

A clinical practice guideline prepared by the American College of Critical Care Medicine of the Society for Critical Care Medicine, and available at [http://www.sccm.org/professional\\_resources/guidelines/table\\_of\\_contents/Documents/Sedatives.pdf](http://www.sccm.org/professional_resources/guidelines/table_of_contents/Documents/Sedatives.pdf). It gives detailed recommendations for ensuring adequate sedation and analgesia for patients on the ICU.

Kollef MH. Ventilator-associated pneumonia. A multivariate analysis. *JAMA*. 1993;270:1965-1970.

This paper describes a cohort study of patients admitted to any of three ICUs in an academic tertiary care center who required mechanical ventilation for longer than 24 hours. Stepwise logistic regression analysis identified four factors that were independently associated with risk of VAP: organ system failure, patient age  $\geq 60$  years, impaired functional status prior to hospitalization, and supine head positioning ( $<30$  degrees of elevation) during the first 24 hours of mechanical ventilation.

Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med*. 2000;342(20):1471-1477.

Randomized controlled trial in 128 adult patients on mechanical ventilation, randomized to daily interruption of sedation irrespective of clinical state or interruption at the clinician's discretion. Daily interruption resulted in a marked and highly significant reduction in time on mechanical ventilation.

MacIntyre NR, Cook DJ, Ely EW Jr, Epstein SK, Fink JB, Heffner JE, Hess D, Hubmayer RD, Scheinhorn DJ; American College of Chest Physicians; American Association for Respiratory Care; American College of Critical Care Medicine. Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. *Chest*. 2001;120(6 Suppl):375S-395S.

A clinical practice guideline, available at [http://www.sccm.org/professional\\_resources/guidelines/table\\_of\\_contents/Documents/Chest-Weaning.pdf](http://www.sccm.org/professional_resources/guidelines/table_of_contents/Documents/Chest-Weaning.pdf), giving detailed recommendations on weaning patients from mechanical ventilation. The paper reviews the evidence that unnecessary delays in weaning increase the complication rate for mechanical ventilation, including pneumonia, as well as the cost. The guidelines draw on an AHRQ-sponsored summary of the literature published in 1999 by the McMaster University Evidence-Based Practice Center.

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Orozco-Levi M, Torres A, Ferrer M, Piera C, el-Ebiary M, de la Bellacasa JP, Rodriguez-Roisin R. Semi recumbent position protects from pulmonary aspiration but not completely from gastroesophageal reflux in mechanically ventilated patients. *Am J Respir Crit Care Med*. 1995;152:1387-1390.

The authors instilled Tc<sup>99</sup> sulphur colloid into the stomachs of 15 patients receiving mechanical ventilation who also had an ng tube in place. Scintigraphic radioactivity counting was performed hourly to identify the presence of gastric contents in oropharyngeal and bronchial secretions. Patients were studied in two positions: supine and semi recumbent (head of bed elevated **45** degrees). At 5 hours gastric contents were present in the oropharynx of patients in both groups. However, gastric contents were present in the bronchial secretions of only those patients who were in the supine position.

Rello J, Lorente C, Bodi M, Diaz E, Ricart M, Kollef MH. Why do physicians not follow evidence-based guidelines for preventing ventilator-associated pneumonia? A survey based on the opinions of an international panel of intensivists. *Chest*. 2002;122:656-661.

This paper describes the findings of a survey of 110 "opinion leaders on VAP" from 22 countries. Respondents were asked to indicate which of 33 evidence-based interventions for the prevention of VAP had been implemented in their ICUs. While the overall implementation rate was reported to be only 80.4%, reported implementation rates were higher for those interventions with better evidence regarding effectiveness, including semi recumbent positioning (91.8%) and removal of the endotracheal tube as soon as clinically feasible (100%). The most common reasons for non adherence were reported to be disagreement with interpretation of clinical trials, unavailability of resources, and costs.

Rello J, Ollendorf DA, Oster G, Vera-Llonch M, Bellm L, Redman R, Kollef MH; VAP Outcomes Scientific Advisory Group. Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. *Chest*. 2002;122(6):2115-2121.

Retrospective matched cohort study from a large US inpatient database examining risk factors for, and the mortality, duration of ventilation, and cost associated with ventilator-associated pneumonia.

Rouby JJ, Laurent P, Gosnach M, Cambau E, Lamas G, Zouaoui A, Leguillou JL, Bodin L, Khac TD, Marsault C. Risk factors and clinical relevance of nosocomial maxillary sinusitis in the critically ill. *Am J Respir Crit Care Med* 1994;150:776-783.

The incidence of infectious maxillary sinusitis (IMS) and its clinical relevance was prospectively studied in 162 consecutive critically ill patients who were mechanically ventilated for a period longer than 7 d. Risk factors for RMS were nasal placement and duration of endotracheal and gastric intubation.

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Shorr AF and O'Malley PG. Continuous Subglottic Suctioning for the Prevention of Ventilator-Associated Pneumonia: Potential Economic Implications. *Chest*. 2001;119:228–235.

Determination of the cost-effectiveness of continuous subglottic suctioning (CSS) as a strategy to decrease the incidence of ventilator-associated pneumonia (VAP) using a decision-model analysis of the cost and efficacy of endotracheal tubes (ETs) allowing CSS. The primary outcome was cases of VAP averted. Model estimates were based on data from published prospective trials of CSS and other prospective studies of the incidence of VAP. A hypothetical cohort of 100 patients requiring nonelective endotracheal intubation and management in an ICU was used and patients were managed with either traditional ETs or ETs capable of CSS.

Smulders K, van der Hoeven H, Weers-Pothoff I, Vandenbroucke-Grauls C. A randomized clinical trial of intermittent subglottic secretion drainage in patients receiving mechanical ventilation. *Chest*. 2002;121:858–862.

One hundred fifty patients with an expected duration of mechanical ventilation > 72 h were randomly assigned to receive either an endotracheal tube for intermittent subglottic secretions drainage or a standard endotracheal tube in a single 12 bed ICU. Incidence of VAP, duration of mechanical ventilation, length of ICU stay, length of hospital stay, and mortality were analyzed.

Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R. Guidelines for preventing health-care-associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *MMWR Recomm Rep*. 2004;53(RR-3):1-36.

This is a 179-page document, available at [http://www.cdc.gov/ncidod/hip/guide/CDCpneumo\\_guidelines.pdf](http://www.cdc.gov/ncidod/hip/guide/CDCpneumo_guidelines.pdf), which gives definitive guidance on prevention of all types of health-care associated pneumonia, including ventilator-associated pneumonia.

Torres A, Serra-Batlles J, Ros E, Piera C, Puig de la Bellacasa J, Cobos A, Lomena F, Rodriguez-Roisin R. Pulmonary aspiration of gastric contents in patients receiving mechanical ventilation: the effect of body position. *Ann Intern Med*. Apr 1 1992;116(7):540-543.

Randomized cross-over study of 19 patients on mechanical ventilation. Tc99m sulphur colloid labeling of stomach contents was performed, followed by sequential radioactivity counts in endobronchial secretions over a 5h period. Patients were randomized to the prone position or semi-recumbency and studied 12h later; the study was repeated 48h later with the patient in the alternate position. Radioactive counts were higher, indicating aspiration of gastric contents, in the prone position, and increased over time.

Task Force on Guidelines. Guidelines for standards of care for patients with acute respiratory failure on mechanical ventilatory support. Task Force on Guidelines; Society of Critical Care Medicine. *Crit Care Med*. Feb 1991;19(2):275-278.

This is one of a series of guidelines published by the Task Force on Guidelines of the Society of Critical Care Medicine and is available at [http://www.sccm.org/professional\\_resources/guidelines/table\\_of\\_contents/Documents/Acute\\_Respiratory\\_Failure.pdf](http://www.sccm.org/professional_resources/guidelines/table_of_contents/Documents/Acute_Respiratory_Failure.pdf). It specifies a number of minimum standards for the care of critically ill patients on mechanical ventilation, including personnel, monitoring equipment, support services, and equipment. There is a brief discussion of clinical management, but no discussion of the supporting evidence.

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Valles J, Artigas A, Rello J, Bonsoms N, Fontanals D, Blanch L, Fernandez R, Baigorri F, Mestre J. Continuous Aspiration of Subglottic Secretions in Preventing VAP. *Annals of Internal Medicine*. 1995; 122(3);179-186.

This is the first randomized, controlled, blinded study to determine whether continuous subglottic aspiration prevents nosocomial pneumonia in mechanically ventilated patients in a medical-surgical intensive care unit with an expected duration of intubation of greater than 72 hours. 76 patients were randomly allocated to receive continuous aspiration of subglottic secretions, and 77 control patients were allocated to receive usual care. The incidence rate of ventilator-associated pneumonia was 19.9 episodes/1000 ventilator days in the patients receiving continuous aspiration of subglottic secretions and 39.6 episodes/1000 ventilator days in the control patients.