Ventilator associated events, conditions and prevention of VAP

Dr .Pratap Upadhya

- Introduction
- Pathogenesis of vap
- Diagnosis of vap
- Ventilator-Associated Events: New Terminology and Its Relationship to VAP
- Prevention of vap

Mechanical ventilation is an essential, life-saving therapy for patients with critical illness and respiratory failure.

These patients are at high risk for complications and poor outcomes, including death.

Chest 2000;118:1100-5.

N Engl J Med 2006;355:41-50

Crit Care Med 2010;38:1947-53.

Ventilator-associated pneumonia (VAP), sepsis, Acute Respiratory Distress Syndrome (ARDS), pulmonary embolism, barotrauma, and pulmonary edema are among the complications that can occur in patients receiving mechanical ventilation

N Engl J Med 2005;353:1685-93

Surveillance for ventilator-associated events in the National Healthcare Safety Network (NHSN) prior to 2013 was limited to VAP.

For the year 2012, VAP incidence for various types of hospital units ranged from 0.0-4.4 per 1,000 ventilator days

Am J Infect Control 2013;41:1148-66.

There is currently **no** valid, reliable definition for VAP, and even the most widely-used VAP criteria and definitions are neither sensitive nor specific

JAMA 2007;297:1583-93

Am J Infect Control 2010;38:237-9

Clin Infect Dis 2008;46:1443-6

Clin Infect Dis 2010;51 Suppl 1:S131-5

Pathogenesis of vap

Ventilator-associated pneumonia (VAP) is an infection of the lower respiratory tract associated with endotracheal intubation and which causes significant morbidity and mortality in the intensive care unit (ICU).

JAMA. 1995;274(8):639–44.

Approximately 10 % of ventilated patients will develop the disease, with the risk of VAP rising as the duration of mechanical ventilation increases reaching a maximum on day 5 post-intubation

Ann Intern Med. 1998;129(6):433–40

VAP is associated with significant morbidity as it significantly increases the length of stay in the ICU, the duration of mechanical ventilation and hospital stay

Crit Care Med. 2005;33(10):2184–93

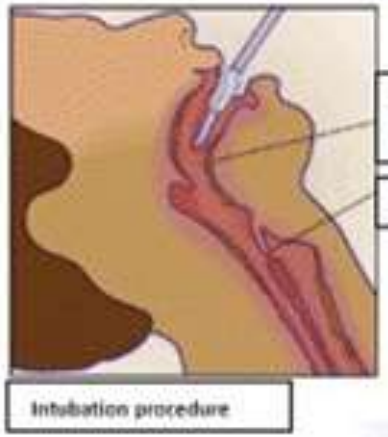
VAP has longitudinal deleterious effects at the level of the individual patient, leading to the increased utilization of the health care system after ICU, further increasing the economic burden of this disease

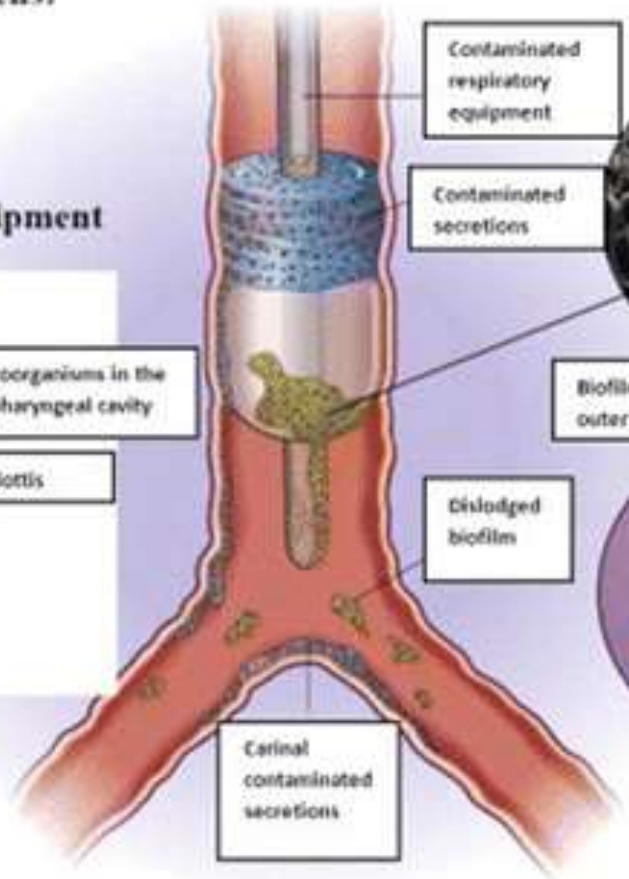
BMC Health Serv Res. 2011;11:289

Pathogenesis of VAP

Common Sources of VAP Pathogens:

- ❑ **Aspiration**
- ❑ **Intubation Procedure**
- ❑ **Biofilm Formation**
- ❑ **Contaminated Secretions**
- ❑ **Contaminated respiratory equipment**





The pathophysiology of VAP is mediated largely by the **introduction of a foreign body,** the endotracheal tube (ETT), into the upper airway This subverts the patient's natural mechanisms for preventing access of microorganisms to the lower respiratory tract.

Crit Care. 2011;15(5):310

Critically ill patients have impaired innate and adaptive immunity

Br J Anaesth. 2013;111(5):778–87

Diagnosis of VAP

The clinical diagnosis of VAP has included a combination of the following:

- clinical symptoms/signs,
- chest radiography, and
- microbiological data

JAMA. 2007;297(14):1583–93

Antimicrob Resist Infect Control. 2012;1(1):28

Respir Care. 2013;58(6):990–1007

Table 1. Centers for Disease Control Diagnosis of Pneumonia

- Radiology
  - Two or more serial chest radiographs with at least one of the following:
    - New or progressive infiltrate
    - Consolidation
    - Cavitation
- Signs/symptoms
  - At least one of the following:
    - Fever (> 38°C)
    - Leukopenia (< 4,000 white blood cells/mL) or leukocytosis (≥ 12,000 white blood cells/mL)
    - Altered mental status, if age ≥ 70 y
  - At least two of the following:
    - New purulent sputum (≥ 25 neutrophils and ≤ 10 squamous epithelial cells per low power field [× 100]) or change in sputum characteristics or amount
    - New or worsening cough, dyspnea, tachypnea
    - Rales
    - Worsening gas exchange
- Microbiology
  - At least one of the following:
    - Positive quantitative culture from minimally contaminated lower respiratory tract specimen. Specimen obtained via endotracheal suctioning is not a minimally contaminated specimen and therefore does not meet the laboratory criteria.
    - Positive culture of pleural fluid
    - Positive culture on lung tissue histological exam
    - Positive growth in blood culture not related to another source of infection

Clinical criteria plus microbiological sampling techniques lack specificity and sensitivity when compared to the demonstration of pneumonia on histological samples obtained by either biopsy or necropsy .

J Crit Care. 2010;25(1):62–8

Accuracy of clinical definitions of ventilator-associated pneumonia: Comparison with autopsy findings

Eva Tejerina MD, PhD [a,*], Andrés Esteban MD, PhD [a,c], Pilar Fernández-Segoviano MD, PhD [b], Fernando Frutos-Vivar MD [a,c], José Aramburu MD [b], Daniel Ballesteros MD [a], José María Rodríguez-Barbero MD [b]

[a] *Intensive Care Unit, Hospital Universitario de Getafe, Carretera de Toledo, kilómetro 12.5, 28905 Getafe (Madrid), Spain*
[b] *Pathology Unit, Hospital Universitario de Getafe, Carretera de Toledo, 28905 Getafe (Madrid), Spain*
[c] *CIBER Enfermedades Respiratorias, Instituto Carlos III, (Madrid), Spain*

Keywords:
Ventilator-associated pneumonia;
Clinical diagnosis;
Microbiological cultures;
Radiographic infiltrates;
Autopsy findings

Abstract

Methods: We studied patients requiring mechanical ventilation for more than 48 hours who died in the intensive care unit and whose bodies were autopsied. We evaluated 3 clinical definitions of ventilator-associated pneumonia: loose definition, defined as chest radiograph infiltrates and 2 of 3 clinical criteria (leukocytosis, fever, purulent respiratory secretions); rigorous definition, defined as chest radiograph infiltrates and all of the clinical criteria; and a clinical pulmonary infection score higher than 6 points. Sensitivity, specificity, and likelihood ratios were calculated by using pathology pattern as criterion standard.

Results: One hundred forty-two (56%) of the 253 patients included had histological criteria of pneumonia. Patients who met the clinical criteria of ventilator-associated pneumonia were 163 (64%) for the loose definition, 32 (13%) for the rigorous definition, and 109 (43%) for the clinical pulmonary infection score. The operative indexes (sensitivity and specificity) of each definition were as follows: loose definition, 64.8% and 36%; rigorous definition, 91% and 15.5%; and clinical pulmonary infection score higher than 6, 45.8% and 60.4%. The addition of microbiological data to the clinical definitions increased the specificity and decreased the sensitivity but not significantly.

Conclusions: Accuracy of 3 commonly used clinical definitions of ventilator-associated pneumonia was poor taking the autopsy findings as reference standard.

The Clinical Pulmonary Infection Score (CPIS) uses a combination of CXR and clinical, physiological and microbiological information for the diagnosis of VAP.

Score>6 correlates with VAP.

Am Rev Respir Dis. 1991;143(5 Pt 1):1121–9

Respir Care. 2011;56(8):1087–94

CPIS points	0	1	2
Tracheal secretions	Rare	Abundant	Purulent
Leukocyte count (mm^3)	>4,000 and <11,000	<4,000 and >11,000	<4,000 or >11,000 + band forms
Temperature (°C)	>36.5 and <38.4	>38.5 and <38.9	>39 or <36
PaO_2/FIO_2 ratio (mmHg)	>240 or ARDS	-	≤240 and no ARDS
Chest radiograph	No infiltrate	Diffuse infiltrate	Localized infiltrate
Culture of tracheal aspirate	Negative	-	Positive

CPIS: Clinical pulmonary infection scoring

Diagnostic Accuracy of Clinical Pulmonary Infection Score for Ventilator-Associated Pneumonia: A Meta-analysis

Jun Shan MM RN, Hong-Lin Chen MM, and Jian-Hua Zhu MD

OBJECTIVE: To assess the diagnostic accuracy of the clinical pulmonary infection score in the diagnosis of ventilator-associated pneumonia in mechanically ventilated patients. METHODS: We searched PubMed and the Cochrane database, and included only studies that compared clinical pulmonary infection score with quantitative microbiological analysis of samples for diagnosing ventilator-associated pneumonia. We constructed 2-by-2 tables of diagnostic accuracy from each article, and meta-analyzed the results by pooling estimates of sensitivity, specificity, likelihood ratio for positive index test, likelihood ratio for negative index test, diagnostic odds ratio, and 95% confidence intervals. RESULTS: Thirteen studies met the inclusion criteria. The pooled estimates for sensitivity and specificity for clinical pulmonary infection score were 65% (95% CI 61–69%) and 64% (95% CI 60–67%), respectively. The combined diagnostic odds ratio was 4.85 (95% CI 2.42–9.71) and the area under the curve was 0.748 (95% CI 0.65–0.85). CONCLUSIONS: The diagnostic performance of the clinical pulmonary infection score for ventilator-associated pneumonia is moderate. However, the clinical pulmonary infection score is simple and easy to perform, and may still be useful in diagnosing ventilator-associated pneumonia. *Key words: ventilator-associated pneumonia; clinical pulmonary infection score; diagnosis; meta-analysis.* [Respir Care 2011;56(8):1087–1094.

Most accurate predictor for autopsy-proven VAP on CXR was the presence of air bronchograms but this was also low.

Chest. 1992;101(2):458–63

The Radiologic Diagnosis of Autopsy-proven Ventilator-associated Pneumonia*

Richard G. Wunderink, M.D., F.C.C.P.; Lee S. Woldenberg, M.D.; Jacob Zeiss, M.D.; Claudia M. Day, R.N., M.S.N.; John Ciemins, M.S.; and David A. Lacher, M.D., M.Ed.

An abnormal chest roentgenogram is essential for the diagnosis of ventilator-associated pneumonia. The diagnostic accuracy of various roentgenographic signs of pneumonia has not been assessed previously in the portable anteroposterior roentgenograms obtained in ventilated patients. Seven roentgenographic signs (air bronchograms, alveolar infiltrates, silhouette sign, cavities, fissure abutment, atelectasis, and asymmetric infiltrates superimposed on diffuse bilateral infiltrates) were evaluated for their accuracy in predicting pneumonia alone, in combination with other signs, or in combination with clinical parameters. The last roentgenogram prior to autopsy of 69 ventilated patients was interpreted by three reviewers and the above signs were correlated with autopsy evidence of pneumonia. Pneumonia was present in 24 (35 percent) of the 69 autopsies. No roentgenographic sign had a diagnostic efficiency of greater than 68 percent. By stepwise logistic regression, the presence of air bronchograms was the only roentgenographic sign that correlated with pneumonia in the total group, correctly predicting 64 percent of pneumonias. In patients without adult respiratory distress syndrome (ARDS), the presence of air bronchograms or alveolar infiltrates correlated with pneumonia, while in patients with ARDS, no roentgenographic sign and only the clinical parameter of purulent sputum correlated with pneumonia. Only a minority (7/22) of worsening alveolar infiltrates in all groups were due to pneumonia and were often confused with ARDS. Alveolar hemorrhage occurred with a surprising frequency (38 percent of autopsies), including 13/45 (29 percent) patients without pneumonia. Alveolar hemorrhage was associated with 29 percent of multiple air bronchograms and 30 percent of bilateral alveolar infiltrates in patients without pneumonia. We conclude that in intubated patients with diffuse bilateral roentgenographic infiltrates, no roentgenographic sign correlates well with pneumonia. No clinical parameter added to the accuracy of either an alveolar infiltrate or an air bronchogram in patients without diffuse infiltrates. Pulmonary hemorrhage and/or infarction are frequent autopsy findings in intubated patients and may be confused radiologically with pneumonia. *(Chest 1992; 101:458-63)*

VAP = ventilator-associated pneumonia

Respiratory tract sampling-

routinely conducted when there is a clinical suspicion of VAP

non-bronchoscopic or bronchoscopic techniques

a recent Cochrane analysis found no change in mortality, days on mechanical ventilation, number of days in the ICU, or antibiotic utilization when compared to semi-quantitative cultures

Cochrane Database Syst Rev. 2014;10, CD006482

[Intervention Review]

Quantitative versus qualitative cultures of respiratory secretions for clinical outcomes in patients with ventilator-associated pneumonia

Danilo Cortozi Berton[1], Andre C Kalil[2], Paulo José Zimermann Teixeira[1]

[1]Department of Pulmonary Medicine - Pavilhão Pereira Filho - Santa Casa de Porto Alegre, Federal University of Health Sciences of Porto Alegre (UFCSPA) and Feevale University, Porto Alegre, Brazil. [2]Department of Internal Medicine, Infectious Diseases Division, University of Nebraska Medical Center, Omaha, Nebraska, USA

Contact address: Paulo José Zimermann Teixeira, Department of Pulmonary Medicine - Pavilhão Pereira Filho - Santa Casa de Porto Alegre, Federal University of Health Sciences of Porto Alegre (UFCSPA) and Feevale University, Rua Prof Annes Dias, 295, Porto Alegre, Rio Grande do Sul, CEP 90020-090, Brazil. paulozt@via-rs.net. paulozt@ufcspa.edu.br.

Editorial group: Cochrane Acute Respiratory Infections Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 10, 2014.
Review content assessed as up-to-date: 21 October 2014.

Citation: Berton DC, Kalil AC, Teixeira PJZ. Quantitative versus qualitative cultures of respiratory secretions for clinical outcomes in patients with ventilator-associated pneumonia. *Cochrane Database of Systematic Reviews* 2014, Issue 10. Art. No.: CD006482. DOI: 10.1002/14651858.CD006482.pub4.

Ventilator-Associated Events: New Terminology and Its Relationship to VAP

Why?
Background and rationale for VAE surveillance
Who?
Age, location
What?
Surveillance definitions
how?
Tools, pitfalls

Why VAE?: the problem

Ventilator-associated pneumonia (VAP) is an important complication of mechanical ventilation

But other bad things also happen to patients on ventilators

No valid, reliable definition for VAP

Need more accurate diagnostics …toconduct surveillance and track prevention progress!

Commonly used definitions include subjective elements and are neither sensitive nor specific for VAP

Not ideal in an era of public reporting of healthcare-associated infection (HAI) rates, comparisons among facilities, pay-for- performance programs

Need a new approach

Combination of x-ray, signs/symptoms and laboratory criteria

- Three sets of criteria: PNU1, PNU2, PNU3
- Chest imaging findings are required
- Signs and symptoms of pneumonia are required Laboratory evidence is optional—but should be used if available

To be "ventilator-associated" —

- Endotracheal tube (ETT)/ventilator must have been in place at some time during the 48 hours preceding or at time of PNEU onset
- No required amount of time that the ETT/ventilator must have been in place for a PNEU to count as a VAP

NHSN Manual: Patient Safety Component Protocol, http://www.cdc.gov/nhsn/TOC_PSCManual.html, updated January 2012

Cdc definitions

Ventilator-associated pneumonia (VAP):

A pneumonia where the patient is on mechanical **ventilation for >2 calendar** days on the date of event, with day of ventilator placement being Day 1, **AND** the ventilator was in place on the date of event or the day before.

Table 1: Specific Site Algorithms for Clinically Defined Pneumonia (PNU1)

Imaging Test Evidence	Signs/Symptoms/Laboratory
Two or more serial chest imaging test results with at least ***one*** of the following[1,2]: • New or progressive and persistent infiltrate • Consolidation • Cavitation • Pneumatoceles, in infants ≤1 year old **Note:** In patients ***without*** underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), one definitive imaging test result is acceptable.[1]	For ANY PATIENT, at least ***one*** of the following: • Fever (>38.0°C or >100.4°F) • Leukopenia (<4000 WBC/mm^3) or leukocytosis (≥12,000 WBC/mm^3) • For adults ≥70 years old, altered mental status with no other recognized cause And at least ***two*** of the following: • New onset of purulent sputum[3] or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, or dyspnea, or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations (e.g., PaO_2/FiO_2 ≤240)[7], increased oxygen requirements, or increased ventilator demand)
	ALTERNATE CRITERIA, for infants ≤1 year old: Worsening gas exchange (e.g., O_2 desaturations [e.g. pulse oximetry <94%], increased oxygen requirements, or increased ventilator demand) And at least ***three*** of the following: • Temperature instability • Leukopenia (<4000 WBC/mm^3) or leukocytosis (≥15,000 WBC/mm^3) and left shift (≥10% band forms) • New onset of purulent sputum[3] or change in character of sputum[4], or increased respiratory secretions or increased suctioning requirements • Apnea, tachypnea[5], nasal flaring with retraction of chest wall or nasal flaring with grunting • Wheezing, rales[6], or rhonchi • Cough • Bradycardia (<100 beats/min) or tachycardia (>170 beats/min)
	ALTERNATE CRITERIA, for child >1 year old or ≤12 years old, at least ***three*** of the following: • Fever (>38. 0°C or >100. 4°F) or hypothermia (<36. 0°C or <96. 8°F) • Leukopenia (<4000 WBC/mm^3) or leukocytosis (≥15,000 WBC/mm^3) • New onset of purulent sputum[3] or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, or dyspnea, apnea, or tachypnea[5]. • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., pulse oximetry <94%], increased oxygen requirements, or increased ventilator demand)

Table 2: Specific Site Algorithms for Pneumonia with Common Bacterial or Filamentous Fungal Pathogens and Specific Laboratory Findings (PNU2)

Imaging Test Evidence	Signs/Symptoms	Laboratory

Two or more serial chest imaging test results with at least ***one*** of the following[1,2]:
• New or progressive and persistent infiltrate
• Consolidation
• Cavitation
• Pneumatoceles, in infants ≤1 year old
 	
Note: In patients *without* underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), one definitive chest imaging test result is acceptable.[1]
	At least ***one*** of the following:
	• Fever (>38.0°C or >100.4°F)
	• Leukopenia (<4000 WBC/mm^3) or leukocytosis (≥12,000 WBC/mm^3)
	• For adults ≥70 years old, altered mental status with no other recognized cause
	
	And at least ***one*** of the following:
	• New onset of purulent sputum[4] or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements
	• New onset or worsening cough, or dyspnea or tachypnea[4]
	• Rales[5] or bronchial breath sounds
	• Worsening gas exchange (e.g., O_2 desaturations [e.g., PaO_2/FiO_2 ≤240][7], increased oxygen requirements, or increased ventilator demand)
		At least ***one*** of the following:
		• Positive growth in blood culture[8] not related to another source of infection
		• Positive growth in culture of pleural fluid[8]
		• Positive quantitative culture[8] from minimally-contaminated LRT specimen (e.g., BAL or protected specimen brushing)
		• ≥5% BAL-obtained cells contain intracellular bacteria on direct microscopic exam (e.g., Gram's stain)
		• Positive quantitative culture[8] of lung tissue
		• Histopathologic exam shows at least ***one*** of the following evidences of pneumonia:
		  ○ Abscess formation or foci of consolidation with intense PMN accumulation in bronchioles and alveoli
		  ○ Evidence of lung parenchyma invasion by fungal hyphae or pseudohyphae

Table 4: Specific Site Algorithm for Pneumonia in Immunocompromised Patients (PNU3)

Imaging Test Evidence	Signs/Symptoms	Laboratory
Two or more serial chest imaging test results with at least ***one*** of the following[1,2]: • New or progressive and persistent infiltrate • Consolidation • Cavitation • Pneumatoceles, in infants ≤1 year old **Note:** In patients ***without*** underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), one definitive chest imaging test result is acceptable.[1]	Patient who is immunocompromised (see definition in footnote [10] has at least ***one*** of the following: • Fever (>38.0°C or >100.4°F) • For adults ≥70 years old, altered mental status with no other recognized cause • New onset of purulent sputum[3], or change in character ofsputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, or dyspnea, or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., PaO_2/FiO_2 ≤240][7], increased oxygen requirements, or increased ventilator demand) • Hemoptysis • Pleuritic chest pain	At least ***one*** of the following: • Matching positive blood and sputum or endotracheal aspirate cultures with *Candida* spp.[11,12] • Evidence of fungi from minimally-contaminated LRT specimen (e.g., BAL or protected specimen brushing) from one of the following: – Direct microscopic exam – Positive culture of fungi – Non-culture diagnostic laboratory test Any of the following from: **LABORATORY CRITERIA DEFINED UNDER PNU2**

Limitations of current definitions-

Current definitions (e.g., definitions used for surveillance in NHSN, Clinical Pulmonary Infection Score) all use combinations of criteria:

Chest x-ray-

Lack specificity for VAP1

Inter-observer variability2

Clinical signs/symptoms-

Lack sensitivity and specificity3

Some are highly subjective

Documentation varies

Microbiological evidence-

Lack sensitivity and specificity4

Practices vary among providers

Controversy about best practices5,6

1Wunderink R, et al., Chest 1992;101;458-63; 2Young M, et al., Arch Intern Med 1994;154:2729-32; 3Fabregas N, et al., Thorax 1999;54:867-73; 4Kirtland SH, et al., Chest 1997;112:445-57; 5Berton DC, et al., Cochrane Database Syst Rev 2008; 6Ruiz M, et al., Am J Respir Crit Care Med 2000;162:119-25

Why VAP rates declining?

- ➢ Evidence-based prevention measures
- ➢ Other reasons—several ways to lower VAP rates without improving patient care ***(Klompas et al., AJIC 2012;40:408-10)***

- ✓ Strict interpretation of clinical signs included in surveillance definitions
- ✓ Strict interpretation of chest x-ray findings included in surveillance definitions
- ✓ Practice of transferring out those patients needing prolonged mechanical ventilation
- ✓ Admission of uncomplicated, vented post-operative patients to unit.

Goals for Modifying Current NHSN Definitions-

- Achieve face validity/clinical credibility
- Improve reliability
- Reduce burden

VAE Surveillance Definition Algorithm—Tiered Approach

Tiers 1 and 2: Definitions suitable for potential use in public reporting

- Objective, general measures of Ventilator-Associated Conditions (VAC) and Infection-related, Ventilator-Associated Complications (IVAC)
- Definitions similar to Tier 1 VAC definition evaluated by *Klompas et al.* identified events associated with longer duration of mechanical ventilation, longer ICU stay, and increased mortality—and were more efficient to apply than current VAP definitions (*PLoS One 2011;6:e18062, Crit Care Med 2012; in press)*

Tier 3: Internal use definitions

- Possible VAP and Probable VAP, incorporating laboratory evidence

Who is eligible?

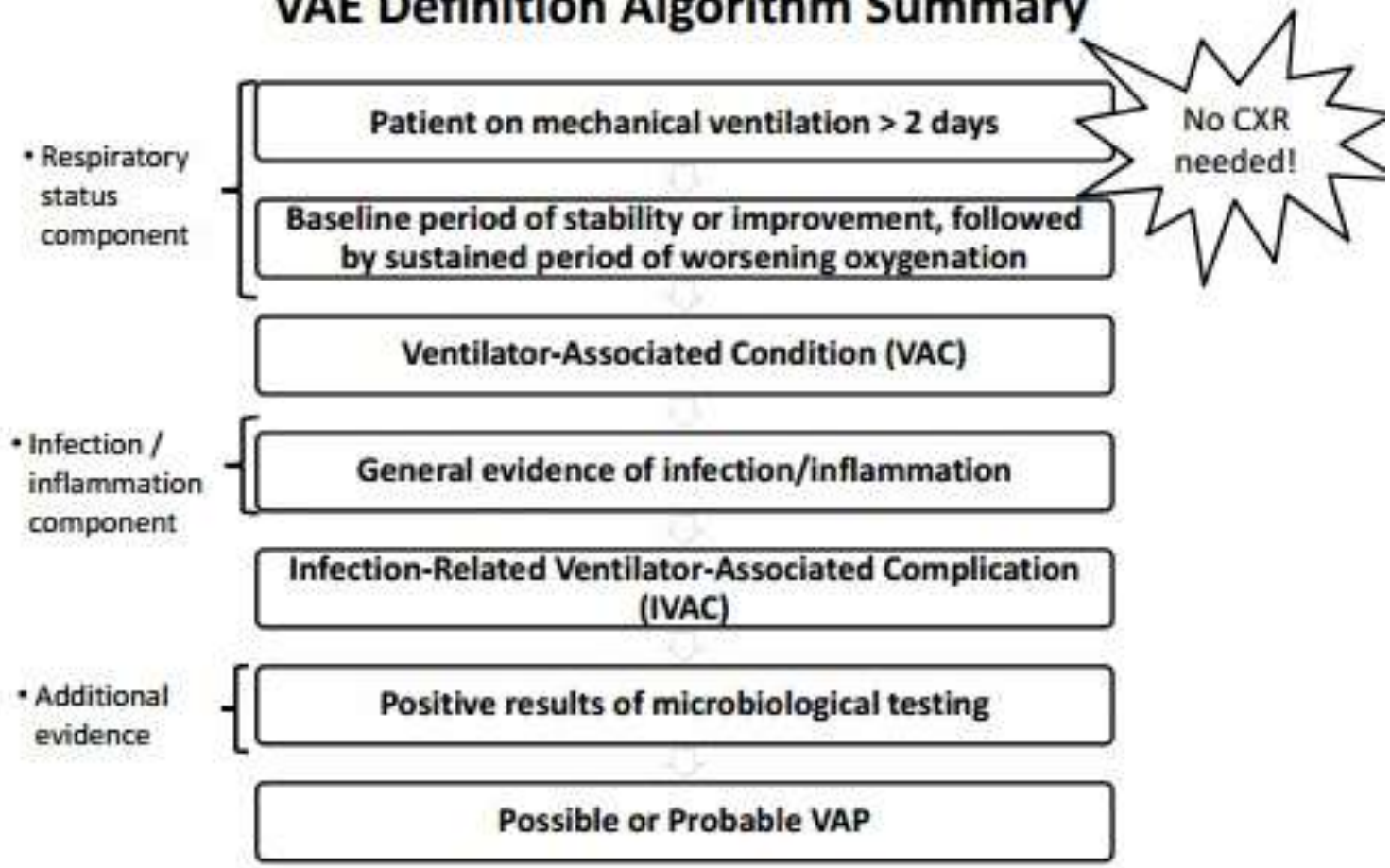
- ≥18 years of age
- Inpatients of acute care hospitals, long term acute care hospitals, inpatient rehabilitation facilities

Who is NOT eligible for VAE surveillance?

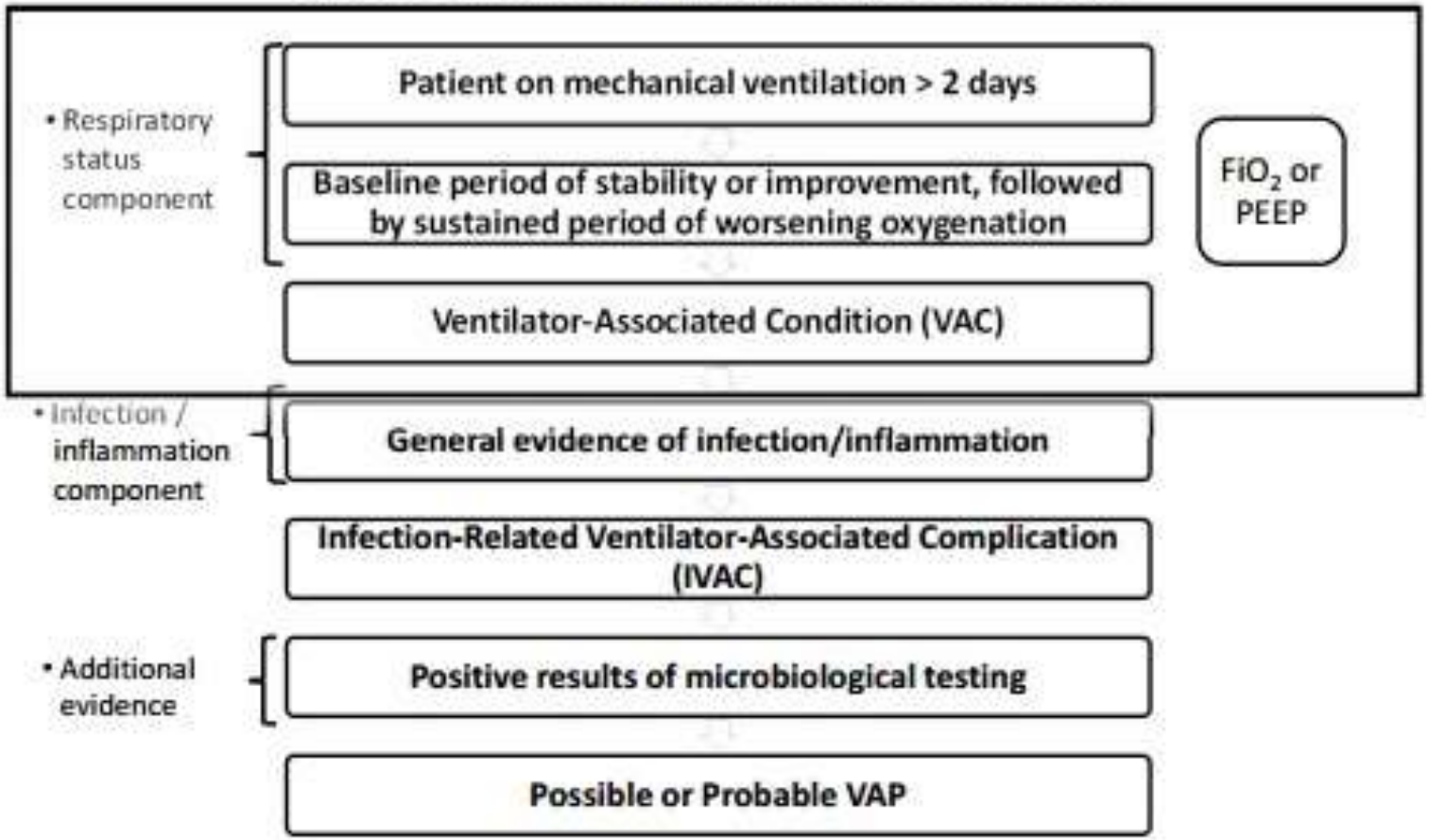
- Children are not eligible.
- Inpatients of facilities other than acute care hospitals, long- term acute care hospitals and inpatient rehabilitation facilities are not eligible.
- Patients on high frequency ventilation or extracorporeal life support are NOT ELIGIBLE for VAE surveillance.

“WHAT” IS VAE? REVIEW OF DEFINITIONS

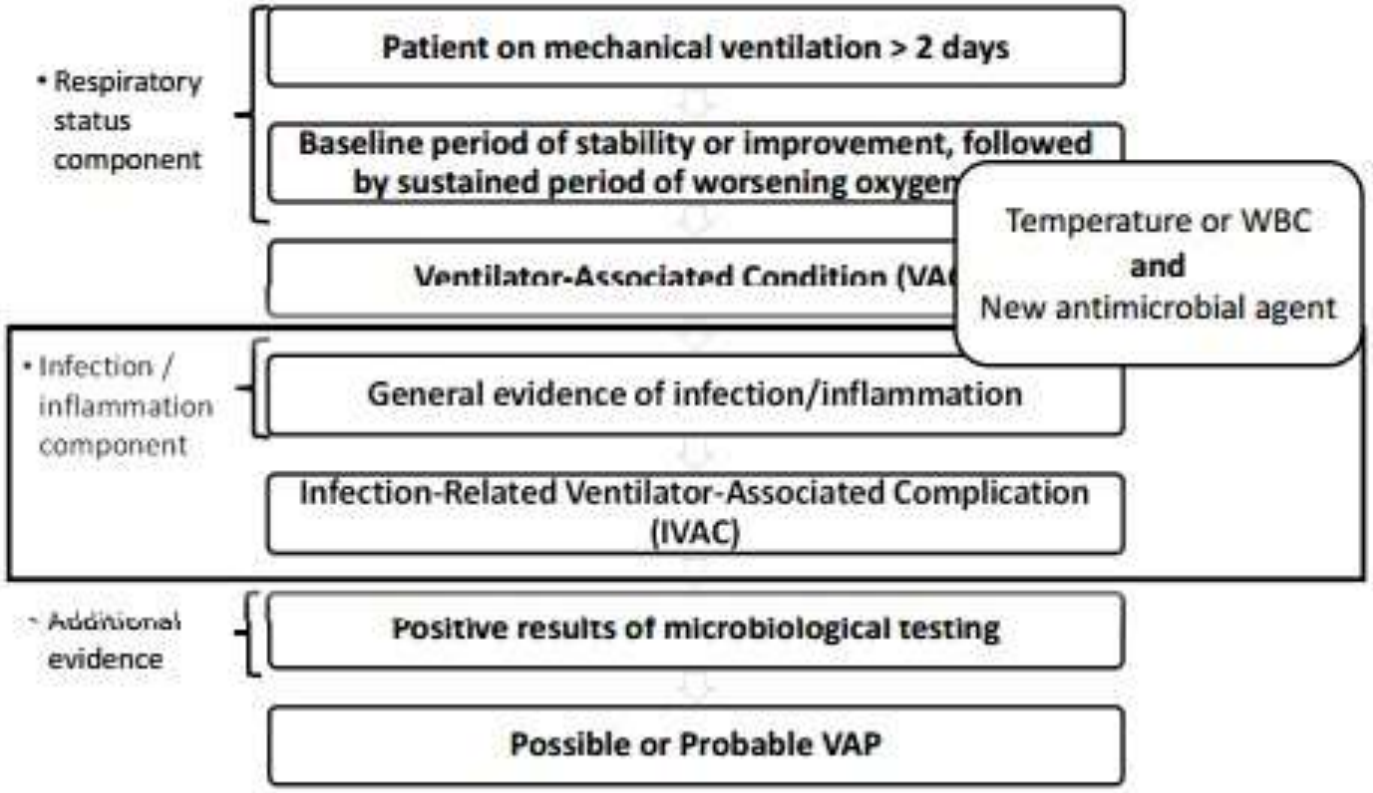
VAE Definition Algorithm Summary



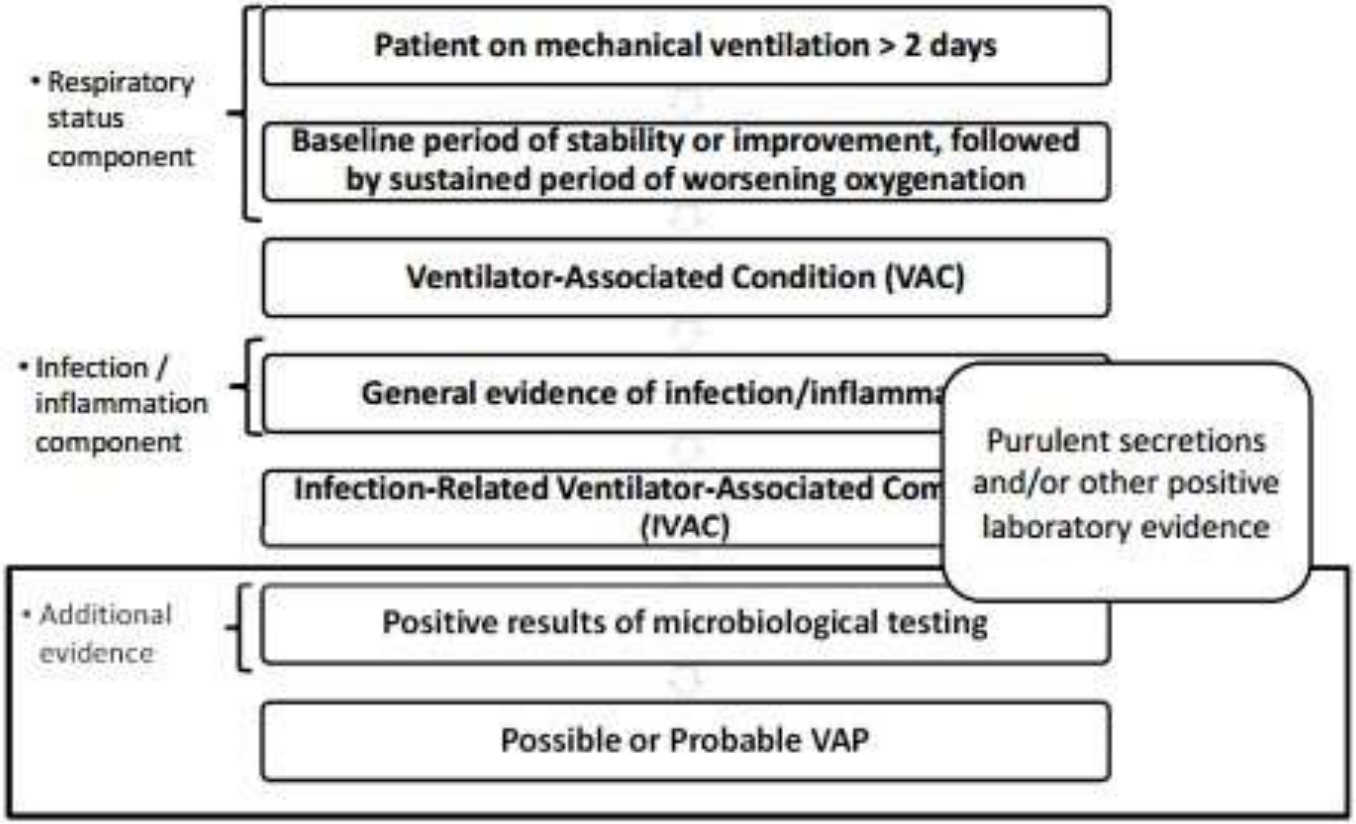
VAE Definition Algorithm Summary



VAE Definition Algorithm Summary



VAE Definition Algorithm Summary



Tier 1: VAC

Patient has a baseline period of stability or improvement on the ventilator, defined by ≥ 2 calendar days of stable or decreasing daily minimum FiO_2 or PEEP values. The baseline period is defined as the two calendar days immediately preceding the first day of increased daily minimum PEEP or FiO_2.

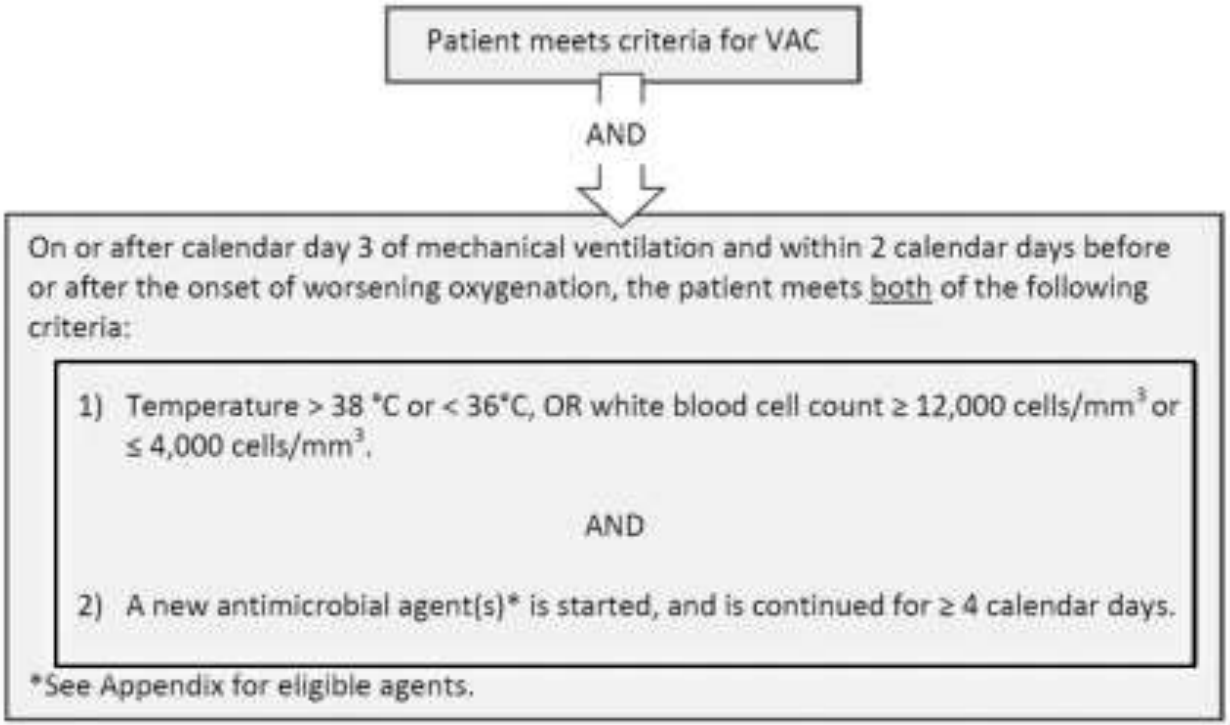
AND

After a period of stability or improvement on the ventilator, the patient has at least one of the following indicators of worsening oxygenation:

1) Increase in daily minimum FiO_2 of ≥ 0.20 (20 points) over the daily minimum FiO_2 in the baseline period, sustained for ≥ 2 calendar days.

2) Increase in daily minimum PEEP values of ≥ 3 cmH_2O over the daily minimum PEEP in the baseline period, sustained for ≥ 2 calendar days.

Tier 2: IVAC


Patient meets criteria for VAC
AND
On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, the patient meets both of the following criteria:
1) Temperature > 38 °C or < 36°C, OR white blood cell count ≥ 12,000 cells/mm3 or ≤ 4,000 cells/mm3.
AND
2) A new antimicrobial agent(s)* is started, and is continued for ≥ 4 calendar days.
*See Appendix for eligible agents.

Tier 3: Possible VAP

Patient meets criteria for VAC and IVAC

AND

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met:

1) Purulent respiratory secretions (from one or more specimen collections)
   - Defined as secretions from the lungs, bronchi, or trachea that contain ≥25 neutrophils and ≤10 squamous epithelial cells per low power field [lpf, x100].
   - If the laboratory reports semi-quantitative results, those results must be equivalent to the above quantitative thresholds.

2) Positive culture (qualitative, semi-quantitative or quantitative) of sputum*, endotracheal aspirate*, bronchoalveolar lavage*, lung tissue, or protected specimen brushing*

**Excludes the following:*

- Normal respiratory/oral flora, mixed respiratory/oral flora or equivalent
- *Candida* species or yeast not otherwise specified
- Coagulase-negative *Staphylococcus* species
- *Enterococcus* species

Tier 3: Probable VAP

VAC, IVAC plus the following…

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met:

1) Purulent respiratory secretions (from one or more specimen collections—and defined as for possible VAP)

AND one of the following (see Table 2):

- Positive culture of endotracheal aspirate*, ≥ 10^5 CFU/ml or equivalent semi-quantitative result
- Positive culture of bronchoalveolar lavage*, ≥ 10^4 CFU/ml or equivalent semi-quantitative result
- Positive culture of lung tissue, ≥ 10^4 CFU/g or equivalent semi-quantitative result
- Positive culture of protected specimen brush*, ≥ 10^3 CFU/ml or equivalent semi-quantitative result

**Same organism exclusions as noted for Possible VAP.*

2) One of the following (without requirement for purulent respiratory secretions):

- Positive pleural fluid culture (where specimen was obtained during thoracentesis or initial placement of chest tube and NOT from an indwelling chest tube)
- Positive lung histopathology
- Positive diagnostic test for *Legionella* spp.
- Positive diagnostic test on respiratory secretions for influenza virus, respiratory syncytial virus, adenovirus, parainfluenza virus, rhinovirus, human metapneumovirus, coronavirus

Hierarchy of definitions:

- If a patient meets criteria for VAC and IVAC, report as IVAC.
- If a patient meets criteria for VAC, IVAC and Possible VAP, report Possible VAP.
- If a patient meets criteria for VAC, IVAC and Probable VAP, report Probable VAP.
- If a patient meets criteria for VAC, IVAC, Possible VAP and Probable VAP, report Probable VAP.

Ventilator associated events [VAE], Ventilator associated pneumonia [VAP] : Definition changes 2015

www.cdc.gov/nhsn/

VAE protocol change #1 :

Third tier of the VAE algorithm is collapsed to include one specific event : PVAP

PVAP replaces possible and probable VAP.

Provides simplification

Three pathways for meeting PVAP definition

- Quantitative or semiquantitative equivalent culture WITHOUT purulent respiratory secretions
- Culture result with purulent secretions
- Other positive laboratory tests.

Patient meets criteria for VAC and IVAC

AND

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met (taking into account organism exclusions specified in the protocol*):

1) Criterion 1: Positive culture of one of the following specimens, meeting quantitative or semi-quantitative thresholds as outlined in protocol, without requirement for purulent respiratory secretions:
   - Endotracheal aspirate, $\geq 10^5$ CFU/ml or corresponding semi-quantitative result
   - Bronchoalveolar lavage, $\geq 10^4$ CFU/ml or corresponding semi-quantitative result
   - Lung tissue, $\geq 10^4$ CFU/g or corresponding semi-quantitative result
   - Protected specimen brush, $\geq 10^3$ CFU/ml or corresponding semi-quantitative result
2) Criterion 2: Purulent respiratory secretions (defined as secretions from the lungs, bronchi, or trachea that contain $\geq$25 neutrophils and $\leq$10 squamous epithelial cells per low power field [lpf, x100])† plus a positive culture of one of the following specimens (qualitative culture, or quantitative/semi-quantitative culture without sufficient growth to meet criterion #1):
   - Sputum
   - Endotracheal aspirate
   - Bronchoalveolar lavage
   - Lung tissue
   - Protected specimen brush

   † If the laboratory reports semi-quantitative results, those results must correspond to the quantitative thresholds. See additional instructions for using the purulent respiratory secretions criterion in the VAE Protocol.
3) Criterion 3: One of the following positive tests:
   - Pleural fluid culture (where specimen was obtained during thoracentesis or initial placement of chest tube and NOT from an indwelling chest tube)
   - Lung histopathology, defined as: 1) abscess formation or foci of consolidation with intense neutrophil accumulation in bronchioles and alveoli; 2) evidence of lung parenchyma invasion by fungi (hyphae, pseudohyphae or yeast forms); 3) evidence of infection with the viral pathogens listed below based on results of immunohistochemical assays, cytology, or microscopy performed on lung tissue
   - Diagnostic test for *Legionella* species
   - Diagnostic test on respiratory secretions for influenza virus, respiratory syncytial virus, adenovirus, parainfluenza virus, rhinovirus, human metapneumovirus,

VAE protocol change 2:

The following community acquired fungal pathogens rarely cause health care associated infections and therefore are no longer available for meeting the PVAP definition-

Cyrptococcus

Histoplasma

Pneumocystis

Blastomyces

VAE protocol change #3:

- Daily minimum PEEP and FiO2 values are defined as the lowest value during the calendar day that is set on the ventilator and maintained for atleast 1 hour.
- Provides simplification and consistency for determining the daily minimum PEEP and FiO2 in select circumstances

VAE new denominator-

Episodes of mechanical ventilation [EMV] is introduced.

defined as a period of days during which the patient was mechanically ventilated for some portion of each consecutive day .

EMV is a total of the number of episodes occurring during a month.

EXAMPLE: On January 1, there are **5** patients on mechanical ventilation in the MICU (2 patients were started on mechanical ventilation on December 24, **2** patients on December 31, and **1** patient on January 1). During the rest of the month, the following are noted**: 1** patient is started on mechanical ventilation on January 8; **2** patients are transferred to the MICU on mechanical ventilation on January 15, and **1** patient who was previously ventilated (from January 1 through January 12) goes back on mechanical ventilation on January 20. No other patients are on mechanical ventilation during the month of January. **The number of EMV for January is nine**. This is calculated as follows: 5 patients(on mechanical ventilation on the first day of the month) + 4 patients who were either started on mechanical ventilation, transferred into the MICU on mechanical ventilation, or re-initiated on mechanical ventilation after being off of the vent for at least 1 calendar day = 9 EMV.

Key points

- Key Take-Home Points Patient must be ventilated more than 2 calendar days.
- Patient must have ≥2 calendar days of stability or improvement of oxygenation followed by ≥2 calendar days of worsening oxygenation.
- Earliest date of event for VAE is mechanical ventilation day 3 (first day of worsening oxygenation).
- First possible day that VAC criteria can be fulfilled is mechanical ventilation day 4

- **Event Date defines the VAE Window Period:**
- ✓ 2 days before, day of and 2 days after the Event Date – 5 days
- ✓ May be shorter if worsening occurs early in the course of ventilation
- **All other criteria (for IVAC, Possible VAP, Probable VAP) must be identified within the VAE Window Period.**
- **The "VAE clock" starts over again when …**
- ✓ The patient begins a new episode of mechanical ventilation
- ✓ A new event period starts (i.e., 14 days have elapsed since previous VAE Event Date)
- ✓ The patient comes off of an excluded therapy (such as HFV or ECMO) and goes back on conventional mode of ventilation.

Prevention of VAP

VAP incidence is 25% of all critical care unit infectious diseases, and 10-25% of ventilated cases develop VAP, >25% of antibiotics prescribed in ICU are for VAP patients.

Craven etal, 2006 Chest 130: 251-260.

VAP increases the length on mechanical ventilation, and ICU stay, longer hospital length of stay, and increase the mortality rate by double.

Safdar etal , 2005 Care Med 33: 2184-2193.

The sources of the VAP have been identified in several places such as oral cavity, subglottic fluid, and the gastric mucosa. The endotracheal tube shows an important matter in the development of VAP, as a source of infection and as a reservoir of the infection from the formation of the biofilm on the inner surface of tube.

Atherton, 1978 Lancet 2: 968-969.

Adair cg etal, 1995 Intensive care medicine 25: 1072-1076

Strategies for VAP prevention-

- Non-invasive positive-pressure ventilation (NIPPV)
- Semi-recumbent position to decrease aspiration of oropharyngeal secretions.
- Oral hygiene with chlorhexidine
- Specialized endotracheal tubes (subglottic secretion drainage; silver-coated)

Current modalities for the prevention of VAP and the evidence for these modalities, are based on the traditional definition of VAP. It is unknown if VACs and iVACs are preventable with the VAP prevention modalities.

Non-invasive Positive Pressure Ventilation (NIPPV)

- Avoiding intubation and limiting the duration of mechanical ventilation reduces the occurrence of VAP.
- Use of NIPPV avoids the need for intubation or terminates mechanical ventilation as early as possible by extubation to NIPPV.

Hess Dr, Respir Care. 2005;50(7):924–9

Burns KE etal, Cochrane Database Syst Rev. 2013;12, CD004127

Noninvasive Positive-Pressure Ventilation and Ventilator-Associated Pneumonia

Dean R Hess PhD RRT FAARC

There is much interest in the use of noninvasive positive-pressure ventilation (NPPV) to prevent intubation and afford a survival benefit for patients. The risk of pneumonia in patients receiving NPPV has been reported in 12 studies. Compared to patients receiving invasive mechanical ventilation (4 studies), the pneumonia rate is lower with the use of NPPV (relative risk [RR] 0.15, 95% confidence interval [CI] 0.04 to 0.58, p = 0.006). Compared to patients assigned to invasive mechanical ventilation (3 studies), in which some of the patients assigned to NPPV did not respond and were eventually intubated, there was also a benefit for the use of NPPV (RR 0.24, 95% CI 0.08 to 0.73, p = 0.01). In studies in which patients assigned to NPPV were compared to patients assigned to standard therapy (5 studies), in which some of the patients in each group were eventually intubated, there was benefit shown for the use of NPPV (RR 0.56, 95% CI 0.31 to 1.02, p = 0.06). When this meta-analysis is repeated without the results of the negative study for NPPV (extubation failure), there is a stronger benefit in support of NPPV to decrease the risk of pneumonia in the remaining 4 studies (RR 0.38, 95% CI 0.20 to 0.73, p = 0.003). A meta-analysis combining the results from the 12 studies reviewed shows a strong benefit for NPPV (RR 0.31, 95% CI 0.16 to 0.57, p = 0.0002). One randomized controlled trial of continuous positive airway pressure compared with standard treatment in patients who developed acute hypoxemia after elective major abdominal surgery reported a lower rate of pneumonia with continuous positive airway pressure (2% vs 10%, RR 0.19, 95% CI 0.04 to 0.88, p = 0.02). In patients who are appropriate candidates for NPPV or continuous positive airway pressure, the available evidence suggests a benefit in terms of a lower risk of pneumonia. Perhaps "endotracheal-tube-associated pneumonia" is a better term than "ventilator-associated pneumonia." *Key words: continuous positive airway pressure, mechanical ventilation, noninvasive positive-pressure ventilation, ventilator-associated pneumonia.* [Respir Care 2005;50(7): 924–929. © 2005 Daedalus Enterprises]

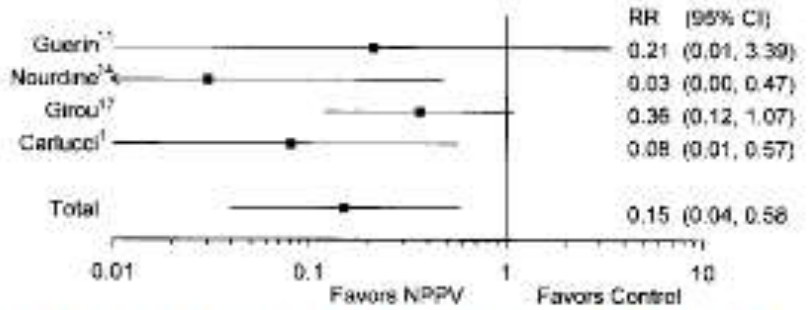


Fig. 1. Pooled analysis of pneumonia in studies comparing noninvasive positive-pressure ventilation (NPPV) with invasive mechanical ventilation. p = 0.13 for heterogeneity. p = 0.006 for overall effect. RR = relative risk. CI = confidence interval.

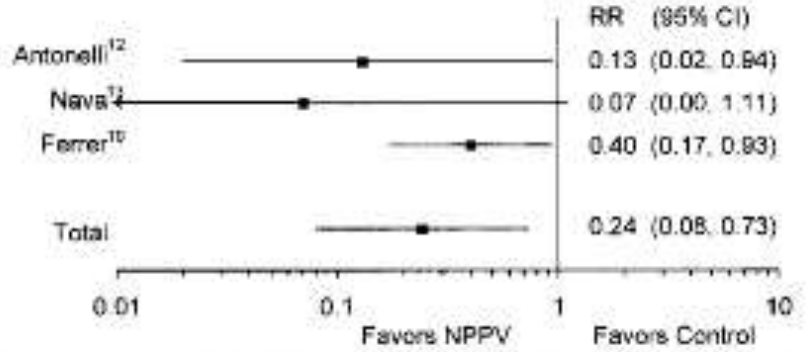


Fig. 2. Pooled analysis of pneumonia in studies where patients were assigned to noninvasive positive-pressure ventilation (NPPV) or invasive mechanical ventilation. p = 0.25 for heterogeneity. p = 0.01 for overall effect. RR = relative risk. CI = confidence interval.

[Intervention Review]

Noninvasive positive-pressure ventilation as a weaning strategy for intubated adults with respiratory failure

Karen EA Burns[1], Maureen O Meade[2], Azra Premji[3], Neill KJ Adhikari[4]

[1]Interdepartmental Division of Critical Care and the University of Toronto, Keenan Research Centre/Li Ka Shing Knowledge Institute, Toronto, Canada. [2]Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Canada. [3]The University of Toronto, Toronto, Canada. [4]Interdepartmental Division of Critical Care, University of Toronto, and Department of Critical Care Medicine and Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, Toronto, Canada

Contact address: Karen EA Burns, Interdepartmental Division of Critical Care and the University of Toronto, Keenan Research Centre/Li Ka Shing Knowledge Institute, St Michael's Hospital, 30 Bond Street, Rm 4-045 Queen Wing, Toronto, Ontario, M5B 1WB, Canada. BurnsK@smh.ca. burnske2@hotmail.com.

Editorial group: Cochrane Anaesthesia Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 12, 2013.
Review content assessed as up-to-date: 1 May 2012.

Citation: Burns KEA, Meade MO, Premji A, Adhikari NKJ. Noninvasive positive-pressure ventilation as a weaning strategy for intubated adults with respiratory failure. *Cochrane Database of Systematic Reviews* 2013, Issue 12. Art. No.: CD004127. DOI: 10.1002/14651858.CD004127.pub3.

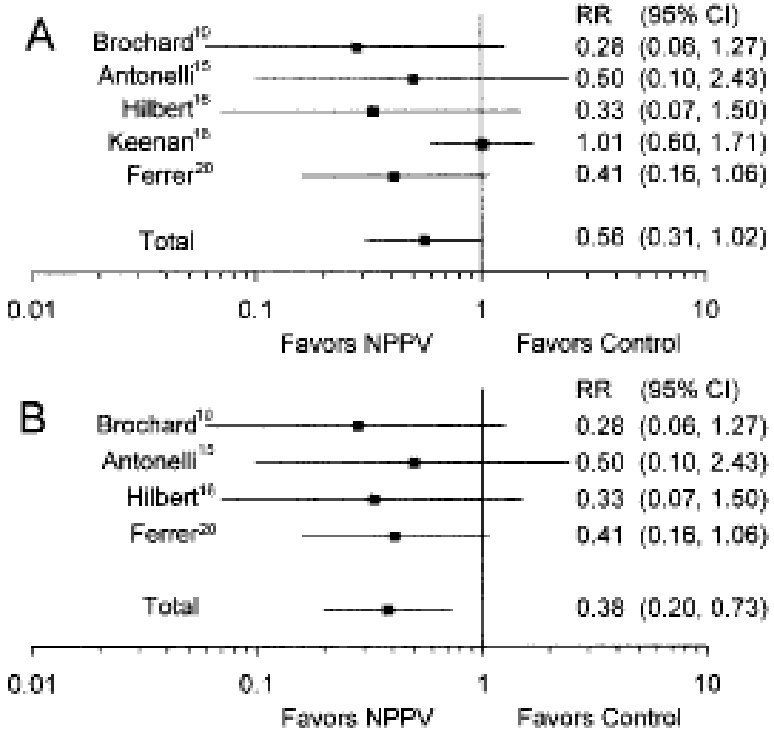


Fig. 3. A: Pooled analysis of pneumonia in studies comparing patients assigned to noninvasive positive-pressure ventilation (NPPV) or assigned to standard therapy. p = 0.19 for heterogeneity. p = 0.06 for overall effect. B: Pooled analysis of pneumonia in studies comparing patients assigned to NPPV or assigned to standard therapy after removal of the study showing no benefit for noninvasive positive-pressure ventilation (NPPV) (failed extubation). p = 0.96 for heterogeneity. p = 0.003 for overall effect. RR = relative risk. CI = confidence interval.

Main results

We identified 16 trials, predominantly of moderate to good quality, involving 994 participants, most with chronic obstructive pulmonary disease (COPD). Compared with IPPV weaning, NPPV weaning significantly decreased mortality. The benefits for mortality were significantly greater in trials enrolling exclusively participants with COPD (risk ratio (RR) 0.36, 95% confidence interval (CI) 0.24 to 0.56) versus mixed populations (RR 0.81, 95% CI 0.47 to 1.40). NPPV significantly reduced weaning failure (RR 0.63, 95% CI 0.42 to 0.96) and ventilator-associated pneumonia (RR 0.25, 95% CI 0.15 to 0.43); shortened length of stay in an intensive care unit (mean difference (MD) -5.59 days, 95% CI -7.90 to -3.28) and in hospital (MD -6.04 days, 95% CI -9.22 to -2.87); and decreased the total duration of ventilation (MD -5.64 days, 95% CI -9.50 to -1.77) and the duration of endotracheal mechanical ventilation (MD - 7.44 days, 95% CI -10.34 to -4.55) amidst significant heterogeneity. Noninvasive weaning also significantly reduced tracheostomy (RR 0.19, 95% CI 0.08 to 0.47) and reintubation (RR 0.65, 95% CI 0.44 to 0.97) rates. Noninvasive weaning had no effect on the duration of ventilation related to weaning. Exclusion of a single quasi-randomized trial did not alter these results. Subgroup analyses suggest that the benefits for mortality were significantly greater in trials enrolling exclusively participants with COPD versus mixed populations.

Authors' conclusions

Summary estimates from 16 trials of moderate to good quality that included predominantly participants with COPD suggest that a weaning strategy that includes NPPV may reduce rates of mortality and ventilator-associated pneumonia without increasing the risk of weaning failure or reintubation.

Positioning

- Limiting aspiration of oropharyngeal secretions is a strategy to prevent VAP. done in part by maintaining a semi-recumbent position to maintain the head of the bed between 30 and 45°.
- Is a simple intervention and it is worth implementing unless there are contraindications in the specific patient.

Alexiou VG etal, a meta-analysis of randomized controlled trials. J Crit Care. 2009;24(4):515–22.

Impact of patient position on the incidence of ventilator-associated pneumonia: A meta-analysis of randomized controlled trials

Vangelis G. Alexiou MD[a], Vrettos Ierodiakonou MD[a], George Dimopoulos MD, PhD, FCCP[a,b], Matthew E. Falagas MD, MSc, DSc[a,c,d,*]

[a]*Alfa Institute of Biomedical Sciences (AIBS), Athens, Greece*
[b]*Department of Intensive Care, University Hospital "ATTIKON", Medical School, University of Athens, Athens, Greece*
[c]*Department of Medicine, Henry Dunant Hospital, Athens, Greece*
[d]*Department of Medicine, Tufts University School of Medicine, Boston, MA, USA*

Table 1 Main characteristics of RCTs included in the meta-analysis

First author/ Reference	Study design/ Year of publication	Country	Positions compared	Study population	Sample size (no. of patients enrolled)	Quality score
Van Nieuwenhoven [15]	MC RCT/ 12 2006	Netherlands	Semirecumbent position; 45° of the head and back vs supine position; standard care; 10° of the head and back	Patients treated in 3 ICUs intubated within 24 h of ICU admission and with duration of ventilation for at least 48 h	221	3
Drakulovic [16]	SC RCT/ 13 1999	Spain	Semirecumbent position; 45° of the head and back vs supine position; 0° of the head and back	Intubated and mechanically ventilated patients of one medical and one respiratory ICU at a tertiary university hospital	86	3
Keeley [17]	SC RCT/ 14 2007	UK	Semirecumbent position 45° of the head of bed vs 25° raised head of bed	Critical care patients intubated within 12 h from ICU admission	30	3
Voggenreiter [18]	MC RCT/ 15 2005	Germany	Prone position for 8-23 h daily vs supine position	Multiple trauma patients with ALI/ARDS and receiving mechanical ventilation treated in 2 trauma ICU	40	3
Mancebo [19]	MC RCT/ 16 2006	Spain and Mexico	Prone position for 20 h daily vs supine position	Intubated, mechanical, ventilated patients with ARDS treated in 13 ICUs	142	3
Beuret [20]	SC RCT/ 17 2002	France	Prone position for 4 h once daily vs supine position (0° and 20° of the head and back)	Comatose patients who needed mechanical ventilation for at least 48 h	51	3
Guerin [12]	MC RCT/ 18 2004	France	Prone position for at least 8 h daily vs supine position (30° of the head and back)	Patients with acute respiratory failure treated in 21 general ICUs with Pao_2/Fio_2 ratio at most 300	791	2

MC: Multi Center, SC: Single Center.

Table 2 Clinical outcomes among patients positioned in an alternative way (prone or semirecumbent) compared with patients in supine position

First author/ Ref. outcome	Van Nieuwenhoven [15]		Drakulovic [16]	Keeley [17]		Voggenreiter [18]	Mancebo [19]		Beuret [20]	Guerin [12]	
	Semirecumbent position					Prone position in patients with ARDS/ALI			Prone position in patients without ARDS/ALI		
VAP clinically suspected	16/112 vs 20/109		3/39 vs 16/47	5/17 vs 7/13		13/21 vs 17/19	14/76 vs 9/60		11/25 vs 14/26	85/413 vs 91/378	
VAP microbiologically documented	13/112 vs 8/109		2/39 vs 11/47	4/17 vs 5/13		N/A	N/A		4/25 vs 10/26	N/A	
Mortality	29/112 vs 30/109 (ICU)	39/112 vs 38/109 (hospital)	7/39 vs 13/47 (ICU)	3/17 vs 4/13 (ICU)	4/17 vs 4/13 (hospital)	1/21 vs 3/19 (day 90)	33/76 vs 35/60 (ICU)	38/76 vs 37/60 (hospital)	7/25 vs 12/26 (day 28)	134/413 vs 119/378 (day 28)	179/413 vs 159/377 (day 90)
Mean duration of ventilation in days (SD)	6 vs 6 median		6(6.2) vs 7.1 (7)	N/A		30 (17) vs 33 (23)	N/A		12.7 (10) vs 14.6 (17.7)	13.7 (7.8) vs 14.1 (8.6)	
Mean duration of ICU stay in days (SD)	9 vs 10 median		9.3 (7.2) vs 9.7 (7.8)	N/A		N/A	20.5 (18.2) vs 19.1 (23.1)		16.5 (12.9) vs 19.4 (24.1)	26.6 (29.6) vs 24.5 (21.9)	
Mean duration of antibiotic therapy in days (SD)	4 (N/A) vs 4 (N/A)		N/A	N/A		20.8 (8.9) vs 18.2 (8.7)	N/A		N/A	N/A	

This meta-analysis provides additional evidence that the usual practice of back-rest elevation of 15° to 30° is not sufficient to prevent VAP in mechanically ventilated patients. Patients positioned semi recumbently 45° have significantly lower incidence of clinically diagnosed VAP compared to patients positioned supinely. On the other hand, the incidence of clinically diagnosed VAP among patients positioned pronely does not differ significantly from the incidence of clinically diagnosed VAP among patients positioned supinely.

probiotics

- Probiotics are living microbial agents of human origin that are able to tolerate the hostile gastrointestinal environment (acid and bile) such that they ultimately persist in the lower alimentary tract to confer health benefits to the host.
- decrease the inflammatory reaction and improve both the immunological response (the balance between T-helper 1 and T-helper 2 cells), and immunological barrier of the gut.

Isolauri E (2001) Probiotics in human disease. Am J Clin Nutr 73: 1142S-1146S.

Ghosh S etal, 2004 Gut 53: 620-622.

[Intervention Review]

Probiotics for preventing ventilator-associated pneumonia

Lulong Bo[1], Jinbao Li[1], Tianzhu Tao[1], Yu Bai[2], Xiaofei Ye[3], Richard S Hotchkiss[4], Marin H Kollef[5], Neil H Crooks[6], Xiaoming Deng[1]

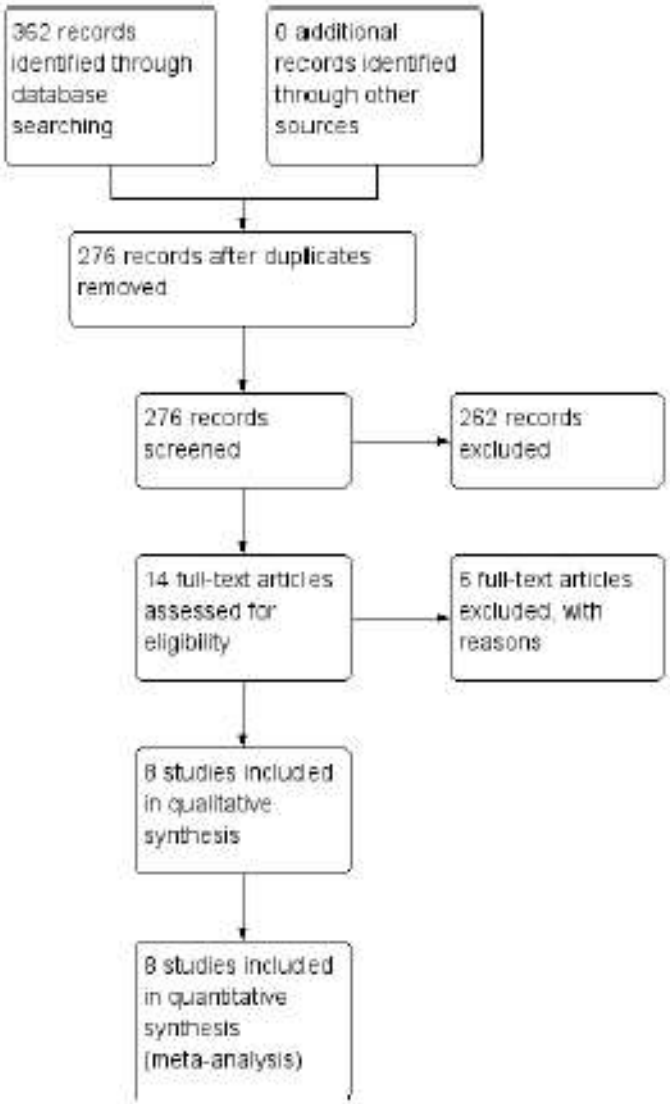
[1]Department of Anaesthesiology and Intensive Care Medicine, Changhai Hospital, Second Military Medical University, Shanghai, China. [2]Department of Gastroenterology/Center for Clinical Epidemiology & Evidence-Based Medicine, Changhai Hospital, Second Military Medical University, Shanghai, China. [3]Department of Health Statistics, Second Military Medical University, Shanghai, China. [4]Department of Anesthesiology, Washington University School of Medicine, St. Louis, Missouri, USA. [5]Division of Pulmonary and Critical Care Medicine, Washington University School of Medicine, St. Louis, Missouri, USA. [6]Academic Department of Anaesthesia, Critical Care & Pain, Birmingham Heartlands Hospital, Birmingham, UK

Contact address: Xiaoming Deng, Department of Anaesthesiology and Intensive Care Medicine, Changhai Hospital, Second Military Medical University, 14th Floor, 168 Changhai Rd, Shanghai, 200433, China. deng_x@yahoo.com. nbastars@126.com.

Editorial group: Cochrane Acute Respiratory Infections Group.
Publication status and date: New, published in Issue 10, 2014.
Review content assessed as up-to-date: 17 September 2014.

Citation: Bo L, Li J, Tao T, Bai Y, Ye X, Hotchkiss RS, Kollef MH, Crooks NH, Deng X. Probiotics for preventing ventilator-associated pneumonia. *Cochrane Database of Systematic Reviews* 2014, Issue 10. Art. No.: CD009066. DOI: 10.1002/14651858.CD009066.pub2.

Figure 1. Study flow diagram: 2014 search



SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Per-protocol analysis: probiotics versus control for preventing ventilator-associated pneumonia

Patient or population: patients receiving mechanical ventilation
Settings: inpatient: China, France, Greece, Slovenia, Sweden, UK and USA
Intervention: per-protocol analysis: probiotics versus control

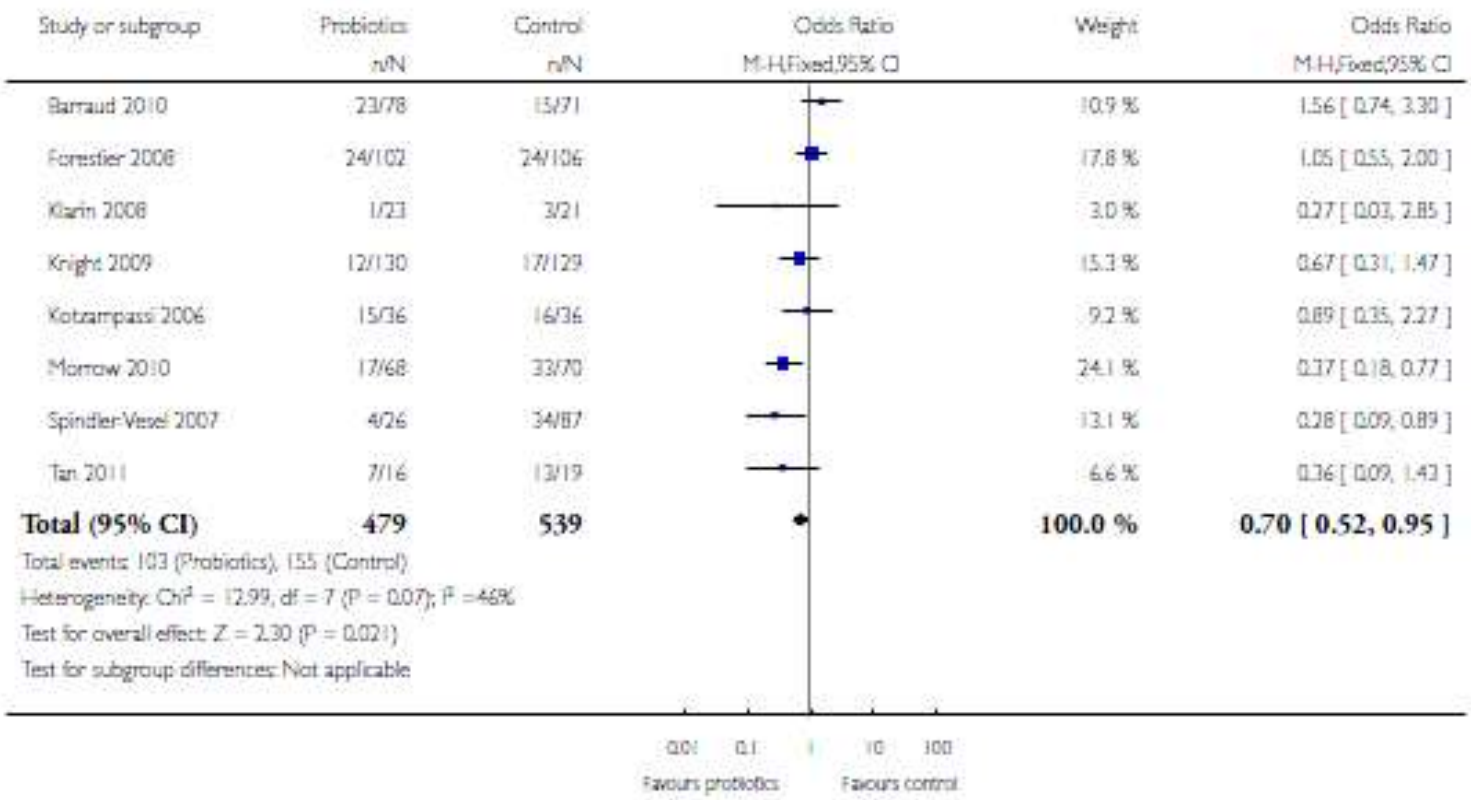
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Per-protocol analysis: probiotics versus control				
Incidence of VAP Follow-up: mean 37 days	**Moderate**[1]		**OR 0.7** (0.52 to 0.95)	1018 (8 studies)	⊕⊕◯◯ **low**[2,3]	
	309 per 1000	**238 per 1000** (189 to 298)				
ICU mortality Follow-up: mean 35 days	**Moderate**[4]		**OR 0.84** (0.58 to 1.22)	703 (5 studies)	⊕◯◯◯ **very low**[3,5,6]	
	214 per 1000	**186 per 1000** (136 to 249)				
Hospital mortality Follow-up: median 37 days	**Moderate**[7]		**OR 0.78** (0.54 to 1.14)	524 (4 studies)	⊕◯◯◯ **very low**[3,6,8]	
	306 per 1000	**256 per 1000** (192 to 335)				
Diarrhoea Follow-up: mean 40 days	**Moderate**[9]		**OR 0.72** (0.47 to 1.09)	618 (4 studies)	⊕◯◯◯ **very low**[3,6,8]	
	435 per 1000	**357 per 1000** (266 to 456)				

Analysis 1.1. Comparison 1 Per-protocol analysis: probiotics versus control, Outcome 1 Incidence of VAP.

Review: Probiotics for preventing ventilator-associated pneumonia

Comparison: 1 Per-protocol analysis: probiotics versus control

Outcome: 1 Incidence of VAP



ETT Modifications-silver coating, SSD

Endotracheal tubes represent a foreign body in the upper airway and are prone to bacterial colonization and the development of biofilms.

The formation of the biofilm is early after the intubation. The biofilm is a source and reservoir of infection to the lower respiratory tract, and a source of the contamination of the respiratory circuits , and it is resistance to the effect of the antibiotic.

Brown MR, 2008 J Antimicrob Chemother 22: 777-780

Rello J etal, 2010 Crit Care Med 38: 1135-1140.

The silver coated tubes have an effect in reduction of the formation of the biofilm, as after 16h of intubation there is no formation of the biofilm in the coated tubes, while the biofilm is formed on a non-coated tubes just after 8h.

Berra L etal,2004 Anesthesiology 100: 1446-1456

Berra et al, 2008 Care Med 34: 1020-1029.

- The use of the silver coated tubes has no additional adverse effects on the patients and shows a decrease in the incidence of VAP (in both early onset and late onset pneumonia), comparing with noncoated tubes, that decrease is around 50%.

Kollef MH, 2008 the NASCENT randomized trial. JAMA : the journal of the American Medical Association 300: 805-813

Reduced burden of bacterial airway colonization with a novel silver-coated endotracheal tube in a randomized multiple-center feasibility study *.

Rello, Jordi; MD, PhD; Kollef, Marin; Diaz, Emili; MD, PhD; Sandiumenge, Albert; del Castillo, Yolanda; Corbella, Xavier; Zachskorn, Regina

Critical Care Medicine. 34(11):2766-2772, November 2006.
DOI: 10.1097/01.CCM.0000242154.49682.B0

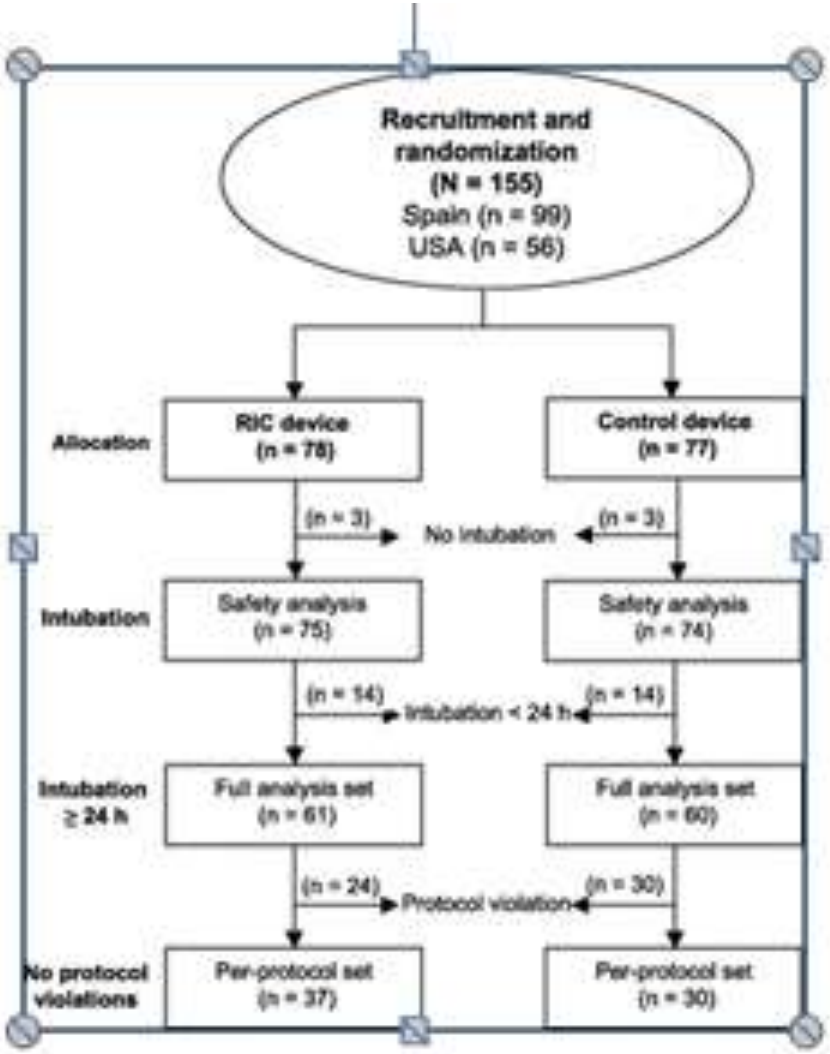

Recruitment and randomization
(N = 155)
Spain (n = 99)
USA (n = 56)
Allocation
RIC device (n = 78)
Control device (n = 77)
(n = 3)
No intubation
(n = 3)
Intubation
Safety analysis (n = 75)
Safety analysis (n = 74)
(n = 14)
Intubation < 24 h
(n = 14)
Intubation ≥ 24 h
Full analysis set (n = 61)
Full analysis set (n = 60)
(n = 24)
Protocol violation
(n = 30)
No protocol violations
Per-protocol set (n = 37)
Per-protocol set (n = 30)

Table 2. Colonization rates on endotracheal tube in the full analysis set

Threshold	RIC Group	Control Group	Relative Risk Reduction (95% CI)	*p* Value[a]
No. of patients with colonization/ total (%)				
Lowest	23/61 (38)	33/60 (55)	0.31 (−0.008 to 0.610)	.07
Intermediate	20/61 (33)	28/60 (47)	0.30 (−0.074 to 0.646)	.14
Highest	18/61 (30)	25/60 (42)	0.29 (−0.115 to 0.677)	.19
No. of days with colonization/ total (%)				
Lowest	54/242 (22)	86/226 (38)	0.41 (0.195 to 0.625)	.04
Intermediate	50/242 (21)	76/226 (34)	0.39 (0.146 to 0.620)	.09
Highest	45/242 (19)	71/226 (31)	0.41 (0.159 to 0.653)	.14

RIC, respiratory infection control; 95% CI, 95% confidence interval; lowest threshold, ++, +++, or $\geq 10^4$ colony-forming units (cfu)/mL; intermediate threshold, ++, +++, or $\geq 10^5$ cfu/mL; highest threshold, ++, +++, or $\geq 10^6$ cfu/mL.

[a] *p* value determined by Fisher's exact test for rates by patients and Wilcoxon's test for rates by days.

Silver-Coated Endotracheal Tubes and Incidence of Ventilator-Associated Pneumonia

The NASCENT Randomized Trial

Marin H. Kollef, MD
Bekele Afessa, MD
Antonio Anzueto, MD
Christopher Veremakis, MD
Kim M. Kerr, MD
Benjamin D. Margolis, MD
Donald E. Craven, MD
Pamela R. Roberts, MD
Alejandro C. Arroliga, MD
Rolf D. Hubmayr, MD
Marcos I. Restrepo, MD
William R. Auger, MD
Regina Schinner, Dipl-Stat
for the NASCENT
Investigation Group

Context Ventilator-associated pneumonia (VAP) causes substantial morbidity. A silver-coated endotracheal tube has been designed to reduce VAP incidence by preventing bacterial colonization and biofilm formation.

Objective To determine whether a silver-coated endotracheal tube would reduce the incidence of microbiologically confirmed VAP.

Design, Setting, and Participants Prospective, randomized, single-blind, controlled study conducted in 54 centers in North America. A total of 9417 adult patients (≥18 years) were screened between 2002 and 2006. A total of 2003 patients expected to require mechanical ventilation for 24 hours or longer were randomized.

Intervention Patients were assigned to undergo intubation with 1 of 2 high-volume, low-pressure endotracheal tubes, similar except for a silver coating on the experimental tube.

Main Outcome Measures Primary outcome was VAP incidence based on quantitative bronchoalveolar lavage fluid culture with 10^4 colony-forming units/mL or greater in patients intubated for 24 hours or longer. Other outcomes were VAP incidence in all intubated patients, time to VAP onset, length of intubation and duration of intensive care unit and hospital stay, mortality, and adverse events.

Results Among patients intubated for 24 hours or longer, rates of microbiologically confirmed VAP were 4.8% (37/766 patients; 95% confidence interval [CI], 3.4%-6.6%) in the group receiving the silver-coated tube and 7.5% (56/743; 95% CI, 5.7%-9.7%) ($P = .03$) in the group receiving the uncoated tube (all intubated patients, 3.8% [37/968; 95% CI, 2.7%-5.2%] and 5.8% [56/964; 95% CI, 4.4%-7.5%] [$P = .04$]), with a relative risk reduction of 35.9% (95% CI, 3.6%-69.0%; all intubated patients, 34.2% [95% CI, 1.2%-67.9%]). The silver-coated endotracheal tube was associated with delayed occurrence of VAP ($P = .005$). No statistically significant between-group differences were observed in durations of intubation, intensive care unit stay, and hospital stay; mortality; and frequency and severity of adverse events.

Conclusion Patients receiving a silver-coated endotracheal tube had a statistically significant reduction in the incidence of VAP and delayed time to VAP occurrence compared with those receiving a similar, uncoated tube.

VENTILATOR-ASSOCIATED PNEUMONIA (VAP) is associated with high morbidity, including increased length of hospital stay, health care costs, and infection with multidrug-resistant pathogens.[1-3] The condition usually occurs within 10 days after endotracheal intubation.[3,4] Reported rates vary by case mix, case definition, diagnostic procedures, and method of ex-

Figure 1. Flow of Participants Through the Trial

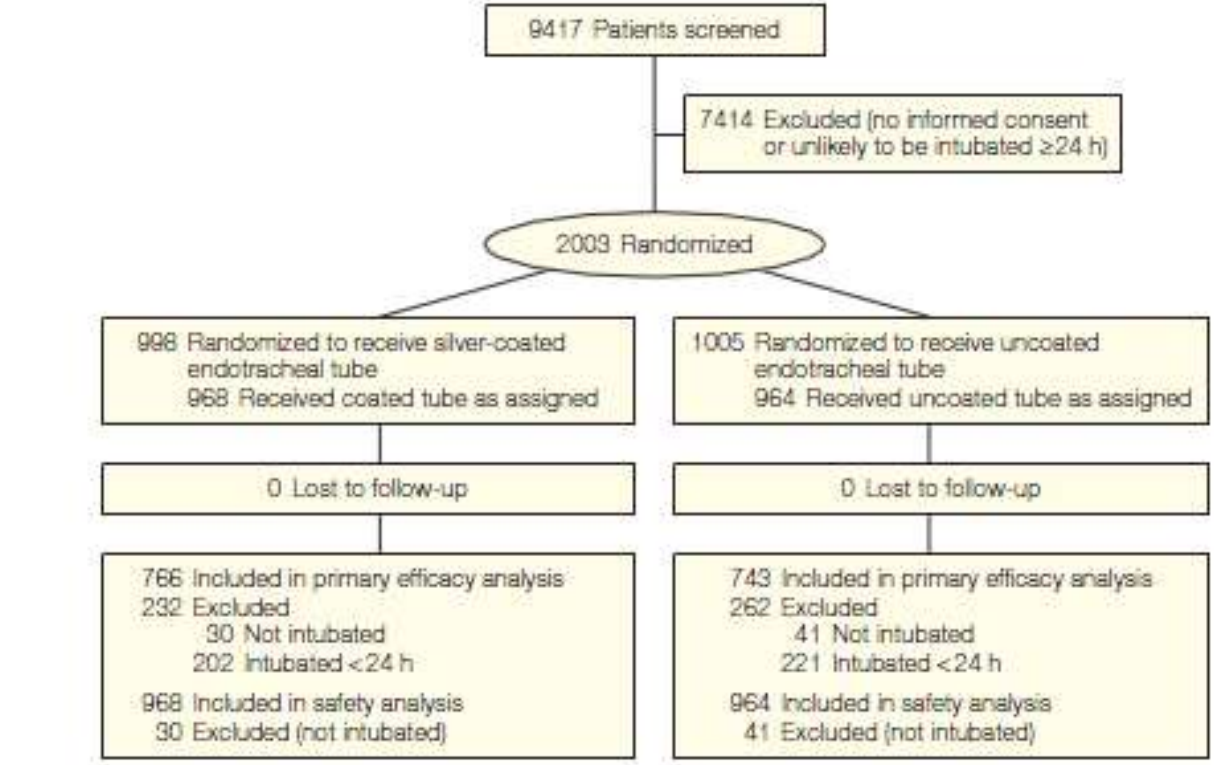


Table 2. Incidence of Microbiologically Confirmed Ventilator-Associated Pneumonia (VAP)[a]

	Evaluable Patients With VAP, No./Total (%) [95% CI]			
	Silver-Coated Tube	Uncoated Tube	RR Reduction, % (95% CI)	*P* Value
VAP at any time				
Intubated ≥24 h	37/766 (4.8) [3.4-6.6]	56/743 (7.5) [5.7-9.7]	35.9 (3.6-69.0)	.03
All intubated	37/968 (3.8) [2.7-5.2]	56/964 (5.8) [4.4-7.5]	34.2 (1.2-67.9)	.04
VAP within 10 d of intubation				
Intubated ≥24 h	27/766 (3.5) [2.3-5.1]	50/743 (6.7) [5.0-8.8]	47.6 (14.6-81.9)	.005
All intubated	27/968 (2.8) (1.9-4.0)	50/964 (5.2) (3.9-6.8)	46.2 (12.6-81.1)	.007
Microbiology[b]				
Staphylococcus aureus	9	16		
Methicillin-resistant *S aureus*	3	7		
Pseudomonas aeruginosa	8	11		
Enterobacteriaceae	10	5		
Yeast	5	7		
Streptococcus species	4	7		
Haemophilus influenzae	3	3		
Acinetobacter baumannii	1	5		
Other[c]	5	17		

Abbreviations: CI, confidence interval; RR, relative risk.

[a] Patients with at least 10^4 colony-forming units/mL in bronchoalveolar lavage fluid.

[b] Twenty patients had polymicrobial infections. In the group receiving the silver-coated endotracheal tube, 6 patients had 2 microorganisms and 1 patient had 3. In the group receiving the uncoated tube, 11 patients had 2 microorganisms and 2 patients had 3.

[c] Other microorganisms in the group receiving the silver-coated endotracheal tube were normal flora (n = 4) and Stenotro

Subglottic secretion drainage-SSD

The presence of secretion in the subglottic space is a source of aspiration in the intubated patients . The subglottic secretion leakage occurs between the cuff and the trachea through the longitudinal folds towards the lungs or through the micro aspiration of the subglottic secretions.

Young PJ, Br J Anaesth 78: 557-562.

Quanes L, 2001, Intensive Care Med 37: 695-700

Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: A systematic review and meta-analysis *.

Muscedere, John; MD, FRCPC; Rewa, Oleksa; Mckechnie, Kyle; Jiang, Xuran; Laporta, Denny; MD, FRCPC; Heyland, Daren; MD, FRCPC

Critical Care Medicine. 39(8):1985-1991, August 2011.
DOI: 10.1097/CCM.0b013e318218a4d9

Table 1. Summary of studies included in the meta-analysis

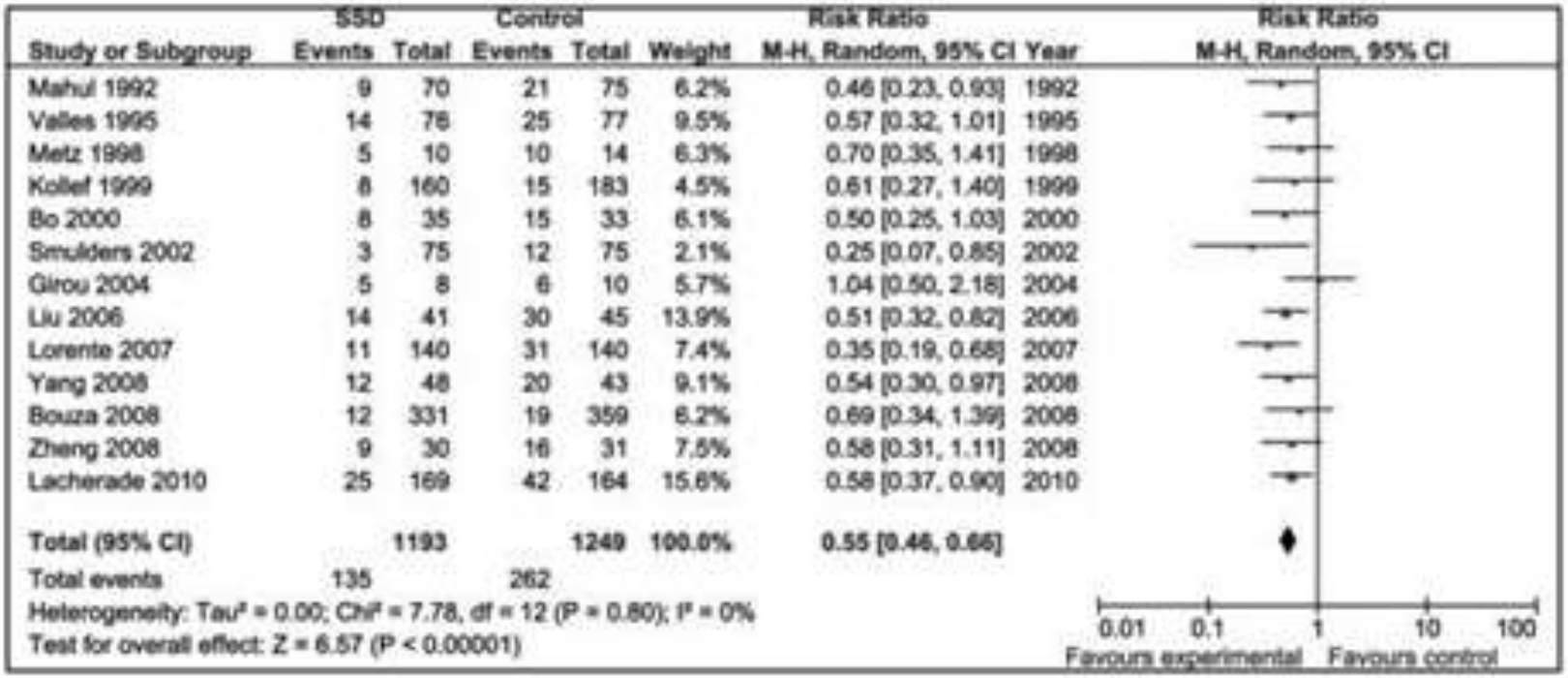
Author, Year	Population (n)	Inclusion Criteria	Clinical Suspicion of VAP*	VAP*	Interventions†	Score‡	Rate of VAP: a. Cases/1000 Ventilator-Days b. Cases/Patients		
							SSD	Control	p
Mahul, 1992	145	Expected duration of MV >3 days	Chest radiograph	BAL	None specified	9	a. 8/1000 b. 9/71	a. 17.5/1000 b. 21/75	a. <.05 b. NR
Valles, 1995	151	Expected duration of MV >3 days	Chest radiograph plus temp >38.3°C, WBC >12 or <4, purulent secretions	BAL or PSB	None specified	9	a. 19.9/1000 b. 14/78	a. 39.6/1000 b. 25/77	a. NR b. NR
Pelz, 1998	24	Expected duration of MV >3 days	Chest radiograph, temp >38.3°C, WBC >12 or <3, purulent secretions	ETA or BAL	None specified	7	a. NA/1000 b. 5/10	a. NA/1000 b. 10/14	a. NA b. NS
Rello, 1999	141	Need for MV after cardiac Surgery	Chest radiograph plus pulmonary abscess on histology or positive blood or pleural cultures or 2 of 3 of the following: fever, leukocytosis, purulent sputum	ETA or no micro	None specified	11	a. 24.5/1000 b. 8/160	a. 43.2/1000 b. 15/162	a. NR b. 0.24
Ibe, 2000	69	Expected duration of MV >72 hrs	Chest radiograph + temp >38.3°C or WBC >12 or <4 or purulent sputum	BAL or PSB	None specified	9	a. NA/1000 b. 6/35	a. NA/1000 b. 15/33	a. NA b. <.05
Heyland, 2002	150	Expected duration of MV >72 hrs	Chest radiograph + evidence for cavitation, histology, positive blood cultures, a positive pleural fluid culture, or any of the 2 following symptoms/ signs: fever (rectal >38°C), WBC <3 or >10, purulent tracheal aspirate (>25 WBC per field	ETA	None specified	9	a. 9.2/1000 b. 3/75	a. 22.3 b. 12/75	a. NR b. .03
Giroy, 2004	14	Expected duration of MV >3 days	Chest radiograph, temp >38.3°C or WBC >12, or purulent sputum	PSB or BAL	Elevation of head of bed in SSD group	9	a. NA/1000 b. 5/8	a. NA/1000 b. 6/10	a. NA b. NS
Liu, 2006	86	Age older than 60 yrs, expected MV >48 hrs	Chest radiograph and 2 of 4: temp >38.0°C or <35.5°C, WBC >10 or <2, >14 WBC high-power field in ETA, or a positive ETA culture	PSB or BAL or positive blood or pleural fluid culture	Elevation of head of bed, gastrointestinal agents in SSD group	9	a. NA/1000 b. 14/41	a. NA/1000 b. 26/45	a. NA b. <.05
Luyento, 2007	290	Expected MV >24 hrs	Chest radiograph, purulent secretions, temp >39°C or <35.5°C, WBC >10 or <4	Quantitative ETA	Tricyanothane cuff in addition to SSD	13	a. 7.5/1000 b. 11/146	a. 19.9/1000 b. 31/146	a. .001 b. .005
Rouzé, 2009	214	Major heart surgery	Chest radiograph and 2 of: temp >38.3°C or <36°C, WBC > 12, purulent secretions, reduction in PF >15% or CPIS >6	Quantitative ETA or PSB	None specified	12	a. 12.8/1000 b. 12/339	a. 27.6 b. 19/331	a. .2 b. .18
Yang, 2009	91	MV >48 hrs	Chest radiograph and 2 of: temp >38.3°C, WBC >12, WBC <4.0, purulent secretions	No micro or ETA or positive blood culture	None specified	9	a. NA/1000 b. 12/49	a. NA/1000 b. 20/43	a. NA b. .03

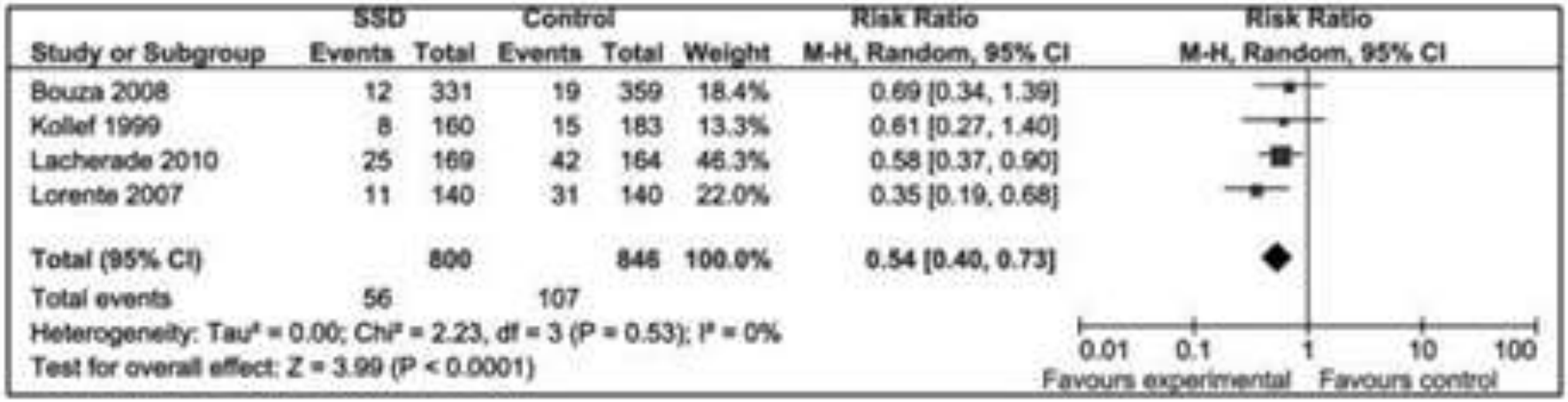
Table 1.—*Continued*

Author, Year	Population (n)	Inclusion Criteria	Clinical Suspicion of VAP[a]	VAP[b]	Cointerventions[c]	Score[d]	Rate of VAP[e] a. Cases/1000 Ventilator-Days b. Cases/Patients		
							SSD	Control	*p*
Zheng, 2008	61	MV >48 hrs	Chest radiograph + temp >38°C or WBC >12 or <4.0 or altered mental status + 2 of purulent sputum, cough, abnormal physical examination, or worsening gas exchange	No micro	None specified	7	a. NA/1000 b. 9/30	a. NA/1000 b. 16/31	a. NA b. <.05
Lacherade, 2010	333	Expected MV >48 hrs	Chest radiograph and 2 of: temp >38.3°C or <36°C, WBC >10 or <4 and purulent tracheal secretions	PSB or BAL	None specified	12	a. 17/1000 b. 25 cases	a. 34/1000 b. 42 cases	a. .002 b. .02

BAL, broncho-alveolar lavage; *CPIS*, clinical pulmonary infection score; *ETA*, endotracheal aspirate; *MV*, mechanical ventilation; *NA*, not applicable; *No micro*, microbiological; *NR*, not reported; *NS*, not significant; *PF*, PaO_2/FIO_2 ratio; *PSB*, protected specimen brush; *SSD*, subglottic secretion drainage; *temp*, temperature; *VAP*, ventilator-associated pneumonia; *WBC*, white blood cell count.

[a]Chest radiograph. Requirement for new or persistent pulmonary infiltrate on a chest radiograph for suspicion of VAP. WBC per 10^9 mL; [b]microbiological criteria for VAP. This refers to the minimum microbiological criteria for the diagnosis of VAP. BAL or PSB = quantitative invasive cultures. No micro = microbiological culture not required for VAP diagnosis; [c]cointerventions. When described, this refers to imbalances between SSD group and control in measures that may have an effect on VAP; [d]methodological score. Refer to SDC Table 1 (see Supplemental Digital Content 1, http://links.lww.com/CCM/A247) for components.


SSD
Control
Risk Ratio
Risk Ratio
Study or Subgroup
Events Total Events Total Weight M-H, Random, 95% CI Year
M-H, Random, 95% CI
Mahul 1992 9 70 21 75 6.2% 0.46 [0.23, 0.93] 1992
Valles 1995 14 76 25 77 9.5% 0.57 [0.32, 1.01] 1995
Metz 1998 5 10 10 14 6.3% 0.70 [0.35, 1.41] 1998
Kollef 1999 8 160 15 183 4.5% 0.61 [0.27, 1.40] 1999
Bo 2000 8 35 15 33 6.1% 0.50 [0.25, 1.03] 2000
Smulders 2002 3 75 12 75 2.1% 0.25 [0.07, 0.85] 2002
Girou 2004 5 8 6 10 5.7% 1.04 [0.50, 2.18] 2004
Liu 2006 14 41 30 45 13.9% 0.51 [0.32, 0.82] 2006
Lorente 2007 11 140 31 140 7.4% 0.35 [0.19, 0.68] 2007
Yang 2008 12 48 20 43 9.1% 0.54 [0.30, 0.97] 2008
Bouza 2008 12 331 19 359 6.2% 0.69 [0.34, 1.39] 2008
Zheng 2008 9 30 16 31 7.5% 0.58 [0.31, 1.11] 2008
Lacherade 2010 25 169 42 164 15.6% 0.58 [0.37, 0.90] 2010
Total (95% CI) 1193 1249 100.0% 0.55 [0.46, 0.66]
Total events 135 262
Heterogeneity: Tau² = 0.00; Chi² = 7.78, df = 12 (P = 0.80); I² = 0%
Test for overall effect: Z = 6.57 (P < 0.00001)
0.01 0.1 1 10 100
Favours experimental Favours control


SSD
Control
Risk Ratio
Risk Ratio
Study or Subgroup
Events Total Events Total Weight
M-H, Random, 95% CI
M-H, Random, 95% CI
Bouza 2008 12 331 19 359 18.4% 0.69 [0.34, 1.39]
Kollef 1999 8 160 15 183 13.3% 0.61 [0.27, 1.40]
Lacherade 2010 25 169 42 164 46.3% 0.58 [0.37, 0.90]
Lorente 2007 11 140 31 140 22.0% 0.35 [0.19, 0.68]
Total (95% CI) 800 846 100.0% 0.54 [0.40, 0.73]
Total events 56 107
Heterogeneity: Tau² = 0.00; Chi² = 2.23, df = 3 (P = 0.53); I² = 0%
Test for overall effect: Z = 3.99 (P < 0.0001)
0.01
0.1
1
10
100
Favours experimental
Favours control

Prevention of Ventilator-Associated Pneumonia and Ventilator-Associated Conditions: A Randomized Controlled Trial With Subglottic Secretion Suctioning*

Damas, Pierre MD, PhD[1]; Frippiat, Frédéric MD, PhD[2]; Ancion, Arnaud MD[2]; Canivet, Jean-Luc MD, PhD[1]; Lambermont, Bernard MD, PhD[2]; Layios, Nathalie MD[1]; Massion, Paul MD, PhD[1]; Morimont, Philippe MD, PhD[2]; Nys, Monique PhD[1]; Piret, Sonia MD[1]; Lancellotti, Patrizio MD, PhD[2]; Wiesen, Patricia MD[1]; D'orio, Vincent MD, PhD[3]; Samalea, Nicolas[1]; Ledoux, Didier MD, PhD[1]

Author Information

[1]Department of General Intensive Care, University Hospital of Liege, Liège, Belgium.

[2]Department of Medicine, University Hospital of Liege, Liège, Belgium.

[3]Department of Emergency Medicine, University Hospital of Liege, Liège, Belgium.

* See also p. 227.

This work was performed at University Hospital of Liege, Liège, Belgium.

Teleflex furnished the endotracheal tubes with subglottic secretion suctioning necessary for the whole study.

The authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail:
pdamas@chu.ulg.ac.be

Abstract

Objectives: Ventilator-associated pneumonia diagnosis remains a debatable topic. New definitions of ventilator-associated conditions involving worsening oxygenation have been recently proposed to make surveillance of events possibly linked to ventilator-associated pneumonia as objective as possible. The objective of the study was to confirm the effect of subglottic secretion suctioning on ventilator-associated pneumonia prevalence and to assess its concomitant impact on ventilator-associated conditions and antibiotic use.

Design: Randomized controlled clinical trial conducted in five ICUs of the same hospital.

Oral chlorhexidine

- there are over 700 bacterial species identified in the oral cavity, with more than 400 are present in periodontal pocket.
- Absence of adequate salivary flow in intubated patients in ICU contributes with the development of oropharyngeal colonization and by molecular analysis of the oral and respiratory bacteria in VAP patients, it is shown that 88% of the cases of VAP had an overlap of pathogens in the lung and the oral cavity.

Bahrani etal, 2007 J Clin Microbiol 45: 1588-1593.

Paster bj, 2006 Periodontol 2000 42: 80-87

[Intervention Review]

Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia

Zongdao Shi[1], Huixu Xie[1], Ping Wang[2], Qi Zhang[3], Yan Wu[4], E Chen[5], Linda Ng[6], Helen V Worthington[7], Ian Needleman[8], Susan Furness[7]

[1]Department of Oral and Maxillofacial Surgery, State Key Laboratory of Oral Diseases, West China College of Stomatology, Sichuan University, Chengdu, China. [2]Department of Dental Implantation, West China College of Stomatology, Sichuan University, Chengdu, China. [3]Department of Oral Implantology, State Key Laboratory of Oral Diseases, West China College of Stomatology, Sichuan University, Chengdu, China. [4]Department of Orthodontics, Chongqing Medical University, Chongqing, China. [5]Department of Paediatric Dentistry, West China College of Stomatology, Sichuan University, Chengdu, China. [6]School of Nursing and Midwifery, University of Queensland, South Brisbane, Australia. [7]Cochrane Oral Health Group, School of Dentistry, The University of Manchester, Manchester, UK. [8]Unit of Periodontology and International Centre for Evidence-Based Oral Healthcare, UCL Eastman Dental Institute, London, UK

Contact address: Susan Furness, Cochrane Oral Health Group, School of Dentistry, The University of Manchester, Coupland III Building, Oxford Road, Manchester, M13 9PL, UK. Susan.Furness@manchester.ac.uk. suefurness@gmail.com.

Editorial group: Cochrane Oral Health Group.
Publication status and date: Edited (no change to conclusions), published in Issue 11, 2013.
Review content assessed as up-to-date: 14 January 2013.

Citation: Shi Z, Xie H, Wang P, Zhang Q, Wu Y, Chen E, Ng L, Worthington HV, Needleman I, Furness S. Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. *Cochrane Database of Systematic Reviews* 2013, Issue 8. Art. No.: CD008367. DOI: 10.1002/14651858.CD008367.pub2.

Cite this article as: BMJ, doi:10.1136/bmj.39136.528160.BE (published 26 March 2007)

BMJ

RESEARCH

Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis

Ee Yuee Chan, nurse educator,[1] Annie Ruest, infectious diseases consultant,[2] Maureen O Meade, associate professor,[3] Deborah J Cook, professor[3]

[1]Department of Nursing Services, Tan Tock Seng Hospital, Singapore
[2]Centre Hospitalier Universitaire de Québec-Hôtel-Dieu, Departments of Medicine and Medical Biology, Québec, Canada
[3]Departments of Medicine, Clinical Epidemiology, and Biostatistics, McMaster University, Hamilton, Canada

Correspondence to: E Y Chan
ee_yuee_chan@ttsh.com.sg

doi 10.1136/bmj.39136.528160.BE

ABSTRACT

Objective To evaluate the effect of oral decontamination on the incidence of ventilator associated pneumonia and mortality in mechanically ventilated adults.

Design Systematic review and meta-analysis.

Data sources Medline, Embase, CINAHL, the Cochrane Library, trials registers, reference lists, conference proceedings, and investigators in the specialty.

Review methods Two independent reviewers screened studies for inclusion, assessed trial quality, and extracted data. Eligible trials were randomised controlled trials enrolling mechanically ventilated adults that compared the effects of daily oral application of antibiotics or antiseptics with no prophylaxis.

Results 11 trials totalling 3242 patients met the inclusion criteria. Among four trials with 1098 patients, oral application of antibiotics did not significantly reduce the incidence of ventilator associated pneumonia (relative risk 0.69, 95% confidence interval 0.41 to 1.18). In seven trials with 2144 patients, however, oral application of antiseptics significantly reduced the incidence of ventilator associated pneumonia (0.56, 0.39 to 0.81). When the results of the 11 trials were pooled, rates of ventilator associated pneumonia were lower among patients receiving either method of oral decontamination (0.61, 0.45 to 0.82). Mortality was not influenced by prophylaxis with either antibiotics (0.94, 0.73 to 1.21) or antiseptics (0.96, 0.69 to 1.33) nor was duration of mechanical ventilation or stay in the intensive care unit.

Conclusions Oral decontamination of mechanically ventilated adults using antiseptics is associated with a lower risk of ventilator associated pneumonia. Neither antiseptic nor antibiotic oral decontamination reduced mortality or duration of mechanical ventilation or stay in the intensive care unit.

INTRODUCTION

Ventilator associated pneumonia remains a leading cause of morbidity and mortality among mechanically ventilated patients, with the incidence ranging from 9% to 27% and a crude mortality that may exceed 50%.[1-4] Aspiration of bacteria from the upper digestive tract is

bacterial load are selective decontamination of the digestive tract, involving administration of non-absorbable antibiotics by mouth and through a nasogastric tube, and oral decontamination, which is limited to topical oral application of antibiotics or antiseptics.

Previous meta-analyses of selective decontamination of the digestive tract found a significant reduction in rates of ventilator associated pneumonia among treated patients.[5-14] The use of this intervention is, however, limited by concern about the emergence of antibiotic resistant bacteria.[15-17] Oral decontamination alone therefore may be more attractive because it requires only a fraction of the antibiotics used in selective decontamination of the digestive tract. To date, trials of oral decontamination using antibiotics have generated conflicting results, some suggesting benefit[18 19 w1] and others showing no benefit.[w2 w3]

One alternative to oral decontamination with antibiotics is to use antiseptics, such as chlorhexidine gluconate or povidone iodine. In contrast to antibiotics, antiseptics act rapidly at multiple target sites and accordingly may be less prone to induce drug resistance.[20] Observational studies suggest that antiseptic oral decontamination can reduce ventilator associated pneumonia,[21 22] but randomised controlled trials are not convincing.[23 w4-w6] Recently a meta-analysis of four trials on chlorhexidine failed to show a significant reduction in rates of ventilator associated pneumonia.[24] Two subsequent randomised controlled trials, however, suggested benefit from this approach.[w7 w8]

Current guidelines from the Centers for Disease Control and Prevention recommend topical oral chlorhexidine 0.12% during the perioperative period for adults undergoing cardiac surgery (grade II evidence).[3] The routine use of antibiotic or antiseptic oral decontamination for the prevention of ventilator associated pneumonia, however, remains unresolved.[3] Despite the lack of firm evidence favouring this preventive intervention, a recent survey across 59 European intensive care units from five countries showed

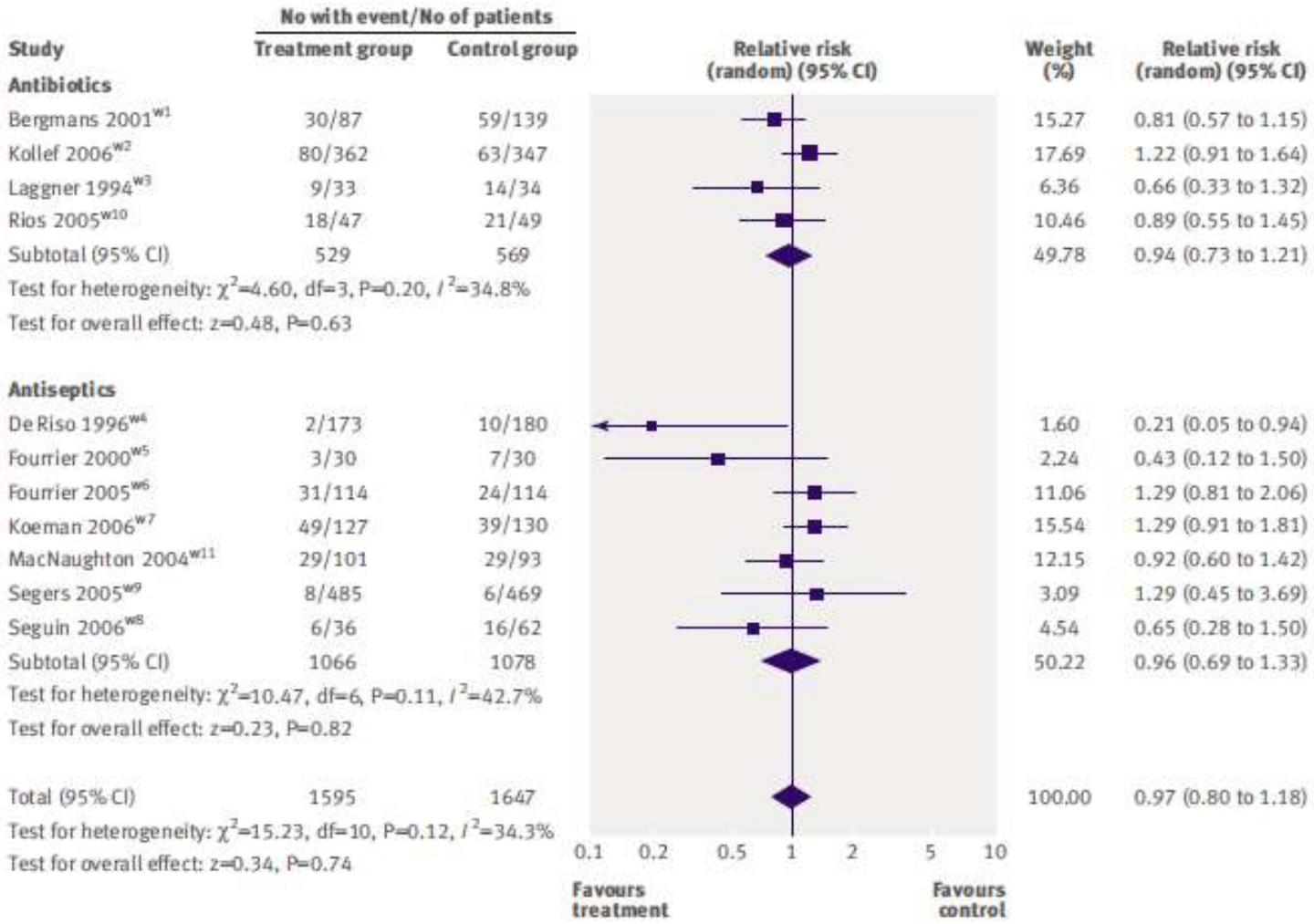


Fig 3 | Forest plot showing effect of oral decontamination prophylaxis compared with no prophylaxis on overall mortality

CHEST

Preintubation Application of Oral Chlorhexidine Does Not Provide Additional Benefit in Prevention of Early-Onset Ventilator-Associated Pneumonia

Cindy L. Munro, PhD, RN, ANP; Mary Jo Grap, PhD, RN; Curtis N. Sessler, MD, FCCP; Ronald K. Elswick Jr, PhD; Devanand Mangar, MD; Rachel Karlnoski-Everall, PhD; and Paula Cairns, BSN, RN

BACKGROUND: Daily application of oral chlorhexidine gluconate (CHX) following intubation to reduce the risk of ventilator-associated pneumonia (VAP) is now the standard of care in many ICUs. This randomized clinical trial evaluated the benefit of adding a preintubation CHX dose to the known benefit of postintubation CHX to reduce the risk of early-onset VAP. A secondary aim was to test the effect of a preintubation oral application of CHX on early endotracheal tube (ETT) colonization.

METHODS: Subjects (N = 314) were recruited from two teaching hospitals and were randomly assigned to oral application of 5 mL CHX 0.12% solution before intubation (intervention group, n = 157), or to a control group (n = 157) who received no CHX before intubation. All subjects received CHX bid after intubation. Groups were compared using a repeated-measures model with Clinical Pulmonary Infection Score (CPIS) as the response variable. In a planned subset of subjects, ETTs were cultured at extubation.

RESULTS: Application of a preintubation dose of CHX did not provide benefit over the intervention period beyond that afforded by daily oral CHX following intubation. ETT colonization at extubation was < 20% in both groups (no statistically significant difference). Mean CPIS remained below 6 (VAP threshold score) in both groups.

CONCLUSIONS: Although it is feasible to deliver CHX prior to intubation (including emergent or urgent intubation), the results suggest that preintubation CHX may be inconsequential when the ventilator bundle, including daily oral CHX, is in place. During the preintubation period, providers should focus their attention on other critical activities.

TRIAL REGISTRY: ClinicalTrials.gov; No.: NCT00893763; URL: www.clinicaltrials.gov

CHEST 2015; 147(2):328-334

Key take home points-

the oral hygiene is effective in decreasing the incidence of early VAP but not the late onset VAP, while comparing the use of chlorhexidine and the toothbrush in the oral care to the regular oral care has shown no statistical difference prevention of VAP.

the use of the probiotic in prevention of VAP is still under analysis, as the results are controversial, and statistics did not show a clear results about different parameters such as the incidence, the days in the hospital, the use of the antibiotics.

Use of NIPPV is one important way to either avoid the need for intubation or terminate mechanical ventilation as early as possible by extubation to NIPPV.

SSD has proved the efficacy in decreasing the early VAP incidence, days on ventilations and use of antibiotics. Both continuous and intermittent suction have proved their efficacy in decreasing the VAP incidence

Table 18: Preventive strategies for VAP

The following strategies are recommended in prevention of VAP:
Oral cavity decontamination with 2% chlorhexidine (1A)[412-415]
Hand hygiene preferably using alcohol-based hand rubs or soap and water (1A)[416]
Use of sedation and weaning protocols (1A)[419,420]
Use of NIV to avoid intubation, where feasible (1A)[264,421]
Subglottic secretion drainage (2A)[422,423]
Heat moisture exchangers in place of heated humidifiers (2A)[424-428]
Closed suction systems (2A)[429-431]
Use of orotracheal intubation as opposed to nasotracheal intubation (2A)[432,433]
Proper and timely disposal of condensates (3A)[434,435]
Maintaining tracheal cuff pressures <25 cm H_2O (2A)[436]
Wipe stethoscopes with alcohol rubs (2A)[437]
Regular postural mobilization to prevent stasis of secretions (2A)
Use of only normal saline for suctioning (3A)
Proper sterilization of nebulizer and other chambers (2A)
Head end elevation to 30°–45° (2A)
The following strategies are not recommended in prevention of VAP:
Antibiotics for prevention of VAP (2A)
Selective digestive tract decontamination (2A)[438]
Routine ventilator circuit changes (2A)[439,440]
Early tracheostomy (2A)

Gupta etal, Lung India. 2012 Jul-Sep; 29(Suppl 2): S27–S62

Conclusion-

VAP is associated with significant morbidity and mortality in critically ill mechanically ventilated patients and has deleterious economic impact on the health care system. The most important step in the approach to VAP is therefore its prevention.

There are many preventative modalities which have been demonstrated to be effective. These include the utilization of NIPPV, oral hygiene measures, modification of ETTs (subglottic secretion drainage or silver-coated) and positioning.

The management of VAP relies upon its prompt diagnosis and involves clinical signs, laboratory investigations, chest radiography, and microbiological data from lung cultures. Unfortunately, a reference standard for VAP remains elusive

There has been significant evolution for the surveillance of VAP. These terms, VAC and iVACs, do not replace the traditional diagnosis of VAP but capture a broader variety of pathologies including pneumonia that may impair gas exchange in mechanically ventilated patients.