Prevention of VAP

Claude MARTIN

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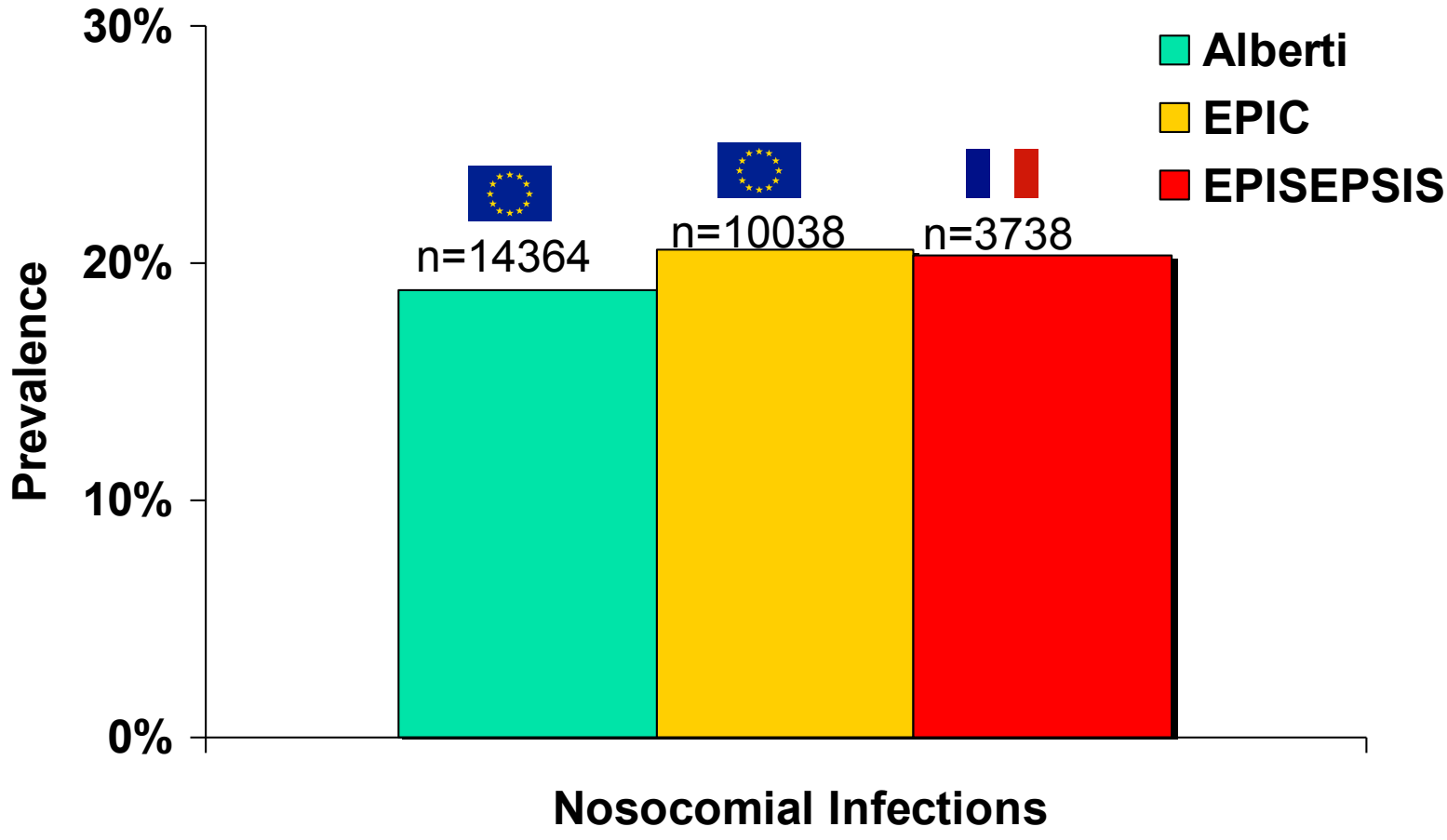
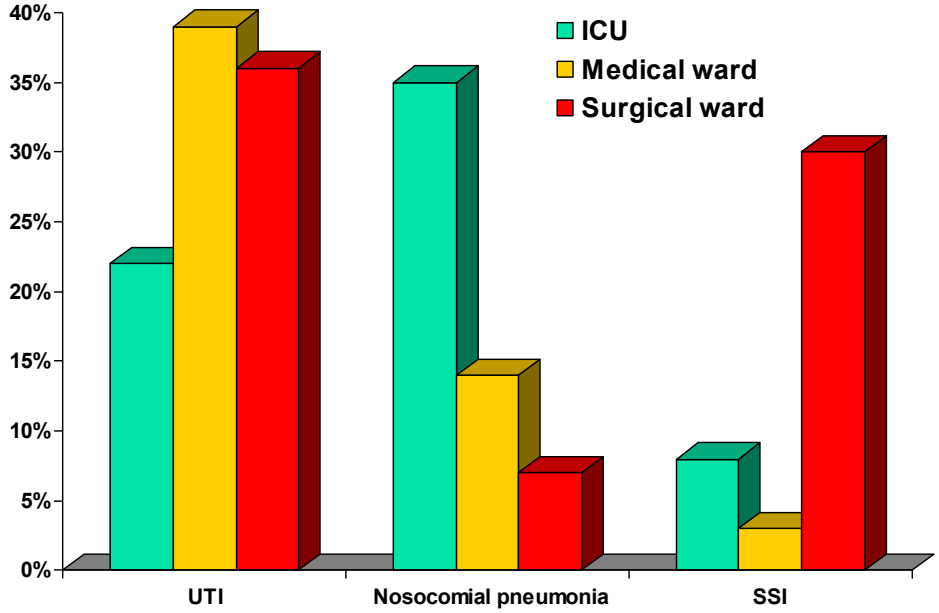
Prevalence of nosocomial infections

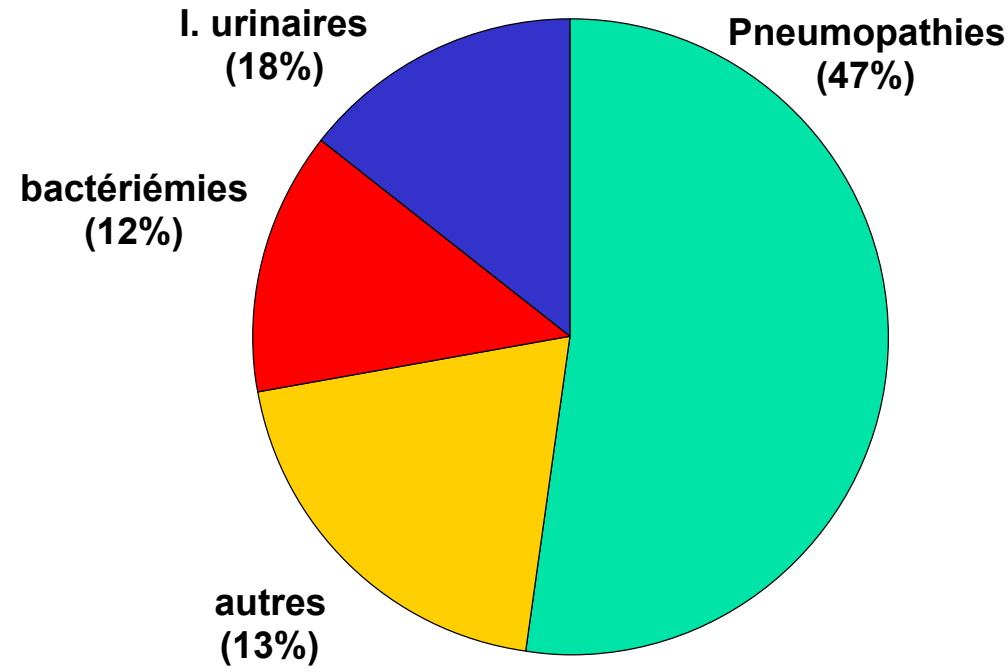


(Alberti, ICM 2002 - EPIIC, JAMA 1995 - EPISEPSIS ICM, 2004)

Nosocomial Pneumonia



Enquête hôpital propre (n=18074)
(J Hosp Infect 2001)



EPIIC Study (n=10518)
(Vincent, JAMA 1995)

Clinical outcomes of health-care-associated infections and antimicrobial resistance in patients admitted to European intensive-care units: a cohort study

Marie-Laurence Lambert, Carl Suetens, Anne Savey, Mercedes Palomar, Michael Hiesmayr, Ingrid Morales, Antonella Agodi, Uwe Frank, Karl Mertens, Martin Schumacher, Martin Wolkewitz

Summary

Background Patients admitted to intensive-care units are at high risk of health-care-associated infections, and many are caused by antimicrobial-resistant pathogens. We aimed to assess excess mortality and length of stay in intensive-care units from bloodstream infections and pneumonia.

Methods We analysed data collected prospectively from intensive-care units that reported according to the European standard protocol for surveillance of health-care-associated infections. We focused on the most frequent causative microorganisms. Resistance was defined as resistance to ceftazidime (*Acinetobacter baumannii* or *Pseudomonas aeruginosa*), third-generation cephalosporins (*Escherichia coli*), and oxacillin (*Staphylococcus aureus*). We defined 20 different exposures according to infection site, microorganism, and resistance status. For every exposure, we compared outcomes between patients exposed and unexposed by use of time-dependent regression modelling. We adjusted results for patients' characteristics and time-dependency of the exposure.

Findings We obtained data for 119 699 patients who were admitted for more than 2 days to 537 intensive-care units in ten countries between Jan 1, 2005, and Dec 31, 2008. Excess risk of death (hazard ratio) for pneumonia in the fully adjusted model ranged from 1·7 (95% CI 1·4–1·9) for drug-sensitive *S aureus* to 3·5 (2·9–4·2) for drug-resistant *P aeruginosa*. For bloodstream infections, the excess risk ranged from 2·1 (1·6–2·6) for drug-sensitive *S aureus* to 4·0 (2·7–5·8) for drug-resistant *P aeruginosa*. Risk of death associated with antimicrobial resistance (ie, additional risk of death to that of the infection) was 1·2 (1·1–1·4) for pneumonia and 1·2 (0·9–1·5) for bloodstream infections for a combination of all four microorganisms, and was highest for *S aureus* (pneumonia 1·3 [1·0–1·6], bloodstream infections 1·6 [1·1–2·3]). Antimicrobial resistance did not significantly increase length of stay; the hazard ratio for discharge, dead or alive, for sensitive microorganisms compared with resistant microorganisms (all four combined) was 1·05 (0·97–1·13) for pneumonia and 1·02 (0·98–1·17) for bloodstream infections. *P aeruginosa* had the highest burden of health-care-acquired infections because of its high prevalence and pathogenicity of both its drug-sensitive and drug-resistant strains.

Interpretation Health-care-associated bloodstream infections and pneumonia greatly increase mortality and pneumonia increase length of stay in intensive-care units; the additional effect of the most common antimicrobial resistance patterns is comparatively low.

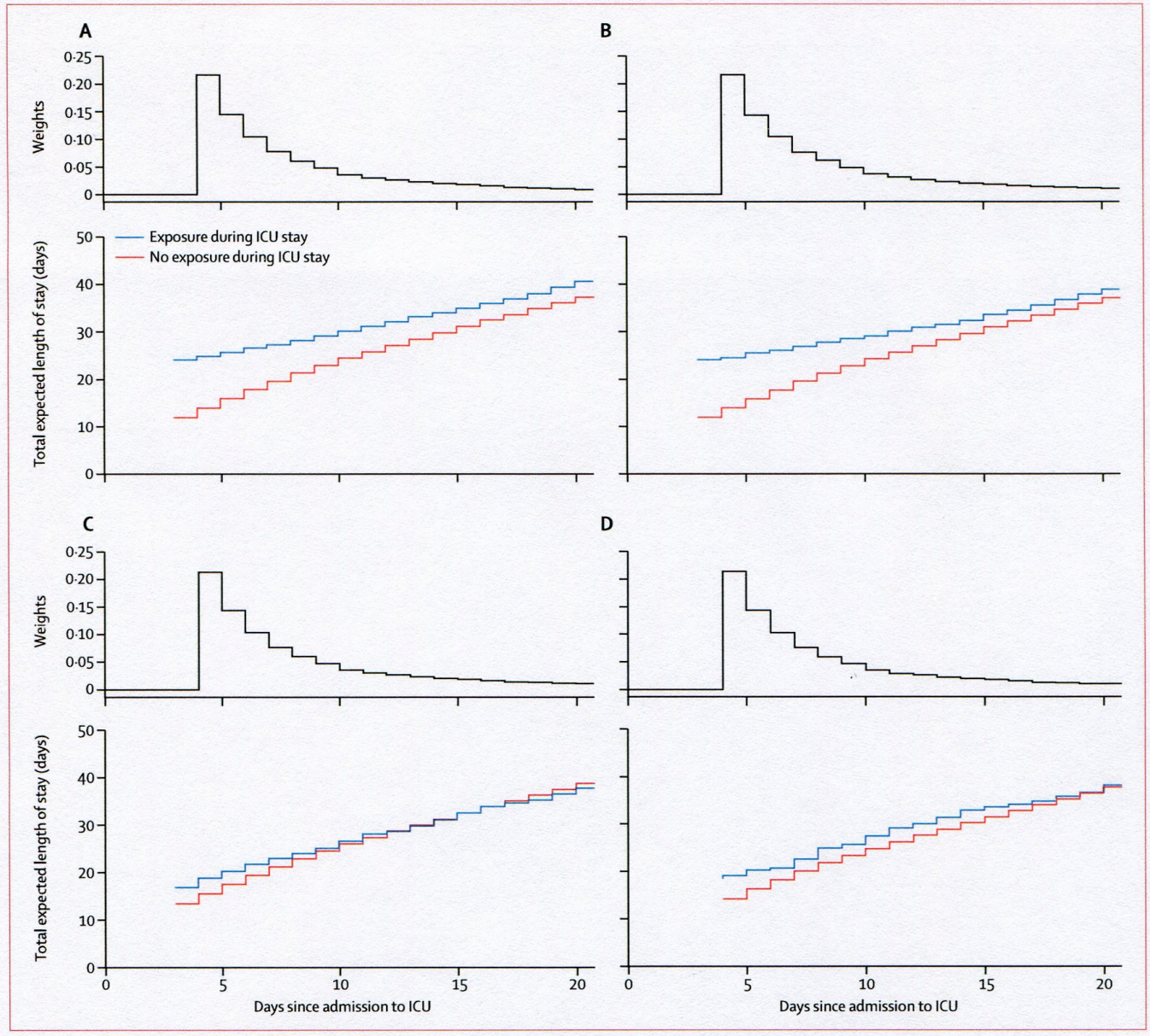
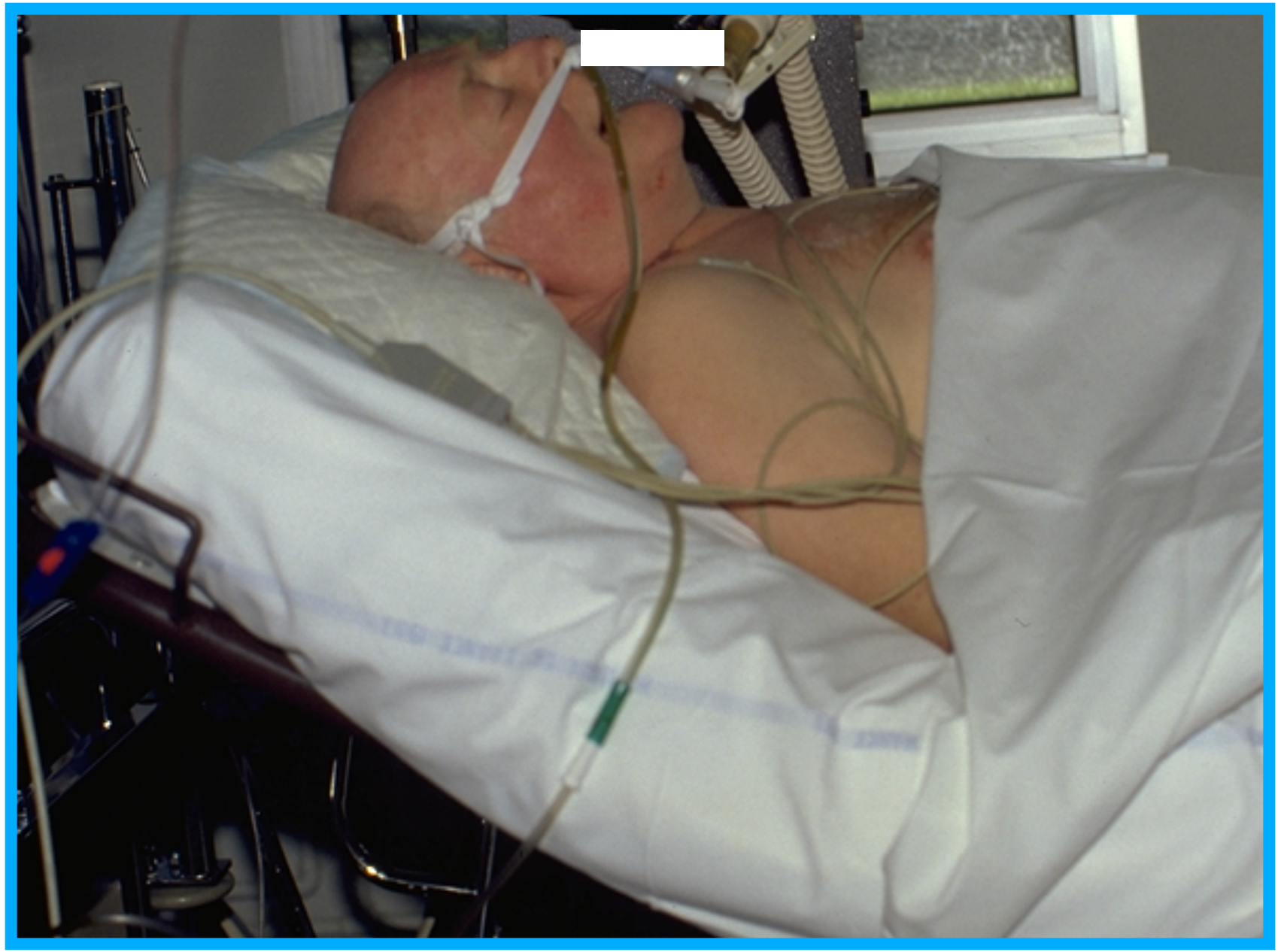


***Figure*: Excess length of stay (days) in intensive-care units related to pneumonia and bloodstream infections (all four microorganisms combined)**
(A) Exposure is pneumonia with drug-sensitive microorganisms. (B) Exposure is pneumonia with drug-resistant microorganisms. (C) Exposure is bloodstream infection with drug-sensitive microorganisms. (D) Exposure is bloodstream infection with drug-resistant microorganisms. Weights were calculated by the distribution of time until group membership (not exposed *vs* exposed) became definite, and show the contribution of events occurring at the corresponding time to the overall estimate (in days, see tables 4 and 5). The difference between the two lines does not depend on the weights. ICU=intensive-care unit.

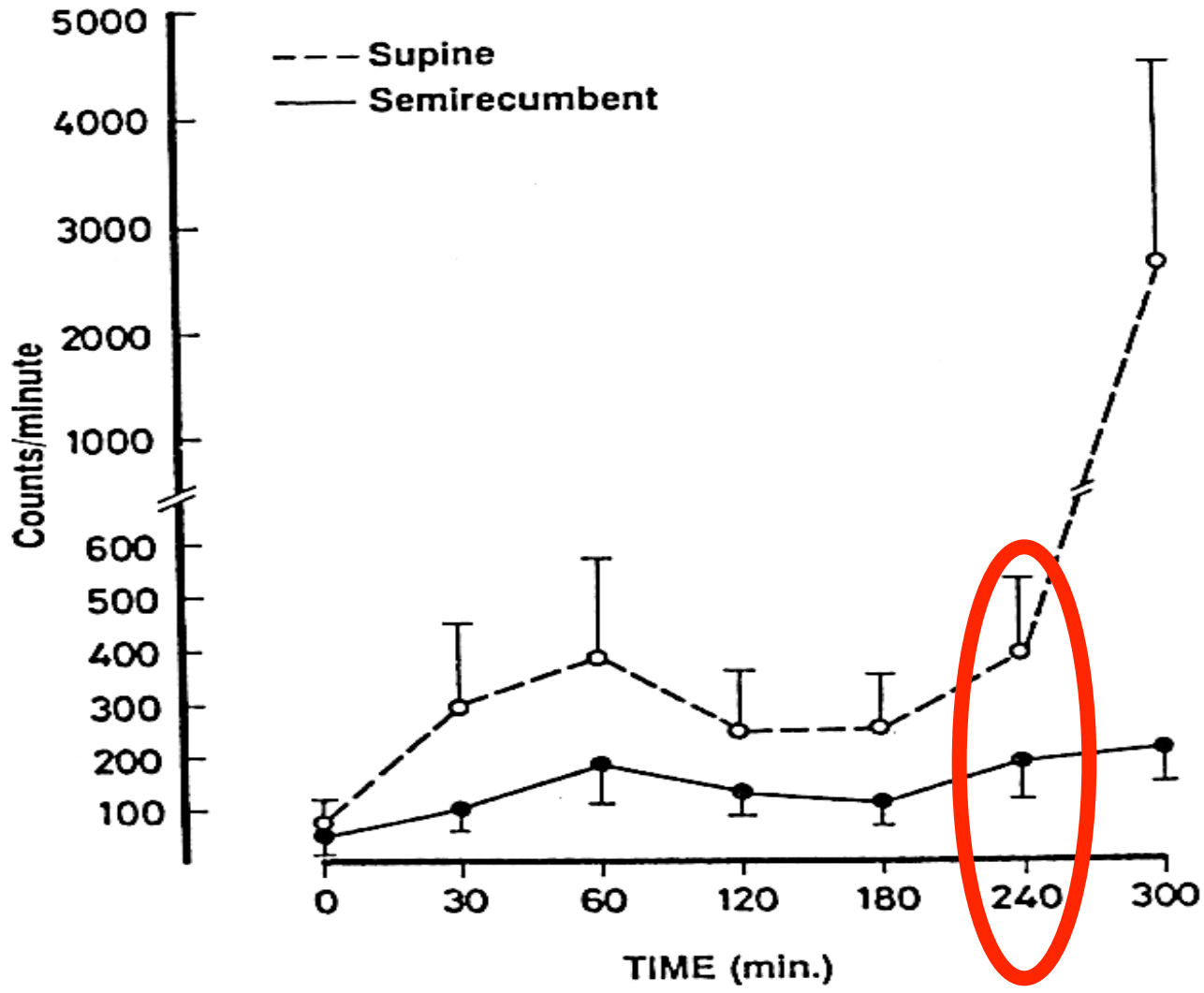
Semirecumbent Position



Semirecumbent Position

in patients receiving M.V.: The effect of body position.

Torres et al, Annals of Internal med. 116: 540-543, 1993



Time-dependent recovery of technetium-99m-labeled gastric contents in endobronchial aspirates at two body positions. Bars represent SE; semirecumbent = 45-degree angle).

Semirecumbent Position

- 86 patients randomized (Drakulovic, Lancet 1999,354 , 1851-58)

	Supine	SR	P
. Clinical pneumonia	34%	8%	0.003
. Microbiological pneumonia	23%	5%	0.01

- **Only independent factor : supine position : OR = 5.7, CI 95% : 1.1. – 39.9**
- **Under - used in clinical practice (Cook, CCM 2002)**
- **CDC : level II**
- **European consensus : supine position must be avoided (Hubmayer, ICM 2002)**

Feasibility and effects of the semirecumbent position to prevent ventilator-associated pneumonia: A randomized study*

Christianne A. van Nieuwenhoven, MD; Christine Vandenbroucke-Grauls, PhD; Frank H. van Tiel, PhD; Hans C. A. Joore, MD; Rob J. M. Strack van Schijndel, MD; Ingeborg van der Tweel, PhD; Graham Ramsay, PhD; Marc J. M. Bonten, PhD

Context: Reducing aspiration of gastric contents by placing mechanically ventilated patients in a semirecumbent position has been associated with lower incidences of ventilator-associated pneumonia (VAP). The feasibility and efficacy of this intervention in a larger patient population, however, are unknown.

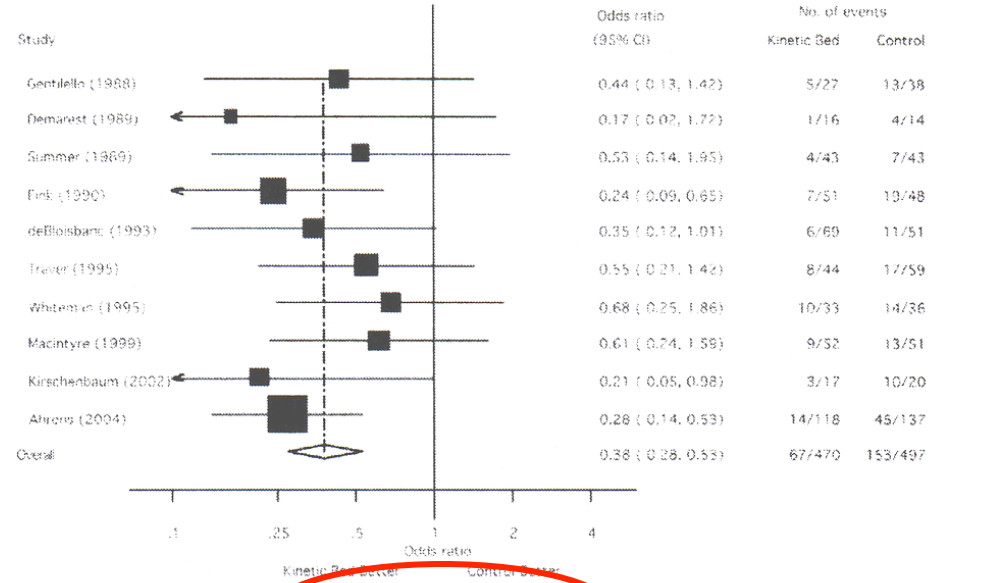
Objective: Assessment of the feasibility of the semirecumbent position for intensive care unit patients and its influence on development of VAP.

Design: In a prospective multicentered trial, critically ill patients undergoing mechanical ventilation were randomly assigned to the semirecumbent position, with a target backrest elevation of 45°, or standard care (i.e., supine position) with a backrest elevation of 10°.

Main Outcome Measures: Backrest elevation was measured continuously during the first week of ventilation with a monitor-linked device. A deviation of position was defined as a change of the randomized position >5°. Diagnosis of VAP was made by quantitative cultures of samples obtained by bronchoscopic techniques.

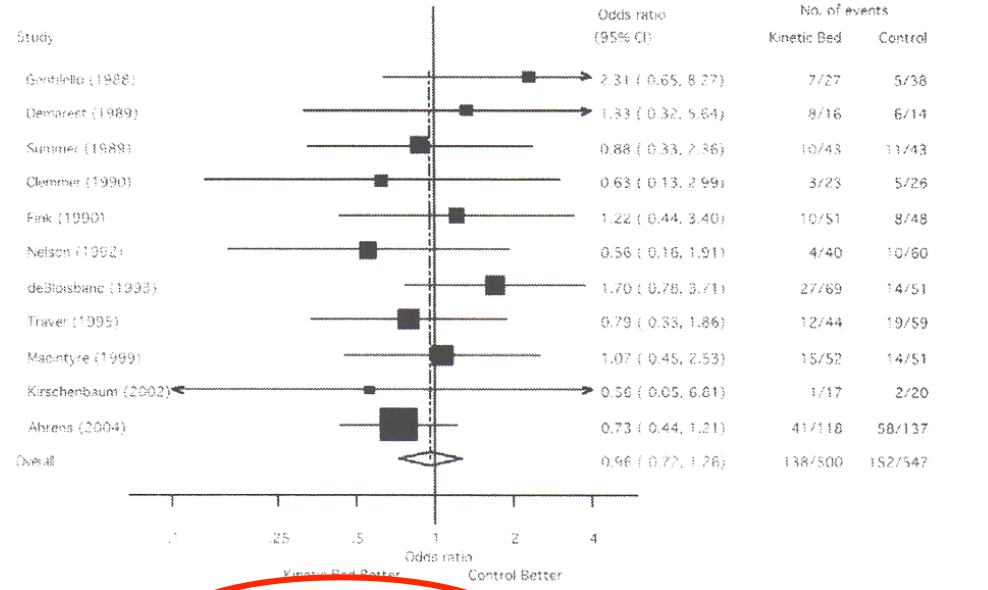
Results: One hundred nine patients were assigned to the supine group and 112 to the semirecumbent group. Baseli characteristics were comparable for both groups. Average elev tions were 9.8° and 16.1° at day 1 and day 7, respectively, for t supine group and 28.1° and 22.6° at day 1 and day 7, respectivel for the semirecumbent group ($p < .001$). The target semirecur bent position of 45° was not achieved for 85% of the study tim and these patients more frequently changed position than supin positioned patients. VAP was diagnosed in eight patients (6.5%) the supine group and in 13 (10.7%) in the semirecumbent grou (NS), after a mean of 6 (range, 3–9) and 7 (range, 3–12) day respectively. There were no differences in numbers of patien undergoing enteral feeding, receiving stress ulcer prophylaxis, developing pressure sores or in mortality rates or duration ventilation and intensive care unit stay between the groups.

Conclusions: The targeted backrest elevation of 45° for semi recumbent positioning was not reached in the conditions of th present randomized study. The achieved difference in treatmen position (28° vs. 10°) did not prevent the development of VA (Crit Care Med 2006; 34:396–402)



Forest plot showing the effect of kinetic bed therapy on nosocomial pneumonia. CI, confidence interval.

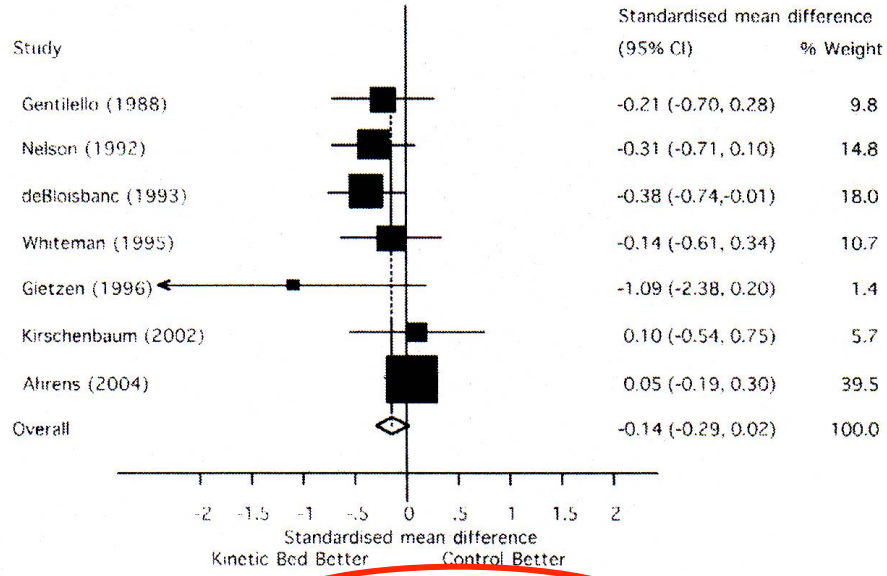
Figure 3



Forest plot showing the effect of kinetic bed therapy on mortality. CI, confidence interval.

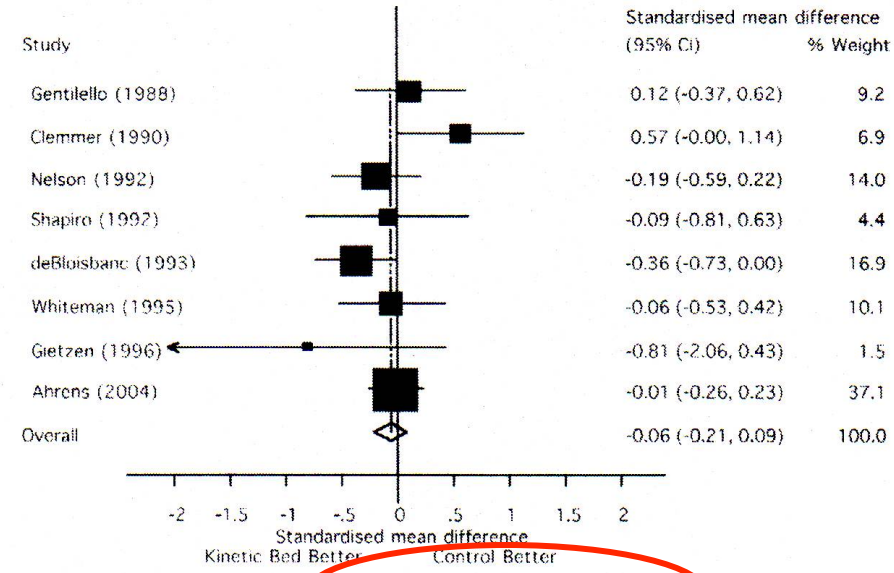
Crit Care 2006,10,R70

Figure 4



Forest plot showing the effect of kinetic bed therapy on duration of mechanical ventilation. CI, confidence interval.

Figure 5

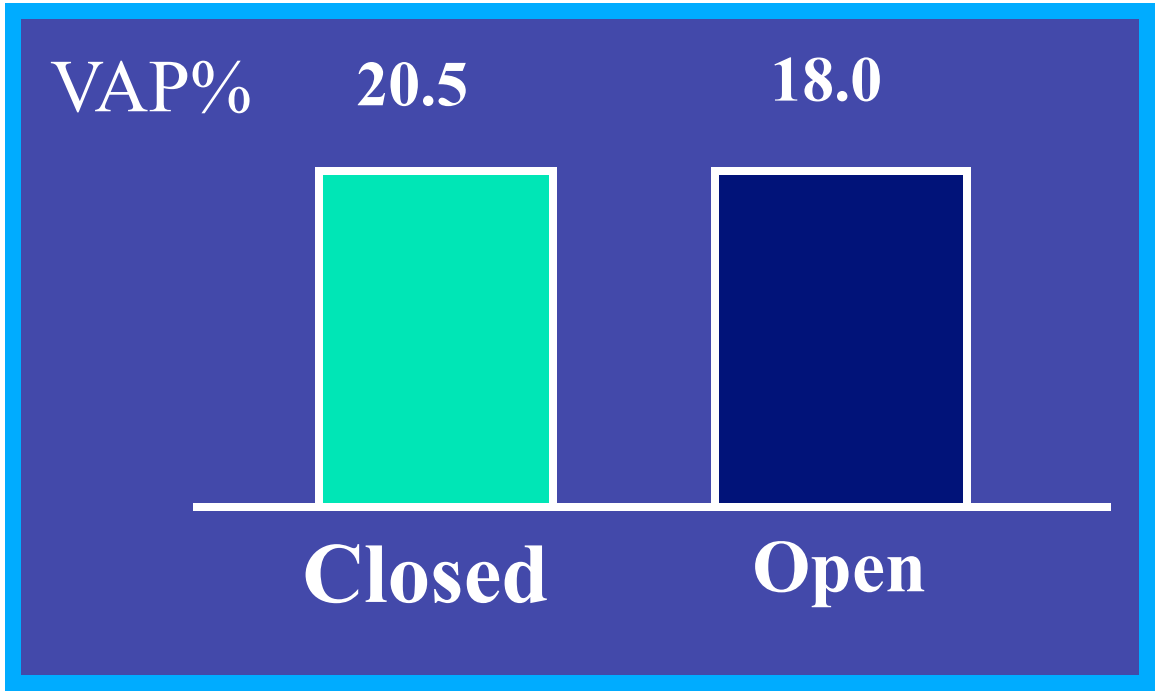


Forest plot showing the effect of kinetic bed therapy on intensive care unit length of stay. CI, confidence interval.

Crit Care 2006,10,R70

VAP : Closed or Open Tracheal Suction System

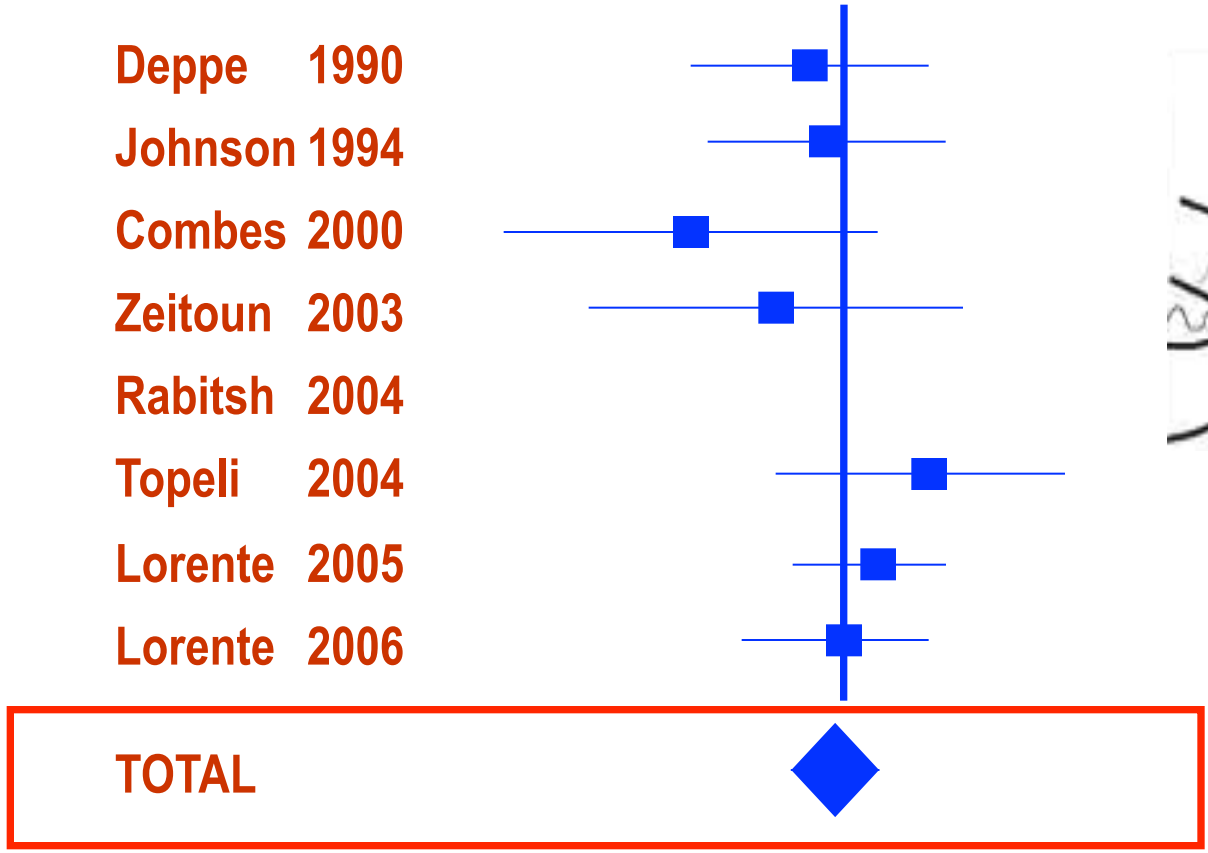
◆ 443 patients

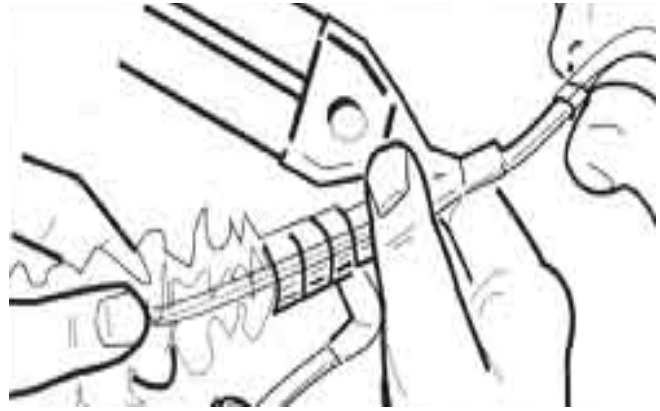


VAP/1000 vent.days
17.6% / 15.8%

Lorente et al CCM 2005, 33, 115

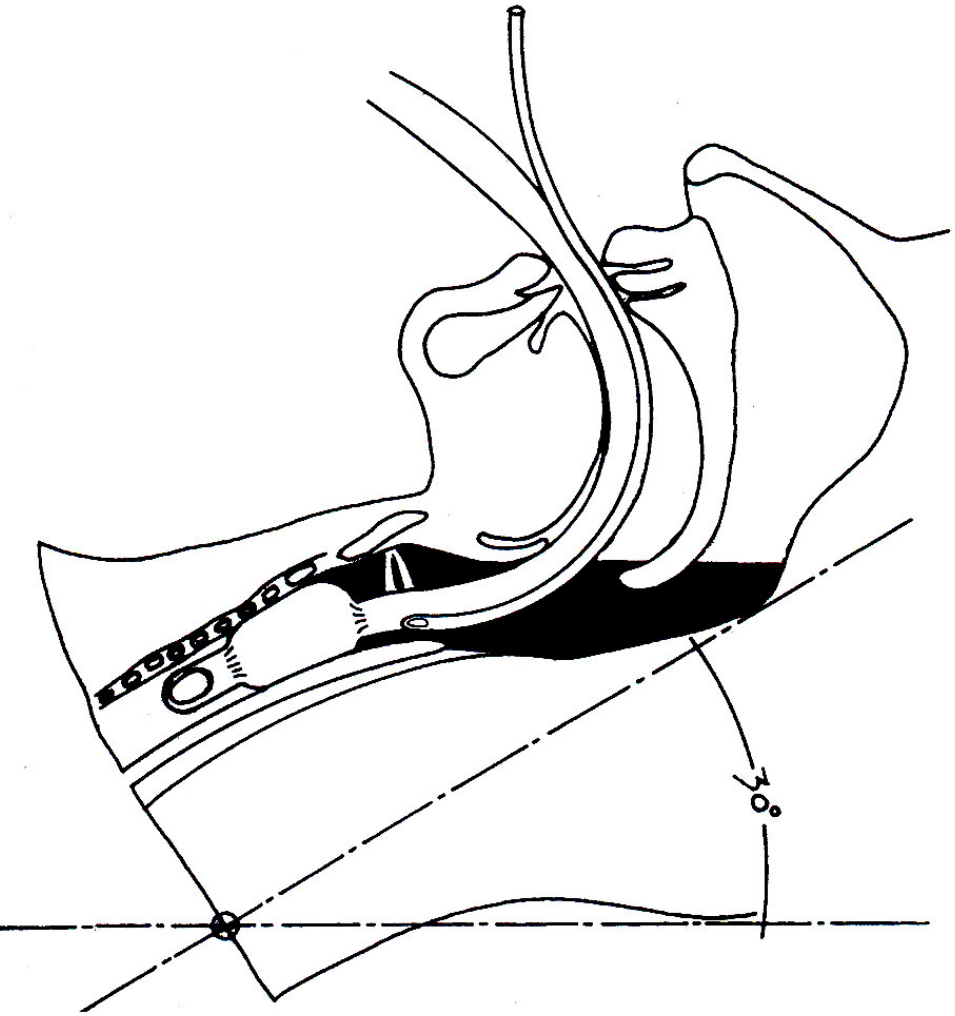
VAP : Closed or Open Tracheal Suction System



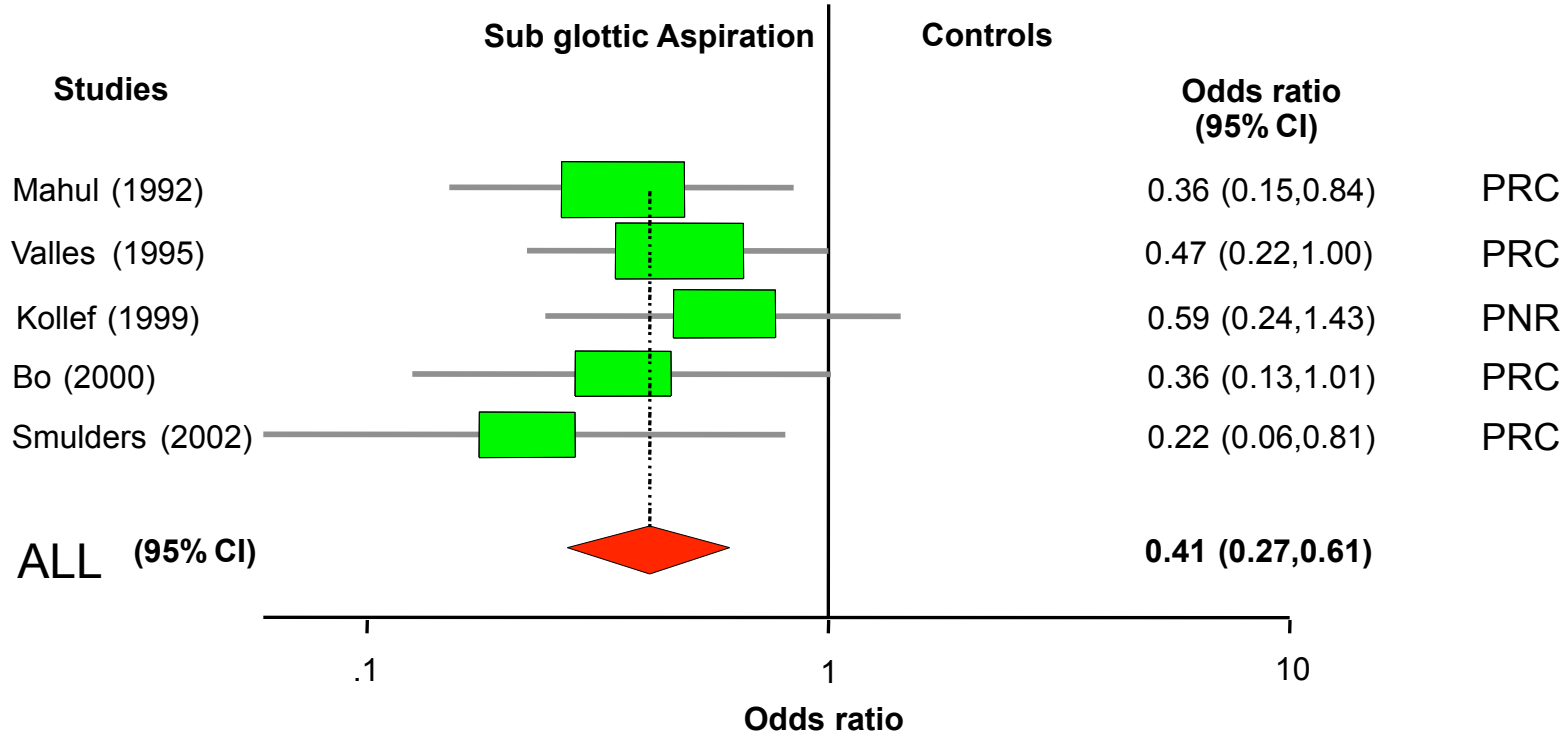


CRIT CARE MED 2007;35: 260

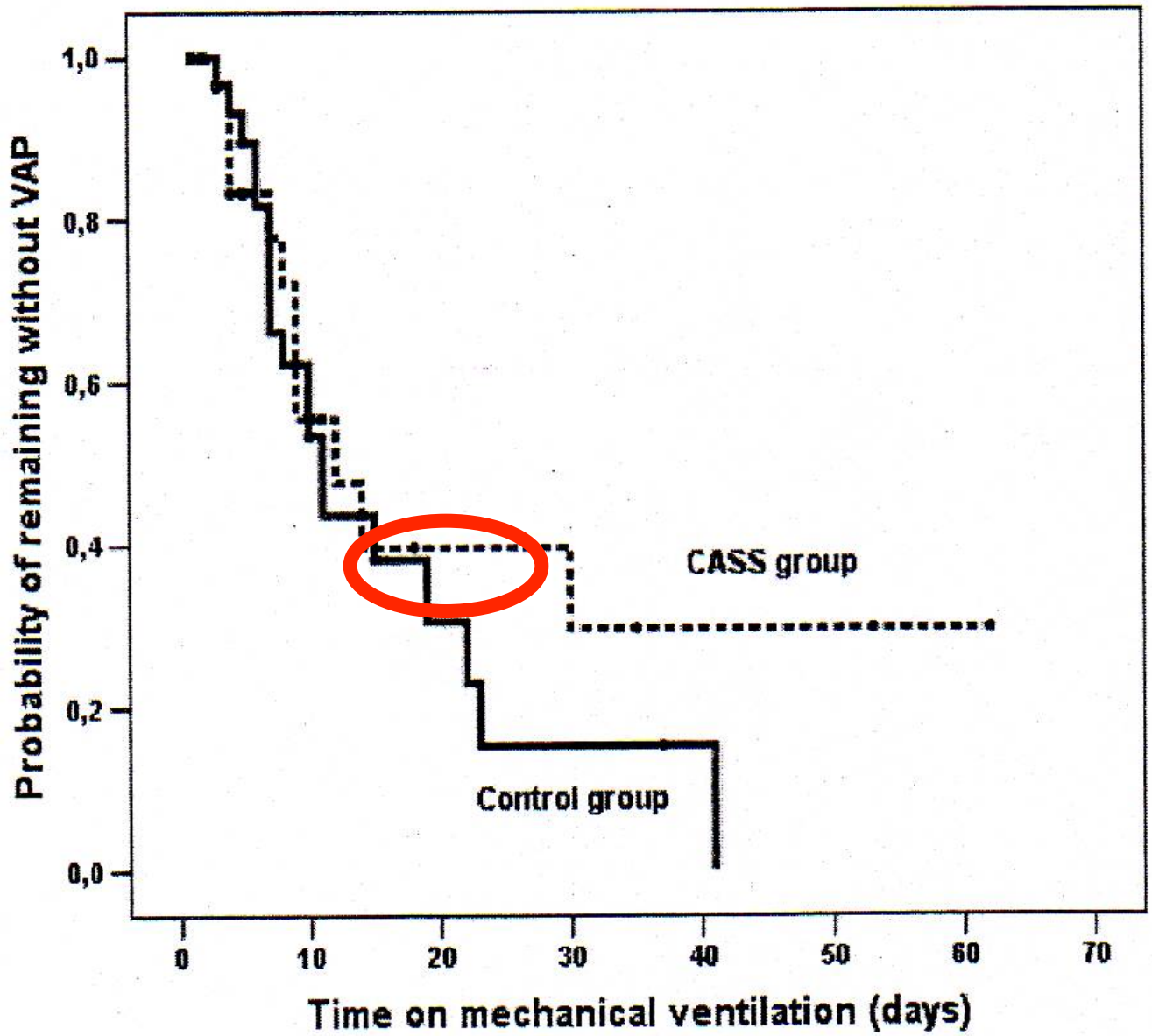
Susbglottic Suctioning



Susbglottic Suctioning



- NO heterogeneity (p=0.77). z=4.31 p<0. 0001
- 859 patients included: 20% VAP control group vs 10% sub – glottic aspiration group .



Number of patients at risk

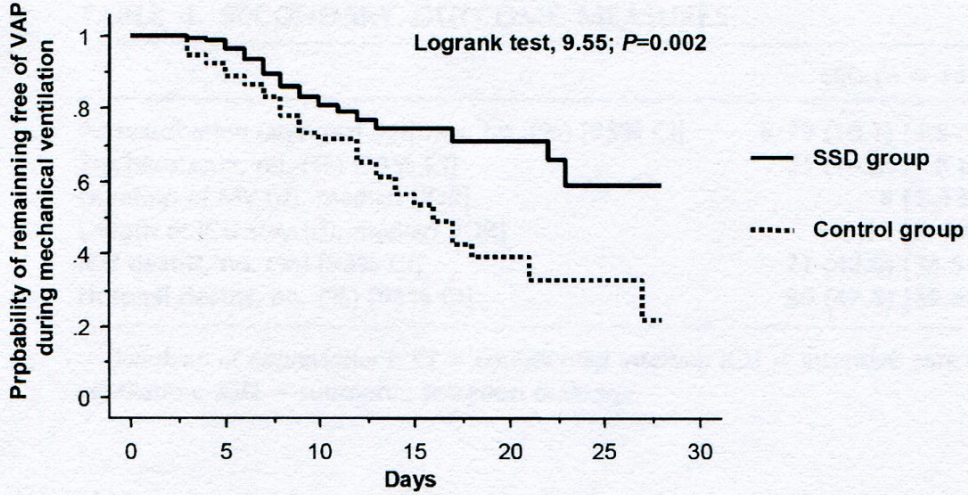
Intermittent Subglottic Secretion Drainage and Ventilator-associated Pneumonia

A Multicenter Trial

Jean-Claude Lacherade[1], Bernard De Jonghe[1], Pierre Guezennec[2], Karim Debbat[3], Jan Hayon[4], Antoine Monsel[1], Pascal Fangio[1], Corinne Appere de Vecchi[1], Cédric Ramaut[5], Hervé Outin[1], and Sylvie Bastuji-Garin[6]

[1]Medicosurgical Intensive Care Unit, Poissy Saint-Germain Hospital, Poissy; [2]Medicosurgical Intensive Care Unit, André Mignot Hospital, Le Chesnay; [3]Medicosurgical Intensive Care Unit, Hospital of Avignon, Avignon; [4]Medicosurgical Intensive Care Unit, Poissy Saint-Germain Hospital, Saint-Germain en Laye; [5]Mobile Intensive Care Unit, Poissy Saint-Germain Hospital, Poissy; and [6]University Paris 12, Laboratoire d'Investigation Clinique, Equipe d'Accueil 4393 and Department of Clinical Research and Public Health, Henri-Mondor Hospital, Assistance Publique-Hôpitaux de Paris, Créteil, France

AJRCCM 2010 182 910-917



SSD, No							
At risk	169	126	58	26	18	8	4
New VAP cases	0	2	15	5	1	2	0
Control, No							
At risk	164	97	44	23	9	4	3
New VAP cases	0	10	16	8	6	1	1

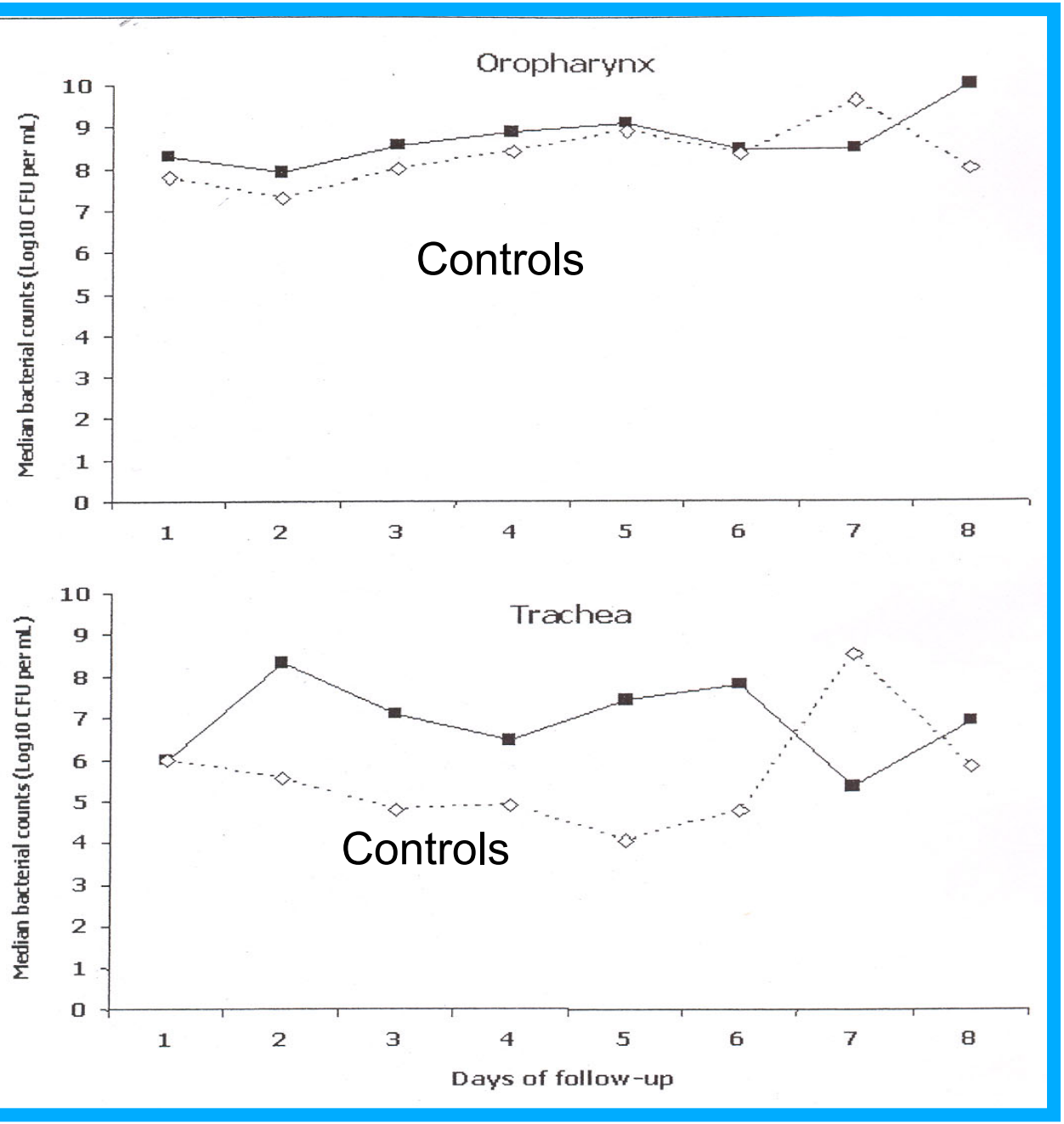
Figure 2. Cumulative rates of patients remaining free of ventilator-associated pneumonia (VAP) in the subglottic secretion drainage (SSD) and control groups, using the Kaplan-Meier method.

Susbglottic Suctioning

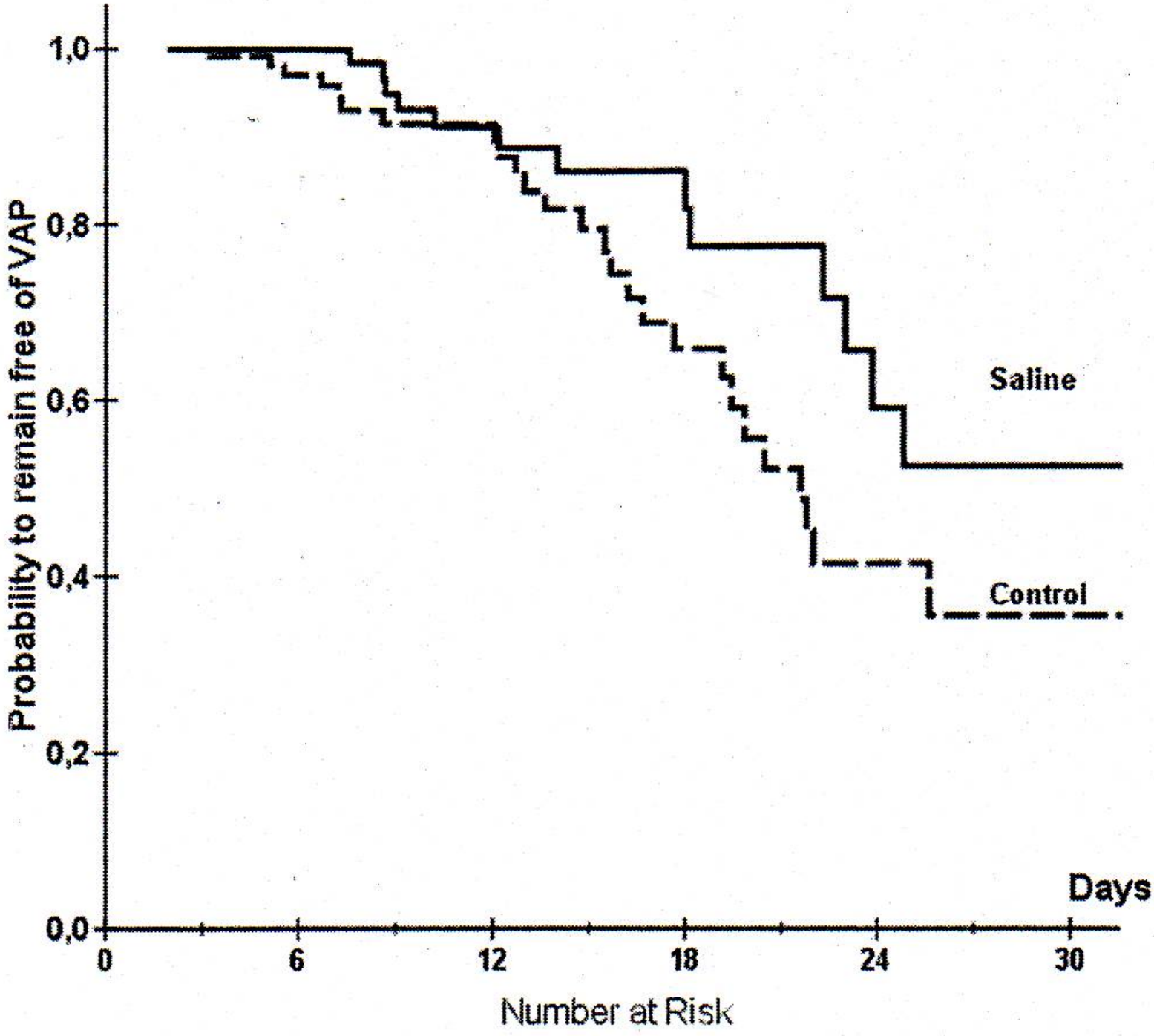
CDC level II

MMWR 2004 , 53 , 1 - 36

Effects of Semirecumbent Position and Susbglottic Suctioning



Girou et al ICM 2004, 30, 225-233


1,0
0,8
0,6
0,4
0,2
0,0
Probability to remain free of VAP
Saline
Control
Days
0
6
12
18
24
30
Number at Risk

Saline instillation before tracheal suctioning decreases the incidence of ventilator-associated pneumonia*

Pedro Caruso, MD, PhD; Silvia Denari, PhD; Soraia A. L. Ruiz, RT; Sergio E. Demarzo, MD, PhD; Daniel Deheinzelin, MD, PhD

LEARNING OBJECTIVES

On completion of this article, the reader should be able to:

1. Describe technique for tracheal installation of saline.
2. Explain benefits and outcomes of tracheal installation of saline.
3. Use this information in a clinical setting.

The authors have disclosed that they have no financial relationships with or interests in any commercial companies pertaining to this educational activity.

All faculty and staff in a position to control the content of this CME activity have disclosed that they have no financial relationship with, or financial interests in, any commercial companies pertaining to this educational activity.

Lippincott CME Institute, Inc., has identified and resolved all faculty conflicts of interest regarding this educational activity.

Visit the *Critical Care Medicine* Web site (www.ccmjournal.org) for information on obtaining continuing medical education credit.

Objectives: **To compare the incidence of ventilator-associated pneumonia (VAP) with or without isotonic saline instillation before tracheal suctioning. As a secondary objective, we compared the incidence of endotracheal tube occlusion and atelectasis.**

Design: **Randomized clinical trial.**

Setting and Patients: **The study was conducted in a medical surgical intensive care unit of an oncologic hospital. We selected consecutive patients needing mechanical ventilation for >72 hrs. Patients were allocated into two groups: a saline group that received instillation of 8 mL of saline before tracheal suctioning and a control group which did not. VAP was diagnosed based on clinical suspicion and confirmed by bronchoalveolar lavage quantitative culture. The incidence of atelectasis on daily chest radiography and endotracheal tube occlusions were recorded. The sample size was calculated to a power of 80% and a type I error probability of 5%.**

Measurements and Main Results: **One hundred thirty patients were assigned to the saline group and 132 to the control group. The baseline demographic variables were similar betwee groups. The rate of clinically suspected VAP was similar in bot groups. The incidence of microbiological proven VAP was signif icantly lower in the saline group (23.5% × 10.8%; $p = 0.008$ (incidence density/1.000 days of ventilation 21.22 × 9.62; $p <$ 0.01). Using the Kaplan-Meier curve analysis, the proportion o patient remaining without VAP was higher in the saline grou ($p = 0.02$, log-rank test). The relative risk reduction of VAP in th saline instillation group was 54% (95% confidence interval, 18%- 4%) and the number needed to treat was eight (95% confidenc interval, 5–27). The incidence of atelectases and endotrachea tube occlusion were similar between groups.**

Conclusions: **Instillation of isotonic saline before tracheal suc tioning decreases the incidence of microbiological proven VAP (Crit Care Med 2009; 37:32–38)**

Key Words: pneumonia; ventilator-associated pneumonia; pre vention; respiratory therapy

CUFF

PRESSION

< 20 cm H_2O

AM J RESPIR CRIT CARE MED 1996; 154: 111

CUFF

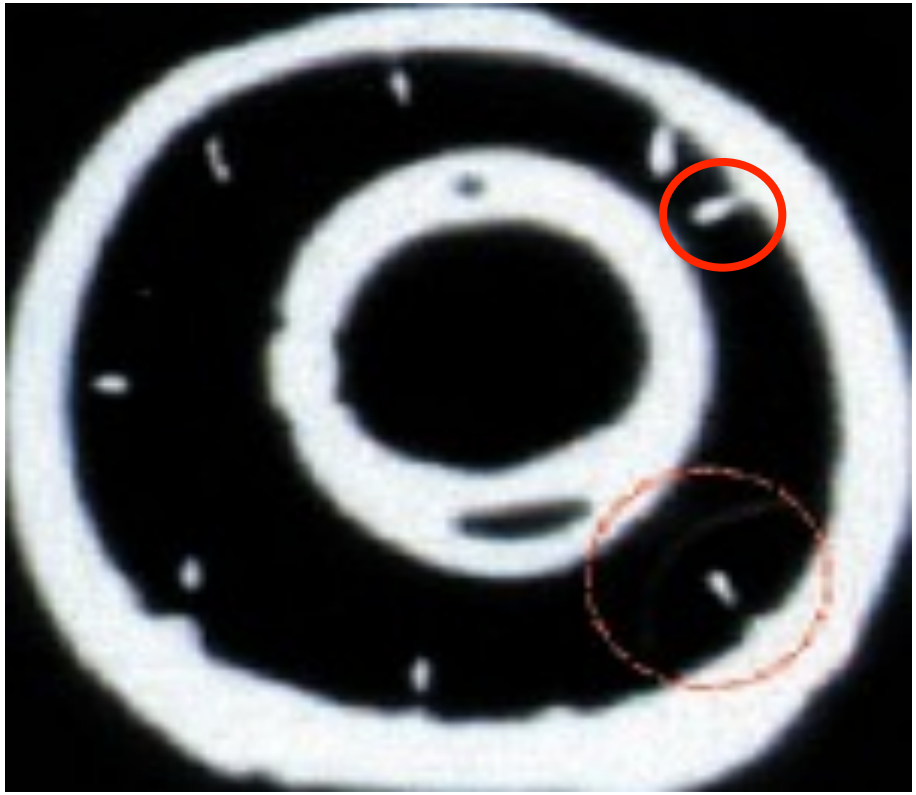
Risk of vap

55 patients **NO ANTIBIOTIC**

FAILURE OF SUBGLOTTIC ASPIRATION	7.52	1.48 – 38.07
LOW CUFF PRESSURE	4.23	1.12 – 15.92
PRIOR HISTORY OF CARDIAC DISEASE	2.17	0.58 – 8.09

AM J RESPIR CRIT CARE MED 1996; 154: 111

CUFF



Classical cuff

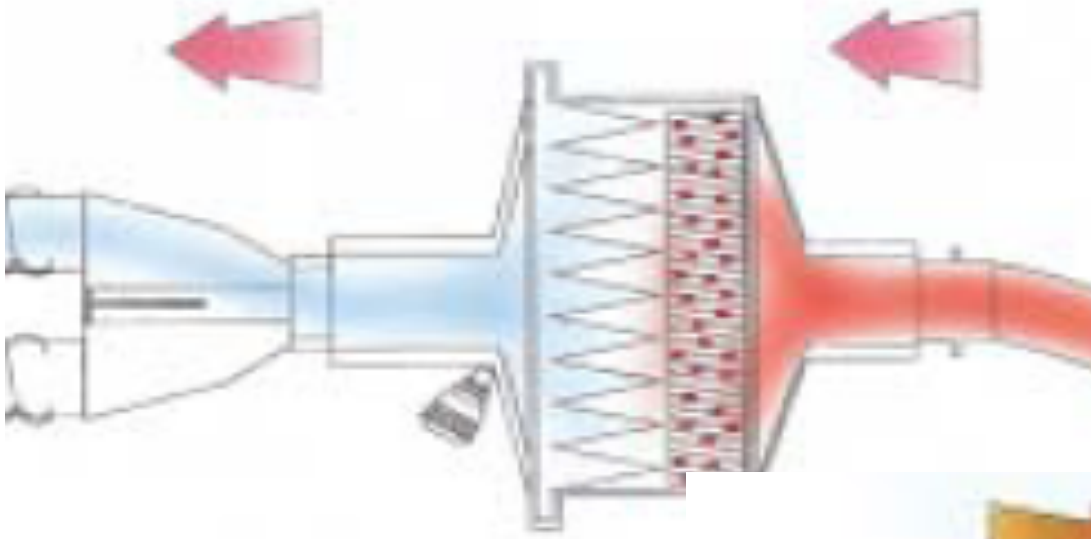
≠ 10 to 50 µm

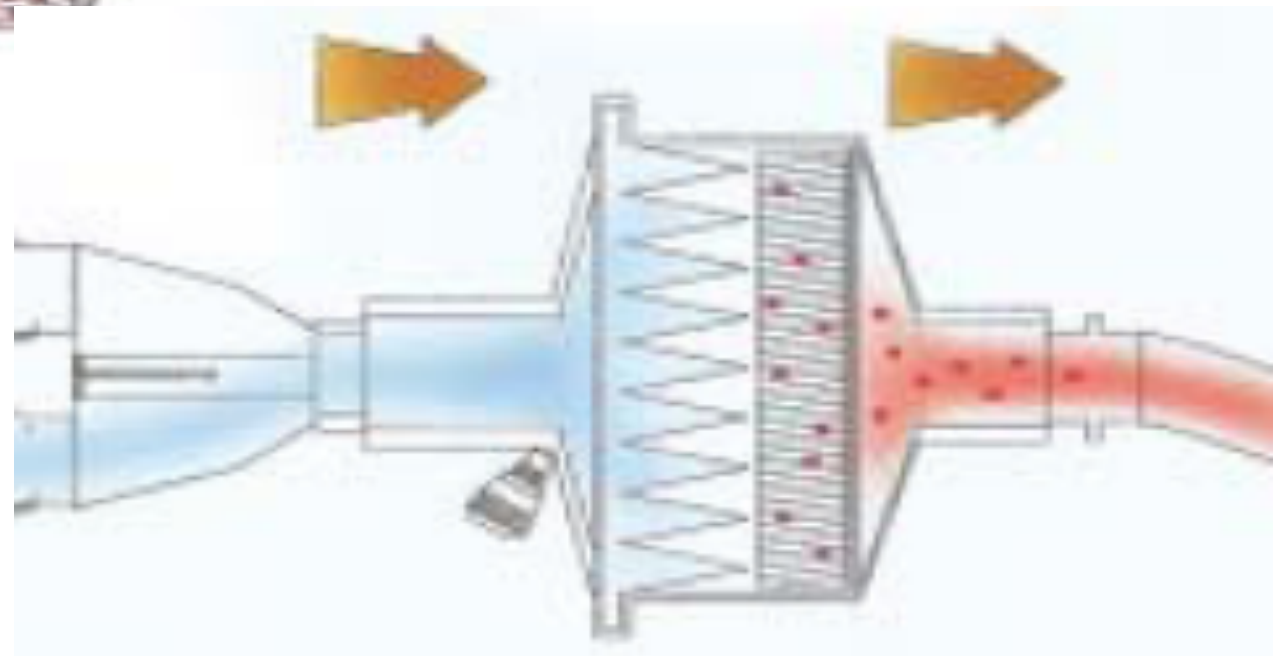
POLYURETHANE cuff

≠ < 10 µm

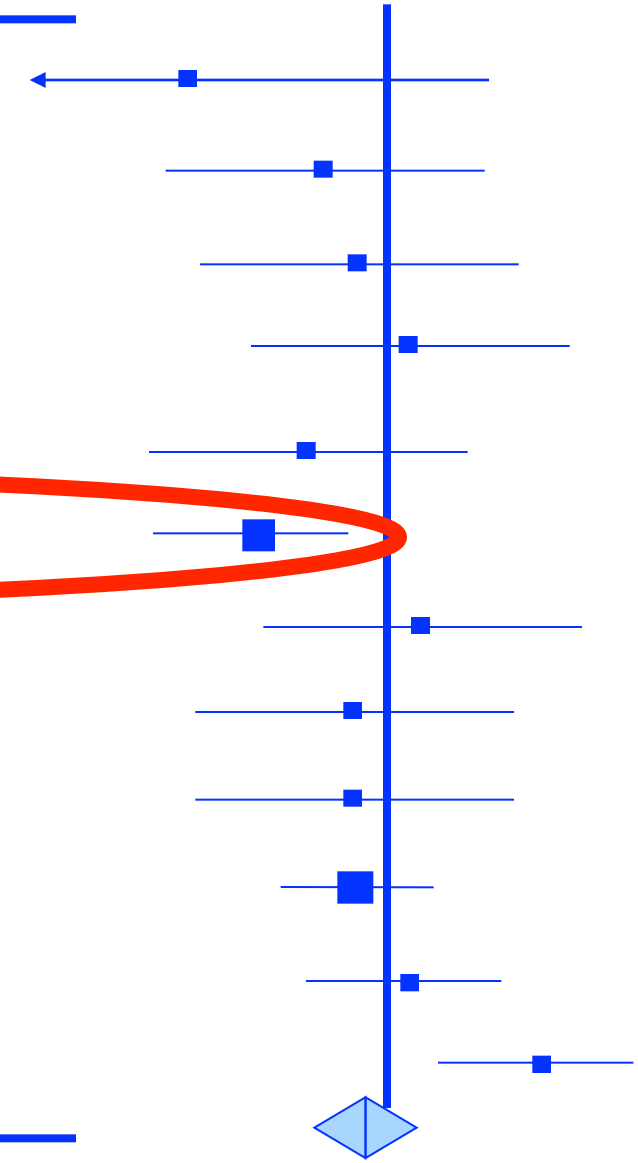
20°C
100
0
9
8
7

HMEs





		TYPE HUMUDIF.		INCIDENCE VAP (%)	
Martin	1990	HDP	+	7	19
Roustan	1992	HDP	+	9	15
Dreyfuss	1995	HDP	+	10	11
Branson	1996	HGS	HW	6	5
Hurni	1997	HGS	+	9	13
Kirton	1997	HDP	+	6	16
Boots	1997	Mixte		19	17
Kollef	1998	HGS	HW	9	10
Memish	2001	HGS	+	11	16
Lacherade	2005	Mixte	HW	25	19
Boots	2006	Mixte	HW	13	12
Lorente	2006	HGS	HW	40	16



CRIT CARE MED 2007; 35: 2843

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

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

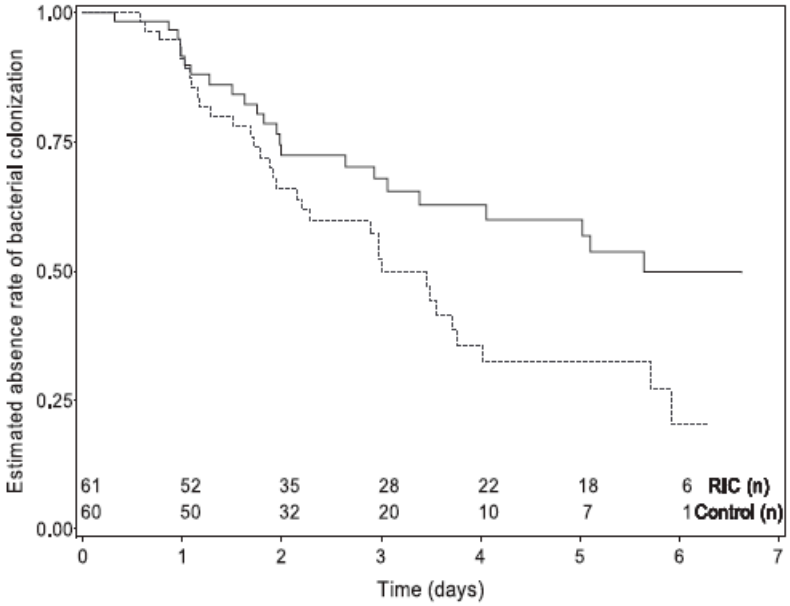


Table 3. Colonization rates in tracheal aspirate in the per-protocol set

Threshold	RIC Group	Control Group	Relative Risk Reduction (95% CI)	*p* Value[a]
No. of patients with colonization/ total (%)				
$\geq 10^5$ cfu/mL	14/37 (38)	16/30 (53)	0.29 (−0.151 to 0.693)	.23
$\geq 10^6$ cfu/mL	8/37 (22)	12/30 (40)	0.46 (−0.088 to 0.970)	.12
No. of days with colonization/ total (%)				
$\geq 10^5$ cfu/mL	26/176 (15)	34/128 (27)	0.44 (0.100 to 0.798)	.14
$\geq 10^6$ cfu/mL	11/176 (6)	24/128 (19)	0.67 (0.272 to 1.099)	.05

RIC, respiratory infection control; CI, confidence interval; cfu, colony-forming units.
[a]*p* value determined by Fisher's exact test for rates by patients and Wilcoxon's test for rates by days.

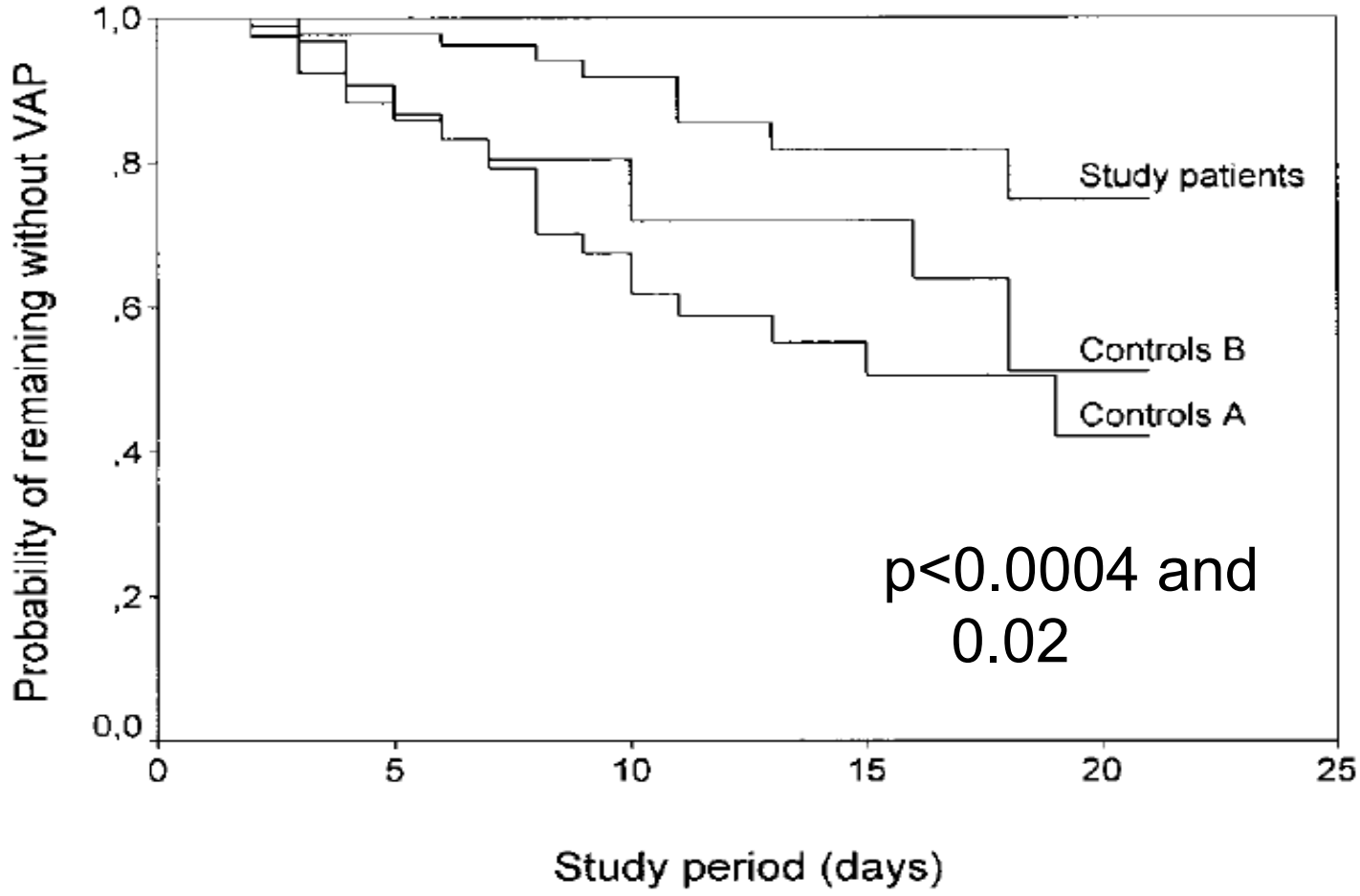
Rello J, Crit Care Med , 2006;34:2766

IV Cefuroxime decreases the Rate of Nosocomial Pneumania

- Prospective , open-label , controlled study
- 100 patients. Cefuroxime 1.5gx2. Placebo

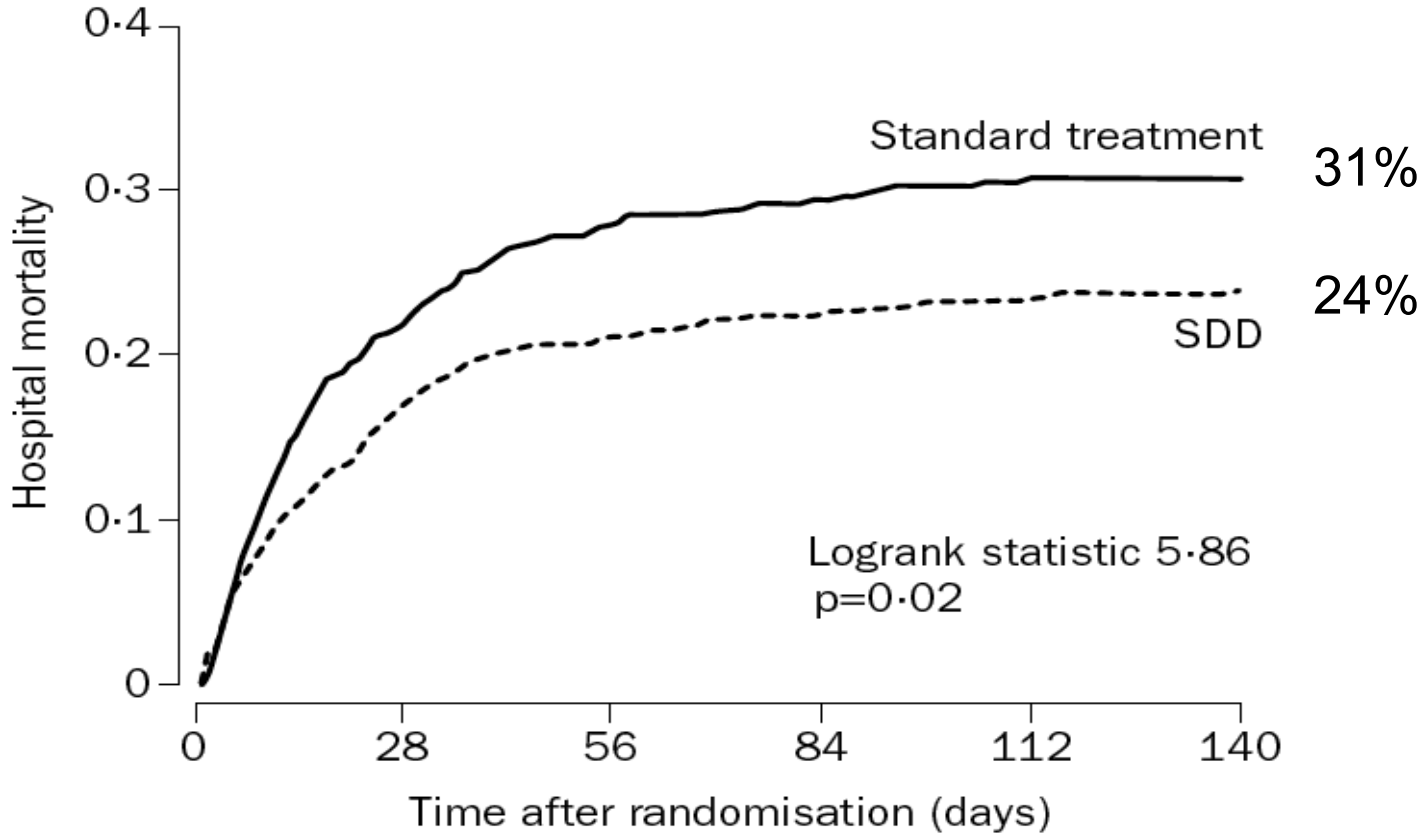
Oropharyngeal Decontamination

n=226



(Bergmans, AJRCCM 2001 ,164 , 382-388)

Mortality



Numbers of patients at risk

SDD	457	383	360	354	350	348
Non-SDD	460	363	331	324	318	318

(De Jonge, Lancet 2003)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Decontamination of the Digestive Tract and Oropharynx in ICU Patients

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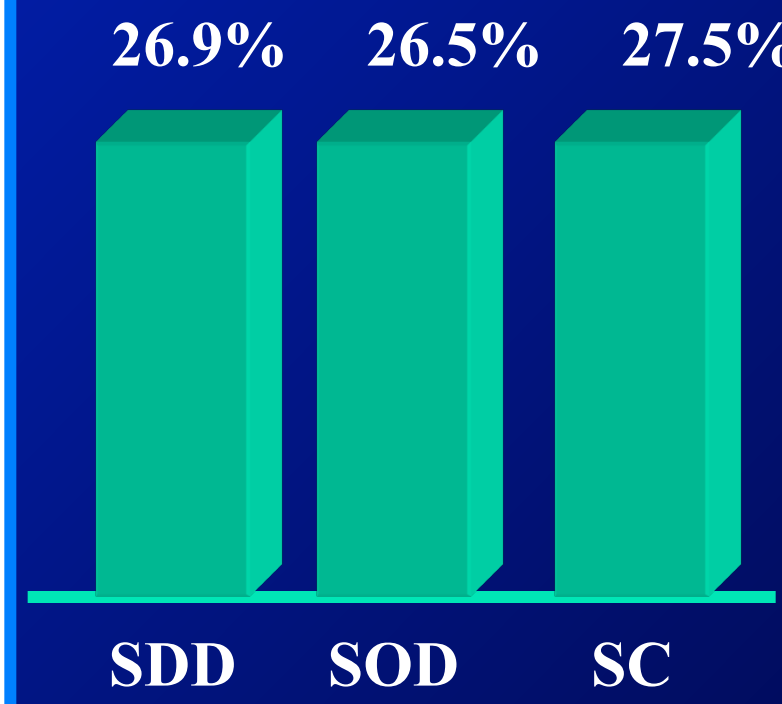
Mortality (D28)

Crude mortality



Adjusted OR (CI 95 %)

SDD : 0.83 (0.72 – 0.97)

P = 0.02

SOD : 0.86 (0.74-0.99)

P = 0.045

Standard Care : 1:00

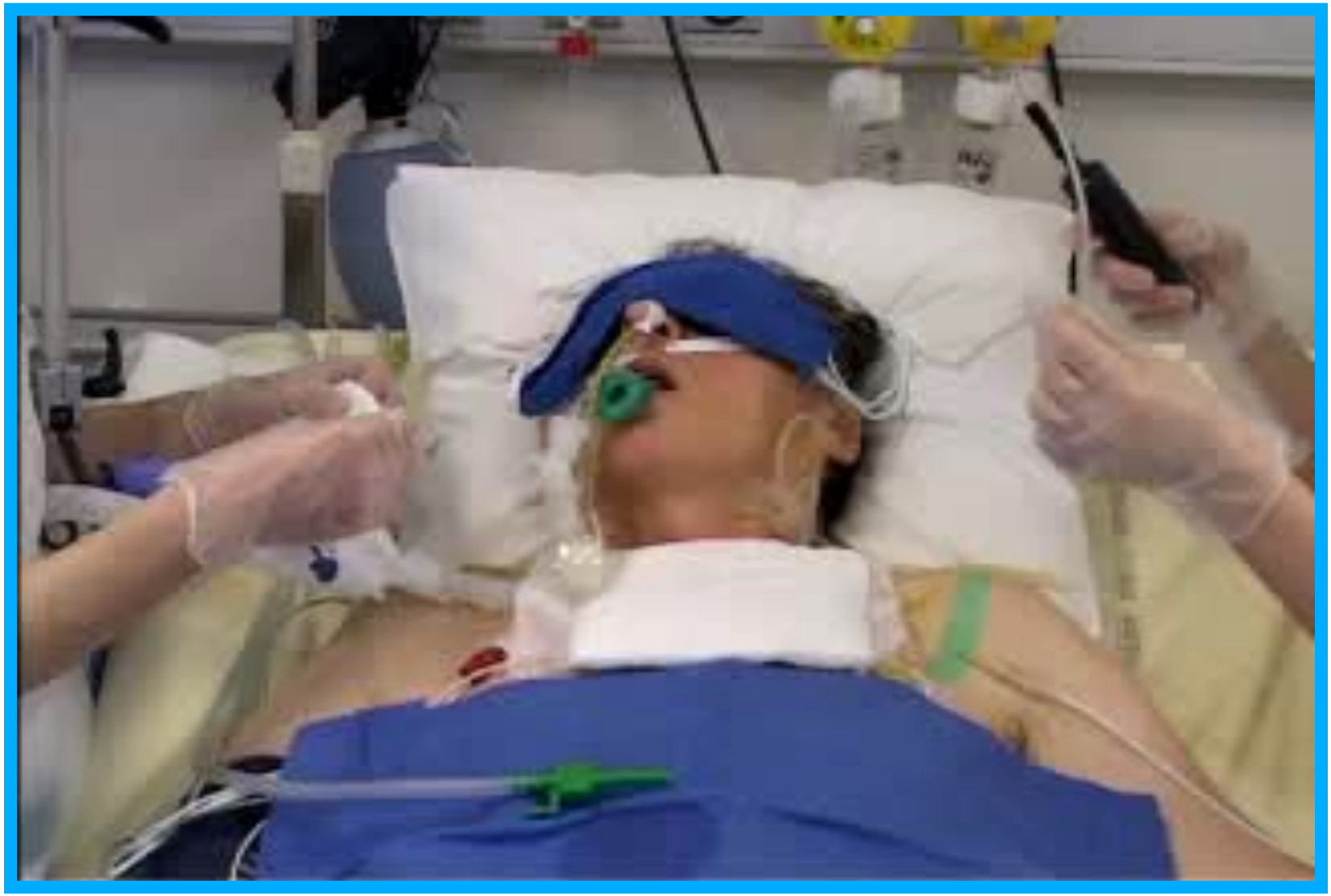
Chlorhexidine

VAP

	n	Type CHX	CHX	Placebo
FOURRIER 2000	30	0.2% gel	5 (17%)	18 (60%)
GRAP 2004	7	0.12%	4 (57%)	3 (60%)
MCNAUGHTON 2004*	91	0.2% sol	8 (9%)	5 (6%)
FOURRIER 2005	114	0.2% gel	13 (11%)	12 (11%)
KOEMAN 2006	127	2%	13 (10%)	23 (18%)
TANTIPONG 2008	102	2%	5 (9%)	10 (19%)

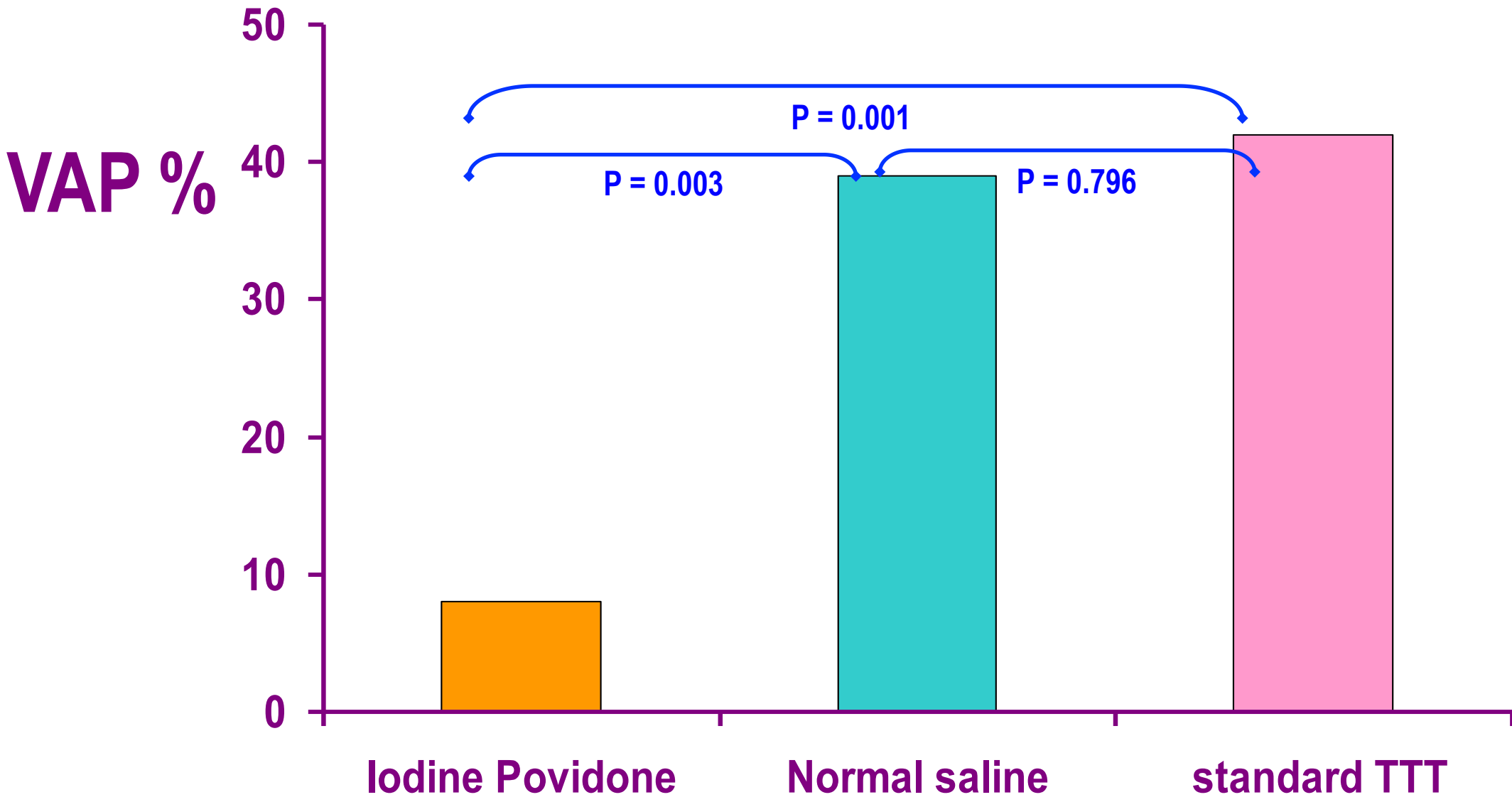
Intensive Care Med 2000; Heart Lung 2004; *Intensive Care Med 2004 (abstract); Crit Care Med 2005; AJRCCM 2006
Infect Control Hosp Epidemiol 2008.

Iodine POVIDONE



Seguin et al CRIT CARE MED 2006; 34: 1514

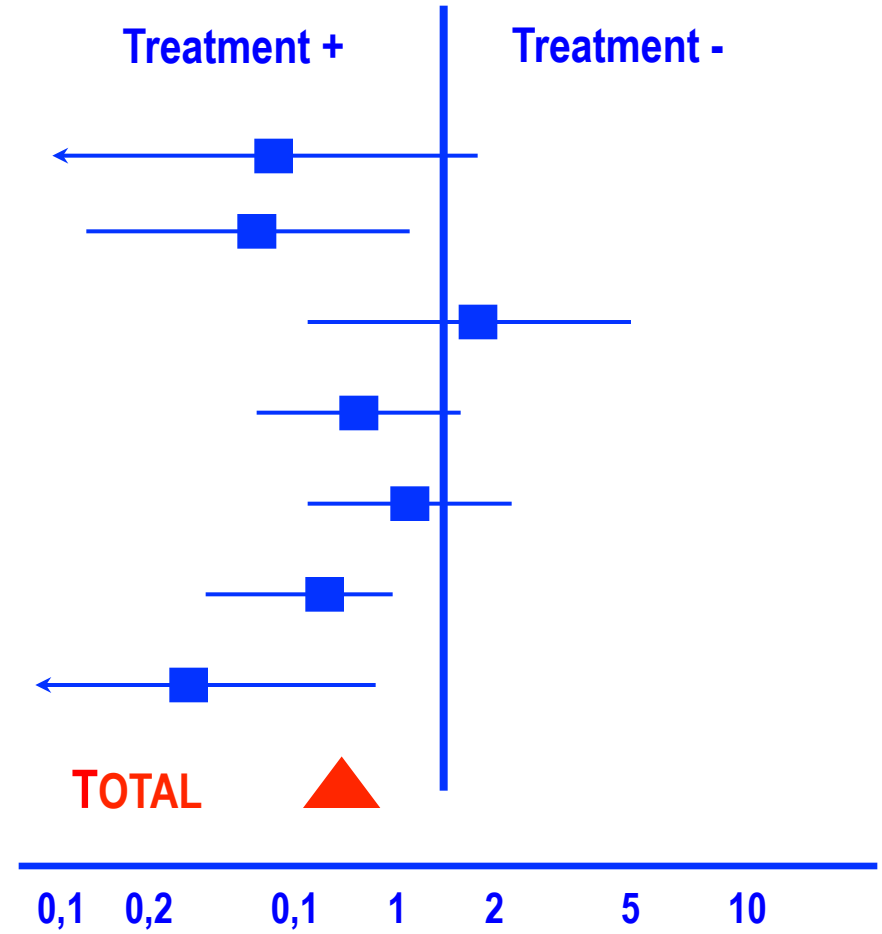
Iodine POVIDONE



CRIT CARE MED 2006; 34: 1514

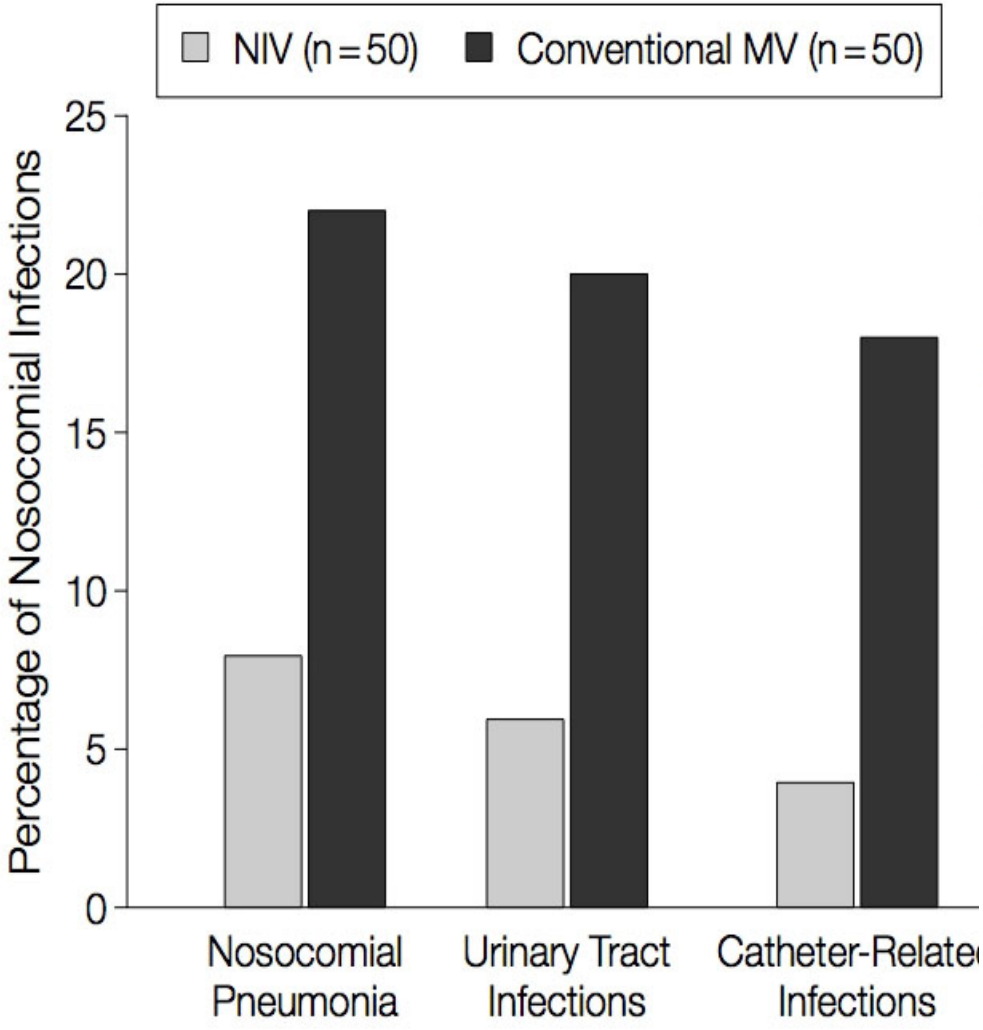
META ANALYSIS – RISK OF VAP

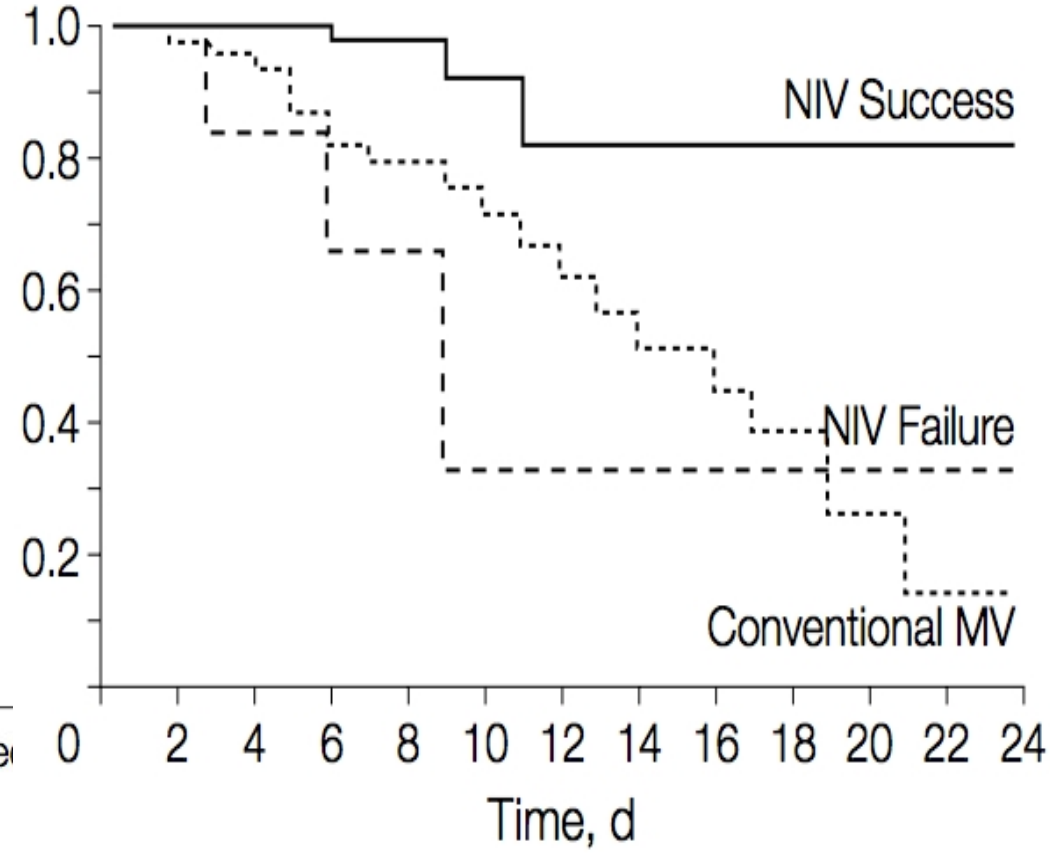
De Riso	1996	3/173	9/180
Fourrier	2000	5/30	13/30
Fourrier	2005	13/114	12/114
Koeman	2006	13/127	23/130
Mac Naughton	2004	21/101	21/93
Segers	2005	35/485	67/469
Seguin	2006	3/36	25/62



BMJ 2007

Non-invasive Ventilation





Girou E. JAMA 2000;284:2361

Hydrocortisone Therapy for Patients With Multiple Trauma

The Randomized Controlled HYPOLYTE Study

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Context The role of stress-dose hydrocortisone in the management of trauma patients is currently unknown.

Objective To test the efficacy of hydrocortisone therapy in trauma patients.

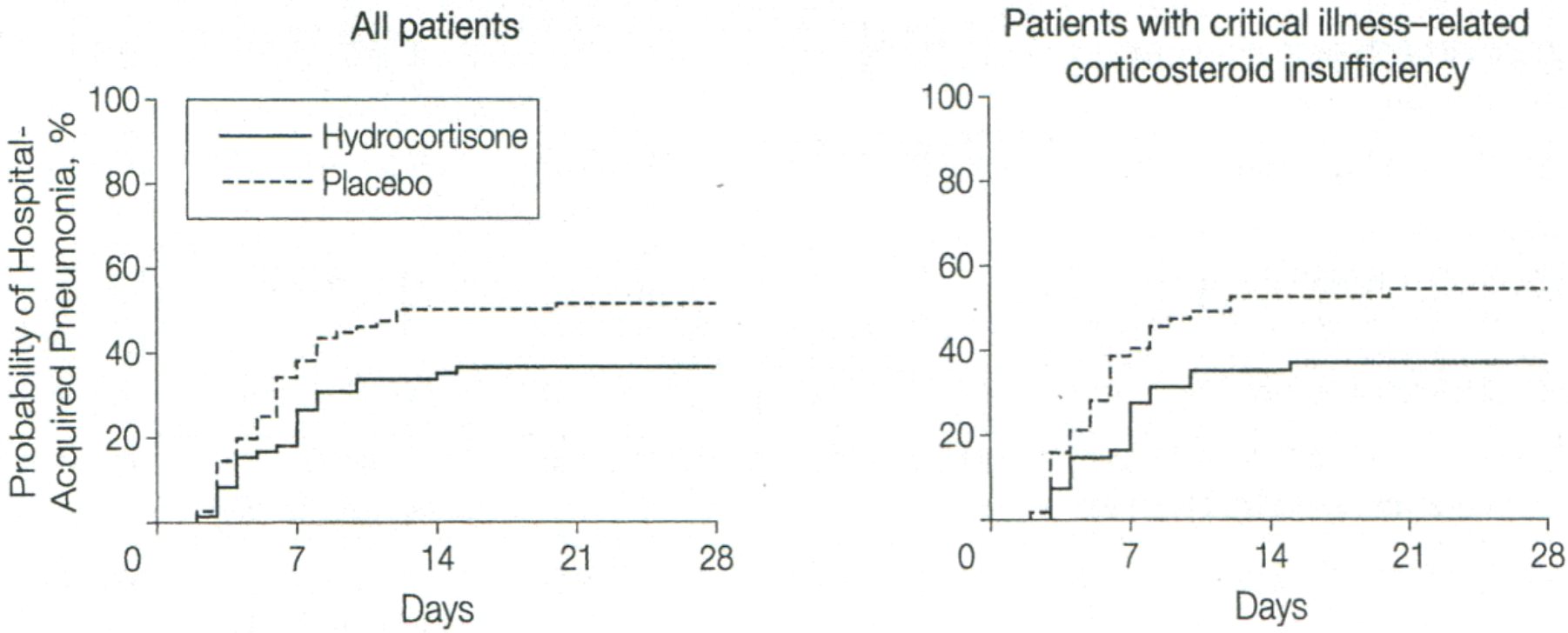
Design, Setting, and Patients Multicenter, randomized, double-blind, placebo-controlled HYPOLYTE (Hydrocortisone Polytraumatise) study. From November 2006 to August 2009, 150 patients with severe trauma were included in 7 intensive care units in France.

Intervention Patients were randomly assigned to a continuous intravenous infusion of either hydrocortisone (200 mg/d for 5 days, followed by 100 mg on day 6 and 50 mg on day 7) or placebo. The treatment was stopped if patients had an appropriate adrenal response.

Main Outcome Measure Hospital-acquired pneumonia within 28 days. Secondary outcomes included the duration of mechanical ventilation, hyponatremia, and death.

Results One patient withdrew consent. An intention-to-treat (ITT) analysis included the 149 patients, a modified ITT analysis included 113 patients with corticosteroid insufficiency. In the ITT analysis, 26 of 73 patients (35.6%) treated with hydrocortisone and 39 of 76 patients (51.3%) receiving placebo developed hospital-acquired pneumonia by day 28 (hazard ratio [HR], 0.51; 95% confidence interval [CI], 0.30-0.83; $P=.007$). In the modified ITT analysis, 20 of 56 patients (35.7%) in the hydrocortisone group and 31 of 57 patients (54.4%) in the placebo group developed

Figure 2. Kaplan-Meier Curves for Hospital-Acquired Pneumonia



Comparison of hydrocortisone group vs placebo using a stratified Cox model.

Implementation of guidelines for management of possible multidrug-resistant pneumonia in intensive care: an observational, multicentre cohort study

*Daniel H Kett, Ennie Cano, Andrew A Quartin, Julie E Mangino, Marcus J Zervos, Paula Peyrani, Cynthia M Cely, Kimbal D Ford, Ernesto G Scerpella, Julio A Ramirez, and the Improving Medicine through Pathway Assessment of Critical Therapy of Hospital-Acquired Pneumonia (IMPACT-HAP) Investigators**

Summary

Background The American Thoracic Society and Infectious Diseases Society of America provide guidelines for management of hospital-acquired, ventilator-associated, and health-care-associated pneumonias, consisting of empirical antibiotic regimens for patients at risk for multidrug-resistant pathogens. We aimed to improve compliance with these guidelines and assess outcomes.

Methods We implemented a performance-improvement initiative in four academic medical centres in the USA with protocol-based education and prospective observation of outcomes. Patients were assessed for severity of illness and followed up until death, hospital discharge, or day 28. We included patients in intensive-care units who were at risk for multidrug-resistant pneumonia and were treated empirically.

Findings 303 patients at risk for multidrug-resistant pneumonia were treated empirically, and prescribed treatment was guideline compliant in 129 patients and non-compliant in 174 patients. 44 (34%) patients died before 28 days in the compliance group and 35 (20%) died in the non-compliance group. Five patients in the compliance group and seven in the non-compliance group were lost to follow-up after day 14. Kaplan-Meier estimated survival to 28 days was 65% in the compliance group and 79% in the non-compliance group ($p=0\cdot0042$). This difference persisted after adjustment for severity of illness. Median length of stay and duration of mechanical ventilation did not differ between groups. Compliance failures included non-use of dual treatment for Gram-negative pathogens in 154 patients and absence of meticillin-resistant *Staphylococcus aureus* coverage in 24 patients. For patients in whom pathogens were subsequently identified, empirical treatment was active in 79 (81%) of 97 of patients receiving compliant therapy compared with 109 (85%) of 128 of patients receiving non-compliant therapy.

Interpretation Because adherence with empirical treatment was associated with increased mortality, we recommend a randomised trial be done before further implementation of these guidelines.

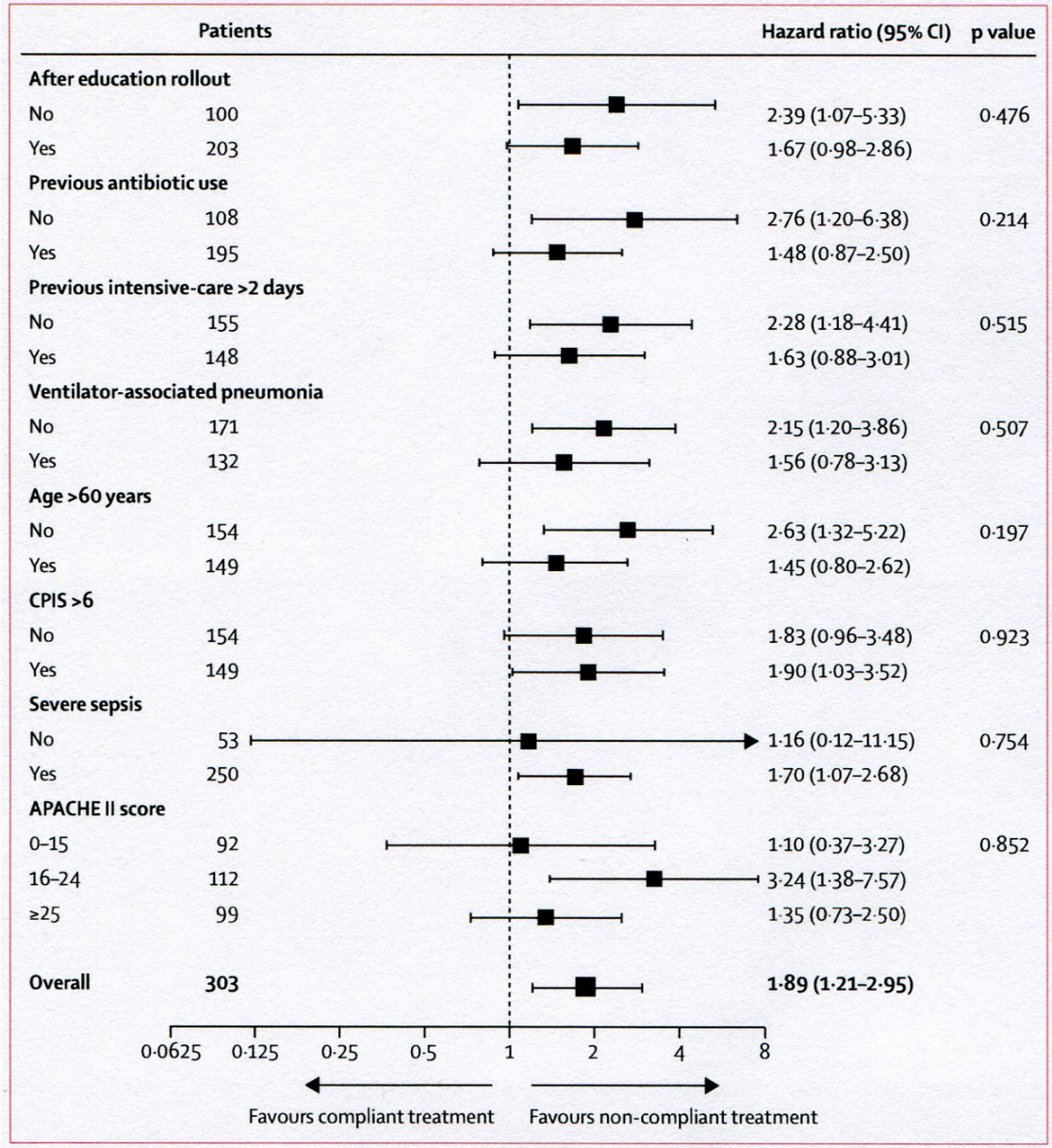
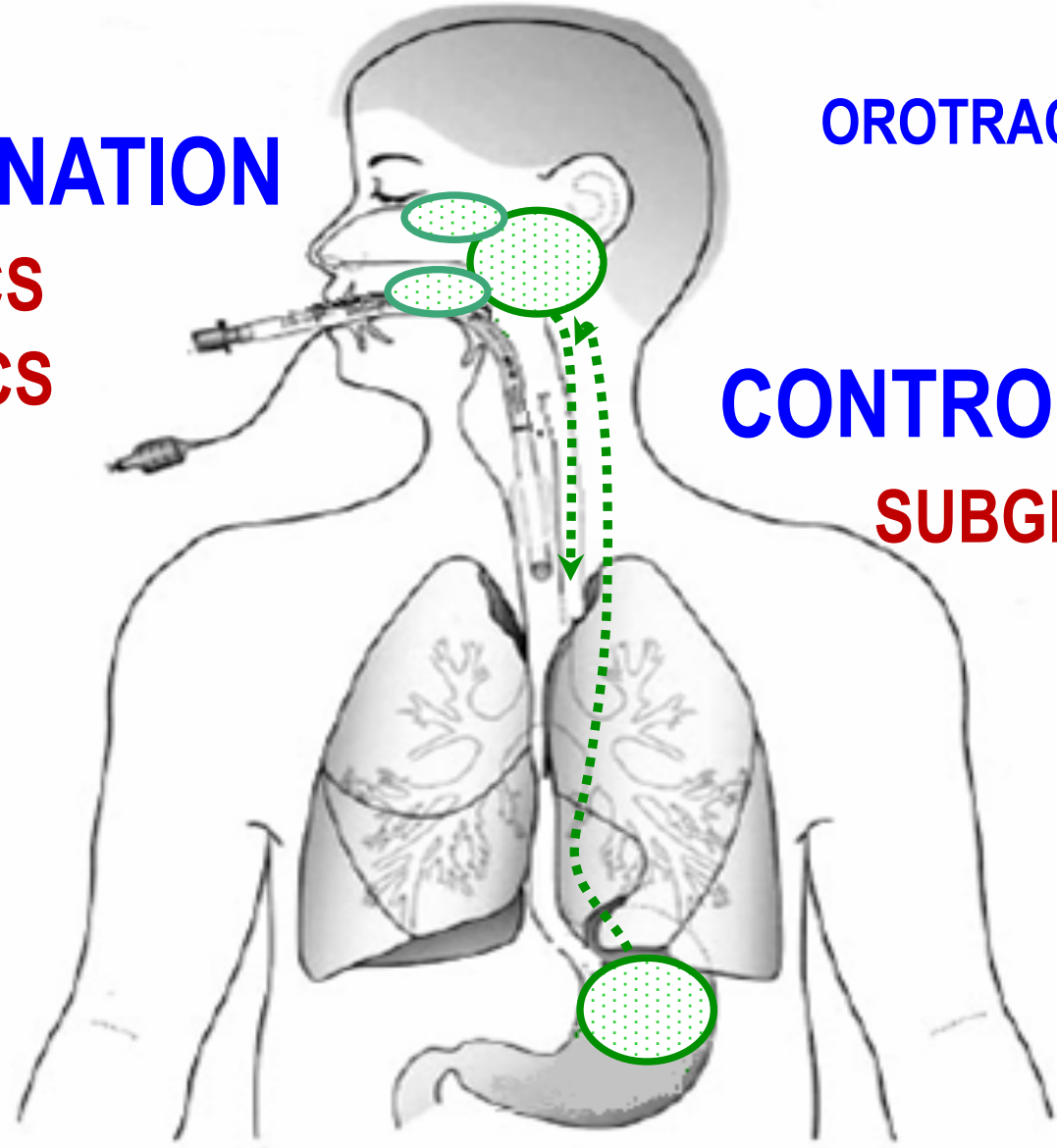


***Figure 2*: Guideline-compliant empirical treatment outcomes for 28-day mortality for key subpopulations**
CPIS=clinical pulmonary infection score. APACHE=acute physiology and chronic health evaluation.

CONCLUSION 1

LIMIT RISK EXPOSURE



OROTRACHEAL INTUBATION

DECONTAMINATION

ANTIBIOTICS

ANTISEPTICS

CONTROL SECRETIONS

SUBGLOTIC ASPIRATION

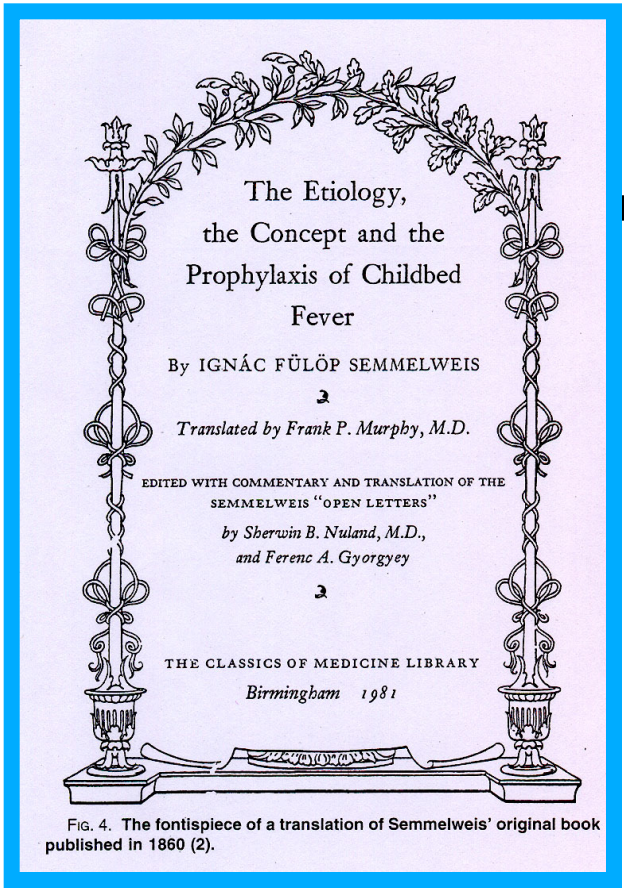
CUFF

REFLUX

POSITION

Conclusion 2

Do not forget the simpliest and most effective methods :


The Etiology,
the Concept and the
Prophylaxis of Childbed
Fever

By IGNÁC FÜLÖP SEMMELWEIS

Translated by Frank P. Murphy, M.D.

EDITED WITH COMMENTARY AND TRANSLATION OF THE SEMMELWEIS "OPEN LETTERS"
by Sherwin B. Nuland, M.D.,
and Ferenc A. Gyorgyey

THE CLASSICS OF MEDICINE LIBRARY
Birmingham 1981

FIG. 4. **The fontispiece of a translation of Semmelweis' original book published in 1860 (2).**

➔**Hand washing**

➔**Hand rubing**