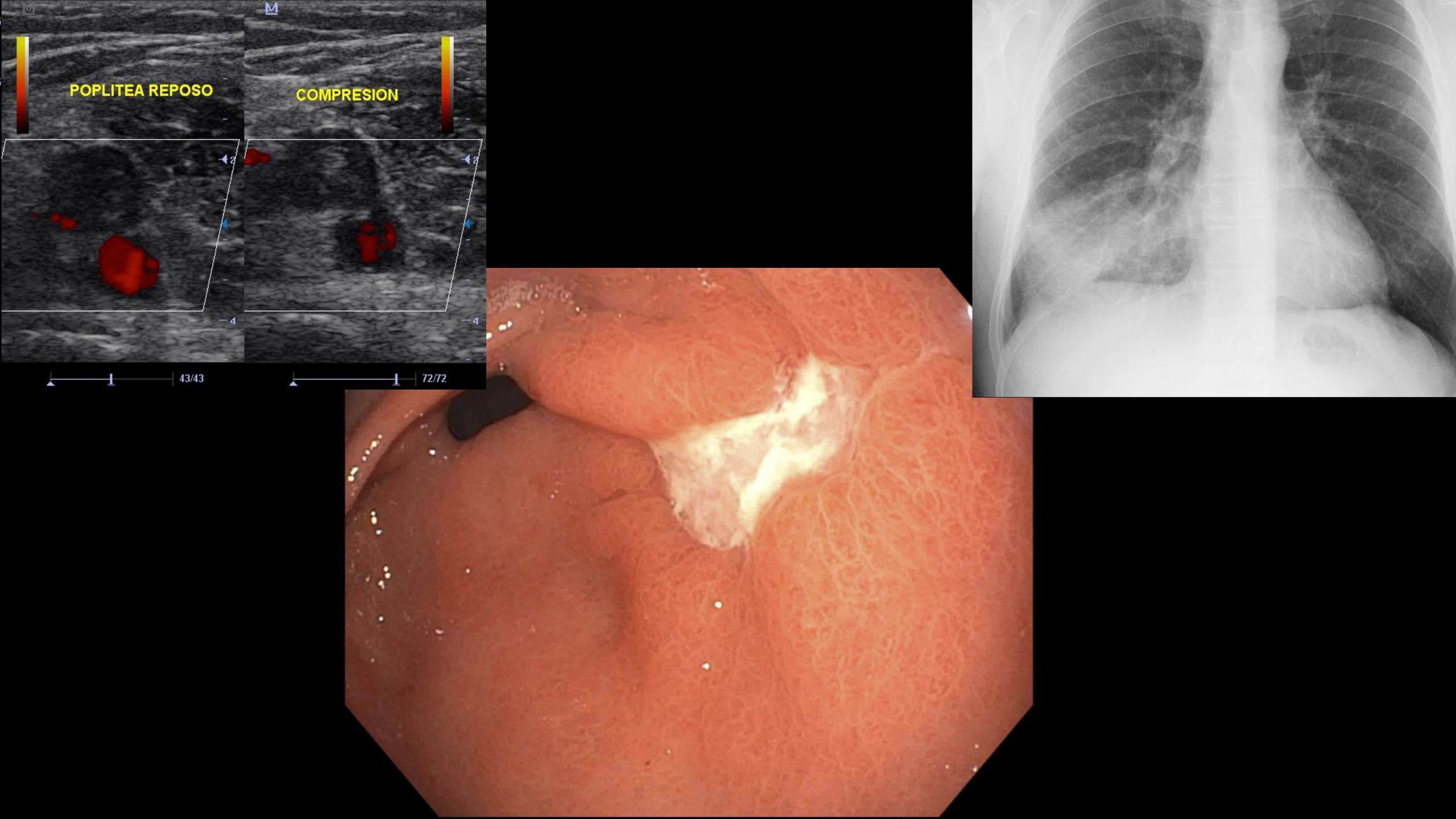
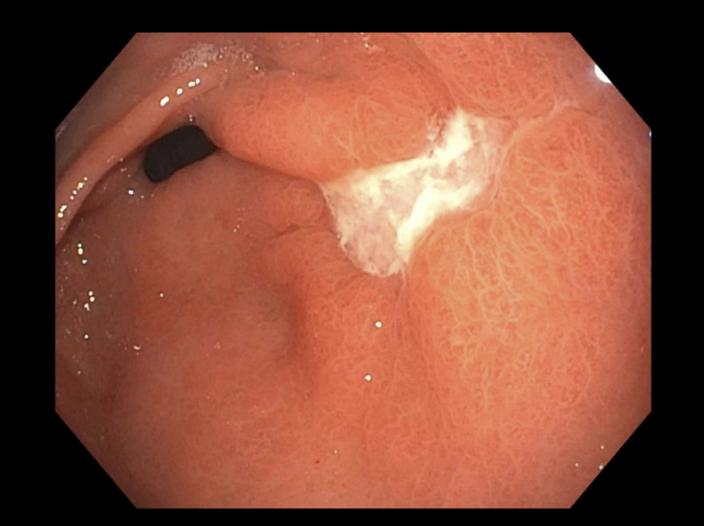
## Prophylaxis in the ICU

Feb 2024





## Stress Ulcer Prophylaxis

#### ORIGINAL ARTICLE

## Pantoprazole in Patients at Risk for Gastrointestinal Bleeding in the ICU

Mette Krag, M.D., Ph.D., Søren Marker, M.D., Anders Perner, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Matt P. Wise, M.D., Ph.D., Joerg C. Schefold, M.D., Frederik Keus, M.D., Ph.D., Anne B. Guttormsen, M.D., Ph.D., Stepani Bendel, M.D., Ph.D., Mark Borthwick, M.Sc., Theis Lange, Ph.D., Bodil S. Rasmussen, M.D., Ph.D., et al.,

for the SUP-ICU trial gr

**Original Investigation** | Caring for the Critically Ill Patient

January 17, 2020

December 6, 2018

N Engl J Med 2018; 379:2199-2208 DOI: 10.1056/NEJMoa1714919 Chinese Translation 中文翻译

## Effect of Stress Ulcer Prophylaxis With Proton Pump Inhibitors vs Histamine-2 Receptor Blockers on In-**Hospital Mortality Among ICU Patients Receiving Invasive Mechanical Ventilation** The PEPTIC Randomized Clinical Trial

The PEPTIC Investigators for the Australian and New Zealand Intensive Care 5 Critical Care Strategic Clinical Network, and the Irish Critical Care Trials Group

Article Information

JAMA. 2020;323(7):616-626. doi:10.1001/jama.2019.22190

JAMA Network"

**QUESTION** What is the comparative effect on in-hospital mortality of using proton pump inhibitors (PPIs) vs histamine-2 receptor blockers (H<sub>2</sub>RBs) for stress ulcer prophylaxis in ICU patients requiring invasive mechanical ventilation?

**CONCLUSION** This clinical trial did not find a statistically significant difference between PPIs and H<sub>2</sub>RBs for stress ulcer prophylaxis in ICU patients receiving mechanical ventilation, but study interpretation may be limited by crossover in medication use.

#### **POPULATION**



**17 137** Men **9691** Women

Adults receiving mechanical ventilation within 24 hours of ICU admission

Mean age: **58** years

#### **LOCATIONS**

50 **International ICUs** 

## 26982 Patients randomized **26771** Patients analyzed 13356

H<sub>2</sub>RB strategy

13415 **PPI strategy** 

INTERVENTION

#### **PRIMARY OUTCOME**

All-cause mortality during index hospitalization within 90 days

#### **FINDINGS**

All-cause mortality within 90 days

**PPI strategy** 

H<sub>2</sub>RB strategy 2459 of 13 415 patients 2333 of 13 356 patients





Absolute risk difference,

0.93 percentage points (95% CI, -0.01 to 1.88); P = .054

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The PEPTIC Investigators. Effect of stress ulcer prophylaxis with proton pump inhibitors vs histamine-2 receptor blockers on in-hospital mortality among ICU patients receiving invasive mechanical ventilation: the PEPTIC randomized clinical trial [published online January 17, 2020], JAMA, doi:10.1001/jama.2019.22190



Contents lists available at ScienceDirect

### Journal of Critical Care

journal homepage: www.jccjournal.org



## Enteral nutrition as stress ulcer prophylaxis in critically ill patients: A randomized controlled exploratory study



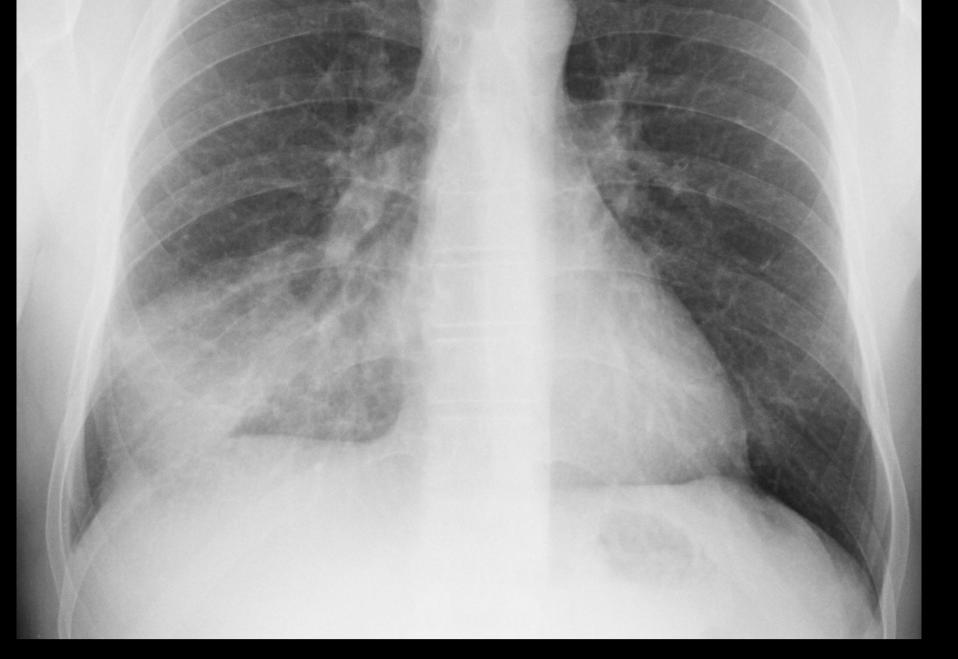
Karim El-Kersh, MD <sup>a,\*</sup>, Bilal Jalil, MD <sup>a</sup>, Stephen A. McClave, MD <sup>b</sup>, Rodrigo Cavallazzi, MD <sup>a</sup>, Juan Guardiola, MD <sup>a</sup>, Karen Guilkey, PT, DPT <sup>a</sup>, Annuradha K. Persaud, MPH <sup>c</sup>, Stephen P. Furmanek, MPH, MS <sup>c</sup>, Brian E. Guinn, MPH <sup>c</sup>, Timothy L. Wiemken, PhD <sup>c</sup>, Bashar Chihada Alhariri, MD <sup>a</sup>, Scott P. Kellie, MD <sup>a</sup>, Mohamed Saad, MD <sup>a</sup>

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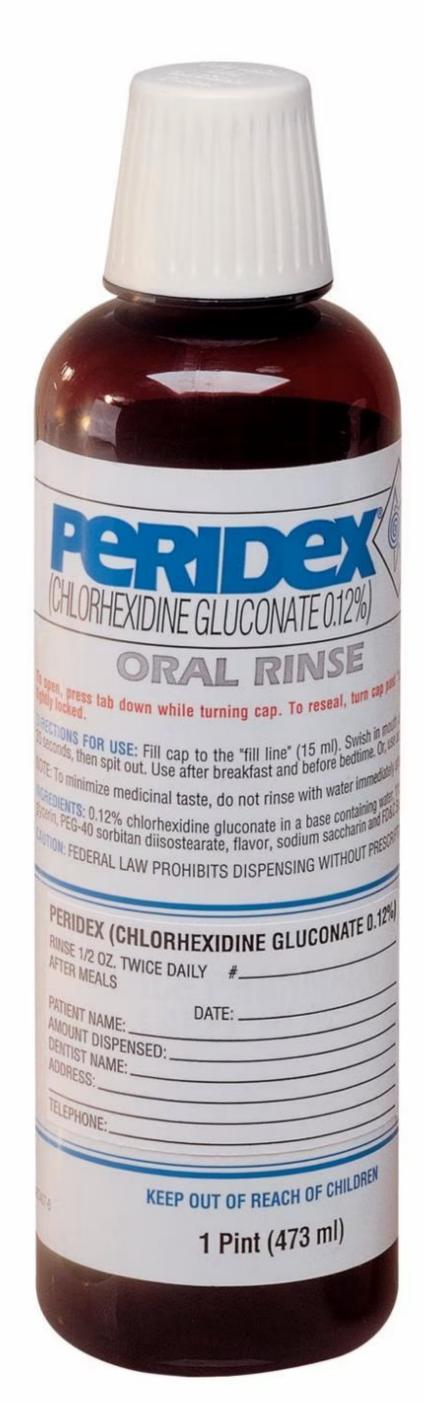
b University of Louisville School of Medicine, Department of Internal Medicine, Division of Gastroenterology, Hepatology and Nutrition, University of Louisville, KY, United States

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## REVISE



VAP





## SAT / SBT

## Selective Decontamination

## Oral Decon

Gastric Decon

Nasal Decon

This Issue Views 24,100 | Citations 0 | Altmetric 155

Original Investigation | Caring for the Critically Ill Patient

October 10, 2023

## Nasal Iodophor Antiseptic vs Nasal Mupirocin Antibiotic in the Setting of Chlorhexidine Bathing to Prevent Infections in Adult ICUs

A Randomized Clinical Trial

## JAMA

**QUESTION** Does nasal iodophor antiseptic work as well as nasal mupirocin antibiotic for preventing *Staphylococcus aureus* clinical cultures in intensive care unit (ICU) patients receiving daily chlorhexidine gluconate (CHG) bathing?

**CONCLUSION** This clinical trial found that nasal iodophor was inferior to nasal mupirocin in preventing S aureus clinical cultures in ICU patients.

### **POPULATION**



**430 764** Men **370 587** Women

**Adult ICU patients** 

Mean age: **63.4** years

### **LOCATIONS**

137
Community
hospitals in the US

### **INTERVENTION**



Iodophor-CHG
Mupirocin-CHG then switched
to twice-daily intranasal
10% povidone-iodine swabs
for 5 days + daily CHG bath

## **Mupirocin-CHG**

Twice-daily intranasal 2% mupirocin ointment for 5 days + daily CHG bath

### **PRIMARY OUTCOME**

S aureus clinical cultures attributed to the ICU (occurring from ICU day 3 through 2 days after ICU discharge) from baseline to intervention period

### **FINDINGS**

**ICU-attributable days** 

## **Iodophor-CHG**

Baseline: 4.3/1000

Intervention period: 5.0/1000

## **Mupirocin-CHG**

Baseline: 4.0/1000

Intervention period: 4.1/1000

Clustered HR, iodophor-CHG: 1.17
Clustered HR, mupirocin-CHG: 0.99

HR difference in differences, 18.4%

(95% CI, 10.7% to 26.6%)

© AMA

Huang SS, Septimus EJ, Kleinman K, et al. Nasal mupirocin vs iodophor in the setting of chlorhexidine bathing to prevent infections in adult ICUs: a randomized clinical trial. *JAMA*. Published October 10, 2023. doi:10.1001/jama.2023.17219

Original Investigation | Caring for the Critically Ill Patient

October 26, 2022

# Effect of Selective Decontamination of the Digestive Tract on Hospital Mortality in Critically Ill Patients Receiving Mechanical Ventilation A Randomized Clinical Trial

The SuDDICU Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group

**Article Information** 

JAMA. 2022;328(19):1911-1921. doi:10.1001/jama.2022.17927

## **JAMA**

FREE

**QUESTION** Among critically ill patients receiving mechanical ventilation, what is the effect of selective decontamination of the digestive tract (SDD) on hospital mortality?

**CONCLUSION** Among critically ill patients receiving mechanical ventilation, SDD did not significantly reduce in-hospital mortality vs standard care, although the confidence interval around the effect estimate includes a clinically important benefit.

© AMA **POPULATION INTERVENTION FINDINGS** In-hospital deaths **SDD Standard care 5982** Patients randomized 753 of 2791 patients 928 of 3191 patients 3780 Men 2202 Women 2791 3191 Adults receiving 27.0% 29.1% **SDD Standard** mechanical ventilation 6-Hourly oral paste and in an intensive care unit care gastric suspension of colistin, Standard care Mean age: **58** years tobramycin, and nystatin, without SDD plus 4-day IV antibiotic course SDD did not significantly reduce **LOCATIONS** in-hospital mortality: **PRIMARY OUTCOME Mean difference, -1.7%** (95% CI, -4.8% to 1.3%) Intensive care 90-Day in-hospital mortality **Odds ratio, 0.91** (95% CI, 0.82-1.02); *P* = .12 units in Australia

Writing Committee for the SuDDICU Investigators. Effect of selective decontamination of the digestive tract on hospital mortality in critically ill patients receiving mechanical ventilation: a randomized clinical trial. JAMA. Published online October 26, 2022. doi:10.1001/jama.2022.17927





### **ORIGINAL ARTICLE**

## Prevention of Early Ventilator-Associated Pneumonia after Cardiac Arrest

Bruno François, M.D., Alain Cariou, M.D., Ph.D., Raphaël Clere-Jehl, M.D., Pierre-François Dequin, M.D., Ph.D., et al., for the CRICS-TRIGGERSEP Network and the ANTHARTIC Study Group\*

### November 7, 2019

N Engl J Med 2019; 381:1831-1842

DOI: 10.1056/NEJMoa1812379

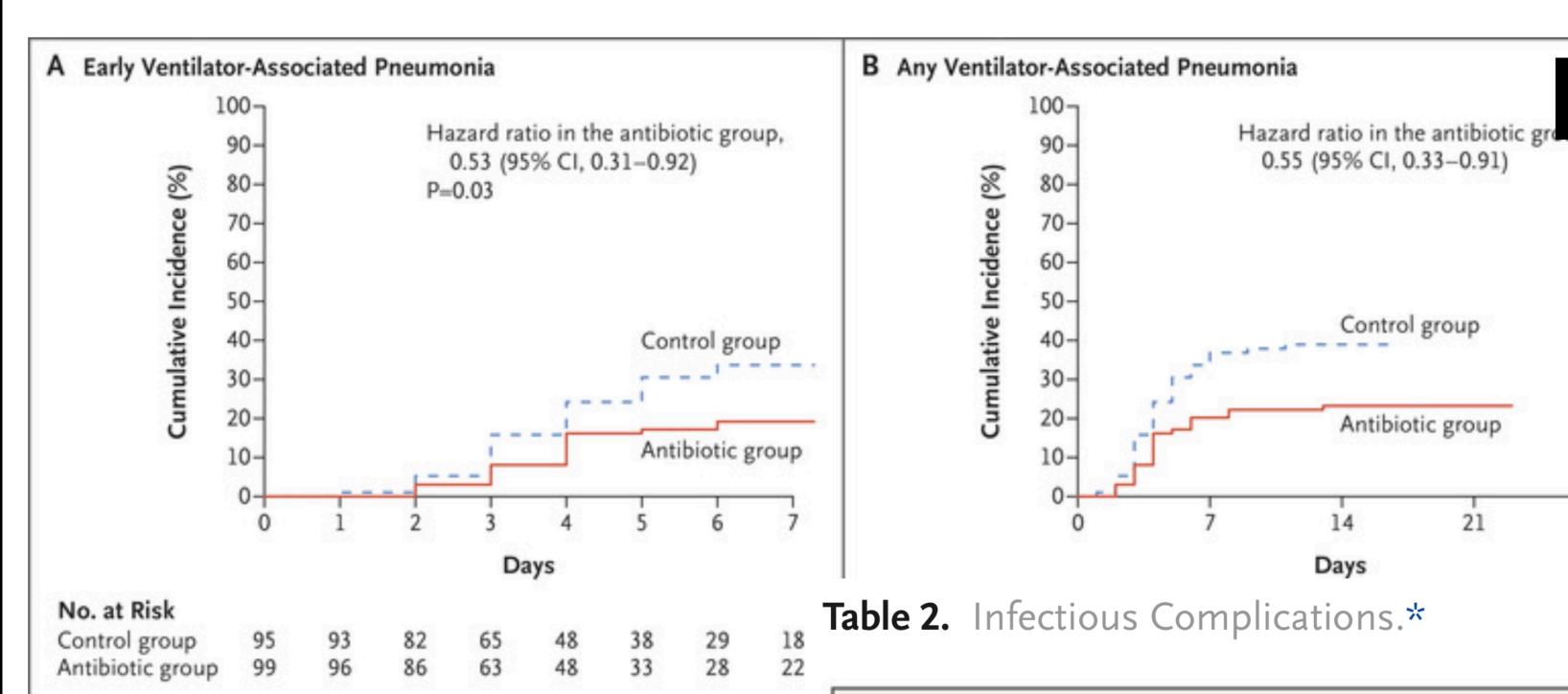
Chinese Translation 中文翻译

THE BOTTOM LINE

## **ANTHARTIC**

Empirical antibiotics after cardiac arrest

Figure 2. Cumulative Incidence of Ventilator-Associated Pneumonia.



Complication	Antibiotic Group (N=99)	Control Group (N = 95)	Hazard Ratio (95% CI)	P Value
	number (	percent)		
Ventilator-associated pneumonia†‡	23 (23)	37 (39)	0.55 (0.33-0.91)	
Early:	19 (19)	32 (34)	0.53 (0.31-0.92)	0.03
Late	4 (4)	5 (5)		
Catheter-related bloodstream infection	1 (1)	1 (1)		
Urinary tract infection	4 (4)	3 (3)		
Other infections§	0	2 (2)		

## **AMIKINHAL Trial**

#### The NEW ENGLAND JOURNAL of MEDICINE

#### RESEARCH SUMMARY

### Inhaled Amikacin to Prevent Ventilator-Associated Pneumonia

Ehrmann S et al. DOI: 10.1056/NEJMoa2310307

#### **CLINICAL PROBLEM**

Ventilator-associated pneumonia is the most frequent presentation of hospital-acquired infection of the lower respiratory tract. Microaspirations around the tracheal-tube cuff and the formation of biofilm can lead to progressive bacterial spread in the tracheobronchial tree, ultimately leading to pneumonia. Inhaled antibiotic therapy enables delivery of very high antibiotic concentrations to the tracheobronchial tree, lung parenchyma, and tracheal-tube biofilm. Whether preventive inhaled antibiotics may reduce the incidence of ventilator-associated pneumonia is unclear.

#### CLINICAL TRIAL

**Design:** A multicenter, double-blind, randomized, placebo-controlled trial in France examined the efficacy and safety of inhaled amikacin in critically ill adults who had undergone invasive mechanical ventilation for ≥72 hours.

Intervention: 847 patients were randomly assigned to receive inhaled amikacin at a dose of 20 mg per kilogram of ideal body weight or placebo once daily for 3 days. The primary outcome was a first episode of ventilator-associated pneumonia through day 28.

#### RESULTS

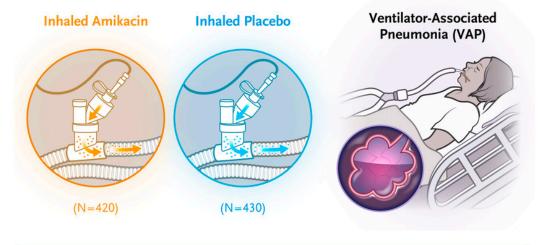
**Efficacy:** At 28 days, ventilator-associated pneumonia had developed in fewer patients in the amikacin group than in the placebo group.

**Safety:** Trial-related serious adverse effects were seen in 7 patients in the amikacin group and 4 patients in the placebo group.

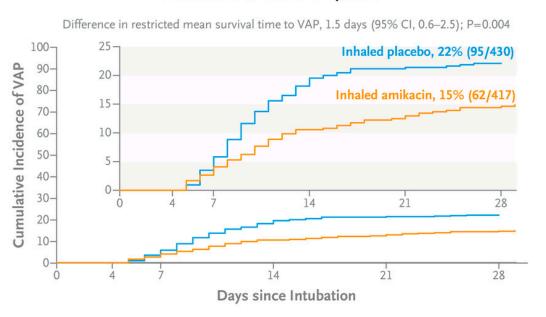
#### LIMITATIONS AND REMAINING QUESTIONS

- The trial was not powered to investigate other patient-centered outcomes, such as death or length of stay in the ICU and hospital.
- The trial was also not powered to detect whether preventive inhaled antibiotics could reduce the use of systemic antibiotics to limit antibiotic-resistance selection pressure.

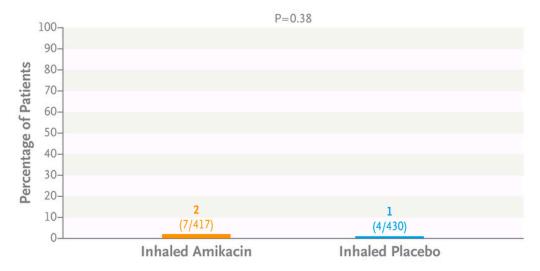
#### Links: Full Article | NEJM Quick Take



#### Incidence of a First VAP Episode



#### **Trial-Related Serious Adverse Effects**

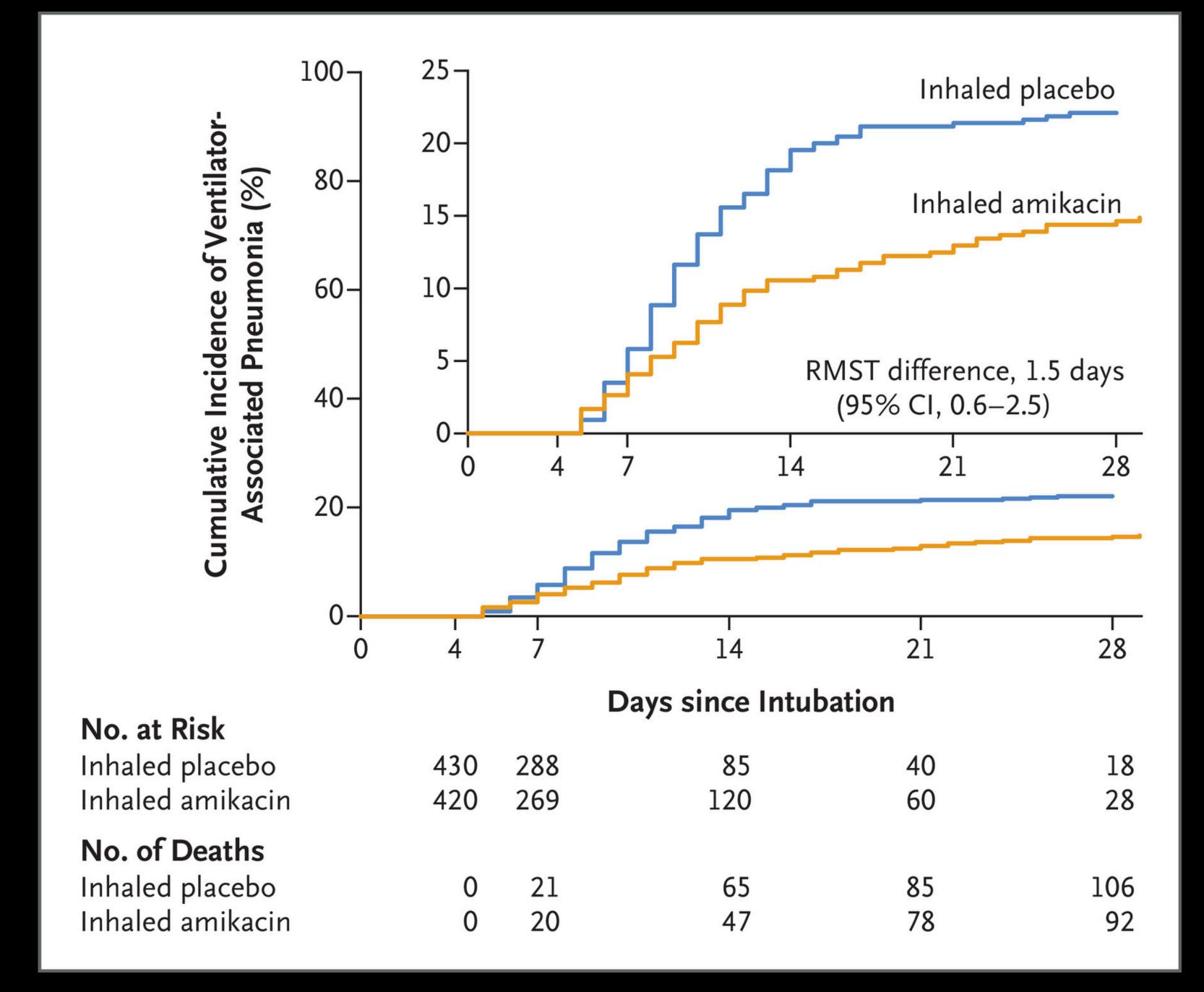


#### CONCLUSIONS

Among critically ill patients who had undergone mechanical ventilation for more than 3 days, a subsequent 3-day course of inhaled amikacin reduced the burden of ventilator-associated pneumonia during 28 days of follow-up.

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## AMIKINHAL Trial





### The Lancet Respiratory Medicine

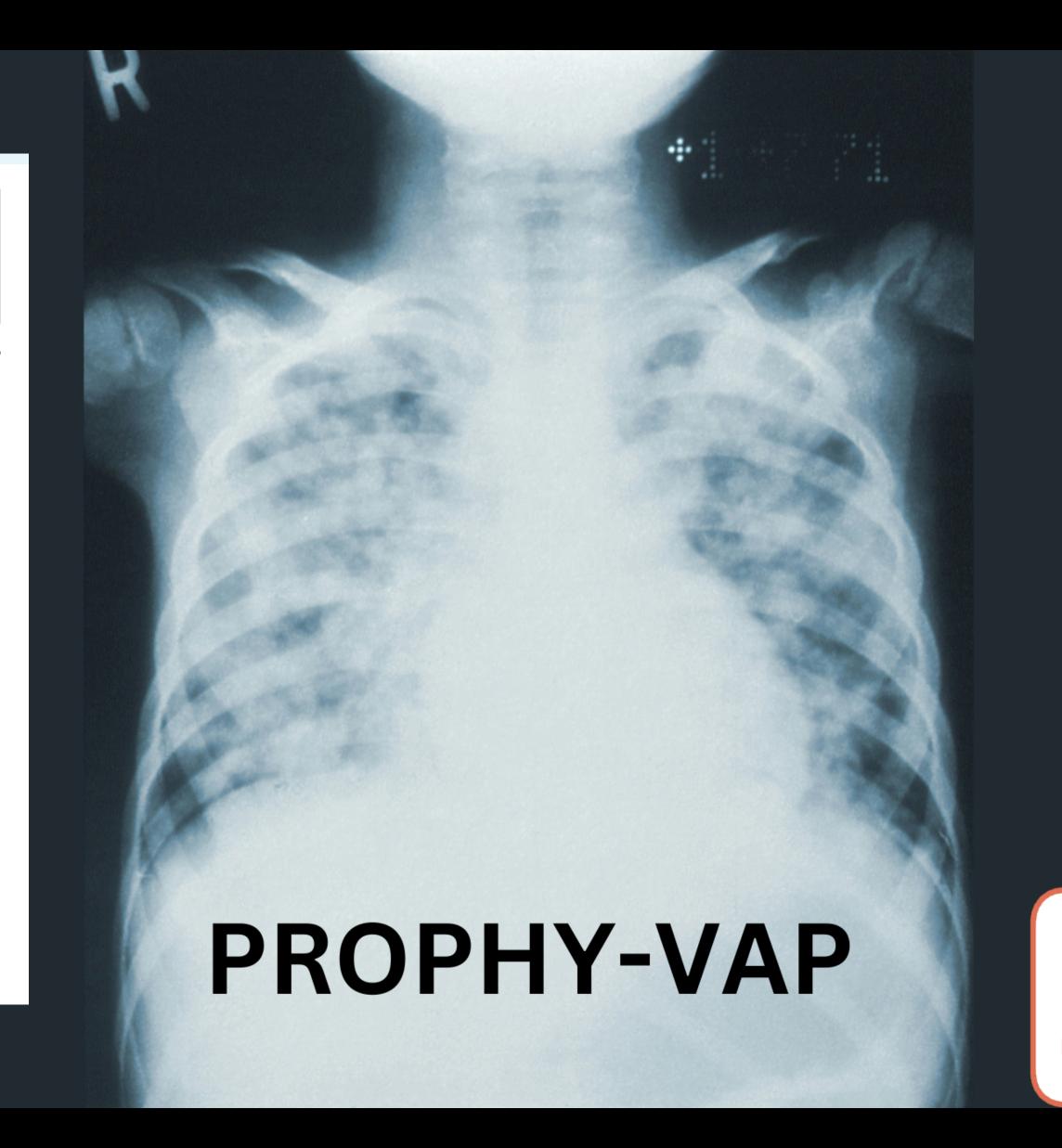
Available online 20 January 2024



Articles

Ceftriaxone to prevent early ventilatorassociated pneumonia in patients with acute brain injury: a multicentre, randomised, double-blind, placebocontrolled, assessor-masked superiority trial

Prof Claire Dahyot-Fizelier MD <sup>a b</sup> A M, Prof Sigismond Lasocki MD <sup>c</sup>, Thomas Kerforne MD <sup>b</sup>, Prof Pierre-Francois Perrigault MD <sup>d</sup>, Prof Thomas Geeraerts MD <sup>e</sup>, Prof Karim Asehnoune MD <sup>f</sup>, Prof Raphaël Cinotti MD <sup>f</sup>, Prof Yoann Launey MD <sup>g</sup>, Vincent Cottenceau MD <sup>h</sup>, Prof Marc Laffon MD <sup>i</sup>, Thomas Gaillard MD <sup>c</sup>, Prof Matthieu Boisson MD <sup>a b</sup>, Camille Aleyrat MSc <sup>j</sup>, Prof Denis Frasca MD <sup>b j</sup>, Prof Olivier Mimoz MD <sup>a k</sup>
PROPHY-VAP Study Group and the ATLANREA Study Group<sup>†</sup>



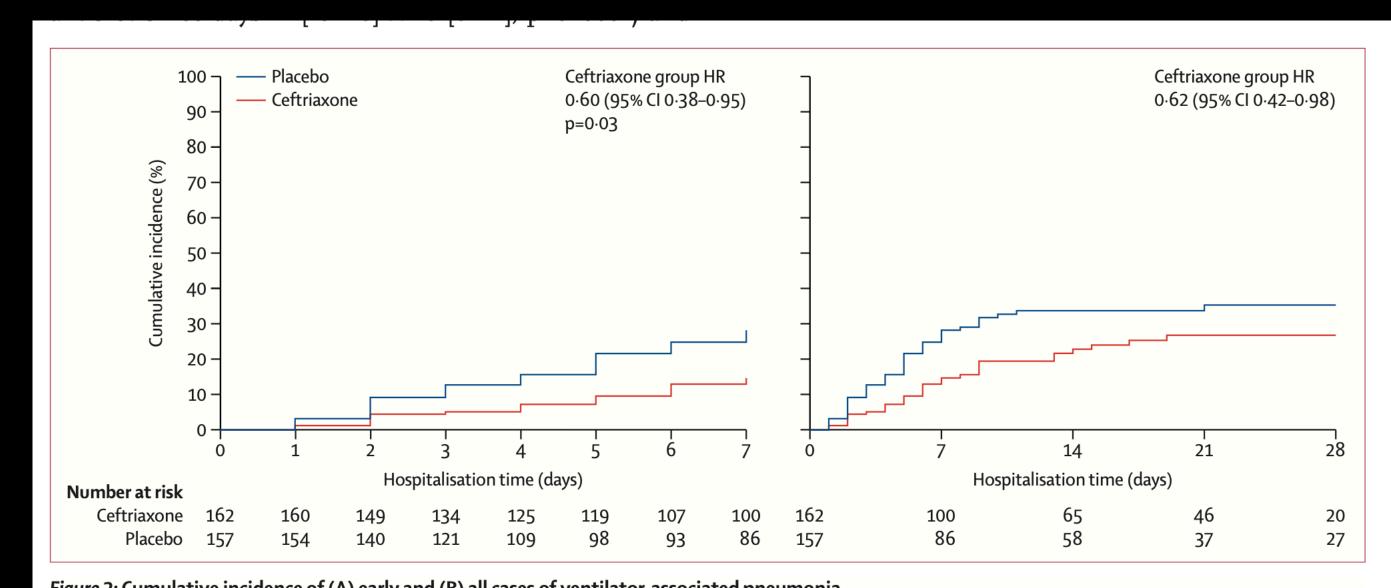


Figure 2: Cumulative incidence of (A) early and (B) all cases of ventilator-associated pneumonia

Cumulative incidence curves of early (from the second to the seventh day of mechanical ventilation) and all cases of ventilator-associated pneumonia were compared using the Fine-Gray approach between patients assigned to receive ceftriaxone and those assigned to receive placebo. HR=hazard ratio.

	Ceftriaxone group (n=162)	Placebo group (n=157)	HR	p value
Primary outcome				
Early VAP	23/23 (14%)	51/51 (32%)	0.60 (0.38-0.95)	0.030
Secondary outcomes on day 28				
AllVAP	35/33 (20%)	58/57 (36%)	0.62 (0.42-0.98)	
Late VAP	12/11 (7%)	7/7 (5%)		
Ventilator-free days	9 (0–22)	5 (0–18)		0.023
Antibiotic-free days	21 (13–28)	15 (8–21)		<0.000
Time between inclusion and first VAP, days	5 (3-9)	4 (2–6)		0.048
Modified Rankin score				0.032
0–1	27/145 (19%)	13/139 (9%)		
2–3	30/145 (21%)	23/139 (17%)		
4–5	63/145 (43%)	64/139 (46%)		
6	25/145 (17%)	39/139 (28%)		
Mortality	25/162 (15%)	39/157 (25%)	0.62 (0.39-0.97)	0.036
Secondary outcomes on day 60				
ICU-free days	34 (15-49)	26 (0-42)		0.003
Hospital-free days	23 (0–39)	8 (0-33)		0.005
Modified Rankin score*				0.17
0–1	44/158 (28%)	31/155 (20%)		
2–3	32/158 (20%)	28/155 (18%)		
4-5	50/158 (32%)	50/155 (32%)		
6	32/158 (20%)	46/155 (30%)		
Mortality	32/161 (20%)	46/157 (30%)	0.66 (0.42-1.04)	0.074

Data are median (IQR), n (%), n/N (%), mean number of events/number of patients evaluated, or HR (95% CI). HR (95% CI) are presented for qualitative variables taking account of competing risk if needed. VAP that occurred during the first 7 days of hospitalisation was defined as early, and VAP that occurred after the first 7 days of hospitalisation was defined as late. The following data were missing: antibiotic-free days for one patient receiving placebo, ICU-free days for one patient receiving placebo, modified Rankin score on day 28 for 17 patients receiving ceftriaxone and 18 receiving placebo, modified Rankin score on day 60 for four patients receiving ceftriaxone and two receiving placebo, and death at day 60 for one patient receiving ceftriaxone. HR=hazard ratio. ICU=intensive care unit. VAP=ventilator-associated pneumonia. \*Modified Rankin scale ranges from 0 to 6, with 0 representing no symptoms, 1 no clinically significant disability, 2 slight disability, 3 moderate disability, 4 moderately severe disability, 5 severe disability, and 6 death.

#### Table 2: Primary and secondary outcomes

# Delirium

Original Investigation | Caring for the Critically Ill Patient

FREE

February 20, 2018

# Effect of Haloperidol on Survival Among Critically Ill Adults With a High Risk of Delirium The REDUCE Randomized Clinical Trial

Mark van den Boogaard, PhD<sup>1</sup>; Arjen J. C. Slooter, MD, PhD<sup>2</sup>; Roger J. M. Brüggemann, PharmD, PhD<sup>3</sup>; et al

Author Affiliations | Article Information

JAMA. 2018;319(7):680-690. doi:10.1001/jama.2018.0160

Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial

Dr Valerie J Page, MBBCh  $\stackrel{>}{\sim}$  • Prof E Wesley Ely, MD • Prof Simon Gates, PhD • Xiao Bei Zhao, RN • Timothy Alce, PhD • Ayumi Shintani, PhD • et al. Show all authors

Open Access • Published: August 21, 2013 • DOI: https://doi.org/10.1016/S2213-2600(13)70166-8 •



### ORIGINAL ARTICLE

# Haloperidol and Ziprasidone for Treatment of Delirium in Critical Illness

Timothy D. Girard, M.D., M.S.C.I., Matthew C. Exline, M.D., M.P.H., Shannon S. Carson, M.D., Catherine L. Hough, M.D., Peter Rock, M.D., M.B.A., Michelle N. Gong, M.D., Ivor S. Douglas, M.D., Atul Malhotra, M.D., Robert L. Owens, M.D., Daniel J. Feinstein, M.D., Babar Khan, M.B., B.S., Margaret A. Pisani, M.D., M.P.H., et al., for the MIND-USA Investigators\*

#### **ORIGINAL ARTICLE**

## Haloperidol for the Treatment of Delirium in ICU Patients

Nina C. Andersen-Ranberg, M.D., Lone M. Poulsen, M.D., Anders Perner, Ph.D., Jørn Wetterslev, Ph.D., Stine Estrup, Ph.D., Johanna Hästbacka, Ph.D., Matt Morgan, Ph.D., Giuseppe Citerio, Ph.D., Jesus Caballero, M.D., Theis Lange, Ph.D., Maj-Brit N. Kjær, M.Sc., Bjørn H. Ebdrup, Ph.D., et al., for the AID-ICU Trial Group\*

Home > Intensive Care Medicine > Article

## Prophylactic melatonin for delirium in intensive care (Pro-MEDIC): a randomized controlled trial

Original | Published: 27 February 2022 Volume 48, pages 414–425, (2022) Cite this article

ORIGINAL ARTICLE

## Early Sedation with Dexmedetomidine in Critically Ill Patients

Yahya Shehabi, Ph.D., M.B., B.S., Belinda D. Howe, R.N., M.P.H., Rinaldo Bellomo, M.D., Ph.D., Yaseen M. Arabi, M.D., Michael Bailey, Ph.D., Frances E. Bass, R.N., Suhaini Bin Kadiman, M.D., Colin J. McArthur, M.B., Ch.B., Lynnette Murray, B.S., Michael C. Reade, M.B., B.S., M.P.H., D.Phil., Ian M. Seppelt, M.B., B.S., Jukka Takala, M.D., Ph.D., et al., for the ANZICS Clinical Trials Group, and the SPICE III Investigators\*

June 27, 2019

N Engl J Med 2019; 380:2506-2517

DOI: 10.1056/NEJMoa1904710

## Take Home Points

- PPI > H2 for now? Priorities early enteral feeds
- Consider adopting mupirocin ointment BID
- Brain injury = 2g Ceftriaxone post intubation
- Tx Hyperactive Delirium as it present