



Prevention in the ICU

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The threat we pose to the critically ill

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ARTICLE

Association between Critical Care Physician Management and Patient Mortality in the Intensive Care Unit

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Table 4. Expected and Actual Hospital Mortality*

Variable	Critical Care Management†			No Critical Care Management†		
	≥95%	5%–95%	≤5%	≥95%	5%–95%	≤5%
Patients, n	18 601	23 324	261	17	37 020	22 609
Mean SAPS II probability	0.1650	0.1733	0.1511	0.0585	0.1102	0.1368
Mean mortality rate	0.1800	0.1884	0.1801	0.0588	0.1004	0.1244
SMR (95% CI)	1.09 (1.05–1.13)	1.09 (1.05–1.12)	1.19 (0.88–1.58)	1.01 (0.03–5.60)	0.91 (0.88–0.94)	0.91 (0.88–0.94)

* SAPS = Simplified Acute Physiology Score; SMR = standardized mortality ratio.

† For the entire stay for patients in the intensive care unit.

Intensivist management increased hospital mortality by 40%, even when controlling for (a) severity of illness and (b) propensity to consult an intensivist

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Association between critical care physician management and patient mortality in the intensive care unit.

Levy MM, Rapoport J, Lemeshow S, Chaffin DS, Phillips G, Daniels M, et al. *Annals of Internal Medicine*. 2008;148(12):923-931.

Abstract

OBJECTIVE: Critically ill patients admitted to intensive care units (ICUs) are thought to gain a added survival benefit from management by critical care physicians. An evidence of this benefit is not clear.

DESIGN: To examine the association between hospital mortality in critically ill patients and management by critical care physicians.

SETTING: This is a retrospective analysis of a large, prospectively collected database of critically ill patients.

SETTING: 122 ICUs in 180 U.S. hospitals.

PATIENTS: 161 452 critically ill adults.

MEASUREMENTS AND MAIN RESULTS: Through use of random-effects logistic regression, investigators compared hospital mortality between patients cared for solely by critical care physicians and patients cared for entirely by non-critical care physicians. An associated 30% increase in hospital mortality was associated with admission to an ICU, and a propensity score was used to adjust for differences in the probability of receiving critical care physician management.

CONCLUSIONS: Critically ill patients who received critical care physician management had a significantly increased mortality rate, and had higher hospital mortality rates than those who did not receive critical care physician management, even when propensity score matched mortality rates were higher for patients who received critical care physician management. The likelihood of admission to an ICU was higher for patients who were sicker and who were assigned to a propensity score to receive critical care physician management.

KEY WORDS: critical care; intensive care; mortality; physician; patient; propensity score; survival.

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Take-home lesson?

vided by trained critical care physicians leads to better outcomes, our data raise an important point: Although we believe that critical care physicians are trained and expertly skilled in the management of critically ill patients, perhaps some routine critical care practices and procedures may not be beneficial or cumulative use of more interventions may take a negative toll. Although further analyses and studies are needed to understand the possibility that care from

Specific topics

- The ICU burden of catheter-related bloodstream infections (CRBSIs) and ventilator-associated pneumonias (VAPs)
- Venous thromboembolism prophylaxis in the critically ill medical patient
- Controlling hyperglycemia—how aggressive should we be?

Case vignette

- You are a hospitalist at a small community hospital, recently appointed to be the medical director of a mixed medical-surgical ICU. Despite not having formal preventative protocols, your predecessor had an enviable record of no ventilator-associated pneumonias (VAPs) or catheter related bloodstream infections (CRSBIs) in over a year.

As the ICU director, you should implement all **except**:

1. Catheter “bundles” designed to prevent CRBSIs
2. Ventilator “bundles” designed to prevent VAPs
3. Bathing patients in a dilute chlorhexidine solution
4. Use of antibiotic-impregnated central lines
5. Honest surveillance of VAPs and CRBSIs

Burden of VAPs/CRBSIs

➤@ 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 Sietens, Anne Sooy, Mercedes Palomar, Michael Hiesmayr, Ingrid Morales, Antonella Agodi, Uwe Frank, Karl Mertens, Martin Schumacher, Martin Wolkewitz

- Lambert et al. Lancet Infectious Diseases 2011
 - 120,000 patients admitted to 537 ICUs in Europe
 - 7% rate of VAPs; 4% bloodstream infections
 - VAP: 2.3 fold increased risk of mortality, increased LOS
 - Bacteremia: 3.1 fold increased risk of mortality
 - Outcomes only modestly worsened by drug resistance

VAPs/CRBSIs are highly prevalent

- Be wary of underreporting bias

A Multifaceted Intervention for Quality Improvement in a Network of Intensive Care Units
A Cluster Randomized Trial

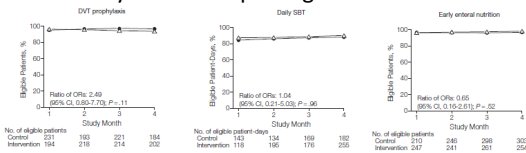
Scales et al. JAMA
Jan 2011

Comment: Evidence-based practice, improved antibiotic use and ICU outcomes, but eligible patients may not receive them. Community hospitals may need additional supports but may have few resources dedicated to quality improvement.
Objective: To determine the effectiveness of a multifaceted quality improvement program to increase delivery of 4 evidence-based ICU practices.
Design, setting, and participants: Prospective cluster-randomized trial among 15 community hospitals in Ontario, Canada. A total of 5038 admissions occurred during the trial period from 2005 to October 2006 and 1743 admissions during a 6-month monitoring period (December 2006 to August 2007).

Implemented protocols for VAP prevention, DVT prophylaxis, spontaneous breathing trials, CRBSI prevention, early enteral feeding, and prevention of decubitus ulcers
– Well known that ICUs are poorly compliant

VAPs/CRBSIs are highly prevalent

- Be wary of underreporting bias



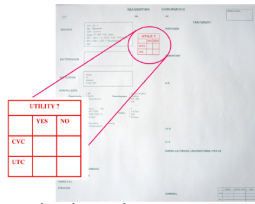
Implemented protocols for VAP prevention, DVT prophylaxis, spontaneous breathing trials, CRBSI prevention, early enteral feeding, and prevention of decubitus ulcers
– Well known that ICUs are poorly compliant
– ICUs self-reported outstanding compliance, even before intervention

Step 1: Remove the underlying problem!

- VAP risk proportionate to ventilator duration (Cook et al. Ann Intern Med 1998)
 - Minimize sedation
 - Bolus preferred to continuous (50% decrease in vent days) Brook et al. Crit Care Med 1999
 - Daily sedation cessation (2 fewer vent days) Kress et al. NEJM 2000
 - Daily sedation cessation with superimposed spontaneous breathing trials (3 fewer vent days) Girard et al. Lancet 2008
 - Respiratory therapist-run weaning protocols
 - 1.5 fewer vent days Ely NEJM 2000; fewer trauma VAPs Marelich Chest 2000
 - Early tracheostomy?
 - Decreases vent time; no change in VAP rates Terragni et al. JAMA 2010

Step 1: Remove the underlying problem!

- Duration of catheterization increases risk
 - Daily reminders to remove catheter
 - Seguin et al. Intensive Care Med 2010



- Decreased catheter days, CRBSIs

Step 2: Clean the site!

- VAPs arise from aspiration of oral contents
 - Oral decontamination
 - 2% chlorhexidine favored in metaanalysis Labeau et al. Lancet Infect Dis 2011
 - Continuous subglottic suctioning Dezfalian Am J Med 2005
 - Antibiotic decontamination of digestive tract?
 - Controversial; drug resistance? Maselli Ther Adv Respir Dis 2011
 - Silver-lined ETT?
 - Decrease biofilm; unclear if cost-effective Maselli Ther Adv Respir Dis 2011
 - Ventilator circuit cleaning?
 - Only change if visibly soiled Han and Liu Respir Care 2010

Step 2: Clean the site!

- CRBSIs
 - Place catheter in the cleanest site
 - Subclavian > IJ >>> femoral McGee NEJM 2003
 - Chlorhexidine baths
 - Bleasdale Arch Intern Med 2007, Climo Crit Care Med 2009
 - Chlorhexidine sponges (with transparent gauze)
 - Beneficial even in low risk patients Timsit et al. JAMA 2009
 - Antibiotic-impregnated lines?
 - Only cost effective if baseline CRBSI rate high Casey et al. Lancet Infect Dis 2008

Step 3: Bundle up!

ICU Bundles—“A group of evidence-based interventions that, when implemented together, result in better outcomes than when implemented individually” (Chittick Crit Care Med 2010)

- Ventilator bundles
 - Hand hygiene, gowns
 - Head of bed elevation > 30°
 - Torres Ann Intern Med 1992
 - ETT cuff pressure > 20 cm H₂O
 - Rello Int Care Med 1996
 - Chlorhexidine oral care
 - Avoiding nonessential vent tubing changes Cook JAMA 1998

Bouadma L et al. Clin Infect Dis 2010

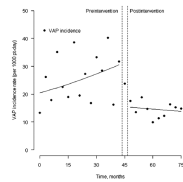


Figure 1. Segmented Poisson regression analysis, comparing incidence rates of ventilator-associated pneumonia (VAP) in the intensive care unit before and after a preventive intervention.

Step 3: Bundle up!

ICU Bundles—“A group of evidence-based interventions that, when implemented together, result in better outcomes than when implemented individually” (Chittick Crit Care Med 2010)

- Catheter bundles
 - Hand hygiene (Yilmaz et al. JPEN 2007)
 - Maximal barrier precautions (Raad et al. Infect Control Hosp Epidemiol 1999)
 - Chlorhexidine (Chaiyakunapruk N et al. Ann Int Med 2002)
 - Discouraging femoral lines
 - Daily review of catheters

Pronovost P et al. NEJM 2006

Table 4. Incidence-Rate Ratios for Catheter-Related Bloodstream Infections.*

Variable	Incidence-Rate Ratio (95% CI)	P Value
Study period		
Baseline	1.00	
During implementation	0.76 (0.57–1.01)	0.063
After implementation		
0–3 mo	0.62 (0.47–0.81)	0.001
4–6 mo	0.56 (0.38–0.84)	0.005
7–9 mo	0.47 (0.34–0.63)	<0.001
10–12 mo	0.42 (0.28–0.63)	<0.001
13–15 mo	0.37 (0.20–0.68)	0.001
16–18 mo	0.34 (0.23–0.50)	<0.001
Teaching hospital	1.34 (0.73–2.46)	0.35
Bed size (per 100 beds)	1.03 (0.97–1.09)	0.33

Case vignette

- You are treating a patient admitted two days previously with variceal hemorrhage. His bleeding has stopped after endoscopic banding upon admission. He has moderate hepatic encephalopathy, with an INR of 2.0 due to cirrhosis.

What form of venous thromboembolism prophylaxis should the patient receive?

1. **None, due to the endogenous elevation in INR**
2. **Sequential compression devices alone**
3. **BID subcutaneous heparin**
4. **TID subcutaneous heparin**
5. **Once-daily low molecular weight heparin**

Burden of VTE in the ICU

- Virchow’s triad common in ICU
 - ~30% incidence of VTE in MICU patients Chan and Schorr Sem Resp Crit Care Med 2010
 - Up to 70% incidence in ischemic stroke
 - Cirrhotic “auto-anticoagulation” is a myth Aldawood et al. Thromb J 2011
- Potentially severe consequences
 - Hemodynamic fragility of the critically ill
 - Difficult to treat (risk of anticoagulation)
 - VTE increases ICU, hospital LOS Cook et al. Crit Care Med 2005
 - CMS will not reimburse Chan and Shorr Sem. Resp Crit Care Med 2010

VTE chemoprophylaxis

- Twice-daily subcutaneous unfractionated heparin
 - Unacceptably high VTE rates in patients ventilated for > 7 days (27%) Ibrahim Crit Care Med 2002
- Thrice-daily subcutaneous unfractionated heparin
 - Superiority to BID suggested by two meta-analyses
 - Fewer DVTs Wein et al. Arch Intern Med 2007
 - Fewer proximal DVT/PEs, but increased bleeding King Chest 2007
 - Similar to BID in one meta-analysis Phung et al. Chest 2011

VTE chemoprophylaxis

- Low molecular weight heparin
 - Fraisse et al. AJRCCM 2000
 - RCT of 223 mechanically-ventilated COPD patients
 - Nadoparin decreased DVT risk compared to placebo (15.5% vs. 28.2%); no difference in bleeding risk
 - PROTECT trial NEJM 2011
 - International RCT of 3764 ICU patients
 - Once-daily dalteparin decreased risk of PE vs. twice-daily subcutaneous heparin. No difference in bleeding
 - Dalteparin prophylaxis safe in renal failure (DIRECT)
 - Douketis J et al. Arch Intern Med 2008
 - No data re: fondaparinux in ICU

Mechanical prophylaxis?

- Little data on efficacy in critically ill
 - In general, mechanical interventions decrease risk of DVT; no effect on PE or death Geerts et al. Chest 2008
 - ICU patients?
 - Better compliance with SCDs. Bockheim et al. J Crit Care 2009
 - Compression stockings better than nothing post-MI. Kierkegaard and Norgren, Eur Heart J 1993
 - ACCP recommendations? Geerts et al Chest 2008
 - Use in patients with major bleeding
 - When bleeding risk subsides, change to heparin/LMWH
 - Can be used in conjunction with heparin/LMWH

Case vignette


- You are caring for a 32 year old female with H1N1 influenza-induced acute lung injury. She is intubated and sedated. While her condition has stabilized, her blood glucose levels are now consistently 180 – 200 mg/dl.

How should you treat this elevated glucose?

1. Do not treat unless glucose persistently > 200 mg/dl
2. Initiate insulin infusion with goal glucose 80 – 110 mg/dl
3. Initiate insulin infusion with goal glucose 144 – 180 mg/dl
4. Initiate subcutaneous insulin therapy with goal 144 – 180 mg/dl

Hyperglycemia in the ICU

- 90% of patients will have blood glucose > 110 mg/dL during their ICU stay Van den Berghe NEJM 2001
 - Consequence of hypermetabolic state, dextrose-containing infusions, steroids, adrenergic agents Egi Chest 2011
 - Associate with poor ICU outcomes Finney JAMA 2003
- Historically, goals were “loose” glycemic control Egi Chest 2011
 - < 200 to 215 mg/dL


 INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS
GREET VAN DEN BERGHE, M.D., Ph.D., PETER WOUTERS, M.Sc., FRANK WIEKERS, M.D., CHARLES VERWAEST, M.D.,
 FRANS BRUYNBOCK, M.D., MIET SOETZ, M.D., Ph.D., DIKE VLASSELAARS, M.D., PATRICK FORDONANDE, M.D., Ph.D.,
 PETER LAUWERS, M.D., AND ROGER BOULLON, M.D., Ph.D.

- Van den Berghe NEJM 2011
 - 1,548 patients from a single Belgian SICU
 - Randomized to “intensive” (80 – 110 mg/dl) versus conventional (180 to 200 mg/dl) glycemic control

VARIABLE	CONVENTIONAL TREATMENT (N=783)	INTENSIVE TREATMENT (N=765)	P VALUE*
Death during intensive care — no./total no. (%)	63/783 (8.0)	35/765 (4.6)	<0.04 (adjusted)
During first 5 days of intensive care	14/783 (1.8)	13/765 (1.7)	0.9
Among patients receiving intensive care for >5 days	49/243 (20.2)	22/208 (10.6)	0.005
In-hospital death — no./total no. (%)			
All patients	85/783 (10.9)	55/765 (7.2)	0.01
Patients receiving intensive care for >5 days	64/243 (26.3)	35/208 (16.8)	0.01

Concerns with tight glycemic control?

- Van den Berghe et al. NEJM 2006
 - “Intensive” insulin therapy did not benefit MICU patients
 - Increased mortality in those admitted for < 3 days
- Brunkhorst et al. NEJM 2008
 - “Intensive” insulin therapy in severe sepsis
 - Stopped early for safety (more severe hypoglycemia)
- Preiser et al. Intensive Care Med 2009
 - “Intensive” insulin therapy in med-surg ICUs
 - Stopped early; no benefit and increased hypoglycemia

Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study Investigators*

- NEJM 2009
 - Multinational RCT of “intensive” insulin vs conventional
 - 6,104 patients enrolled

Table 3. Outcomes and Adverse Events.*

Outcome Measure	Intensive Glucose Control	Conventional Glucose Control	Odds Ratio or Absolute Difference (95% CI)†	Statistical Test	P Value
Death — no. of patients/total no. (%)				Logistic regression	
At day 90	829/3010 (27.5)	751/3012 (24.9)	1.14 (1.02 to 1.28)		0.02
At day 28	670/3010 (22.3)	627/3012 (20.8)	1.09 (0.96 to 1.23)		0.17

- Increased risk of hypoglycemia was noted
 - Interestingly, not the cause of the increased mortality

Recommendations for glucose control?

- Do not push glucose too low
 - Unclear cause of excess mortality
- Do not abandon glucose control efforts!
 - American Diabetes Association Diabetes Care 2011:
 - Start intravenous insulin once glucose > 180 mg/dl
 - Goal 144 to 180 mg/dl
 - Intravenous insulin protocol recommended
