



**Stress ulcer prophylaxis in the intensive care unit:  
unanswered research questions**

*A systematic review*

**Principal investigator:**

Morten Hylander Møller, MD PhD

Department of Intensive Care

Copenhagen University Hospital Rigshospitalet

Blegdamsvej 9

2100 Copenhagen, Denmark

+45 22555343

[mortenhylander@gmail.com](mailto:mortenhylander@gmail.com)

[www.sup-icu.com](http://www.sup-icu.com)

Protocol 1.1  
30/06/2012



## **1. BACKGROUND**

### **I. Summary**

In the context of critical illness, there is a risk of stress-related gastrointestinal (GI) mucosal damage, which can progress to ulceration and GI bleeding. One of the first reports on GI stress ulcerations in patients in the intensive care unit (ICU) was published by Skillman and colleagues in 1969<sup>1</sup>. In 7 out of 150 patients (5%) with the triade respiratory failure, sepsis and hypotension, postmortem examination revealed multiple superficial ulcers in the gastric fundus. Following this report, clinical trials have shown that stress ulcer prophylaxis (SUP) can reduce the frequency of GI bleeding in ICU patients compared to placebo or no prophylaxis<sup>2-7</sup>. Based on this research, SUP is regarded as the standard of care in critically ill patients, as outlined by The Joint Commission, The Institute for Healthcare Improvement, and in the Surviving Sepsis Campaign International Guidelines<sup>8</sup>. A number of randomized clinical trials (RCTs) and meta-analyses, have sought to determine the better SUP agent by balancing efficacy and harm<sup>9-12</sup>. However, recent research has questioned the rationale and level of evidence of SUP in the ICU, because of limited data and methodological flaws in some of the trials<sup>9-12</sup>.

### **II. Aim**

The aim of the present review is to highlight the unanswered clinical research questions on the topic of SUP in critically ill patients.

### **III. Hypothesis**



We hypothesized, that the rationale of SUP in the ICU is widely unresolved, and that the level of evidence is poor.

#### IV. Research Question

Is stress ulcer prophylaxis in critically ill patients indicated?

#### V. PICO

Population: critically ill patients in the intensive care unit

Intervention: stress ulcer prophylaxis

Comparator: any

Outcome: gastrointestinal bleeding; mortality; colitis; pneumonia; cardiovascular events

## 2. METHODS

### I. Search strategy

The following databases will be searched for literature: MEDLINE including MeSH, EMBASE, and the Cochrane Library.

### II. Search terms

critically ill OR ICU OR intensive care unit OR intensive care

AND

stress ulcer prophylaxis OR SUP

AND



mortality OR death OR gi bleeding OR gastrointestinal bleeding OR pneumonia OR morbidity OR clostridium difficile

### **III. Selection criteria**

Adult critically ill patients in the intensive care unit receiving stress ulcer prophylaxis.

### **IV. Additional limits on type, study design?**

None.

### **V. Quality assessment**

Risk of bias will be assessed according to GRADE <sup>13</sup>.

### **VI. Data extraction**

The following key data will be extracted: the incidence of gastrointestinal bleeding in the critically ill patients, and efficacy and harm of the different pharmacological agents.

### **VII. Data synthesis**

Data synthesis will be given in tables.

## **3. PROCESS**

### **I. Target audience**

Physicians treating critically ill patients.



## II. Publication type

A systematic review.

## III. Communication media

Results will be presented at national and international conferences. The paper will be published in an international peer-reviewed journal.

## 4. TIMETABLE

Draft protocol for internal review:	June 2012
Searching and study selection:	July 2012
Data extraction	July 2012
Quality assessment	July 2012
Draft report for peer review	July 2012
Submit for publication	Fall 2012

## 5. REFERENCES

1. Skillman JJ, Bushnell LS, Goldman H, Silen W. Respiratory failure, hypotension, sepsis, and jaundice. A clinical syndrome associated with lethal hemorrhage from acute stress ulceration of the stomach. *Am J Surg* 1969;117:523-30.
2. Shuman RB, Schuster DP, Zuckerman GR. Prophylactic therapy for stress ulcer bleeding: a reappraisal. *Ann Intern Med* 1987;106:562-7.
3. Cook DJ, Reeve BK, Guyatt GH, Heyland DK, Griffith LE, Buckingham L, Tryba M. Stress ulcer prophylaxis in critically ill patients. Resolving discordant meta-analyses. *JAMA* 1996;275:308-14.
4. Cook DJ, Witt LG, Cook RJ, Guyatt GH. Stress ulcer prophylaxis in the critically ill: a meta-analysis. *Am J Med* 1991;91:519-27.



Protocol 1.1

---

5. Tryba M. Prophylaxis of stress ulcer bleeding. A meta-analysis. *J Clin Gastroenterol* 1991;13 Suppl 2:S44-55.
6. Lasky MR, Metzler MH, Phillips JO. A prospective study of omeprazole suspension to prevent clinically significant gastrointestinal bleeding from stress ulcers in mechanically ventilated trauma patients. *J Trauma* 1998;44:527-33.
7. Phillips JO, Metzler MH, Palmieri MT, Huckfeldt RE, Dahl NG. A prospective study of simplified omeprazole suspension for the prophylaxis of stress-related mucosal damage. *Crit Care Med* 1996;24:1793-800.
8. Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut JF, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent JL. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med* 2008;36:296-327.
9. Huang J, Cao Y, Liao C, Wu L, Gao F. Effect of histamine-2-receptor antagonists versus sucralfate on stress ulcer prophylaxis in mechanically ventilated patients: a meta-analysis of 10 randomized controlled trials. *Crit Care* 2010;14:R194.
10. Lin PC, Chang CH, Hsu PI, Tseng PL, Huang YB. The efficacy and safety of proton pump inhibitors vs histamine-2 receptor antagonists for stress ulcer bleeding prophylaxis among critical care patients: a meta-analysis. *Crit Care Med* 2010;38:1197-205.
11. Marik PE, Vasu T, Hirani A, Pachinburavan M. Stress ulcer prophylaxis in the new millennium: a systematic review and meta-analysis. *Crit Care Med* 2010;38:2222-8.
12. Quenot JP, Thiery N, Barbar S. When should stress ulcer prophylaxis be used in the ICU? *Curr Opin Crit Care* 2009;15:139-43.
13. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schunemann HJ. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924-6.