Guardians of the Gut

Review of the Stress Ulcer Prophylaxis Guidelines

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Disclosures

The planner(s) and speaker(s) have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

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Learning Objectives

Describe the pathophysiology of stress ulcers in critically ill patients

Review current practice and summarize the new stress ulcer prophylaxis (SUP) guidelines

Discuss the therapeutic options for SUP and their associated risk

Apply updated SUP recommendations to eligible patient populations

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Outline

- Background
- Previous Guidance
- 2024 Society of Critical Care Medicine Guidelines
- Pharmacologic Agents
- Summary

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Abbreviation Key

- aPTT: activated partial thromboplastin time
- ASHP: American Society of Health-System Pharmacists
- C. diff: Clostridioides difficile
- CI: confidence interval
- CIB: clinically important bleed
- EN: enteral nutrition
- GI: gastrointestinal
- H2RAs: histamine 2 receptor antagonists
- ICU: intensive care unit
- INR: international normalized ratio
- IPA: International Pharmaceutical Abstracts
- IV: intravenous
- LOS: length of stay
- MOA: mechanism of action
- MOD: multiorgan dysfunction
- NG: nasogastric
- PICO: Patient, Intervention, and Outcome Question
- PLT: platelets
- PO: by mouth
- PPIs: proton pump inhibitors
- RCTs: randomized controlled trials
- RE: relative effect
- RR: relative risk
- RRT: renal replacement therapy
- SCCM: Society of Critical Care Medicine
- SCLE: Systemic and Cutaneous Lupus Erythematosus
- SUP: stress ulcer prophylaxis
- TOC: transitions of care
- UGIB: upper gastrointestinal bleed

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Definition

Stress ulcers are acute erosions or lesions of the gastric mucosa that develop in response to severe pathophysiological stress, predisposing them to clinically important stress-related upper gastrointestinal bleeding (UGIB)

Moody FG, et al. Stress ulcers: their pathogenesis, diagnosis, and treatment. *Surg Clin North Am*. 1976

Epidemiology

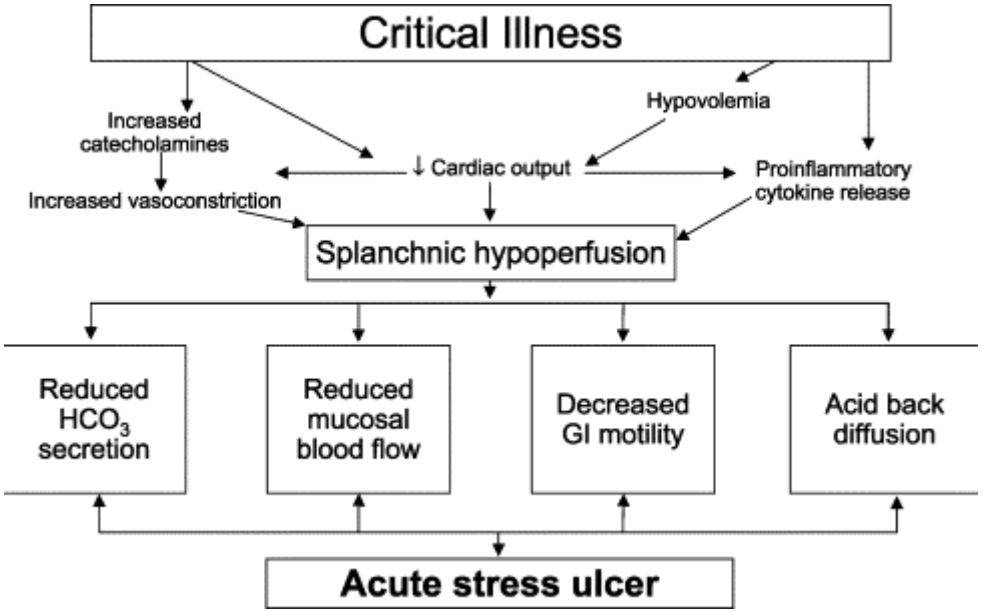
Superficial focal lesions in mucosa of gastric fundus found in critically ill patient (1969)

Early on- 25% of critically ill patients developed overt gastrointestinal bleeding

Now more infrequent- 0.6-4 % of patients

Plummer MP, et al. Stress ulceration: prevalence, pathology and association with adverse outcomes. *Crit Care*. 2014

Pathophysiology



Stollman N, et al. Pathophysiology and prophylaxis of stress ulcer in intensive care unit patients. *J Crit Care*. 2005

Assessment Question #1

Which of the following is NOT a proposed mechanism behind the pathophysiology of stress ulcers?

A. Increased catecholamine release
B. Splanchnic hypoperfusion
C. Increased GI motility
D. Hypovolemia/Hypotension

Previous Guidance

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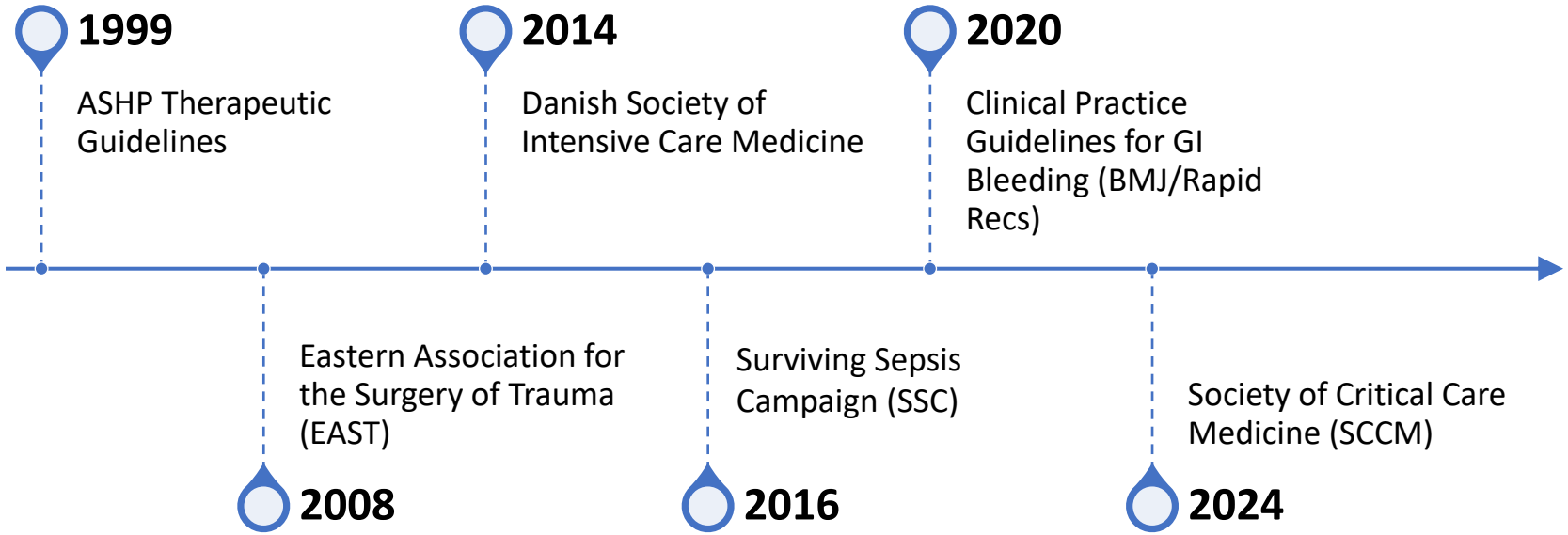
1999
ASHP Therapeutic Guidelines
2008
Eastern Association for the Surgery of Trauma (EAST)
2014
Danish Society of Intensive Care Medicine
2016
Surviving Sepsis Campaign (SSC)
2020
Clinical Practice Guidelines for GI Bleeding (BMJ/Rapid Recs)
2024
Society of Critical Care Medicine (SCCM)

1999 ASHP Guidelines

Objective: To evaluate literature on the use of stress ulcer prophylaxis in critically ill patients and form a concise guideline

Methods: Detailed and exhaustive literature searches of MEDLINE from 1966 to 1997 and IPA from 1970 to 1997 were performed

Results: Formal recommendations on SUP indications, agents, and monitoring

ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis. ASHP Commission on Therapeutics and approved by the ASHP Board of Directors on November 14, 1998. *Am J Health Syst Pharm*. 1999

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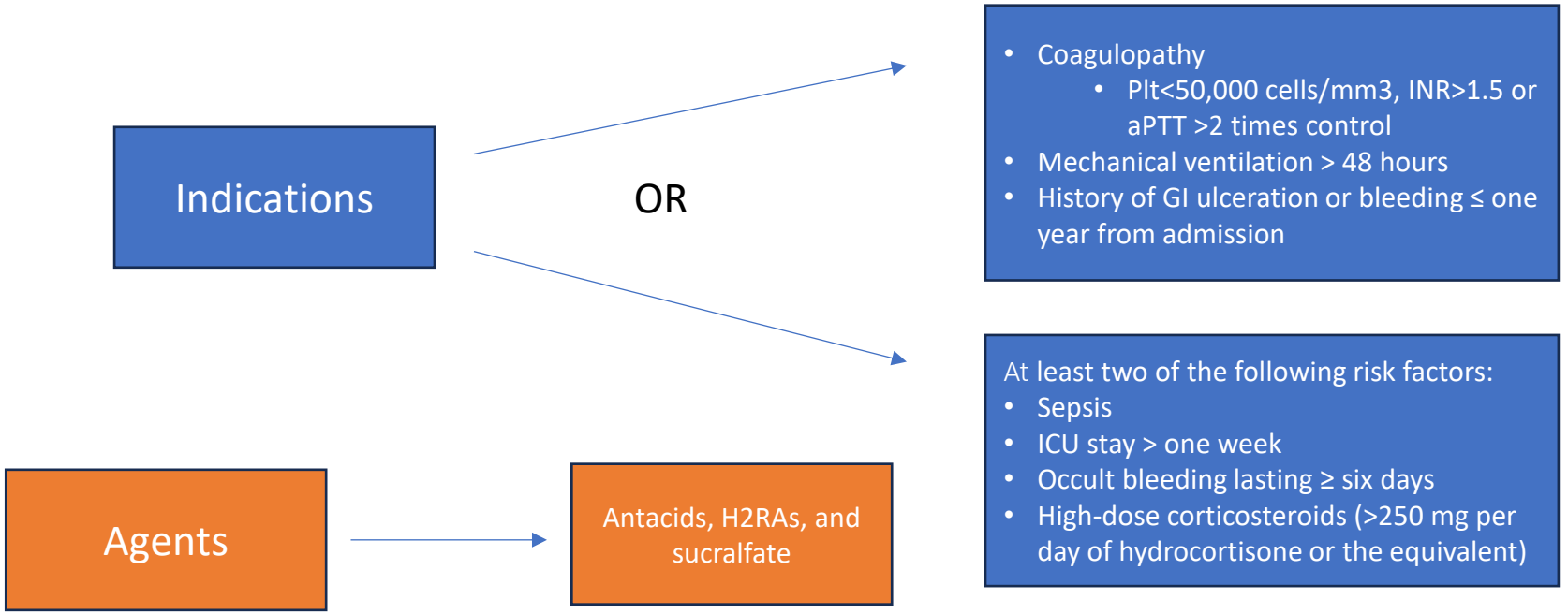
1999 ASHP Guidelines



ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis. ASHP Commission on Therapeutics and approved by the ASHP Board of Directors on November 14, 1998. *Am J Health Syst Pharm*. 1999

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2016 Surviving Sepsis

Objective: To provide an update to “Surviving Sepsis Campaign Guidelines for Management of Sepsis and Septic Shock: 2012”

Methods: Generated a list of questions, searched for best available evidence, and followed GRADE system to assess evidence and form recommendations

Results: The panel provided 93 statements on early management and resuscitation of patients with sepsis or septic shock

Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Intensive Care Med*. 2017;43(3):304-377. doi:10.1007/s00134-017-4683-6

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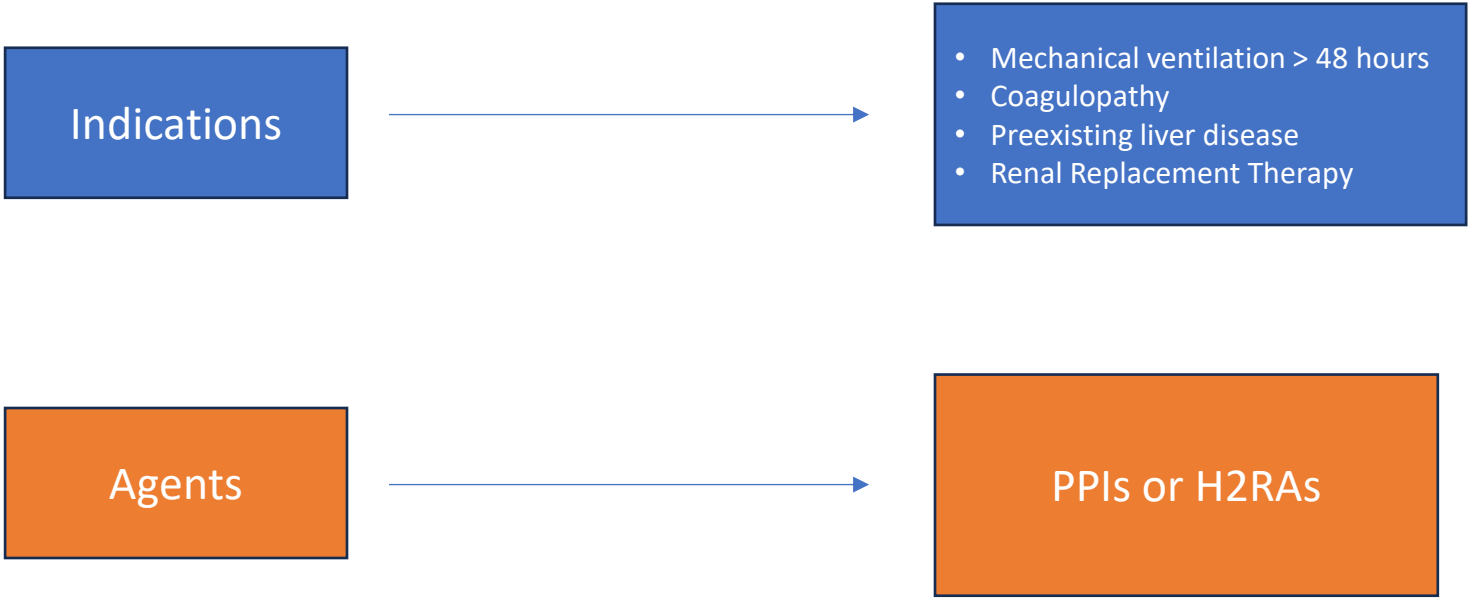
2016 Surviving Sepsis



ASHP Therapeutic Guidelines on Stress Ulcer Prophylaxis. ASHP Commission on Therapeutics and approved by the ASHP Board of Directors on November 14, 1998. *Am J Health Syst Pharm*. 1999

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2024 Society of Critical Care Medicine Guidelines

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Overview

Objective: To develop evidence-based recommendations for the prevention of UGIB in adults in the ICU

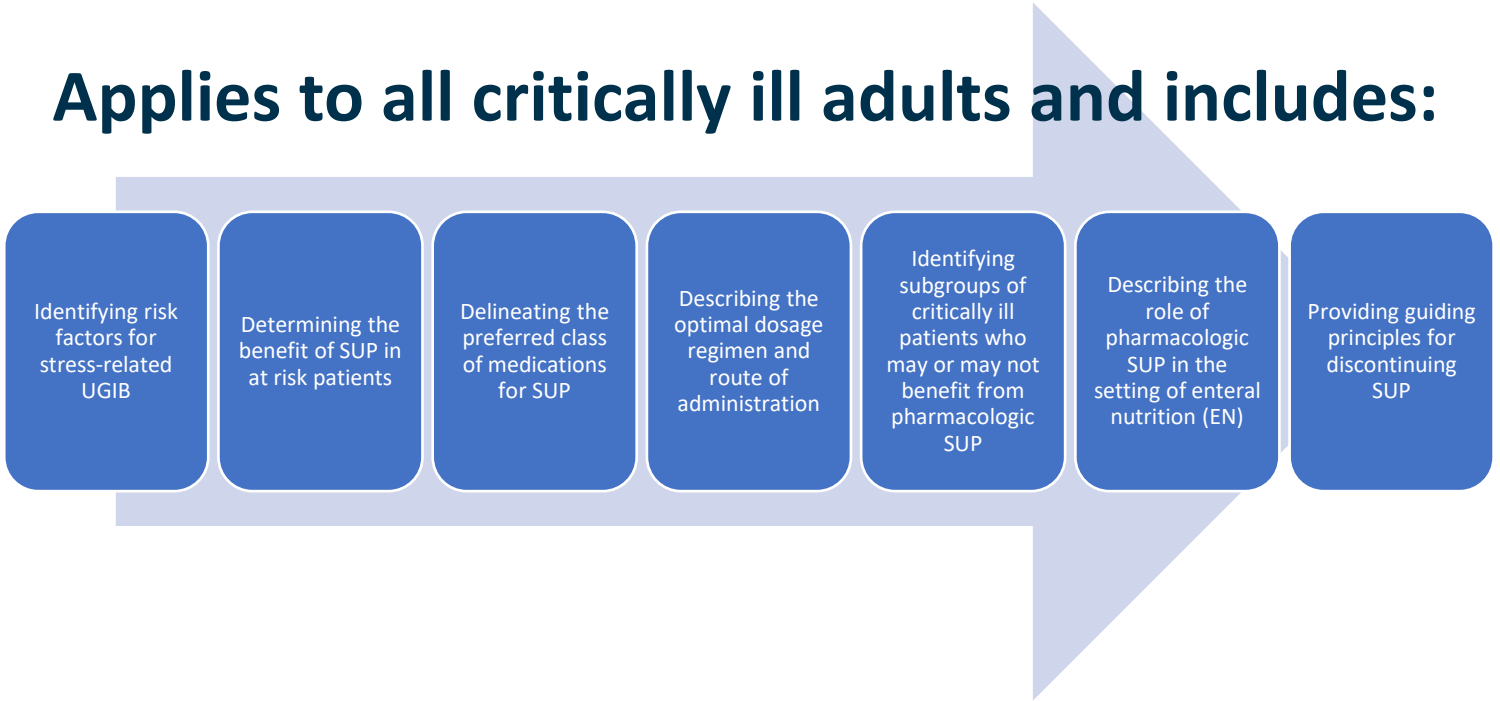
Methods: The panel conducted a systematic review of the published scientific literature, focusing on patient-oriented, clinically relevant outcomes to answer Population, Intervention, Comparison, and Outcome (PICO) questions regarding clinically important and overt stress-related UGIB in the ICU

Results: The panel generated nine conditional recommendations and made four good practice statements

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

Scope

Applies to all critically ill adults and includes:



MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

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Recommendations

PICO Question (Population, Intervention, Comparison, Outcome*)	Recommendation
• Critically ill adults (ICU) with coagulopathy or shock or chronic liver disease • SUP vs No SUP	• Critically ill adults with coagulopathy, shock, or chronic liver disease be considered at risk for clinically important UGIB
• Critically ill adults (ICU) with risk factors for developing stress-related UGIB • Enteral nutrition vs No enteral nutrition	• Administer enteral nutrition to reduce clinically important stress-related UGIB in critically ill adults
• Critically ill adults (ICU) with risk factors for developing stress-related UGIB • SUP vs No SUP	• Critically ill adults with coagulopathy, shock, or chronic liver disease be considered at risk for overt UGIB

*All outcomes: Reduced occurrence of clinically important stress-related UGIB

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MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

Recommendations cont.

PICO Question (Population, Intervention, Comparison, Outcome*)	Recommendation
• Neurocritically ill adults (ICU) with risk factors for developing stress-related UGIB • SUP vs no SUP	• Use SUP in neurocritical care adults
• Critically ill adults with risk factors for developing stress-related UGIB who are enterally fed during ICU admission • SUP vs no SUP	• Use SUP for critically ill adults who are enterally fed and possess one or more risk factor(s)
• Critically ill adults who are at low risk for developing stress-related UGIB and are enterally fed during ICU admission • SUP vs no SUP	• Do NOT use SUP for critically ill adults who are enterally fed and at low risk for clinically important stress-related UGIB

*All outcomes: Reduced occurrence of clinically important stress-related UGIB

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MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

Recommendations cont.

PICO Question (Population, Intervention, Comparison, Outcome*)	Recommendation
• Critically ill adults (ICU) with risk factors for developing stress-related UGIB • PPIs or H2RAs vs NO PPIs or H2RAs	• We suggest using either PPIs or H2RAs as first-line agents for SUP in critically ill adults with risk factors
• Critically ill adults (ICU) with risk factors for developing stress-related UGIB • Enteral or IV SUP vs No SUP	• We suggest using either enteral or IV routes when administering SUP in critically ill adults with risk factors compared to no SUP
• Critically ill adults (ICU) with risk factors for developing stress-related UGIB • Low-dose SUP vs High-dose SUP	• Low-dose SUP should be administered compared with high-dose SUP (good practice statement).

*All outcomes: Reduced occurrence of clinically important stress-related UGIB

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MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

Recommendations cont.

PICO Question (Population, Intervention, Comparison, Outcome*)	Recommendation
• Critically ill adults (ICU) with risk factors for developing stress-related UGIB that are no longer present • Discontinued vs continued use of SUP	• SUP should be discontinued when the risk factor(s) is no longer present • Discontinuation of SUP before transfer out of the ICU is necessary to prevent inappropriate prescribing (good practice statement)
• Critically ill adults who do not have risk factors for developing stress-related UGIB but are on SUP before ICU admission • Discontinued vs continued use of SUP	• The indications for these medications should be reviewed and consideration made for discontinuing them (good practice statement)
• Critically ill adults who have risk factors for developing stress-related UGIB but are on SUP before ICU admission • Continued vs discontinued use of SUP	• The consideration to change the medication to the most preferred agent for SUP must be weighed against the indication that required the SUP therapy before ICU admission (good practice statement)

*All outcomes: Reduced occurrence of clinically important stress-related UGIB

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MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

Risk Factors

We suggest critically ill adults with **coagulopathy, shock, or chronic liver disease** be considered at risk for clinically important UGIB

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

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At Risk Definition

*"At risk" -critically ill and **presence** of coagulopathy, shock, or chronic liver disease*

*"Low-risk" -critically ill and **absence** of coagulopathy, shock, or chronic liver disease*

Note: Mechanical ventilation ALONE probably is not a risk factor and does not necessitate SUP

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

Prevalence and Outcome of GI Bleeding (2015)

Methods	• International, prospective 7-day cohort study • Adults without GI bleeding acutely admitted to the ICU during a 7-day period • Primary outcome: clinically important bleeding in the ICU • Secondary outcome: overt GI bleeding in ICU and mortality 90 days after inclusion
Results	• 1,034 patients in 97 ICUs in 11 countries were included • Variables associated with CIB: **three or more co-existing diseases** (OR 8.9, 2.7–28.8), **co-existing liver disease** (7.6, 3.3–17.6), **use of RRT** (6.9, 2.7–17.5), **co-existing coagulopathy** (5.2, 2.3–11.8), **acute coagulopathy** (4.2, 1.7–10.2), **use of acid suppressants** (3.6, 1.3–10.2) and **higher organ failure score** (1.4, 1.2–1.5) • 49 of 1,034 patients (4.7 %, 3.4–6.0) had at least one episode of overt GI bleeding during the ICU stay • Crude and adjusted odds for mortality were 3.7 (1.7–8.0) and 1.7 (0.7–4.3), respectively
Conclusion	• Co-existing diseases, liver failure, coagulopathy and organ failures are the main risk factors for GI bleeding

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Krag M, et al. Prevalence and outcome of gastrointestinal bleeding and use of acid suppressants in acutely ill adult intensive care patients. *Intensive Care Med*. 2015

Predictors of GI Bleeding in Adult ICU (2019)

Methods	• Systematic review and meta-analysis of cohort studies • Eligible studies assessed **potential predictors** of clinically important GI bleeding (CIB; primary outcome) or overt GI bleeding (secondary outcome)
Results	• 8 studies (116,497 patients) were included • **Coagulopathy** (RE 4.76, 95% CI 2.62–8.63, moderate certainty), **shock** (RE 2.60, 95% CI 1.25–5.42, low certainty), and **chronic liver disease** (RE 7.64, 95% CI 3.32–17.58, moderate certainty) were associated with increased incidence of CIB • The effect of mechanical ventilation on CIB was unclear (RE 1.93, 0.57–6.50, very low certainty)
Conclusion	• These findings may be used to identify ICU patients at higher risk of GI bleeding who are most likely to benefit from stress ulcer prophylaxis

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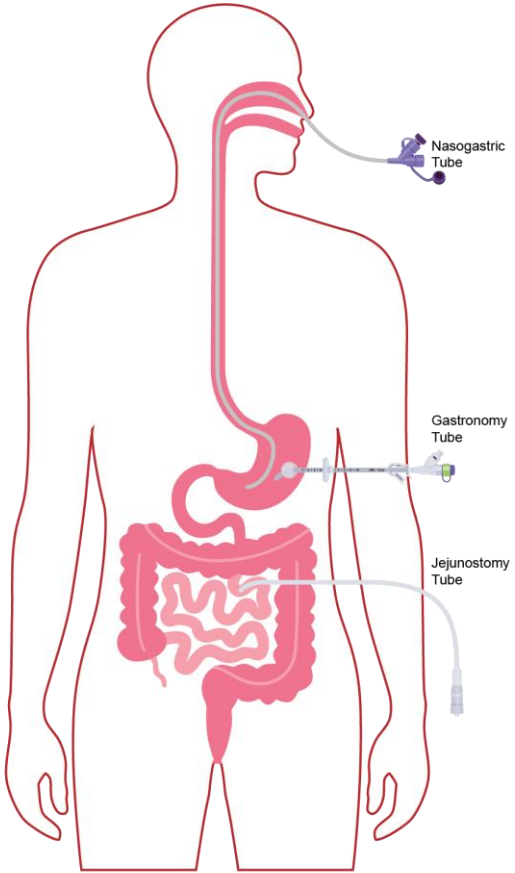
Granholm A, Zeng L, Dionne JC, et al. Predictors of gastrointestinal bleeding in adult ICU patients: a systematic review and meta-analysis. *Intensive Care Med*. 2019

Enteral Nutrition

We suggest clinicians **administer EN** to reduce clinically important stress-related UGIB in critically ill adults



Credit: iStock and ASPEN, American Society for Parenteral and Enteral Nutrition

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

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Risk Factors for CIB for Patients Requiring Ventilation (1999)

Methods	• Cohort of 1,200 ventilated ICU patients enrolled in a multicenter, randomized trial of sucralfate vs. ranitidine to determine rates of upper gastrointestinal bleeding, pneumonia, and mortality
Results	• 1,077 patients, 30 (2.8%) developed CIB • Factors associated with bleeding were **low platelet count**, **maximum serum creatinine**, and **maximum multiple organ failure (MOD) score** • **Enteral nutrition** (relative risk = 0.30 [95% CI = 0.13-0.67]) and SUP with ranitidine (relative risk = 0.39 [95% CI = 0.17-0.83]) were **protective**
Conclusion	• In critically ill ventilated patients, renal failure was independently associated with an increased risk of clinically important gastrointestinal bleeding, whereas **enteral nutrition** and stress ulcer prophylaxis with ranitidine conferred significantly lower bleeding rates

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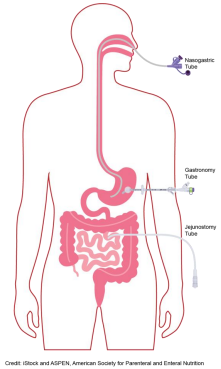
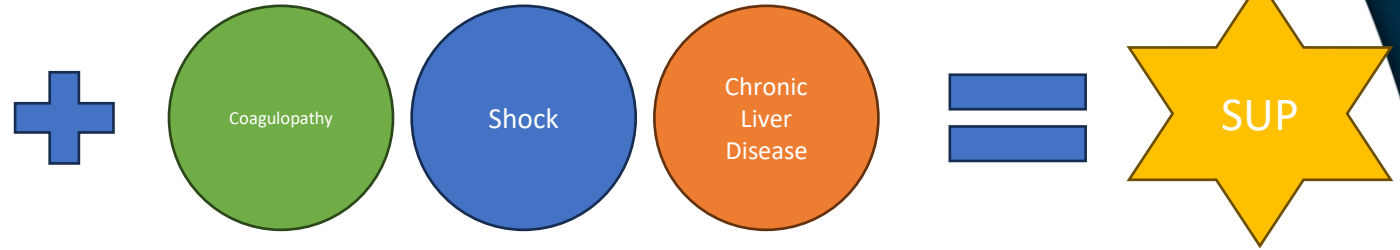
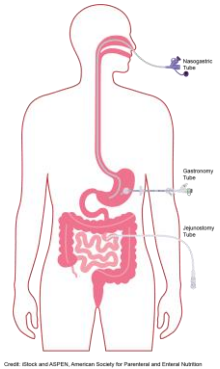
Cook D, et al. Risk factors for clinically important upper gastrointestinal bleeding in patients requiring mechanical ventilation. Canadian Critical Care Trials Group. *Crit Care Med*. 1999

Enteral Nutrition

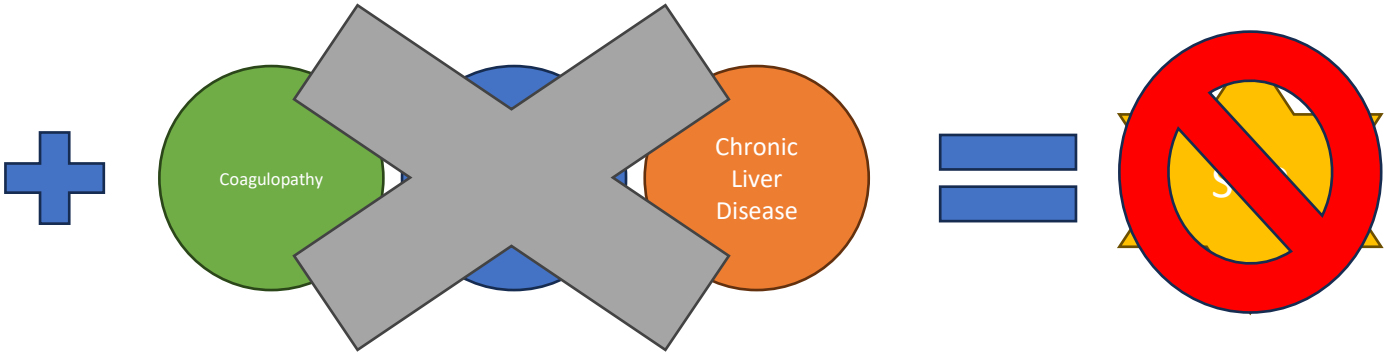


Credit: iStock and ASPEN, American Society for Parenteral and Enteral Nutrition





Credit: iStock and ASPEN, American Society for Parenteral and Enteral Nutrition



**Remark- Concurrent administration of SUP with EN may increase pneumonia risk.

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

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SUP in ICU Patients Receiving EN (2018)

Methods	• A meta-analysis of RCTs comparing pharmacologic SUP to either placebo or no prophylaxis • Enterally fed patients in the ICU
Results	• 7 studies (n=889 patients) included • No statistically significant difference in GI bleeding between groups • SUP had no effect on overall mortality, C. diff infection, length of stay in ICU, or duration of mechanical ventilation • **There was an increased risk of hospital-acquired pneumonia (RR 1.53; 95% CI, 1.04 to 2.27; *p* = 0.03)**
Conclusion	• The results suggested that in patients receiving enteral feeding, pharmacologic SUP is not beneficial, and combined interventions may even increase the risk of nosocomial pneumonia

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Huang HB, et al. Stress ulcer prophylaxis in intensive care unit patients receiving enteral nutrition: a systematic review and meta-analysis. *Crit Care*. 2018

Neurocritical Care

We suggest using SUP in **neurocritical care adults** to reduce clinically important stress-related UGIB compared with no SUP

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

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Risks and Benefits of SUP in adult Neurocritical Care Patients (2015)

Methods	• Meta analysis of RCTs in which researchers compared the effects of SUP (PPIs or H2RAs) with placebo or no prophylaxis **in neurocritical care patients** • Primary outcome: UGI bleeding • Secondary outcome: all-cause mortality and nosocomial pneumonia
Results	• 8 RCTs comprising 829 neurocritical care patients • **SUP was more effective than placebo or no prophylaxis at reducing UGI bleeding** (random effects: RR 0.31; 95 % CI 0.20–0.47; $P < 0.00001$; $I^2 = 45$ %) **and all-cause mortality** (fixed effects: RR 0.70; 95 % CI 0.50–0.98; $P = 0.04$; $I^2 = 0$ %) • There was no difference between SUP and placebo or no prophylaxis regarding nosocomial pneumonia (random effects: RR 1.14; 95 % CI 0.67–1.94; $P = 0.62$; $I^2 = 42$ %)
Conclusion	• In neurocritical care patients, SUP seems to be more effective than placebo or no prophylaxis in preventing UGI bleeding and reducing all-cause mortality while not increasing the risk of nosocomial pneumonia

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Liu B, et al. Risks and benefits of stress ulcer prophylaxis in adult neurocritical care patients: a systematic review and meta-analysis of randomized controlled trials. *Crit Care*. 2015

Assessment Question #2

An 80-year-old male a past medical history of hypertension and hyperlipidemia admitted with pneumonia. Upon admission he intubated and started on norepinephrine. Current labs Na 167, K 3.8, WBC 12, PLT 30,000, INR 1.3

How many risk factors does this patient have?

A. 0

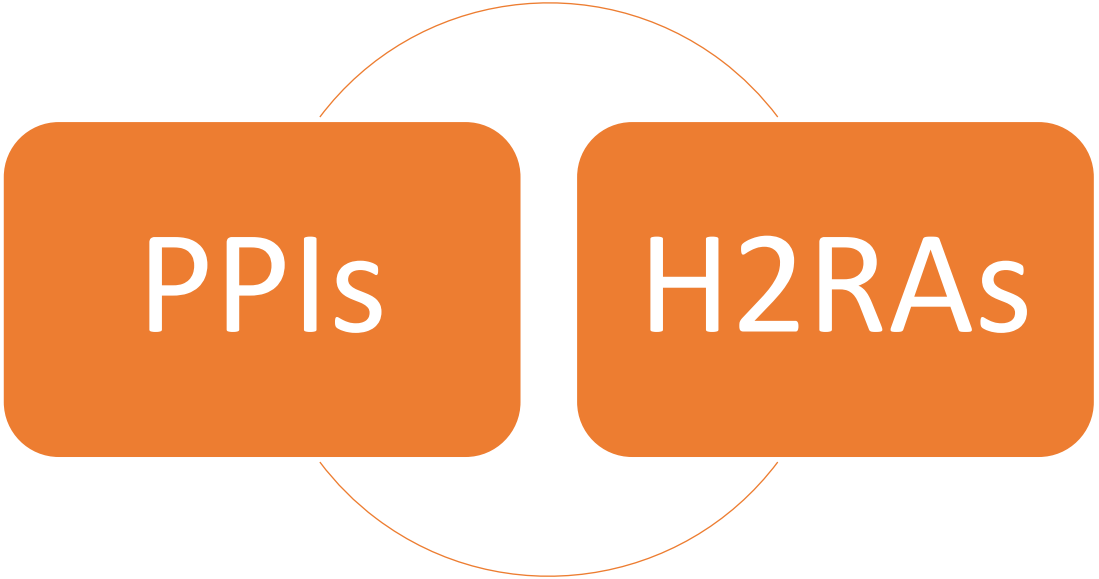
B. 1

C. 2

D. 3

Pharmacologic Agents

Agents for SUP



MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

PEPTIC 2020

Objective

- To compare in-hospital mortality rates using PPIs vs H2RAs for stress ulcer prophylaxis

Design

- Open-label, Cluster crossover RCT
- 50 ICUs in 5 countries
- August 2016 and January 2019
- Age ≥ 18 years old, invasive mechanical ventilation within 24 hours of ICU admission

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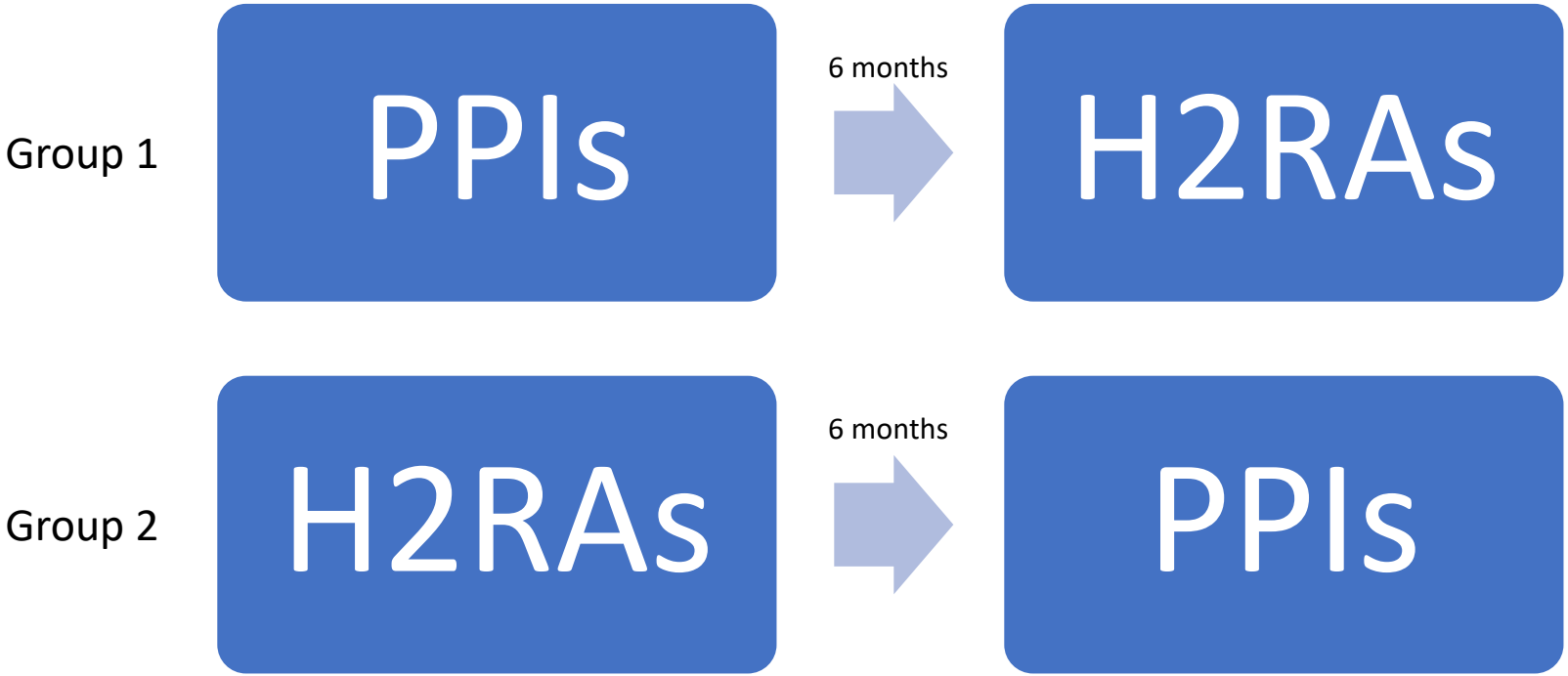
PEPTIC Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group, et al. Effect of Stress Ulcer Prophylaxis With Proton Pump Inhibitors vs Histamine-2 Receptor Blockers on In-Hospital Mortality Among ICU Patients Receiving Invasive Mechanical Ventilation: The PEPTIC Randomized Clinical Trial. *JAMA*. 2020

Methods



PEPTIC Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group, et al. 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. *JAMA*. 2020

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Outcomes

Primary Outcome:

- All-cause mortality within 90 days during hospitalization

Secondary Outcome:

- CIB
- Clostridioides difficile infection
- ICU and hospital LOS

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PEPTIC Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group, et al. 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. *JAMA*. 2020

Results

26,828 patients were analyzed

Primary Outcome

- 18.3 % in PPI group and 17.5% in H2RA group died at day 90 (**p = 0.54)**

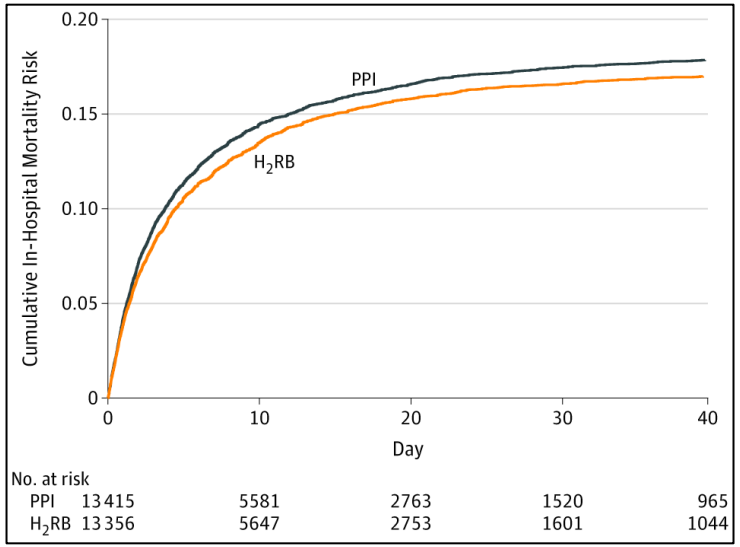

Figure 2 from : The PEPTIC Randomized Clinical Trial. *JAMA*. 2020

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PEPTIC Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group, et al. 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. *JAMA*. 2020

Results cont.

Secondary Outcomes:

Outcome	PPI N=13415	H2RA N=13356	RR (95% CI)	P value
CIB	172/13436 (1.3%)	239/13392 (1.8%)	0.73 (0.57 to 0.92)	0.009
C. Diff infection	40/13436 (0.30%)	57/13392 (0.43%)	0.74 (0.51 to 1.09)	0.13
ICU LOS	3.6 days (1.6 to 10.4)	3.3 days (1.5 to 10.0)	1.00 (0.97 to 1.03)	0.85
Hospital LOS	12.2 days (6.0 to 40)	12.0 days (6.0 to 39.3)	1.01 (0.98 to 1.03)	0.66

PEPTIC Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group, et al. 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. *JAMA*. 2020

Conclusions

Takeaways: Among ICU patients requiring mechanical ventilation, SUP with PPI vs H2RA did not show a difference in mortality rate

Limitations:

- Open label
- Asymmetrical nonadherence
- Lack of C.diff testing
- Variety in drug and routes used

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PEPTIC Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group, et al. 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. *JAMA*. 2020

REVISE 2024

Objective

- To compare in-hospital mortality rates using PPIs vs H2RAs for stress ulcer prophylaxis

Design

- International, multicenter, randomized, blinded
- 68 hospitals
- July 2019 - October 2023
- Age ≥ 18 yo, invasive mechanical ventilation in ICU

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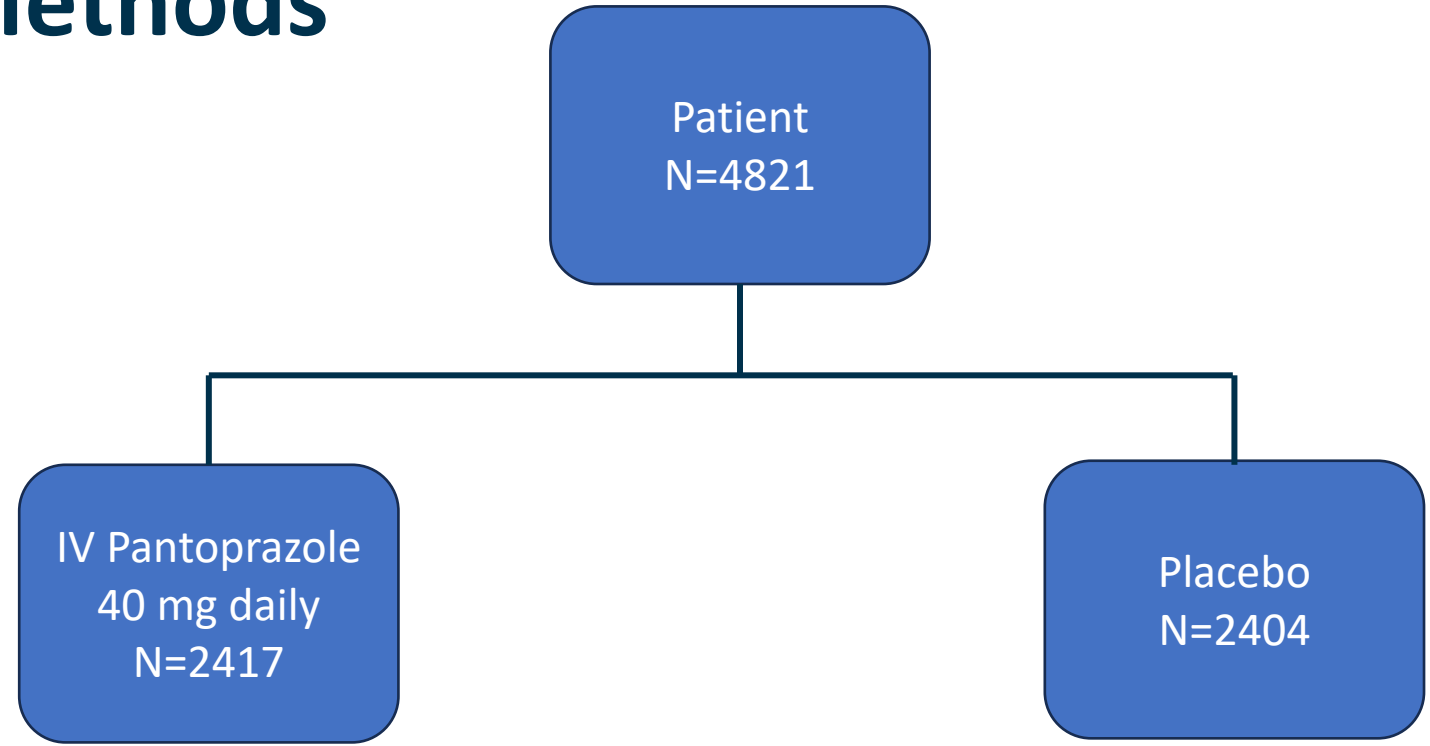
Cook D, et al. Stress Ulcer Prophylaxis during Invasive Mechanical Ventilation. *N Engl J Med*. 2024;391(1):9-20. doi:10.1056/NEJMoa2404245

Methods



Cook D, et al. Stress Ulcer Prophylaxis during Invasive Mechanical Ventilation. *N Engl J Med*. 2024;391(1):9-20. doi:10.1056/NEJMoa2404245

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Outcomes

Primary Outcome: CIB (hemodynamic compromise or therapeutic interventions)

Secondary Outcome:

- Ventilator associated pneumonia
- C. Diff infection
- Initiation of RRT
- Patient-important bleeding

Primary Safety Outcome: Death from any cause at 90 days

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Cook D, et al. Stress Ulcer Prophylaxis during Invasive Mechanical Ventilation. *N Engl J Med*. 2024;391(1):9-20. doi:10.1056/NEJMoa2404245

Results

4821 patients were randomized

Primary + Primary Safety Outcome:

Outcome	Pantoprazole N=2417	Placebo N=2404	Hazard Ratio (95% CI)	P value
CIB	25/2385 (1%)	84/2377 (3.5%)	0.30 (0.19 to 0.47)	<0.001
90 day-mortality	696/2390 (29.1%)	734/2379 (30.9%)	0.94 (0.85 to 1.04)	0.25

Cook D, et al. Stress Ulcer Prophylaxis during Invasive Mechanical Ventilation. *N Engl J Med*. 2024;391(1):9-20. doi:10.1056/NEJMoa2404245

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Results cont.

Secondary Outcomes:

Outcome	Pantoprazole N=2417	Placebo N=2404	Hazard Ratio (95% CI)	P value
VAP	556/2394 (23.2%)	567/2381 (23.8%)	1.00 (0.98 to 1.12)	0.93
C. Diff infection	28/2385 (1.2%)	16/2377 (0.7%)	1.78 (0.96 to 3.29)	0.50
New RRT	146/2385 (6.1%)	142/2380 (6.0%)	1.04 (0.83 to 1.31)	0.98
Patient Important UGIB	36/2385 (1.5%)	100/2377 (4.2%)	0.36 (0.25 to 0.53)	<0.001

Cook D, et al. Stress Ulcer Prophylaxis during Invasive Mechanical Ventilation. *N Engl J Med*. 2024;391(1):9-20. doi:10.1056/NEJMoa2404245

Conclusions

In mechanically ventilated patients, IV pantoprazole reduced the risk of clinically important upper gastrointestinal bleeding but did not affect mortality

Limitations:

- Only assessed ventilated patients

Cook D, et al. Stress Ulcer Prophylaxis during Invasive Mechanical Ventilation. *N Engl J Med*. 2024;391(1):9-20. doi:10.1056/NEJMoa2404245

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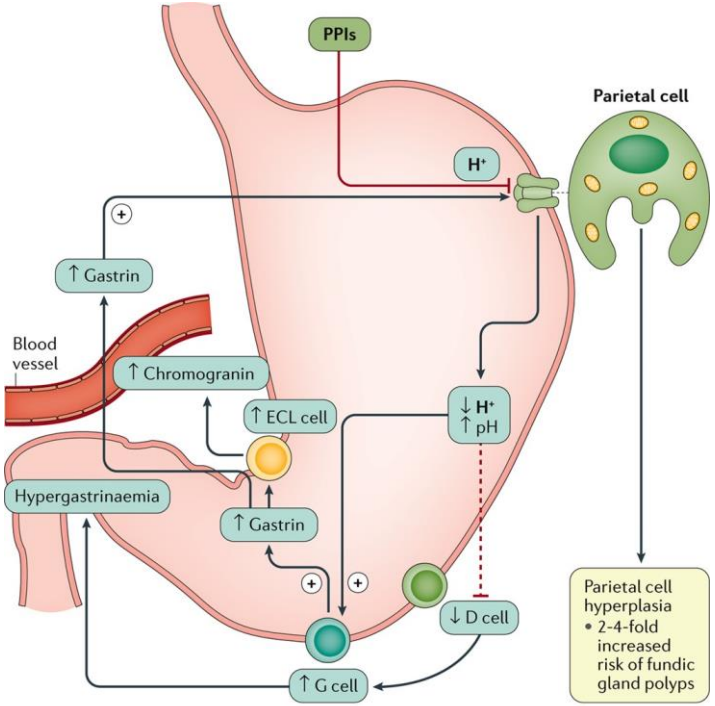
SCCM Panel Meta-Analysis (2024)

Objective	• Compared PPIs, H2RAs, and sucralfate for the outcomes of clinically important UGIB, overt UGIB, pneumonia, and mortality
Results	• Compared with H2RAs, PPIs were associated with reduced clinically important UGIB (RR, 0.53; 95% CI, 0.34–0.83), but increased mortality (RR, 1.05; 95% CI, 1–1.10) • Sucralfate was associated with less pneumonia than PPIs and H2RAs • Unable to assess incidence of C. diff

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

Comparison	Study	Design	Population	CIB	Notes
Sucralfate vs H2RA	Alquraini M, et al. *J Crit Care*.2017;40:21-30.	Meta-analysis 21 RCT	3121 critically ill patients	No difference in CIB (RR 1.19; 95% CI 0.79, 1.80; *P* = 0.42)	Lower risk of ICU acquired pneumonia with sucralfate
H2RA vs PPI	Alshamsi F, et al. Crit Care. 2016;20(1):120.	Meta-analysis 19 RCT	2117 ICU patients	CIB reduced with PPI (RR 0.39; 95% CI 0.21-0.71; p = 0.002)	No difference in mortality or VAP
H2RA vs PPI	PEPTIC Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group, et al. *JAMA*. 2020	RCT	26,828 patients requiring invasive mechanical ventilation within 24 hours of ICU admission	CIB occurred in 1.3% of PPI group and 1.8% of H2RA group (p = 0.009)	No difference in mortality or C.diff
PPI vs Placebo	REVISE Cook D, et al. N Engl J Med. 2024;391(1):9-20	RCT	4821 critically ill patients undergoing invasive ventilation	CIB reduced with PPI (HR 0.30; 95% CI 0.19 to 0.47; P<0.001)	No difference in mortality

Proton Pump Inhibitors



Malfertheiner P, Kandulski A, Venerito M. Proton-pump inhibitors: understanding the complications and risks. *Nat Rev Gastroenterol Hepatol*. 2017;14(12):697-710. doi:10.1038/nrgastro.2017.117

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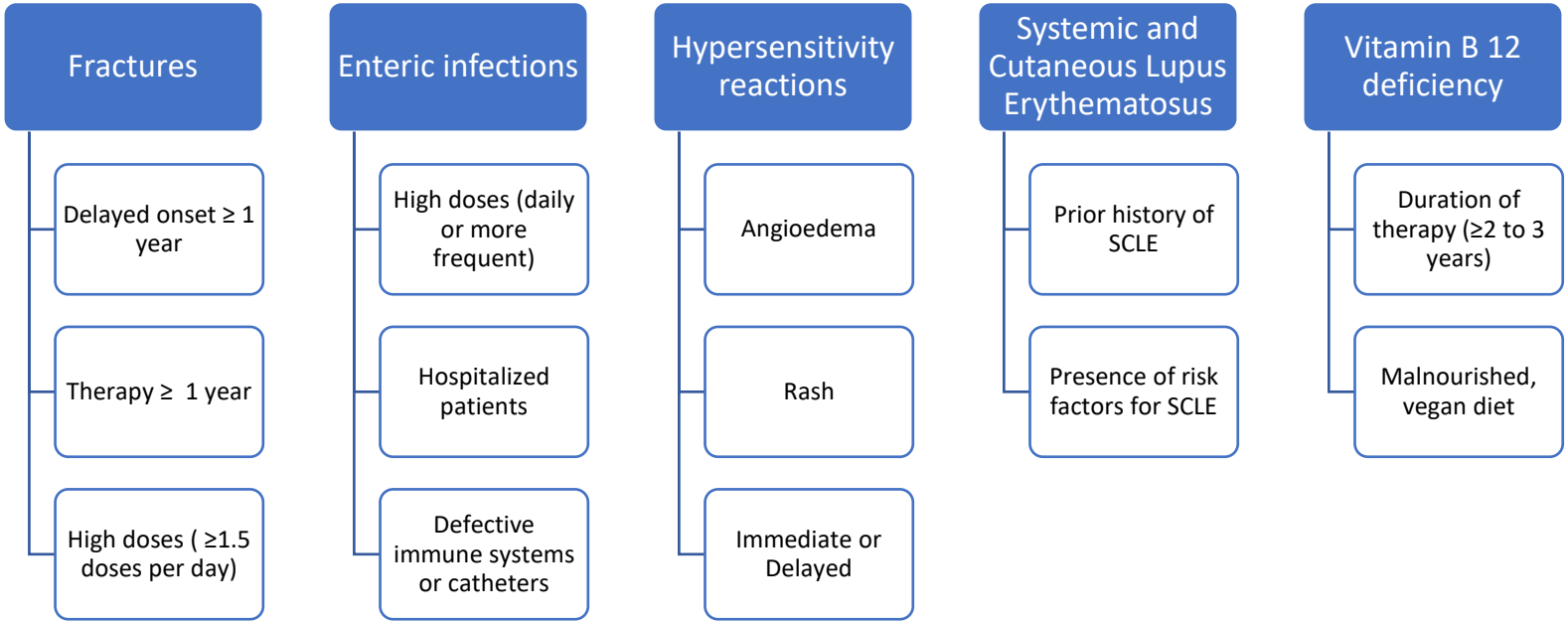
Recommended PPIs - SCCM 2024

- Pantoprazole 40 mg IV/PO/NG daily
- Esomeprazole 40 mg IV/PO daily
- Omeprazole 40 mg PO/NG daily
- Lansoprazole 30 mg PO daily

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

Adverse Effects



Lexicomp; Pantoprazole, Omeprazole

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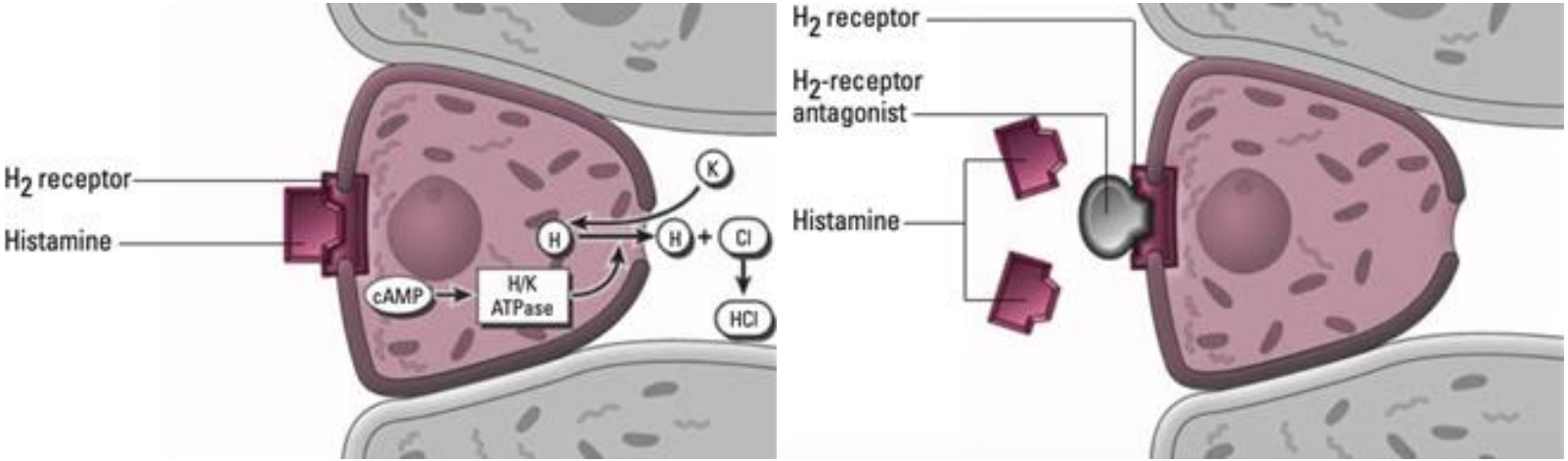
Histamine H_2 Receptor Antagonists



Myrna S. Histamine (H2) Receptor Antagonists: How Do They Work?. *Lippincott NursingCenter*. 2023;2017.

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Recommended H2RAs – SCCM 2024

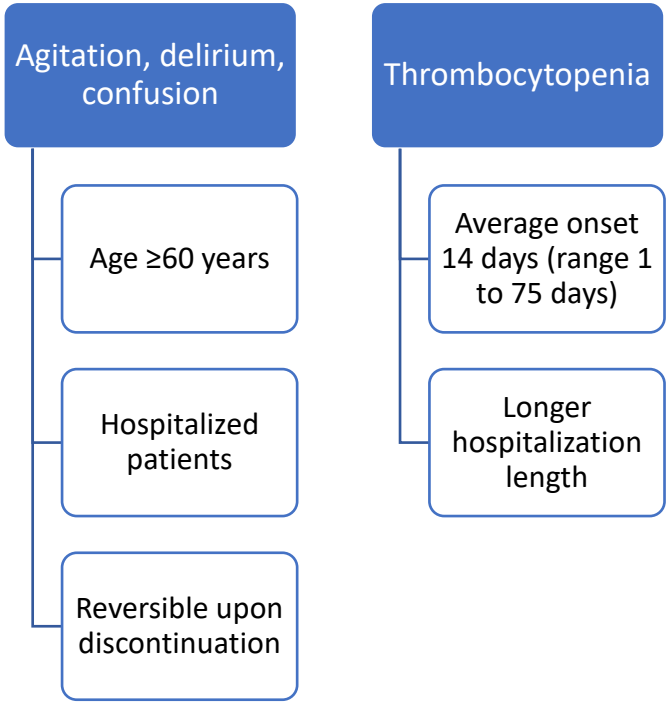
Famotidine 20 mg IV/PO/NG twice daily

Cimetidine 300 mg PO four times daily

Note: renal adjustments

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

Adverse Effects



Lexicomp; Famotidine, Cimetidine

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Good Practice Statements SCCM 2024

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Statement 1

Low Dose SUP

High Dose SUP

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Statement 2

SUP should be discontinued when the risk factor(s) is no longer present

Discontinuation of SUP before transferring out of the ICU is necessary to prevent inappropriate prescribing

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

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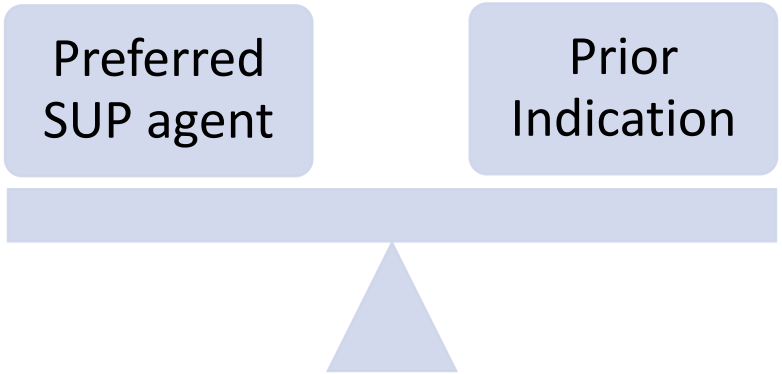
Statement 3

- Adults with no risk factors but are on a SUP agent before ICU admission, the indications for these medications should be reviewed and considerate discontinuing them

MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

Statement 4



MacLaren R, et al. Society of Critical Care Medicine and American Society of Health-System Pharmacists Guideline for the Prevention of Stress-Related Gastrointestinal Bleeding in Critically Ill Adults. *Crit Care Med*. 2024

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Assessment Question #3

A 62-year-old female (70kg) is admitted to the ICU with acute respiratory distress syndrome (ARDS) and is currently on mechanical ventilation (Day 3). She has developed Acute Kidney Injury (AKI) with a current CrCl of 15 mL/min. Labs: PLT 38,000/mm^3, INR 2.1. She is NPO.

Which of the following is the most appropriate SUP regimen considering her current renal status and risk factors?

A. Famotidine 20 mg IV BID
B. Famotidine 20 mg IV every 48 hours
C. Pantoprazole 40 mg IV daily
D. Sucralfate 1g via OG tube every 6 hours

Assessment Question #4

A 74-year-old male with a history of atrial fibrillation (on Dabigatran) and chronic COPD is being transferred from the ICU to the step-down unit. He was intubated for 5 days but is now extubated. He is no longer in shock. His labs have normalized (PLT 155,000/mm^3 INR 1.1). He is started on a soft food diet.

The surgical resident wants to continue Pantoprazole 40 mg PO daily because "the patient is on an oral anticoagulant and has a history of COPD exacerbations requiring steroids." What is the most evidence-based recommendation?

A. Continue Pantoprazole; the use of Dabigatran justifies SUP on the floor
B. Discontinue Pantoprazole; the patient no longer meets ICU-specific criteria for SUP
C. Switch to Famotidine 20 mg daily as a "middle ground" for floor prophylaxis
D. Continue Pantoprazole as patient may require steroids bursts for his COPD

Summary

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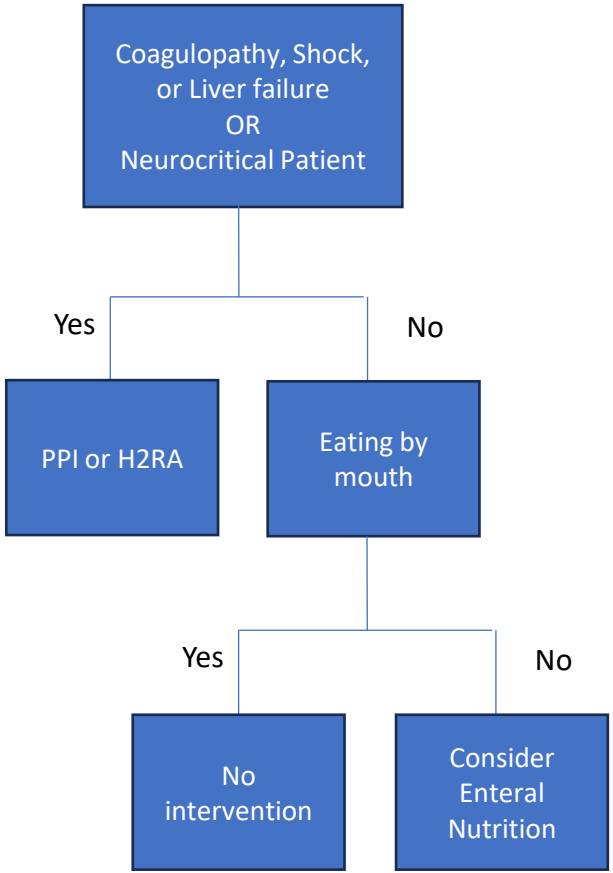
Review



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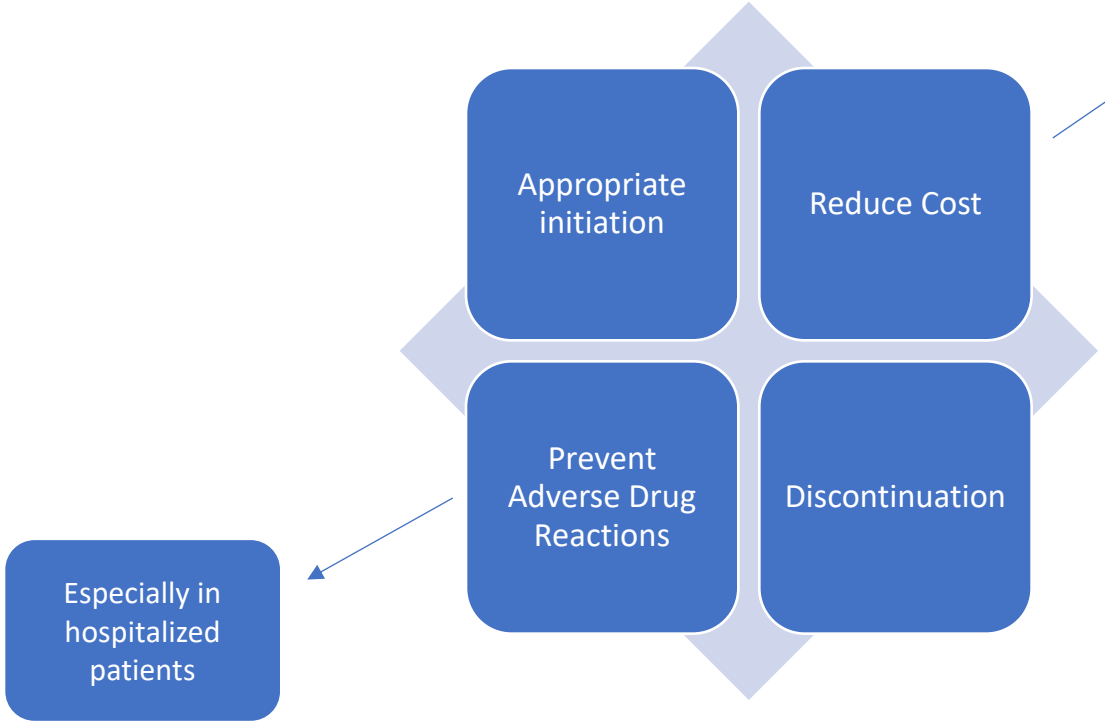
Pharmacists Role



Drug	Cost
Famotidine 20mg Injection	$0.48
Famotidine 20 mg tablet	$0.06
Pantoprazole 40 mg injection	$2.80
Pantoprazole 40 mg tablet	$0.12

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Conclusion

Previous practice has lacked updated guidance

New guidelines narrow indications based on recent data

Pharmacists can have a large role in the implementation within TOC

Future data should examine long term effects of SUP therapies

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Questions?

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