SEPSIS AND SEPTIC SHOCK

INTERNATIONAL GUIDLINES 2016

Sepsis is defined as organ dysfunction due to excessive reaction to infection

It is a consequence of sepsis

Needs vasoactive drug administration for maintainig a MAP equal or greater than 65 mmHg.

Lactate levels higher than 2 mmol/L despite correct fluid resuscitation

It is associated with metabolic or cardiovascular alteration.

CLINICAL CRITERIA FOR DIAGNOSIS OF SEPSIS

How to recognise organ dysfunction:

SOFA (sequential organ failure assessment): the best score used in the clinical practice to quantify the severity of organ dysfunction.

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score[a]

	Score				
System	0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Abbreviations: Fio_2, fraction of inspired oxygen; MAP, mean arterial pressure; Pao_2, partial pressure of oxygen.

[a] Adapted from Vincent et al.[27]

[b] Catecholamine doses are given as μg/kg/min for at least 1 hour.

[c] Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

Organ dysfunction is associated with a SOFA score > 2 (mortality 10%).

Pt with suspected infection in the ward can be identified by using the q SOFA:

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Box 4. qSOFA (Quick SOFA) Criteria

Respiratory rate ≥22/min

Altered mentation

Systolic blood pressure ≤100 mm Hg

What to do in pateints with septic shock

FLUIDS THERAPY

-Sepsis and septic shock: medical emergencies that need fluids ASAP!

-30 ml/kg of crystalloids in the first 3 hours

- Ri-evaluate frequently haemodinamics variables and, if needed, give more fluids!

- Administer albumin in case of elevated administartion of crystallods. (weak evidence)

FLUIDS THERAPY

- **Do not use HES in presence of septic shock.**
- **Do not use gelatins**

- **Use crystalloids**

HESs are colloids for which there are safety concerns in patients with sepsis. A meta-analysis of nine trials (3456 patients) comparing 6% HES 130/0.38–0.45 solutions to crystalloids or albumin in patients with sepsis showed no difference in all-cause mortality (RR 1.04; 95% CI 0.89–1.22) [250]. However, when low risk of bias trials were analyzed separately, HES use resulted in higher risk of death compared to other fluids (RR 1.11; 95% CI 1.01–1.22; high-quality evidence), which translates to 34 more deaths per 1000 patients. Furthermore, HES use led to a higher risk of RRT (RR 1.36; 95% CI 1.08–1.72; high-quality evidence) [250]. A subsequent network meta-analysis focused on acute resuscitation of patients with sepsis or septic shock and found that HES resulted in higher risk of death (10 RCTs; OR 1.13; CrI, 0.99–1.30; high-quality evidence) and need for RRT (7 RCTs; OR 1.39; CrI, 1.17–1.66; high-quality evidence) compared to crystalloids. When comparing albumin to HES, albumin resulted in lower risk of death (OR 0.73; CrI, 0.56–0.93; moderate-quality evidence) and a trend toward less need for RRT (OR 0.74; CrI, 0.53–1.04; low-quality evidence) [237]. Overall, the undesirable con-

Evaluate cardiac function.

Evaluate dynamic variables (stroke volume, pulse pressure, variation).

Try to reach a MAP of 65 mmHg, with vasoactive drug.

Try to normalise the level of lactate.

High versus Low Blood-Pressure Target in Patients with Septic Shock

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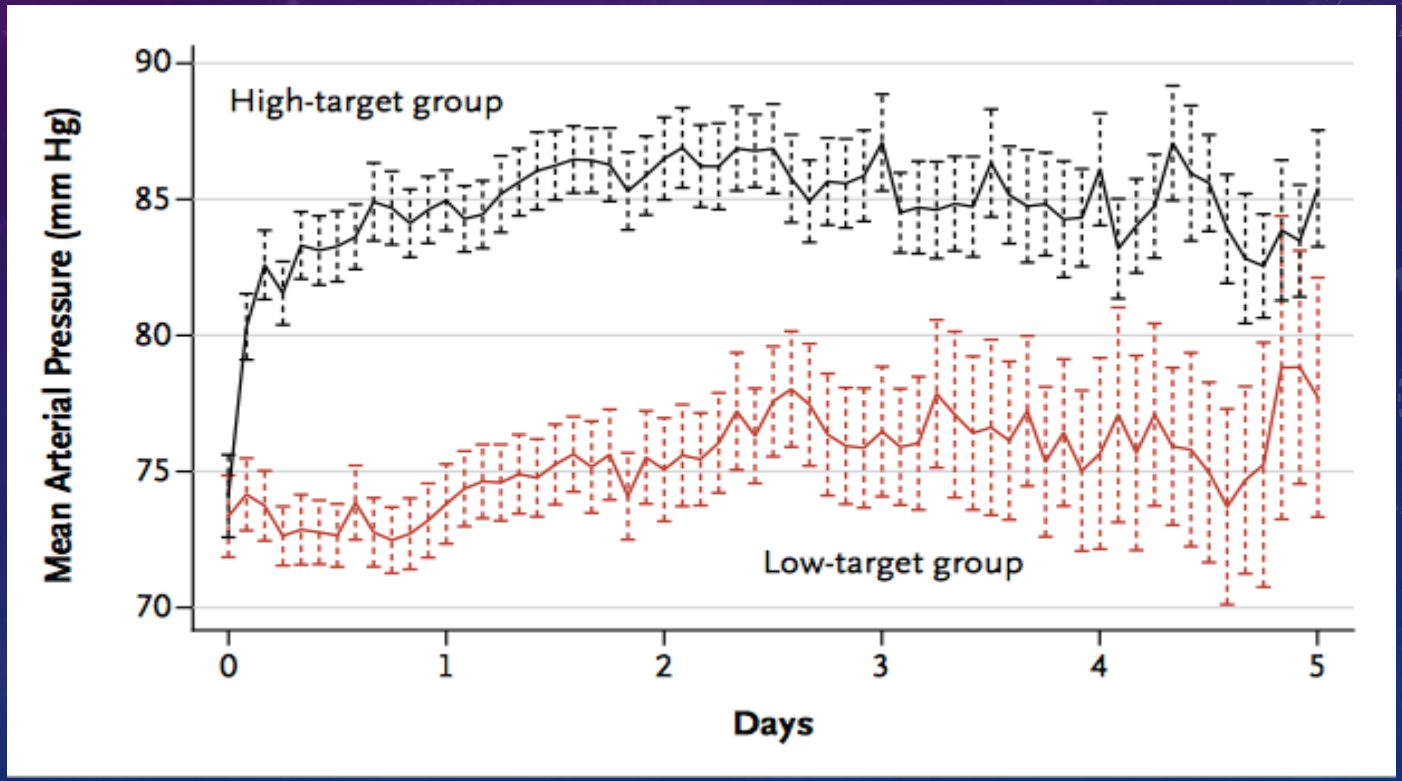

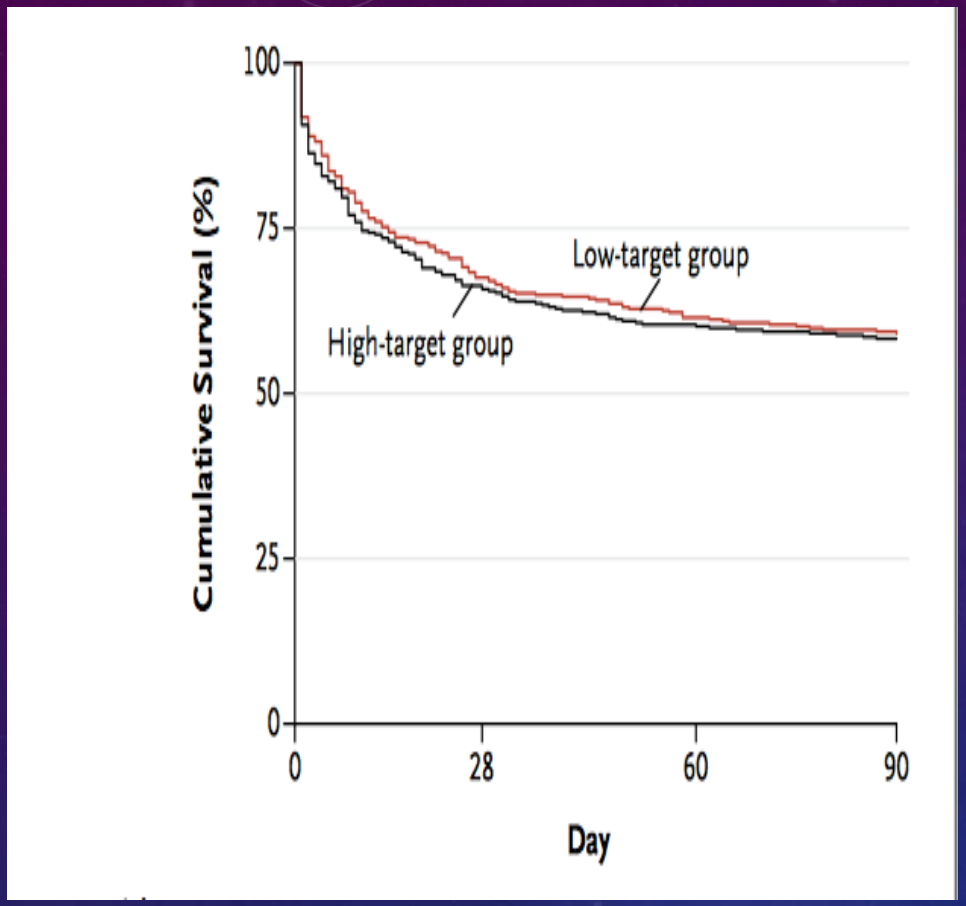

Group PAM 80-85 mmHg

vs

Group PAM 65-70 mmHg

No difference:

1. Survival at 28 day;
2. Organ dysfunction
3. Mortality at 90 days

DIAGNOSIS

- Hemocolture (2 sets, aerobic and anaerobic bacteria)) and routine colture before atb administration
- Start empirically atb therapy within 1 huors after the diagnosis. (if not, increased mortality and organ damage)
- If a cannuled vein is not avalible, use im route

Empiric therapy	Initial therapy started in the absence of definitive microbiologic pathogen identification. Empiric therapy may be mono-, combination, or broad-spectrum, and/or multidrug in nature.
Targeted/definitive therapy	Therapy targeted to a specific pathogen (usually after microbiologic identification). Targeted/definitive therapy may be mono- or combination, but is not intended to be broad-spectrum.
Broad-spectrum therapy	The use of one or more antimicrobial agents with the specific intent of broadening the range of potential pathogens covered, usually during empiric therapy (e.g., piperacillin/tazobactam, vancomycin, and anidulafungin; each is used to cover a different group of pathogens). Broad-spectrum therapy is typically empiric since the usual purpose is to ensure antimicrobial coverage with at least one drug when there is uncertainty about the possible pathogen. On occasion, broad-spectrum therapy may be continued into the targeted/definitive therapy phase if multiple pathogens are isolated.
Multidrug therapy	Therapy with multiple antimicrobials to deliver broad-spectrum therapy (i.e., to broaden coverage) for empiric therapy (i.e., where pathogen is unknown) or to potentially accelerate pathogen clearance (combination therapy) with respect to a specific pathogen(s) where the pathogen(s) is known or suspected (i.e., for both targeted or empiric therapy). This term therefore includes combination therapy.

Combination therapy	The use of multiple antibiotics (usually of different mechanistic classes) with the specific intent of covering the known or suspected pathogen(s) with more than one antibiotic (e.g., piperacillin/tazobactam and an aminoglycoside or fluoroquinolone for gram-negative pathogens) to accelerate pathogen clearance rather than to broaden antimicrobial coverage. Other proposed applications of combination therapy include inhibition of bacterial toxin production (e.g., clindamycin with β-lactams for streptococcal toxic shock) or potential immune modulatory effects (macrolides with a β-lactam for pneumococcal pneumonia).

Rhodes et al. – Intensive Car Med, 2017

VASOPRESSORS

- Norephinefrin is the first choice vasoactive drug
- It can be associated with adrenaline or vasopressine to reach the target MAP or to reduce the dosage of norephinefrin

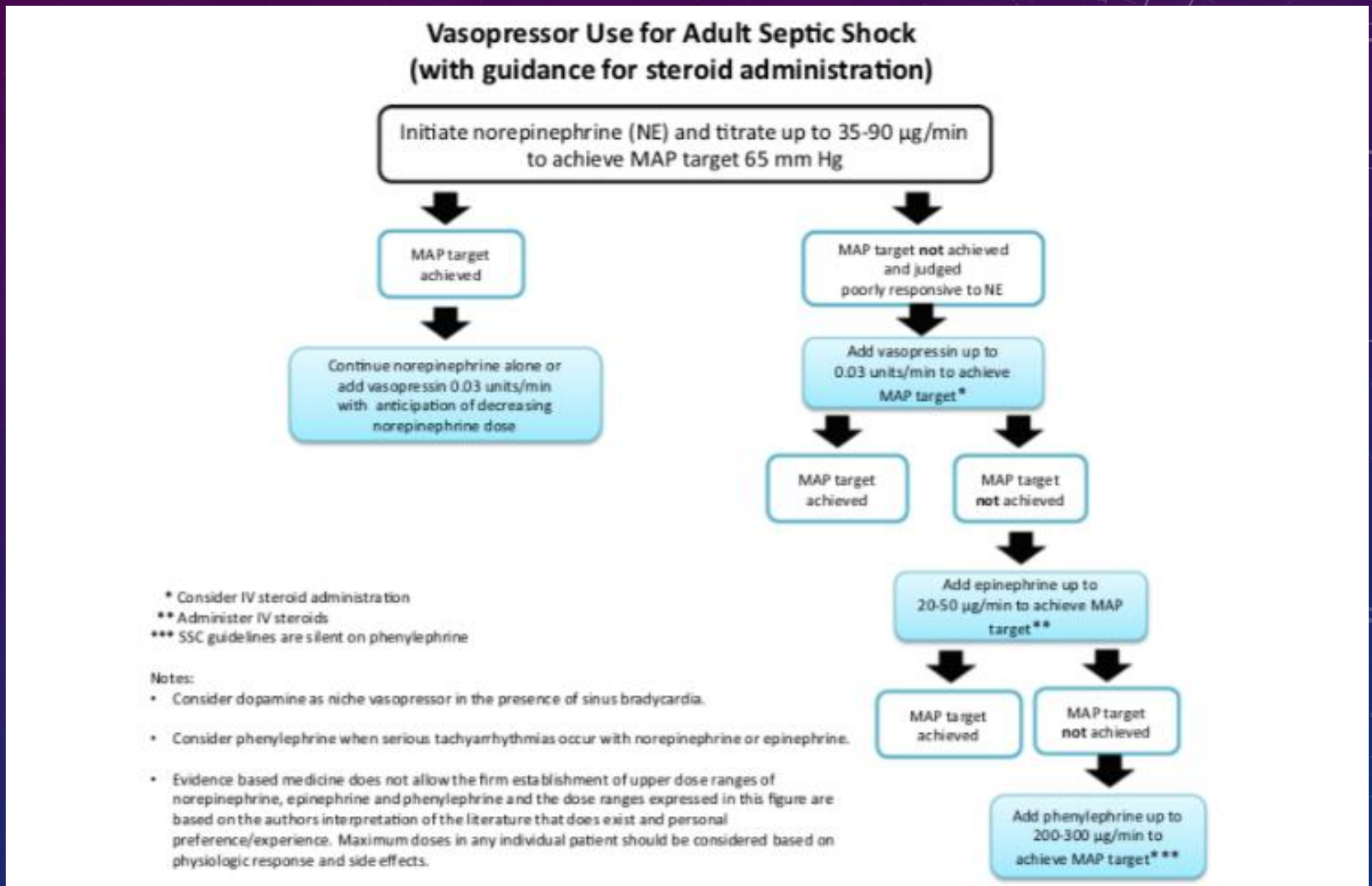

Fig. 3 This figure demonstrates how the guideline recommendations on vasopressor and steroid use can be molded into a flow diagram approach to the management of septic shock

BLOOD

- Tranfusion is needed for Hb<7 g/dl (absence of miocardial infartion…)
- No eritropietin in case of acute anemia
- No fresch frozen plasma in absence of hemorragia.

IMMUNOGLOBULINS

- **We suggest against the use of IV immunoglobulins**
- **in patients with sepsis or septic shock (weak**
- **recommendation, low quality of evidence).**

- - IVIgG
- Cochrane meta-analysis:
- - IVIgGM

- - Placebo

BLOOD-PURIFICATION TECHNIQUES

- **We make no recommendation regarding the use**
- **of blood purification techniques.**

- **High volume Hemofiltration**

- **Hemoadsorption**

- **Plasma exchange**

- **Plasmafiltration**

MECHANICAL VENTILATION

‘’We recommend using a target tidal volume of 6 mL/kg predicted body weight (PBW) compared with 12 mL/kg in adult patients with sepsis induced ARDS (strong recommendation, high quality of evidence).’’

‘’We recommend using an upper limit goal for plateau pressures of 30 cmH2O over higher plateau pressures in adult patients with sepsis-induced severe ARDS (strong recommendation, moderate quality of evidence)’’

MECHANICAL VENTILATION

ARDS

- MILD : P/F < 300
- MODERATE: P/F < 200
- SEVERE : P/F < 100

Mortality decreases in patiens with a pressure and volume limited strategy

RENAL REPLACEMENT THERAPY.

- **We suggest that either continuous RRT (CRRT)**
- **or intermittent RRT be used in patients with sepsis**
- **and acute kidney injury (weak recommendation,**
- **moderate quality of evidence).**

- Absence of significant differences in hospital mortality between patients who receive CRRT and intermittent RRT.

- Kellum JA, Angus DC, Johnson JP et al (2002) Continuous versus intermittent renal replacement therapy: a meta-analysis. Intensive Care Med 28(1):29–37
- Tonelli M, Manns B, Feller-Kopman D (2002) Acute renal failure in the intensive care unit: a systematic review of the impact of dialytic modality on mortality and renal recovery. Am J Kidney Dis 40(5):875–885

RENAL REPLACEMENT THERAPY

- **We suggest using CRRT to facilitate management**
- **of fluid balance in hemodynamically unstable**
- **septic patients (weak recommendation, very low**
- **quality of evidence).**

- **Better hemodynamic tolerance (MAP/systolic) with no improvement in regional perfusion and no survival benefit.**

- John S, Griesbach D, Baumgartel M, Weihprecht H, Schmieder RE, Geiger H (2001) Effects of continuous haemofiltration vs intermittent haemodialysis on systemic haemodynamics and splanchnic regional perfusion in septic shock patients: a prospective, randomized clinical trial. Nephrol Dial Transplant 16(2):320–327.

GLUCOSE CONTROL

- **We recommend a protocolized approach to blood glucose management in ICU patients with sepsis, commencing insulin dosing when two consecutive blood glucose levels are >180 mg/dL. This approach should target an upper blood glucose level ≤180 mg/dL rather than an upper target blood glucose level ≤110 mg/dL (strong recommendation, high quality of evidence).**

- **We recommend that blood glucose values be monitored every 1–2 h until glucose values and insulin infusion rates are stable, then every 4 h thereafter in patients receiving insulin infusions (BPS)**

NUTRITION

- **We recommend against the administration of early parenteral nutrition alone or parenteral nutrition in combination with enteral feedings**
- **(but rather initiate early enteral nutrition) in critically ill patients with sepsis or septic shock who can be fed enterally (strong recommendation, moderate quality of evidence).**

- This may represent an advantage over enteral nutrition, especially when patients may be underfed due to GI intolerance, which may be pertinent over the first days of care in the ICU. However, parenteral delivery is more invasive and has been associated with complications, including an increased risk of infections

NUTRITION

- **We recommend against the use of glutamine to**
- **treat sepsis and septic shock (strong recommendation,**
- **moderate quality of evidence)**

- Rationale: exogenous supplementation can improve gur mucosal athrophy and permeability,possibly leading to reduced bacterial translocation

- Enhanced immune cell function, decreased proinflammatory cytokine production, and higher levels of glutathione and antioxidative capacity.

- Bertolini G, Iapichino G, Radrizzani D et al (2003) Early enteral immunonutrition in patients with severe sepsis: results of an interim analysis of a randomized multicentre clinical trial. Intensive Care Med 29(5):834–840.

BICARBONATE THERAPY

- **We suggest against the use of sodium bicarbonate**
- **therapy to improve hemodynamics or to**
- **reduce vasopressor requirements in patients**
- **with hypoperfusion-induced lactic acidemia with**
- **pH ≥ 7.15 (weak recommendation, moderate**
- **quality of evidence).**

- **Limit TV in ARDS/hypercapnia**
- **Sodium and fluid overload**
- **Decrease of serum calcium**

VENOUS THROMBOEMBOLISM PROPHILAXIS

- **We recommend pharmacologic prophylaxis**
- **[unfractionated heparin (UFH) or low-molecular-**
- **weight heparin (LMWH)] against venous**
- **thromboembolism (VTE) in the absence of contraindications**
- **to the use of these agents (strong**
- **recommendation, moderate quality of evidence**

VENOUS THROMBOEMBOLISM PROPHILAXIS

- **We recommend LMWH rather than UFH for**
- **VTE prophylaxis in the absence of contraindications**
- **to the use of LMWH (strong recommendation,**
- **moderate quality of evidence)**

- **We suggest combination pharmacologic VTE**
- **prophylaxis and mechanical prophylaxis, whenever**
- **possible (weak recommendation, low quality**
- **of evidence)**

STRESS ULCER PROPHILAXIS

- **We recommend that stress ulcer prophylaxis be**
- **given to patients with sepsis or septic shock who**
- **have risk factors for gastrointestinal (GI) bleeding**
- **(strong recommendation, low quality of evidence).**

- **We suggest using either proton pump inhibitors**
- **(PPIs) or histamine-2 receptor antagonists**
- **(H2RAs) when stress ulcer prophylaxis is indicated**
- **(weak recommendation, low quality of evidence**