

SUPPLEMENTAL DIGITAL CONTENT 1

PICO QUESTIONS

<i>In patients with sepsis or septic shock, should we use crystalloid with supplemental albumin for initial resuscitation versus crystalloids alone?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Crystalloids and supplemental Albumin	Crystalloids alone	Mortality Renal replacement therapy
<i>In patients with sepsis or septic shock, should we be using HES versus crystalloids for acute resuscitation?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	HES	Crystalloids	Mortality Renal replacement therapy
<i>In patients with severe sepsis or septic shock, should we be using gelatin versus crystalloid for acute resuscitation?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Gelatins	Crystalloids	Mortality Renal replacement therapy
<i>In patients with sepsis or septic shock, should we use using balanced crystalloid solutions versus normal saline?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Balanced crystalloid Solutions	Crystalloids	Mortality

			Renal Replacement Therapy
<i>In patients with sepsis or septic shock, should we recommend using repeated fluid challenge based on hemodynamic variables?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock, that are suspected to be hypovolemic	Repeated fluid challenge as long guided by hemodynamic improvement in dynamic or static variables	Not continue fluid challenges or use alternative criteria	Mortality
<i>In patients with sepsis or septic shock, should we use early goal directed therapy protocol for resuscitation?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	EGDT protocol	Other protocols or physician guided therapy	Mortality
<i>In patients with sepsis or septic shock with elevated serum lactate, should we incorporate resuscitation goals aiming to normalize lactate levels?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock and elevated lactate level	Resuscitation targeting normalization of lactate levels	Resuscitation targeting other goals Not including lactate	Mortality
<i>In patients with septic shock requiring vasopressors, should we target mean arterial pressure (MAP) of 65 mmHg vs. higher MAP?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with septic shock requiring vasopressors	MAP of 65 mmHg	MAP above 65 mmHg	Mortality

<i>In patients with septic shock requiring vasopressors, should we use norepinephrine versus other agents?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with septic shock requiring vasopressors	Norepinephrine	Other vasopressors	Mortality
<i>In patients with septic shock not responding to single vasopressors, should we add epinephrine?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with septic shock not responding to single vasopressor	Addition of epinephrine	Other vasopressors	Mortality Arrhythmia
<i>In patients with septic shock requiring vasopressors, should we use norepinephrine alone versus combination with vasopressin?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with septic shock requiring vasopressin	Norepinephrine alone	Norepinephrine and Vasopressin	Mortality Renal replacement therapy Arrhythmia Limb ischemia
<i>In patients with septic shock requiring vasopressors, should we use of vasopressin versus other agents?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with septic shock requiring vasopressors	Vasopressin	Other agents	Mortality Renal replacement therapy Arrhythmia Limb ischemia
<i>In patients with septic shock requiring vasopressors, should we use dopamine versus other agents?</i>			

Population	Intervention	Comparator	Outcome(s)
Adult patients with septic shock requiring vasopressors	Dopamine	Other agents	Mortality Arrhythmia
<i>In patients with septic shock and persistent hypoperfusion, should we use alternative inotropic agents to increase cardiac output?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with septic shock with evidence of persistent hypoperfusion and cardiac dysfunction	levosimendan	Dobutamine	Mortality
<i>In patients with sepsis or septic shock, should we use dynamic parameters (versus static parameters) to predict fluid responsiveness?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Dynamic parameters	Static parameters	Improvement in hemodynamics
<i>Should hospitals use formal resourced performance improvement program for sepsis including sepsis screening for acutely ill, high risk patients?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult acutely ill patients with sepsis	Hospital-based performance programs	No program	Mortality Costs
<i>In patients with sepsis, should we use broad empiric antimicrobial coverage?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis	Antimicrobials with activity against all likely pathogens	Narrow coverage	Mortality

	(broad empiric coverage)		
<i>In patients with septic shock, should we administer empirically appropriate antimicrobials (within one hour of recognition)?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with septic shock	Administer empirically appropriate within 1 hour	Administration after 1 hour of recognition	Mortality
<i>In patients with sepsis, should we administer empirically appropriate antimicrobials (within one hour of recognition)?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis	Administer empirically appropriate antimicrobials within 1 hour	Administration after 1 hour of recognition	Mortality
<i>In critically ill septic patients, should we implement pharmacokinetic dosing optimization for each antimicrobial?</i>			
Population	Intervention	Comparator	Outcome(s)
Critically ill adult septic patients	Pharmacokinetic dosing optimization	Standard dosing	Mortality Clinical cure Microbiologic cure
<i>In patients with sepsis and neutropenia, should we use empiric combination antimicrobial therapy versus mono-therapy?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis and neutropenia	Combination empiric antimicrobial therapy	Single empiric antimicrobial therapy	Mortality
<i>In patients with sepsis at high risk for multi-drug resistant pathogens, should we use empiric combination antibiotic therapy (versus mono-therapy) until sensitivities are determined?</i>			
Population	Intervention	Comparator	Outcome(s)

Adult patients with sepsis caused by difficult-to-treat, multidrug-resistant pathogens, such as <i>Acinetobacter</i> and <i>Pseudomonas</i> spp.	Combination antibiotic therapy	monotherapy	Mortality
<i>In patients with septic shock, should we use empiric double-coverage antibiotic agents until hemodynamic stabilization and pathogen identification?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with septic shock	Combination empiric antibiotic therapy with a beta-lactam and an aminoglycoside or fluoroquinolone	Empiric monotherapy	Mortality
<i>In patients with sepsis who are receiving antimicrobials, should we assess for de-escalation of therapy daily?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis who are on antimicrobials	Assess antimicrobials daily for de-escalation	Continue antimicrobial course without daily assessment	Mortality Drug resistance Adverse events
<i>In patients with uncomplicated infections causing sepsis or septic shock, should we recommend a duration of therapy of 7-10 days versus longer course?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Antimicrobial therapy for 7-10 days	Therapy for >10 days	Mortality
<i>In patients with sepsis or septic shock who are receiving empiric combination of antimicrobials should we assess for de-escalation of therapy daily?</i>			
Population	Intervention	Comparator	Outcome(s)

Adult patients with sepsis or septic shock who are on empiric combination of antimicrobials (excluding patients with endocarditis)	De-escalation in 3 to 5 days to the most appropriate single antimicrobial agent as soon as the susceptibility profile is known and/or clinical stability is achieved.	Continue antimicrobial course without daily assessment	Mortality Drug resistance Adverse events
<i>In patients with sepsis, should we use procalcitonin levels to support de-escalation of antimicrobial therapy?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with a diagnosis of sepsis	Use procalcitonin levels or similar biomarkers to assist in empiric antimicrobial discontinuation	Not use biomarkers to assist in empiric antimicrobial discontinuation	Mortality Drug resistance Adverse events
<i>In patients with sepsis or septic shock, should we attempt early (within 12 hours) source control?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock, and remediable source of infection is identified	Source control intervention within first 12 hours	Intervention beyond 12 hours	Mortality
<i>In patients with severe inflammatory state of non-infectious origin should we use systemic prophylactic antimicrobials?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult critically ill patients with severe inflammatory state of non-infectious cause	Prophylactic antimicrobials	No prophylaxis	Mortality
<i>In patients with septic shock, should we use intravenous corticosteroids (versus not)?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with septic shock	Intravenous corticosteroids	Placebo or no intervention	Mortality

<i>In patients with sepsis, should we use plasma filtration therapy?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis	Blood purification	No Blood purification	Mortality Vasopressor use Organ dysfunction
<i>In patients with sepsis, should we use a hemoperfusion therapy?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis	plasma filtration therapy	No plasma filtration therapy	Mortality Vasopressor use Organ dysfunction
<i>In patients with sepsis, should we use a restrictive transfusion strategy versus liberal transfusion?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis	Restrictive blood transfusion threshold (< 7-8 g/dL hemoglobin)	Liberal blood transfusion threshold (9-10 g/dL)	Mortality Amount of blood transfused Myocardial ischemia
<i>In patients with sepsis and anemia, should we use erythropoietin to treat anemia?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis and anemia	erythropoietin	No erythropoietin	Mortality VTE
<i>In non-bleeding patients with sepsis and coagulation abnormalities, should we use prophylactic FFP?</i>			

Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis and laboratory coagulation abnormalities (prolonged PT, PTT), non-bleeding	Fresh frozen plasma	No FFP	Mortality Major bleeding
<i>In non-bleeding patients with sepsis and thrombocytopenia, should we use prophylactic platelet transfusion based on specific platelet levels?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis and thrombocytopenia, non-bleeding	Platelet transfusion for specific threshold (platelet counts \leq 10,000/mm ³ , \leq 20,000/mm ³ if bleeding risk, or \leq 50,000/mm ³ active bleeding, surgery or invasive procedures)	Different platelet transfusion threshold	Mortality Major bleeding
<i>In adult patients with sepsis or septic shock, should we use intravenous immunoglobulins (versus not)?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Intravenous immunoglobulins	Placebo or no intervention	Mortality
<i>In adult patients with sepsis or septic shock, should we antithrombin (versus not)?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Antithrombin	Placebo or no intervention	Mortality

			Major bleeding
<i>Should we use stress ulcer prophylaxis in critically ill septic patients?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock and risk factors for stress ulcer	PPIs or H2RA	Placebo or No prophylaxis	Clinically important bleeding Pneumonia C. difficile infection Mortality ICU length of stay
<i>Should we use PPIs (versus H2RA) for stress ulcer prophylaxis in critically ill septic patients?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock and risk factors for stress ulcer	PPIs	H2RA	Clinically important bleeding Pneumonia C. difficile infection Mortality ICU length of stay
<i>Should we use pharmacologic VTE prophylaxis (UFH or LMWH) in critically ill patients with sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult, critically ill patients with sepsis or septic shock	Pharmacologic prophylaxis (UFH or LMWH)	Placebo or No Prophylaxis	Mortality DVT PE Major Bleeding
<i>Should we use LMWH (versus UFH) for VTE prophylaxis in critically ill patients with sepsis or septic shock?</i>			

Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	prophylactic LMWH	prophylactic UFH	Mortality DVT PE Major Bleeding
<i>Should we use mechanical VTE prophylaxis in critically ill patients with sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Mechanical prophylaxis (intermittent compression devices)	No prophylaxis	Mortality DVT PE
<i>Should we use a combination of pharmacologic and mechanical prophylaxis vs. either alone in critically ill patients with sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult, critically ill patients with severe sepsis or septic shock	Pharmacologic prophylaxis (UFH or LMWH) and mechanical prophylaxis	Pharmacologic or mechanical prophylaxis alone	Mortality DVT PE Major Bleeding
<i>Should we use early TPN versus early full enteral feeding in critically ill patients with sepsis or septic shock who can be fed enterally?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock without contraindications for enteral feeding	Early TPN +/- trophic enteral feeding (started ≤48 hrs) in the first 7 days	Early full enteral feeding alone (started ≤48 hrs and to goal ≤72 hrs)	Mortality Infections ICU length of stay
<i>Should we use early TPN versus no or early trophic enteral feeding in critically ill patients with sepsis or septic shock who have contraindications for early full enteral feeding?</i>			

Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock with contraindications for early full enteral feeding	Early TPN +/- trophic enteral feeding in the first 7 days	No or early trophic enteral feeding alone, or enteral feeding according to usual/standard care	Mortality Infections ICU length of stay
<i>Should we use early full enteral feeding versus no initial enteral feeding (except IV glucose/dextrose) in critically ill patients with sepsis or septic shock without contraindications to enteral feeding?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock without contraindications for enteral feeding	Early full enteral feeding	Fasting or intravenous glucose/dextrose with delayed enteral feeding started >48 hours	Mortality Infections ICU length of stay
<i>Should we use early full enteral feeding versus early trophic enteral feeding in patients with sepsis or septic shock without contraindications to enteral feeding?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock without contraindications for enteral feeding	Early trophic feeding (trophic $\leq 70\%$ of standard goal)	Early full enteral feeding	Mortality Infections ICU length of stay
<i>Should we use early trophic enteral feeding versus no early enteral feeding (except IV glucose/dextrose) in patients with sepsis or septic shock without contraindications to enteral feeding?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock without contraindications for enteral feeding	Early trophic feeding	Fasting or IV glucose/dextrose with delayed enteral feeding started >48 hrs	Mortality Infections ICU length of stay
<i>Should we use omega-3 supplementation in patients with sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)

Adult patients with sepsis or septic shock	Enteral or parenteral feeding with omega-3 as an immunomodulating supplement	Enteral or parenteral feeding alone	Mortality Infections ICU length of stay
<i>Should we measure gastric residuals when enterally feeding critically ill patients with sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock receiving enteral feeding	Measuring gastric residuals and withholding feeding when residuals exceed a given threshold	No measurement of gastric residuals	Mortality Aspiration pneumonia ICU length of stay
<i>Should we use enteral feeding via a gastric tube versus a post-pyloric tube in patients with sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock receiving enteral feeding	Enteral feeding with a gastric tube	Enteral feeding with a post pyloric feeding tube	Mortality Aspiration or aspiration pneumonia ICU length of stay
<i>Should we use of prokinetic agents for enterally fed patients with sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock who can be enterally fed	Use of pro-kinetic agents (metoclopramide, domperidone, erythromycin)	Placebo; or intervention	Mortality Aspiration or aspiration pneumonia ICU length of stay Successful post pyloric tube placement
<i>Should we use selenium therapy in patients with severe sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)

Adult patients with sepsis or septic shock	Selenium in therapeutic doses	Placebo or No selenium	Mortality Pneumonia ICU length of stay DMV
<i>Should we recommend glutamine therapy in critically ill patients with severe sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Glutamine in therapeutic doses	Placebo or No glutamine	Mortality ICU LoS DMV
<i>Should we use arginine therapy in patients with sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Arginine in therapeutic doses	Placebo or No arginine	Mortality ICU LoS DMV
<i>Should we use carnitine therapy patients with sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Carnitine in therapeutic doses	Placebo or No carnitine	Mortality ICU LoS DMV
<i>Should we use intensive insulin therapy in patients with sepsis or septic shock?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Intensive insulin therapy	Conventional insulin therapy	Mortality Hypoglycemia

<i>Should we use arterial blood glucose level (versus to point of care resting) in critically ill patients with severe sepsis or septic shock on insulin infusion?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock	Arterial glucose level measurement	Point of care testing	Accuracy of glucose level
<i>In patients with sepsis, should we recommend discussion of goals of cares and prognosis with family?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult, critically ill patients with sepsis or septic shock	Goals of care and prognosis discussed with patients and families	No discussion	Communication and understanding Family satisfaction Stress Anxiety Depression Facilitated decision-making ICU LOS for moribund patients
<i>In patients with sepsis, should we recommend incorporating palliative and end-of-life care?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult, critically ill patients with sepsis or septic shock	Palliative and end-of-life planning incorporated into treatment in ICU	Limited use of palliative or end-of-life care in ICU	Percent of patients receiving a palliative care consult

			<p>Percent of patients receiving end-of-life care in the ICU</p> <p>Withdrawal of life support/DNR rates</p> <p>Family hospital anxiety and depression score</p> <p>Family satisfaction</p> <p>Family member quality of dying score</p> <p>Nurse quality of dying score</p> <p>Health care provider satisfaction score</p> <p>ICU LOS for moribund patients</p>
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Should we recommend addressing goals of care early (within 72 hours) during ICU stay?

Population	Intervention	Comparator	Outcome(s)
Adult, critically ill patients with sepsis or septic shock	Goals of care addressed within 72 h of admission, as early as feasible	Address goals of care after 72 h	<p>Family care conference held within 72 h of ICU admission</p> <p>Communication and understanding</p> <p>Family satisfaction</p> <p>Facilitated decision-making</p> <p>Staff moral distress, staff burnout</p>

			ICU LOS
<i>In patients with sepsis induced ARDS, should we use low tidal volume ventilation?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis induced ARDS	Target Vt of 6 mL/kg PBW	Target Vt of 12 mL/kg PBW	Mortality Duration of mechanical ventilation
<i>In patients with sepsis induced ARDS who are mechanically ventilated, should we use plateau pressures less than 30 cm H2O?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis induced ARDS	Upper limit of plateau pressure: 30 cmH2O	Plateau pressure > 30 cmH2O	Mortality Barotrauma
<i>In patients with sepsis induced ARDS who are mechanically ventilated, should we use high PEEP strategy?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis-induced moderate to severe ARDS	“Higher” PEEP	“Lower” PEEP	Mortality
<i>In patients with sepsis induced ARDS, should we use recruitment maneuvers?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis-induced ARDS and refractory hypoxemia	Recruitment maneuvers	No recruitment maneuvers	Mortality Oxygenation
<i>In patients with sepsis induced severe ARDS, should we use prone ventilation?</i>			

Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis-induced severe ARDS	Prone ventilation	No proning	Mortality Oxygenation Complications
<i>In patients with sepsis who are mechanically ventilated, should we elevate the head of the bed?</i>			
Population	Intervention	Comparator	Outcome(s)
Mechanically ventilated adult patients with sepsis	Head of bed between 30 and 45 degrees	No head of bed elevation	Mortality Pneumonia
<i>In patients with sepsis induced ARDS, should we use non-invasive ventilation?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis-induced ARDS	Noninvasive ventilation (NIV)	Invasive mechanical ventilation	Mortality
<i>In patients with sepsis who are mechanically ventilated and ready for weaning, should we use weaning protocol versus physician guided weaning?</i>			
Population	Intervention	Comparator	Outcome(s)
Mechanically ventilated adult patients with sepsis who are can tolerate weaning from mechanical ventilation	Weaning protocol	No protocol	Mortality Successful extubation Duration of mechanical ventilation

<i>In patients with sepsis who are mechanically ventilated and ready for weaning, should we use spontaneous breathing trials (SBT)?</i>			
Population	Intervention	Comparator	Outcome(s)
Mechanically ventilated adult patients with sepsis who are can tolerate weaning from mechanical ventilation	Regular SBT	No SBT	Mortality Successful extubation Duration of mechanical ventilation
<i>In patients with sepsis induced ARDS, should we use pulmonary artery catheter (PAC)?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis-induced ARDS	Use of PAC	No PAC	Mortality Duration of mechanical ventilation
<i>In patients with sepsis induced ARDS, should we use conservative fluid strategy?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis-induced ARDS, and no signs of tissue hypoperfusion	“Conservative” fluid strategy	“Liberal” fluid strategy	Mortality Duration of mechanical ventilation ICU length of stay
<i>In patients with sepsis induced ARDS, should we use inhaled Beta agonists?</i>			
Population	Intervention	Comparator	Outcome(s)

Adult patients with sepsis-induced ARDS and no bronchospasm	Use of inhaled Beta agonists	No Beta agonists or placebo	Mortality Duration of mechanical ventilation
<i>In patients with sepsis induced ARDS, should we use ECMO treatment?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis-induced ARDS	ECMO/expert therapy	Usual Care	Mortality Duration of mechanical ventilation
<i>In patients with sepsis induced ARDS, should we use High Frequency Oscillation (HFO) versus conventional ventilation?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis-induced ARDS	HFO ventilation	Conventional Mechanical Ventilation	Mortality Duration of mechanical ventilation
<i>In patients with sepsis induced respiratory failure without ARDS, should we use low tidal volume ventilation?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis-induced respiratory failure	Low tidal volume ventilation	Conventional Mechanical Ventilation	Mortality Duration of mechanical ventilation Development of ARDS

<i>In mechanically ventilated patients with sepsis, should we use sedation targets?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult mechanically ventilated patients with sepsis	Sedation targets “specific endpoints”	No targets used to guide sedation	Mortality Duration of mechanical ventilation ICU length of stay
<i>In patients with severe ARDS who are mechanically ventilated, should we use neuromuscular blocking agents?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis induced ARDS	Neuromuscular blocking agent	Placebo	Mortality Ventilator-free days ICU-acquired weakness Barotrauma
<i>In patients with sepsis and indication for hemodialysis, should we use CRRT versus intermittent hemodialysis?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis and acute kidney injury requiring dialysis	CRRT	IHD	Mortality
<i>In patients with sepsis and AKI with no indication for hemodialysis, should we use renal replacement therapy versus not?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis and acute kidney injury without indication for hemodialysis	Renal replacement therapy (early initiation of renal replacement therapy)	No dialysis	Mortality

<i>In patients with sepsis or septic shock and hypoperfusion-induced lactic acidosis, should we use sodium bicarbonate therapy?</i>			
Population	Intervention	Comparator	Outcome(s)
Adult patients with sepsis or septic shock and hypoperfusion-induced lactic acidosis	Intravenous sodium bicarbonate	Placebo or no intervention	Mortality

HES: Hydroxyethyl starches; EGDT: Early goal directed therapy; MAP: Mean arterial pressure; PT: prothrombin time; PTT: Partial thromboplastin time; FFP: Fresh frozen plasma; PPI: Proton pump inhibitor; H2RA: Histamine 2 receptor antagonist; UFH: Unfractionated heparin; LMWH: Low molecular weight heparin; TPN: Total parenteral nutrition; ICU: Intensive care unit; DMV: Duration of mechanical ventilation; LOS: length of stay; DNR: Do not resuscitate; Vt: Tidal volume; PBW: Per body weight; PEEP: Peak end expiratory pressure; SBT: Spontaneous breathing trial; PAC: Pulmonary arterial catheter; ECMO: Extra-corporeal membrane oxygenation; HFO: High frequency oscillation; CRRT: Continuous renal replacement therapy