The STOP Sepsis Bundle Toolkit
Strategies to Timely Obviate the Progression of Sepsis

Department of Emergency Medicine
Division of Pulmonary and Critical Care Medicine
Department of Anesthesiology and Surgical Intensive Care
Department of Quality Resource Management
Loma Linda University Medical Center

for the STOP Sepsis Working Group

Version 9.3
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www.llu.edu/llumc/emergency/patientcare
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   a. Therapeutic outline to guide clinicians and nurses in recognizing and providing early
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8. STOP Sepsis Quality Measurement Tool
   a. A quality improvement checklist to ensure standard of care.
   b. A list of patients with severe sepsis or septic shock is obtained from admission records
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9. STOP Sepsis Quality Indicators
   a. Definitions of evidence-based quality indicators applicable in the treatment of severe
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INTRODUCTION

What is a bundle?
A bundle is a group of interventions related to a disease that when performed together result in better outcome than when individually done. It increases the use of evidence-based science in clinical practice and provides a mechanism to enforce teamwork. A bundle is not guidelines, but a method to implement the guidelines. In creating a bundle, several rules have to be met: 1) the components of the bundle are solid and accepted into clinical practice, 2) the components must be completed in the same space and time interval, 3) the completion of each component can be answered by a “Yes” or “No”, 4) the delivery of the whole bundle can be answered by a “Yes” or “No”, and 5) the function of the bundle or the disease process it targets needs to be frequently occurring.

What is the STOP Sepsis Bundle?
The STOP Sepsis Bundle is an implementation of an early sepsis treatment model specific to the emergency department at Loma Linda University. It focuses on the first 6 hours of care after severe sepsis or septic shock is recognized. While it was designed for the emergency department setting, the bundle can be applied in any location where care is being given to patients with severe sepsis or septic shock; e.g. the medical ward, the recovery room, or the intensive care unit. It has additionally evolved to incorporate care in the intensive care unit, beyond the first 6 hours of disease presentation.

What is the evidence and support for the STOP Sepsis Bundle?
The Surviving Sepsis Campaign guidelines for the management of severe sepsis and septic shock serve as framework for the bundle. The advances in therapy behind the bundle are early goal-directed therapy (EGDT), corticosteroids, and activated protein C. Most important in the first 6 hours of therapy for severe sepsis or septic shock is the implementation of EGDT as originally presented by Rivers et al. The STOP Sepsis Bundle was not conceived to replace or modify EGDT, but is presented as an adaptation of the original EGDT research, and with the hope of making EGDT as widely implemented as possible. This suggested bundle is a practical application of the sepsis bundles provided by the Institute for Health Care Improvement to the clinical environment at our institution. It also takes into consideration quality indicators being considered as sepsis core measures. Completion of the entire 6-hour bundle at our institution was associated with an 18.7% absolute decreased in mortality.

Disclaimer
The content of this toolkit is a clinical template and will change with time. The clinician should use judgment for individual patient encounters. We would appreciate any feedback or suggestions to improve on the quality of the toolkit.

H. Bryant Nguyen, MD, MS
hbnguyen@llu.edu
for the STOP Sepsis Working Group

The STOP Sepsis Bundle
Loma Linda University

Two or more of the following:
1) Temp > 38.3°C (100.9°F) or < 36.0°C (96.8°F)
2) Heart Rate > 90
3) Resp Rate > 20 or PaCO₂ < 32 mmHg
4) WBC > 12K, < 4K or > 10% Bands

ScvO₂ < 70
NO
YES

Lactate > 4 mmol/L or Multi-Organ Dysfunction
NO
YES

OBTAIN APPROPRIATE CULTURES

Suspected Infection

Septic Shock

Severe Sepsis High Risk

Severe Sepsis Low Risk

Sepsis

Antibiotics & IVF

Re-Assess

Early Goal-Directed Therapy

Initiate Sepsis Orders

Central Line Placement for CVP/ScvO₂ Monitoring

Supplemental Oxygen OR Mechanical Ventilation with Lung Protective Strategies

Initiate Broad Spectrum Antibiotics

CVP 8-12

CVP < 8

CVP > 15 and SBP > 160 (MAP > 110)

SBP > 90-140 (MAP 65-90)

SBP < 90 (MAP < 65)

SBP > 160 (MAP > 110)

ScvO₂ < 70

ScvO₂ ≥ 70

Intubation and Mechanical Ventilation with Lung Protective Strategies

Heart Rate

HR > 120

HR < 120

Goals Achieved

Lactate > 2

APACHE II ≥ 25

Hgb < 10

Transfuse PRBC

Consider Digoxin 0.25 – 0.5 mg IV

Hgb ≥ 10

Consider Drotrecogin alfa activated 24 mcg/kg/hr x 96 hr

1. Nitroglycerin 10-60 mcg/min until CVP < 12 or SBP < 140 (MAP < 90)

Nitroglycerin 10-60 mcg/min until CVP < 12 or SBP < 140 (MAP < 90)

1. Arterial Line Placement (preferred)
2. Norepinephrine 2-20 mcg/min
3. Dopamine 5-20 mcg/kg/min
4. Phenylephrine 40-200 mcg/min (if HR > 120)
5. Vasopressin 0.01-0.04 U/min (if on another Vasopressor)
6. Epinephrine 2-10 mcg/min
7. Dexamethasone 2 mg IV q 6 hrs OR Hydrocortisone 50 mg IV q 6 hrs after CST (if on Vasopressor or Adrenal Insufficiency)

1. NS 500 mL Bolus until CVP 8-12, then Continue at 150 mL/hr
2. Consider Adding Colloid if CVP < 4

6-Hour STOP Sepsis Bundle Goals for Severe Sepsis or Septic Shock

- Initiate CVP/ScvO₂ Monitoring within 2 hours
- Give Broad Spectrum Antibiotics within 4 hours
- Achieve Hemodynamic Goals within 6 hours
  - CVP ≥ 8 mmHg
  - MAP ≥ 65 mmHg / SBP ≥ 90 mmHg
  - ScvO₂ ≥ 70%
- Monitor for Decreasing Lactate
- Give Steroid if on Vasopressor or suspect Adrenal Insufficiency

Disclaimer (v9.3)
This is a clinical template and clinician should use judgment for individual patient encounters.
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Sepsis has recently received renewed interest, beginning with a revised international definition. Therapies that significantly decrease sepsis mortality include: early and appropriate antibiotics, early goal-directed therapy, corticosteroid, recombinant human activated protein C, lung protective strategies, and tight glucose control.

These advances have resulted in a management guidelines from the international Surviving Sepsis Campaign. In implementing the new guidelines, the Institute for Healthcare Improvement recommends the development of sepsis change bundles. These bundles include a group of interventions that must be given to patients with severe sepsis as they present and are admitted to the hospital. These efforts are endorsed by 11 international medical societies with the goal of decreasing sepsis mortality by 25 percent.


24-Hour STOP Sepsis Bundle Goals for Severe Sepsis or Septic Shock

- Initiate steroids for catecholamine resistance/adrenal insufficiency
- Initiate drotrecogin alfa activated if APACHE II >25
- Maintain blood glucose control < 150 mg/dL
- Achieve plateau pressure <30 cmH2O if mech ventilation
- Reassess antimicrobial therapy
- Maintain sedation/analgesia for ventilator synchrony & comfort
- Initiate stress ulcer and DVT prophylaxis
- Nutrition within 24 hours of admission
- Titrate off vasopressors while maintaining:
  - CVP > 8 mmHg
  - MAP > 65 mmHg / SBP > 90 mmHg
  - SvO2/ScvO2 > 70% on FiO2 < 0.5

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Diagnostic criteria for sepsis
Infection, documented or suspected, and some of the following:

- General variables
  - Fever (core temperature >38.3°C)
  - Hypothermia (core temperature <36°C)
  - Heart rate >90/min or >2 SD above the normal value for age
  - Tachypnea
  - Altered mental status
  - Significant edema or positive fluid balance (>20 mL/kg over 24 hrs)
  - Hyperglycemia
  - Plasma glucose >120 mg/dL in the absence of diabetes

- Inflammatory variables
  - Leukocytosis (WBC count >12,000/µL)
  - Leukopenia (WBC count <4000/µL)
  - Normal WBC count with >10% bands
  - Plasma C-reactive protein >2 SD above normal
  - Plasma procalcitonin >2 SD above normal

- Hemodynamic variables
  - Arterial hypotension
    - SBP <90 mm Hg
    - MAP <70 mm Hg or SBP decrease >40 mm Hg in adults
    - ScvO2/ScvO2 >85% or <65%
    - Cardiac index > 3.5 L/min/m²

- Organ dysfunction variables
  - Arterial hypoxemia (PaO2/FIO2 <300)
  - Acute oliguria (urine output <0.5 mL/kg/hr)
  - Creatinine increase >0.5 mg/dL
  - Coagulation abnl (INR >1.5 or aPTT >60 secs)
  - Ileus (absent bowel sounds)
  - Thrombocytopenia (platelet count <100,000/µL)
  - Hyperbilirubinemia (total bilirubin > 4 mg/dL)

- Tissue perfusion variables
  - Hyperlactatemia (>2 mmol/L)
  - Decreased capillary refill or mottling

Discontinue Steroid Therapy

Change dexamethasone to hydrocortisone and fludrocortisone, continue for 7 days
A CLINICAL OUTLINE FOR THE CARE OF PATIENTS WITH SEVERE SEPSIS AND SEPTIC SHOCK

for the STOP Sepsis Bundle - Strategies to Timely Obviate the Progression of Sepsis
Version 9.3

SEPSIS DEFINITIONS:

Note: These definitions are used by the STOP Sepsis Working Group and are adaptation of the formal definitions. Refer to bibliography for formal definitions.1, 2

**Infection:** A microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms. An infection can be recognized as:

1. Presence of white cells in a normally sterile body fluid **OR**
2. Positive culture (urine, blood, sputum) **OR**
3. Perforated viscous **OR**
4. Radiographic evidence of pneumonia in association with the production of purulent sputum

**Signs of Inflammation:** A systemic response to inflammation and is manifested by two or more of the following:

1. Temperature > 38.3°C/100.9°F or < 36°C/96.8°F
2. Heart rate > 90 beats/min (sinus rhythm)
3. Respiratory rate > 20 breaths/min or PaCO₂ < 32 mmHg
4. WBC > 12,000 cells/mm³, < 4000 cells/mm³, or > 10% bands

**Sepsis:** The systemic response to an infection, and can be recognized by the presence of suspected or confirmed infection AND the systemic inflammatory response.

**Severe Sepsis:** Sepsis associated with more than one acute organ dysfunction or hypoperfusion. Hypoperfusion may include, but are not limited to lactic acidosis (or lactate > 2 mmol/L), oliguria, or an acute alteration in mental status. Organ dysfunction can be defined as: respiratory failure, acute renal failure, acute liver failure, coagulopathy, or thrombocytopenia. Laboratories that will suggest organ dysfunction include:

1. PaO₂(mmHg)/FiO₂ < 300
2. Creatinine > 2.0 OR Creatinine Increase > 0.5 mg/dL
3. INR > 1.5
4. PTT > 60 s
5. Platelets < 100,000/uL
6. Total bilirubin > 4 mg/dL

**Septic Shock:** Sepsis with hypotension, despite adequate fluid resuscitation of 20 ml/kg crystalloid, along with the presence of perfusion abnormalities that may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status. Patients who are on inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured. **Cryptic** septic shock is sepsis with severe lactic acidosis (lactate > 4 mmol/L) irrespective of blood pressure, and is considered to be equivalent to traditional septic shock (sepsis with hypotension).

**Hypotension:** A systolic blood pressure (SBP) < 90 mmHg or mean arterial pressure < 65 mmHg or a reduction in SBP of > 40 mmHg from baseline in the absence of other causes for hypotension.
PATIENTS WHO WILL BENEFIT FROM EARLY GOAL-DIRECTED THERAPY:

1. Two or more signs of inflammation
   AND
2. Suspected or confirmed infection
   AND
3. Systolic blood pressure < 90 mmHg after a 20 ml/kg fluid bolus OR
   Lactate ≥ 4 mmol/L

Exclusion criteria (used in the trial):
- Age < 18 yrs
- Pregnancy
- Stroke
- Acute coronary syndrome
- Acute pulmonary edema
- Status asthmaticus
- Active GI hemorrhage
- Seizure
- Drug overdose
- Burn
- Trauma
- Emergent surgery
- Uncured cancer
- Immunosuppression
- Do-not-resuscitate order.

LABORATORY DATA OBTAINED WITHIN ONE HOUR AFTER PHYSICIAN EVALUATION:

1. Baseline
   a. CBC with differential, comprehensive metabolic panel, PT/PTT, D-Dimer, Troponin I, urine analysis, type & screen
   b. CXR, ECG
   c. Urine culture, blood culture, sputum culture and sensitivities
2. Baseline and every 3 hours
   a. ScvO₂ (central venous blood gas if using intermittent measurements)
   b. Lactate (grey-top tube on ice)

HEMODYNAMIC MONITORING WITHIN 2 HOURS AFTER PHYSICIAN EVALUATION:

1. Cardiac monitoring
2. Pulse oximetry
3. Central venous pressure (CVP) monitoring with intermittent ScvO₂ measurements
   a. Central venous catheterization via internal jugular or subclavian vein method
4. OR (Preferred) Continuous central venous oxygen saturation (ScvO₂) monitoring
   a. ScvO₂ catheterization via internal jugular or subclavian vein method
5. Intra-arterial catheterization (preferred)

TREATMENT PROTOCOL (TO BE COMPLETED WITHIN 6 HOURS AND UNTIL ICU ADMISSION):

1. Initiate mechanical ventilation when indicated
   a. Maintain low tidal volume to achieve peak inspiratory plateau pressure ≤ 30 cm H₂O
2. Give appropriate antimicrobial agent(s) within 4 hours
3. Central venous pressure (CVP) - Preload
   a. CVP < 8 mmHg
      i. 500 mL bolus of normal saline every 30 minutes until CVP reaches 8-12 mmHg, then continue at 150 mL/hr
      ii. Consider lactate ringer instead of normal saline if hyperchloremic acidosis is present
      iii. Consider adding colloid to crystalloid if CVP < 4 mmHg
   b. CVP > 15 mmHg and MAP > 110 (or SBP > 160) mmHg
      i. Initiate nitroglycerin 10-60 mcg/min until CVP < 12 mmHg or MAP > 90 (or SBP < 140) mmHg
4. Mean arterial pressure (MAP) - Afterload
   a. MAP < 65 (or SBP < 90) mmHg after 2 liters of crystalloid
      i. Initiate vasopressors in the order below until MAP > 65 (or SBP > 90) mmHg
         1. Norepinephrine 2-20 mcg/min (first line therapy in severe sepsis)
2. Dopamine 5-20 mcg/kg/min
3. Phenylephrine 40-200 mcg/min (preferred if HR > 120 bpm)
4. Vasopressin 0.01-0.04 U/min\(^{10-12}\) (if on another vasopressor)
5. Epinephrine 2-10 mcg/min (may increase lactate)
   ii. Consider adrenal insufficiency if vasopressor dependent\(^{13}\)
      1. Perform cosyntropin stimulation test (CST)
         a. Measure baseline cortisol level
         b. Administer ACTH (Cosyntropin/Cortrosyn) 250 mcg IV
         c. Measure cortisol level at 30 min and 60 min after given ACTH
            i. Change in cortisol < 9 ug/dl suggests relative adrenal
               insufficiency\(^{14}\)
   2. Give Hydrocortisone 50 mg IV (OR dexamethasone 2 mg IV if not performing
      CST) q 6 hrs
   3. Give Fludrocortisone 50 mcg PQ qd
      b. MAP > 110 (or SBP > 160) mmHg\(^7,8\)
         i. Initiate nitroglycerin 10-60 mcg/min until MAP < 90 (or SBP < 140) mmHg
         ii. Consider hydralazine 10-40 mg IV
   5. Central venous oxygen saturation (ScvO\(_2\))\(^3,5\) – Contractility and oxygen content
      a. ScvO\(_2\) < 70% after above therapy and Hb < 10 g/dL
         i. Transfuse packed red blood cells
      b. ScvO\(_2\) < 70% after above therapy and Hb > 10 g/dL
         i. Dobutamine 2.5–20 mcg/kg/min titrated until ScvO\(_2\) ≥ 70% OR MAP < 70 (or SBP < 100) mmHg OR heart rate > 100 bpm
      1. Caution with starting Dobutamine when MAP < 70 (or SBP < 100 mmHg) OR
         heart rate > 100 bpm
         ii. Dopamine 5-10 mcg/kg/min
      c. Consider intubation and mechanical ventilation to decrease respiratory muscle oxygen
         consumption
         i. Maintain low tidal volume to achieve peak inspiratory plateau pressure ≤ 30 cm H\(_2\)O
   6. Heart rate:
      a. Heart rate > 120 bpm
         i. Consider digoxin 0.25-0.5 mg IV (possible benefit as inotrope and in controlling heart
            rate in sepsis with underlying cardiomyopathy)\(^{15}\)
   7. Obtain intensive care consult for admission after above goals are met
   8. Go back to each step above until patient is transferred to intensive care unit

THERAPEUTIC GOALS TO BE ACHIEVED WITHIN 24 HOURS, AND MAINTAINED AFTER ICU
ADMISSION\(^{4,9,16-18}\):

1. Mechanical ventilation if indicated, with low tidal volume to maintain peak inspiratory plateau pressure
   ≤ 30 cm H\(_2\)O
   a. Decreases absolute mortality by 9 percent\(^{19}\)
2. Hemodynamic monitoring established (within 2 hours)
3. Appropriate broad-spectrum antibiotics administered
   a. Given within 4 hours decreases length of stay by 2 days, and decreases absolute mortality by 24
      percent\(^{20-23}\)
   b. Every hour delay in antibiotic increases the odds-ratio for mortality and decreases the chance
      for survival by 7.6%\(^{24}\)
4. Early goal directed therapy goals
   a. Achieved within 6 hours decreases absolute mortality by 16 percent\(^{3}\)
   b. Central venous pressure 8-12 mmHg
   b. Mean arterial pressure 65 to 90 OR systolic blood pressure 90 to 140 mmHg
   c. Central venous oxygen saturation (ScvO\(_2\)) ≥ 70%
d. Urine output > 0.5 ml/kg/hr

6. Decreased lactic acidosis
   a. Lactate ≥ 4 mmol/L in non-hypotensive patients has 96% specificity of predicting mortality\(^{25}\)
   b. Lactate ≥ 4 mmol/L in the ED was associated with 28.4% in-hospital mortality, and 22.4% mortality within 3 days\(^{26}\)
   c. Lactate normalized to < 2 mmol/L within 24 hours decreases absolute mortality by 25 percent\(^{27,28}\)
   d. Lactate clearance (or decrease) of ≥ 10% after 6 hours of resuscitation in the emergency department is associated with improved outcome\(^{29}\)

7. Administer steroid if on chronic steroid, vasopressor dependent, or suspect adrenal insufficiency
   a. Decreases absolute mortality by 10 percent\(^{13}\)

8. Consider drotrecogin alfa activated/Xigris (recombinant human activated protein C)
   a. Decreases absolute mortality by 13 percent in patients with APACHE II score ≥ 25\(^{30}\)
   b. ENHANCE Study suggests that Xigris given on day 1 compared to day 2 (or after) is associated with a lower mortality\(^{31}\)
   c. No benefit and FDA warning for use in patients with single organ dysfunction and recent surgery within 30 days (ADDRESS Trial)\(^{32}\)

9. Consider insulin if required to maintain glucose 80-110 mg/dl
   a. Decreases absolute mortality by 3.4 percent at 12 months in surgical intensive care patients\(^{33}\)
   b. Decreases morbidity (renal failure, mechanical ventilation, length of stay) but not mortality in medical intensive care patients\(^{34}\)

REFERENCES:


### Clinical Pathway (v9.3)

**Case Type:** Severe Sepsis or Septic Shock  
**Target ICU LOS:** 7 days

<table>
<thead>
<tr>
<th>DESIRED OUTCOME</th>
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<tbody>
<tr>
<td>1. Early identification of severe sepsis and septic shock</td>
</tr>
<tr>
<td>2. Early hemodynamic monitoring</td>
</tr>
<tr>
<td>3. Early intervention of severe sepsis and septic shock</td>
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<tr>
<td>4. Prevent the progression of multi organ failure and increase chances of survival</td>
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<table>
<thead>
<tr>
<th>DAY</th>
<th>0-6 hours</th>
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<tbody>
<tr>
<td>LOCATION</td>
<td>ED/ PACU/ ICU</td>
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<table>
<thead>
<tr>
<th>Assessments</th>
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<tbody>
<tr>
<td>Primary Assessment (nurse Triage): Assign treatment category based on assessment, vital signs every hour</td>
</tr>
<tr>
<td>Secondary Assessment: vital signs every hour, pain control, physician evaluation, determine sepsis category (sepsis, severe sepsis, or septic shock)</td>
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<tr>
<th>Tests</th>
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<tr>
<td>CBC w/ diff, comprehensive metabolic panel, PT, PTT, D-Dimer, Troponin I, urine analysis, Lactate, type and screen</td>
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<tr>
<td>CXR, ECG</td>
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<tr>
<td>Appropriate cultures and sensitivities prior to antibiotics</td>
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<tr>
<th>Activity</th>
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<tbody>
<tr>
<td>Bedrest</td>
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<table>
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<tr>
<th>Treatments</th>
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<tbody>
<tr>
<td>Cardiac monitoring, Pulse oximetry</td>
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<tr>
<td>Supplemental Oxygen or Mechanical Ventilation</td>
</tr>
<tr>
<td>Central Line Placement for CVP/ScvO2 Monitoring</td>
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<tr>
<td>Arterial Line Placement if needed</td>
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<tr>
<td>Early antibiotics and Source control</td>
</tr>
<tr>
<td>Hemodynamic optimization (early goal-directed therapy)</td>
</tr>
<tr>
<td>Monitor input and output</td>
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<thead>
<tr>
<th>Medications</th>
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<tbody>
<tr>
<td>Broad-spectrum IV antibiotics</td>
</tr>
<tr>
<td>Crystalloid, colloid, PRBC</td>
</tr>
<tr>
<td>Norepinephrine, Dopamine, Phenylephrine, Vasopressin, Epinephrine, Dobutamine</td>
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<tr>
<td>Dexamethasone, Hydrocortisone</td>
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<tr>
<th>Nutrition</th>
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<td>NPO</td>
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<thead>
<tr>
<th>Teaching</th>
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<tbody>
<tr>
<td>Review treatment plan with patient/family.</td>
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<table>
<thead>
<tr>
<th>Consults</th>
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<tbody>
<tr>
<td>Intensive care consult, surgical consult if needed</td>
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<table>
<thead>
<tr>
<th>Goals prior to ICU admission</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. CVP/ScvO2 monitoring within 2 hours</td>
</tr>
<tr>
<td>2. Broad spectrum antibiotics within 4 hours</td>
</tr>
<tr>
<td>3. Optimal hemodynamics: CVP ≥ 8 mmHg, MAP ≥ 65 mmHg (or SBP ≥ 90 mmHg), ScvO2 ≥ 70% within 6 hours</td>
</tr>
<tr>
<td>4. Resolution of tissue hypoperfusion (decreasing lactate)</td>
</tr>
<tr>
<td>5. Initiate corticosteroid if on vasopressor or suspect adrenal insufficiency</td>
</tr>
</tbody>
</table>
# Clinical Pathway (v9.3)

## Case Type: Severe Sepsis or Septic Shock

**Target ICU LOS:** 7 days

### Desired Outcome

1. Titrate vasopressor while maintaining optimal hemodynamics and resolving tissue hypoperfusion
2. Assess and initiate optimal therapies for severe sepsis and septic shock
3. Prevent complications of severe sepsis and septic shock

### Day 1: Admission Day 1

<table>
<thead>
<tr>
<th>Location</th>
<th>ICU</th>
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**Assessments**
- Continuous cardiac monitoring, hemodynamic monitoring, CVP/ScvO2 every hour, VS every hour, input/output every hour

**Tests**
- CBC w/ diff, comprehensive metabolic panel, PT, PTT, D-Dimer, Troponin I, Lactate
- ABG, VBG (for ScvO2 monitor calibration)
- APACHE II calculation
- Cosyntropin stimulation test
- CXR, ECG
- Imaging studies if needed

**Activity**
- Bedrest

**Treatments**
- Mechanical Ventilation if indicated with Lung Protective Strategies
- CVP/ScvO2 or pulmonary artery catheter (SvO2) for hemodynamic monitoring
- Hemodynamic optimization
- Antibiotics and source control
- Corticosteroid
- Recombinant human activated protein C
- FAST HUG (Feeding, Analgesia, Sedation, Thromboembolic prevention, Head of bed elevation, stress Ulcer prophylaxis, Glucose control)

**Medications**
- Appropriate IV antibiotics
- Crystalloid, colloid, PRBC
- Norepinephrine, Dopamine, Phenylephrine, Vasopressin, Epinephrine, Dobutamine
- Hydrocortisone and fludrocortisone if on vasopressor and adrenal insufficiency
- Drotrecogin alfa activated
- Insulin infusion
- Opiate, Sedative
- H2-blocker, Proton pump inhibitor, Heparin

**Nutrition**
- Nutrition consult within 24 hours of admission

**Teaching**
- Review treatment plan with patient/family.

**Consults**
- Nutrition, Subspecialties

### Goals at 24-hour after ICU admission

1. Optimal hemodynamics CVP ≥ 8 mmHg, MAP ≥ 65 mmHg (or SBP ≥ 90 mmHg), ScvO2 (or SvO2) ≥ 70% while titrating vasopressors
2. Corticosteroid if on vasopressor and adrenal insufficiency
3. Drotrecogin alfa activated if APACHE II ≥ 25
4. Glucose < 150 mg/dL
5. Plateau pressure ≤ 30 cmH2O if mechanical ventilation
6. Sedation/analgesia for patient comfort (using Ramsay Sedation Scale)
7. Antimicrobial appropriateness
8. Stress ulcer and DVT prophylaxis
9. Early nutrition
**Clinical Pathway (v9.3)**

**Case Type:** Severe Sepsis or Septic Shock  
**Target ICU LOS:** 7 days

### DESIRED OUTCOME
1. Titrate vasopressor while maintaining optimal hemodynamics and resolving tissue hypoperfusion  
2. Assess and initiate optimal therapies for severe sepsis and septic shock  
3. Prevent complications of severe sepsis and septic shock  
4. Weaning from mechanical ventilator  
5. Decrease ICU length of stay and in-hospital mortality

### DAY

<table>
<thead>
<tr>
<th>DAY</th>
<th>Day 2 until Day 7 (ICU Discharge)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOCATION</td>
<td>ICU</td>
</tr>
</tbody>
</table>
| Assessments | Continuous cardiac monitoring, hemodynamic monitoring, CVP/ScvO2 every hour, VS every hour, input/output every hour  
Assess risks for bleeding, DVT, nosocomial infection |
| Tests | CBC w/diff, comprehensive metabolic panel, Lactate  
ABG, VBG (for ScvO2 monitor calibration)  
CXR, ECG  
Imaging studies if needed |
| Activity | Bedrest |
| Treatments | Mechanical Ventilation if indicated with Lung Protective Strategies  
CVP/ScvO2 or pulmonary artery catheter (SvO2) for hemodynamic monitoring  
Hemodynamic optimization  
Antibiotics and source control  
Corticosteroid  
Recombinant human activated protein C (discontinued if bleeding)  
FAST HUG (Feeding, Analgesia, Sedation, Thromboembolic prevention, Head of bed elevation, stress Ulcer prophylaxis, Glucose control) |
| Medications | Appropriate IV antibiotics  
Crystalloid, colloid, PRBC  
Norepinephrine, Dopamine, Phenylephrine, Vasopressin, Epinephrine, Dobutamine  
Hydrocortisone and fludrocortisone (total of 7 days)  
Drotrecogin alfa activated (total infusion of 96 hours)  
Insulin infusion  
Opiate, Sedative  
H2-blocker, Proton pump inhibitor, Heparin |
| Nutrition | Enteral versus parenteral feeding |
| Teaching | Review treatment plan with patient/family. Reassess patient for continued aggressive support. |
| Consults | Physical Therapy, Occupational Therapy, Case Manager, Subspecialties |

### Goals on each day after ICU admission
1. Optimal hemodynamics CVP ≥ 8 mmHg, MAP ≥ 65 mmHg (or SBP ≥ 90 mmHg), ScvO2 (or SvO2) ≥ 70% while titrating vasopressors  
2. Discontinue corticosteroid if not adrenal insufficiency (responder to cosyntropin stimulation test)  
3. Assess for bleeding if on drotrecogin alfa activated  
4. Glucose < 150 mg/dL  
5. Plateau pressure ≤ 30 cmH2O if mechanical ventilation, weaning off ventilator as appropriate  
6. Sedation/analgesia for patient comfort (using Ramsay Sedation Scale)  
7. Antimicrobial appropriateness  
8. Stress ulcer and DVT prophylaxis  
9. Nutrition  
10. ICU discharge planning
### Adult Severe Sepsis Orders (version 9.3)

| Diagnosis: | Severe Sepsis | Septic Shock |
| Condition: | Critical |
| Code Status: | Full | DNR |

#### Routine Nursing Orders
- Cardiac Monitoring & Continuous Pulse Oximetry
- Supplement oxygen to keep O₂ sat > 92%
- Vitals q 1 hr with Progress Note Documentation by Nurse or MD
- Monitor input and output q 1 hr
- Activity: Bed Rest
- Diet: NPO
- IV Saline lock with flush of Normal Saline 3 mL q 12 hours
- Calibrate & Initiate Central Venous Pressure and ScvO₂ Monitoring after line placement verified by MD
- Mechanical ventilator: Mode __, Freq __, Vₜ __, FiO₂ __, PEEP __, mPaw __, I:E __, PS __, PEEPₕ __, PEEPₐ __, HIGHₜ __, Seconds Amplitude __, %I-time __
- Alert MD if Central Venous Pressure is < 8 mmHg or > 15 mmHg
- Alert MD if Systolic Blood Pressure < 90 mmHg or > 160 mmHg (Mean Arterial Pressure < 65 mmHg or > 90 mmHg)
- Alert MD if ScvO₂ < 70%
- Alert MD if Hemoglobin (or Hemacue) < 10 g/dL
- Alert MD if Lactate > 2 mmol/L
- Alert MD if O₂ saturation < 88% or peak-inspiratory plateau pressure > 30 cm H₂O (on mechanical ventilation)

#### Diagnostics
- Blood culture & sensitivity, urine culture & sensitivity, sputum culture & sensitivity, urinalysis, CBC with differential, comprehensive metabolic panel, PT/PTT/INR, D-Dimer, Trop I
- Lactate level (drawn in grey tube on ice) now and repeat in 6 hours
- Venous blood gas from central line & arterial blood gas
- Cosyntropin stimulation test: Obtain cortisol level, administer ACTH 250 mcg IV, then obtain cortisol at 30 and 60 min
- Measure peak-inspiratory plateau pressure every 4 hours
- Glucose level every 4 hours
- 12-lead ECG

#### Chest X-ray
- Reason: __________________________________________________________________________

#### Ultrasound
- Location and Reason: __________________________________________________________________________

#### CT scan
- Location and Reason: __________________________________________________________________________

#### Medications (Date and time must be entered for each order)

<table>
<thead>
<tr>
<th>Physician Signature</th>
<th>Date and Time</th>
<th>ALLERGIES:</th>
<th>Weight (kg):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous fluids - NS 500 mL IV bolus until Central Venous Pressure 8 to 12 mmHg, then continue NS to run at 150 mL/hour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics - See Parenteral Antibiotics Order Form</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tylenol 1 gm PO q 4 hr PRN Temperature &gt; 38.3 °C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin 5,000 units SQ q 12 hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Famotidine 20 mg IV q 12 hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midazolam 100 mg/NS 100 mL at 1-10 mg/hr, titrate to sedation scale</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine 100 mg/NS 100 mL at 1-10 mg/hr, titrate to pain relief</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasopressors - (SBP = Systolic Blood Pressure)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norepinephrine 8 mg/D,W 250 mL at 2-20 mcg/min, titrate to SBP &gt; 90 mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dopamine 800 mg/D,W 250 mL at 5-20 mcg/kg/min, titrate to SBP &gt; 90 mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenylephrine 10 mg/NS 250 mL at 40-200 mcg/min, titrate to SBP &gt; 90 mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasopressin 20 units/NS 100 mL at 0.01-0.04 units/min, titrate to SBP &gt; 90 mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epinephrine 1 mg/NS 250 mL at 2-10 mcg/min, titrate to SBP &gt; 90 mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dobutamine 500 mg/NS 250 mL at 2.5-20 mcg/kg/min, titrate to ScvO₂ &gt; 70%, maintaining SBP &gt; 90 mmHg and Heart Rate &lt; 140 per min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitroglycerin 100 mg/D,W 250 mL at 10-60 mcg/min, titrate to SBP &lt; 140 mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type &amp; Cross 2 units</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfuse ____ unit PRBC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone 50 mg IV q 6 hr, and Fludrocortisone 50 mcg PO qd</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xigris (Drotrecogin alfa activated) 24 mcg/kg/hr for 96 hr - See Institutional Guidelines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular Insulin 100 units/NS 100 mL titrate to keep glucose &lt; 150 mg/dL</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
MEDICATION ORDER FORM (Version 9.3)
Xigris (Drotrecogin alfa activated) for Adult Patients with Severe Sepsis or Septic Shock

INDICATIONS (Circle “Yes” or “No” for each of the following below):
NOTE: Patient must have all three indications to receive Xigris (drotrecogin alfa activated)

1. Yes / No - **Patient has high risk for mortality due to severe sepsis or septic shock defined as:**
   a. (2) and (3) below AND
   b. Cardiovascular dysfunction: Arterial systolic blood pressure < 90 mmHg or the mean arterial pressure < 70 mmHg despite adequate fluid resuscitation, requiring the use of vasopressor AND
   c. APACHE II Score ≥ 25 or the presence of two or more organ dysfunction

2. Yes / No - **Patient has known or suspected infection defined as:**
   a. Presence of white cells in a normally sterile body fluid OR
   b. Positive culture (urine, blood, sputum) OR
   c. Perforated viscous OR
   d. Radiographic evidence of pneumonia in association with the production of purulent sputum

3. Yes / No - **Patient has three or more signs of inflammation defined as:**
   a. Temperature > 38.3°C (100.9°F) or < 36.0°C (96.8°F)
   b. Heart Rate > 90 beats per minute
   c. Respiratory > 20 breaths per minute or PaCO₂ < 32 mmHg
   d. WBC > 12,000/mm³ or < 4,000/mm³ or > 10% bands

CONTRAINDICATIONS and WARNINGS (Circle “Yes” or “No”):
NOTE: Patient MUST NOT receive Xigris (drotrecogin alfa activated) if one or more of the absolute contraindications exist

<table>
<thead>
<tr>
<th>Absolute Contraindications</th>
<th>Warnings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes / No – Active internal bleeding</td>
<td>Yes / No – Concurrent therapeutic dosing of heparin to treat an active thrombotic or embolic event</td>
</tr>
<tr>
<td>Yes / No – Recent hemorrhagic stroke within 3 months</td>
<td>Yes / No – Platelet count &lt; 30,000 x 10⁶/L, even if the platelet count is increased after transfusions</td>
</tr>
<tr>
<td>Yes / No – Recent intracranial, intraspinal surgery, or severe head trauma within 2 months</td>
<td>Yes / No – Prothrombin time-INR &gt; 3.0</td>
</tr>
<tr>
<td>Yes / No – Trauma with an increased risk of life-threatening bleeding</td>
<td>Yes / No – Recent gastrointestinal bleeding within 6 weeks</td>
</tr>
<tr>
<td>Yes / No – Presence of an epidural catheter</td>
<td>Yes / No – Recent administration of thrombolytic therapy within 3 days</td>
</tr>
<tr>
<td>Yes / No – Intracranial neoplasm or mass lesion or evidence of cerebral herniation</td>
<td>Yes / No – Recent administration of oral anticoagulants or glycoprotein IIb/IIIa inhibitors within 7 days</td>
</tr>
<tr>
<td>Yes / No – Known hypersensitivity to drotrecogin alfa (activated) or any component of this product</td>
<td>Yes / No – Recent administration of aspirin &gt; 650 mg per day or other platelet inhibitors within 7 days</td>
</tr>
<tr>
<td>Yes / No – Known hypersensitivity to drotrecogin alfa (activated) or any component of this product</td>
<td>Yes / No – Recent ischemic stroke within 3 months</td>
</tr>
<tr>
<td>Yes / No – Known bleeding diathesis</td>
<td>Yes / No – Intracranial arteriovenous malformation or aneurysm</td>
</tr>
<tr>
<td>Yes / No – Known bleeding diathesis</td>
<td>Yes / No – Known bleeding diathesis</td>
</tr>
<tr>
<td>Yes / No – Chronic severe hepatic disease</td>
<td>Yes / No – Any other condition in which bleeding constitutes a significant hazard or would be particularly difficult to manage because of its location</td>
</tr>
<tr>
<td>Yes / No – Single organ dysfunction and recent surgery less than 30 days</td>
<td>Yes / No – Single organ dysfunction and recent surgery less than 30 days</td>
</tr>
</tbody>
</table>

Allergies: _______________ Patient Weight = ________ kg APACHE II Score: _______

<table>
<thead>
<tr>
<th>Patient Weight Range (kg)</th>
<th>Dosing: Check [✓] dose that applies to patient’s weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>27-43</td>
<td>[ ] Xigris 10 mg in NS 100 mL to run at 8 mL/hour for 8 bags total</td>
</tr>
<tr>
<td>44-60</td>
<td>[ ] Xigris 15 mg in NS 150 mL to run at 13 mL/hour for 8 bags total</td>
</tr>
<tr>
<td>61-78</td>
<td>[ ] Xigris 20 mg in NS 200 mL to run at 17 mL/hour for 8 bags total</td>
</tr>
<tr>
<td>79-95</td>
<td>[ ] Xigris 25 mg in NS 250 mL to run at 21 mL/hour for 8 bags total</td>
</tr>
<tr>
<td>96-113</td>
<td>[ ] Xigris 30 mg in NS 300 mL to run at 25 mL/hour for 8 bags total</td>
</tr>
<tr>
<td>114-130</td>
<td>[ ] Xigris 35 mg in NS 350 mL to run at 29 mL/hour for 8 bags total</td>
</tr>
<tr>
<td>131-135</td>
<td>[ ] Xigris 40 mg in NS 400 mL to run at 33 mL/hour for 8 bags total</td>
</tr>
</tbody>
</table>

Attending Physician Signature: ___________________________ Date and Time: ___________________________
### APACHE II Score Calculation

<table>
<thead>
<tr>
<th>1. Temperature (°C / °F)</th>
<th>Points</th>
<th>6. Arterial pH</th>
<th>Points</th>
<th>11. White Blood Count (per mm³)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 41°C / &gt; 105.8°F</td>
<td>4</td>
<td>&gt; 7.70</td>
<td></td>
<td>&gt; 40</td>
<td>4</td>
</tr>
<tr>
<td>39.4-40.9 / 102.1-105.7</td>
<td>3</td>
<td>7.60-7.69</td>
<td>3</td>
<td>20-39.9</td>
<td>2</td>
</tr>
<tr>
<td>38.5-38.9 / 101.3-102</td>
<td>1</td>
<td>7.50-7.59</td>
<td>1</td>
<td>15-19.9</td>
<td>1</td>
</tr>
<tr>
<td>36-38.4 / 96.8-101.2</td>
<td>0</td>
<td>7.33-7.49</td>
<td>0</td>
<td>3-14.9</td>
<td>0</td>
</tr>
<tr>
<td>34-35.9 / 93.1-96.7</td>
<td>1</td>
<td>7.25-7.32</td>
<td>2</td>
<td>1-2.9</td>
<td>2</td>
</tr>
<tr>
<td>32-33.9 / 89.5-93</td>
<td>2</td>
<td>7.15-7.24</td>
<td>3</td>
<td>&lt; 1</td>
<td>4</td>
</tr>
<tr>
<td>30-31.9 / 85.9-89.4</td>
<td>3</td>
<td>&lt; 7.15</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 29.9 / ≤ 85.8</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. MAP = [(2 x DBP) + SBP] / 3 (mm Hg)</th>
<th>Points</th>
<th>7. Serum Sodium (mmol/L)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 180</td>
<td>4</td>
<td>Eyes Opening</td>
<td>4</td>
</tr>
<tr>
<td>≥ 160</td>
<td>4</td>
<td>160-179</td>
<td>3</td>
</tr>
<tr>
<td>130-159</td>
<td>3</td>
<td>155-159</td>
<td>2</td>
</tr>
<tr>
<td>110-129</td>
<td>2</td>
<td>150-154</td>
<td>1</td>
</tr>
<tr>
<td>70-109</td>
<td>0</td>
<td>130-149</td>
<td>0</td>
</tr>
<tr>
<td>50-69</td>
<td>2</td>
<td>120-129</td>
<td>2</td>
</tr>
<tr>
<td>≤ 49</td>
<td>4</td>
<td>111-119</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Heart Rate (beats per min)</th>
<th>Points</th>
<th>8. Serum Potassium (mmol/L)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 180</td>
<td>4</td>
<td>Incomprehensible</td>
<td>2</td>
</tr>
<tr>
<td>140-179</td>
<td>3</td>
<td>&gt; 7</td>
<td>4</td>
</tr>
<tr>
<td>110-139</td>
<td>2</td>
<td>6-6.9</td>
<td>3</td>
</tr>
<tr>
<td>70-109</td>
<td>0</td>
<td>5.5-5.9</td>
<td>1</td>
</tr>
<tr>
<td>55-69</td>
<td>2</td>
<td>3.5-5.4</td>
<td>0</td>
</tr>
<tr>
<td>40-54</td>
<td>3</td>
<td>3-3.4</td>
<td>1</td>
</tr>
<tr>
<td>&lt; 39</td>
<td>4</td>
<td>2.5-2.9</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Respiratory Rate (breaths per min)</th>
<th>Points</th>
<th>9. Serum Creatinine (mg/dL)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>4</td>
<td>Absent</td>
<td>1</td>
</tr>
<tr>
<td>35-49</td>
<td>3</td>
<td>&gt; 3.5 &amp; acute renal failure</td>
<td>8</td>
</tr>
<tr>
<td>25-34</td>
<td>1</td>
<td>2.0-3.4 &amp; acute renal failure</td>
<td>6</td>
</tr>
<tr>
<td>12-24</td>
<td>0</td>
<td>1.5-1.9 &amp; acute renal failure</td>
<td>4</td>
</tr>
<tr>
<td>10-11</td>
<td>1</td>
<td>&gt; 3.5 &amp; chronic renal failure</td>
<td>4</td>
</tr>
<tr>
<td>6-9</td>
<td>2</td>
<td>2.8-3.4 &amp; chronic renal failure</td>
<td>3</td>
</tr>
<tr>
<td>≤ 5</td>
<td>4</td>
<td>1.5-1.9 &amp; chronic renal failure</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Oxygenation</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. A-a gradient if FiO₂ ≥ 0.5</td>
<td></td>
</tr>
<tr>
<td>&gt; 50</td>
<td>4</td>
</tr>
<tr>
<td>&lt; 50</td>
<td>1</td>
</tr>
<tr>
<td>&lt; 50</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>10. Hematocrit (%)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60</td>
<td>4</td>
</tr>
<tr>
<td>&lt; 60</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>11. White Blood Count (per mm³)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 40</td>
<td>4</td>
</tr>
<tr>
<td>20-39.9</td>
<td>2</td>
</tr>
<tr>
<td>15-19.9</td>
<td>1</td>
</tr>
<tr>
<td>3-14.9</td>
<td>0</td>
</tr>
<tr>
<td>1-2.9</td>
<td>2</td>
</tr>
<tr>
<td>&lt; 1</td>
<td>4</td>
</tr>
<tr>
<td>≤ 7.15</td>
<td>4</td>
</tr>
</tbody>
</table>

### APS Points (Sum of 12 points above) = APS Points + Age Points + Chronic Health Points

### Age Points

<table>
<thead>
<tr>
<th>Age</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-74</td>
<td>5</td>
</tr>
<tr>
<td>60-64</td>
<td>3</td>
</tr>
<tr>
<td>55-59</td>
<td>2</td>
</tr>
<tr>
<td>50-59</td>
<td>1</td>
</tr>
<tr>
<td>45-54</td>
<td>0</td>
</tr>
</tbody>
</table>

### Chronic Health Points

<table>
<thead>
<tr>
<th>Chronic Health</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, Non-operative</td>
<td>5</td>
</tr>
<tr>
<td>Yes, Emergency post-operative</td>
<td>5</td>
</tr>
<tr>
<td>Yes, Elective post-operative</td>
<td>2</td>
</tr>
</tbody>
</table>

### APACHE II Score

```latex
\text{APACHE II Score} = \text{APS Points} + \text{Age Points} + \text{Chronic Health Points}
```

### Chronic Health:

**Organ insufficiency or immunocompromised state must have been evident prior to this hospital admission and conform to the following criteria:**

- **LIVER:** Biopsy-proven cirrhosis and documented portal hypertension; episodes of past upper GI bleeding attributed to portal hypertension; or prior episodes of hepatic failure/encephalopathy/coma.
- **CARDIOVASCULAR:** New York Heart Association Class IV
- **RESPIRATORY:** Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction; i.e. unable to climb stairs or perform household duties, or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (>40 mm Hg), or respiratory dependency.
- **RENAL:** Receiving chronic dialysis.
- **IMMUNOCOMPROMISED:** Patient has received therapy that suppresses resistance to infection; e.g. immunosuppression, chemotherapy, radiation, long-term or recent high-dose steroids, or has a disease that is sufficiently advanced to suppress resistance to infection; e.g. leukemia, lymphoma, AIDS.

---

**NOTE:** Points are determined from the worst physiologic variables in the first 24 hours after patient presentation.
### CRITERIA FOR INITIATING BUNDLE

1) Two or more signs of inflammation:
   a) Temperature $>38.3^\circ C$ (100.9F) or $<36^\circ C$ (96.8F)
   b) Heart rate $>90$ beats/min
   c) Respiratory rate $>20$ breaths/min or PaCO$_2$ $<32$ mmHg
   d) WBC $>12,000$ cells/mm$^3$, $<4000$ cells/mm$^3$, or $>10\%$ bands

2) Suspected or confirmed infection

3) Systolic blood pressure $<90$ mmHg after fluid bolus (septic shock) OR
   Lactate $\geq 4$ mmol/L (high risk severe sepsis / cryptic shock) OR
   Evidence of $>1$ organ dysfunction (severe sepsis)

### LABORATORIES AND PROCEDURES (within 2 hours after meeting bundle criteria)

1) Peripheral IV, cardiac monitor, oxygen, pulse oximetry
2) Obtain Sepsis panel (Blood culture, sputum culture, urine culture, sensitivities, urine analysis, CBC w/differential, comprehensive metabolic panel, PT/PTT, D-Dimer, Troponin I, Lactate)
3) Calibrate and initiate CVP and ScvO$_2$ monitoring after CXR verification of line placement
4) Obtain central venous blood gas from central line
5) Repeat lactate at 6 hours after 1st draw

### THERAPY (within 6 hours after meeting bundle criteria)

1) Broad Spectrum Antibiotics within 4 hours

2) Normal saline 500 mL bolus until CVP 8-12 mmHg, then continue at 150 ml/hr

3) Intervention is required if:
   a) Pulse Ox $< 93\%$ (Consider intubation and mechanical ventilation)
   b) Peak inspiratory plateau pressure $> 30$ cm H$_2$O (Consider decreasing tidal volume)
   c) Lactate $> 2$ mmol/L (Repeat lactate in 6 hours)
   d) CVP $> 15$ mmHg (Consider nitroglycerin if SBP $> 160$ mmHg or MAP $> 110$ mmHg)
   e) SBP $< 90$ mmHg (MAP $< 65$ mmHg) after 2 Liters IVF (Consider vasopressor)
   f) SBP $> 160$ mmHg (MAP $> 110$ mmHg) (Consider afterload reducer)
   g) ScvO$_2$ $< 70\%$ (Consider transfusion for hemoglobin $< 10$ g/dL and/or dobutamine)

4) Target hemodynamic goals by 6 hours and maintained until ICU transfer:
   a) CVP $\geq 8$ mmHg
   b) MAP $\geq 65$ mmHg / SBP $\geq 90$ mmHg
   c) ScvO$_2$ $\geq 70\%$

5) If patient is on vasopressor and/or APACHE II score $\geq 25$, consider:
   a) Corticosteroid and perform Cosyntropin Stimulation Test
   b) Recombinant human Activated Protein C (Drotrecogin alfa activated)
What is SvO₂?

1. Venous oxygen saturation (SvO₂) reflects a balance between oxygen delivery (DO₂) and oxygen consumption (VO₂).

2. DO₂ comprises of cardiac output and arterial oxygen content:
   a. \[ \text{DO}_2 = \text{CO} \times [(1.34 \times \text{Hb} \times \text{SaO}_2) + (0.0031 \times \text{PaO}_2)] \]
   b. DO₂ results in 100% oxygen delivered to the tissue.
   c. The tissue will consume (VO₂) with an oxygen extraction ratio of 25-35%.
   d. The remainder in the venous side (or venous oxygen content) is 65-75%.

3. When DO₂ and VO₂ are balanced, the optimal venous oxygen content will be reflected by a mixed venous oxygen saturation (SvO₂) of 65-75%.

4. SvO₂ is traditionally measured in the pulmonary artery via a pulmonary artery catheter (Swan-Ganz catheter).

5. SvO₂ has diagnostic, prognostic, and therapeutic value in the care of critically ill patients with acute myocardial infarction, severe heart failure, cardiogenic shock, traumatic and hemorrhagic shock, septic shock, and general medical and surgical intensive care.
What is ScvO\textsubscript{2} and Why use ScvO\textsubscript{2}? 

1. The central venous oxygen saturation (ScvO\textsubscript{2}) reflects central venous oxygen content, excluding the venous oxygen delivered from the coronary sinus (from the heart).
2. ScvO\textsubscript{2} can be measured in the superior vena cava or right atrium.
3. ScvO\textsubscript{2} has been shown to correlate well with SvO\textsubscript{2}.
4. An accepted normal SvO\textsubscript{2} > 65%.
5. An accepted normal ScvO\textsubscript{2} > 70%, which is about 7% higher than SvO\textsubscript{2}, since ScvO\textsubscript{2} does not mix with the de-saturated venous blood of the coronary sinus.
6. ScvO\textsubscript{2} can be measured via a central venous blood gas or a central venous catheter with oximetry technology.
7. ScvO\textsubscript{2} measured via a central venous catheter with oximetry technology allows for continuous ScvO\textsubscript{2} monitoring; i.e. analogous to continuous arterial pulse oximetry (SaO\textsubscript{2}) monitoring. 
   a. Continuous ScvO\textsubscript{2} allows for monitoring dynamic changes in ScvO\textsubscript{2} in response to treatments.
   b. Continuous ScvO\textsubscript{2} monitoring via a central venous catheter is practical and more easily performed than continuous SvO\textsubscript{2} monitoring via the pulmonary artery catheter.
8. The addition of continuous ScvO\textsubscript{2} monitoring in a protocolized approach to resuscitation of severe sepsis and septic shock has been shown to significantly improve outcome.

What do abnormalities in ScvO\textsubscript{2} mean?

1. Troubleshooting an abnormal ScvO\textsubscript{2} requires understanding of the causes of abnormal DO\textsubscript{2} and VO\textsubscript{2}.
   a. For example, a low DO\textsubscript{2} in the presence of normal VO\textsubscript{2} will result in less oxygen delivered to the venous circulation; therefore, a low ScvO\textsubscript{2}.
   b. A critically ill patient will have various combinations of DO\textsubscript{2} and VO\textsubscript{2}.
      i. For example, sepsis patients can have a hypodynamic low DO\textsubscript{2} state resulting in low ScvO\textsubscript{2}; or a hyperdynamic high DO\textsubscript{2} state combined with a low VO\textsubscript{2} state from cellular mitochondria defect, resulting in high ScvO\textsubscript{2}.

<table>
<thead>
<tr>
<th>Low ScvO\textsubscript{2} (&lt;&lt; 70%)</th>
<th>High ScvO\textsubscript{2} (&gt;&gt; 70%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low DO\textsubscript{2}</td>
<td>High VO\textsubscript{2}</td>
</tr>
<tr>
<td>Hypoxia, Suctioning (low SaO\textsubscript{2})</td>
<td>Exercise</td>
</tr>
<tr>
<td>Anemia, Hemorrhage (low Hb)</td>
<td>Pain</td>
</tr>
<tr>
<td>Cardiac dysfunction, Hypovolemia, Shock, Arrhythmia (low CO)</td>
<td>Hyperthermia, Shivering, Seizure</td>
</tr>
</tbody>
</table>
How do we treat an abnormal ScvO₂?

1. Low ScvO₂ – usually results from low DO₂, a scenario that is treatable by optimizing DO₂. Figure below illustrates the components of DO₂. DO₂ is increased to normal range by increasing these various components. Note that normalizing DO₂ is not the same as increasing DO₂ to supranormal values.¹²-¹⁴

   a. Optimizing Preload – increase central venous pressure (or pulmonary capillary wedge pressure) by increasing end-diastolic volume with fluid resuscitation.
   b. Optimizing Afterload – increase mean arterial pressure (or systemic vascular resistance) with vasopressor agents. Sometimes a vasodilator may be necessary to decrease afterload in order to optimize DO₂.¹⁵
   c. Optimizing Oxygen content – \((1.34 \times \text{Hb} \times \text{SaO}_2) + (0.0031 \times \text{PaO}_2)\)
      i. Increase PaO₂/SaO₂ with oxygen supplementation; e.g. mechanical ventilation.
      ii. Increase hemoglobin with transfusion.
   d. Optimizing Contractility – increase with inotrope agent; e.g. dobutamine.¹⁶,¹⁷
   e. Oxygen content and contractility should be targeted when ScvO₂ is persistently low after preload and afterload have been optimized.
      i. For example, transfusion and/or inotrope should be considered when CVP > 12 mmHg, MAP > 90, and ScvO₂ < 70%. Simply giving a fluid bolus when ScvO₂ < 70% in this scenario may not be appropriate.

2. High ScvO₂ – resulting from high DO₂, or low VO₂.
   a. Usually it is difficult to treat a high ScvO₂, except to optimize the current therapies: maintaining optimal preload, afterload, contractility and oxygen content.
      i. For example, prognosis is poor when a patient is on multiple vasopressors with significant lactic acidosis, and ScvO₂ > 90%.¹⁸,¹⁹
What other references do we have about $\text{SvO}_2$/$\text{ScvO}_2$ or organ hypoperfusion in sepsis:

### The STOP Sepsis Bundle
#### Quality Measurement Tool

<table>
<thead>
<tr>
<th>Date of Admission:</th>
<th>Time of ED / ICU Arrival:</th>
</tr>
</thead>
<tbody>
<tr>
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<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>MRN:</th>
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</table>

<table>
<thead>
<tr>
<th>Age:</th>
<th>Sex:</th>
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### Quality Indicators:

<table>
<thead>
<tr>
<th>Criteria for Severe Sepsis Bundle:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. [ ] Two or more Signs of Inflammation AND</td>
</tr>
<tr>
<td>2. [ ] Suspected infection OR positive cultures AND</td>
</tr>
<tr>
<td>3. [ ] SBP &lt; 90 mmHg after fluid bolus OR Lactate ≥ 4 mmol/L OR mechanical ventilation OR vasopressor dependent OR evidence of ≥ 2 acute organ dysfunction*</td>
</tr>
</tbody>
</table>

**Patient met all three criteria:** Y / N

**Date & Time meeting Criteria:**

**Location meeting Criteria:** ED / Ward / PACU / ICU

---

### Signs of Inflammation:

- Manifested by two or more of the following conditions:
  - Temperature >38.3°C or <36°C (value= )
  - Heart rate >90 beats/min (value= )
  - Respiratory rate >20 breaths/min or PaCO₂ <32 mmHg (value= )
  - WBC > 12,000 cells/mm³, <4000 cells/mm³, or >10% bands (value= )

### Sepsis:

- Signs of inflammation & suspected infection+

### Severe Sepsis:

- Sepsis associated with > 2 organ dysfunction, or hypoperfusion (lactate > 2 mmol/L)

### Septic Shock:

- Sepsis with hypotension (BP < 90/60), despite a fluid bolus of 20 mL/kg

---

### Early Recognition of High Risk Patient – Lactate Measured:

<table>
<thead>
<tr>
<th>LA:</th>
<th>Y / N</th>
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### Within 2+1 hours of meeting Bundle Criteria:

<table>
<thead>
<tr>
<th>Initiate hemodynamic monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Triple lumen catheter</td>
</tr>
<tr>
<td>□ Pulmonary artery catheter</td>
</tr>
<tr>
<td>□ CVP monitoring</td>
</tr>
<tr>
<td>□ ScvO₂ monitoring</td>
</tr>
<tr>
<td>□ SvO₂ monitoring</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>Completed by 2 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Y / N</td>
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</tbody>
</table>

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### Within 4+1 hours of meeting Bundle Criteria:

<table>
<thead>
<tr>
<th>Cultures obtained prior to antibiotic administration</th>
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<tbody>
<tr>
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<table>
<thead>
<tr>
<th>Give broad spectrum antibiotic(s)</th>
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<tbody>
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<table>
<thead>
<tr>
<th>Time</th>
<th>Completed by 4 hrs</th>
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<tbody>
<tr>
<td></td>
<td>Y / N</td>
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</tbody>
</table>

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### After 6+1 hours of meeting Bundle Criteria and/or at ICU adm:

<table>
<thead>
<tr>
<th>Achieve and maintain hemodynamic goals (all three goals below)</th>
</tr>
</thead>
<tbody>
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</table>

<table>
<thead>
<tr>
<th>CVP ≥ 8 mmHg</th>
<th>MAP ≥ 65 mmHg or SBP ≥ 90 mmHg</th>
<th>ScvO₂ (or SvO₂) ≥ 70%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y / N</td>
<td>Y / N</td>
<td>Y / N</td>
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<table>
<thead>
<tr>
<th>Time</th>
<th>Completed after 6 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Y / N</td>
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### After 24+2 hours of meeting Bundle Criteria and/or ICU adm:

<table>
<thead>
<tr>
<th>Cosyntropin Stimulation Test Performed</th>
</tr>
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<tbody>
<tr>
<td></td>
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<table>
<thead>
<tr>
<th>ΔCortisol:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y / N</td>
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</table>

<table>
<thead>
<tr>
<th>Corticosteroid if on Vasopressor and/or ΔCortisol ≤ 9 mcg/dL</th>
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<tbody>
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<table>
<thead>
<tr>
<th>APACHE II Score computed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>APACHE II:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y / N</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Drotrecogin Alfa (activated) Eligibility Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>APACHE II ≥ 25 and/or Vasopressor Dependent</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drotrecogin Alfa (activated) Indicated and Administered (within 48hrs)</th>
</tr>
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<tbody>
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<table>
<thead>
<tr>
<th>Time</th>
<th>Completed after 24 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Y / N</td>
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</tbody>
</table>

### Achieve and maintain median glucose level < 150 mg/dL:

<table>
<thead>
<tr>
<th>Glucose (0hr)</th>
<th>(2hr)</th>
<th>(4hr)</th>
<th>(6hr)</th>
<th>(8hr)</th>
<th>(10hr)</th>
<th>(12hr)</th>
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<table>
<thead>
<tr>
<th>Time</th>
<th>Completed after 24 hrs</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Y / N</td>
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</tbody>
</table>

### Achieve and maintain median plateau pressure < 30 cm H₂O if mechanical ventilation:

<table>
<thead>
<tr>
<th>Pplat (0hr)</th>
<th>(4hr)</th>
<th>(8hr)</th>
<th>(12hr)</th>
<th>(16hr)</th>
<th>(20hr)</th>
<th>(24hr)</th>
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<table>
<thead>
<tr>
<th>Time</th>
<th>Completed after 24 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Y / N</td>
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### Rx in first 24 hours:

- IVF _______ mL, Vasopressor ( Y / N ), Inotrope ( Y / N ), Transfusion ( Y / N ), Mech Vent ( Y / N )

---

### STOP Sepsis Bundle Quality Achieved (All Quality Indicators Met):

<table>
<thead>
<tr>
<th>Y / N</th>
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</table>

- Bundle Quality was NOT targeted because of patient advanced directive or clinician judgment (noted in the chart)

---

### Total Lengths of Stay:

- Total Length of Stay in the Emergency Department (if applicable) _______ (hrs)
- Total Days of Mechanical Ventilation (if applicable) _______ (days)
- Total Length of Stay in the ICU _______ (days)
- Total Length of Hospital Stay _______ (days)
- In-Hospital Mortality Died / Lived
STOP Sepsis Bundle Quality Indicators (v9.3)
Loma Linda University

**Denominator:** Number of patients (monthly) meeting criteria for septic shock or severe sepsis with lactate $\geq 4$ mmol/L.

**Process Measures (Numerator):** Percentage of patients having each of the following *process measures* completed within the first 48 hours of meeting criteria for septic shock or severe sepsis with lactate $\geq 4$ mmol/L.

- LLU-SS-1 – Lactate measured
- LLU-SS-2 – CVP/ScvO$_2$ monitoring within 2 hours
- LLU-SS-3 – Cultures obtained prior to antibiotics
- LLU-SS-4 – Antibiotics within 4 hours
- LLU-SS-5 – CVP $\geq 8$ mmHg within 6 hours
- LLU-SS-6 – MAP $\geq 65$ mmHg or SBP $\geq 90$ mmHg within 6 hours
- LLU-SS-7 – ScvO$_2$ (or SvO$_2$) $\geq 70\%$ within 6 hours
- LLU-SS-8 – Corticosteroid if vasopressor dependent and/or adrenal insufficiency
- LLU-SS-9 – Assess for drotrecogin alfa activated (APACHE II calculated) within 24 hours
- LLU-SS-10 – Drotrecogin alfa activated within 48 hours if indicated
- LLU-SS-11 – Median glucose maintained < 150 mg/dL
- LLU-SS-12 – Median plateau pressure maintained $\leq 30$ cmH$_2$O if on mech ventilation

**Outcome measures (for all patients in the denominator):**
- LLU-SS-13 – Mechanical ventilator days
- LLU-SS-14 – ICU length of stay
- LLU-SS-15 – In-hospital mortality

Note: These indicators are measurable at our institution, and are adapted from ongoing efforts by the Surviving Sepsis Campaign / Institute for Healthcare Improvement (Adv Sepsis 2005;4(3):108-111), Volunteer Hospitals of America Transforming the ICU (TICU) Project, JCAHO, and the STOP Sepsis Quality Improvement Project (LLUMC).