Contact for Content:
Name: Pierre Kory, MD- Medicine- Pulmonary Medicine
Phone Number: (608) 265-5532
Email Address: pkory@medicine.wisc.edu

Name: Brian Sharp, MD- Emergency Medicine- General
Phone Number: (608) 262-2398
Email Address: bsharp@medicine.wisc.edu

Contact for Changes:
Center for Clinical Knowledge Management (CCKM)
Email Address: CCKM@uwhealth.org

Coordinating Team Members:
Robert Hoffman, MD – Hospital Medicine
Jeffrey Pothof, MD – Emergency Medicine
Leslie Thompson, MD – Hospital Medicine
Ann O’Rourke, MD – Trauma Surgery
Derrick Chen, MD – Laboratory
Jayne McGrath, CNS – Emergency Medicine
Joanna Dagenais, CNS – Nursing Education
Christine Hellenbrand, RT – Respiratory Therapy
Jeffrey Fish, PharmD – Inpatient Pharmacy
Lucas Schulz, PharmD – Inpatient Pharmacy
Josh Vanderloo, PharmD – Drug Policy Program
Diana Renken, PharmD – Center for Clinical Knowledge Management
Katherine Le, PharmD – Center for Clinical Knowledge Management

Committee Approvals/Dates:
Clinical Knowledge Management (CKM) Council (9/27/18)
**Introduction**

In the United States, sepsis caused the death of over 38,000 patients in 2013 and is considered to be a high-burden healthcare problem with mortality exceeding 20% in severe sepsis and nearly 50% in patients with septic shock. The Surviving Sepsis Campaign (SSC) was developed in 2002 in an attempt to reduce the mortality rate by calling for improvements and outlining best practice in care for this patient population. Implementation of and compliance with the evolving Surviving Sepsis Campaign recommendations (updated in 2005 and 2012) has resulted in a 25% relative risk reduction in mortality rate. In 2015, the Centers for Medicare & Medicaid Services (CMS) issued core measure standards to drive quality care. The following guideline outlines the expected care at UW Health which includes recommendations based on recent evidence and/or expert opinion/consensus.

**Scope**

**Intended Users:** Physicians, Advanced Practice Providers, Nursing, Pharmacists

**Objective(s):** To outline evidence-based recommendations for the diagnosis and management of sepsis, severe sepsis, and septic shock.

**Target Population:** Adult patients age 18 years or older who present with suspected or confirmed sepsis, severe sepsis or septic shock in the emergency department or following inpatient admission.

**Clinical Questions Considered:**
- When should intravenous hydrocortisone, ascorbic acid and thiamine be considered for treating sepsis?
- What interventions should be completed within first 3 hours of presentation?
- What interventions should be completed by 6 hours from initial presentation?

**Definitions**

**NOTE:** The following definitions were developed using literature evidence and local consensus/expert opinion and align with requirements of external reporting metrics. While recent literature has introduced the use of the Sequential (Sepsis-Related) Organ Failure Assessment (SOFA) score or qSOFA score in place of SIRS criteria to define sepsis and septic shock (SEP-3 definitions), the methodology and validity of these new definitions has been questioned in emerging literature, and further publications are desired prior to incorporation in this guideline or practice at UW Health. Documentation of sepsis using the SOFA or qSOFA score alone is inadequate; however, these tools could be considered as *adjunctive* tools to support stratification of patients following initial identification/documentation via SIRS criteria.

**Sepsis:** Suspected source of clinical infection and 2 or more systemic inflammatory response syndrome (SIRS) criteria.

<table>
<thead>
<tr>
<th>SIRS Criteria&lt;sup&gt;12-14&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core temperature &lt; 36°C (96.8°F) or &gt; 38°C (100.4°F)</td>
</tr>
<tr>
<td>Heart rate &gt; 90 bpm</td>
</tr>
<tr>
<td>Respiratory rate &gt; 20 breaths/min or paCO₂ &lt; 32 mmHg or the requirement of invasive mechanical ventilation for an acute process</td>
</tr>
<tr>
<td>White blood cell count (WBC) &gt; 12 x 10⁹ mm⁻³ or &lt; 4 x 10⁹ mm⁻³ or &gt; 10% immature band forms</td>
</tr>
</tbody>
</table>
**Severe Sepsis:** Suspected source of clinical infection, 2 or more systemic inflammatory response syndrome (SIRS) criteria, and the presence of sepsis-induced organ dysfunction not attributed to baseline medical condition or medication (e.g., chronic kidney disease or use of warfarin).

<table>
<thead>
<tr>
<th>SIRS Criteria&lt;sup&gt;12-14&lt;/sup&gt;</th>
<th>Sepsis-induced organ dysfunction&lt;sup&gt;15&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core temperature &lt; 36°C (96.8°F) or &gt; 38°C (100.4°F)</td>
<td>SBP &lt; 90 mm Hg</td>
</tr>
<tr>
<td>Heart rate &gt; 90 bpm</td>
<td>MAP &lt; 65 mm Hg</td>
</tr>
<tr>
<td>Respiratory rate &gt; 20 breaths/min or paCo2 &lt; 32 mmHg or the requirement of invasive mechanical ventilation for an acute process</td>
<td>Creatinine &gt; 2.0 mg/dL or increase of &gt; 0.5 mg/dL from previous value</td>
</tr>
<tr>
<td>WBC &gt; 12 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &lt; 4 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &gt; 10% immature band forms</td>
<td>Urine output &lt; 0.5 mL/kg/hr for &gt; 2 hours</td>
</tr>
<tr>
<td>WBC &gt; 12 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &lt; 4 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &gt; 10% immature band forms</td>
<td>Bilirubin &gt; 2.0 mg/dL</td>
</tr>
<tr>
<td>WBC &gt; 12 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &lt; 4 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &gt; 10% immature band forms</td>
<td>Platelets &lt; 100,000/µL</td>
</tr>
<tr>
<td>WBC &gt; 12 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &lt; 4 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &gt; 10% immature band forms</td>
<td>INR &gt; 1.5 or PTT &gt; 60 secs</td>
</tr>
<tr>
<td>WBC &gt; 12 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &lt; 4 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &gt; 10% immature band forms</td>
<td>Lactate above upper limits laboratory normal (e.g., &gt; 2.0 mmol/L)</td>
</tr>
<tr>
<td>WBC &gt; 12 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &lt; 4 x 10&lt;sup&gt;9&lt;/sup&gt; mm&lt;sup&gt;3&lt;/sup&gt; or &gt; 10% immature band forms</td>
<td>Acute respiratory failure with invasive or non-invasive ventilation</td>
</tr>
</tbody>
</table>

**Septic Shock:** Patients meeting criteria for severe sepsis with sepsis-induced hypoperfusion, using markers of either systolic blood pressure (SBP) < 90 mm Hg or mean arterial pressure (MAP) < 65 mm Hg persisting despite adequate fluid resuscitation OR lactate ≥ 4 mmol/L (regardless of timing of fluid administration).<sup>16</sup>

Blood pressure thresholds for sepsis-induced hypoperfusion should not be attributable to baseline medical condition, medication, or individual patient state (e.g., patients with end-stage liver disease and/or cirrhosis).

**Recommendations**

**Screening and Diagnosis**

1) Routine screening of potentially infected seriously ill patients in the Emergency Department for severe sepsis to increase the early identification of sepsis and allow implementation of early sepsis therapy is recommended.<sup>15,17-19</sup> *(UW Health Low quality evidence, recommendation C)*

2) Obtain appropriate cultures before antimicrobial therapy is initiated if such cultures do not cause significant delay (> 45 min.) in the start of antimicrobial administration.<sup>15</sup> *(SSC Grade 1C)* For more information on blood cultures in adult patients, refer to *UW Health Policy 2.5.6 – Blood Cultures for Adult Patients*.

3) It is recommended to perform imaging studies promptly in attempts to confirm a potential source of infection.<sup>15</sup> *(UW Health Very low quality evidence, recommendation S)* Potential sources of infection should be sampled as they are identified and in consideration of patient risk for transport and invasive procedures (e.g., careful coordination and aggressive monitoring if the decision is made to transport for a CT-guided needle aspiration). Bedside studies, such as ultrasound, may avoid patient transport.
Initial Resuscitation

Within 3 hours of Presentation

1) Patients with suspected or confirmed severe sepsis and hypotension or elevated lactate (≥ 4 mmol/L) should receive in total a minimum of 30 mL/kg (total body weight) intravenous fluid challenge, generally administered as quickly as possible. Greater amounts of fluid may be needed in some patients.15 (SSC Grade 1C)

Crystalloids (normal saline or lactated Ringer’s solution) are recommended as the initial fluid of choice in the resuscitation of severe sepsis and septic shock.15 (SSC Grade 1B) Use of hydroxyethyl starches (HES) is not recommended for fluid resuscitation.15 (SSC Grade 1B) For recommendations related to the use of albumin, refer to the UW Health Albumin – Adult – Inpatient Clinical Practice Guideline.

2) Obtain and use lactate level as a marker of shock in patients with suspected severe sepsis or septic shock.20-24 (UW Health Moderate quality evidence, recommendation S) An association exists between elevated lactate levels and increased risk of need for ICU support25 and increased mortality.21,24,26-30

3) The administration of effective intravenous antimicrobials within the first hour of recognition of septic shock (SSC Grade 1B) and severe sepsis without septic shock (SSC Grade 1C) should be the goal of therapy.15,31 It is recommended that initial empiric anti-infective therapy include one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into the tissues presumed to be the source of sepsis.15 (SSC Grade 1B)

For Gram-negative infections, reference the UW Health Pharmacokinetic/Pharmacodynamic Dose Optimization of Antibiotics for the Treatment of Gram-Negative Infections – Adult – Inpatient Clinical Practice Guideline.

For skin and soft tissue infections, refer to the UW Health Skin, Skin Structure, and Soft Tissue Infection Diagnosis and Treatment - Adult -Inpatient/Ambulatory Clinical Practice Guideline.

For urinary tract infections, refer to the UW Health Diagnosis and Treatment of Infections of the Urinary Tract – Adult – Inpatient/Ambulatory Clinical Practice Guideline.

For suspected or confirmed Clostridium difficile infections, refer to the UW Health Prevention, Diagnosis, and Treatment of Clostridium difficile Infection- Adult/Pediatric – Inpatient/Ambulatory Clinical Practice Guideline.

For sepsis of unknown origin, a general approach to empiric treatment is to use broad-spectrum antibiotics such as antipseudomonal β-lactam and anti-MRSA agents (e.g., cefepime and vancomycin or piperacillin/tazobactam and vancomycin; combination piperacillin/tazobactam and vancomycin may be a risk factor for acute kidney injury). For patients in septic shock, a second Gram-negative agent (e.g., aminoglycoside or ciprofloxacin) is recommended.32 For patients with a history of multidrug-resistant (MDR) organisms, empiric therapy should be tailored according to previous sensitivities. The use of prior antibiotic regimens should be considered when selecting therapy32-34 (UW Health Low
Clinicians may also consult UW Health antibiograms when selecting therapy as well.

Patients in the ICU receiving β-lactam antibiotics for treatment of severe sepsis or septic shock should receive their first dose of antibiotic as a 30-minute infusion to reduce the time to a therapeutic concentration.33,34 (UW Health Moderate quality of evidence, recommendation S) In addition, patients with severe sepsis or septic shock may have augmented renal clearance and thus require higher doses than what calculated renal function predicts and from what is outlined in the UW Health Renal Function-Based Dose Adjustments clinical practice guideline.35

Within 6 hours of Presentation

1) Protocolized hemodynamic therapy using specific targets for resuscitation (i.e., strict ScVO2 monitoring, red blood cell transfusion if Hgb > 7 g/dL) of severe sepsis or septic shock is no longer recommended.12-14,36,37 (UW Health High quality evidence, recommendation S) Indications for blood transfusion are outlined within the UW Health Indications for Blood Product Transfusion – Adult – Inpatient/Ambulatory Clinical Practice Guideline.

2) An association exists between elevated lactate levels and increased risk of need for ICU support25 and increased mortality.27-30 Repeat lactate monitoring within six hours of an initial elevated level (> 2.0 mmol/L) in all patients with severe sepsis or septic shock is a CMS Sepsis Core Measure (2015). Therefore, drawing repeat levels is recommended in patients with severe sepsis or septic shock and an initial lactate level of > 2.0 mmol/L29,38 in the emergency department, intensive care or intermediate care settings11,13, (UW Health Low quality evidence, recommendation S) and also in general care patients. (UW Health Very low quality, recommendation C)

3) Vasopressor therapy may be applied in patients with septic shock following initial fluid challenge to initially target a MAP of 65 mm Hg.15 (SSC Grade 1C) It is recommended that all patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available.15

Norepinephrine is recommended as the first-choice vasopressor.15 (SSC Grade 1B) Vasopressin can be added to norepinephrine with the intent of raising MAP to target or decreasing norepinephrine dosage.15 Epinephrine (added to and potentially substituted for norepinephrine) is suggested when an additional agent is needed to maintain adequate blood pressure.15 (SSC Grade 2B)

Dopamine is suggested as an alternative vasopressor agent to norepinephrine only in highly selected patients (e.g., low risk of tachyarrhythmia and absolute or relative bradycardia).15 (SSC Grade 2C) Low-dose dopamine is not recommended to be used for renal protection.15 (SSC Grade 1A)

Phenylephrine is not recommended in the treatment of septic shock except in the following circumstances15 (SSC Grade 1C):

- Norepinephrine is associated with serious arrhythmias
- Cardiac output is known to be high and blood pressure is persistently low
- Salvage therapy when combined inotrope/vasopressor drugs and low-dose vasopressin have failed to achieve MAP target.
A trial of dobutamine infusion is recommended to be administered in patients with septic shock and in the presence of severe myocardial dysfunction or ongoing signs of hypoperfusion, despite achieving adequate intravascular volume and adequate mean arterial pressure. (UW Health Very low quality of evidence, recommendation C)

For additional recommendations, see the UW Health Vasoactive Continuous Infusions – Adult – Inpatient Clinical Practice Guideline.

4) In intensive care patients requiring greater amounts of fluid, it is recommended that a fluid challenge technique is applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (e.g., change in pulse pressure, stroke volume variation) or static (e.g., arterial pressure, heart rate) variables.\(^\text{15}\)

Reassessment of tissue perfusion after initial fluid resuscitation and within 6 hours of presentation is recommended in patients with septic shock. (UW Health Very low quality evidence, recommendation C) Preference should be given to non-invasive monitoring techniques. (UW Health Very low quality evidence, recommendation C)

Reassessment may include a focused clinical exam with documentation of vital signs, cardiopulmonary exam, capillary refill, peripheral pulse evaluation, skin findings, mental status, and urine output OR any two of the following:

- Invasive monitoring (i.e., CVP, ScvO\(_2\))\(^\text{15}\); or
- Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge\(^\text{39,40}\); or
- Bedside cardiovascular ultrasound.\(^\text{41-43}\)

Table 1. Interventions to complete within 3 and 6 hours of presentation for patients with suspected severe sepsis or septic shock*

<table>
<thead>
<tr>
<th>Within 3 hours of presentation</th>
<th>Within 6 hours of presentation</th>
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<tbody>
<tr>
<td>• Assess level of shock by measuring lactate level</td>
<td>• Repeat lactate monitoring within six hours of an initial elevated level (&gt; 2.0 mmol/L) in all patients with severe sepsis or septic shock i</td>
</tr>
<tr>
<td>• Obtain blood culture prior to initiating antimicrobial therapy if culture will not cause significant delay in administration</td>
<td>• Vasopressor therapy may be applied in patients with septic shock following initial fluid challenge to initially target a MAP of 65 mm Hg.</td>
</tr>
<tr>
<td>• Administer IV antimicrobial within first hour of recognition</td>
<td>• Reassess tissue perfusion (i.e., lactate level) after initial fluid resuscitation in patients with septic shock.</td>
</tr>
</tbody>
</table>
| • Patients with suspected or confirmed severe sepsis and hypotension or elevated lactate (≥ 4 mmol/L) should receive in total a minimum of 30 mL/kg (total body weight) IV fluid challenge, generally administered as quickly as possible. | *

* SSC recommends interventions to be completed as a single “hour-1” bundle to encourage resuscitation and management immediately in seriously ill patients.\(^\text{44}\)
Ongoing Management and Treatment

Goals of Care
1) It is recommended to discuss the goals of care and prognosis with patients and families. \(^{15}\) (SSC Grade 1B) The goals of care should be incorporated into treatment and end-of-life care planning, utilizing palliative care principles where appropriate. \(^{15}\) (SSC Grade 1B)

2) It is suggested that goals of care be addressed as early as feasible, but no later than 72 hours following ICU admission. \(^{15}\) (SSC Grade 2C)

Source Control
1) A specific anatomical diagnosis of infection requiring consideration for emergent source control (e.g., necrotizing soft tissue infection, peritonitis, cholangitis, intestinal infarction) is recommended to be sought and diagnosed or excluded as rapidly as possible, and intervention should be undertaken for source control within the first 12 hours after the diagnosis is made, if feasible. \(^{15}\) (SSC Grade 1C) When source control in a severely septic patient is required, the effective intervention associated with the least physiologic insult should be used (e.g., percutaneous rather than surgical drainage of an abscess).

2) It is suggested that when infected peripancreatic necrosis is identified as a potential source of infection, definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has occurred. \(^{15}\) (SSC Grade 2B)

3) If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established. \(^{15}\) (UW Health Very low quality evidence, recommendation S)

4) Once a source pathogen is identified (i.e., culture, PCR testing), and/or patient is hemodynamically stable, consider antimicrobial deescalation. (UW Health Very low quality evidence, recommendation C)

Corticosteroids and Vitamin Infusion Therapy
1) If adequate fluid resuscitation and vasopressor therapy restore a patient’s hemodynamic stability, intravenous hydrocortisone is not suggested as a treatment for sepsis. If hemodynamic stability is not achieved or patient requires high dosages of vasopressor therapy, intravenous hydrocortisone alone at a dose of 200 mg per day can be considered. \(^{15}\) (SSC Grade 2C)

2) Corticosteroids should not be administered for the treatment of sepsis in the absence of shock. \(^{15}\) (SSC Grade 1D) The ACTH stimulation test should not be used to identify adults with septic shock who should receive hydrocortisone. \(^{15}\) (SSC Grade 2B)

3) For patients with septic shock, intravenous hydrocortisone, ascorbic acid (Vitamin C) and thiamine may be considered (i.e., iHAT therapy) with the following dosing\(^{45,46}\) (UW Health Low quality of evidence, recommendation C):
   - Hydrocortisone 50 mg every 6 hours\(^{45}\)
   - Intravenous ascorbic acid 1.5 grams every 6 hours\(^{45}\)
   - Intravenous thiamine 200 mg every 12 hours\(^{45}\)
Glucose Control
A protocolized approach to blood glucose management which describes insulin infusion initiation when two consecutive blood glucose levels are > 180 mg/dL in ICU patients with severe sepsis is recommended.\textsuperscript{15,47,48} This approach should target an upper blood glucose level < 180 mg/dL, rather than an upper target blood glucose ≤ 110 mg/dL.\textsuperscript{15,47} \textit{(SSC Grade 1A)}

Glucose levels obtained with point-of care testing of capillary blood in patients with sepsis should be interpreted with caution; as such measurements may not accurately estimate arterial blood or plasma glucose values. For protocolized care, refer to the \textit{Wisconsin Insulin Infusion – Adult - Inpatient Practice Protocol}.

Bicarbonate Therapy
Sodium bicarbonate is not recommended for the purpose of improving hemodynamics or reducing vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH ≥ 7.15.\textsuperscript{15} \textit{(SSC Grade 2B)}

Disclaimer
Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician’s judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

Methodology
Development Process
Each guideline is reviewed and updated a minimum of every 3 years. All guidelines are developed using the guiding principles, standard processes, and styling outlined in the UW Health Clinical Practice Guideline Resource Guide. This includes expectations for workgroup composition and recruitment strategies, disclosure and management of conflict of interest for participating workgroup members, literature review techniques, evidence grading resources, required approval bodies, and suggestions for communication and implementation.

Methods Used to Collect the Evidence:
The following criteria were used by the guideline author(s) and workgroup members to conduct electronic database searches in the collection of evidence for review.

Literature Sources:
- Electronic database search (e.g., PubMed)
- Hand-searching journals, external guidelines, and conference publications

Time Period: June 2018 to September 2018

The following is a list of various search terms that were used individually or in combination with each other for literature searches on PubMed: sepsis, vitamin c, ascorbic acid, guideline, lactate.

Methods to Select the Evidence:
Literary sources were selected with the following criteria in thought: English language, subject age, publication in a MEDLINE core clinical journal and strength of expert opinion (e.g., professional organization or society).
Methods Used to Formulate the Recommendations:
The workgroup members agreed to adopt recommendations developed by external organizations and/or created recommendations internally via a consensus process using discussion of the literature and expert experience/opinion. If issues or controversies arose where consensus could not be reached, the topic was escalated appropriately per the guiding principles outlined in the UW Health Clinical Practice Guideline Resource Guide.

Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations:
Recommendations developed by external organizations maintained the evidence grade assigned within the original source document and were adopted for use at UW Health.

Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (see Figure 1).

Figure 1. GRADE Methodology adopted by UW Health

<table>
<thead>
<tr>
<th>Step 1: Identify Type of Evidence</th>
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<tbody>
<tr>
<td>Randomized controlled trial (HIGH)</td>
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<tr>
<td>Observational study (LOW)</td>
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<tr>
<td>Expert consensus (VERY LOW)</td>
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<tr>
<th>Step 2: Consider Downgrade or Upgrade</th>
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<tbody>
<tr>
<td>Risk of bias</td>
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<tr>
<td>Inconsistency</td>
</tr>
<tr>
<td>Indirectness</td>
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<tr>
<td>Imprecision</td>
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<tr>
<td>Publication bias</td>
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<tr>
<td>Large consistent effect</td>
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<tr>
<td>Dose response</td>
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<tr>
<td>Confounders only reducing size of effect</td>
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<tr>
<th>Step 3: Assign Quality of Evidence</th>
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<tbody>
<tr>
<td>High</td>
</tr>
<tr>
<td>Moderate</td>
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<tr>
<td>Low</td>
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<tr>
<td>Very Low</td>
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<tr>
<th>Step 4: Consider External Factors</th>
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<tbody>
<tr>
<td>Balance of benefits/harms</td>
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<tr>
<td>Patient preferences</td>
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<tr>
<td>Cost-effectiveness</td>
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<th>Step 5: Assign Strength of Recommendation</th>
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<tbody>
<tr>
<td>Strong</td>
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<tr>
<td>Weak/Conditional</td>
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GRADE Ranking of Evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
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<tbody>
<tr>
<td>High</td>
<td>We are confident that the effect in the study reflects the actual effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.</td>
</tr>
<tr>
<td>Low</td>
<td>The true effect may differ significantly from the estimate.</td>
</tr>
<tr>
<td>Very Low</td>
<td>The true effect is likely to be substantially different from the estimated effect.</td>
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GRADE Ratings for Recommendations For or Against Practice

<table>
<thead>
<tr>
<th>Rating</th>
<th>Description</th>
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<tbody>
<tr>
<td>S</td>
<td>Generally should be performed (i.e., the net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.)</td>
</tr>
<tr>
<td>C</td>
<td>May be reasonable to perform (i.e., may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.)</td>
</tr>
</tbody>
</table>
Surviving Sepsis Campaign (SSC) Determination of the Quality of Evidence

<table>
<thead>
<tr>
<th>Underlying methodology</th>
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<tbody>
<tr>
<td>A (high) RCTs</td>
</tr>
<tr>
<td>B (moderate) Downgraded RCTs or upgraded observational studies</td>
</tr>
<tr>
<td>C (low) Well-done observational studies with control RCTs</td>
</tr>
<tr>
<td>D (very low) Downgraded controlled studies or expert opinion based on other evidence</td>
</tr>
</tbody>
</table>

Factors that may decrease the strength of evidence

1. Poor quality of planning and implementation of available RCTs, suggesting high likelihood of bias
2. Inconsistency of results, including problems with subgroup analyses
3. Indirectness of evidence (differing population, intervention, control, outcomes, comparison)
4. Imprecision of results
5. High likelihood of reporting bias

Main factors that may increase the strength of evidence

1. Large magnitude of effect (direct evidence, relative risk > 2 with no plausible confounders)
2. Very large magnitude of effect with relative risk > 5 and no threats to validity (by two levels)
3. Dose-response gradient

RCT = randomized controlled trial.

Surviving Sepsis Campaign (SSC) Factors Determining Strong vs Weak Recommendation

<table>
<thead>
<tr>
<th>What Should be Considered</th>
<th>Recommended Process</th>
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</thead>
<tbody>
<tr>
<td>High or moderate evidence</td>
<td>The higher the quality of evidence, the more likely a strong recommendation.</td>
</tr>
<tr>
<td>(Is there high or moderate quality evidence?)</td>
<td></td>
</tr>
<tr>
<td>Certainty about the balance of benefits vs. harms and burdens (Is there certainty?)</td>
<td>The larger the difference between the desirable and undesirable consequences and the certainty around that difference, the more likely a strong recommendation. The smaller the net benefit and the lower the certainty for that benefit, the more likely a weak recommendation.</td>
</tr>
<tr>
<td>Certainty in or similar values (Is there certainty or similarity?)</td>
<td>The more certainty or similarity in values and preferences, the more likely a strong recommendation.</td>
</tr>
<tr>
<td>Resource implications, (Are resources worth expected benefits?)</td>
<td>The lower the cost of an intervention compared to the alternative and other costs related to the decision—i.e., fewer resources consumed—the more likely a strong recommendation.</td>
</tr>
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Collateral Tools & Resources

**Metrics**

CMS Core Measures

Within 3 Hours of Presentation:
1. Lactate level
2. Blood culture prior to antibiotic administration
3. Broad spectrum antibiotics
4. Fluid resuscitation

Within 6 Hours of Presentation:
5. Vasopressor
6. Reassessment of volume status and tissue perfusion
7. Repeat lactate level

**Best Practice Alerts (BPA)**

UWIP B SEPSIS NURSE; UWIP B SEPSIS PHYSICIAN; UWIP B SEPSIS PHARMACIST
UWIP B BED REQUEST PNEUMONIA/SEPSIS
Clinical Practice Guidelines
1. Skin, Skin Structure, and Soft Tissue Infection Diagnosis and Treatment – Adult – Inpatient/Ambulatory Guideline
2. Diagnosis and Treatment of Infections of the Urinary Tract – Adult – Inpatient/Ambulatory Guideline
3. Use of Procalcitonin Monitoring Related to the Diagnosis and Treatment of Respiratory Tract Infections and Emerging Sepsis – Adult – Inpatient/Ambulatory Guideline
4. Intravenous Vancomycin Use – Adult – Inpatient Guideline
5. Ventilator Associated Events (VAE) – Adult – Inpatient Guideline
6. Albumin – Adult – Inpatient Guideline
7. Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory

Patient Resources
1. Health Facts For You #5715- Group B Streptococcal Infection

Policies
1. UWHC Clinical Laboratory Policy 1507.P014- Blood Culture Collection

Delegation Protocols
Sepsis Treatment Initiation – Adult – Emergency Department [101]

Practice Protocols
Wisconsin Insulin Infusion – Adult – Inpatient [6]

Order Sets & Smart Sets
ED – Suspected Sepsis Treatment – Adult [5510]
ED – Severe Sepsis Treatment – Adult [3049]
ED – Anti-infectives – Adult Supplemental [4949]
IP – Empiric – Anti-infective Treatment – Adult – Supplemental [6474]
References


