Early Care of Adults With Suspected Sepsis in the Emergency Department and Out-of-Hospital Environment: A Consensus-Based Task Force Report

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INTRODUCTION

Sepsis is a major cause of hospital death in the United States (US)[1] and is associated with over 850,000 annual emergency department visits.[2] Despite advances in care, patients with serious infection continue to have a high inpatient mortality rate, reaching 20% or more in some settings. This makes sepsis and septic shock one of the highest mortality conditions treated in the ED. Additionally, many survivors never fully recover, and instead, long-term morbidities, chronic critical illness, or post-intensive care syndrome develops in them.[3,4]

Public health and policy efforts seek to reduce the morbidity and mortality associated with sepsis and septic shock through state regulations mandating care, public reporting of hospital performance, the creation of national learning networks, and patient-facing public awareness campaigns.[5-8] Despite these efforts, death and incomplete recovery in the following 2 years remains elevated.[9,10] Risk-adjusted mortality varies between regions and hospitals, suggesting that nonstandard clinical treatment pathways leave opportunities to improve.[11,12]

Sepsis care may be most consequential during the earliest phase of treatment. Sepsis in most hospitalized patients in the US (86%) is diagnosed on admission, and up to 80% receive initial care in the ED.[2,13] Furthermore, over 75% of ED sepsis patients are treated by emergency medical services (EMS) providers in the out-of-hospital environment.[14,15] Thus, both out-of-hospital and inhospital emergency care are key in identifying sepsis and initiating early care for those with life-threatening infection.

Many aspects of emergency sepsis care—recognition, prompt and adequate antibiotic therapy, and circulatory support with fluids and vasopressors for those with septic shock—have evidence-based guiding actions that improve outcomes. Given the inherent difficulty in establishing the early diagnosis of sepsis, any guidance must recognize care elements that influence the timeliness and outcomes of care. Aspects that challenge early care include competing ED diagnoses and care, varying levels of evidence for sepsis recommendations, and treating patients with unnecessary therapy when they ultimately have diagnoses other than sepsis.

Recent policy efforts have intensified the scrutiny placed on clinicians, hospitals, and health systems that deliver sepsis care. In July 2018, the US Centers for Medicare and Medicaid Services (CMS) began public reporting of a national sepsis bundle quality measure, commonly referred to as SEP-1. Early data demonstrated that only half of sepsis patients nationally received the full CMS-recommended bundle for emergency and hospital care.[7,16] This finding is unsurprising because clinicians often adjust adherence to guideline-based recommendations based on individual patients and local capabilities. The Surviving Sepsis Campaign offers recommendations on comprehensive sepsis care.[17] These efforts support better care and outcomes, but they have also raised concerns for those in acute care settings, such as EDs, because they initially applied to undifferentiated patients before the diagnosis of sepsis could be confirmed.[18]

To address controversies and opportunities for improvement in the emergency care of patients with sepsis in acute early care settings, the American College of Emergency Physicians (ACEP) convened a multispecialty task force in 2019. A core group of emergency physicians initially created a list of areas where concerns existed, using their individual experiences and accumulated feedback from the ACEP, and then a group majority agreement identified which topics the panel would address. We sought to identify key elements of early sepsis care, offer insight to aid future efforts, and suggest practical consensus-based approaches to certain parts of ED sepsis management. The group did not intend to create a new or comprehensive set of ED sepsis care guidelines.

To ensure the inclusion of diverse opinions and perspectives, the ACEP engaged a broad array of experts to address the topics chosen, with the goal of maximizing the consensus of task force recommendations across many audiences. Task force members reviewed existing guidelines, evidence, and medical professional society recommendations; then, a writing committee crafted sections based on an October 2019 in-person meeting of the task force. The consolidated document was shared over 6 months with the full panel for revision and approval. All of the final areas and recommendations reached super majority (75%) approval, eliminating the need for other consensus mechanisms.

We summarize the task force's assessment of current knowledge and recommendations in this report. We use a format that addresses common steps in the initial emergency care of adults with suspected sepsis. We focused this work on adult sepsis diagnosis and management given recent collaborative pediatric sepsis care guidelines.[19] The task force product was not created to define a practice standard; we intended to inform physicians' judgment at the bedside and to help future guideline development by noting areas of concern.

RECOGNIZING SEPSIS AND SEPTIC SHOCK IN THE FIRST MINUTES TO HOURS OF CARE

Principles of Sepsis Recognition

Key Points:

(1) Sepsis is a confirmed or suspected infection with new or worsening organ dysfunction and dysregulated host response to infection; it is not defined by a single datum or finding.
   - Septic shock exists in a subset of sepsis patients with circulatory dysfunction, and it confers higher mortality.
   - Septic shock—like sepsis—has a spectrum of disease, ranging from hypotension alone to hypotension requiring vasopressor support with an elevated blood lactate level after initial sepsis resuscitation. All patients with impaired cardiovascular function from sepsis are best managed with early detection and prompt treatment, similar to those with more severe presentations of septic shock.

(2) Any guideline or care pathway or bundle must accommodate the reality that sepsis detection can be difficult. The clinical findings of sepsis overlap with many other conditions and often require extended time and effort to detect. Therefore, guidance is most applicable when the diagnosis of sepsis is established rather than simply considered as one of multiple potential causes of illness.
   - The differential diagnosis of sepsis in patients is often broad, and accurate diagnosis of sepsis may require advanced or repeated testing and observation to distinguish it from other causes of acute illness.

Recognizing sepsis early is challenging given the overlapping findings that exist in those with sepsis and those with other acute illnesses. Sepsis is a clinical diagnosis based on a dysregulated response to an infection. Over the last 3 decades, definitions of sepsis from international consensus groups have evolved (Table 1).[20-22] Consistent with the current consensus nomenclature, we considered the definition of sepsis to be an infection with new or worsening organ dysfunction; a specific pathogen does not need to be identified for a patient to have sepsis.

Septic shock is a severe form of sepsis with cardiovascular dysfunction, usually manifested as hypotension. Recent consensus definition efforts (Sepsis-3)[22] have narrowed the definition of septic shock to those

Table 1. Evolution of sepsis definitions.

	First Consensus Definitions (1991)[21]	Second Consensus Definitions (2001)[22]	Third Consensus Definitions (2016)[23]
Infection	Pathology caused by invasion of normally sterile environment by pathogenic microorganisms	No change	Not defined
Sepsis	Inflammatory response from infection with the SIRS criteria proposed to define an inflammatory response	Suspected or confirmed infection with ≥2 SIRS criteria, as defined below: - Temperature of >38 °C or <36 °C - Heart rate >90 beats/min - Respiratory rate >20 breaths/min or PaO_2 <32 mm Hg - White blood cell count >12,000 or <4,000 cells/mm^3 or >10% band neutrophils	Organ dysfunction (defined by increase in SOFA score of ≥2) caused by dysregulated response to infection with a threat to survival
Severe sepsis	Sepsis associated with organ dysfunction	Sepsis with organ dysfunction, defined as any of the following: - Hypotension - Lactate 2 mmol/L or greater - International normalized ratio > 1.5 - Creatinine > 2.1 mg/dL or urine output < 0.5 mL/kg per hour - Platelet count < 110,000/L - Oxygen saturation < 90%	Eliminated (now redundant with "sepsis")
Septic shock	Sepsis with concurrent hypotension despite adequate fluid resuscitation plus perfusion abnormalities, such as elevated lactate levels, low urine output, or altered mental status	Sepsis with concurrent hypotension despite adequate fluid resuscitation	Sepsis with vasopressors required to maintain MAP >65 mm Hg and lactate >2 mmol/L after fluid resuscitation

SIRS, Systemic inflammatory response syndrome.

with hypotension requiring vasopressor therapy *plus* an elevated blood lactate level (2 mmol/L or above) after initial resuscitation (see later discussion) to identify a subgroup at very high risk of mortality. Previous definitions used broader inclusions for defining septic shock, including those with hypotension alone.

We acknowledge that sepsis and septic shock exist on a continuum and that patients with infection-induced cardiovascular failure benefit from prompt recognition and care, no matter what current term defines their status. We also recognize that patients with infection-induced hypotension are an important population in the out-of-hospital and ED settings, as vital signs alone are harbingers of the need for time-sensitive care, even if these patients fail to meet the Sepsis-3 definition of septic shock. A singular episode of hypotension portends a worse outcome, underscoring the need for an inclusive early approach to identifying patients at higher risk of death or harm from sepsis.[23]

No single test accurately and reliably establishes a diagnosis of sepsis. Although some patients present with overt findings of sepsis, many have vague symptoms or examination features that overlap with those of other conditions (eg, tachycardia, tachypnea, laboratory changes, and other findings). Sepsis can be difficult to recognize in the immunocompromised, the elderly, and those presenting very early in the course of illness, when intact or robust compensatory responses may shroud overt signs.

The differential diagnoses of both sepsis and septic shock include other causes of organ dysfunction, many of which require different methods of care. For example, 20% to 40% of patients with *suspected* sepsis in the ED are ultimately diagnosed with a noninfectious sepsis mimic, such as pulmonary embolism, cardiogenic shock, or overdose.[24-26] These patients with sepsis mimics rarely benefit from all aspects of sepsis-directed care. Anchoring on a diagnosis of sepsis early in the illness course can result in missed or delayed diagnosis and treatment of the true cause of acute illness.

The care of those with sepsis should be monitored for impact to identify best practices as well as opportunities for improvement. Sepsis outcomes worsen with delays in care, but giving sepsis-specific care when sepsis does not exist may not offer benefit and can risk harm, though the latter is

not routinely assessed. Further complicating surveillance are initiatives that utilize the easily available time of ED arrival as the starting point for sepsis care, which both ignores sepsis mimics and creates quality benchmarks of limited clinical validity. As a result, and in response to input from the ACEP and others in emergency care, the Surviving Sepsis Campaign revised the start time of bundle initiation from the easily identified *time of ED arrival* to the more difficult to track—but more relevant—*time of sepsis diagnosis*.

We support a paradigm of defining sepsis and septic shock terms and care steps for use across all care settings and clinicians of different specialties, done best with meaningful contribution by all key stakeholders.

Early Screening and Detection of Those With Sepsis

Key Points:

(1) Standardized early sepsis screening tools may improve sepsis recognition and care. However, there is no validated evidence-based tool or strategy to reliably accomplish this goal in the ED or out-of-hospital setting.

Many performance improvement programs aim to improve early sepsis recognition through systematic screening manually or in the electronic health record.[27-29] Presently, although many can improve certain care tasks, there are no early screening systems that are demonstrably effective in improving outcomes of this critical task. Many screening methods tailor activities to the needs and capabilities of individual hospitals or health systems rather than to broadly identifying those in need of sepsis-related interventions. Some early sepsis screening tools have improved timeliness of care, but insight into reliability and patient-focused outcomes is lacking. This question creates uncertainty regarding whether the key feature leading to care improvement is the use of a specific screening tool or the inclusion of healthier patients in the sepsis denominator, or whether the general act of performing quality improvement activities simply increases recognition of sepsis.[30] It is incumbent on clinicians to understand which elements of screening lead to improved outcomes and to embrace those that are best supported.

INITIAL CARE STEPS IN THE EMERGENCY DEPARTMENT AND THE OUT-OF-HOSPITAL ENVIRONMENT

Principles of Early Sepsis Management

Key Points:

(1) History and physical examination may help to detect infection and organ dysfunction.

(2) Once sepsis is recognized, prompt action to treat infection and reverse or prevent hypotension and hypoperfusion is important. However, time thresholds for care must be based on distinguishing sepsis from other clinical diagnoses.

- Accruing evidence of infection, organ dysfunction, and hypotension or hypoperfusion requires longitudinal observation, meaning thresholds based on searchable administrative times alone may not be feasible.

We agree that prompt evaluation and management of patients with suspected sepsis in the out-of-hospital setting and ED are important. Whereas current evidence supports that sepsis care is time sensitive, our review identified a variety of elements that may affect how rapidly the diagnosis of sepsis can be established, especially when presenting signs and symptoms suggest alternate diagnoses. Accordingly, we offer readily deployable and early action for patient care while sepsis is being discerned from other competing diagnoses (Table 2). Once the diagnosis of sepsis is confirmed, current guidelines offer thresholds for time-based action to support optimal care.

Many patients with sepsis have relative or absolute hypovolemia. A variety of management strategies help address plasma volume expansion and other resuscitative actions in those with sepsis and septic shock. One such resuscitation strategy by Rivers et al[31] is termed "early goal-directed therapy," which delineates an algorithmic approach to the recognition and management of patients with sepsis and either hypotension or elevated lactate levels; the Rivers et al did not study all types of patients with sepsis. Early goal-directed therapy relied on central venous pressure, mean arterial pressure (MAP), central venous oxygen saturation, and hematocrit to guide resuscitation. That seminal trial showed that early recognition and resuscitation improved outcomes, but 3 subsequent large multicenter trials spanning from 2008 to 2014 comparing early goal-directed therapy with usual care did not demonstrate improved outcomes with early goal-directed therapy.[32-34] It is important to note that the latter trials employed nonalgorithmic but still early recognition and resuscitation patterns adopted in the interim as "usual care." Therefore, the key aspects of early goal-directed therapy—early recognition and prompt resuscitation—are now foundational to septic shock care.

Out-of-Hospital Care

Key Points:

(1) EMS providers can expedite sepsis care through a focused history and by obtaining corroborating data prior to transport.

Table 2. Key principles in the initial management of patients with suspected sepsis in the out-of-hospital setting and emergency department.

Topic	Out-of-Hospital	Emergency Department
Evaluation for source of infection	Obtain historical elements of when the patient became ill and time course of symptoms.	Focused history and physical examination. Recommended testing includes bacterial and viral specimens for culture or analysis, urinalysis, chest x-ray, and selective cross-sectional imaging as directed by presenting signs, symptoms, and the results of other diagnostic tests.
Severity assessment	Obtain vital signs. Administer supplemental oxygen to maintain SpO_2 $\geq$92%.	Assess for organ dysfunction by physical examination and laboratory assessment. Recommended evaluation for most patients includes blood lactate, complete blood count with differential, chemistry panel, liver function tests, mental status assessment, cardiovascular assessment (heart rate, blood pressure), and respiratory assessment (rate, work of breathing, SpO_2). Administer supplemental oxygen to maintain $\geq$92%.
Treatment and prevention of hypotension	Establish whether hypotension (typically defined as a MAP $<$65 mm Hg or SBP $<$90–100) is present.	Use intravenous fluids and/or vasopressors to resolve hypotension/hypoperfusion.
Intravenous fluid	We recommend using a bolus of isotonic crystalloid (a balanced crystalloid solution is preferred) in patients with systolic blood pressure $<$100 mm Hg and without signs of fluid overload. An initial administration of 500–1,000 mL of isotonic crystalloid is an acceptable, common approach.	Current data do not identify a specific fluid volume that optimizes patient outcomes. In patients with SBP $<$100 mm Hg, MAP $<$65 mm Hg, or other signs of hypoperfusion and without signs of fluid overload, initial administration of 500–2,000 mL (or up to approximately 30 mL/kg) of isotonic crystalloid is an acceptable, common approach. Frequent assessments of fluid status and assessment of the hemodynamic response to fluid administration should guide whether additional fluid is given. Balanced crystalloid solutions are the preferred type of fluid.
Vasopressors	Insufficient data are available to make a recommendation about administration of out-of-hospital vasopressors.	The timing of vasopressor use—after how much volume and based on what response—is not evidence-based. Many initiate a vasopressor infusion (norepinephrine recommended as first-line therapy) for profound shock or persistent hypotension after initial intravenous fluid delivery. Earlier vasopressor use before completing a set volume of fluid administration may be an acceptable alternative. Vasopressors may be administered by peripheral intravenous line or intraosseous line without central venous access. Titrate vasopressors to maintain MAP $\geq$65 mm Hg.
Antibiotics	Insufficient data are available to make a recommendation about administration of out-of-hospital antibiotics.	We recommend prompt administration of antibiotics in the ED, but we reserve very short time thresholds for those with infection and shock and note there are insufficient data to recommend a specific time threshold for administration of antibiotics. In a patient without a confirmed source of infection, broad-spectrum antibiotics with activity against gram-negative and gram-positive bacteria according to local antibiotic susceptibility should be administered. Patients with identified sources of infection (eg, pneumonia, UTI) may have therapy targeted according to source-specific guidelines.
Infection source control	No specific action.	Remove accessible temporary devices that appear infected (eg, temporary urinary and vascular catheters). Consult surgical or procedural specialists for evaluation of patients with infectious sources potentially amenable to procedural source control (eg, abscess, necrotizing soft tissue infection, toxic megacolon).

SBP, Systolic blood pressure; *UTI*, urinary tract infection.

(2) Selecting and rapidly transporting sepsis patients to an ED capable of providing necessary early sepsis care are important factors in out-of-hospital sepsis care.
(3) Out-of-hospital antibiotic therapy has the potential to improve outcomes, but it is not currently supported by data and cannot yet be recommended for routine use.

In the out-of-hospital setting, a key priority is rapidly transporting a patient with potential sepsis to a site capable of providing the care needed. Obtaining a focused history from the patient, family members, caregivers, and others immediately available at the time of patient transport can aid in identifying the cause and severity of illness. EMS providers should communicate this history to ED personnel during the care transition to ensure timely sepsis diagnosis and therapy. Other field diagnostic testing is currently of unproven benefit and is not commonly available. Although giving antibiotics during this very early care interval has theoretic benefit for those with sepsis, the accurate identification of the best patients to receive this therapy is difficult, and the current data do not support a clear benefit of this approach.[35] Future research assessing out-of-hospital diagnostics and interventions may alter recommendations for field care.

Evaluation for Source of Infection

Key Points:

(1) We support obtaining blood cultures in the ED without delaying care in those with suspected sepsis.
(2) In those without an identified source of infection, we support obtaining a chest x-ray and urinalysis (with urine culture if urinalysis is suggestive of infection) in the ED.
(3) We support sampling possible infection sources based on medical history, symptoms, and physical examination findings (eg, cerebrospinal fluid, peritoneal fluid, wounds).
(4) Targeted computed tomography (CT) based on clinical suspicion is preferred to routine whole-body imaging.

In the ED, evaluation for the source of infection should include a history and physical examination, with a review of available and relevant medical records. If a source is not identified with initial examination and testing, we recommend that providers reassess and focus attention on areas of potential cryptic infection that can be difficult to fully examine, including the genitourinary region, perianal region, and sites of medical devices and indwelling catheters.[36]

Although sending samples for culture does not affect initial treatment, isolation of a pathogen from samples collected early and prior to antibiotics can provide source confirmation and enhance appropriate antibiotic tailoring because cultures taken after antibiotics have substantially lower yields.[37-39] We recommend collecting blood cultures as early as feasible and before administration of antibiotics, unless culture collection will delay antibiotic administration. Taking 2 sets of blood cultures (1 aerobic bottle and 1 anaerobic bottle in each set) obtained from separate sites over a short time period is common practice, using techniques to minimize the risk of contamination.[40,41] In a patient with a suspected infection involving an indwelling vascular catheter, collecting one set of blood cultures from the catheter in addition to peripheral blood cultures (with time-to-positivity testing) is one strategy to aid diagnosis of a catheter-related bloodstream infection.

Pneumonia and urinary tract infection are the 2 most common infection sources in sepsis.[36] Absent a clear alternative source, we support chest imaging (usually with chest x-ray) and urinalysis (with subsequent urine culture) in the appropriate clinical circumstances. Additional testing for sources of infection is based on history and examination. For patients presenting with respiratory symptoms when local influenza or severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is prevalent, many clinicians choose molecular viral testing (eg, reverse transcriptase polymerase chain reaction, or RT-PCR) of a nasopharyngeal or respiratory specimen in any patient with respiratory symptoms, fever, or other symptoms of the prevalent infection.[42]

In patients with suspected infection *and* signs of clinical instability (eg, hypotension), we recommend starting antibiotic therapy promptly after blood cultures are drawn. This often means that some culture specimens, such as urine, cerebrospinal fluid, or synovial fluid, follow an initial dose of antibiotics in the ED.

CT may detect other infectious sources.[43-45] We advocate for targeted use of CT based on likely sources of infection after a clinical assessment rather than untargeted "whole-body" CT. Early ED identification of a culprit infection source also supports rapid source control for abscess, intestinal perforation, infected medical prosthesis, or necrotizing soft tissue infection.

Severity Assessment

Key Points:

(1) Clinicians should use multiple clinical and laboratory findings to detect sepsis and guide care.

(2) We support initially measuring blood lactate levels in the ED (venous or arterial) and repeating lactate measurement after initial resuscitation only if elevated above 4 mmol/L or if there is suspicion of clinical deterioration.
(3) After noting whether hypotension is present, no scoring system accurately stratifies individual sepsis patient risk at the earliest stages of care. We recommend assessment of sepsis severity through identifying acute organ dysfunction; collecting data needed to calculate the Sequential Organ Failure Assessment (SOFA) score is one reasonable systematic approach.

Lactate. Blood lactate level is not a specific diagnostic test for sepsis, and elevations can exist for many reasons.[46] Nonetheless, lactate elevations correlate with a higher risk of short-term mortality.[22,47] We endorse the use of venous lactate specimens because this approximates arterial lactate values, is supported by most sepsis literature, and facilitates timelier sampling.

Convenient thresholds used to note abnormal elevation in blood lactate are more than 2.0 mmol/L (evidence of cellular dysfunction) and more than 4.0 mmol/L (evidence of more severe cellular dysfunction).[22,48,49] Just as increasing lactate concentration correlates with a worsening clinical status and an increased risk of death, declining lactate levels with resuscitation are favorable indicators.[46,50]

We agree that obtaining an initial lactate level aids in characterizing sepsis patients, but the most convincing data of benefit from repeat measurements studied those with an initial lactate level of at least 4 mmol/L.[50] The optimal timing to define changes in lactate level that indicate meaningful improvement is not known, but a common practice includes measuring lactate in 2-hour intervals, with a 10% relative decline in lactate between measurements indicating improvement.[50]

SOFA Score. The SOFA scoring system organizes and classifies sepsis-associated organ dysfunction. Like many similar tools, the trajectory of the SOFA score has more prognostic and therapeutic utility than a singular measurement.[22,51] Using the SOFA system to characterize sepsis severity also facilitates serial assessments and communication between providers by supplying a shared nomenclature.

The SOFA score assesses dysfunction across 6 organ systems—respiratory, coagulation, liver, cardiovascular, central nervous, and renal—with a score for each system, ranging from 0 (no dysfunction) to 4 (most severe dysfunction) (Table 3). The total SOFA score is the sum of the component scores for each of the 6 systems, resulting in a range from 0 (no dysfunction) to 24 (most severe dysfunction).

We support testing to assess organ function, which also allows SOFA scoring. Collecting SOFA score data (Table 3) entails an assessment of oxygenation, a complete blood count with platelet count, liver function tests with serum total bilirubin concentration, blood pressure checks and the need for vasopressors, the Glasgow Coma Scale score, and a basic chemistry panel with serum creatinine concentration. Using the original SOFA criteria, scoring respiratory system dysfunction depends on availability of a PaO_2 value to calculate a PaO_2/FiO_2 ratio. We do not advocate performing an arterial blood gas only to obtain PaO_2 for the purposes of calculating a respiratory SOFA score. Patients with a change in SOFA score of at least 2 points compared with baseline (before illness) have life-threatening organ dysfunction and an inhospital mortality risk of at least 10%.[22,52]

An adaptation of the SOFA score may make organ failure–based scoring more feasible for ED assessment (Table 3). In Table 3, we included pulse oximetry (SpO_2) values on specific oxygen flow rates that approximate PaO_2/FiO_2 thresholds in the original SOFA scoring system.[53] SpO_2 and supplemental oxygen flow rate do not precisely correlate with PaO_2 and FiO_2; however, these parameters can provide an estimate of the severity of respiratory dysfunction that is much more feasible in common ED practice. Another option is the modified SOFA, tested in the ED.[54,55]

The "quick SOFA" (qSOFA) scoring tool sought to simplify the key aspects of SOFA scoring for identification of patients at highest risk for poor outcomes. Drawn from ED and hospitalized patients, the qSOFA score identifies infected patients at higher risk of death if 2 or more of the following features are present: respiratory rate of at least 22 breaths/min, altered mental status, and systolic blood pressure of at least 100 mm Hg; these vital sign abnormalities are not unique to patients with sepsis.[22] ED-based validation studies show that qSOFA is less sensitive and more specific for short-term mortality than the 2001 systemic inflammatory response syndrome criteria.[21] Screening with qSOFA is potentially useful for identifying patients at the highest risk for clinical deterioration and need for intensive care, but this tool is not sensitive enough to be used as the sole strategy for sepsis screening. It also was not intended to identify patients with infection, as it was developed to assess outcomes in patients already diagnosed with infection. Only 1 of every 3 patients who are qSOFA-positive on admission has infection, and 1 in 6 has sepsis. The qSOFA score also has low sensitivity for identifying suspected infection and sepsis, and its

Table 3. The Sequential Organ Failure Assessment (SOFA) scoring system modified for use in the ED. Modified from Singer et al[23] and Vincent et al.[51].

System (Measurement)	Score 0	1	2	3	4	Recommended Action in ED
Respiratory						Assess SpO_2 without supplemental oxygen if feasible. Apply oxygen to maintain SpO_2 ≥92%. Note SpO_2 and oxygen delivery once SpO_2 has stabilized at ≥92%.
PaO_2/FiO_2 ratio	≥400	300–399	200–299 or <200 without invasive or noninvasive ventilation	100–199 with invasive or noninvasive ventilation	<100 with invasive or noninvasive ventilation	
Approximate SpO_2 and oxygen delivery						
Without invasive or noninvasive ventilation	SpO_2 ≥97% on room air	SpO_2 92%–96% on room air	Supplemental O2 to maintain SpO_2 ≥92%	NA	NA	
With invasive or noninvasive ventilation	SpO_2 97%–100%		SpO_2 92%–96% on FiO_2=0.3	FiO2 0.31–0.69 to maintain SpO_2 ≥92%	FiO_2 ≥0.7 to maintain SpO_2 ≥92%	
Coagulation						Obtain CBC with platelet count.
Platelets ($10^3/\mu L$)	≥150	100–149	50–99	20–49	<20	
Liver						Obtain liver function tests with total bilirubin concentration.
Total bilirubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0	
Cardiovascular						Assess initial MAP. Initiate fluid resuscitation. Administer vasopressors as needed to maintain MAP ≥65 mm HG.
MAP and vasopressor use	MAP ≥70 without vasopressors	MAP <70 without vasopressors	Dopamine <5 or dobutamine any dose	Dopamine 5.1–15, epinephrine ≤0.1, or norepinephrine ≤0.1	Dopamine >15, epinephrine >0.1, or norepinephrine >0.1	
Central nervous system						Note highest Glasgow Coma Scale in ED (after resuscitation).
Glasgow Coma Scale	15	13–14	10–12	6–9	<6	
Renal						Obtain chemistry panel with creatinine concentration.
Serum creatinine (mg/dL)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9	≥5.0	

CBC, Complete blood count; *NA,* not applicable.

prognostic significance is not specific to infection. More sensitive and specific tools for sepsis screening and risk stratification are needed.[56]

Based on the absence of a single optimal screening method to accurately capture those with sepsis, we think clinicians should employ multiple complementary approaches to identify those with infection accompanied by organ dysfunction to aid care.

Intravenous Fluid and Timing of Vasopressors

Key Points:

(1) We agree with delivering an intravenous (IV) fluid bolus during initial management of patients who have hypotension or findings of hypoperfusion absent signs of fluid overload.
   - We do not support a prespecified volume or body mass–adjusted volume of fluid for all patients, though we recognize many patients benefit from 30 mL/kg of crystalloid. Patient response may serve as the best indicator of the appropriateness of fluid resuscitation volume, rather than the delivery of a prespecified volume.
   - We do not recognize a specific minimum fluid amount before starting vasopressor support.
     i. Vasopressor support may be coupled with plasma volume expansion to prevent cardiovascular collapse in those with severe hypotension or life-threatening hypoperfusion without requiring that a fluid administration threshold be reached prior to vasopressor initiation.
   - We think serial examinations (using more than one bedside tool to assess the adequacy of resuscitation) are best, with no one approach demonstrated as superior to alternative approaches.

(2) We support using balanced crystalloid solutions (Ringer's solution or Plasmalyte) as the primary resuscitation fluid in patients with sepsis, especially if volumes of more than 1 L are used.
   - Infusions of saline solution can cause hyperchloremic metabolic acidosis and may impair renal performance in commonly prescribed resuscitative doses.

Fluid Volume and Concurrent Titration of Vasopressors. Despite the widespread use of intravenous fluids for the management of sepsis, there remains controversy regarding the volume and rate of fluid administration.[57] For the past 2 decades, large mean volumes of intravenous fluid (eg, more than 3,000 to 5,000 mL) have been common in the care of ED patients with sepsis, especially those with septic shock.[58] Whereas intravenous fluid loading can optimize cardiac preload, recent data suggest that the effects of a fluid bolus on hemodynamics are often transient—an observation that may find some explanation in the well-described capillary leak observed with life-threatening infection.[59,60] Recognition of secondary abdominal compartment syndrome and combined outcomes such as the major adverse kidney event assessment show that excessive fluid administration can worsen clinical outcomes.[61-63] Determining how much fluid a given patient needs to abrogate hypovolemia remains a vexing issue. While doing so, one must vigilantly monitor for unintended fluid overload during resuscitation. Furthermore, certain clinical entities may degrade the elasticity of the cardiopulmonary system, as described during the SARS-CoV-2 pandemic, establishing additional concerns regarding fluid prescription titration.[64]

Many trials have used body mass–based intravenous fluid dosing (20 or 30 mL/kg) to guide initial fluid resuscitation, but rigorous clinical trials of different volumes of intravenous fluids are challenging to conduct because of variations in comorbidities, time of presentation, and prevalence of obesity. Practical issues limit the feasibility of body mass–based dosing, including poor estimates of body mass and unit doses of 500 mL and 1,000 mL, which make for natural break-points to assess for clinical response. Finally, patients with sepsis treated with the largest volumes of intravenous fluid in observational studies had less favorable outcomes. These observations raise questions of whether large and continued boluses of fluid improve clinical outcomes or are markers of severity of illness.[63,65-68] Additionally, assessments of fluid administration are confounded by the indication for fluid delivery and the specific endpoints that were assessed.

We do not believe data that support a singular body mass–based volume for all or most patients, although we recognize that many will receive and respond to certain targets like 30 mL/kg. We believe any new guidelines should incorporate titration and response assessment along with defined aliquots, including body mass–based, to optimally improve care. However, some patients will need more than the current guideline-suggested volume, whereas others may need a lesser volume or the same volume administered at a different rate. These different patient elements require bedside reevaluation during the course of resuscitation. Administration of an initial volume of 500 to 1,000 mL of crystalloid is a common and reasonable practice, as it affords the opportunity to gauge the patient's response to the bolus, does not establish an endpoint for fluid therapy, and provides early insight into the need for concomitant vasopressor support.

Table 4. Signs that can assist clinicians with evaluating patient volume status.

Clinical Signs of Hypoperfusion	Clinical Signs of Fluid Overload
SBP <100 mm Hg (or less than baseline SBP for patients with baseline SBP <100 mm Hg)[23]	Development of pulmonary crackles with fluid administration
MAP <65 mm Hg (or less than baseline MAP for patients with baseline MAP <65 mm Hg)	Increased jugular venous distention with fluid administration
Heart pulse rate >110 beats/min	Increased work of breathing with fluid administration
Shock index (pulse rate/SBP) >1.0	Increased hypoxemia with fluid administration
Elevated serum lactate levels	Chest x-ray signs of pulmonary edema
Peripheral capillary refill time >3 seconds[124]	Ultrasound signs consistent with pulmonary edema (eg, B-lines)
Depressed mental status	
Decreased urine output (<0.5 mL/kg per hour)	

The assessment of fluid status and fluid responsiveness is commonly desired to guide care. Table 4 highlights methods currently available to help clinicians with volume status assessment.[69,70] None of these methods is clearly superior to the others at improving sepsis survival; they are only some of the tools available to the bedside clinician to manage sepsis patients. In practice, using multiple tools to guide therapy is preferred, recognizing that the ability to collect some variables may differ across sites.

In addition to simple volume assessment maneuvers, quantitative methods to predict which patients will respond favorably to a fluid bolus ("fluid responsiveness") exist. These methods include measuring collapsibility of the inferior vena cava with bedside ultrasound, directly measuring stroke volume in response to a fluid bolus, and measuring the change in stroke volume or cardiac output in response to a passive leg raise (Table 4).[69-73] Although these methods are physiologically rational, clinical outcome data are insufficient at this time to support a recommendation for their use.

Fluid Type. The 2 major categories of resuscitation fluids are isotonic crystalloids and colloids (Figure 1).

Extravascular leakage of fluid is a physiologic hallmark of sepsis. Infusion of large volumes of crystalloid can contribute to extravascular leakage (edema), which potentially interferes with cellular function, including in the kidneys, liver, heart, and lungs.[59,74,75] The use of colloids is based on the theory that higher-weight molecules limit extravascular leakage and increase long-term intravascular volume.[76] Colloids have properties that potentially make them a better choice for sepsis resuscitation than crystalloids, but sepsis physiology leads to increased capillary permeability, limiting the physiologic benefit in disease. Clinical outcome data have not consistently demonstrated the superiority of colloids over crystalloids.[77-80] We agree that the lack of established benefits and the higher cost of colloids support crystalloid solutions over colloids for initial volume expansion in sepsis.

Among crystalloids, the primary choices are saline solution (0.9% sodium chloride, or "normal saline") and balanced crystalloids.[76] Saline solution contains a supraphysiologic concentration of chloride (154 mmol/L), which can lead to hyperchloremic metabolic acidosis and may increase renal inflammation and impair renal

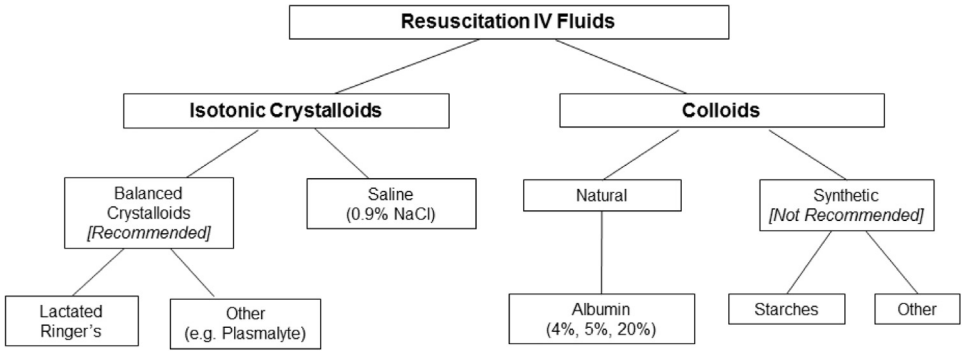

Figure 1. Major types of intravenous fluid available for resuscitation. We recommend balanced crystalloid solutions as the primary fluid type for resuscitation in sepsis. We do not recommend using colloids.

perfusion.[81,82] Balanced crystalloids have a higher physiologic electrolyte composition and include lactated Ringer's solution (chloride concentration 109 mmol/L), Plasmalyte (chloride concentration 98 mmol/L), and Normosol-R (chloride concentration 98 mmol/L).[76] Recent data suggest that fluid resuscitation with balanced crystalloids leads to improved patient outcomes compared with saline solution among a general ED population, those who are critically ill, and those with sepsis.[83-85] Data supporting sepsis patient resuscitation using balanced crystalloids over saline solution are largely based on single-center trials.[83-85] The results of ongoing multicenter trials will more fully characterize the comparative effects of balanced crystalloids and saline solution, but we believe that current evidence coupled with known risks of saline solution are sufficient to favor the use of balanced crystalloids for those with sepsis.[86]

Vasopressors

Key Points:

(1) Norepinephrine is an excellent first-line vasopressor for patients with septic shock.
(2) Titrating vasopressors to maintain a MAP of at least 65 mm Hg in most patients is a common target.
(3) Early vasopressors can be administered through a well-secured nondistal peripheral IV catheter.

Norepinephrine is the preferred first-line agent for patients with septic shock.[87,88] Adding vasopressin (0.03 to 0.04 U/min) is a reasonable approach to reduce norepinephrine requirements and decrease complications, especially at high doses.[88,89] In patients with ongoing hypotension despite high doses of norepinephrine, or in patients with echocardiographic evidence of myocardial depression, epinephrine is a second-line vasopressor and inotropic agent.[90,91]

We recommend titrating vasopressors to maintain a MAP of at least 65 mm Hg unless the patient has baseline hypertension and evidence of hypoperfusion with a MAP of more than 65.[92,93] Consider titration of vasopressors to achieve improvement in markers of organ perfusion (urine output, lactate) as an approach to management of patients with baseline hypertension.

Central venous access was historically required before initiating vasopressor therapy in many sites. This practice affects early sepsis care by delaying the initiation of vasopressor infusion therapy, which may increase large-volume fluid administration while awaiting catheter placement, evaluation, and clearance for use. Current limited data suggest that early administration of peripheral norepinephrine through large-bore peripheral intravenous catheters for short intervals with appropriate monitoring is safe during resuscitation.[94-98]

Antimicrobials

Key Points:

(1) We support early antibiotics once sepsis is diagnosed or deemed likely. The strongest support for initial intravenous antibiotics is in those with suspected diagnosis of septic shock—that is, patients with infection and any hypotension or hypoperfusion.
   - Shorter time to antibiotics is preferred, but the precise time frame to optimally support outcomes remains to be defined.
   - Emerging data will help address the impact of the timing of subsequent doses, especially for patients who remain in the ED due to the lack of an appropriate inpatient bed.
   - Antivirals are less clearly time sensitive in the earliest phases of disease.
(2) For sepsis patients without an identified pathogen, we recommend initiation of broad-spectrum antibiotics with activity against gram-negative and gram-positive bacteria according to local susceptibility patterns.

Antimicrobials: General Principles. Most sepsis patients receive initial doses of antimicrobials in the ED prior to the availability of culture results. In general, clinicians should base the initial selection of antimicrobials on the most likely and most harmful potential pathogens rather than targeting a specific pathogen, unless the clinical presentation directs such a focused approach. Narrow-spectrum therapy is uncommon and should not be anticipated in usual practice. Clinicians should treat patients with broad-spectrum antibacterial agents. Specific patients may require additional coverage for influenza or fungal infections, both of which have been characterized in guidelines or consensus documents; this may be further informed and adjusted by local patient population–appropriate antibiogram data.[42,99-108]

Timing of Antibiotics. Whereas some data suggest that an earlier administration of antibiotics is associated with better survival,[5,109-112] other data suggest that small variations in the timing of a first dose of antibiotics are not associated with mortality differences.[35,113,114] Guidelines often outline time-based approaches to drive earlier action—for example, the Surviving Sepsis Campaign that included the administration of antibiotics by the first hour. We agree that once the diagnosis of sepsis is established, rapid and comprehensive therapy—not just antibiotic administration—is optimal. But the current data do not recommend a singular time

target that clearly improves outcomes for all. In those with the most severe form of sepsis—septic shock—the data and collective experience support a shorter time window; otherwise, the relationship between time and outcome is less clear.[115,116]

Viruses. Viral infections, such as those caused by influenza and SARS-CoV-2, can cause sepsis. Specific treatment recommendations for these viral infections are beyond the scope of this effort. Antiviral therapy can be initiated in the ED, although no timing threshold data exist.

Fungi. Fungi can trigger sepsis, and the most common cause of fungal sepsis is *Candida*. Risk factors for invasive *Candida* infection include prior invasive *Candida* infection, current *Candida* colonization, total parenteral nutrition, recent major abdominal surgery, recent exposure to broad-spectrum antibiotics, recent prolonged hospitalization, acute necrotizing pancreatitis, neutropenia, chronic corticosteroid use, and chronic indwelling vascular catheters.[100] In patients at high risk of fungal sepsis, antifungal therapy with activity for likely pathogens should be initiated in the ED.[117,118]

Infection Source Control

Key Points:

(1) We support early identification of infections requiring source control, and we recommend early consultation and procedural intervention to control infection sources.
(2) No specific timing threshold for achieving source control currently exists.

When infections are suspected that have an easily removable source (eg, indwelling vascular access catheter, soft tissue abscess), early action is appropriate. Focal sources of infection should prompt consultation by procedural specialists for source control, including tunneled vascular catheters, hemodialysis lines, vascular ports, implanted devices, infected ureteral stones, biliary ductal obstruction with cholangitis, deep space or body cavity abscesses, intestinal perforation or obstruction with ischemia, necrotizing soft tissue infection, and complications of infections such as those related to *Clostridium difficile* colitis.[119] Source control should not delay the initiation of resuscitation or antibiotics; resuscitation and source control often need to occur concurrently.

TITRATION OF CARE

Titration of care—that is, delivering ongoing fluids, vasopressor, respiratory support, or other interventions based on the individual response to the first care steps—is relevant to emergency care providers, especially when sepsis patients board in the ED awaiting inpatient bed availability or interfacility transfer.

Ongoing Fluid Administration

Key Points:

(1) Fluid administration after an initial bolus should be based on serial assessments of the patient and response to therapy.
(2) No singular assessment approach is superior, and we recommend using multiple assessments, including basic vital signs and physical examination methods (a clinical evaluation) or more advanced physiologic measurements (quantitative evaluation) at multiple time intervals.
(3) If using a quantitative resuscitation approach, we recommend dynamic measures over static measures.

Up to 50% of patients with septic shock fail to increase cardiac output in response to fluid administration, and when fluid loading does lead to increased cardiac output, the response is often transient.[59,69,120-123] Identifying patients who respond to fluids is one way to tailor an appropriate volume of fluid administration. Septic shock can manifest as a combination of preload-dependent, distributive, and cardiogenic shock, and all patients with ongoing hypotension or elevated lactate levels after initial fluid resuscitation need repeated hemodynamic assessment.

Because no specific method of hemodynamic assessment in treating sepsis patients is clearly superior in altering survival, we present 2 approaches: (1) a *clinical evaluation*, which focuses on basic assessment techniques that are widely available in emergency care settings; and (2) a *quantitative evaluation*, which uses more advanced assessment methods with equipment and expertise that may not be available in all emergency care settings. Both clinical and quantitative evaluations are reasonable approaches for monitoring and serial assessment. Using either method, a key principle is that sepsis assessment should iteratively use multiple parameters to guide therapy.

Clinical Evaluation. The clinical evaluation uses changes in vital signs and the physical examination to assess response to care. Although vital signs (eg, blood pressure and heart rate) and physical examination findings are poorly sensitive markers when taken alone, changes in these parameters are often important indicators to guide therapy. Patients who improve with the initial bolus of fluid are candidates for subsequent fluid boluses, using aliquots (such as 500 to 1,000 mL) followed by repeat serial clinical examinations to evaluate response to fluid administration and evidence of volume overload (Table 4). Clinicians may assess peripheral perfusion (eg, capillary refill), which, in

one trial, performed similarly to lactate clearance in identifying adequacy of fluid resuscitation and selecting fluid resuscitation volumes.[124] Urine output is another tool to assess ongoing resuscitation success, but it is not helpful for the common shorter ED care intervals and is eased by indwelling catheter use, the latter sometimes avoided to lessen iatrogenic infections.[125]

Quantitative Evaluation. Quantitative measures of cardiovascular function assess physiologic changes in response to fluid administration. Current data do not support improved survival with any specific quantitative evaluation, but quantitative methods add insight to those titrating shock therapy. The term "quantitative evaluation" encompasses both static and dynamic measures of volume status. Static measures (eg, central venous pressure) are typically pressures or volumes measured in isolation, whereas dynamic measures evaluate physiologic changes in response to a fluid bolus, passive leg raise, or respiratory variation. We recommend using dynamic measures over static measures because dynamic measures are stronger predictors of a patient's clinical response to fluid administration.[126]

Many dynamic measures exist, including pulse pressure variation, stroke volume variation, passive leg raise measurement with continuous stroke volume or cardiac output measurement, inferior vena cava collapsibility on ultrasound, and the aortic valve velocity time integral.[69,70,127-132] At this time, no data exist to demonstrate that assessment or care provision on the basis of specific dynamic measures are associated with survival more than others.

Vascular Access and Invasive Monitoring

Key Points:

(1) Vasopressor administration through peripheral intravenous or intraosseous catheters that are monitored for signs of good functioning is acceptable for short-term use.
(2) Invasive hemodynamic devices, including central venous and arterial catheters, may aid but are not routinely needed in early sepsis care.

Septic shock patients may have vasopressor therapy initiated through large, well-functioning peripheral intravenous catheters or intraosseous catheters without delay for central venous access. Monitor peripheral catheters used for vasopressor therapy frequently for signs of malfunction or extravasation and obtain central venous access if access challenges exist or if prolonged therapy is anticipated.[95,96,133]

During the early period of resuscitation, noninvasive blood pressure measurement is reasonable, especially if blood pressure normalizes with fluid or vasopressor administration.[134-137] Patients with poor or unreliable blood pressure measurements by noninvasive blood pressure cuffs may benefit from arterial catheter placement for blood pressure monitoring and titration of therapy.

Subsequent Doses of Antibiotics

Key Points:

(1) Patients who remain in the ED for prolonged periods should have subsequent doses of antibiotics administered according to the optimal dosing schedule for each medication.

For patients remaining in the ED for prolonged periods, second and subsequent doses of antibiotics are important to optimize the antimicrobial effect. These doses must be scheduled and administered regardless of where the patient is located. Delays in follow-up antibiotics are associated with worse outcomes, and EDs must ensure safe transitions and ongoing dosing.[138]

Adjunctive Early Sepsis Therapies

Key Points:

(1) Routine corticosteroid therapy does not benefit sepsis patients unless there is concomitant adrenal insufficiency or the patient is on high-dose corticosteroid therapy for comorbid disease management prior to the onset of sepsis.
(2) Other adjuncts, including angiotensin II (or analogs), vitamin C, vitamin D, and thiamine—alone or in combination—lack strong evidence supporting benefit and are not recommended.

Patients with sepsis who have been chronically taking corticosteroid therapy[139] or who have preexisting adrenal insufficiency should receive stress-dose hydrocortisone (50 to 100 mg intravenously). However, outside selected sepsis patients, routine corticosteroid use has been controversial. An early randomized trial showed improved survival in patients with poor adrenal response ("relative adrenal insufficiency") and very high illness severity.[140] Subsequent trials have shown varying results, with the most recent evidence suggesting that corticosteroid therapy may speed resolution of shock and shorten intensive care unit and hospital length of stay. Recent meta-analyses have come to varying conclusions on the impact of steroids on mortality, and some now recommend their use.[141-148] We believe that steroids may play a role in patients with hypotension resistant to vasopressor therapy, but that is uncertain; otherwise, the current data do not support routine use outside of adrenal failure or suppression or to treat another condition (eg, immune-modulated respiratory failure).

Other sepsis adjuncts, such as combination therapy with vitamin C, thiamine, and hydrocortisone, as well as novel therapeutics such as angiotensin II, have insufficient evidence to support incorporation into routine ED practice.[63,149-151]

Role of Interhospital Transfer, Inpatient Boarding, and Care Transitions in Sepsis Management

Key Points:

(1) ED boarding (defined as prolonged care awaiting inpatient transfer) presents additional risk for sepsis patients. If local facilities do not have the capabilities to promptly care for critically ill patients, we recommend transfer of sepsis patients from the initial ED to an accepting facility with capabilities for managing these patients.
(2) Each institution should develop a plan that defines explicit accountability for sepsis patients receiving prolonged ED care.

Some facilities do not have the capability to manage patients with complex infections or organ failure syndromes.[152,153] In those centers, prompt recognition and identification for interhospital transfer is important and may parallel existing injury–related care transfer approaches. Because of the importance of early antimicrobial therapy and resuscitation, delivery of antibiotics, IV fluids, and vasopressors should be started prior to transfer, as noted earlier. Some high-performing regional sepsis networks include collaboration with referral centers, providing feedback about patient outcomes, and screening for subsequent inpatient transfers.

Inpatient boarding (eg, prolonged ED care while awaiting inpatient bed availability) is linked to increased mortality in observational studies of patients with severe infection.[111,154-160] Hypothesized reasons for worse outcomes include delayed administration of subsequent doses of antibiotics, limited monitoring resulting in delayed recognition of changes in patient status, high patient-to-nurse ratios, and provider focus on new patient evaluation.[157,161] To optimize outcomes, we advise prioritizing septic shock patients for early inpatient bed availability owing to increased resource and time demands in care management. Furthermore, hospitals should develop systems to provide the necessary care for patients with sepsis who remain in an ED while awaiting an inpatient bed.[161] During periods of boarding, some facilities incorporate procedures whereby inpatient physician or nurse teams assume care of admitted patients in the ED. These procedures should be clearly delineated so that all members of the care team understand who is responsible and accountable for care. Other facilities have dedicated spaces for critical care management, whereas others, as noted earlier, have dedicated spaces, teams, and supplies. During transitions of care between hospitals, treatment units, or providers, we recommend timely provider-to-provider and nurse-to-nurse communication and the use of standardized care transition protocols.

RELATED CONTROVERSIES

Key Points:

(1) We support recommendations and quality assessment tools required by government or regulatory bodies as important ways to improve the outcomes of those with sepsis, and we believe these should be based on the best available evidence and should undergo regular reevaluation.
(2) The creation of recommendations, guidelines, and quality assessment tools must include input from all relevant stakeholders engaged at each phase of care and must incorporate assessment of impact on both targeted patients and others receiving care.

Quality Metrics. Guidelines for sepsis care include standardized recommendations, such as the Severe Sepsis and Septic Shock (SEP-1) quality reporting measure within the National Hospital Inpatient Quality Reporting program[162] and the Surviving Sepsis Campaign Guidelines. We recognize that these and other efforts raise awareness and performance and potentially improve outcomes. It is also important to recognize that some clinical realities trigger situation-dependent decisionmaking that is requisite for management of the ED sepsis patient. Instead, those decisions may reflect unique patient physiology or response to therapy that requires rapid readjustment. When faced with such clinical challenges, bedside clinicians should not be penalized for responding to patient response to therapy.

When seeking to improve sepsis care, the input of experts with emergency care backgrounds is essential, alongside that of other experts, to ensure that the important early steps align with the knowledge and capabilities of the emergency care system. Those creating recommendations, guidelines, or quality metrics should reach to this pool of partners to optimize the applicability of what is considered optimal and feasible care.

Sepsis Care in Constrained Settings. We focused on care settings with advanced emergency and critical care medicine capabilities, including close hemodynamic monitoring, administration of vasopressors, and mechanical ventilation. We recognize that resource-constrained settings place practical limitations on the care options available; care

Organizations that participated and endorsed the recommendations

American College of Emergency Physicians

American Academy of Emergency Medicine

American College of Osteopathic Emergency Physicians

American Osteopathic Board of Emergency Medicine

Association of Academic Chairs of Emergency Medicine

Council of Emergency Medicine Residency Directors

Emergency Medicine Residents' Association

Emergency Nurses Association

Infectious Diseases Society of America

National Association of EMS Physicians

Society for Academic Emergency Medicine

Society of Hospital Medicine

Society of Critical Care Medicine

Organizations that participated and provided input on the recommendations

American College of Emergency Physicians

American Academy of Emergency Medicine

American Board of Emergency Medicine

American College of Chest Physicians

American College of Osteopathic Emergency Physicians

American Osteopathic Board of Emergency Medicine

American Thoracic Society

Association of Academic Chairs of Emergency Medicine

Council of Emergency Medicine Residency Directors

Emergency Medicine Residents' Association

Emergency Nurses Association

Infectious Diseases Society of America

National Association of EMS Physicians

Society for Academic Emergency Medicine

Society for Hospital Medicine

Society of Critical Care Medicine

Figure 2. Organizations involved in the development of the recommendations.

must be modified in those settings. For example, recent clinical trials in settings where different patient and pathogen patterns existed and where advanced critical care capabilities were uncommon suggested that lower volumes of intravenous fluid administration may lead to better patient outcomes.[61,62] Sepsis remains a leading cause of death in the world, especially in the very young and very old and in resource-limited settings. Improving care in these settings must be distinct in composition from that in highly resourced hospitals in the United States.

In conclusion, our multidisciplinary task force identified opportunities to improve recommendations, guidance, and quality metrics for early sepsis care. The points reviewed and suggested within this document seek to foster the next set of improvements for a leading cause of mortality. We identified many specific content and process opportunities in which research and collaboration could advance care, health, and outcomes. These include clear opportunities to guide fluid, vasopressor, and antibiotic therapy and thoughts on ancillary care and future guideline development. Optimal future sepsis recommendations will rely on a collaborative multiple stakeholder engagement approach to evaluating current processes, designing iterative improvements, and discovering new knowledge in the quest to conquer sepsis.

Members of the American College of Emergency Physicians Multispecialty Sepsis Review Panel reviewed the drafts after initial composition and offered input: Jennifer Alexband, DO, Michael Benham, MD, David A. Farcy, MD, Marianne Gausche-Hill, MD, Sean Hickey, MD, Ryan C. Jacobsen, MD, Chadwick Miller, MD, Michael Puskarich, MD, Chanu Rhee, MD, MPH, Lisa Shieh, MD, PhD, Elizabeth Tedesco, DNP, RN, CEN, PHRN, Julie Winkle Mayglothling, MD, Christopher Zabbo, DO, and Jerry Zimmerman, MD, PhD

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