Early Recognition: The Rate-Limiting Step to Quality Care for Severe Sepsis Patients in the Emergency Department
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ABSTRACT
• **Objective:** To detail strategies to improve sepsis recognition and the quality of care provided to the septic patient.
• **Methods:** Review of the literature.
• **Results:** Severe sepsis affects nearly 3 million individuals each year in the United States, and cost estimates for these hospitalizations exceed $24 billion. Effective management is predicated on timely recognition. In this review, we detail strategies to improve early identification of potentially septic patients as well as the quality of care provided to the septic patient in the emergency department (ED). The strategies discussed are based upon an understanding of the signs and symptoms of sepsis and the clinical risk factors associated with sepsis, which can be used to design novel strategies to screen patients for sepsis and risk stratify patients at risk for clinical deterioration.
• **Conclusion:** ED structures and processes can be used to increase adherence with sepsis management guidelines to improve patient outcomes.

Severe sepsis affects nearly 3 million individuals each year in the United States and cost estimates for these hospitalizations exceed $24 billion [1–3]. Sepsis is a life-threatening condition characterized by a suspected or identified infection accompanied by a vigorous host inflammatory response. In severe sepsis, end-organ dysfunction manifests in myriad forms, including altered mental status, acute kidney injury, liver dysfunction, pulmonary dysfunction, and hemodynamic compromise [4,5]. This protean presentation of a deadly condition makes identification and risk stratification both challenging and essential to improving patient outcomes. The majority of patients with severe sepsis will receive their initial care within an emergency department (ED) [6,7]. It is essential that emergency medicine providers have the means to appropriately identify patients presenting with severe sepsis in a timely manner—thus facilitating life-saving measures such as early intravenous fluid resuscitation and administration of timely and appropriate antimicrobials.

In this review, we detail strategies to improve sepsis recognition and the quality of care provided to the septic patient in the ED. The strategies discussed are based upon an understanding of the signs and symptoms of sepsis and the clinical risk factors associated with sepsis, which can be used to design novel strategies to screen patients for sepsis and risk stratify patients for clinical deterioration. Then, we review suggested ED structures and processes to increase adherence with sepsis-based guidelines to improve patient outcomes. Successful implementation is predicated on hospital administrative support towards the efforts given the time and resources required and strong and committed leadership across the health care system.

**Epidemiology of Severe Sepsis**

Estimates of annual cases of severe sepsis vary, ranging from 1 million to 3 million cases in the United States [1–3]. In-hospital mortality for this condition ranges from 14% to 30% [5]. The incidence of severe sepsis in the United States has been increasing at a rate of 13% annually, with an estimated cost of greater than $24 billion per year [1,2]. In 2 large cohorts of hospitalized patients, it was found that sepsis contributed to 1 in every 2 to 3 deaths following inpatient admission [8]. Coincident with these increased estimates, advances in the early identification and treatment of sepsis have led to decreasing mortality rates over the past decade [1,9].

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Of importance to the ED clinician, an episode of sepsis has long-term effects on cognitive and physical function, quality-of-life, and survival [10,11]. Post-discharge, approximately one-quarter of sepsis survivors will be readmitted within 30 days [12–14]. In as many as half of these instances, another life-threatening infection is the cause for readmission, making the past medical history, including a detailed accounting of recent episodes of sepsis, an important part of the initial ED evaluation [12]. Furthermore, severe sepsis survivors spend a large proportion of their time following discharge within a health care facility, and will frequently present to the ED with an acute condition from such an environment. Important factors for predicting readmission after a sepsis hospitalization include patient age, severity of illness, hospital length of stay, and the need for intensive care during the initial hospitalization [12–14].

**Principles of Effective Sepsis Management**

The principles of effective sepsis management begin with early identification in the pre-hospital setting, at triage, or when a patient begins to decompensate in the hospital. After the point of initial recognition, core principles include risk stratification, timely and appropriate antimicrobial administration, initial intravenous fluid boluses and ongoing resuscitation guided by physical examination and objective resuscitation end-points [4,5]. These practices have been operationalized in the care bundles of the Surviving Sepsis Campaign Guidelines [4]. Within 3 hours, the resuscitation bundle includes measuring serum lactate to risk stratify patients, obtaining blood cultures, administering broad-spectrum antibiotics, and administering 30 mL/kg crystalloid in patients with hypotension or hyperlactatemia [4]. The 6-hour bundle expands upon these initial measures and includes additional management recommendations based on resuscitation end-points.

As effective management is predicated on timely recognition, an understanding of the impact of delayed recognition is essential to provide optimal care for the severe sepsis patient in the ED. Decades of research has revealed that certain markers predict adverse outcomes, including transition to septic shock and death, as do delayed processes of care. Importantly, while early quantitative resuscitation was demonstrated to improve outcomes in a meta-analysis, there was no demonstrable benefit when resuscitation was initiated late (> 24 hours) in the course in the ICU (odds ratio of death, 1.16 [95% confidence interval, 0.60–2.22]) [15].

**Strategies to Improve Recognition**

**Pre-Hospital Environment**

As many as 40% of severe sepsis cases admitted to the hospital from the ED will present to the ED via emergency medical services (EMS) transport, and this rate appears to be increasing over time [16]. Thus, efforts to improve identification and risk-stratification of potential cases of severe sepsis should begin in the pre-hospital environment. These EMS encounters frequently exceed 45 minutes [16], pre-hospital interventions appear to be uncommon [16,17], and establishment of intravenous access paired with fluid resuscitation in the pre-hospital environment may improve survival [18]. Further, when EMS providers recognize sepsis, ED care processes (eg, time to antibiotics, protocol-directed resuscitation) are improved, with shorter time to antibiotics and initiation of early goal-directed therapy (EGDT) [19] and a trend towards achieving goal mean arterial pressure earlier [17]. In sum, while further investigation is required to facilitate this transition, efforts to improve sepsis outcomes should also include the interface between the pre-hospital environment and the ED (Figure).

**From EMS to ED Triage**

Borrowing the principle “time equals tissue” from a variety of time sensitive conditions (eg, myocardial infarction management [“time equals muscle”] and stroke care [“time equals brain”]), clinicians and researchers have realized that expedited recognition of severe sepsis patients begins at the time of initial contact with the health care system. For severe sepsis patients, clinicians need to think “time equals organ function.” Given the frequency with which sepsis patients arrive to the ED via EMS, effective communication between EMS and ED providers could be leveraged to prepare the ED team to provide timely care for the sepsis patient via a “sepsis alert.” While confirmation of its applicability to sepsis care is required in the absence of a regionalized network of sepsis centers, the rationale is based on the experience of the effectiveness of trauma and stroke alert systems [20–22]. For patients not recognized as potentially being infected by EMS providers during transport, repeat vital signs during ED triage can be screened to identify patients exhibiting signs of the systemic inflammatory response syndrome (SIRS) [4,23]. The same principles of effective communication apply for patients being sent from medical clinics to the ED for evaluation and treatment of potential severe sepsis. For patients arriv-
Vital Signs and SIRS Criteria in the ED
The vast majority of patients who are hypotensive in triage are expedited to a treatment room and early resuscitation is begun. However, these patients represent a minority of severe sepsis patients seen in triage; therefore, all available data need to be analyzed to capture the highest percentage of severe sepsis patients. Acknowledging that SIRS criteria are not specific for sepsis [24], will miss as many as 1 out of 8 patients initially [25], and may not predict mortality [26], their presence is nonetheless characteristic of sepsis. As such, identifying the presence of SIRS at triage, or during the ED stay via serial vital signs, facilitates sepsis recognition, as do strategies that leverage routine vital signs to calculate predictors of instability including the shock index (heart rate/systolic blood pressure), where a shock index ≥ 0.7 has been associated with illness severity [27]. An increased respiratory rate has been demonstrated to identify risk for transfer from a floor bed to the ICU within 24 hours of ED admission [28]. Further, clinical manifestations of sepsis, including end-organ dysfunction, are protean, and patients frequently present with nonspecific, constitutional symptoms (eg, weakness, malaise, fever, chills, nausea) that could reflect one of many diseases (Table 1).

The Afferent Arm: Multimodal Screening Strategies
While institutional practice improvement initiatives to facilitate sepsis recognition and care should incorporate educational strategies, led by champions with expertise in sepsis, the complex presentation of sepsis requires multimodal approaches [29]. These multimodal approaches, beginning at the time of ED triage, should be designed to harness information technology to screen patients to improve severe sepsis recognition (the afferent arm) and to utilize structures and processes of care efficiently and effectively (the efferent arm) to guide severe sepsis management according to sepsis-care bundles espoused by guidelines (Figure) [4].

Operational processes to screen for sepsis in the ED will need to account for ED organizational flow (eg,
average time from registration to triage, average time from triage to being seen by a physician, average length of stay in the ED, number of hospital beds) and hand-off practices (e.g., care transition from ED team to floor or ICU team, or within ED at shift change). For ED organizations with shorter ED lengths of stay (e.g., < 2 hours), screening practices at ED triage will serve as the focal point to identify cases of sepsis. Boarding, defined

Table 1. Epidemiologic Risk Factors, Signs, Symptoms, and Organ Dysfunction Associated With Severe Sepsis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Prevalence</th>
<th>Reference</th>
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<tbody>
<tr>
<td><strong>Clinical risk factors</strong></td>
<td></td>
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</tr>
<tr>
<td>Age</td>
<td></td>
<td>2,4–5, 23,43</td>
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<tr>
<td>Diabetes mellitus</td>
<td></td>
<td>2,4–5, 23,43</td>
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<tr>
<td>Alcohol abuse</td>
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<td>2,4–5, 23,43</td>
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<td>Malignancy</td>
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<td>Transplant</td>
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<td>2,4–5, 23,43</td>
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<td>Immunosuppression</td>
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<td>2,4–5, 23,43</td>
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<tr>
<td>Recent hospitalization</td>
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<td>12–14</td>
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<tr>
<td>Recent sepsis hospitalization</td>
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<tr>
<td><strong>Vital signs</strong></td>
<td></td>
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<tr>
<td>Temperature*</td>
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<td>23</td>
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<tr>
<td>Tachycardia*</td>
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<td>23</td>
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<tr>
<td>Shock index (heart rate/systolic blood pressure)</td>
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<td>27</td>
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<tr>
<td>Tachypnea*</td>
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<td>23</td>
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<tr>
<td><strong>Inflammatory variables</strong></td>
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<tr>
<td>White blood cell count*</td>
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<tr>
<td>Bandemia</td>
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<td>23</td>
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<td>Hyperglycemia</td>
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<td><strong>Organ dysfunction in the emergency department†</strong></td>
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<tr>
<td>Serum lactate (≤ 2 mmol/L)</td>
<td>76%</td>
<td>43</td>
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<tr>
<td>Systolic blood pressure &lt; 90 mm Hg‡</td>
<td>42%</td>
<td>43</td>
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<tr>
<td>Acute kidney injury, creatinine &gt; 0.5 above baseline</td>
<td>33%</td>
<td>43</td>
</tr>
<tr>
<td>Mean arterial pressure &lt; 60 mm Hg‡</td>
<td>30%</td>
<td>43</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>27%</td>
<td>43</td>
</tr>
<tr>
<td>Acute kidney injury, creatinine &gt; 2.0 mg/dL</td>
<td>27%</td>
<td>43</td>
</tr>
<tr>
<td>Shock (refractory hypotension)‡</td>
<td>24%</td>
<td>43</td>
</tr>
<tr>
<td>Acute thrombocytopenia‡</td>
<td>15%</td>
<td>43</td>
</tr>
<tr>
<td>Coagulation dysfunction‡</td>
<td>11%</td>
<td>43</td>
</tr>
<tr>
<td>Arterial hypoxemia‡</td>
<td>11%</td>
<td>43</td>
</tr>
<tr>
<td>Hyperbilirubinemia‡</td>
<td>8%</td>
<td>43</td>
</tr>
<tr>
<td>Acute kidney injury, oliguria</td>
<td>6%</td>
<td>43</td>
</tr>
<tr>
<td>Ileus</td>
<td>Not available</td>
<td>23</td>
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*Traditional SIRS criteria defined as temperature > 38.3 or < 36.0, heart rate > 90/minute, tachypnea > 20/minute or PaCO2 < 32 mm Hg, white blood cell count > 12,000 or < 4000.
†In descending order of prevalence, based on published data.
‡Hypotension defined as systolic blood pressure < 90 mm Hg, mean arterial pressure < 70 mm Hg, or a systolic blood pressure decrease > 40 mm Hg from baseline; arterial hypoxemia defined as a partial pressure of arterial oxygen to fraction of inspired oxygen of less than 300; hyperbilirubinemia defined as total bilirubin > 4 mg/dL; acute kidney injury as oliguria (< 0.5 mL/kg/hour for 2 or more hours despite fluid resuscitation) or creatinine increase > 0.5 mg/dL; coagulation dysfunction as international normalized ratio (INR) > 1.5 or activated partial thromboplastin time > 60s; platelet count < 100.
as caring for a patient in the ED pending transfer, is common, increasing as a result of ED closures [30,31], and associated with prolonged hospital length of stay and increased in-hospital mortality when ICU transfer is delayed [32]. Sepsis patients in particular appear to be a vulnerable group of patients. While many explanations exist to account for the relationship between delayed transfer and adverse outcomes, timely recognition and management of the septic patient could be compromised with prolonged boarding. To combat this potential effect, continual assessment during the entire ED stay may unmask an initially unclear presentation of sepsis.

One strategy to identify sepsis in ED organizations with prolonged ED lengths of stay is through the use of a track-and-trigger system, or early warning system. Traditionally, track-and-trigger systems were implemented on the hospital wards, as means to identify physiological deterioration in a timely manner to prevent clinical deterioration [33]. More recently, early warning systems have been used to identify patients with sepsis on the hospital wards and within EDs, as these systems rely on physiological parameters such as SIRS that are cardinal features of sepsis [34]. However, given the potential for alert fatigue, designing a system that operates with high accuracy is imperative.

Efforts are underway to redefine sepsis, using a simplified approach and readily available physiological variables, with the main goal of targeting those most at-risk of an adverse outcome during the hospitalization. Simultaneously, an understanding of the overt and more occult manifestations are essential to incorporate into the clinical decision-making and pattern recognition required to identify sepsis in a timely and accurate manner. In Table 2, the signs and symptoms that may serve as flags for severe sepsis are presented.

Mature early warning systems, designed to leverage the electronic medical record (EMR) by capturing vital signs, laboratory measures, (eg, elevated serum creatinine compared to a recent hospitalization) and symptoms (eg, altered mental status), are well-positioned to herald clinical deterioration (eg, cardiac arrest) with improved accuracy [35] and to be applied to sepsis specifically [34]. While sophisticated analytical strategies, such as machine learning, are being used to improve the test characteristics of these early warning systems, iterative, prospective chart review is an essential and complementary performance improvement step to refine the process. Further, chart review affords the opportunity to ensure compliance with sepsis care bundles.

Knowledge of the risk factors associated with development of sepsis is critical for the front-line emergency physician and nurse. Additionally, as many of these risk factors are associated with adverse outcomes, including unplanned ICU transfer and in-hospital mortality, which occur in as many as one out of 8 patients admitted directly to the ward, they have utility for early risk-stratification and triaging purposes in the ED. Advanced age and pre-existing comorbid conditions, particularly an oncologic diagnosis and/or chronic organ dysfunction, are major risk factors for sepsis and worse outcomes result in those who develop sepsis [2]. Further, illness severity, including an elevated serum lactate level, is associated with adverse outcomes. These factors can be incorporated into triage decisions and/or close monitoring for patients admitted to the general ward [36]. Conversely, because patients admitted to the ICU setting and subsequently stepped down through their hospitalization may experience better outcomes compared to patients admitted to the general ward who then require step-up to an ICU setting (37,38), attention to triage practices is critical.

These complementary strategies, which serve as the afferent arm of the system, summon health care providers to the bedside of a vulnerable patient. However, clinical effectiveness in the management of severe sepsis requires a robust, sophisticated, and mature efferent arm capable of delivering expert care to the now recognized septic patient.

### Principles of Effective Management Post-Recognition

#### Risk Stratification

An elevated serum lactate level was initially described in pathological states in the mid 19th century by Johann Joseph Scherer [39] and has long been associated with increased mortality in hospitalized patients [40]. Lactate is a useful biomarker for risk stratification in a variety of patients arriving to the ED, particularly those who have been identified at high risk for sepsis. Jansen and colleagues examined the measurement of pre-hospital serum lactate at the time of paramedic on-scene assessment in a group of acutely ill patients [41]. Patients with point-of-care lactate levels of 3.5 mmol/L or greater were found to have an in-hospital mortality of 41% versus 12% for those with lactate levels less than 3.5 mmol/L. Within the population with an elevated lactate, patients with a
systolic blood pressure greater than 100 mgHg experienced a mortality of nearly 30%, while it was greater than 50% in hypotensive patients with an elevated lactate, highlighting the value of both hemodynamic and serum lactate measures. Upon arrival to the ED, lactate measurements have a strong correlation with mortality. In one retrospective cohort, lactate level was linearly associated with mortality in a broad array of patients older than age 65 years [42]. An initial serum lactate level in the ED in the intermediate (2.0 – 3.9 mmol/L) or high range (≥ 4 mmol/L) has been associated with increased odds of death 2 to 5 times higher independent of organ dysfunction in severe sepsis specifically [43].

As the association between serum lactate levels and death is independent of organ dysfunction, serum lactate is a simple and reliable tool to both enhance detection and risk-stratify patients presenting to the ED with severe sepsis. Given the frequency with which hyperlactatemia is present in patients with suspected infection [43], operationalizing serum lactate measures with the initial phlebotomy draw is an important step to risk-stratify patients. This step can be coupled later with intravenous fluid resuscitation for those with marked elevations (≥ 4 mmol/L), in accord with guideline recommendations [4]. Screening of initial lactate values can be further expedited by utilizing fingerstick point-of-care lactate devices [44]. Last, while serial lactate measures can be incorporated into triage decisions, there is no clear threshold that warrants ICU admission. Rather, persistent elevations in serum lactate can be used to identify patients who require close observation regardless of their admission location.

Several scoring systems have been developed to augment sepsis risk stratification within the ED. The most prominent of these are the Predisposition Insult Response and Organ failure (PIRO), Sequential Organ Failure Assessment (SOFA), and Mortality in the Emergency Department Sepsis (MEDS) scores, and the National early warning score (NEWS) [45-48]. The MEDS score incorporates host factors including age and co-morbid illness, as well as physiologic and laboratory tests which can be obtained rapidly in an ED setting. Multiple prospective and retrospective examinations of the MEDS scoring systems have demonstrated that it performs optimally in ED patients with sepsis but not those with severe sepsis, in terms of predicting 30-day mortality [46,47]. The PIRO score more extensively incorporates predisposing co-morbidities, physiologic and laboratory parameters, and has been modified to consider presumed source of infection, leading to a stronger predictive ability for mortality in more severely ill patients. In patients presenting to the ED with severe sepsis and septic shock, a prospective observational study found the PIRO to be the best predictor of mortality, compared to SOFA and MEDS scores [45]. In a recent study by Corfield et al, sepsis patients with a higher NEWS, according to initial ED vital signs (temperature, pulse, respiratory rate, systolic blood pressure, oxyhemoglobin saturation) and consciousness level, were significantly more likely to be admitted to an ICU within 48 hours or to experience in-hospital mortality [48].

Timely and Appropriate Antibiotics

In a landmark study published by Kumar and colleagues in 2006, the relationship between timing of antibiotics and mortality was established [49]. In 2731 adult septic shock patients, mortality increased 7.6% for every hour delay in effective antimicrobial administration. A striking finding, given that the study population was limited to patients cared for in the ICU, was the fact that only 50% of patients received appropriate antibiotics within 6 hours of onset of shock and nearly one-quarter of patients did not receive antibiotics until the 15th hour. As a direct result, in-hospital mortality was observed to be 58% in this study.

Over the ensuing decade, a series of studies have demonstrated a narrowing of the quality gap in this regard, and the result has coincided with a significant improvement in survival. In 2010, Giaieski and colleagues demonstrated a significant improvement in the prompt administration of antibiotic delivery in patients presenting to an ED with severe sepsis, with the median time from shock onset (sustained hypotension or lactate ≥ 4 mmol/L) to antibiotics down to 42 minutes [50]. Importantly, consistent with the Kumar study, time to appropriate antibiotics, rather than simply initial antibiotics, remained associated with in-hospital mortality independent of initiating early goal-directed therapy. In 2011, Puskarich and colleagues revealed that time to antibiotics continued to improve and, as a result, the investigators did not identify a relationship between time from triage to antibiotics and in-hospital mortality [51]. However, when antibiotics were delayed until after shock recognition, consistent with the study by Kumar and colleagues, survival decreased. Until recently, this important observation was challenging to operationalize clinically as little was known about how to facilitate risk-stratification of those at risk to develop shock. However,
Capp and colleagues recently found that deterioration to septic shock 48 hours after ED presentation occurs in approximately one out of eight patients and identified gender (female), transient hypotension, and/or hyperlactatemia upon presentation as risk factors associated with such a deterioration [52].

As an essential element of sepsis care bundles, a focus on timely use of antibiotics in patients with suspected infection, has the potential to increase the use of antibiotics in the ED in patients determined subsequently to not be infected. To combat this acknowledged downstream effect, reconsideration of the utility of empiric antibiotics 48 to 72 hours after admission is required. This step can be accomplished through the use of a sepsis care pathway and/or a formal antibiotic stewardship program.

**Quantitative Resuscitation**

Rivers and colleagues, in a landmark 2001 trial, examined the effectiveness of a protocolized resuscitation strategy in the most proximal phase of severe sepsis and septic shock [53]. A distinguishing characteristic between the usual care arm and the intervention in this ED-based study, in addition to whether mixed central venous oxygen saturation was measured as a resuscitation end-point, was the inclusion of an ED provider at the bedside to attend to clinical management. The intervention, aimed at achieving physiologic targets, resulted in significantly more fluid resuscitation (3.5 L vs. 5.0 L within the first 6 hours) and a significant decrease in inhospital mortality compared to the usual care arm (46.5 vs. 30.5%). The study revolutionized the culture and practice of sepsis care, in part by shining a light on the importance of timely resuscitation at the most proximal point of contact between the patient and the healthcare system. It also highlighted the importance of integrating serum lactate measurement into the early screening and risk stratification processes for sepsis care delivery.

The 2014 randomized trial of Protocol-Based Care for Early Septic Shock (ProCESS) revisited this concept, comparing the Rivers 2001 protocol to both a current guideline-based non-invasive algorithmic protocol and what had become usual ED care in the interim [54]. The ProCESS trial, which operationalized a team of bedside providers to direct care for each of the 3 distinct arms, found no significant difference between the arms in terms of 90-day and 1-year mortality, but mortality was approximately 10% less in all arms compared with the intervention arm of the Rivers trial. Further, subjects in each of the 3 arms received in excess of 2 L intravenous fluid resuscitation pre-randomization and 4.4–5.5 L when resuscitation spanned from pre-randomization to 6 hours post-randomization. The conclusion drawn is that the commonalities between the arms—early fluid resuscitation, early antibiotics, and the option to use physiologic measures as markers of the adequacy of treatment, all guided by bedside ED providers—are the most important factors for surviving sepsis. And the result is that practitioners have refined these tools over a decade, leading to steady improvements in survival.

Consistent with the ProCESS trial, a recent Australia and New Zealand trial confirmed no significant difference in 90-day mortality between protocolized EGDT and current usual care for septic shock within an ED [55]. Consistent with ProCESS and ProMISe [56], subjects enrolled in ARISE received in excess of 2.5 L in resuscitation pre-randomization, which when paired with fluid resuscitation in the 0-6 hour post-randomization period (1.96 L in the EGDT arm and 1.71 L in the usual-care arm) resulted in resuscitation in the 4.5 to 5L range during the initial resuscitation. The ARISE trial was unique in that appropriate antibiotic administration was a requirement prior to randomization, ensuring that this important driver of mortality reduction was standardized between the two arms of the trial. In summary, while the ideal fluid resuscitation amount is unknown, requires a personalized approach, and further investigation is required to effectively incorporate non-invasive measures to guide fluid responsiveness, early and aggressive resuscitation paired with early antibiotic administration are essential aspects of effective sepsis management.

**The Efferent Arm: Structure and Processes to Improve Outcomes**

The efferent arm of the system, beyond risk stratification, requires the implementation of optimal staffing and processes to care for the septic patient. While options will vary, preparation is a requisite, as are strategies that efficiently lead the clinician at the bedside to the use of evidence-based medicine (Table 2).

**Personnel and Staffing**

Quality care for the septic patient requires immediate availability of a multidisciplinary care team, including physicians and nurses with critical care experience who can be rapidly deployed to the bedside. The location of care provision may include on-going care in the initial
ED room assignment or transfer to a dedicated area for the care of the critically ill patient within the ED.

To provide optimal care in the era of overcrowding and delayed transfer to an ICU, a movement towards ED intensive care units (ED-ICUs) has emerged [57]. The models of practice range from a model based upon ED intensivists, with expertise in critical care medicine, providing care within the traditional structure of an ED, to a model wherein a portion of the ED is assigned for the care of the critically ill for extended periods of time beyond the initial resuscitation. As these models mature from resuscitation bays capable of scaling up based on need to dedicated ED-ICUs, investments in shared Unit leadership (physician and nursing), staffing (physician, critical care nursing, respiratory therapy, critical care pharmacist) and processes of care (eg, multidisciplinary rounds) in line with established ICUs will be necessary.

While attractive conceptually, large-scale implementation of this movement is unlikely to occur outside of tertiary care academic medical centers. In the many EDs across the US without ED intensivists, and confronted with limited clinician resources, flexible physician and nursing staffing models will be necessary to ensure that care provisions are in accord with established guidelines. Potential solutions to provide the resources to meet the needs of these high-intensity patients include critical care consultation and a strategy traditionally applied to the ICU, telemedicine [58]. Last, given the relationship between hospital volume and mortality in severe sepsis [59,60], timely transfer to a high-volume center for specific cases may be appropriate, although the optimal timing, case selection, and impact of transfer on outcomes warrant further examination.

### Clinical Decision Support Strategies

To complement the identification and risk-stratification available by screening and scoring systems, clinical decision support systems are novel tools to improve outcomes in the era of electronic medical records (EMR). Specific to sepsis care delivery, performance improvement initiatives including audit-and-feedback practice can increase severe sepsis guideline adherence, and even modest improvements in adherence appear to lead to sustained improvements that contributed to a 25% relative risk reduction in the observed mortality rate [61,62]. Clinical decision support tools can be used to link early recognition to optimal care processes, such as the Surviving Sepsis Campaign resuscitation and management bundles. The use of prompts as strategies to ensure that bundles of care are ordered and carried out is an important aspect to operationalize during the design phase [63].

Significant preparation is required to effectively carry out the clinical decision support design strategy. For example, to ensure timely antibiotic dispensing, a number of process steps will be required, including prompt notification to a central pharmacist or preferably, an ED pharmacist with access to a local pharmacy pre-stocked with commonly used antibiotics [64]. In addition, the use of an institution-specific antibiogram within the physician computer-order entry sepsis order set, that

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**Table 2. Strategies to Improve Sepsis Recognition and Quality of Care**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>References</th>
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</thead>
<tbody>
<tr>
<td>Implement a quality improvement program focused on sepsis care delivery</td>
<td>4,61–62</td>
</tr>
<tr>
<td>Coordinate efforts between pre-hospital, ED, and hospital providers</td>
<td>16–19,32</td>
</tr>
<tr>
<td>Automate alert using EMR to improve sepsis recognition</td>
<td>33–35,46–48</td>
</tr>
<tr>
<td>Automate serum lactate measurements into triage process to risk stratify patients presenting with sepsis</td>
<td>40–44</td>
</tr>
<tr>
<td>Design and implement a standardized sepsis protocol, including sepsis care bundles</td>
<td>4,61,62</td>
</tr>
<tr>
<td>Design and implement sepsis-specific clinical decision support processes</td>
<td>61–63</td>
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<tr>
<td>Design new or identify existing resuscitation rooms for rapid initial management of patients with potential severe infections</td>
<td>57</td>
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<tr>
<td>Streamline the process from antibiotic order to antibiotic delivery, including the use of an antibiogram for antibiotic selection</td>
<td>49–51,64</td>
</tr>
<tr>
<td>Measure adherence to guideline recommendations (eg, blood cultures obtained, time to antibiotics)</td>
<td>61,62</td>
</tr>
<tr>
<td>Review performance at set intervals as part of an audit-and-feedback component of the program</td>
<td>29,61,62</td>
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EMR = electronic medical record.
includes site-specific recommendations (eg, pulmonary, gastrointestinal source) and susceptibility patterns, is an essential aspect of optimal sepsis processes of care. Last, the antibioticogram will need to be frequently updated to include season-specific (eg, oseltamivir administration for high-risk cases during influenza season) recommendations to ensure that providers are prompted with the most up-to-date clinical information.

Audit and Feedback and Continuous Performance Improvement

The multimodal approach required to translate knowledge (eg, guidelines) into sepsis care implemented at the bedside is an iterative process. An ED armed with a robust track-and-trigger system and an effective efferent arm, including sophisticated clinical decision support strategies, will require frequent auditing in the plan-do-study-act model of quality improvement to yield clinical effectiveness [61,62,65]. Auditing, paired with feedback to frontline providers, is essential to refine and improve the complex process required to provide expert care to the septic patient [29,65]. Sustained success in optimizing sepsis care delivery is the goal, yet significant work is required to determine the best strategies to achieve this endpoint.

Conclusion

Severe sepsis affects millions of individuals each year in the United States. Delays in recognition result in increased morbidity and mortality, at a tremendous cost to the patient and society. By designing strategies to identify sepsis in a timely, efficient, and effective manner, and by implementing ED structures and processes to increase adherence with sepsis-based guidelines, improved patient-centered outcomes can be realized.

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