

Identifying Patients With Sepsis on the Hospital Wards



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Sepsis contributes to up to half of all deaths in hospitalized patients, and early interventions, such as appropriate antibiotics, have been shown to improve outcomes. Most research has focused on early identification and treatment of patients with sepsis in the ED and the ICU; however, many patients acquire sepsis on the general wards. The goal of this review is to discuss recent advances in the detection of sepsis in patients on the hospital wards. We discuss data highlighting the benefits and limitations of the systemic inflammatory response syndrome (SIRS) criteria for screening patients with sepsis, such as its low specificity, as well as newly described scoring systems, including the proposed role of the quick sepsis-related organ failure assessment (qSOFA) score. Challenges specific to detecting sepsis on the wards are discussed, and future directions that use big data approaches and automated alert systems are highlighted.

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The incidence of sepsis has been rising over the past decade, and it is one of the most common reasons for hospitalization, with an estimated 1.6 million cases annually in the United States.^{1,2} This leads to approximately \$20 billion dollars in health-care spending in the United States, which will likely continue to increase as the population ages. Although most prior research has focused on patients in the ICU or ED, up to 50% of patients with sepsis are treated on the hospital wards.^{3,4}

Longitudinal trends from observational data suggest that outcomes in patients with sepsis are improving. However, mortality remains as high as 50% for those with septic shock.⁵⁻⁷ It has been shown that early interventions,

such as appropriate antibiotic therapy, improve outcomes in patients with sepsis, making early diagnosis critical.^{8,9} As such, the Surviving Sepsis Campaign (SSC) has made it their mission to raise sepsis awareness and decrease sepsis-related mortality.^{10,11} Still, recognition and treatment of sepsis remain a challenge given that more than one-half of patients with severe sepsis are not documented to have this diagnosis by their physicians.⁴ Therefore, work aimed at improving the recognition of patients with sepsis is critical to improving their short- and long-term outcomes.

In this review, we discuss how the definition of sepsis has evolved over time and the

ABBREVIATIONS: EHR = electronic health record; ICD-9 = International Classification of Diseases, Ninth Revision; NPV = negative predictive value; PPV = positive predictive value; qSOFA = quick sepsis-related organ failure assessment; SIRS = systemic inflammatory response syndrome; SSC = Surviving Sepsis Campaign

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potential benefits of active sepsis screening on the wards. In addition, we review recent studies that use automated sepsis screening tools for patients on the general wards and their clinical utility. Finally, we end with gaps in knowledge and future directions in this important area of research.

Defining Sepsis: An Evolution

The concept of sepsis has been around since 700 BC when Homer used the term “sepo” to describe human death as “rot” in his poems.¹² Since then, the idea of sepsis has undergone many iterations. Hippocrates expanded on Homer’s idea in *Corpus Hippocraticum*, in which he described it as a dangerous odiferous biological decay. It was not until 600 years later that Galen linked sepsis to blood infections and began treating patients with sepsis using abscess drainage and bloodletting.

Even by the 1980s, sepsis literature reported significant disparities in sepsis incidence and mortality due to the fact that there was no universally accepted definition.¹³⁻¹⁷ Finally, in 1992, the American College of Chest Physicians and the Society of Critical Care Medicine held a consensus conference that introduced the systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome hoping that these definitions would improve clinicians’ aptitude for early detection and treatment as well as standardize future sepsis-related clinical trials.¹⁸

This definition was quickly met with criticism. Many felt that SIRS was too nonspecific and that it did not adequately describe the underlying physiology of sepsis.¹⁹ In addition, there was concern that using this definition of sepsis would lead to clinical trials with patient populations that were too heterogeneous, thus precluding comparisons of patients with sepsis and negating the original intent behind SIRS.²⁰ Furthermore, a survey of 1,100 critical care physicians in 2000 revealed that 67% “cited no common definition of sepsis” and < 20% of respondents agreed on any one definition.²¹ Together, these factors prompted the 2001 International Sepsis Definitions Conference to revisit the definitions proposed in 1991.²² However, apart from expanding the list of signs and symptoms of sepsis, the experts thought there was not enough new evidence to support a change to the original criteria.

Because of these controversies and advances made in understanding the pathophysiology, epidemiology, and treatment of sepsis, the Society of Critical Care Medicine and the European Society of Intensive Care Medicine convened a task force in 2015 to update the definitions

of sepsis and septic shock.²³ The new consensus guidelines define sepsis as life-threatening organ dysfunction, with suspected or documented infection and an acute two-point increase in the sepsis-related organ failure assessment (SOFA) score. In addition, septic shock was redefined as the need for vasopressors to maintain the mean arterial pressure at > 65 mm Hg and a lactate level > 2 mmol/L after adequate fluid resuscitation. It is important to note that the term “severe sepsis” and the SIRS criteria are no longer part of the updated definition.

Screening for Sepsis on the Wards

Because patients on the ward may become septic at any point during hospitalization, screening is often performed longitudinally rather than at one point in time. This requires additional resource strain and burden on caregivers compared with a one-time screening on admission. In addition, there are few data to support optimal treatment strategies for patients with sepsis identified on the wards, as discussed in further detail by a recent review.²⁴ Despite these considerations, several studies suggest that actively screening patients on the wards is associated with improved process measures and patient outcomes, as discussed further on.

Manual Screening Tools

Despite ongoing controversy surrounding the sepsis definitions, prior studies suggest that sepsis screening using the 2001 consensus definitions may decrease mortality.^{25,26} For example, the SSC conducted a 2-year retrospective study that evaluated quarterly bundle compliance and hospital mortality after initiation of sepsis screening programs in the ED, wards, and ICU. Results from 252 hospitals showed a significant increase in compliance rates with the 6-hour treatment bundle (10.9% vs 31.3%) and 24-hour treatment bundle (18.4% vs 36.1%). This correlated temporally with a decrease in unadjusted mortality rates from 37.0% to 30.8% at the end of the 2-year study.²⁵ The most recent SSC study extended the follow-up period to 7½ years. This study reaffirmed the mortality benefit of high compliance with both treatment bundles by demonstrating a 25% relative risk reduction in mortality.²⁷ As a result, the SSC advocates routine screening for sepsis with the use of a paper-based screening tool to be used in all levels of acute care.^{28,29} However, it is important to note that before and after studies such as these and others that are discussed further on run the risk of patient selection bias, temporal bias, and investigator bias. Thus, future

TABLE 1] Characteristics of Studies Evaluating Automated Sepsis Screening Tools

Reference	Study Design	Test Sites	Gold Standard for Sepsis	Definition of Alert	Alert Frequency	Primary Outcome	Secondary Outcome
Thiel et al, 2010 ⁴⁸	Retrospective cohort	One academic hospital	ICD-9 codes for acute infection + acute organ dysfunction + need for vasopressors	Decision trees with and without ABG data	Continuous	Diagnostic accuracy	...
Sawyer et al, 2011 ⁴⁹	Prospective observational pilot study	One academic hospital	2001 consensus criteria	Decision tree without ABG data	Continuous	Rate of IV antibiotics/fluids, respiratory support, vasopressor initiation, laboratory results/imaging within 12 h of alert	Rate of ICU transfer, rate of ICU transfer within 12 h of alert, in-hospital mortality, LOS, LOS after alert
Buck, 2014 ³⁹	Prospective observational pilot study	One community hospital	ICD-9 code for sepsis, severe sepsis, or septic shock	≥ 2 SIRS criteria + 1 sign of organ dysfunction in a 24-h window	Once per 24 h	Diagnostic accuracy	Any intervention from MD or RN
Palleschi et al, 2014 ³³	Retrospective before and after study	4 hospitals within 1 medical center	ICD-9 code for sepsis, severe sepsis, or septic shock	≥ 2 SIRS ± 1 sign of organ dysfunction ± elevated lactate level	Continuous	Lactate determination, blood culture results, time to antibiotic treatment	Timing of early intervention in ED vs acute care
McRee et al, 2014 ⁴²	Retrospective before and after study	1 community hospital	ICD-9 code for sepsis, severe sepsis, or septic shock	≥ 2 SIRS + manual nurse evaluation deeming patient "high risk"	...	Stage of sepsis, length of stay, discharge location, mortality	...
Brandt et al, 2015 ³⁶	Prospective observational pilot study	1 academic hospital	ICD-9 code for sepsis, severe sepsis, or septic shock	Must have had acute infection, organ dysfunction, or change in mental status prior to screening for SIRS; then must have met ≥ 2 SIRS criteria	Continuous	Diagnostic accuracy	Difference in time of alert prior to recognition by MD (determined by chart review)

(Continued)

TABLE 1] (Continued)

Reference	Study Design	Test Sites	Gold Standard for Sepsis	Definition of Alert	Alert Frequency	Primary Outcome	Secondary Outcome
Amland et al, 2015 ³⁸	Prospective observational study	1 community hospital	ICD-9 code for septicemia, sepsis, severe sepsis, or septic shock	≥ 3 SIRS criteria (including elevated glucose levels in patients without diabetes) ± 1 sign of organ dysfunction + post-alarm cross-check by MD	Continuous	Diagnostic accuracy	...
Kurczewski et al 2015 ⁴⁰	Retrospective before and after study	1 academic hospital	ICD-9 code for sepsis, severe sepsis, or septic shock	≥ 2 SIRS criteria inclusive of either abnormal temperature or WBC count	...	Time to any sepsis-related intervention (IV antibiotics/fluids, blood work)	Time to individual, sepsis-related intervention, LOS, LOS in ICU, mortality
Umscheid et al, ⁴¹ 2015	Retrospective before and after study	Multicenter	ICD-9 code for sepsis	Risk score of ≥ 4 points: 1 point for each SIRS criterion, 1 point for SBP < 100 mm Hg, 1 point for lactate level > 2.2 mmol/L	Continuous; stopped once patient triggered alert	Predictive ability for composite of ICU transfer, RRT data, or death across all 3 hospitals	Rate of IV antibiotics/fluids, blood work, imaging
Amland and Hahn-Cover, 2016 ³⁷	Retrospective cohort	Multicenter	ICD-9 code for sepsis, severe sepsis, or septic shock	≥ 3 SIRS (including elevated glucose levels in patients without diabetes) ± 1 sign of organ dysfunction	Continuous	Diagnostic accuracy	Sepsis prevalence, incidence, and patient outcomes after the alert

ABG = arterial blood gas; ICD-9 = *International Classification of Diseases*, Ninth Revision; LOS = length of stay; MD = medical doctor; RN = registered nurse; RRT = rapid response team; SBP = systolic blood pressure; SIRS = systemic inflammatory response syndrome.

randomized controlled trials are needed to confirm these findings.

Automated Screening Tools

Although manual sepsis screens are commonly used, they have several disadvantages.³⁰ First, they are susceptible to transcription and calculation errors, which can lead to inaccurate screening results. In addition, manual screens can only be performed intermittently, often once every nursing shift.³¹⁻³³ This can lead to considerable delays in recognition and treatment. Finally, manual screening typically requires a caregiver to contact the physician to initiate a plan of care. Delays in calling or failure to call may also impact patient outcomes. In contrast, automated screening tools have the potential to decrease diagnostic delays and increase screen accuracy. Several institutions have developed automated screening tools to expedite the diagnosis of sepsis and the delivery of subsequent sepsis bundles (Table 1). It is important to note that all of these are based on before and after studies, with the exception of one randomized controlled trial that was conducted in patients in the ICU.³⁴

SIRS-Based Screening Tools

Many automated sepsis screening tools described in the literature are primarily based on SIRS criteria, with additional specifications that are tailored to individual hospital systems. Modifying the SIRS criteria for automated screening to improve specificity is an important concept given that a recent study suggested that up to one-half of patients on the wards will meet SIRS criteria at least once during their admission.³⁵

Several studies have investigated the diagnostic accuracy of SIRS-based screening tools (Table 2). In a prospective pilot study, Brandt et al³⁶ required the presence of infection, organ dysfunction, or altered mental status in the patient's active problem list prior to allowing an automated system to search for SIRS criteria. The alert

was issued to a sepsis surveillance group consisting of an intensivist and critical care nurse, who performed a chart review to determine if the primary team should be notified. This automated method relied heavily on adequate provider documentation (ie, the physician had to add an infection or acute organ dysfunction diagnosis to the active problem list) and resulted in a positive predictive value (PPV) of 16.5% and sensitivity of 100% for the diagnosis of severe sepsis based on expert adjudication of all patients identified by the alert.

An initial study performed by Amland and Hahn-Cover³⁷ triggered an alert in patients meeting either SIRS criteria alone or with at least one sign of organ dysfunction. During a silent testing period, the alert resulted in a sensitivity of 83% and a PPV of 46% for the diagnosis of sepsis, using an *International Classification of Diseases, Ninth Revision* (ICD-9) code of septicemia, sepsis, severe sepsis, or septic shock. In a subsequent study with the alert running live, a post-alarm cross-check had to be completed by the covering physician in the electronic health record (EHR).³⁸ If the physician checked a box labeled "suspected infection," an automated order set for blood cultures and lactate levels was populated. The addition of this second component to the screening tool increased the PPV to 94% and maintained similar sensitivity (81%).

The impact of SIRS-based automated screening tools on improving sepsis-related interventions has also been studied (Tables 3, 4). For example, in a prospective pilot study, Buck³⁹ noticed that 40% of the patients identified by the alert received escalated care in the form of repeated evaluation by a physician, additional medications or intravenous fluids, laboratory tests, respiratory support, or transfer to the ICU. Additionally, in the pilot study mentioned earlier, Brandt et al³⁶ showed that the alert resulted in a diagnosis of sepsis approximately 27 minutes earlier when compared with the time of sepsis diagnosis based on chart review.

TABLE 2] Predictive Ability of Automated Sepsis Screening Tools

Reference	Type of Alert	Diagnosis of Sepsis, Severe Sepsis, or Septic Shock			
		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Thiel et al, 2010 ⁴⁸ (without ABG)	Non-SIRS decision tree	17.1	96.0	20.5	95.9
Brandt et al, 2015 ³⁶	SIRS-based	100	62.0	16.5	100
Buck, 2014 ³⁹	SIRS-based	17	...
Amland and Hahn-Cover, 2016 ³⁷	SIRS-based	83	92	46	99
Amland et al, 2015 ³⁸	SIRS-based	81	87	94	63

NPV = negative predictive value; PPV = positive predictive value. See Table 1 legend for expansion of other abbreviation.

TABLE 3] Frequency of Initiation of Clinical Process Measures After Implementation of an Automated Sepsis Screening Tool

Reference	Type of Alert	Antibiotic Escalation (%)		Administer IV Fluids (%)		Draw for Lactate Determination (%)		Blood for Cultures Drawn (%)	
		Before Alert	After Alert	Before Alert	After Alert	Before Alert	After Alert	Before Alert	After Alert
Umscheid et al, 2015 ⁴¹	SIRS based	18	27	27	37	19	36	19	24
Sawyer et al, 2011 ⁴⁹	Non-SIRS decision tree	24	36	24	38
Palleschi et al, 2014 ³³	SIRS based	50	89	72	75

See Table 1 legend for expansion of abbreviation.

In a before and after interventional study, Kurczewski et al⁴⁰ evaluated a tool that used at least two SIRS criteria to trigger the sepsis alert but modified it so that one of them had to include an abnormal WBC count or temperature. Rather than diagnostic accuracy, differences in time to sepsis-related therapies in patients discharged with an ICD-9 code for sepsis, severe sepsis, or septic shock were evaluated. Once a patient met the criteria, providers were forced to address the alert in the EHR before any other tasks could be performed, and there were no limits to how frequently the alert could fire. In patients who triggered the alert, there was a significant decrease in median time to any sepsis-related intervention (0.6 hours vs 4.1 hours), blood culture collection (1.1 hours vs 13.1 hours), and lactate determination (2.4 hours vs 40.5 hours). In another study using a similar screening tool, with the added component of an interprofessional sepsis education program, Palleschi et al³³ also showed improvements in obtaining lactate levels (50% vs 89%; $P < .001$), and blood cultures (72% vs 75%).

Rather than using the traditional definition of sepsis to develop an alert system, Umscheid et al⁴¹ performed a before and after study using a tool that translated SIRS criteria into a risk score in which patients earned one point for each SIRS criterion as well as for a systolic blood pressure < 100 mm Hg or a lactate level > 2.2 mmol/L. Once an alert was triggered, the covering

provider, bedside nurse, and rapid response team gathered at the patient's bedside within 30 minutes. This group then had to assess and document the most likely condition that triggered the alert and whether clinical management should be modified. The screening tool was then silenced for the remainder of that patient's hospital stay. Using four points as the trigger threshold resulted in a screen-positive rate of 6%, sensitivity of 17%, specificity of 97%, PPV of 28%, and negative predictive value (NPV) of 95% for the composite outcome of ICU transfer, rapid response activation, or death. After initiation of the alert on the wards, there was a significant increase in sepsis-related interventions within 3 hours of the alert, including ordering of antibiotics (10% vs 16%), determination of lactate levels (10% vs 23%), and blood product administration (5% vs 10%). Of note, review of the alert assessments revealed that one-half of the alerted clinicians did not think the patient was critically ill, > 30% believed the diagnosis was sepsis, and more than 90% knew of this diagnosis prior to the alert.

Aside from the results of the most recent SSC study, the impact of automated sepsis screening on patient outcomes, such as mortality, has been mixed (Table 5). One study suggesting an improvement in patient outcomes was performed by McRee et al,⁴² who used an alert triggered by two SIRS criteria with the additional component of a manual risk assessment by a nurse in

TABLE 4] Time to Initiation of Clinical Process Measures After Implementation of an Automated Sepsis Screening Tool

Reference	Type of Alert	Antibiotic Therapy Escalation (h)		Administer IV Fluids (h)		Lactate Levels Determined (h)		Blood for Cultures Drawn (h)	
		Before Alert	After Alert	Before Alert	After Alert	Before Alert	After Alert	Before Alert	After Alert
Kurczewski et al, 2015 ⁴⁰	SIRS based	5.2	3.9	7.1	1.9	40.5	2.4	13.2	1.1
Palleschi et al, 2014 ³³	SIRS based	3.0	1.5

See Table 1 legend for expansion of abbreviation.

TABLE 5] Frequency of Patient Outcomes After Implementation of an Automated Sepsis Screening Tool

Reference	Type of Alert	ICU Transfers (%)		Mortality (%)	
		Before Alert	After Alert	Before Alert	After Alert
Sawyer et al, 2011 ⁴⁹	Non-SIRS decision tree	23	26	12	10
McRee et al, 2014 ⁴²	SIRS based	9.3	1.0
Kurczewski et al, 2015 ⁴⁰	SIRS based	47	27
Umscheid et al, 2015 ⁴¹	SIRS based	35	35	17	13

See Table 1 legend for expansion of abbreviation.

a before and after study. When compared with patients who were discharged with an ICD-9 code for sepsis, severe sepsis, or septic shock before alert implementation, those who had triggered the alert had a substantial decrease in mortality (9.35% vs 1.0%) and a higher likelihood of being discharged home (25.3% vs 49.0%) but no difference in length of stay. However, the two studies noted previously by Kurczewski et al⁴⁰ and Umscheid et al,⁴¹ which demonstrated an increase in sepsis-related interventions, failed to show any differences in overall length of stay and mortality after alert implementation.

These results suggest that more data are needed from clinical trials to conclusively determine if automated SIRS-based screening tools improve important clinical outcomes such as mortality in patients on hospital wards.

Non-SIRS-Based Screening Tools

Over the past several years, many groups have developed risk-stratification tools for identifying high-risk patients outside the ICU.^{43,44} The modified early warning score is one example that is already in place in several hospitals in the United States and around the world and has been shown to predict patient outcomes, including cardiac arrest, ICU transfers, and in-hospital mortality. Given the lack of specificity of the SIRS criteria, there has been significant interest in evaluating the performance of early warning scores in predicting outcomes for patients with sepsis. To date, most work in this area has been performed in the ED, with evidence that these scores can accurately predict mortality.^{45,46} On the wards, one prospective study of patients with sepsis demonstrated that the simple clinical score and rapid emergency medicine score, which are based on patient demographics and vital signs, were accurate predictors of mortality (area under the curve, 0.77 for both).⁴⁷

Other groups have developed sepsis risk scores using patient-level data from the EHR. For example, Thiel et al⁴⁸ developed an automated screening tool for septic

shock using a decision tree model that included vital signs, such as systolic blood pressure, and laboratory tests, including blood urea nitrogen, albumin, and bilirubin determinations. This resulted in a PPV of 21.4% and a NPV of 96.1% for the diagnosis of septic shock in one of their validation cohorts. They subsequently performed a prospective observational study using the developed model on the wards.⁴⁹ Of patients who triggered the alert, 70.8% received at least one sepsis-related intervention. In this group, there was a significant increase in escalation of antibiotic therapy (36% vs 24%), IV fluid administration (38% vs 24%), and oxygen therapy (20% vs 8%). There was no difference in the rate of transfers to the ICU and hospital mortality in this study.

A recently developed risk stratification tool that was presented along with the new sepsis definitions is termed the quick sepsis-related organ failure assessment (qSOFA).⁵⁰ This tool was developed using EHR data from 12 hospitals within the University of Pittsburgh health system. In this study, suspicion of infection was defined as antibiotic administration and culture orders within a specific time window. Optimal cut points of different vital signs were determined in univariate analyses, and these variables were combined in a logistic regression model. The final qSOFA score consisted of altered mental status, systolic blood pressure \leq 100 mm Hg, and a respiratory rate of at least 22 breaths per minute. A score of 2 or higher had $>$ 60% sensitivity for in-hospital mortality in the University of Pittsburgh Medical Center validation cohort, which included patients in the ICU and patients not in the ICU. The proposed use of qSOFA is at the bedside to identify high-risk infected patients outside the ICU and to prompt clinicians to consider additional diagnostic tests or escalation of therapy. However, it is not currently part of the recent consensus definition of sepsis. In addition, the SSC still recommends screening with SIRS criteria and using the qSOFA to screen for organ dysfunction in those who meet the traditional definition of sepsis.⁵¹

Current Controversies and Gaps in Knowledge

Identifying Infected Patients

One of the biggest challenges facing sepsis research, especially for studies that use retrospective EHR data, is to determine which patients are truly infected. Even caregivers of the same patient may disagree on whether the patient might be infected. For example, in a single-center prospective study by our group, we found that bedside nurses and ordering providers agreed on the presence of infection only 17% of the time ($\kappa = 0.12$).⁵² Furthermore, progression to severe sepsis or shock was significantly higher when both providers suspected infection in a SIRS-positive patient (17.7%) and lowest when neither suspected infection (1.5%), with single-provider suspicion conferring intermediate risk (6.0%). Studies using EHR data to define infection are equally challenging, as the accuracy of culture orders, antibiotic prescriptions, and other interventions for defining infection are unknown. The impact of different definitions of infection and their effect on variable importance in screening models and algorithm accuracy as well as their benefit to patients is unknown and an important area of future research.

Optimal Screening Frequency

Ideally, automated screening tools perform continuous background monitoring allowing for real-time sepsis detection. Of the studies that allowed for continuous or repeated alerts, alert fatigue or high rates of false-positive results were common.^{39,40} Some studies attempted to decrease alert fatigue by limiting the number of times the screening tool could fire per day or per hospitalization. This does not capture the dynamic longitudinal nature of a patient's clinical course on the wards nor does it maximize the use of an automated system. It also highlights the need for more specific screening tools that have been validated on the wards and that provide clinicians with meaningful information that is actionable.

Treatment of Screen-Positive Patients

As noted earlier, current data on automated sepsis screening on the wards suggest that these tools improve delivery of the sepsis management bundle without altering rates of ICU transfers and mortality. These results raise the issue of the optimal treatment of patients on the wards who are flagged as high risk by the screening tools. The SSC's recommendations for severe sepsis and shock are based on evidence that primarily includes patients in the ICU or ED. In fact, as outlined

in a recent review, of the 122 studies used to develop these recommendations, only one prospective clinical trial, which examined the duration of empirical antibiotics, included any patients on the wards.²⁴ There were no patients on the wards in any trial supporting aggressive fluid resuscitation, which not only is a frequent intervention on the wards for septic patients but also is a commonly reported outcome for the efficacy of sepsis screening tools. Future research in sepsis treatment for patients on the wards is clearly needed to optimize outcomes in this population.

Future Directions

In addition to the gaps in knowledge noted earlier, future work in the use of biomarkers and EHR data may lead to important developments in the care of patients with sepsis. For example, one of the most promising biomarkers in use today is procalcitonin, as its values rise rapidly with invasive bacterial infection and decrease once that infection has cleared.⁵³ However, procalcitonin is also elevated in other conditions, such as trauma. Thus, the current suggested use of procalcitonin is limited to guiding the cessation of antibiotic therapy.^{28,54,55} Another promising alternative includes an advanced polymerase chain reaction followed by electrospray ionization and mass spectrometry, which can detect more than 800 pathogens in a single assay within 6 hours.⁵⁶ As our understanding of sepsis pathophysiology continues to grow, discovery of novel biomarkers that provide diagnostic information, as well as risk stratification, will allow providers to deliver optimal care to patients with sepsis. Finally, as EHR data that can be used for research becomes more widespread, using advanced machine learning techniques to develop highly accurate tools will become more common.^{57,58}

Limitations

None of the sepsis screening tools reviewed relied on the new definition of sepsis, and it is unclear how this impacts patient care. Additionally, we did not perform a standardized regimented literature search of all studies on sepsis detection because our article focused only on studies performed in the past 5 years.

Conclusions

Because of the increased awareness of sepsis driven by previous landmark studies and the SSC, there have been a multitude of efforts to improve sepsis detection in hospitalized patients. Many of the studies in this review

offer promising screening tools for patient surveillance and increased sepsis-specific interventions, but their effect on patient outcomes is less clear. Future work is needed to determine the optimal way to identify patients with sepsis on the wards that will most likely benefit from earlier and more aggressive interventions.

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