REVIEW

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Sepsis Performance Improvement Programs: From Evidence Toward Clinical Implementation

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Abstract

This article is one of ten reviews selected from the Annual Update in Intensive Care and Emergency Medicine 2022. Other selected articles can be found online at https://www.biomedcentral.com/collections/annualupdate2022. Further information about the Annual Update in Intensive Care and Emergency Medicine is available from https://link.springer.com/bookseries/8901.

Introduction

Since its launch in the early 2000s, the international Surviving Sepsis Campaign (SSC) has provided guidelines for the management of sepsis, most recently updated in 2021 [1]. The SSC aims to provide a standard of care for sepsis while increasing awareness among healthcare professionals and the general public. The goal is to reduce morbidity and mortality from sepsis and septic shock worldwide [2].

To facilitate the clinical implementation of the guidelines, the SSC bundles their recommendations into small groups of care processes that physicians should perform within a specific timeframe and that provides them with a concrete plan of action [1, 2]. Despite efforts to facilitate the successful implementation of the guidelines, adherence has been suboptimal, particularly regarding the microbiological work-up and administration of appropriate antibiotics [3]. Non-compliance to the SSC guidelines seems most prominent among emergency medicine and internal medicine physicians [4].

In response to the low adoption rates of (SSC) sepsis guidelines, individual hospitals and organizations have introduced sepsis performance improvement programs.

Usually, dedicated physicians or research teams lead these initiatives and use screening tools, process changes in sepsis care pathways, and sepsis educational programs to optimize adherence to the standard of care [5]. The latest update of the SSC guidelines recommends that all hospitals and health systems have sepsis performance improvement programs [1].

In this chapter, we discuss the literature on the use and benefits of sepsis performance improvement programs to improve protocol adherence and provide practical insights for the clinical implementation of such programs in your hospital.

Do 'One-Size-Fits-All' Care Bundles Improve Sepsis Outcomes?

Sepsis performance improvement programs aim to improve adherence to a guideline or protocol for sepsis care, and they are almost exclusively studied in the context of the SSC care bundles [5]. When one aims to improve compliance rates to any guideline, one should first be convinced that this is a goal worth pursuing. In the case of the SSC guidelines, this debate has been ongoing for many years, and this paragraph presents only a brief overview of this reflective and meaningful discussion [6, 7].

Expert panelists on sepsis have created the SSC bundles, spearheaded by the Society of Critical Care

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Schinkel *et al. Critical Care* (2022) 26:77

Page 2 of 8

Medicine (SCCM) and European Society of Intensive Care Medicine (ESICM), and endorsed by numerous medical societies [1, 6]. However, the evidence base for these bundles and the timeframes in which they should be performed have been a matter of debate [7–9]. One prominent example concerns adherence to early goal-directed therapy (EDGT), an early form of bundled care that was associated with significantly lower in-hospital mortality rates (30.5% vs. 46.5% in the usual care group) in a randomized study of 263 patients with sepsis or septic shock presenting to the emergency department of a tertiary hospital in the United States [10]. However, these results were not replicated in subsequent large randomized trials and meta-analyses [11–13]. Furthermore, the value of individual bundle items, such as the 30 ml/kg fluid bolus and administration of antibiotics within 1 h to all patients, has been heavily debated because of conflicting results regarding the benefits [7, 14–16]. Moreover, fear exists that pressure to perform bundle items within a specific timeframe may promote harmful diagnostic tests and treatments, as was the case with the 2002 quality measure for the management of community-acquired pneumonia by the Centers for Medicare & Medicaid Services, which was later removed [9, 17].

Despite the limited evidence base that underlies some of the recommendations in the SSC bundles, the overall consensus, underscored by the endorsements from 35 international medical societies, seems to be that most of the care processes in the bundles will positively contribute to the management of the majority of sepsis patients [6]. Numerous observational studies have shown associations between improved bundle compliance and a reduction in mortality. An extensive 7.5-year study in 280 hospitals across Europe, South America, and the United States showed that overall mortality was significantly lower in high-compliance hospitals (29.0%) compared with low-compliance hospitals (38.6%) [18]. This study included 29,470 patients with sepsis or septic shock from emergency departments, regular wards, and intensive care units (ICUs) between January 1st 2005 and June 30th 2021. Notably, compliance was defined as high when sites completed the resuscitation bundle within 6 h for as few as 15% of their patients, suggesting that complete bundle adherence is only practical in a small subset of patients [18]. A similar project in Portugal studied the effects of adherence to the 6-h bundle in 897 patients with community-acquired sepsis in 17 ICUs [19]. Among those 897 patients, the core bundle was only completed within 6 h in 12% of the patients. The highest compliance was seen for the administration of vasopressors (78%) and the collection of cultures before antibiotic treatment (77%). In comparison, the lowest adherence was seen for blood culture collection in general (48%) and administration of antibiotics (52%) [19]. Compliance with the complete bundle was associated with decreased 28-day mortality, with an adjusted odds ratio (OR) of 0.44 (95% confidence interval [CI] 0.24–0.80) in sepsis and 0.49 (95% CI 0.25–0.95) in septic shock. Other studies have found similar mortality benefits associated with improved SSC bundle adherence [20–22].

Sepsis Improvement Programs: What Is the Evidence?

Adherence to the SSC guidelines in hospitals and healthcare systems that have adopted them is still suboptimal [3, 5]. For example, a nationwide study in Finland showed complete guideline adherence in only 6 out of 92 ICU patients during the four-month study period, similar to rates found in other studies [5, 23]. Sepsis performance improvement programs may help improve compliance, and a 2015 systematic review and meta-analysis by Damiani and colleagues tried to quantify this effect [5]. The reviewers identified 50 observational studies with highly diverse improvement programs and study designs. Despite this heterogeneity, the meta-analysis showed that sepsis performance improvement programs were consistently associated with increased compliance with 6-h (OR 4.12, 95% CI 2.95–5.76) and 24-h (OR 2.57, 95%-CI 1.74–3.77) bundles and with reduced mortality (OR 0.66, 95%-CI 0.61–0.72). The mortality estimates are hard to interpret in this meta-analysis since they include in-hospital mortality as well as short- and long-term mortality.

Among the 50 studies included in the systematic review of Damiani et al., combinations of interventions using screening tools, process changes, and educational programs were independently associated with increased bundle compliance and reduced mortality [5]. It thus appears that having a sepsis performance improvement program in itself is more important than the specific content of the program. However, the best results were observed in programs with various simultaneous interventions for performance improvement and in hospitals where the initial compliance was lowest [5]. The following sections will discuss the most-studied interventions (implementation of sepsis screening tools, process changes in sepsis care pathways, and educational programs) and their effects in further detail.

Sepsis Screening Tools

A primary focus of many performance improvement programs is using screening tools to identify sepsis early. Correct treatment can be initiated earlier if sepsis is recognized sooner, which is expected to improve

Schinkel *et al. Critical Care*   (2022) 26:77

Page 3 of 8

patient outcomes [2]. Three randomized controlled trials (RCTs) have studied whether the use of screening tools can improve patient outcomes in sepsis [24–26]. Downing et al. used an electronic health record (EHR) alert to detect sepsis early in medical and surgical wards, based on modified sepsis criteria including laboratory results and vital signs [24]. However, the alert did not result in improved performance measures or patient outcomes.

Hooper and colleagues studied the effects of pager alerts whenever a patient in the medical ICU satisfied a modified version of the systemic inflammatory response syndrome (SIRS) criteria [25]. Again, the alerts did not result in any improved performance measures or decreased mortality rates. Only Shimabukuro and colleagues were able to show improvements in patient outcomes using automatically generated alerts in the EHR with their machine learning-based sepsis screening tool [26].

Among 142 patients in the US-based medical-surgical ICUs, the hospital length-of-stay (− 2.30 days), ICU length-of-stay (− 2.09 days), and in-hospital mortality (− 12.3%, absolute) were all significantly lower in the intervention group that used the automated sepsis screening tool [26]. One explanation for why this study was able to find beneficial effects is that it was the only one of the three to combine the alert with a mandatory and immediate evaluation of the patient to specifically address the potential diagnosis of sepsis, which can be regarded as an additional process change.

A problem in sepsis screening is that there is a plethora of different risk scores and screening tools which are currently used, such as the SIRS criteria, Modified Early Warning Score (MEWS), National Early Warning Score (NEWS), and quick Sequential Organ Failure Score (qSOFA). The accuracy of these risk scores is highly variable in the emergency department, regular wards, and the ICU [27].

Several extensive studies and reviews have evaluated which screening tool is most effective for suspected infection or sepsis [27–31]. The NEWS and MEWS consistently show a balance between sensitivity and specificity, both usually ranging between 0.40 and 0.80 [27, 29]. SIRS is more sensitive than specific, and qSOFA more specific than sensitive. None of these instruments seems superior to the others in identifying sepsis across studies [27–31]. The SSC guideline consequently does not recommend using a particular tool [1]. Physicians should be aware of the benefits and limitations of the tools they use, and choices should be based on local preferences. The only exception is the use of qSOFA, which the guideline recommends against as a screening tool [1]. Although the qSOFA is highly specific, the poor sensitivity makes it unsuitable for screening purposes.

A limitation to all currently used tools is that they are susceptible to false positives because of the relatively low prevalence of sepsis, particularly in the general emergency department and ward populations [30]. Advanced computational approaches such as machine learning could provide a solution for this and may eventually replace the current, less complex risk scores. A systematic review and meta-analysis evaluating seven studies showed that machine learning algorithms outperform MEWS, SIRS, and qSOFA for sepsis prediction [32]. Additionally, monitoring through EHR systems with continuous data streams can detect sepsis even earlier than static risk scores. Van Wyk et al. showed this when their algorithm predicted sepsis onset in 377 ICU patients in the USA on average 205 min earlier than SIRS criteria would have [33]. However, many challenges still need to be overcome before safely introducing machine learning tools for sepsis into everyday clinical practice [34]. Some of these challenges were recently illustrated by the external validation of the Epic Sepsis Model, the machine learning-based screening tool for sepsis provided by the EHR vendor, Epic (Verona, WI, USA) [35]. This algorithm is widely adopted for sepsis screening, particularly in the USA. In a population of 2552 sepsis patients among 38,455 hospitalizations, the Epic Sepsis Model reached an area under the curve (AUC) of only 0.63 for sepsis recognition in an external validation [35]. Physicians using this tool evaluated an average of 109 patients based on sepsis screening alerts to detect only one case earlier than they would have without, putting a disproportionate burden on the healthcare system.

Process Changes in Sepsis Care Pathways

Several studies have examined the effect of sepsis performance improvement programs using process changes to improve adherence to the SSC care bundles. After identifying a patient who may have sepsis, the diagnostic work-up and treatments should be promptly initiated. The most critical process change in sepsis care pathways studied in this regard is the implementation of sepsis (response) teams. Instead of putting the responsibility to act on a sepsis screening alert on one consulting physician, who may already care for multiple patients, dedicated teams are created to respond to sepsis alerts collectively. A pre-post study by Viale et al. in Italian emergency departments showed that implementing a dedicated sepsis response team was associated with increased bundle adherence from 4.6 to 32%, improved appropriateness of the initial antibiotic therapy from 30 to 79%, and a hazard ratio of 0.64 (95% CI 0.43–0.94) for 14-day all-cause mortality [3]. In another study from Italy, these results were replicated in a multidisciplinary ICU [36]. In this setting,

Schinkel *et al. Critical Care* (2022) 26:77

Page 4 of 8

implementing a dedicated sepsis team was reported to be associated with a significant decrease in in-hospital mortality from 68 to 23%. Furthermore, the use of the dedicated sepsis team was significantly associated with decreased mortality in univariate logistic analysis (OR 0.28, 95% CI 0.10–0.79) [36]. However, the results of these studies should be interpreted cautiously, given their observational design and potential for confounding by indication.

Process changes other than implementing a dedicated sepsis team may also contribute to better bundle adherence when they improve the efficiency of the care workflow. Examples that have been extensively studied are printed or easily accessible protocols, standardized EHR order sets, daily auditing with weekly feedback, and nurse-driven sepsis protocols [5]. Nurse-driven sepsis protocols are a practical approach that acknowledges the essential role of nurses in the sepsis care pathways [37]. Their role is not formally described in the SSC guidelines, but they are often the first to triage patients and respond to their deteriorating condition. As an example, a Dutch study by Tromp et al. showed that a nurse-driven sepsis care bundle increased compliance with the complete bundle from 3.5 to 12.4% and the mean number of performed bundle elements within the appropriate timeframe from 3.0 to 4.2 [37]. Completion of four of the six individual bundle items, such as the measurement of serum lactate (23% to 80%) and the start of antibiotics within 3 h (38% to 56%), increased significantly. No significant changes in the in-hospital mortality rates or hospital length of stay were observed [37].

Sepsis Educational Programs

Arguably, increased sepsis awareness is one of the primary reasons for better patient outcomes through SSC care bundle use. Therefore, education is an essential aspect of sepsis performance improvement programs, as it helps raise awareness among healthcare professionals. The 2015 systematic review about sepsis performance improvement programs by Damiani et al. included 17 studies in which only educational programs were used [5]. These included educational materials, lectures, bedside teaching, and simulation training, among others. Many of these education-only programs showed significantly increased bundle adherence and decreased mortality rates. An early observational cohort study in the USA by Nguyen et al. studied the effects of a comprehensive sepsis education program in a small cohort of 96 patients with sepsis in their ICU [38]. A mortality rate of 45% was observed when the compliance with SSC care bundles

was high, but was 73% when SSC guidelines were largely disregarded ($p = 0.006$). Another example of the effects of educational programs is the more extensive study by van Zanten and colleagues, which also reduced the limitations of the observational approach by using control groups and propensity score matching [22]. Implementation of educational programs in 52 participating hospitals was associated with an absolute increase of 23.6% in SSC bundle adherence and an absolute decrease in mortality rates of 5.8% in 8031 ICU patients with sepsis during the study period. No such associations were found in 8387 ICU patients in 30 non-participating hospitals over the same period.

The Road Ahead

The discussion about the precise value of the SSC care bundles and the care processes within them will inevitably continue [6, 7]. Standardized expert care recommendations are indispensable for a syndrome with a mortality rate as high as it is in sepsis. However, such recommendations are often challenging to develop given the heterogeneity of sepsis and the weak and often contradicting evidence for its different treatment modalities [1, 13, 39]. Still, bundle adherence has consistently been associated with improved patient outcomes. An unanswered question is whether improved patient outcomes are caused by the items in the care bundles, by increased awareness irrespective of bundle adherence, or whether they are just artifacts of confounding by indication. Well-controlled trials could potentially find a definitive answer to this question, further determining what matters most while implementing sepsis performance improvement programs. Such a trial will, however, be hard to carry out and needs sophisticated methodological design.

Sepsis improvement programs are associated with improved protocol compliance and can be helpful to improve protocol adherence when a hospital or healthcare system implements either the SSC sepsis guidelines or their version of a protocol for sepsis detection and treatment. Therefore, these programs should be used in any hospital with low adherence rates to local protocols. The program should ideally consist of various simultaneous interventions to promote bundle compliance optimally [5]. Those interventions can be sepsis screening tools, process changes in sepsis care pathways, and sepsis educational programs. However, the goal should never be to mandate 100% guideline adherence but to leave room to deviate from standardized protocols when appropriate.

Schinkel *et al. Critical Care*   (2022) 26:77

Page 5 of 8

In our university medical center, we initiated a sepsis performance improvement program in 2021. As an illustration, we provide the details about this program, including early lessons learned from the implementation process in Box 1. The flowchart for our sepsis response team set-up is visually presented in Fig. 1. A major takeaway is that the engagement of only a few clinical leaders per department seems insufficient in an emergency department's dynamic and continuous environment. Furthermore, the involvement of patient representatives is important when initiating a sepsis performance improvement program, as the values and perspectives of the main stakeholder should not be overlooked. In high-pressure situations, such as acute care for patients with suspected sepsis in the emergency department, treatment of the patient's physical state is prioritized over the mental state. However, systematically addressing important questions the patient may have could alleviate much of the mental stress they will likely experience. In Box 2, we summarize important questions to address from the viewpoint of a sepsis survivor who has been involved with our sepsis performance improvement program.

Box 1 An example from the emergency department: creating a sepsis performance improvement program in a large university medical center. The different phases of implementing a sepsis performance improvement program in the Amsterdam University Medical Center

Pre-implementation phase:

• Retrospective and prospective evaluation of the current situation to identify opportunities for improvement. We noted:

  - Sequential ED consultations by various specialists, which delayed appropriate care.

  - Non-urgent triage codes in (elderly) patients with suspected sepsis.

• Involvement of patient representatives.

  Interventions:

• Screening tool selected: MEWS (already in use and thus easy to incorporate).

• Process changes: Initiation of a sepsis response team, standardized notes and EHR order sets, daily audit and weekly feedback.

• Education: Launch of a dedicated website, pocket cards, talks at morning hand-over.

  Lessons learned so far:

• Early challenges include behavior change and trust among all stakeholders that the new workflow will be efficient and may improve outcomes.

• The engagement of only a few clinical leaders per department seems insufficient for successful implementation, especially in the dynamic environment of an ED.

ED emergency department, *ICU* intensive care unit, *MEWS* Modified Early Warning Score, *EHR* electronic health record
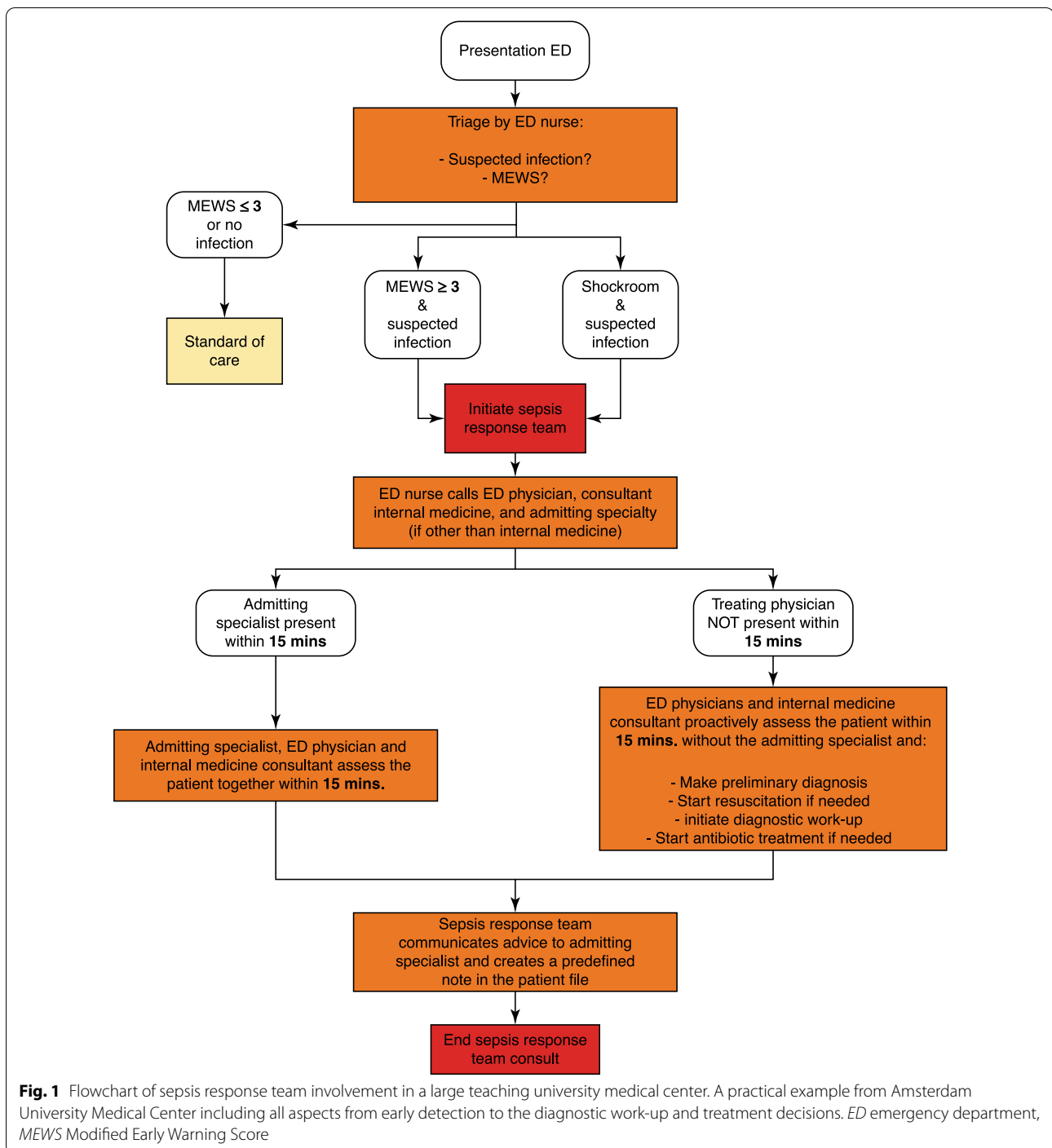
Box 2 Essential aspects of emergency department sepsis care from the patient's point of view. A summary of aspects to address during the evaluation of and conversation with a patient who may have sepsis

• Acknowledge the signs that a patient is worried and take them seriously

• Communicate about the word "sepsis" and what it means

• Communicate the urgency that the potential sepsis is recognized

• Inform the patient about the use of a sepsis team or sepsis protocol

• Inform the patient about the plan of action, including possible tests, treatments, and other decisions to be made over the following hours

• Inform the patient about the effects/symptoms that can be expected from the treatment or progression of the syndrome

Finally, most studies investigating the benefits of bundled care and sepsis performance improvement programs used mortality reduction as an endpoint [5]. Already in 2005, an International Sepsis Forum (ISF) colloquium provided a broad set of outcome measures that sepsis studies can use beyond survival as the only and ultimate goal of sepsis care [40]. Nevertheless, the literature is still dominated by the pursuit of short-term survival benefits. During the coronavirus disease 2019 (COVID-19) pandemic, the ISF proposed an adjusted version of the original outcome set, which was adopted globally [40, 41]. Improving outcome parameters such as resource use, duration of invasive treatments, and the development of organ dysfunction that requires higher levels of care, suddenly became extremely valuable in a resource-scarce setting [42]. Future studies on sepsis performance improvement programs and sepsis care bundles should similarly expand the core set of outcome measures to capture these additional benefits. In the era of shared decision-making and patient-centered care, we should acknowledge that there is more to life than death [43].

Conclusion

Sepsis performance improvement programs can optimize compliance to sepsis care protocols, which have been associated with improved patient outcomes in various studies. These programs should ideally combine screening tools, process changes in sepsis care pathways, and educational programs to create awareness about sepsis care. The consequent gains through swift and adequate recognition of sepsis can be used to diagnose and treat patients accurately and timely according to (SSC) care protocols and deliberately think about when it is necessary to deviate from the general recommendations. Trust and behavior change are essential aspects of implementing sepsis care bundles. These aspects can be reinforced by performance improvement programs but need time. Engaging a large group

Schinkel *et al. Critical Care* (2022) 26:77

Page 6 of 8

Fig. 1 Flowchart of sepsis response team involvement in a large teaching university medical center. A practical example from Amsterdam University Medical Center including all aspects from early detection to the diagnostic work-up and treatment decisions. *ED* emergency department, *MEWS* Modified Early Warning Score

of multidisciplinary clinical leaders for sepsis improvement programs seems essential for their success.

Authors' contributions
MS and WJW conceived the study. MS, PWBN, and WJW analysed and interpreted the literature. MS drafted the work. PWBN and WJW substantially revised the work. MS, PWBN, and WJW all read and approved the final version of the manuscript and agree to be accountable for the integrity of the work. All authors read and approved the final manuscript.

Schinkel *et al. Critical Care* (2022) 26:77

Page 7 of 8

Availability of data and material
Not applicable.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
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Competing interests
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Schinkel *et al. Critical Care*   (2022) 26:77

Page 8 of 8

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