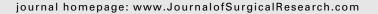


Available online at www.sciencedirect.com

# **ScienceDirect**





## **Association for Academic Surgery**

# Sooner is better: use of a real-time automated bedside dashboard improves sepsis care



Andrew D. Jung, MD,<sup>a</sup> Jennifer Baker, MD,<sup>a</sup> Christopher A. Droege, PharmD,<sup>b</sup> Vanessa Nomellini, MD PhD,<sup>a</sup> Jay Johannigman, MD,<sup>a</sup> John B. Holcomb, MD,<sup>c</sup> Michael D. Goodman, MD,<sup>a</sup> and Timothy A. Pritts, MD PhD<sup>a,\*</sup>

### ARTICLE INFO

Article history:
Received 1 March 2018
Received in revised form
4 May 2018
Accepted 31 May 2018
Available online 29 June 2018

Keywords:
Sepsis
Septic shock
Sepsis screening score
Clinical decision support tools
Guideline compliance
Antibiotic treatment

#### ABSTRACT

Background: Minimizing the interval between diagnosis of sepsis and administration of antibiotics improves patient outcomes. We hypothesized that a commercially available bedside clinical surveillance visualization system (BSV) would hasten antibiotic administration and decrease length of stay (LOS) in surgical intensive care unit (SICU) patients. Methods: A BSV, integrated with the electronic medical record and displayed at bedside, was implemented in our SICU in July 2016. A visual sepsis screen score (SSS) was added in July 2017. All patients admitted to SICU beds with bedside displays equipped with a BSV were analyzed to determine mean SSS, maximum SSS, time from positive SSS to antibiotic administration, SICU LOS, and mortality.

Results: During the study period, 232 patients were admitted to beds equipped with the clinical surveillance visualization system. Thirty patients demonstrated positive SSS followed by confirmed sepsis (23 Pre-SSS versus 7 Post-SSS). Mean and maximum SSS were similar. Time from positive SSS to antibiotic administration was decreased in patients with a visual SSS (55.3  $\pm$  15.5 h versus 16.2  $\pm$  9.2 h; P < 0.05). ICU and hospital LOS was also decreased (P < 0.01).

Conclusions: Implementation of a visual SSS into a BSV led to a decreased time interval between the positive SSS and administration of antibiotics and was associated with shorter SICU and hospital LOS. Integration of a visual decision support system may help providers adhere to Surviving Sepsis Guidelines.

© 2018 Elsevier Inc. All rights reserved.

<sup>&</sup>lt;sup>a</sup> Department of Surgery, University of Cincinnati, Cincinnati, Ohio

<sup>&</sup>lt;sup>b</sup> Department of Pharmacy Services, UC Health-University of Cincinnati Medical Center, Cincinnati Ohio

<sup>&</sup>lt;sup>c</sup> Department of Surgery, University of Texas Health Science Center at Houston, Houston Texas

<sup>\*</sup> Corresponding author. Department of Surgery, University of Cincinnati, 231 Albert Sabin Way, ML 0558, Cincinnati, OH 45267-0558. Tel.: +513 558 8467; fax: +513 558 8677.

E-mail address: prittsta@ucmail.uc.edu (T.A. Pritts). 0022-4804/\$ — see front matter © 2018 Elsevier Inc. All rights reserved.

#### Introduction

Despite advances in modern critical care, sepsis remains a leading contributor to in-hospital morbidity and mortality. It is estimated that 750,000 patients are treated for severe sepsis and septic shock in the United States each year. Sepsis is a common diagnosis among intensive care unit admissions, and mortality rates have been shown to be at least 25%. Sepsis is a common diagnosis among intensive care unit admissions, and mortality rates have been shown to be at least 25%.

The Surviving Sepsis Campaign was launched in 2004 and provided guidelines for the diagnosis and treatment of severe sepsis and septic shock.<sup>4</sup> The Third International Consensus Definitions for Sepsis and Septic Shock defines sepsis as a serious blood infection and associated acute organ dysfunction as outlined by the Sequential Organ Failure Assessment (SOFA) score: vasopressors, mechanical ventilation, elevated creatinine, elevated total bilirubin, thrombocytopenia, and elevated lactate. 5-7 The most recent guidelines were published in 2016 and emphasize early fluid resuscitation, source control, and administration of intravenous antibiotics.8 Previous studies have shown that optimal outcomes in the treatment of severe sepsis and septic shock are achieved when treatments are administered utilizing clinical care bundles.9 Unfortunately, widespread implementation and compliance with trauma clinical practice and sepsis treatment bundles is inconsistent. 10-12 In the treatment of sepsis, Seymour et al. showed that rapid completion of sepsis treatment bundles was associated with lower in-hospital mortality. 13 Time to antibiotic administration may be the most crucial variable, as further studies have demonstrated increases in mortality with each hour of delay in antibiotic administration.14

Clinical decision support tools have the potential to improve treatment of various medical conditions cared for in the intensive care setting. 15-17 Their utility lies in enhancing awareness of worsening and critical disease states to

clinicians. Because the treatment of severe sepsis and septic shock is multidisciplinary, clinical decision support tools visible to the patient, patient families, and the entire health care team may augment or expedite the delivery of appropriate, timely medical care. The effect of a visual clinical decision support tool on the time to antibiotic administration in patients with sepsis or potential sepsis is unknown. We hypothesized that implementation of a commercially available bedside clinical surveillance visualization system would be associated with improved patient outcomes, including earlier antibiotic administration, decreased length of stay (LOS), and reduced mortality in surgical intensive care unit (SICU) patients.

## **Methods**

## Automated clinical surveillance visualization system

In July 2016, an automated clinical surveillance visualization system (Decisio Health Inc, Houston, TX; www.decisiohealth.com) was implemented within the SICU at the University of Cincinnati Medical Center. This visualization system was integrated with our electronic medical record (EPIC, Verona, WI) and displays patient vital signs and laboratory values in real time on a 42-inch dedicated monitor mounted above the patient's hospital bed (Fig. 1). This visualization system has the ability to integrate with multiple electronic medical records and was initially used with the Cerner EMR (Kansas City, MO). The monitor is visible to physicians and nurses, as well as the patient and family. The patient display is conditionally color-coded to allow for rapid identification of abnormal vital signs and laboratory values. Vital signs and laboratory values within normal clinical ranges are displayed bright green. As the

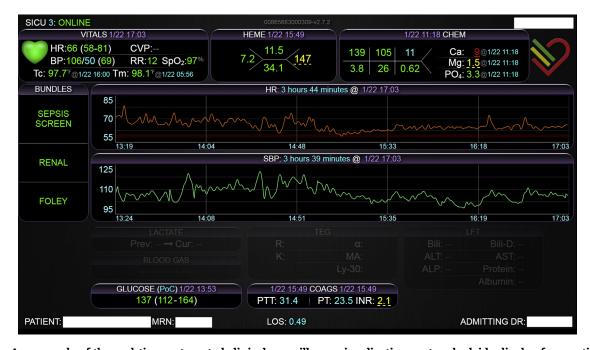


Fig. 1- An example of the real-time automated clinical surveillance visualization system bedside display for a patient admitted to the surgical intensive care unit. (Color version of figure is available online.)

values approach the upper or lower limits of normal, the relevant portion of the display switches to yellow. Bright red values are displayed when vital signs and laboratory values are critically abnormal and serve as a visual stimulus for action by physicians. The clinical surveillance system automatically collected data via the electronic medical record on all 34 beds within the SICU, but bedside displays were installed in 12 of 34 patient beds. Patient displays for all beds were also viewable from a centrally located computer within the intensive care unit, as well as on mobile workstations on wheels.

## Sepsis screen score

In July 2017, an automated sepsis screen score (SSS) was activated within the clinical surveillance system and made viewable on the bedside display system. The SSS is a numerical score based on prior validated definitions and is composed of heart rate, body temperature, respiratory rate, and white blood cell count. <sup>18</sup> Each value is assigned a value, which is then totaled to provide the SSS (Table 1). A positive SSS is defined as a score greater than or equal to 4. On identification of a positive SSS, physicians proceeded to initiate a pre-existing sepsis care pathway (which included blood cultures, imaging, and additional laboratory tests) to confirm a diagnosis of sepsis.

#### Clinical outcomes with an SSS displayed at bedside

From July 2016 to September 2017, patient data were collected on all patients admitted to the 12 SICU rooms that contained the automated clinical surveillance visualization system bedside display (n=232). Patients who did not receive antibiotics for sepsis based on the SSS were excluded (n=195). Of the remaining 37 patients screening positive for sepsis and receiving antibiotics, 30 patients were confirmed to have sepsis based on positive cultures. These 30 patients were separated into two groups. The pre-Sepsis Screen Score (Pre-SSS) group included patients admitted only to SICU beds that had the clinical surveillance visualization system displayed at bedside before the implementation of the visible SSS (July 2016-June 2017, n=23), and the post-Sepsis Screen Score

(Post-SSS) group included patients admitted only to SICU beds that had the clinical surveillance visualization system displayed at bedside after the SSS was made visible to physicians (July 2017-September 2017, n=7). Time to antibiotics was calculated as the length of time from the moment the SSS turned positive to when the first dose of intravenous antibiotics was recorded as administered via barcode scan in the electronic medical record.

#### Statistical methods

The primary outcome measured was time to antibiotic administration after a positive SSS. Secondary outcomes measured included mean sepsis score, maximum sepsis score, SICU LOS, hospital LOS, and in-hospital mortality. Univariate analysis for continuous variables was performed with a two-tailed Student's t-test and ANOVA when appropriate. Analyses were performed using Stata 13.1 software (College Station, TX), and significance was defined as P value less than 0.05. This study was approved by the Institutional Review Board before data collection.

#### **Results**

From July 2016 to September 2017, a total of 232 patients were admitted to beds with bedside clinical surveillance visualization systems in the SICU. Thirty patients (12.9%) demonstrated a positive SSS and were confirmed to have sepsis based on positive cultures. Twenty-three of 30 patients were admitted before the deployment of the SSS on the bedside display system (Pre-SSS), and seven of 30 patients were admitted after the SSS was activated on the bedside display (Post-SSS). Patient demographics are presented in Table 2. There were no significant differences between age, gender, comorbidities, or reason for admission to the SICU. The mean SSS was similar between the two groups (1.6  $\pm$  0.1 versus $1.9 \pm 0.4$ , P = NS; Fig. 2A), as well as the maximum sepsis score (6.2  $\pm$  0.5 versus 5.7  $\pm$  0.5, P = NS; Fig. 2B). Time from positive SSS to antibiotic administration was significantly shorter after activation of the SSS on the bedside display (55.3  $\pm$  15.5 h

Component	Points					
	0	1	2	3	4	
HR (bpm)	70-109		55-69	40-54	≤39	
			110-139	140-179	≥180	
Temp (°C)	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9	
		38.5-38.9		39-40.9	≥41	
RR (br/m)	12-24	10-11	6-9	35-49	≤5	
		25-34			≥50	
WBC (kcell/mm³)	3-14.9	15-19.9	1-2.9		≤1	
			20-39.9		>40	

HR = heart rate; bpm = beats per minute; temp = temperature; C = Celsius; RR = respirator rate; br/m = breaths per minute; WBC = white blood cell.

Table 2 – Patient demographics.						
Component	Pre-SSS (n = 23)	Post-SSS $(n=7)$	P value			
Gender, n (%)			NS			
Male	12 (52.2)	3 (42.9)				
Female	11 (47.8)	4 (57.1)				
Age in y, mean $\pm$ STD	$54.7\pm18.1$	$50.6 \pm 22.1$	NS			
CAD, n (%)	3 (13.0)	1 (14.3)	NS			
CKD, n (%)	4 (17.4)	0 (0)	NS			
DM, n (%)	9 (39.1)	2 (28.5)	NS			
Tobacco, n (%)	10 (43.5)	4 (57.1)	NS			
Reason for admission, n (%)			NS			
Emergency surgery	3 (13.0)	3 (42.9)				
Elective surgery	4 (17.4)	0 (0)				
Trauma	10 (43.5)	2 (28.5)				
Other	6 (26.1)	2 (28.5)				

 $y=year;\ CAD=coronary\ artery\ disease;\ CKD=chronic\ kidney\ disease;\ DM=diabetes\ mellitus.$ 

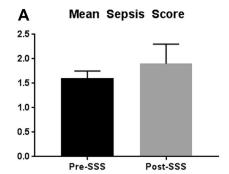
versus 16.2  $\pm$  9.2 h, P < 0.05; Fig. 3). SICU LOS was significantly shorter in the Post-SSS group (19.1  $\pm$  3.3 d versus 7.6  $\pm$  2.5 d, P < 0.01; Fig. 4A) as was the total hospital LOS (29.6  $\pm$  4.3 d versus 10.8  $\pm$  3.1 d, P < 0.01; Fig. 4B). There was no significant difference in mortality between the two patient cohorts.

## Discussion

The present study examined the effect of implementation of an SSS within an automated visual clinical surveillance system in the SICU at a single center, large-volume, academic institution. The visible SSS was implemented into the bedside clinical surveillance system in July 2017. When comparing patients admitted to SICU beds with a bedside display only installed, the inclusion of the visible SSS was associated with a significant reduction in the time to antibiotic administration and decreased ICU and overall hospital LOS.

Clinical variables used in the calculation of the SSS overlap with traditional definitions of systemic inflammatory response syndrome. 19 Many patients presenting to the SICU, either from the operating room or the trauma bay, exhibit the signs and symptoms of a systemic, noninfectious inflammatory response. This can potentially lead to a higher number of SICU patients with a false positive SSS. Therefore, once a patient had a positive SSS, the clinicians collected further data (e.g., physical examination, blood cultures, urine cultures, chest radiographs, computed tomography scans) to make a diagnosis of sepsis or septic shock. Although this study lacks the sample size to calculate an accurate sensitivity and specificity for the SSS in SICU patients, the sepsis screening score had a sensitivity of 96.5%, specificity of 96.7%, a positive predictive value of 80.2%, and a negative predictive value of 99.5% in a previous study. 20 Therefore, we are confident that the accuracy of the SSS is valid in our patient population.

The Surviving Sepsis Campaign was developed in 2002 with a primary goal to reduce sepsis-related mortality by 25% in 5 y by improving clinician diagnosis and developing standardized guidelines for appropriate treatment of sepsis and septic shock.<sup>21</sup> Initial definitions of sepsis were published in 2004, and its specifics were refined over the following decade.<sup>4</sup> Most recently, the fourth edition of the Surviving Sepsis Campaign International Guidelines for Management of Sepsis and Septic Shock was published in 2016 and focused on early sepsis screening and if positive, resuscitation guided by lactate levels, early source control, and early administration of intravenous antibiotics.8 Although these standardized guidelines have led to improvements in diagnosis and treatment of sepsis and septic shock, compliance remains an ongoing issue. Rhodes et al.<sup>22</sup> looked at global compliance of 3- and 6-h Surviving Sepsis Campaign bundles and found that compliance rates were low. Overall compliance with the 3-h bundle was only 19% (340 patients), and little improvement was seen in compliance with the 6-h bundle (35.5%, 637 patients). Surveys of critical care and internal medicine physicians



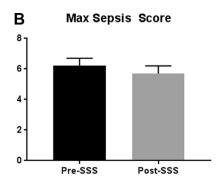


Fig. 2 – (A) Mean sepsis score of all patients admitted to a bed with a real-time automated clinical surveillance visualization system before the display of the sepsis score (Pre-SSS) and after the display of the sepsis score (Post-SSS). Values displayed as mean  $\pm$  standard error of the mean, and significance determined using two-tailed Student's t-test. 1.6  $\pm$  0.1 versus 1.9  $\pm$  0.4, P = NS. (B) Max sepsis score of all patients admitted to a bed with a real-time automated clinical surveillance visualization system before the display of the sepsis score (Pre-SSS) and after the display of the sepsis score (Post-SSS). Values displayed as mean  $\pm$  standard error of the mean, and significance determined using two-tailed Student's t-test. 6.2  $\pm$  0.5 versus 5.7  $\pm$  0.5, P = NS.

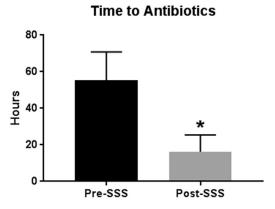


Fig. 3 — Average time from a positive sepsis score to administration of antibiotics in all patients admitted to a bed with a real-time automated clinical surveillance visualization system before the display of the sepsis score (Pre-SSS) and after the display of the sepsis score (Post-SSS). Value displayed as mean  $\pm$  standard error of the mean, and significance determined using two-tailed Student's t-test. 55.3  $\pm$  15.5 h versus 16.2  $\pm$  9.2, \*P < 0.05.

regarding sepsis guideline adherence demonstrated similar results of poor compliance.<sup>23</sup> Despite awareness efforts and standard treatment protocols, there are ongoing areas of improvement that need to be addressed.

Initiatives have been put in place in an attempt to improve compliance, including educational programs and dedicated medical staff for care of septic patients. <sup>24,25</sup> One potential method to improve guideline compliance is with the use of clinical decision tools for patient care, and early studies have shown promising results in compliance with antibiotic administration. <sup>26</sup> Barriers to full compliance arise given the multidisciplinary and time-sensitive approach to sepsis treatment, and clinical decision support tools may assist in guideline adherence. <sup>10,11</sup> Although all aspects of the Surviving Sepsis Guidelines are imperative for effective treatment of sepsis and septic shock, time to antibiotic administration may be the most crucial. Kumar et al. <sup>14</sup> found that when administering

antibiotics, each hour of delay from onset of hypotension was associated with a 7.6% decrease in hospital survival. Another study demonstrated that decreased time to antibiotic administration was associated with decreased in-hospital mortality. 13 However, in the latter study, adherence to the 3-h bundle ranged from 60% to 90%; and while the study did not postulate on reasons for noncompliance, the highest compliance was at small nonteaching hospitals with a low patient census compared with large referral centers. The fewer the distractions, the faster the care team is able to identify a patient in sepsis. Large academic centers may provide more opportunity for uncoordinated process of care. At these institutions, the implementation of bedside display systems and clinical decision support tools can assist in early diagnosis of sepsis and septic shock. Thus, antibiotics can be administered sooner, and in-hospital survival can improve. A recent meta-analysis demonstrated that programs aimed at improving education, diagnosis, and treatment of sepsis and septic shock were associated with increased compliance with Surviving Sepsis Campaign Guidelines.<sup>27</sup> The novelty of the technology used in our study is the combination of the bedside screen with easy to interpret labels in addition to the implementation of a sepsis screening score to prompt clinician response. Some electronic medical records already have notification capabilities but require accessing a patient's chart via a computer. The technology presented in our article provides real-time alerts that only require easy to interpret visual cues about a patient's status displayed on a large screen visual to all team members involved in the patient's care. In addition, the bedside surveillance system has the ability to send text alerts to mobile phones, but this specific aspect was not implemented in our present study. Future utilization of a remote alert system may improve guideline compliance with antibiotic administration. It is an area of ongoing investigation.

Our study found that the bedside display system in conjunction with the SSS bundle was associated with improved time to antibiotic administration. Although the 11-h time to antibiotic administration is longer than the 3-h window suggested in the Surviving Sepsis Campaign, the benefits of shortened ICU and overall hospital stay were nevertheless

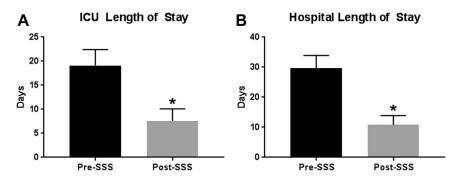


Fig. 4 - (A) Average intensive care unit days for all patients admitted to a bed with a real-time automated clinical surveillance visualization system before the display of the sepsis score (Pre-SSS) and after the display of the sepsis score (Post-SSS). Values displayed as mean  $\pm$  standard error of the mean, and significance determined using two-tailed Student's t-test. 19.1  $\pm$  3.3 d versus 7.6  $\pm$  2.5, \*P < 0.01. (B) Average hospital LOS for all patients admitted to a bed with a real-time automated clinical surveillance visualization system before the display of the sepsis score (Pre-SSS) and after the display of the sepsis score (Post-SSS). Values displayed as mean  $\pm$  standard error of the mean, and significance determined using two-tailed Student's t-test. 29.6  $\pm$  4.3 d versus 10.8  $\pm$  3.1 d, \*P < 0.01.

achieved. Given the limited number of ICU beds with a clinical visualization surveillance system installed at the bedside, our study is underpowered to show a difference in in-hospital mortality when comparing patients admitted only to beds equipped with the bedside display. The reduction in time to antibiotic administration is likely due to earlier identification of patients who are exhibiting signs and symptoms of sepsis, prompt initiation of a confirmatory sepsis work-up, and thus a more timely diagnosis of sepsis. Surviving Sepsis provides hospitals with sepsis bundles for streamlined treatment of severe sepsis, but timing is crucial. The bedside display system can quickly notify physicians of a possible septic patient and lead to more efficient initiation of a predesigned sepsis bundle. Discordance between antibiotic administration times likely lies within the patient population. Many of the studies looking at antibiotic administration involve patients presenting to the emergency department, not patients within an SICU. The clinical picture of sepsis is also complicated by a systemic inflammatory response that is not related to an infections process in patients in the SICU, and further investigative studies are performed to confirm sepsis before initiating antibiotics; and finally, the time span was calculated from the moment the SSS turned positive to the time that antibiotic were administered, not the time from actual diagnosis of sepsis and antibiotic order placement to administration. Because the SSS does not diagnose sepsis but rather assists in the identification of patients who show signs and symptoms of sepsis, additional diagnostic measures were taken before antibiotic administration, to minimize overuse of antibiotics. Surveys of physicians have demonstrated wide variation in their knowledge and application of sepsis definitions, leading to underrecognition. <sup>28,29</sup> Unfortunately, these additional steps inherently prolong the time to antibiotics, but with the use of the visual SSS, the duration can be optimized.

Historically, patients who developed severe sepsis had a mortality ranging from 20% to 50%. <sup>30</sup> As advances in medical care improve sepsis treatment, the in-hospital mortality rate has been decreasing by 3.3% per year. <sup>31</sup> Unfortunately, the improvement in mortality is negated by the rising incidence of sepsis. <sup>3,32</sup> Current literature estimates sepsis-specific in-hospital mortality at 15.0%. <sup>31</sup> In this study, there was no mortality benefit for inclusion of a sepsis score on the bedside display when specifically analyzing patients admitted only to ICU beds with the automated clinical surveillance visualization system displayed at bedside. This is likely due to a small sample size (n = 30), as there were only a total of six deaths. Monitoring of this patient population is ongoing, and we anticipate analysis of data every 6 mo to proactively follow the effects of bedside display system implementation.

There are several limitations to the study. First, patient data at a single large academic center were analyzed. This limits our conclusions about the benefit of widespread application of the clinical display system to similar hospitals. Unfortunately our data are underpowered to reveal a mortality benefit for rooms that display the bedside clinical surveillance visualization decision support system. Second, the bedside display system uses a sepsis screening score that focuses on temperature, white blood cell count, blood pressure, and heart rate. Current Sepsis-3 guidelines emphasize the use of SOFA or Quick SOFA (qSOFA). However, Sepsis-3 states that SOFA

and qSOFA are not the "stand-alone definitions for sepsis," and that SIRS criteria can "still be useful in identification of infection."5 SOFA and qSOFA use subjective data that require manual input into the electronic medical record. This manual input can be a source of delay in alert notification and identification of sepsis. Thus, the authors decided to incorporate the SSS, which is calculated based on automatically populated objective data, into the surveillance system. Nevertheless, physical examination and patient evaluation remain of utmost importance, and the authors stress that this alert system is a screening tool and does not replace bedside evaluation and sound clinical judgment. In addition, the analysis is between a historical cohort (Pre-SSS) instead of a contemporary cohort. While patient demographics and indications for admission are similar, a seasonal bias may have been introduced into the data. Fourth, although the display system is visible in patient rooms and on computers within the ICU, there was no standardized response system in place for appropriate nurse and physician response to a positive SSS. This is a future area of study. Fifth, four of the 11 patients who were given antibiotics in the Post-SSS group later had their antibiotics stopped, compared with three of the 26 patients in the Pre-SSS group. The concern for overuse of antibiotics is legitimate, and further ongoing analysis is needed to identify if a significant overuse of antibiotics will result from this visual SSS.

#### Conclusion

Implementation of an SSS for a bedside clinical surveillance visualization decision support system was associated with a decreased time interval between the diagnosis of sepsis or septic shock and administration of antibiotics, resulting in decreased ICU and hospital LOS. Integration of clinical decision support systems in the ICU setting may help providers to adhere to Surviving Sepsis Guidelines for identification and treatment of surgical patients with infections and improve quality of care.

## Acknowledgment

Authors' contributions: A.D.J. and J.B. involved in data analysis, preparation of article, and critical revisions of article. C.A.D. involved in concept design, data analysis, preparation of article, and critical revisions of article. V.N., J.J., M.D.G., and T.A.P. involved in concept design, data acquisition and analysis, preparation of article, and critical revisions of article. J.B.H. involved in concept design, preparation of article, and critical revisions of article.

## **Disclosures**

J.B.H. is a member of board of directors and has equity in Decisio Health and is the CMO of Prytime Medical. Although he was involved in conceptualization of study design, preparation of article, and critical revisions of article, he did not participate in data collection or data analysis to minimize the confounding effect of his conflict of interest.

#### REFERENCES

- Jones AE, Shapiro NI, Roshon M. Implementing early goal directed therapy in the emergency setting: the challenges and experiences of translating research innovations into clinical reality in academic and community settings. Acad Emerg Med. 2007;14:1072-1078.
- Angus DC, Linde-Zwirble WT, Lidicker J, et al. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med. 2001;29:1303–1310.
- 3. Dombrovskiy VY, Martin AA, Sunderaam J, et al. Rapid increase in hospitalization and mortality rates in the United States: a trend analysis from 1993 to 2003. Crit Care Med. 2007;35:1244–1250.
- Dellinger RP, Carlet JM, Masur H, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med. 2004;32:858–873.
- Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315:801–810.
- Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315:762–774.
- Vincent JL, Moreno R, Takala J, et al. Working group on sepsisrelated problems of the European Society of intensive care medicine. The SOFA (Sepsis-related organ failure assessment) score to describe organ dysfunction/failure. *Intensive Care Med.* 1996;22:707–710.
- 8. Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med. 2017;43:304—377.
- 9. Nguyen HB, Corbett SW, Steele R, et al. Implementation of a bundle of quality indicators for the early management of severe sepsis and septic shock is associated with decreased mortality. Crit Care Med. 2007;35:1105–1112.
- Carlbom DJ, Rubenfeld GD. Barriers to implementing protocol-based sepsis resuscitation in the emergency department: results of a national survey. Crit Care Med. 2007;35:2525–2532.
- Fong JJ, Cecere K, Unterborn J, Garpestad E, Klee M, Devlin JW. Factors influencing variability in compliance rates and clinical outcomes among three different sepsis bundles. Ann Pharmacother. 2007;41:929–936.
- 12. Shafi S, Barnes SA, Rayan N, et al. Compliance with recommended care at trauma centers: association with patient outcomes. *J Am Coll Surg.* 2014;219:189–198.
- Seymour CW, Gesten F, Prescott HC, et al. Time to treatment and mortality during mandated emergency care for sepsis. N Engl J Med. 2017;376:2235–2244.
- 14. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006;34:1589–1596.

- Garg AX, Adhikari NKJ, McDonald H, et al. Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. JAMA. 2005;293:1223–1238.
- Lehmann ED. Computerized decision-support tools in diabetes care: hurdles to implementation. Diabetes Technol Ther. 2004;6:422–429.
- Schurink CA, Lucas PJ, Hoepelman IM, et al. Computer assisted decision support software for the diagnosis and treatment of infectious diseases in intensive care units. Lancet Infect Dis. 2005;5:305–312.
- Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest. 1992;101:1644–1655.
- **19.** Simpson SQ. SIRS in the time of Sepsis-3. *Chest.* 2018;153:34–38.
- Moore LJ, Jones SL, Kreiner LA, et al. Validation of a screening tool for the early identification of sepsis. *J Trauma*. 2009;66:1539–1546.
- Powell C. Surviving sepsis campaign: history. Available at:http://survivingsepsis.org . Accessed February 6, 2018.
- 22. Rhodes A, Phillips G, Beale R, et al. The surviving sepsis campaign bundles and outcome: results from the international multicentre prevalence study on sepsis (the IMPreSS study). Intensive Care Med. 2015;41:1620—1628.
- 23. Djurkovic S, Baracaldo JC, Guerra JA, et al. A survey of clinicians addressing the approach to the management of severe sepsis and septic shock in the United States. *J Crit Care*. 2010;25:658.e1–658.e6.
- 24. Levy MM, Dellinger RP, Townsend SR, et al. The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. *Intensive Care Med.* 2010;36:222–231.
- Berg GM, Vasquez DG, Hale LDS, Nyberg SM, Moran DA. Evaluation of process variations in noncompliance in implementation of evidence-based sepsis care. J Healthc Qual. 2013;35:60-69.
- Giuliano KK, Lecardo M, Staul LA. Impact of protocol watch on compliance with the Surviving Sepsis Campaign. Am J Crit Care. 2011;20:330–331.
- 27. Damiani E, Donati A, Serafini G, et al. Effect of performance improvement programs on compliance with sepsis bundles and mortality: a systematic review and meta-analysis of observational studies. PLoS One. 2015;10:e0125827.
- 28. Whittaker SA, Mikkelsen ME, Gaieski DF, Koshy S, Kean C, Fuchs BD. Severe sepsis cohorts derived from claims-based strategies appear to be biased toward a more severely ill patient population. Crit Care Med. 2013;41:945–953.
- 29. Rhee C, Kadri SS, Danner RL, et al. Diagnosing sepsis is subjective and highly variable: a survey of intensivists using case vignettes. Crit Care. 2016;20:89.
- 30. Wheeler AP, Bernard GR. Treating patients with severe sepsis. N Engl J Med. 1999;340:207—214.
- 31. Rhee C, Dantes R, Epstein L, et al. Incidence and trends of sepsis in US hospitals using clinical vs claims data, 2009-2014. *JAMA*. 2017;318:1241–1249.
- Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003;348:1546–1554.