

OPEN

A Multimodal Sepsis Quality-Improvement Initiative Including 24/7 Screening and a Dedicated Sepsis Response Team-Reduced Readmissions and Mortality

Muhtadi H. Alnababteh, MD¹; Sean Shenghsiu Huang, PhD²; Andrea Ryan, MSN³;
Kevin M. McGowan, MS⁴; Seife Yohannes, MD⁵

Objectives: To evaluate if a hospitalwide sepsis performance improvement initiative improves compliance with the Centers for Medicare and Medicaid Services-mandated sepsis bundle interventions and patient outcomes.

Study Design: Retrospective analysis comparing 6 months before and 14 months after intervention.

Setting: Tertiary teaching hospital in Washington, DC.

Subjects: Patients admitted with a diagnosis of sepsis to a tertiary hospital.

Interventions: Implementation of a multimodal quality-improvement initiative.

Measurements and Main Results: A total of 4,102 patients were diagnosed with sepsis, severe sepsis, or septic shock during the study period, 861 patients (21%) were diagnosed during a 6-month preintervention period, and 3,241 (79%) were diagnosed in a 13-month postintervention period. Adjusted for patient case-mix, the prevalence of simple sepsis increased by 12%, but it decreased for severe sepsis and septic shock by 5.3% and 6.9%, respectively. Compliance with

all sepsis bundle interventions increased by 31.1 percentage points ($p < 0.01$). All-cause hospital readmission and readmission due to infection were both reduced by 1.6% and 1.7 percentage points ($p < 0.05$). Death from any sepsis diagnosis was reduced 4.5% ($p < 0.01$). Death from severe sepsis and septic shock both was reduced by 5% ($p < 0.01$) and 6.5% ($p < 0.01$), respectively.

Conclusions: After the implementation of multimodal sepsis performance initiatives, we observed a higher prevalence of sepsis secondary to screening but a lower prevalence of severe sepsis and septic shock, an improvement in compliance with the sepsis bundle interventions bundle, as well as reduction in hospital readmission and all-cause mortality rate.

Key Words: early warning system; infection; performance improvement; sepsis response team; sepsis

¹Department of Internal Medicine, MedStar Washington Hospital Center, Washington, DC.

²Department of Health Systems Administration, Georgetown University, Washington, DC.

³Department of Quality and Outcomes, MedStar Washington Hospital Center, Washington, DC.

⁴Georgetown University School of Medicine, Washington, DC.

⁵Department of Critical Care, MedStar Washington Hospital Center, Washington, DC.

Copyright © 2020 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of the Society of Critical Care Medicine. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Crit Care Expl 2020; 2:e0251

DOI: 10.1097/CCE.0000000000000251

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Sepsis remains a leading cause of death globally, with a global estimate of 31.5 million sepsis and 19.4 million severe sepsis cases, with potentially 5.3 million deaths annually (1). Septic shock occurs at a rate of 19 per 1,000 hospitalizations in the United States, contributing to a mortality of 39–51% (2). Cost of sepsis, severe sepsis, and septic shock are estimated to be \$16,324, \$24,638, and \$38,298 per case, respectively. According to the National Inpatient Hospital Costs report, sepsis is the most expensive condition to be treated, accounting for \$23.7 billion or 6.2% of the aggregate costs for all hospitalizations (3). With high mortality, morbidity, and cost, efforts have been directed toward developing guidelines for sepsis managements. Rivers et al (4) showed that early goal-directed therapy (EGDT) decreases mortality and length of hospital stay. Other studies showed improvement in reversal of persistent shock and decreases in in-hospital mortality rates with the use of goal-directed therapy (5). Although subsequent randomized controlled trials did not show the benefit of some of the interventions within

TABLE 1. Three- and Six-Hour Bundle Elements as Mandated by Centers for Medicare and Medicaid Services

3-hr Bundle	
Obtain statum (immediately) lactate as soon as criteria met for sepsis along with complete blood count/complete metabolic panel and additional labs based on situation	
Obtain blood cultures (×2) before initiation of antibiotics (if unable to obtain within 15 min, please document reason)	
Administer broad-spectrum antibiotics (based on hospital guideline)	
Administer at least 30 mL/kg of actual body weight IV fluids for hypotension (SBP < 90; MAP < 65) or a lactate ≥ 4 mmol/L	
Consider inotropic support for inadequate myocardial performance	
6-hr Bundle	
Repeat lactate level if initial is > 2 to trend	
Initiate vasopressors and/or additional volume for hypotension to maintain SBP > 90 or MAP ≥ 65 mm Hg	
Consider inotropic support for inadequate myocardial performance	
If septic shock criteria are present, the physician/nurse practitioner/physician assistant must document the presence of septic shock and document within 6 hr of septic shock presentation a repeat assessment to include:	
A focused examination with review of all elements of:	Or any two of the following four:
Vital signs review	Bedside cardiovascular ultrasound to assess volume status and myocardial performance
Cardiopulmonary examination	
Capillary refill evaluation	Passive leg raise examination or response to a fluid challenge
Peripheral pulse evaluation	Central venous pressure measurement
Skin examination	Central venous oxygen measurement

MAP = mean arterial pressure, SBP = systolic blood pressure.

the EGDT, the studies provided a construct on early resuscitation of patients with sepsis that includes early antibiotics, correction of hypovolemia, and restoring adequate perfusion.

The Surviving Sepsis Campaign (SSC) came as initiative to develop guidelines for the early management of sepsis and septic shock through timely 3- and 6-hours bundles (6). **Table 1** summarizes the SSC Guideline 3- and 6-hour interventions. SSC was associated with sustained and continuous quality improvement (CQI) in sepsis care, and a reduction in reported hospital mortality rates was associated with participation (7).

With a goal to improve compliance with bundled treatments per the SSC, the Centers for Medicare and Medicaid Services (CMS) has implemented the 2012 SSC Guidelines in a Sepsis Core Measure (sepsis bundle interventions) Inpatient Quality Reporting Metric mandate for hospitals to implement CQI including early identification of patients with sepsis and septic shock as well as implementation of elements of the 3- and 6-hour bundle interventions (8).

Since implementation of the mandate, some have argued that apart from the timely administration of antibiotics, all other elements of the 3- and 6-hour resuscitation bundles are devoid of supporting scientific evidence and do not positively influence patient outcomes (9).

At our hospital, a 912-bed tertiary hospital, with average annual 45,500 inpatient and observation discharges and 64,300 emergency department visits, a multimodal sepsis performance

initiative was implemented in 2016. In this study, we aim to analyze the effects of the sepsis performance initiative on sepsis bundle compliance and patient outcomes.

MATERIALS AND METHODS

A Sepsis Performance Improvement Committee was formed in February 2016. The committee was coled by nurse and physician champions, with hands-on sponsorship from the hospital chief medical officer. The committee was composed of physicians, advance practice providers (APPs), nurses, and members from hospital pharmacy, laboratory, IT, phlebotomy, coding and documentation, quality improvement, and process improvement. The committee instituted five new interventions: a clinical decision support (CDS) tool, sepsis response team, education campaign, electronic templates and order set, and data monitoring and quality improvement. The initiative was implemented sequentially over a 13-month period between May 1, 2016, and May 31, 2017. The period of implementation was excluded from the pre- and postanalysis of this study.

1) Clinical Decision Support Tool: In April 2016, a new 24/7 electronic CDS tool for sepsis screening, called St John's Alert (Cerner Corporation, Kansas City, MO), embedded in the electronic health record (EHR), was implemented in the emergency department and hospital wards. The CDS uses the American College of Chest Physicians/Society of Critical Care Medicine

TABLE 2. Clinical Decision Support Tool for Sepsis Screening, St John's Alert (Cerner Corporation, Kansas City, MO), Embedded in the Electronic Health Record in the Emergency Department and Hospital Wards

Alert 1	Alert 2
When ≥ 3 SIRS criteria are met as below	When ≥ 2 SIRS criteria and ≥ 1 of the following four organ system dysfunction criteria are met:
Temperature > 38.3 or $< 36.0^{\circ}\text{C}$	Systolic blood pressure < 90 mm Hg and/or mean arterial pressure < 65 mm Hg
Heart rate > 90	
WBC $> 12\text{k}$ or $< 4\text{k}$ or $> 10\%$ bands	Serum lactate > 2.0 mmol/L
Respiratory rate > 20	Total bilirubin ≥ 2.0 mg/dL and < 10.0 mg/dL
	Serum creatinine $\Delta \uparrow 0.5$ mg/dL from baseline

SIRS = systemic inflammatory response syndrome.

Sepsis 2 definition from 2001 to identify risk patients. The CDS was validated by Amland and Hahn-Cover (10), showing 83% sensitivity and 92% specificity for sepsis detection, and it was shown to recognize sepsis before a provider suspected infection and ordered diagnostic tests or antibiotics indicating a suspicion of infection, 24% of the time. Confirmed infection rate of patients identified by the CDS was 65% (10).

The CDS screens for systemic inflammatory response syndrome (SIRS) and for end-organ dysfunction, as shown in Table 2. Two types of alerts were developed. The first alert screens for SIRS and triggers when at least three of the four SIRS criteria are met. The second alert screens for end-organ dysfunction and triggers when at least two SIRS criteria and at least one of the four organ system dysfunction criteria are met.

The CDS displays at-risk patients on a live dashboard embedded in the EHR. The dashboard is actively monitored by the sepsis response nurse team and can also be monitored by any provider in the hospital. The dashboard also displays SIRS criteria that are met and provides a link to a sepsis-documentation template.

- 2) Sepsis Response Team: By broadening the scope of existing emergency response and critical care teams, our hospital puts together a sepsis response team that included critical care trained sepsis response nurses (SRNs) and critical care trained sepsis APPs. The team was implemented twice a week in July 2016 and coverage was increased to 24 hours a day, seven days a week starting in April 2017. The SRNs have no patient assignments and are dedicated to responding to emergency situations including rapid response, acute strokes, and ST segment elevation myocardial infarctions in addition to sepsis responses. They assist emergency department and ward nurses in drawing lactates and blood cultures, as well as infusing antibiotics and fluids as early as possible. For this study, the postintervention period was designed to begin after implementation of the response team 24/7.

The SRN gets alerted with patient identification and location via an inhouse phone, when the CDS identifies a patient with SIRS who needs to be screened for sepsis. The SRN notifies and collaborates with the Sepsis APP. The Sepsis APP reviews the electronic chart of every patient identified by the CDS and communicates with the patient's primary team to discuss if implementation of

the sepsis bundle should be initiated. **Figure 1** shows the current workflow between the SRN and sepsis APP.

- 3) Education Campaign: Starting in May 2016, a hospitalwide education campaign focused on sepsis was initiated. Members of the sepsis committee participated in every clinical departmental conference, huddle, and grand rounds focusing on sepsis early identification and treatment at least once and more times if requested. Brochures, pocket guides, and newsletters on the topic of early recognition, treatment, and appropriate documentation of sepsis were prepared and widely disseminated. A presentation on the sepsis campaign was placed on the hospital online learning platform as mandatory education for nurses and residents.

Part of the education was on coding and documentation in order to improve appropriate capture of patients with sepsis. This education was provided by physicians, APPs, and nurses to their corresponding peers. The education included the use of appropriate terms to rule in and rule out sepsis, to capture severity of illness, and to correctly document the time of sepsis onset.

- 4) Electronic Templates and Order Sets: Electronic templates were prepared for documentation of sepsis 3- and 6-hour bundles and rolled out at the same time as the CDS tool. A sepsis order set was prepared to streamline ordering of sepsis bundles and rolled out hospitalwide in early 2017. Antibiotic recommendations were incorporated on the order set based on the recommendations of the hospital Antibiotic Stewardship Committee.
- 5) Data Monitoring and Quality Improvement: CMS mandates that a sample of all sepsis charts be audited by independent abstractors, for the implementation of each sepsis bundle element. The audit, representing 10% of our severe sepsis and septic shock cases, is reported quarterly to CMS via an online portal. In addition, we developed an internal database of all patients identified by the CDS tool, and times to each intervention were monitored. The Sepsis Performance Improvement Committee met monthly to review data, identify long lags in bundle implementation, and institute changes and improvements as necessary.

A clinical nurse specialist was hired as a Sepsis Committee coordinator and later changed to cochair. The cochair organized and oversaw the campaign and maintained sepsis-related databases. The cochair also performed manual chart reviews of patients identified by the CDS to monitor if subsequent cultures and provider documentation confirmed the diagnosis of sepsis.

In this study, we analyzed patient outcomes for the 6 months prior to implementation of the above interventions, from October 1, 2015, to March 31, 2016. We excluded a 13-month implementation period from April 1, 2016, to April 30, 2017. The postintervention period was a 14-month period after complete implementation, May 1, 2017, to June 30, 2018. Clinical Outcome, expected mortality, and severity of illness data was gathered from the Vizient Clinical Database/Resource Manager (used by permission of Vizient, all rights reserved). Vizient is an alliance of 117 U.S. academic medical centers and 300 of their affiliated hospitals. Members that participate in the clinical database/resource manager submit demographic data, medication data, and up to 99 International Classification of Diseases diagnosis and procedure codes per encounter for all inpatient and outpatient encounters. Vizient performs rigorous quality assessments of submitted data before the data are loaded into the clinical database/resource manager. Vizient also calculates a severity-of-illness score, which accounts for demographic variables, hospital diagnoses, and comorbid conditions that were present upon hospital admission (11). The Vizient dataset has been used in a range of scientific studies and quality improvement initiatives (12).

The study was submitted for approval to the hospital Institutional Review Board and received approval (exemption). Statistical analysis was performed by an independent statistician at Georgetown University in Washington, DC.

The following equation describes the main multivariate regression model used in our analysis. $F(.)$ represents a functional form that varies depending on the outcomes. For patient mortality, hospital readmission, and bundle compliance, $Q_{i,t}$ is a binary outcome for patient i in year t . We will estimate a logistic model for the nonlinear outcomes. For length of stays, because the measures are continuous, we will estimate a linear model.

$$Q_{i,t} = F(\text{Intervention}_t, \delta + \text{Patient}_{i,t}, \partial)$$

where “Intervention” takes a value of 1 for sepsis patients admitted after the sepsis initiatives have been fully implemented.

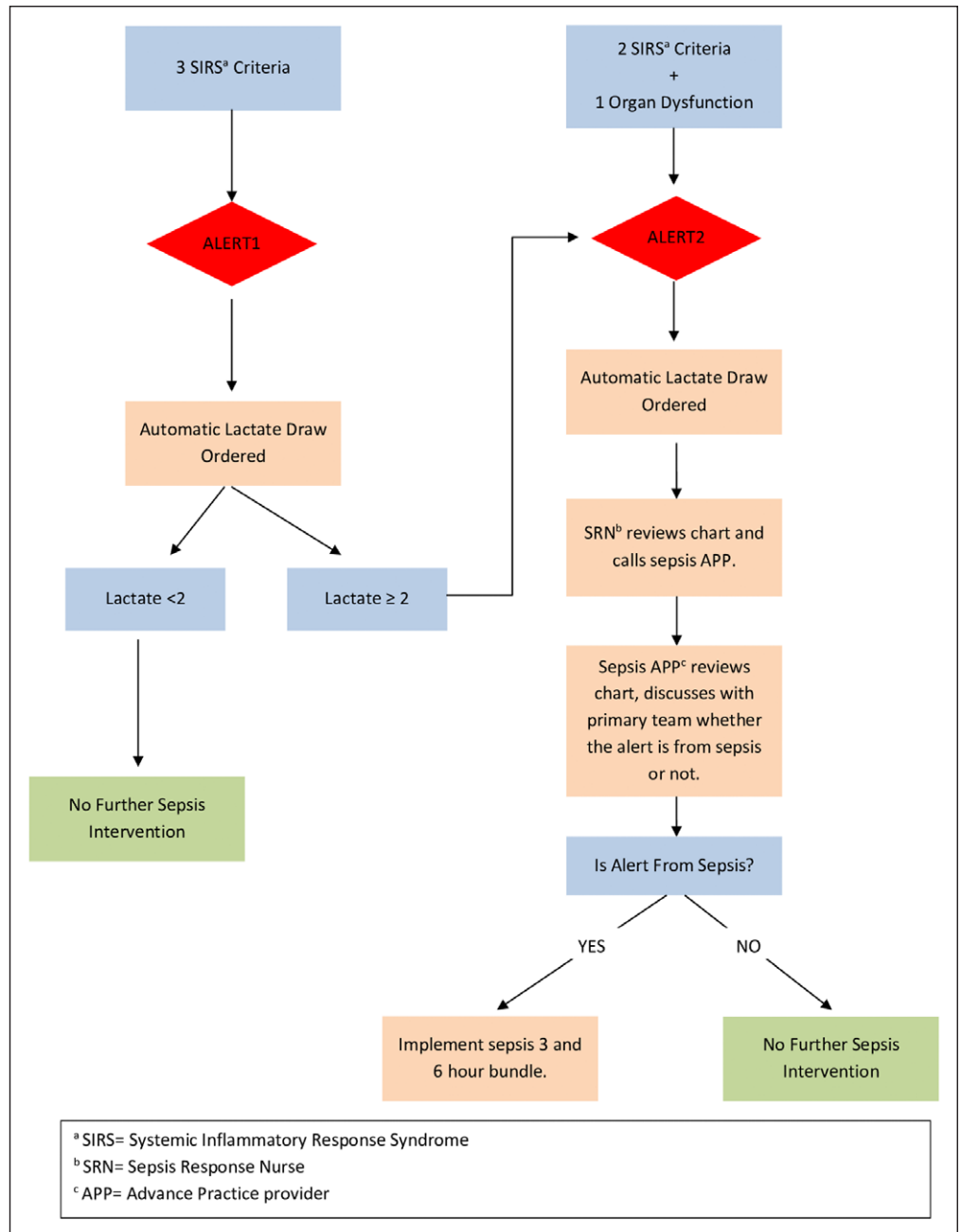


Figure 1. Workflow between sepsis response nurse and sepsis response advance practice provider.

“Patient” is a set of patient demographic and case-mix variables. These variables include age, gender, admission sources, race and ethnicity, as well as expected mortality risk. The expected mortality risk was derived from the third-party logistic regression analysis, Vizient Clinical Database/Resource Manager, based on coding data and used for hospital comparison and estimation of expected outcomes. Statistical analyses were conducted in Stata 15.1 (StataCorp LLC, 2017, College Station, TX).

RESULTS

Summary Statistics

The summary statistics are reported in Table 3. A total of 4,102 patients were diagnosed with sepsis, severe, sepsis, or septic

TABLE 3. Summary Statistics of Control Variables

Control Variable	Before the Intervention	After the Intervention	Total	<i>p</i>
Observations, <i>n</i> (%)	861	3,241	4,102	
Mean Age—yr (sd)	60.030	61.370	61.090	0.040
Female, <i>n</i> (%)	428 (49.7)	1,500 (46.3)	1,928 (47)	0.077
Black, <i>n</i> (%)	648 (76.6)	2,334 (73.8)	2,982 (74.4)	0.10
White, <i>n</i> (%)	138 (16.3)	497 (15.7)	635 (15.8)	0.67
Other race, <i>n</i> (%)	351 (8.8)	49 (5.8)	302 (9.6)	< 0.001
Ethnicity: Hispanic, <i>n</i> (%)	38 (4.6)	218 (7.3)	256 (6.7)	0.006
Mean expected mortality risk (sd)	0.116 (0.177)	0.123 (0.191)	0.122 (0.188)	0.46

shock during the study period. About 861 of patients (21%) were diagnosed during the preintervention period and 3,241 (79%) were diagnosed in the postintervention period. The average patient age was 61 years old and more than 80% of the patients were admitted through the emergency department. The majority of patients were Black (72.7%). The patient characteristics (age, gender, race, and ethnicity) were similar in the pre- and postintervention samples.

Table 4 shows the summary statistics of the outcome variables before and after the sepsis initiatives. We find that all-cause hospital mortality decreased from 20% to 16% in the postintervention period. The prevalence of septic shock decreased from 34% to 27%, and the prevalence of severe sepsis

decreased from 17% to 12%. Both the all-cause hospital readmission and readmission due to infection were lower in the postintervention period. The bundle compliance rate increased from 10.7% to 36.9%. We also see a slightly shorter length of hospital stay and ICU stay.

Regression Results

Table 5 reports the multivariate regression results after adjusting for patient demographics and severity of illness differences. Because the estimation of binary outcomes relies on the logistic model, to better interpretation of the results, we estimate and report the marginal effects of the intervention. We find that sepsis mortality was reduced by 4.6 percentage points ($p < 0.01$). The

TABLE 4. Summary Statistics of Patient Outcomes

Outcome	Before the Intervention	After the Intervention	Total	<i>p</i>
Observations, <i>n</i> (%)	861	3,241	4,102	
Death, <i>n</i> (%)	175 (20.3)	523 (16.1)	698 (17)	< 0.01
Septic shock, <i>n</i> (%)	291 (33.8)	872 (26.9)	1,163 (28.4)	< 0.01
Severe sepsis, <i>n</i> (%)	146 (17)	379 (11.7)	525 (12.8)	< 0.01
All-cause readmission, <i>n</i> (%)	51 (5.9)	129 (4)	180 (4.4)	0.02
Infection readmission, <i>n</i> (%)	48 (5.6)	116 (3.6)	164 (4)	0.01
Bundle compliance, <i>n</i> (%)	10.7	36.9	30.4	< 0.01
Mean ICU length of stay (sd)	4.186 (7.889)	3.763 (8.631)	3.852 (8.481)	0.02
Mean hospital length of stay (sd)	15.970 (19.310)	14.080 (15.460)	14.480 (16.360)	< 0.01

The sample of bundle compliance only has 224 observations.

TABLE 5. Reported Marginal Effects

Death	Septic Shock Incidence	Severe Sepsis Incidence	Bundle Compliance	All-Cause Hospital Readmission	Infection Readmission	Hospital Length of Stay	ICU Length of Stay
-0.0457 ***	-0.0654 ***	-0.0499***	0.3105***	-0.0158**	-0.0166**	-1.8105 **	-0.4407
[0.0124]	[0.0139]	[0.0118]	[0.0843]	[0.0072]	[0.0069]	[0.7079]	[0.2945]

All regressions include control variables listed in Table 3.

Numbers reported in the brackets are sds.

*, **, and *** represent statistically significant at 10%, 5%, and 1% levels.

prevalence of septic shock and severe sepsis were reduced by 6.5 and 5.0 percentage points, respectively ($p < 0.01$). Compliance with all elements of the 3- and 6-hour bundle interventions increased by 31.1 percentage points ($p < 0.01$). We also find lower all-cause hospital readmission and readmission due to infection rates by 1.6 and 1.7 percentage points ($p < 0.05$). In terms of length of stay, hospital length of stay was reduced by 1.8 days ($p < 0.05$) in the postintervention period. There was no difference in ICU length of stay. Although not shown, when we limit the sample to only the septic shock or severe sepsis patients, the mortality rates were reduced by 6.5% and 5.0 percentage points, respectively.

DISCUSSION

This study has demonstrated that the implementation of a multimodal hospitalwide sepsis performance program improved outcomes from before to after implementation of the program. After adjusting for severity of illness using multivariate regression, we saw improvements in sepsis bundle compliance, all-cause mortality, hospital length of stay, and hospital readmission rates. In addition, a decrease in the number of severe sepsis and septic shock cases was seen, whereas the incidence of uncomplicated sepsis increased. We believe that the decrease in severity of illness was due to two reasons. First, with the implementation of the 24/7 screening, we saw a significant increase in the number of uncomplicated sepsis cases in the postintervention period due to improved identification and increased awareness, which led to an increase in the denominator. In addition, we believe that the improved screening may have contributed to the early identification of some patients with uncomplicated sepsis, leading to early identification and intervention prior to clinical deterioration to severe sepsis or septic shock.

We believe the improvement in mortality was primarily due to earlier identification as well as an early implementation of the sepsis bundles. Along with the increased diagnosis of sepsis cases, there was a corresponding improvement in early treatment. Implementation of all sepsis bundle elements improved from 11% to 37% in the postintervention period. Even though compliance in the postintervention period was only at 37%, it should be noted that this metric was measured only in 5.5% of all cases. The 5.5% of charts represents the number of charts abstracted for sepsis bundle compliance, as mandated by CMS. This abstraction takes place on 10–20% of patients, with severe sepsis or septic shock, and who were not transferred from another acute care facility. The small sampling size and the exclusion of uncomplicated sepsis from the bundle compliance mandate led to a smaller representative sample. It should also be noted that this number indicates cases where all elements of the bundle are met, as shown in Table 4. Over time, we are seeing an increase in the number of bundle elements that are timely implemented per case, even when all the elements are not implemented. We are specifically seeing an increase in the number of patients appropriately screened for severe sepsis/septic shock and given timely antibiotics.

The concept of a sepsis-treatment bundle, such as that used in this study, where none of the elements of the bundle are based on high- or moderate-level evidence and is mandated by public authorities, remains controversial (13). One large study has shown

that only the rapid implementation of the 3-hour bundle and early antibiotics, but not rapid completion of an initial IV fluid bolus, were associated with improved mortality (14). In addition to the controversy on the elements of the bundle, there is also emerging literature that different phenotypes of sepsis may respond to different interventions (15).

Prior studies by Seymour et al (14) and Levy et al (16) have reported improvements in sepsis mortality after New York state mandated care for sepsis. However, neither of these studies looked at and correlated with the quality improvement measures that were implemented to improve compliance with the sepsis bundles. CMS allows hospitals flexibility in the strategy implemented to identify patients with sepsis. Our goal in this article is to show a correlation between the specific interventions we implemented and an overall improvement in patient outcomes.

We recognize that a multimodal sepsis intervention, such as that implemented in this study, is unfunded and must be paid for by savings in utilization and patient outcomes. We have not included a cost-benefit analysis in this study, and more studies are needed to prove the financial benefit. However, based on our outcomes, for a hospital of our size with an average of 2,000 sepsis cases per month, the improvements amount to annual savings of 90 lives, reduction in 32 hospital readmissions, and a cumulative reduction in hospital length of stay by 3,600 days.

Although the treatment of sepsis needs further refining in the selection of elements of the bundle as well as an improved selection of patients or patient phenotypes, this study demonstrates that the sepsis 3- and 6-hour bundles are showing promising responses in patient outcomes.

Our study has some limitations; this was a retrospective single-site study, and our findings may not be generalizable to hospitals serving different populations. Although our study shows a correlation in improvement in compliance with sepsis 3- and 6-hour bundles and patient outcomes, it does not identify which elements of the bundle or which performance improvement initiatives contributed most to the outcomes. There need to be more targeted evaluations of each intervention and targeted treatment based on sepsis phenotype in future studies. Additionally, it is likely that some of the improvements in outcome are a result of improved coding and documentation of patients with sepsis. However, given that we see improvements in bundle compliance, early antibiotics, and early screening, the change in coding and documentation is unlikely to drive significantly the results.

CONCLUSIONS

In this study, we report an improvement in sepsis outcomes after initiation of a multimodal sepsis performance-improvement initiative. With the improvement in sepsis 3-hour and 6-hour bundle implementation, we are seeing continued improvement in patient outcomes. As hospitals continue to implement sepsis performance initiatives as mandated by CMS, it is essential to find the most impactful and efficient interventions to improve outcomes. This study confirms the beneficial effects of the combined use of the interventions that we have implemented at our center. Analyzing the impact of the different elements of the sepsis bundle would be warranted in future studies.

Drs. Alnababteh and Yohannes contributed equally to this work.

All the authors contributed to the access to all the data in the study; are responsible for the integrity of the data and the accuracy of the data analysis; contributed to drafting and reviewing of the manuscript; and contributed to intellectual content. Drs. Yohannes, Alnababteh, and Huang designed the study concept. All authors contributed to acquisition, analysis, or interpretation of data. Dr. Huang helped in statistical analysis. Dr. Alnababteh and Yohannes obtained funding.

Supported, in part, by Medstar Washington Hospital Center, Graduate Medical Education, which was utilized for external statistical analyses.

The abstract was presented at the 2019 Georgetown University/MedStar Health Research Institute Research Symposium and selected as one of three best scientific abstracts out of more than 400.

The authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: seife.yohannes@medstar.net

REFERENCES

1. Fleischmann C, Scherag A, Adhikari NK, et al; International Forum of Acute Care Trialists: Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. *Am J Respir Crit Care Med* 2016; 193:259–272
2. Kadri SS, Rhee C, Strich JR, et al: Estimating ten-year trends in septic shock incidence and mortality in United States Academic Medical Centers using clinical data. *Chest* 2017; 151:278–285
3. Torio CM, Moore BJ: National Inpatient Hospital Costs: The Most Expensive Conditions by Payer, 2013: Statistical Brief #204. Rockville, MD, Agency for Healthcare Research and Quality (US), 2006
4. Rivers E, Nguyen B, Havstad S, et al; Early Goal-Directed Therapy Collaborative Group: Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; 345:1368–1377
5. Lin SM, Huang CD, Lin HC, et al: A modified goal-directed protocol improves clinical outcomes in intensive care unit patients with septic shock: A randomized controlled trial. *Shock* 2006; 26:551–557
6. Dellinger RP, Levy MM, Rhodes A, et al; Surviving Sepsis Campaign Guidelines Committee Including the Pediatric Subgroup: Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med* 2013; 41:580–637
7. Levy MM, Dellinger RP, Townsend SR, et al; Surviving Sepsis Campaign: The Surviving Sepsis Campaign: Results of an international guideline-based performance improvement program targeting severe sepsis. *Crit Care Med* 2010; 38:367–374
8. Aaronson EL, Filbin MR, Brown DF, et al: New mandated centers for medicare and medicaid services requirements for sepsis reporting: Caution from the field. *J Emerg Med* 2017; 52:109–116
9. Marik PE, Norfolk F, Joshua Farkas VD, et al: Should the surviving sepsis campaign guidelines be retired? Yes on behalf of collaborating authors. *Chest* 2018; 155:12–14
10. Amland RC, Hahn-Cover KE: Clinical decision support for early recognition of sepsis. *Am J Med Qual* 2016; 31:103–110
11. Greenberg JA, Hohmann SF, James BD, et al: Hospital volume of immunosuppressed patients with sepsis and sepsis mortality. *Ann Am Thorac Soc* 2018; 15:962–969
12. Chaudhary NS, Donnelly JP, Wang HE: Racial differences in sepsis mortality at U.S. Academic Medical Center-Affiliated Hospitals. *Crit Care Med* 2018; 46:878–883
13. Pepper DJ, Natanson C, Eichacker PQ: Evidence underpinning the Centers for Medicare & Medicaid Services' severe sepsis and septic shock management bundle (SEP-1). *Ann Intern Med* 2018; 168:610–612
14. 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
15. Seymour CW, Kennedy JN, Wang S, et al: Derivation, validation, and potential treatment implications of novel clinical phenotypes for sepsis. *JAMA* 2019; 376:2003–2017
16. Levy MM, Gesten FC, Phillips GS, et al: Mortality changes associated with mandated public reporting for sepsis. The results of the New York State initiative. *Am J Respir Crit Care Med* 2018; 198:1406–1412