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Managing sepsis: Electronic recognition, rapid response teams, and standardized care save lives^{★,★★,★★★}

Faheem W. Guirgis, MD^{a,*}, Lisa Jones, MD^b, Rhemar Esma, MD^c, Alice Weiss, RN^c, Kaitlin McCurdy, MD^d, Jason Ferreira, PharmD^e, Christina Cannon, MD^a, Laura McLauchlin, DNP^f, Carmen Smotherman, MS^g, Dale F. Kraemer, PhD^g, Cynthia Gerdik, DNP, MBA^h, Kendall Webb, MD^a, Jin Ra, MDⁱ, Frederick A. Moore, MD^j, and Kelly Gray-Eurom, MD, MMM^a

^aUniversity of Florida College of Medicine, Jacksonville, Department of Emergency Medicine, Jacksonville, FL, USA

^bUniversity of Florida College of Medicine, Jacksonville, Division of Pulmonary Critical Care Medicine, Department of Medicine, Jacksonville, FL, USA

^cUF Health Jacksonville, Quality Management, Jacksonville, FL, USA

^dUniversity of Florida College of Medicine, Jacksonville, Department of Medicine, USA

^eUniversity of Florida College of Pharmacy, Jacksonville, USA

^fUniversity of Florida College of Medicine, Jacksonville, Department of Neurosurgery, USA

^gUniversity of Florida College of Medicine, Jacksonville, Center for Health Equity and Quality Research, USA

^hUF Health Jacksonville, USA

ⁱUniversity of Florida College of Medicine, Jacksonville, Department of Surgery, USA

^jUniversity of Florida College of Medicine, Gainesville, Department of Surgery, USA

Abstract

★Study site: All patients were enrolled at UF Health Jacksonville, 655 West 8th Street, Jacksonville, FL 32209, USA.

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*Corresponding author at: Department of Emergency Medicine, UF Health Jacksonville, 655 West 8th Street, Jacksonville, FL 32209, USA.

Ethical approval and consent to participate

Approval for this retrospective study was obtained from the UF Health Jacksonville Institutional Review Board.

Competing interests

The authors have no disclosures or conflicts of interest to report.

Author contributions

FWG, LJ, RE, AW, JF, CG, KW, JR and KGE devised the study. FWG, LJ, RE, AW, CC, KM, LM, CS, DFK, CG and KGE supervised the data collection and chart reviews. CS, DFK, FAM provided methodological and statistical advice on study design and data analysis. FWG, LJ, JF, JR, and FAM provided expertise on sepsis. RE and KW provided IT expertise. AW and KGE provided expertise in quality improvement. FWG, RE, KM, JF, CC, LM, CS, DFK, and KGE drafted the manuscript and all authors contributed substantially to its revision.

Availability of supporting data

Not applicable.

Purpose—Sepsis can lead to poor outcomes when treatment is delayed or inadequate. The purpose of this study was to evaluate outcomes after initiation of a hospital-wide sepsis alert program.

Materials and methods—Retrospective review of patients 18 years treated for sepsis.

Results—There were 3917 sepsis admissions: 1929 admissions before, and 1988 in the after phase. Mean age (57.3 vs. 57.1, $p = 0.94$) and Charlson Comorbidity Scores (2.52 vs. 2.47, $p = 0.35$) were similar between groups. Multivariable analyses identified significant reductions in the after phase for odds of death (OR 0.62, 95% CI 0.39–0.99, $p = 0.046$), mean intensive care unit LOS (2.12 days before, 95% CI 1.97, 2.34; 1.95 days after, 95% CI 1.75, 2.06; $p < 0.001$), mean overall hospital LOS (11.7 days before, 95% CI 10.9, 12.7 days; 9.9 days after, 95% CI 9.3, 10.6 days, $p < 0.001$), odds of mechanical ventilation use (OR 0.62, 95% CI 0.39, 0.99, $p = 0.007$), and total charges with a savings of \$7159 per sepsis admission ($p = 0.036$). There was no reduction in vasopressor use (OR 0.89, 95% CI 0.75, 0.1.06, $p = 0.18$).

Conclusion—A hospital-wide program utilizing electronic recognition and RRT intervention resulted in improved outcomes in patients with sepsis.

Keywords

Sepsis; Rapid response teams; Clinical decision support; Resuscitation

1. Introduction

Sepsis is a life-threatening, dysregulated host response to infection that leads to organ dysfunction [1] and is the primary cause of death from infection [2]. Over 750,000 cases of sepsis occur annually in the United States, with the number and rate of hospitalizations tripling over the last two decades and continuing to climb each year [2–4]. Sepsis was also the most expensive condition billed to Medicare in 2011, costing over \$20 billion that year [5]. Care for sepsis patients frequently involves prolonged length of stay (LOS) incurring higher overall healthcare costs [6]. According to the Centers for Disease Control, patients hospitalized for sepsis had an average LOS that was 75% longer than patients hospitalized for other conditions [2]. Given that the rate of hospitalization for sepsis is much higher for those aged 65 and over, the incidence is expected to continue to grow with the aging U.S. population [3,6,7].

Sepsis mortality decreases with early recognition and treatment [1, 8]. Therefore, sepsis screening and early, aggressive care is vital to increasing the chance of survival. Implementation of Surviving Sepsis Campaign (SSC) guidelines, an international effort promoting widespread early recognition and implementation of treatment bundles, have been associated with mortality reduction in sepsis [8,9]. At our institution, we implemented a multidisciplinary, hospital-wide program which included an electronic health record (EHR) sepsis recognition tool, education, standardized management bundles, and designated team responders for each area of the hospital including the rapid response team (RRT) for inpatients. The purpose of this study was to determine the effect of the sepsis alert program on the primary outcome of inpatient mortality and secondary outcomes including intensive

care unit (ICU) LOS, hospital LOS, mechanical ventilation use, vasopressor use, and hospital charges per sepsis admission.

2. Methods

2.1. Study design

We conducted a retrospective review of all patients treated at UF Health Jacksonville for sepsis from October 1, 2013 to November 10, 2015 to evaluate sepsis outcomes before and after implementation of the program. UF Health Jacksonville is a not-for-profit, academic medical center and is a 696-bed level 1 trauma center with 142 intensive care beds and is a regional referral center. The sepsis alert program was initiated on November 19, 2014, and groups were dichotomized as “before” and “after” based on this time point and outcomes were then compared by group. The study period therefore included approximately 13 months in the before phase and 12 months in the after phase.

2.2. Selection of subjects

Patients from all units including the emergency department (ED), ICU, and general wards were included. Using methods similar to those previously described by Angus et al. [3], patients with a discharge ICD-9 code for sepsis, severe sepsis, or septic shock were identified electronically via our EHR system (see appendix for ICD-9 codes). Patients were also required to meet clinical criteria for sepsis including two of four SIRS criteria: HR > 90, respiratory rate > 20 or PaCO₂ < 32 mm Hg, white blood cell count > 12,000/mm³ or <4000/mm³ or > 10% bands, and temperature > 38 °C or <36 °C as well as a documented source of infection. Only patients 18 years of age and older were included in the retrospective study. Patients were excluded if they were incarcerated.

2.3. Interventions

2.3.1. Sepsis educational initiatives—In order to effectively implement the sepsis alert program, a hospital-wide educational effort was developed and executed. All physicians from a service line which could encounter a sepsis patient were educated. Lectures were given by the Committee Co-chairs to the Emergency Medicine, Internal Medicine, Surgery, Orthopedic Surgery, Urology, Obstetrics and Gynecology, Neurology and Hospitalist Departments/Divisions as well as to the ICUs and RRT nurses. All providers, nurses, and technicians were allowed adequate time to ask questions and were given the Co-Chairs’ contact information should they have questions.

2.3.2. Sepsis recognition

2.3.2.1. Clinical screening: Patients were systematically screened for sepsis in ED triage, the ICU, and the general wards using clinical criteria. After completing the institution wide educational program as well as an introduction to the sepsis alert program on the EHR home page, sepsis alert pocket cards were distributed to providers and nurses in all areas detailing the sepsis alert criteria: two of four SIRS criteria plus suspicion of infection and the presence of new altered mental status, or a systolic blood pressure (SBP) < 90 mm Hg, or a serum lactate level > 3 mmol/L. In ED triage, sepsis alert criteria were posted and the attending ED physician was directly notified when sepsis was suspected by the triage nurse. The ED

attending would then perform a bedside evaluation and determine if criteria were met, and if so, page a sepsis alert by entering the order set. On the general wards, all nurses were educated on sepsis criteria and were to screen for sepsis whenever vitals were taken. If suspicion for sepsis was present, RRT or the primary team was paged. ICU screening for sepsis occurred regularly with vital sign evaluations, in addition to the ICU team rounding and closely monitoring patients for sepsis. They also evaluated patients upon admission or transfer to the ICU from another unit. Concerned providers were also encouraged to page a sepsis alert in patients not meeting criteria but in whom a high clinical suspicion for sepsis was present.

2.3.2.2. Rapid response team screening: The RRT consists of a critical care trained nurse, most of whom have many years of critical care nursing experience, and is available 24 h per day, seven days per week. RRT nurses can be reached via in-house phone directly to their cell phone or can be paged via the operator. Providers or nurses may also page a rapid response activation, which pages designated responders immediately including the RRT nurse, the on-call ICU physicians as well as critical care pharmacists and respiratory therapists. In addition to being called or paged by bedside nurses when sepsis was suspected, RRT performed clinical screening for sepsis on the general wards through proactive rounding on all high-risk patients. Proactive rounding occurs when the RRT nurse seeks out high-risk patients on the general wards, adds them to his/her census, and then checks on them on a daily basis. These patients are identified because the RRT nurse surveys the ward nurses, staff, and physicians for patients who are either high-risk by vital signs or by pre-determined high-risk conditions [10]. In the event of clinical suspicion for sepsis, the RRT nurse directly paged the patient's provider who would then assesses the patient for sepsis within 1 h. If sepsis was confirmed, a sepsis alert was initiated via the sepsis order set. If the provider did not believe the patient to be septic, a note was placed in the chart detailing the decision not to page a sepsis alert, but the RRT would continue to proactively round on the patient. RRT nurses facilitate care delivery for ward septic patients by performing stabilizing interventions including establishing intravenous access, administering fluids and antibiotics, and facilitating transfer to a higher level of care when indicated.

2.3.2.3. Automated sepsis screening: Sepsis screening also occurred via an automated possible sepsis notification based on EHR data surveillance applying an adjusted Modified Early Warning Signs–Sepsis Recognition Score (MEWS-SRS) [11]. Eight different algorithms were tested including combinations of vital signs and laboratory criteria, with a goal positive predictive value of 50% or greater for sepsis. Test protocols were run in 48 h blocks, after which a 20% sample of cases of “possible sepsis” identified by the test protocol were manually adjudicated by a trained research assistant. The MEWS score, which was originally designed for nurses to assist in the recognition of decompensating ward patients, was successfully adapted to the MEWS-SRS score specifically for the surgical ICU patient population to identify sepsis [11]. Based on the testing described above in our patient population, we further adjusted the MEWS-SRS to include lower thresholds for white blood cell count and removed points for hypertension to make the score more generalizable (Table 1). The tool was then approved by the sepsis committee and was developed to be EHR-agnostic and work in the EHR background, transparently scanning all admitted patient

records for the adjusted MEWS-SRS parameters on an hourly basis. For patients meeting 5 criteria, a “possible sepsis” page was sent via an electronic paging system to the patient’s responsible provider for all areas of the hospital. For general ward patients, the RRT nurse was also paged. The paged notification contained the “possible sepsis” header and the abnormal values from the adjusted MEWS-SRS. After sending an alert, the program marked the EHR and continued to monitor the trends of each criterion. It did not send another alert for 24 h unless the trend in at least 1 criterion was found to be worsening in a consecutive 4 h period. If the diagnosis of sepsis, severe sepsis, or septic shock was entered into the EHR problem list, or the sepsis alert order set was utilized, the tool recognized this as confirmation of the alert and thus no further page alerts would be sent for 72 h. Alternatively, a diagnosis of SIRS added to the EHR problem list served to silence the alerts in non-septic patients.

2.3.3. Sepsis alert implementation—A sepsis alert order set was created for hospital-wide use. The order set was constructed using both the National Quality Forum and Centers for Medicare and Medicaid Services’ SEP-1 quality measures and mirrored the 3-hour bundle. The order set includes point-of-care serum lactic acid, antibiotic recommendations, two sets of blood cultures, and a 30 mL/kg initial fluid bolus. Options for further infectious workup and closer vital sign monitoring and nursing care are also included. Initiation of this order set also triggers an automated sepsis alert to be paged out to providers and responders after which, primary providers, nurses, clinical pharmacists, and technicians administered the sepsis protocol by delivering the care bundle. For general ward patients, the patient’s primary hospital physician and nurse with the assistance of a RRT nurse, clinical pharmacist, and a respiratory technician would initiate treatment for sepsis in consult with medical or surgical ICU services. Preferred empiric antimicrobial therapy for purposes of the sepsis alert program were chosen based on susceptibility profiles at our institution and included options for patients with and without allergies to penicillins. When available, clinical pharmacists reviewed each patient’s microbiologic history at bedside for requirement of alternative antimicrobials or reasons in which standard agents would be inappropriate. Addition of double gram negative, anaerobic, or fungal coverage was considered on a case-by-case basis by the treating team.

2.4. Outcomes and covariates

The primary outcome was inpatient mortality. Secondary outcomes were ICU LOS, hospital LOS, mechanical ventilation use, vasopressor use, and hospital charges for sepsis patients treated during the study period. Basic demographic information including age, race, sex, and comorbidities were retrospectively collected from the EHR. To adjudicate the sepsis diagnosis we used the classic definition of sepsis defined by the presence of 2 or more systemic inflammatory response (SIRS) criteria in conjunction with a documented infection [12]. Septic shock was defined by a need for vasopressors during admission in the presence of infection. A comprehensive chart review was performed which included initial vital signs, laboratory values and culture results, inpatient mortality, ICU LOS, hospital LOS, mechanical ventilation use, vasopressor use, hospital charges, treatment period (before or after sepsis alert program), and readmissions for sepsis. Comorbidities were quantitated using the Charlson Comorbidity Index [13]. Hospital charges reflected the documented full

established rate for each chargeable item for the entire admission. These amounts included room and board, medications, procedure service, diagnostic services, and supplies.

2.5. Data analysis

Categorical variables were summarized using counts and percentages, and analyzed using Chi-square or Fisher's tests. Continuous data was summarized using means, standard deviations, and medians, and analyzed using Wilcoxon rank sum test. In the multivariable analyses, since some of the patients included in the sepsis data set had more than one inpatient episode, repeated measures models were fit to these data to account for these potential repeated measures. Generalized linear mixed models using a logistic link function were fit with a random intercept for each subject, for inpatient mortality, mechanical ventilation use, and vasopressor use. For hospital LOS and total charges, the log-transformed data were approximately normal so a mixed model repeated measures analysis was used. For ICU LOS, zero-inflated negative binomial models were each fit to these data.

Candidate predictors were encounter age, Charlson Score, number of prior sepsis admissions, after phase, gender, sepsis status on admission, and race (black, white, and other). All order interactions among the categorical variables were also fit. These models assessed the impact of the after phase on outcomes after adjusting for all the other predictors. Five different variance-covariance structures (including first-order autoregressive, compound symmetry, and "unstructured") were fit for each outcome in the generalized linear mixed models. The structure with the smallest corrected Akaike Information Criterion was selected for that outcome [14]. The likelihood ratio test was used to compare between models for each outcome. Least squares (adjusted) means were estimated for log-normal outcomes and odds ratios for other outcomes. Comparisons were made using Tukey-Kramer adjustments for multiple comparisons. All models were fit using SAS® 9.4 Stat Version 13.1.

3. Results

3.1. Details of overall cohort

There were 3205 unique patients with 3917 sepsis admissions over the study period: 1637 unique patients with 1929 admissions in the before phase, and 1568 unique patients with 1988 admissions in the after phase. Of these, there were 2585 (81%) unique patients with sepsis present on admission (POA), and 620 unique patients with non-POA (19%) sepsis, or sepsis acquired during admission. There were 3186 sepsis POA admissions (1558 before, 1628 after), and 731 non-POA sepsis admissions (371 before, 360 after). One hundred and fifty three patients were admitted with sepsis in both the before and after phases.

3.2. Differences in patient characteristics between before phase and after phase

For the comparison of baseline demographics, there was no significant difference in mean age (before 57.3, SD 16.9; after 57.1, SD 18.0, $p = 0.94$) or overall Charlson Score (before 2.52, SD 2.62; after 2.47, SD 2.66, $p = 0.35$) between groups. There was a slightly lower representation of African Americans in the after phase (before 855, 52%; after 748, 48%, $p = 0.04$) as well as a decrease in the number of uncomplicated diabetics (before 496, 30%;

after 419, 27%, $p = 0.04$). There was an increase in the number of patients with congestive heart failure in the after group (before 325, 20%; after 355, 23%, $p = 0.04$). All other baseline characteristics were similar (Table 2). Univariate comparisons of the features of sepsis admissions across both phases are displayed in Table 3.

3.3. Effects of intervention on in-hospital mortality

Multivariable analysis identified a significant reduction in the odds of death in the after phase compared to the before phase (OR 0.62, 95% CI 0.39–0.99, $p = 0.046$), adjusting for all other variables in the model. Patients with sepsis POA had a significantly reduced odds of death (OR 0.35, 95% CI 0.28–0.45) in comparison to non-POA sepsis across both phases, as did patients with more than one previous sepsis admission (OR 0.78, 95% CI 0.65–0.94, $p = 0.01$). The odds of inpatient death decreased by about 22% for each additional previous ED visit (OR 0.78, 95% CI 0.65, 0.94, $p = 0.01$). Predictors of increased mortality were increasing Charlson Score (OR 1.17, 95% CI 1.13–1.16, $p < 0.001$) and increasing age (OR 1.04, 95% CI 1.03–1.04, $p < 0.001$). Males had a significantly lower odds of death in the after phase compared to the before phase (OR = 0.35, 95% CI 0.13, 0.93, $p = 0.03$). In the after phase, 25% (499/1988) of sepsis admissions had utilized the sepsis alert order set but there was no significant mortality reduction specifically associated with order set utilization ($p = 0.93$). A graphical representation of the results for inpatient mortality is displayed in Fig. 1. The results of both univariate and multivariable analyses for the six outcomes of interest are displayed in Table 4.

3.4. Effects of intervention on ICU and hospital resource utilization

For ICU LOS using the zero-inflated negative binomial model, there was a significant reduction in the number of ICU days from a mean of 2.12 days (95% CI 1.97, 2.34) in the before phase compared with 1.95 days (95% CI 1.75, 2.06) in the after phase ($p < 0.001$). A more significant reduction in ICU LOS was observed for sepsis POA patients for whom ICU LOS was reduced from a mean of 1.82 days (95% CI 1.62, 2.01) in the before phase to 1.50 days (95% CI 1.28, 1.60) in the after phase ($p < 0.001$). For overall LOS, there was also a significant reduction in the number of hospital days in the after phase compared with the before phase ($p < 0.001$). The estimated ratio of the two means comparing after- to before - phase was 0.85 with a 95% CI of 0.79–0.90. After adjustment for all the other factors, the estimated before phase adjusted LOS was 11.7 days (95% CI 10.9, 12.7 days) and after phase was 9.9 days (95% CI 9.3, 10.6 days), indicating an approximate 1.8 day reduction in hospital LOS.

In the after phase, there was a significantly reduced odds of mechanical ventilation use compared with the before group (OR 0.62, 95% CI 0.39, 0.99, $p = 0.007$). However, there was no significant reduction in the odds of vasopressor use (OR 0.89, 95% CI 0.75, 0.1.06, $p = 0.18$). For total charges per admission, there was a significant reduction between the estimated before phase adjusted mean charges of \$87,562 compared with the after phase charges of \$80,403 ($p = 0.04$), an approximate savings of \$7159 per sepsis admission.

4. Discussion

In this retrospective study, we have demonstrated that a comprehensive, program for sepsis recognition and management is associated with improved outcomes. Our findings demonstrate that a hospital-wide initiative as well as a team approach to sepsis care was associated with reductions in inpatient sepsis mortality, ICU LOS, hospital LOS, mechanical ventilation use, and hospital charges.

Our program involved a multifaceted approach to the complex problem of sepsis. The main goal of the program was a culture change regarding sepsis care throughout our institution. The four components of the sepsis alert program that we believe contributed to its success were: 1) interactive educational sessions, 2) electronic recognition, 3) a sepsis alert order set for simplified, standardized bundled care, and 4) a designated response team for each area of the hospital including RRT for care delivery on the wards. Our program emphasized the 3-hour bundle elements because we felt that, at a minimum, we wanted the 3-hour bundle elements administered to as many patients as possible in all areas of the hospital. The provision of more aggressive early goal directed therapy was left at the discretion of providers [15–17].

In this study, we note improved compliance rates with the 3-hour bundle at 25% compared with a recent Surviving Sepsis Campaign study which noted only a 19% compliance rate [9]. Though there was no significant mortality reduction with order set utilization, we believe that it was the culture change regarding sepsis care that resulted in improved care, so that whether the order set was utilized or not, patients were benefitting from elements of the bundle outside the order set. Other studies of sepsis bundle implementation have yielded mixed results. One study by Kumar et al. demonstrated improved compliance to the sepsis six (oxygen, blood cultures, antibiotics, lactate measurement, intravenous fluids, and urine output monitoring) from 29% pre-intervention to 63% post-intervention, but without demonstrable improvement in outcomes [18]. However, most studies indicate improved outcomes even with modest adherence to bundled care [9] [19–22]. Our program was similar to others with regards to provision of the 3-hour bundle, with our institution adding components of education, electronic recognition, designated response teams, and RRT.

We recognized during our design of the program that two of the greatest barriers to early, aggressive care for sepsis are a failure to recognize sepsis and a feeling that the bundle was unnecessary [19]. For this reason, we concentrated educational efforts to the weeks prior to implementation and emphasized the need for the key bundle elements including early antibiotics, intravenous fluids, lactate surveillance, and blood cultures. We reminded all providers and hospital staff that the purpose of a sepsis alert is to mobilize resources for efficient delivery of care to the septic patient, particularly nursing support through the RRT, clinical pharmacists for rapid antibiotics, and respiratory therapy for respiratory care and point of care lactate testing. We have previously demonstrated that novel uses of our RRT for surveillance of “at risk” ward patients has been effective at reducing mortality [10,23] and believe that sending automated “possible sepsis” pages to the RRT facilitated early recognition and treatment.

Previous success has been demonstrated with the implementation of the MEWS-SRS tool in the surgical ICU setting for sepsis screening [11]. After testing several different vital sign and laboratory-based protocols to electronically screen all patients in the hospital for sepsis, we successfully developed the adjusted MEWS-SRS that yielded the most favorable results with a PPV of 70% for sepsis. Because of the limitation of resources and technology available at our institution, we were unable to execute real-time background EHR data analysis for automated possible sepsis notifications and instead were restricted to hourly notifications, though real-time notifications are in future plans. Another innovation was the ability to adapt the electronic screening tool to a particular clinical setting and to silence “possible sepsis” pages by the addition of a sepsis diagnosis to the patient’s EHR problem list or by using the order set, acknowledging that sepsis had been recognized and treatment initiated. We allowed particular clinical areas to silence the page for shorter or longer periods (ICUs were allowed to silence the page for 72 h, general ward patients for 24 h) based on the level of monitoring in each unit to prevent alarm fatigue. However, the tool continued monitoring patients in the background, and could re-alert if the adjusted MEWS-SRS increased by 1 point.

Interestingly, in addition to demonstrating improvements in 5 of the 6 study outcomes, we identified that patients diagnosed with sepsis at the time of admission had a significantly reduced odds of death in comparison to patients who developed sepsis after admission. There may be several reasons for this, including delayed recognition in patients with other primary diagnoses (e.g., a patient with a stroke develops sepsis from aspiration pneumonia) or delayed or partial treatment of sepsis. In addition, aggressive care is more easily instituted in the ED or ICU than the general ward setting. However, with the assistance of RRT nurses we believe we have overcome much of the challenge to providing rapid care on the wards. Another potential cause for increased mortality of non-POA sepsis may include nosocomial pathogens with increased resistance. In all likelihood, it is a combination of these factors that may have contributed to increased mortality for non-POA sepsis patients and we intend to elucidate this and improve upon it in future studies. We also identified a reduced mortality for patients with an increased number of previous sepsis admissions. Though this is initially counterintuitive, it may have been a higher baseline suspicion for sepsis in a patient with a recent sepsis admission that contributed to earlier or more aggressive care. Another contributing factor may include having culture results from previous sepsis admissions to guide appropriate antibiotic selection.

Our program was developed prior to the new Sepsis-3 definitions, however, our study protocol used criteria similar to the recently described quick SOFA (qSOFA) criteria for hospital-wide sepsis screening [24]. We used a SBP < 90 rather than a SBP < 100, and we also used the presence of altered mental status. We did not however, include a criterion based on respiratory rate, and instead included a point-of-care lactate result of 3 mmol/L or greater as our cut-off for a sepsis alert. In addition, we added a specific recommendation for “provider concern”, that allowed concerned healthcare providers to page a sepsis alert even without meeting specific criteria. We feel that in general, a provider gestalt risk of sepsis is valuable, and because sepsis is a disease which can be diagnostically challenging, allowing providers to initiate timely care even when hard signs of sepsis are not yet present allows for earlier bundled care.

Finally, the reduction in charges of approximately \$7159 per sepsis admission is not surprising, given the reduction in the need for mechanical ventilation as well as the reduction in ICU and hospital LOS. This underscores that earlier, aggressive care can prevent the late complications of sepsis which frequently occur due to under-resuscitation and inadequate care in the early phase and provides further motivation for hospitals to improve sepsis care while reducing the expense of potentially unnecessary critical care utilization.

This study had several limitations. The retrospective nature of the study has inherent limitations with regards to the accuracy of the sepsis diagnosis, particularly using diagnostic codes [25]. Though this may have been an issue, we utilized previously described methods from experts in sepsis research to minimize the inclusion of non-septic patients in the study [3]. Determining the particular elements of care each patient received is difficult in a retrospective study and was beyond the scope of this study. In future studies, we hope to better elucidate particular elements of sepsis care so that we may address inadequacies in treatment and further reduce mortality. Though the electronic sepsis recognition tool was sending pages to providers and RRT nurses, we do not currently have data on the percentage of time that providers responded and initiated a formal sepsis alert. Our suspicion is that many more electronic alerts were sent than were responded to by providers. In future studies, we plan to merge the data between each particular electronic alert and the medical record to determine if the patient received the appropriate sepsis care. We are currently developing a method to do this efficiently and provide rapid feedback to providers.

5. Conclusion

In conclusion, the implementation of a comprehensive, hospital-wide program for sepsis recognition and management may significantly improve inpatient sepsis mortality, ICU LOS, overall hospital LOS, mechanical ventilation use, and hospital charges.

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Abbreviations

LOS	length of stay
SSC	Surviving Sepsis Campaign
EHR	electronic health record
RRT	rapid response team
ED	emergency department
ICU	intensive care unit

SBP	systolic blood pressure
MEWS-SRS	Modified Early Warning Signs–Sepsis Recognition Score
SIRS	systemic inflammatory response syndrome
POA	present on admission
Non-POA	non-present on admission
SD	standard deviation
OR	odds ratio
CI	confidence interval
SOFA	sequential organ failure assessment

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Fig. 1. Multivariable analysis demonstrating odds ratios (far right) for prediction of inpatient mortality from sepsis.

Table 1

Adjusted MEWS-SRS Score for identifying all patients with sepsis.

Adjusted modified early warning signs - sepsis recognition score									
Score	3	2	1	0	1	2	3		
T	<32	<35	<36	36–38.4	38.5–38.9	39–40.9	41		
HR	<40	40–44	45–50	51–100	101–110	111–129	>130		
RR	7	8	9	10–14	15–20	21–29	30		
SBP	70	71–80	81–100	101					
Latest WBC	<1	1–2.9		3–12.9	13–17.9	18–37.9	38		

Table 2

Baseline demographics of sepsis patients.

Variable	Overall (<i>n</i> = 3205)	Before (<i>n</i> = 1637, 51%)	After (<i>n</i> = 1568, 49%)	<i>p</i> -Value
Age, mean (SD)	57.1 (17.3)	57.3 (16.9)	57.1 (18.0)	0.94 ^a
Gender, female	1575 (49)	826 (51)	749 (48)	0.13 ^b
Race, Black	1603 (50)	855 (52)	748 (48)	0.04 ^b
White	1444 (45)	704 (43)	740 (47)	
Other	158 (5)	78 (5)	80 (5)	
AIDS	139 (4)	76 (5)	63 (4)	0.41 ^b
Cancer	364 (11)	198 (12)	166 (11)	0.21 ^b
CHF	680 (21)	325 (20)	355 (23)	0.04 ^b
COPD	1032 (32)	513 (31)	519 (33)	0.29 ^b
CVD	286 (9)	147 (9)	139 (9)	0.97 ^b
DM (no complications)	915 (29)	496 (30)	419 (27)	0.04 ^b
DM (complications)	226 (7)	96 (6)	130 (8)	0.006 ^b
Dementia	100 (3)	49 (3)	51 (3)	0.64 ^b
ESRD	251 (8)	142 (9)	109 (7)	0.07 ^b
Liver (mild)	367 (11)	189 (12)	178 (11)	0.93 ^b
Liver (moderate-severe)	83 (3)	40 (2)	43 (3)	0.57 ^b
Myocardial infarction	238 (7)	134 (8)	104 (7)	0.11 ^b
Metastatic cancer	132 (4)	70 (4)	62 (4)	0.68 ^b
Charlson Index, mean (SD)	2.67 (2.72)	2.52 (2.62)	2.47 (2.66)	0.35 ^a
Sepsis on admission (POA)	2585 (81)	1320 (81)	1265 (81)	0.97 ^b

Note: data are count (percentage), unless otherwise specified.

^aWilcoxon rank-sum test.^bPearson's Chi-square test.

Table 3

Features of sepsis for all encounters.

Variable	Overall (<i>n</i> = 3917)	Before (<i>n</i> = 1929, 49%)	After (<i>n</i> = 1988, 51%)	<i>p</i> -Value
Systolic blood pressure (mm Hg)	123.6 (30.5); <i>n</i> = 3013	122.9 (30.9); <i>n</i> = 1472	124.3 (30.1); <i>n</i> = 1541	0.23 ^a
Initial HR (beats/min)	101.3 (23.6); <i>n</i> = 3663	100.3 (24.0); <i>n</i> = 1775	102.18 (23.2); <i>n</i> = 1888	0.009 ^a
Initial RR (breaths/min)	19.7 (5.1); <i>n</i> = 3742	19.6 (5.3); <i>n</i> = 1833	19.75 (5.31); <i>n</i> = 1909	0.05 ^a
Initial temperature (°F)	98.8 (2.1); <i>n</i> = 3749	100.3 (24.0); <i>n</i> = 1833	98.9 (2.3); <i>n</i> = 1916	0.0007 ^a
Oxygen saturation (%)	93.4 (7.0); <i>n</i> = 1010	93.4 (7.4); <i>n</i> = 515	93.5(6.7); <i>n</i> = 495	0.42 ^a
Initial WBC (thous/mm ³)	13.6 (8.1); <i>n</i> = 3786	13.6 (8.0); <i>n</i> = 1857	13.2 (8.2); <i>n</i> = 1929	0.85 ^a
Lactate (mmol/L)	2.7 (2.8); <i>n</i> = 1967	3.0 (3.0); <i>n</i> = 968	2.6 (2.6); <i>n</i> = 999	0.05 ^a
Lactate ^c n (%)				
4 mmol/L	315 (16)	170 (18)	145 (15)	0.07 ^b
<4 mmol/L	1652 (84)	798 (82)	854 (85)	
Creatinine mg/dL	1.8 (2.3); <i>n</i> = 3842	1.9 (2.3); <i>n</i> = 1872	1.78 (2.3); <i>n</i> = 1970	0.15 ^a
Positive culture, n (%)				0.34 ^b
Blood	1284 (35)	700 (35)	584 (35)	
Respiratory	1093 (30)	573 (29)	520 (31)	
Urine	1088 (30)	606 (31)	482 (29)	
Wound	201 (5)	102 (5)	99 (5)	
Total	3666 (100)	1981 (54)	1685 (46)	

^aWilcoxon rank-sum test.^bPearson's Chi-square test.^cLactate at first admission.

Table 4

Univariate and multivariable analyses: after versus before phase comparisons of outcomes.

Outcome	Univariate (unadjusted) comparisons		p ^U	Multivariable (adjusted) comparisons		p ^M
	Overall (n = 3205)	Before (n = 1637)		After (n = 1568)	After vs. Before	
Inpatient mortality, n (%)	428 (11)	226 (12)		202 (10)	0.62 (0.39, 0.99) ^c	0.046
ICU LOS (days)	0 (0;3)	0 (0;5)		0 (0;3)	1.95 vs. 2.13 ^d	<0.001
Hospital LOS (days)	7 (4;16)	8 (4;17)		7 (4;15)	9.92 vs. 11.74 ^d	<0.0001
Mechanical ventilation use, n (%)	371 (9)	214 (11)		157 (8)	0.70 (0.54, 0.91) ^c	0.007
Vasopressor use, n (%)	1166 (30)	588 (30)		578 (29)	0.89 (0.75, 1.06)	0.181
Charges in USD	62,304 (31,648;143,472)	64,041 (30,739;148,684)		60,849 (32,631;137,317)	87,562 vs. 80,402 ^d	0.036

Note: Data are median (25th p;75th p) unless otherwise specified; 25th p = 25th percentile; 75th p = 75th percentile.

p^U = p-value from univariate analysis; p^M = p-value from multivariable analysis; USD = United States dollars.

^a Pearson's Chi-square test

^b Wilcoxon rank-sum test.

^c OR (95% CI).

^d Adjusted means.