Research and Applications

Evaluating the impact of a computerized surveillance algorithm and decision support system on sepsis mortality

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ABSTRACT

Objective: We created a system using a triad of change management, electronic surveillance, and algorithms to detect sepsis and deliver highly sensitive and specific decision support to the point of care using a mobile application. The investigators hypothesized that this system would result in a reduction in sepsis mortality.

Methods: A before-and-after model was used to study the impact of the interventions on sepsis-related mortality. All patients admitted to the study units were screened per the Institute for Healthcare Improvement Surviving Sepsis Guidelines using real-time electronic surveillance. Sepsis surveillance algorithms that adjusted clinical parameters based on comorbid medical conditions were deployed for improved sensitivity and specificity. Nurses received mobile alerts for all positive sepsis screenings as well as severe sepsis and shock alerts over a period of 10 months. Advice was given for early goal-directed therapy. Sepsis mortality during a control period from January 1, 2011 to September 30, 2013 was used as baseline for comparison.

Results: The primary outcome, sepsis mortality, decreased by 53% ($P = 0.03$; 95% CI, 1.06-5.25). The 30-day readmission rate reduced from 19.08% during the control period to 13.21% during the study period ($P = 0.05$; 95% CI, 0.97-2.52). No significant change in length of hospital stay was noted. The system had observed sensitivity of 95% and specificity of 82% for detecting sepsis compared to gold-standard physician chart review.

Conclusion: A program consisting of change management and electronic surveillance with highly sensitive and specific decision support delivered to the point of care resulted in significant reduction in deaths from sepsis.

Key words: sepsis, septic shock, clinical decision support, change management, electronic surveillance, sepsis mortality

BACKGROUND

Sepsis is a leading cause of death in the United States. Annually, there are 750 000 deaths from severe sepsis in the United States.[1] A significant financial burden is associated with treating septic patients; the estimated treatment cost is around $20 billion annually in the United States, making sepsis the costliest medical condition to treat in this country.[2] A strong body of evidence correlates early goal-directed therapy (prompt diagnosis, antimicrobial therapy, risk stratification, and hemodynamic stabilization) to significant

reductions in sepsis-related mortality.[3–7] Despite this evidence, healthcare organizations continue to struggle to identify and treat sepsis in a timely manner. Evidence suggests that patients who develop sepsis on general hospital wards may experience delays in diagnosis, treatment, and transfer to the intensive care unit (ICU), resulting in poor outcomes.[8–10] Change management consisting of sepsis education, screening protocols, process improvement, and sepsis analytics has been shown to improve sepsis outcomes,[11] but change management can be resource-intensive, and changes are

often difficult to sustain over time. This underscores the potential for intelligent and prompt sepsis decision support at the point of care. This impetus has led to the development of several systems that use automated, computerized surveillance for detecting sepsis.[12–19] However, to date, these clinical decision support (CDS) systems either lack sensitivity for sepsis detection or have poor specificity, adding to provider alert fatigue and disuse of the CDS system.[12,13,15,17,19,20] As a result, electronic surveillance systems have not managed to dramatically improve sepsis mortality.[16,17,19,20] With an aim to fill the void for highly sensitive and specific automated sepsis surveillance and point-of-care CDS, we developed and implemented a CDS system, then evaluated its test characteristics and the resultant sepsis-related outcomes.

A sepsis improvement program was implemented at Huntsville Hospital in Huntsville, Alabama, using a triad of techniques: (1) change management, (2) an electronic surveillance system, created using detailed rules to achieve high sensitivity and specificity, and (3) decision support delivered at the point of care using a mobile application. Sepsis algorithms based on the Institute for Healthcare Improvement's (IHI) Surviving Sepsis Guidelines, in addition to hundreds of CDS rules tailored to the prevalence of comorbid medical conditions in the study population that could mimic or explain sepsis symptoms, were implemented for automated sepsis screening. The investigators hypothesized that this program would result in a significant reduction of sepsis-related mortality.

METHODS

The study site was Huntsville Hospital, a tertiary care teaching hospital in Huntsville, Alabama. Huntsville Hospital has 941 beds and an average of 42 000 inpatient discharges annually. Sepsis surveillance was initiated on two hospital floors, containing two respiratory units and one general medicine unit, comprising a total 58 inpatient beds.

The training and implementation phase of the study was from October 1, 2013 to February 28, 2014. The implementation for the computerized sepsis surveillance and mobile alerting system was complete on March 6, 2014. Data from patients admitted to the two study floors in Huntsville Hospital were collected during the study period – March 1-December 31, 2014 (Figure 1). In addition, hospital data on baseline sepsis incidence and other health quality indicators were gathered from a control period – January 1, 2011 to September 30, 2013.

Ethics Approval
The Institutional Review Committee at Huntsville Hospital deemed this study exempt, because it was a part of hospital quality improvement initiative to reduce sepsis-related mortality. All selected patient data were accessible only to authorized personnel and stored using institutionally recommended security protocols.

Study Design
This was a single center, quasi-experimental study, with pre- and post-test analysis comparing patients admitted to two hospital floors on which a sepsis improvement program was implemented. The primary endpoint for the study was a comparison of sepsis-related mortality before and after the implementation of the sepsis improvement program. The sepsis improvement program consisted of a combination of sepsis education, process improvement through change management, and an electronic CDS system. The CDS system conducted

real-time surveillance of electronic medical record (EMR) data and delivered alerts to nursing staff's mobile devices at the point of care. Evidence-based advice was also delivered to nursing staff for all patients that screened as positive for sepsis. The advice included the 3- and 6-h bundles recommended by the Society of Critical Care's Surviving Sepsis Campaign.[4]

In a secondary analysis, the investigators also compared 30-day readmission and average length of hospital stay in the control and study group populations. Additionally, as a sub-analysis, the validity of sepsis alerts in comparison to the gold standard for diagnoses of sepsis of chart review was assessed.

Implementation Training and Change Management
The training and implementation period was utilized for change management, to create sepsis protocols and order sets, to establish unit teams, and to educate unit staff about sepsis and the use of the electronic sepsis alerting system. The governance process for establishing sepsis protocols was handled by the creation of nursing ward teams, a Sepsis Steering Committee, and a Physician Steering Committee. These teams' duties included:

- Creating sepsis order sets based on the Society for Critical Care's Surviving Sepsis Campaign Guidelines.
- Defining sepsis protocols for testing, communication, and follow-up.
- Establishing nursing protocols for lactate testing at the point of care for positive sepsis screening alerts.
- Creating electronic nursing documentation within the hospital EMR system that contained key discrete data elements necessary for sepsis screening algorithms.
- Educating hospital staff about sepsis and the sepsis screening protocols, including both formal, didactic sessions as well as ongoing instruction and feedback.
- Educating staff about the use of the electronic sepsis screening program.
- Facilitating progress across the unit teams.
- Creating excitement, awareness, and adoption of the sepsis program amongst the diverse clinical staff.
- Leading the overall sepsis initiative at the hospital.

Implementation of Electronic Sepsis Surveillance and Alerting System
Sepsis Alerting Algorithms
An electronic sepsis surveillance and alerting system that assessed patient demographics, vital signs, medications, lab values, and discrete documentation elements from nursing documentation, including medical problems, infectious diagnoses, as well as signs and symptoms of infection, was put in place in the study wards (Figure 2). During the system's implementation period, the nursing documentation within the hospital's EMR was evaluated and adjusted to ensure that appropriate discrete clinical elements would be documented for use by the system's rules engine. Discrete clinical data from the nursing documentation forms and other data were exported to an external rules engine using real-time Health Level Seven International interfaces.

The sepsis surveillance algorithms were created based on directives issued by the Office of National Coordinator and the Health Information and Management Systems Society Clinical Decision Support Workgroup and Task Force guidelines on CDS implementation.[21] The algorithms were also reviewed by subject matter experts with clinical experience in sepsis and clinical informatics. Through

Table 1. Patient Characteristics and Comorbidities in Control and Study Periods

	Control Period	Study Period	P-Value
Age	64 ± 0.22 years	63 ± 0.38 years	0.77
Female, n (%)	2587 (48)	975 (49)	0.22
Comorbidities, n (%)			
AIDS/HIV	8 (0.33)	7 (0.7)	0.5
Alcohol abuse	25 (1.04)	6 (0.6)	
Blood loss anemia	6 (0.25)	3 (0.3)	
Cardiac arrhythmias	132 (5.4)	58 (5.7)	
Chronic pulmonary disease	215 (8.9)	82 (8.1)	
Coagulopathy	51 (2.1)	13 (1.3)	
Congestive heart failure	139 (5.7)	51 (5)	
Deficiency anemia	38 (1.5)	14 (1.4)	
Depression	97 (4)	34 (3.4)	
Diabetes, complicated	58 (2.4)	38 (3.8)	
Diabetes, uncomplicated	150 (6.2)	55 (5.4)	
Drug abuse	23 (0.9)	17 (1.7)	
Fluid and electrolyte disorders	263 (10.8)	109 (10.8)	
Hypertension	367 (15.2)	160 (15.8)	
Hypothyroidism	100 (4.1)	54 (5.3)	
Liver disease	37 (1.5)	19 (1.9)	
Lymphoma	10 (0.4)	4 (0.4)	
Metastatic cancer	18 (0.75)	5 (0.5)	
Neurodegenerative disorders	148 (6.13)	55 (5.4)	
Obesity	72 (2.9)	42 (4.2)	
Paralysis	38 (1.5)	7 (0.7)	
Peptic ulcer disease, no bleeding	6 (0.2)	3 (0.3)	
Peripheral vascular disease	37 (1.5)	18 (1.8)	
Psychoses	5 (0.21)	6 (0.6)	
Pulmonary circulation disorders	32 (1.3)	20 (2)	
Renal failure	143 (5.9)	61 (6)	
Rheumatoid arthritis/collagen vascular diseases	26 (1)	12 (1.2)	
Solid tumor without metastasis	34 (1.4)	12 (1.2)	
Valvular disease	39 (1.6)	15 (1.5)	
Weight loss	97 (4)	31 (3.1)	

iterative development, decision support algorithms were built to diagnose sepsis, severe sepsis, and septic shock, taking into account comorbid acute and chronic diseases and associated parameters that can lead to misclassification errors in sepsis diagnosis. For example, creatinine was assessed differently for patients with renal disease; serum lactate, bilirubin, and platelet count results were assessed differently for patients with end-stage liver disease; and heart rate for patients on beta blockers had a different alerting threshold. The investigators reviewed all lab and vital sign parameter values after examining all the alerts that occurred during the implementation period, and adjusted these values for the specific patient population in the study screening units. The two physician investigators (S.M., S.R.C.) reviewed cases with comorbidities and adjusted the clinical parameters based on a combination of data analysis, literature review, and expert consensus. For patients that screened as positive for sepsis, therapeutic advice was delivered, based on evidence-based best practice recommendations, including, but not limited to, the Society of Critical Care Surviving Sepsis Campaign Guidelines for sepsis.[22–24] Further details on the overview of the alerting system and treatment protocols can be found in the Supplementary Appendix.

Real-time electronic sepsis surveillance was initiated in the two study medical units in March 2014. All patients admitted to the participating units were automatically enrolled for electronic sepsis screening. Nurses received alert notifications on mobile and desktop computer devices on a secured hospital network. The sepsis CDS system communicated important patient-specific information to nursing staff using four types of alerts: (1) informational prompts, like isolated tachycardia, isolated hypothermia, etc.; (2) diagnostic alerts that informed nurses about new positive sepsis screening results or signs of worsening sepsis in patients who previously screened as positive for sepsis; (3) advice alerts containing narratives for evidence-based care for sepsis, such as intravenous fluids, antibiotics, lactate testing, and recommended site-specific sepsis order sets, communication protocols, etc. (the advice mirrored and supported the protocols created during the change management effort); and (4) reminder alerts, which ensured that all alerts were acknowledged and that staff were complying with the recommended treatment plans. Nurses were directed to contact physicians about all patients diagnosed with sepsis.

Severe sepsis and septic shock alerts were also sent in tandem and escalated after periodic intervals to unit charge nurses to ensure the delivery of care and to ensure that all alerts were addressed in a timely fashion.

Data Sources

The nursing staff were required to accept or override all positive sepsis screening alerts. All sepsis screening alerts and respective clinician responses were later utilized for calculating test characteristics for the application. The diagnosis of sepsis was established using administrative claims data for analyzing sepsis-related mortality during the control and study periods.[25] This method involved utilizing the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for each patient's discharge diagnosis. Claims data have been widely used to identify septic patients, based on any of the three explicit sepsis ICD codes: sepsis (995.91), severe sepsis (995.92), or septic shock (785.52). This method has been validated to be a highly specific approach to identifying severe sepsis.[26] All patients assigned at least one of the sepsis ICD-9 codes who were admitted to the screening units were included in the study and control sets (depending on when they were admitted).

Data were collected retrospectively for all patients who were admitted to either of the two screening floors of the hospital from March 1-December 31, 2014, for the study period, and from January 1, 2011 to September 30, 2013, for the control period.

The investigators excluded cases that could not be impacted by the sepsis surveillance system from the analysis, including patients admitted directly to the ICU or who had received care in the ICU before being admitted to the sepsis study units. These patients were excluded from the study because the bulk of their sepsis care was administered before their enrollment in the sepsis screening program. Patients who had documentation or designation to intentionally receive limited care (eg, comfort measures only) were also excluded from both periods of the analysis.

Test Characteristics

The investigators evaluated patients screened using the surveillance program and alerts from April 1-June 30, 2014 to analyze the rules driving the sepsis-related alerts based on parameters sent from the surveillance engine. Sepsis diagnosis was compared against gold-standard chart review to calculate the positive predictive value, sensitivity, and specificity of the interventions.

Table 2. Patients Included in the Study

	Control Period	Study Period
Patients with sepsis (hospital-wide)	5414	1974
Patients with sepsis (screening units)	1170	464
After exclusions[a]	566	212
Deaths from sepsis[b]	51	9

ICU, intensive care unit.

[a]Exclusions included patients who were admitted to the ICU before being admitted to the screening units and patients that received limited interventions.

[b]Total deaths from sepsis after excluding ICU admissions and patients undergoing only limited care.

In order to confirm the sepsis diagnosis for calculating sensitivity and specificity, two physicians did a comprehensive chart review on all patients that received care in the study units from April-June 2014.

Case Definitions
Case definitions for systemic inflammatory response (SIRS), sepsis, and severe sepsis were based on the Society of Critical Care Surviving Sepsis Campaign Guidelines' evidence-based recommendation.[22–24,27] Sepsis was defined as the presence of two or more SIRS criteria secondary to infection. Severe sepsis was deemed present when there was evidence of organ dysfunction due to sepsis. Septic shock was defined as hypotension that was persistent after an initial fluid challenge in patients with sepsis or a serum lactate level of >4 mmol/L that was deemed to be elevated as a result of sepsis.

"Limited care" was defined as an instance in which appropriate sepsis care was intentionally withheld. Limited care did not include do not resuscitate/do not intubate (DNR/DNI) status unless it resulted in intentional withholding of care. Limited care did not include withdrawal of care after care had been provided and found to be futile because the patient had end-stage sepsis.

We used the Elixhauser scoring system[28,29] to evaluate comorbidities prevalent in the control and study populations. Patients were classified into one of two groups: the comorbidity present group or the comorbidity absent. We calculated a modified Elixhauser score by adding assigned points for each patient condition, excluding conditions with a negative Elixhauser score. All patients that had a modified Elixhauser score of greater than zero were included in the comorbidity present group.

The two physician investigators reviewed all patient records from April-June 2014 to diagnose the presence and severity of sepsis for positive screenings, in order to calculate alert test characteristics. All disagreements were reviewed and adjudicated. To assess reviewer agreement on the sepsis diagnosis, a subset of cases was reviewed by an independent physician with expertise in sepsis diagnosis and management. A Kappa statistic was calculated to assess inter-rater agreement for sepsis diagnosis between the two initial physician investigators and the independent physician reviewer.[30]

In a secondary analysis, the investigators also compared 30-day readmission rates and patients' average length of stay in the hospital. Additionally, the validity of sepsis alerts in comparison to gold-standard chart review for diagnoses of sepsis was assessed.

Analysis
The primary outcome of interest was sepsis-related mortality on the floors where screening was performed using the electronic sepsis surveillance system, comparing the control and study periods.

ICD-9 codes from insurance claims were retrospectively evaluated to confirm each patient's sepsis diagnosis. All patients who had been assigned one of the three ICD-9 codes (sepsis, septicemia, and septic shock) were deemed positive for sepsis. This method was used for all patients admitted during the control and study periods.

RESULTS

Site Characteristics
The average patient age for the study group population was 63 years, and 49% of the study participants were female. No significant differences in age or sex were noted in the control population (Table 1).

> **Key Findings**
>
> - First study to use a combination of change management, computerized surveillance, and mobile based point of care alerting.
>
> - 53% decrease in sepsis mortality on hospital units where sepsis initiative was implemented.
>
> - Alert sensitivity 95%; specificity was 82% compared to gold standard physician chart review.

Side Bar 1 – Key Findings
We used ICD-9 codes to generate Elixhauser scores,[28,29] compared comorbidities, and noted that there was no significant difference in the overall prevalence of comorbid conditions in the control and study populations (Table 1).

A total of 7388 patient records were evaluated (from the combined study and control periods), out of which 1634 were patients in the sepsis screening units (1170 in the control group and 464 in the study group, respectively). After all exclusions (ie, limited care and ICU admissions, as described previously), 778 of the patients reviewed were included in the study.

The observed coding of sepsis diagnoses by ICD-9 coding in the study units was 116 cases per 100 hospital days during the control period, compared to 151 cases per 100 hospital days while the electronic sepsis surveillance system was in place.

The sepsis-related mortality rate was 90 deaths per 1000 cases of sepsis during the control period, compared to 42 deaths per 1000 sepsis cases during the study phase, amounting to 53% fewer deaths per 1000 cases after the electronic sepsis surveillance system was implemented. This difference in sepsis-related mortality was statistically significant ($P = 0.03$; 95% confidence interval [CI], 1.06-5.25). Because the exclusive use of explicit ICD-9 codes for tracking sepsis is known to have high specificity but lower sensitivity,[26] we also evaluated sepsis prevalence by including patients with three explicit IDC-9 codes or Angus implementation codes.[25,26] The mortality rate in this cohort was 85 deaths per 1000 cases of sepsis during the control period, and 50 deaths per 1000 cases of sepsis during the study period, which amounted to a 41% lower mortality rate during the post-system implementation period ($P = 0.06$).

We noted a 43% decrease in sepsis mortality calculated based on deaths from sepsis per day of hospital stay, with 51 sepsis-related deaths occurring in 1004 days during the control period, and only 9 deaths occurring in 305 days during the study period. There was an
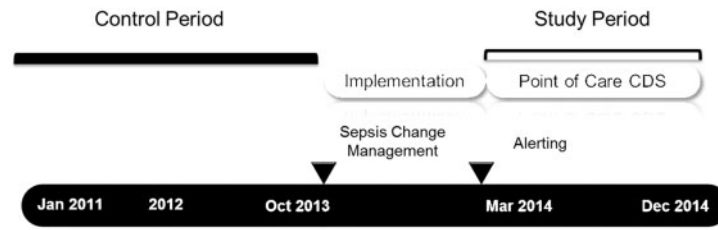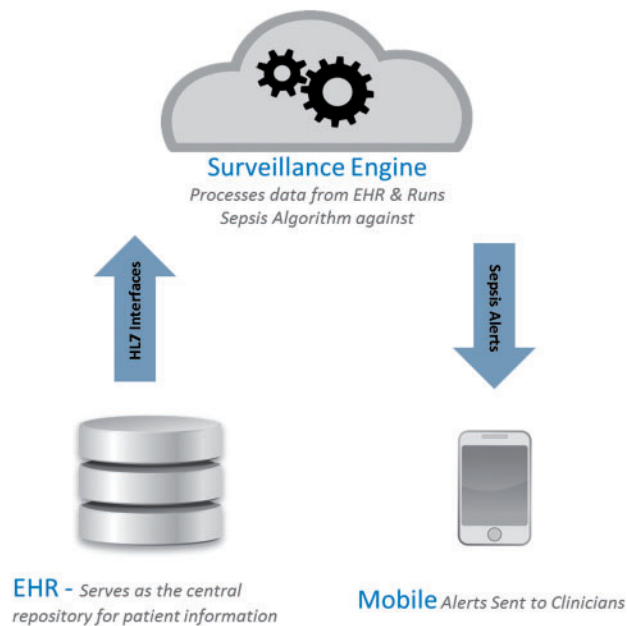
Figure 1. Study Timeline.

Figure 2. Overview of Clinical Decision Support Surveillance.

average of 315 sepsis-related deaths annually, determined by ICD-9 code, hospital-wide (excluding the study units) during the control period, compared to 322 deaths in 2014.

For patients with sepsis diagnosed by ICD-9 coding, a multivariate logistic regression analysis after adjusting for patient age, gender, presence of comorbidities, and hospital nursing unit showed that patients screened using the sepsis CDS system had a 2.1 times lower risk of death (odds ratio: 0.474; 95% CI, 0.228-0.988; $P = .04$), compared to patients in the pre-implementation period group.

The total number of sepsis cases captured by explicit ICD-9 codes increased throughout the control and study periods both in the study units and on all other floors hospital-wide (Figure 4).

There was no statistical difference in the year-to-year means when comparing explicit ICD-9-coded sepsis diagnoses, including for the 10 months of study period and the year before (Table 3). Moreover, the rate of increase in ICD-9 code capture of sepsis was the same hospital-wide, on non-sepsis screening floors. This suggests that the sepsis initiative was not the primary reason for the increase in the ICD-9 coding of sepsis.

A secondary analysis was done for 30-day readmission rates for all patients in the study units who had been assigned sepsis ICD-9 codes. A −30.8% change was noted in the study screening units, with an observed readmission rate of 19.08% during the control period and 13.21% during the study period ($P = 0.057$; 95% CI, 0.97-2.52).

The average length of stay in the study units for patients with sepsis ICD-9 codes decreased from 6.72 days during the control period to 6.68 days post-surveillance system implementation, but did not reach statistical significance ($P > 0.05$).

As a sub-analysis, we also tested the accuracy of the electronic sepsis diagnosis. We analyzed data for all patients admitted to the study screening units over the course of 3 months and compared those diagnosed with sepsis using the electronic system to those diagnosed using the gold standard of comprehensive chart review. There was substantial agreement between the investigators and the independent physician on the diagnosis of sepsis, with a Kappa statistic of 0.67 (95% CI, 0.41-0.92).

The electronic system had excellent accuracy for detecting sepsis or severe sepsis, with sensitivity of 95% for sepsis cases and 82% specificity, compared to the gold standard of physician chart review described earlier (Table 4).

DISCUSSION

To our knowledge, this study is unique in its attempt to measure the synergistic impact of a triad of change management with evidence-based guideline education, electronic surveillance, and advanced mobile-based point-of-care alerting on sepsis outcomes. This study is also an important addition to the existing body of knowledge on sepsis CDS systems because of its high sensitivity and specificity for real-time surveillance and point-of-care alerting. Previous CDS systems have generated a high number of false positive alerts caused by co-morbid medical conditions and ongoing medications. Many comorbid conditions alter clinical and laboratory data, thereby triggering false positive alerts in these CDS systems.[12,13,15,17,19,31,32] The sepsis screening algorithms used in the current study were based on standard IHI guidelines. However, these algorithms also contained additional specifications to adjust for comorbid medical conditions and medications. We believe that the complexity of the system's algorithms are responsible for its high sensitivity and high specificity and are key contributors to the impressive outcomes reported in our results.

Previous electronic surveillance systems have either had issues with high alert fatigue, when they have been successful in detecting sepsis (high sensitivity with low specificity), or have had modest alert fatigue, but missed a significant number of sepsis cases (high specificity, low sensitivity).[15–20,32] Likely as a result of this, previously published electronic surveillance systems have not been shown to have a significant impact on mortality.[16,17,19,20,32] We believe that the highly accurate alerts (sensitive and specific) in the system designed for this study minimized alert fatigue, allowing optimal clinician utilization of the system, and, when combined with the timely detection of sepsis allowed by the system, resulted in the positive outcome of significantly reduced sepsis mortality in the study population.
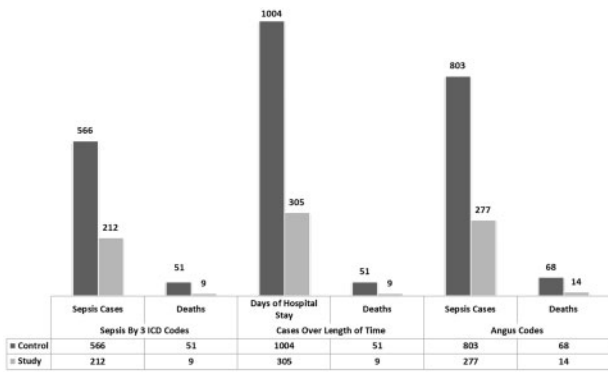
Figure 3. Sepsis mortality (by ICD-9 code) in the study population. ICD-9, International Classification of Diseases – 9.
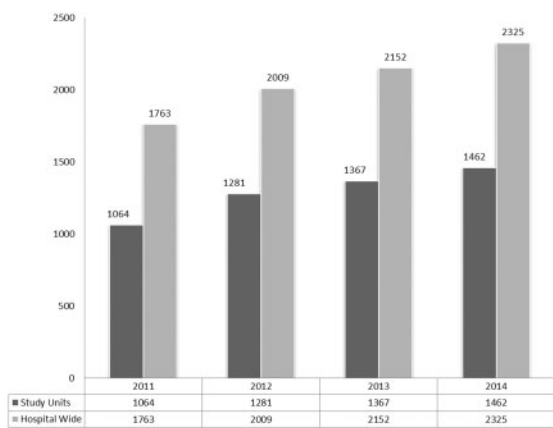

Figure 4. Total number of sepsis cases (hospital-wide, by ICD-9 codes). ICD-9, International Classification of Diseases – 9.

Table 3. Year-wise Comparison for Explicit ICD-9-Code-Captured Sepsis in Study Units

Year Comparison	Difference in Means	Simultaneous 95% CI
2013–2014[a]	−14.956	−41.361,11.450
2012–2014[a]	−29.983	−54.591,−5.376*
2012–2013	−15.028	−40.370,10.314
2011–2014[a]	−50.483	−75.091,−25.876*
2011–2013	−35.528	−60.870,−10.186*
2011–2012	−20.500	−43.962,2.962

CI, confidence interval; ICD-9, International Classification of Diseases – 9.

[a]2014 was limited to the 10 months of the study period.

*Comparison is significant at the 0.05 level.

Table 4. Test Characteristics for the Electronic Diagnosis of Sepsis vs. Gold-Standard Comprehensive Chart Review

Statistic	Result (95% CIs)
True positives	118
False negatives	6
False positives	117
True negatives	530
Sensitivity	95.16 (89.77-98.20)
Specificity	81.92 (78.73-84.8)
Positive likelihood ratio	5.26 (4.45-6.23)
Negative likelihood ratio	0.06 (0.03-0.13)
Sepsis prevalence[a]	16.08 (13.56, 18.87)
Positive predictive value[a]	50.21 (43.64, 56.78)
Negative predictive value[a]	98.88 (97.58, 99.59)

CI, confidence interval; ICD-9, International Classification of Diseases – 9.

[a]Sepsis prevalence calculated by chart review, not by ICD-9 coding. The calculated sepsis prevalence is for the 3-month duration that patients spent in the sepsis study units. Sepsis prevalence may be different hospital-wide and in the total Huntsville patient population. The true positive predictive value and negative predictive value may also be different, because they are based on true sepsis prevalence and not ICD-9 code proxy for sepsis.

Data analysis also showed a relative increase in the number of ICD-9-code-based sepsis diagnoses during the study period. It can be argued that this was due to an increased awareness of sepsis, increased documentation, and, therefore, increased ICD-9 coding of sepsis. This may indeed account for the modest increase in the improvement in sepsis coding seen in this study, but, more likely, there was greater impact from the sepsis documentation improvement initiative that started years prior to the study period. The documentation initiative implemented hospital-wide resulted in higher sepsis rates throughout the hospital, including the sepsis study units. We noted that there was a steady increase in the number of sepsis cases from 2011, and there was no significant change in the number of cases from the year before this sepsis program was implemented (2013–2014).

Regardless of the reason for the increase in cases assigned ICD-9 codes for sepsis, the increase complicates the mortality assessment; capturing more sepsis cases may artificially seem to improve outcomes when mortality is assessed as deaths per case of sepsis by ICD-9 code criteria. Because the capture rate went up from the control period to the study period, the 53% mortality reduction is an overestimation of the true mortality reduction.

When assessed using the number of ICD-9-code-identified sepsis deaths per number of total patient hospital stay days, the mortality rate went down by 43%. Because the improvement in ICD-9 code capture of sepsis cases can be expected to increase the number of sepsis cases in the study population, it would also be expected to increase the documentation and capture of sepsis-related deaths. Thus, calculating the number of deaths from sepsis per hospital stay days possibly underestimates the true impact of our interventions on sepsis-related mortality rates. The true reduction in sepsis-related mortality as a result of our interventions was likely between 43 and 53%.

We employed another method to evaluate the reduction in sepsis-related mortality observed in this study. In this method, patients were considered to be sepsis-positive if they met Angus implementation criteria or had an ICD-9 code for sepsis. This method also revealed a 41% lower mortality rate in the study group. This reduction is slightly lower than our other estimates, because the Angus implementation criteria method had a significantly lower specificity,[26] and thereby also captured non-sepsis cases that were not impacted by the sepsis system. Nevertheless, it serves as another appropriate check to confirm that the system reduced mortality.

Sepsis mortality was reduced in the study group, based on four assessments: (1) measuring sepsis prevalence and mortality using ICD-9 codes for sepsis; (2) calculating sepsis mortality over a period of time; (3) calculating sepsis prevalence and mortality using Angus implementation criteria; and (4) measuring sepsis mortality after adjusting for patient-level parameters.

In addition, further analysis showed that sepsis mortality did not improve on units that did not implement our electronic surveillance and alerting system. We thus infer that the sepsis initiative was the primary driver of the improvement in sepsis-related mortality in the study population.

This sepsis initiative did not include any additional hospital discharge planning or education. We postulate that the improvement in 30-day readmission rates for sepsis patients observed in this study was due to an expedient sepsis diagnosis and improved care, factors that have been well-established to decrease morbidity, length of hospital stay, and readmission rates in multiple studies.[5,6,18,33]

There is often an inverse relationship between length of hospital stay and risk of readmission within 30 days in initiatives that impact these metrics. However, patients' length of hospital stay did not increase despite a reduction in the 30-day readmission rate in this study. It can be inferred that the impact on 30-day readmission is due to improvement of the care process and not an increased length of stay in the hospital, which could artificially reduce the 30-day readmission rate.

The trend we saw toward improvement in patients' average length of hospital stay post-implementation of the sepsis surveillance and alerting system did not achieve statistical significance. We hypothesize that a hospital-wide implementation of the electronic sepsis surveillance and alerting system would result in standardized sepsis screening and early detection, improved sepsis guideline adherence, and a substantially bigger sample size to test the system with, which are known determinants for significant improvement in length of hospital stay for sepsis patients. Levy et al.[6] and Jones et al.,[34] suggest that all sepsis quality characteristics, including mortality, 30-day readmission rate, and average length of hospital stay and ICU stay are significantly improved with improved sepsis guideline adherence for bundle compliance. Because the primary focus of our program was to improve sepsis care by following IHI bundle compliance, we hypothesize that these same quality indicators will all improve.

The Third International Consensus Definitions Task Force recently updated its definitions of sepsis.[35] We welcome the new definitions, acknowledge the need to simplify the process of diagnosing of sepsis, and second the task force's nod to the continued usefulness of SIRS criteria for the identification of infection. However, the task force's comment about the SIRS criteria's "poor discriminant validity"[35] may not hold true for intelligent CDS systems, including the one evaluated in this study. As previously described in this article, the CDS system designed for this study leveraged EHR data to account for multiple patient comorbidities that may otherwise trigger false positive alerts for patients without sepsis.

It has been established that early detection and treatment of sepsis significantly decreases sepsis-related mortality.[3–7] However, there remains a paucity of evidence regarding which definition of sepsis (ie, Sepsis-2 or Sepsis-3) detects sepsis earlier. Thus, until the new sepsis definition has been vetted by the clinical community and validated in multiple patient populations and hospital settings, we recommend a hybrid approach, comprising a combination of the existing SIRS and severe sepsis criteria that have been carefully weighed and adjusted based on patient comorbidities and medications, augmented with the new simplified quick Sequential Organ Failure Assessment (qSOFA) and SOFA scoring. We intend to update our algorithms with the new hybrid criteria and revalidate the findings in a separate study. Nonetheless, because our methods for developing and implementing the sepsis CDS system are based on established informatics standards,[21] we argue that the methods employed in this study can be utilized to replicate equally impressive results using newer sepsis definitions.

Our study has several limitations. The sample size, particularly for the study period, is relatively modest. Moreover, this was a quasi-experimental study comparing two different time periods. The control population was a patient population from several years before the study period. However, we noted that the control and study group patient populations were not different in terms of clinical setting, age, gender, and comorbidities present (Table 1). Race and ethnicity information was missing for a large number of patients and thus was not utilized in the multivariate analysis. It is possible that secular trends and improvements in medical knowledge, staff training, guideline adherence, and quality of care over time may have influenced the quality of sepsis care in this study and, hence, may have improved outcomes. However, Huntsville Hospital did not have an established Rapid Response Team during the control or study period, and there was no significant change in hospital-wide sepsis mortality during the control and study periods. Because a similar decrease in sepsis mortality was not seen elsewhere in the hospital, we assume that the improvements in sepsis outcomes observed on the study floors at the hospital can be attributed to the electronic sepsis surveillance and alerting initiative. We infer that the alert system resulted in low alarm fatigue because of its high specificity (true negative rate). This should be re-evaluated in a mixed-methods analysis involving the system end users. We did not study guideline adherence and bundle compliance for electronically screened sepsis patients and impact of these factors on sepsis quality metrics, but intend to explore this in follow-up studies. Additionally, another potential limitation that could impact the study is that administrative data (ie, ICD-9 codes) used to diagnose sepsis in our study are known to have low sensitivity.[25,26] We were, however, consistent in employing this method of identifying septic patients during the control and study periods.

CONCLUSION

An electronic surveillance and alerting system for sepsis can achieve both high sensitivity and high specificity with a design focused on building many patient-specific detection rules. We observed a significant improvement in sepsis-related quality metrics, including decreased mortality and decreased 30-day readmissions, using a triad of change management, electronic surveillance with highly sensitive and specific alerting rules, and decision support delivered to the point of care. These results should be externally validated in larger and differing patient populations.

CONTRIBUTORS

Both authors acknowledge their contributions to and responsibilities for the content of this work. S.M. provided the concept and design of the study and manuscript. S.M. and S.R.C. performed clinical data collection, analysis, and interpretation of results and wrote the manuscript.

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REFERENCES

1. Gaieski DF, Edwards JM, Kallan MJ, Carr BG. Benchmarking the incidence and mortality of severe sepsis in the United States. *Crit Care Med.* 2013;41(5):1167–1174.

2. Torio CM, Andrews RM. National inpatient hospital costs: the most expensive conditions by payer, 2011. 2013.

3. Kumar A, Zarychanski R, Light B, *et al.* Early combination antibiotic therapy yields improved survival compared with monotherapy in septic shock: a propensity-matched analysis. *Crit Care Med.* 2010;38(9):1773–1785.

4. Dellinger RP, Levy MM, Rhodes A, *et al.* Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med.* 2013;41(2):580–637.

5. Rivers E, Nguyen B, Havstad S, *et al.* Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med.* 2001;345(19):1368–1377.

6. Levy MM, Rhodes A, Phillips GS, *et al.* Surviving Sepsis Campaign: association between performance metrics and outcomes in a 7.5-year study. *Intensive Care Med.* 2014;40(11):1623–1633.

7. Gao F, Melody T, Daniels DF, Giles S, Fox S. The impact of compliance with 6-hour and 24-hour sepsis bundles on hospital mortality in patients with severe sepsis: a prospective observational study. *Crit Care.* 2005;9(6):R764–R770.

8. Young MP, Gooder VJ, Bride K, James B, Fisher ES. Inpatient transfers to the intensive care unit. *J General Internal Med.* 2003;18(2):77–83.

9. Lundberg JS, Perl TM, Wiblin T, *et al.* Septic shock: an analysis of outcomes for patients with onset on hospital wards versus intensive care units. *Crit Care Med.* 1998;26(6):1020–1024.

10. Thiel SW, Asghar MF, Micek ST, Reichley RM, Doherty JA, Kollef MH. Hospital-wide impact of a standardized order set for the management of bacteremic severe sepsis. *Crit Care Med.* 2009;37(3):819–824.

11. Kliger J, Singer SJ, Hoffman FH. Using the Integrated Nurse Leadership Program to Reduce Sepsis Mortality. *Jt Commission J Qual Patient Safety.* 2015;41(6):264–272.

12. Paul M, Andreassen S, Nielsen AD, *et al.* Prediction of Bacteremia Using TREAT, a Computerized Decision-Support System. *Clin Infect Dis.* 2006;42(9):1274–1282.

13. Harrison AM, Herasevich V, Gajic O. Automated Sepsis Detection, Alert, and Clinical Decision Support: Act on It or Silence the Alarm? *Crit Care Med.* 2015;43(8):1776–1777.

14. Henry KE, Hager DN, Pronovost PJ, Saria S. A targeted real-time early warning score (TREWScore) for septic shock. *Sci Transl Med.* 2015;7(299):299ra122.

15. Nguyen SQ, Mwakalindile E, Booth JS, *et al.* Automated electronic medical record sepsis detection in the emergency department. *Peer J.* 2014;2:e343.

16. Bailey TC, Chen Y, Mao Y, *et al.* A trial of a real-time alert for clinical deterioration in patients hospitalized on general medical wards. *J Hosp Med.* 2013;8(5):236–242.

17. Semler MW, Weavind L, Hooper MH, *et al.* An electronic tool for the evaluation and treatment of sepsis in the ICU: a randomized controlled trial. *Crit Care Med.* 2015;43(8):1595–1602.

18. Nelson JL, Smith BL, Jared JD, Younger JG. Prospective trial of real-time electronic surveillance to expedite early care of severe sepsis. *Ann Emerg Med.* 2011;57(5):500–504.

19. Buck KM. Developing an early sepsis alert program. *J Nurs Care Qual.* 2014;29(2):124–132.

20. Umscheid CA, Betesh J, VanZandbergen C, *et al.* Development, implementation, and impact of an automated early warning and response system for sepsis. *J Hosp Med.* 2015;10(1):26–31.

21. HIMSS Clinical Decision Support Workgroup and Task Force. *Improving Outcomes With Clinical Decision Support: an Implementer's Guide.* 2nd edn. Osheroff JA, ed. HIMSS; 2011.

22. Neviere R, Parsons P, Wilson K. Sepsis and the systemic inflammatory response syndrome: definitions, epidemiology, and prognosis. UpToDate, Parsons PE, Ed. UpToDate [Internet]. April 24, 2015 [cited 3/27/2015 3:09:39 PM; 3/27/2015 3:09:39 PM; 3/27/2015 12:31:02 PM]:May 27, 2015.

23. Bone RC, Balk RA, Cerra FB, *et al.* Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest J.* 1992;101(6):1644–1655.

24. Dellinger RP, Levy MM, Rhodes A, *et al.* Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med.* 2013;39(2):165–228.

25. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med.* 2001;29(7):1303–1310.

26. Iwashyna TJ, Odden A, Rohde J, *et al.* Identifying patients with severe sepsis using administrative claims: patient-level validation of the Angus implementation of the international consensus conference definition of severe sepsis. *Med Care.* 2014;52(6):e39–e43.

27. Levy MM, Fink MP, Marshall JC, *et al.* 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Intensive Care Med.* 2003;29(4):530–538.

28. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care.* 1998;36(1):8–27.

29. van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. *Med Care.* 2009:626–633.

30. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. *Fam Med.* 2005;37(5):360–363.

31. Brandt BN, Gartner AB, Moncure M, *et al.* Identifying severe sepsis via electronic surveillance. *Am J Med Qual.* 2015;30(6):559–565.

32. Ehrlichman P, Trach L, Patel B, Maheshwari V, Seckel M. 983: sensitivity and positive predictive value of CERNER EMR based sepsis recognition tool. *Crit Care Med.* 2014;42(12):A1597.

33. Jones S, Mullally M, Ingleby S, Buist M, Bailey M, Eddleston JM. Bedside electronic capture of clinical observations and automated clinical alerts to improve compliance with an Early Warning Score protocol. 2011.

34. Jones TK, Fuchs BD, Small DS, *et al.* Post-acute care use and hospital readmission after sepsis. *Ann Am Thorac Soc.* 2015;12(6):904–913.

35. Singer M, Deutschman CS, Seymour C, *et al.* The third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA.* 2016;315(8):801–810.