OBSERVATIONAL STUDY

OPEN

Order Set Usage is Associated With Lower Hospital Mortality in Patients With Sepsis

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IMPORTANCE: The Surviving Sepsis Campaign recommends standard operating procedures for patients with sepsis. Real-world evidence about sepsis order set implementation is limited.

OBJECTIVES: To estimate the effect of sepsis order set usage on hospital mortality.

DESIGN: Retrospective cohort study.

SETTING AND PARTICIPANTS: Fifty-four acute care hospitals in the United States from December 1, 2020 to November 30, 2022 involving 104,662 patients hospitalized for sepsis.

MAIN OUTCOMES AND MEASURES: Hospital mortality.

RESULTS: The sepsis order set was used in 58,091 (55.5%) patients with sepsis. Initial mean sequential organ failure assessment score was 0.3 lower in patients for whom the order set was used than in those for whom it was not used (2.9 SD [2.8] vs 3.2 [3.1], $p < 0.01$). In bivariate analysis, hospital mortality was 6.3% lower in patients for whom the sepsis order set was used (9.7% vs 16.0%, $p < 0.01$), median time from emergency department triage to antibiotics was 54 minutes less (125 interquartile range [IQR, 68–221] vs 179 [98–379], $p < 0.01$), and median total time hypotensive was 2.1 hours less (5.5 IQR [2.0–15.0] vs 7.6 [2.5–21.8], $p < 0.01$) and septic shock was 3.2% less common (22.0% vs 25.4%, $p < 0.01$). Order set use was associated with 1.1 fewer median days of hospitalization (4.9 [2.8–9.0] vs 6.0 [3.2–12.1], $p < 0.01$), and 6.6% more patients discharged to home (61.4% vs 54.8%, $p < 0.01$). In the multivariable model, sepsis order set use was independently associated with lower hospital mortality (odds ratio 0.70; 95% CI, 0.66–0.73).

CONCLUSIONS AND RELEVANCE: In a cohort of patients hospitalized with sepsis, order set use was independently associated with lower hospital mortality. Order sets can impact large-scale quality improvement efforts.

KEY WORDS: clinical decision support; health services; order set; sepsis; quality improvement

Sepsis is present in up to 52% of hospitalizations and is the leading cause of hospital mortality in the United States (1). The Surviving Sepsis Campaign recommends "standard operating procedures for treatment as a "strong" recommendation despite "very low-quality evidence" (2). Healthcare systems use Electronic Medical Record (EMR)-embedded order sets to implement "standard operating procedures." Order sets may increase health equity and improve patient outcomes (3, 4).

Because many investigations of sepsis order sets have been single-institution or of short duration, we sought to understand the association between order set usage and clinical outcomes in a large, integrated delivery system in the United States (5–9). In adult patients discharged with sepsis, we hypothesized that the use of a sepsis order set was associated with greater survival to

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KEY POINTS

Question: In patients hospitalized with sepsis, is use of a sepsis order set associated with lower hospital mortality?

Findings: In this retrospective cohort study of 104,662 patients hospitalized for sepsis in a large U.S. healthcare system, use of a sepsis order set was independently associated with lower hospital mortality. Time to antibiotics and total time hypotensive only partially mediated the association between sepsis order set use and hospital mortality.

Meaning: Sepsis order set use is associated with lower hospital mortality in a large cohort of patients in the United States.

hospital discharge compared with not using an order set. Second, we hypothesized that the effect of order set usage is mediated via both a shorter time to antibiotics and a shorter duration of hypotension. Finally, we hypothesized that order set use would be associated with improved outcomes across all race/ethnicity groups.

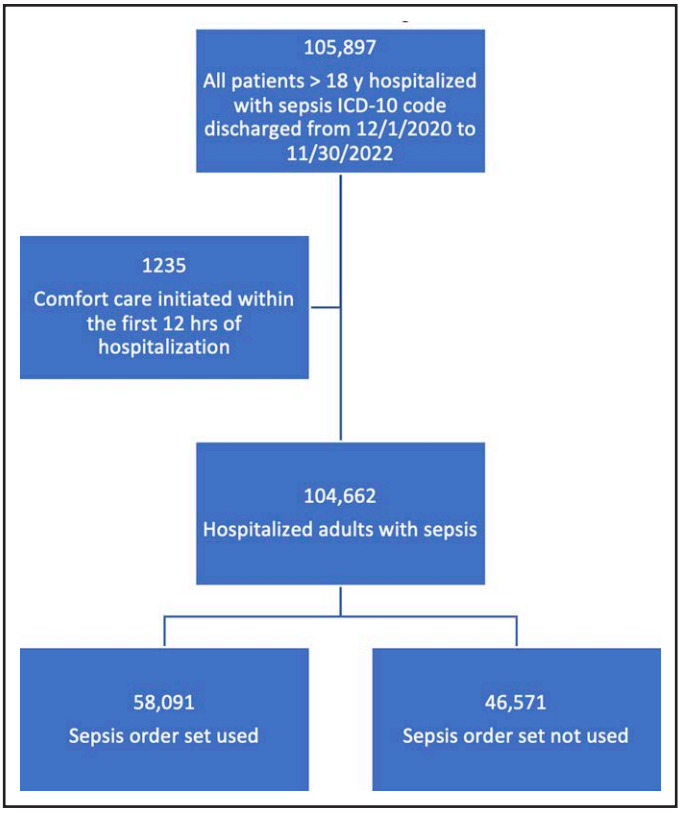

Figure 1. Patient selection CONSORT flow diagram. Sepsis *International Classification of Diseases*, Tenth Revision (ICD-10) codes as per Center for Medicare and Medicade Services sepsis early management bundle quality measure (https://qualitynet.cms.gov/inpatient/specifications-manuals).

MATERIALS AND METHODS

Study Design and Patients

We performed a retrospective cohort study of all patients 18 years or older who were admitted to a Providence hospital as an inpatient and discharged between December 1, 2020, and November 30, 2022, with a diagnosis of sepsis from the set of diagnoses used as inclusion criteria for the Centers for Medicare and Medicaid Services (CMS) CMS sepsis early management bundle quality measure (10). Patients with comfort care ordered within the first 12 hours of admission were excluded (**Fig. 1**). The study was approved by the Providence Human Research Protection Program/institutional review board (Study MOD2022001653, Title: Retrospective Chart Review: Order Set Usage in Patients with Sepsis Improves Survival to Hospital Discharge, Approved November 30, 2022) and the study adhered to Declaration of Helsinki.

Patient demographic, clinical, and treatment data were extracted from the EMR. Severe sepsis and septic shock were determined by the International Classification of Diseases, Tenth Revision codes. The presence of COVID-19 during the admission and "present on admission" (POA) versus "not-present on admission" was based on discharge diagnoses and coding, respectively. Hypotension onset was defined as the first of two consecutive systolic blood pressures (SBPs) below 90 mm Hg or the first of two consecutive mean arterial pressures (MAPs) less than 65 mm Hg and resolution of hypotension was defined as the first of two consecutive SBPs greater or equal to 90 mm Hg or the first of two consecutive MAPs greater than or equal to 65 mm Hg. An episode of hypotension was calculated from the time difference between hypotension onset and hypotension resolution and the total time hypotensive for hospitalization was the sum of the durations of hypotension for each episode. Sequential Organ Failure Assessment scores were abstracted from the EMR (11, 12).

Sepsis Order Set

The sepsis order set was designed by the Providence Sepsis Focus Group, a quality improvement collaborative, to make guideline-concordant sepsis care. The sepsis order set was available in the EMR of 54 hospitals across the Providence system. Order set usage was determined by the use of an embedded "Sepsis Management" order and was abstracted as a binary variable. Order sets could be used on presentation in the emergency department (ED) or later during hospitalization. The sepsis order set included (**eTable 1**, http://links.lww.com/CCX/B194):

- A "Sepsis Management" order to denote the patient as a "septic patient."
- Nursing orders for more frequent "sepsis vital signs," with licensed independent provider call parameters.
- Serum lactate measurement every 2 hours for two measurements.
- A 30 mL/kg crystalloid bolus with options for normal saline or Ringer's Lactate.
- Noninvasive cardiac monitoring to assess fluid responsiveness, where available.
- Norepinephrine infusion for hypotension.
- Antimicrobial decision support based on source of infection and type of sepsis (sepsis vs severe sepsis or septic shock), risk of multidrug-resistant organisms, and local antibiograms.

The "Sepsis Management" order placed the patient on an EMR-based census generating an at-a-glance display of 3- and 6-hour bundle element completion (bolus, lactate, blood cultures, antibiotics, lactate repeat if indicated, vasopressor if indicated). Some facilities assigned a dedicated sepsis nurse to ensure that guideline-concordant care was delivered to patients on the sepsis census. All orders could be independently selected in the order set.

Statistical Analysis

We used descriptive statistics to assess the distribution of the variables relative to order set usage. Continuous variables are presented as mean with SD or median with interquartile range (IQR). Categorical variables are presented as frequency with percentage. For comparisons between groups, Welch *t* or Wilcoxon rank-sum tests, and Chi-square tests were performed for continuous, and categorical variables, respectively. Patients with missing time from ED triage to antibiotic administration and patients with no time hypotensive were excluded from those analyses. Multivariable logistic regression analyses were performed to test the association of order set usage with hospital mortality, our primary endpoint. Risk factors including age, race/ethnicity, patient primary language, Sequential Organ Failure Assessment (SOFA) score, initial lactate level, COVID status, sepsis POA status, payer, hospital, and administrative region within the Providence system were evaluated in the univariate and multivariable analyses. We did not include sex or hospital/administrative region in the final model as these did not affect the association between order set usage and hospital mortality and the model performed better without them.

For our secondary a priori-specified analysis, we conducted bootstrap mediation analyses with 1,000 samples to examine the indirect effects of time to antibiotics and total time hypotensive on the association between sepsis order set use and hospital mortality (13, 14). Mediation analysis is a statistical technique to estimate the extent to which a mediator variable, each of time to antibiotics and total time hypotensive independently in this case, "mediate" or explain the relationship between the predictor of interest (order set use) and outcome (hospital mortality). We hypothesized that the order set would impact mortality via shorter time to antibiotics and less time hypotensive and mediation analysis allowed us to test that hypothesis. Statistical tests were considered significant at a p value of less than 0.05 and all testing was two-sided. Statistical analyses were performed in R Studio, Version 2022.12.0 + 353 (Boston, MA).

RESULTS

We identified 104,662 patients discharged with a sepsis diagnosis over the 2-year study period, 58,091 (55.5%) for whom the sepsis order set was used and 46,571 (44.5%) for whom the order set was not used. Patients for whom the order set was used were older (65.4 vs 64.4 yr; $p < 0.01$) and less likely to be male (53.5% vs 54.5%; $p < 0.01$). Use of order set by race/ethnicity category varied from 60% (Asian, 5.2% of total population) to 45% ("Other/unknown," 6.7% of total, $p < 0.01$) and the order set was used for 56% of patient who identified English as their primary language, 57% Spanish, and 48% "other" languages ($p < 0.01$). More patients for whom the order set was used had severe sepsis (30.4% vs 22.8%; $p < 0.01$), fewer had septic shock (22.0% vs 25.4%; $p < 0.01$), and more had

sepsis POA (96.2% vs 87.9%; $p < 0.01$). Additional patient characteristics are shown in **Table 1**.

Sepsis order set use was associated with a shorter median time from ED triage to antibiotic administration (125 min [IQR, 68–221] vs 179 min [IQR, 98–379]; $p < 0.01$) in all patients and in patients with sepsis POA (122 min [IQR, 66–213] vs 163 min [IQR, 91–297]; $p < 0.01$) (**eTable 2**, http://links.lww.com/CCX/B194). More patients for whom sepsis order sets were used received antibiotics within 1 hour (19.6% vs 7.6%;

TABLE 1.
Baseline Patient Characteristics by Order Set Use

	Patients (% of Total)	Sepsis Order Set Used by Patient Characteristic, *n* (% Using Order Set)	Sepsis Order Set Not Used by Patient Characteristic, *n* (% Not Using Order Set)	*p*
All patients	104,662 (100)	58,091 (55.5)	46,571 (44.5)	
Patient age (yr), mean (SD)	64.9 (17.7)	65.4 (17.9)	64.4 (17.5)	< 0.01
Male sex, *n* (%)	56,466 (54.0)	31,091 (53.5)	25,375 (54.5)	< 0.01
Race/ethnicity, *n* (%)				< 0.01
White	68,697 (65.6)	38,840 (66.9)	29,857 (64.1)	
Asian	5451 (5.2)	3265 (5.6)	2186 (4.7)	
Black	4236 (4.0)	2265 (3.9)	1971 (4.2)	
Hispanic	16,634 (15.9)	9193 (15.8)	7441 (16.0)	
Native American/Alaska Native	1685 (1.6)	846 (1.5)	839 (1.8)	
Native Hawaiian/Pacific Islander	888 (0.8)	485 (0.8)	403 (0.9)	
Unknown/other	7050 (6.7)	3183 (5.5)	3867 (8.3)	
Primary language, *n* (%)				< 0.01
English	90,864 (86.8)	50,806 (87.5)	40,058 (86.0)	
Spanish	7713 (7.4)	4382 (7.5)	3331 (7.2)	
Other	6064 (5.8)	2889 (5.0)	3175 (6.8)	
Payer, *n* (%)				< 0.01
Medicare	58,477 (55.9)	32,627 (56.2)	25,850 (55.5)	
Medicaid	20,816 (19.9)	11,595 (20.0)	9221 (19.8)	
Commercial	20,805 (19.9)	11,796 (20.3)	9009 (19.3)	
Other	2604 (2.5%)	1373 (2.4)	1231 (2.6)	
Severe sepsis, *n* (%)	28,277 (27.0)	17,668 (30.4)	10,609 (22.8)	< 0.01
Septic shock, *n* (%)	24,616 (23.5)	12,793 (22.0)	11,823 (25.4)	< 0.01
Sepsis present on admission, *n* (%)	96,837 (92.5)	55,902 (96.2)	40,935 (87.9)	< 0.01
Hypotensive episode, *n* (%)	40,675 (38.9)	23,652 (40.7)	17,023 (36.6)	< 0.01
COVID positive, *n* (%)	14,544 (13.9)	6487 (11.1)	8057 (17.3)	< 0.01
Initial lactate (mg/dL), mean (SD)	.5 (2.2)	2.5 (2.1)	2.5 (2.3)	< 0.01
Initial Sequential Organ Failure Assessment score for first hospital day, mean (SD)	3.0 (2.9)	2.9 (2.8)	3.2 (3.1)	< 0.01

$p < 0.01$) and 3 hours of ED triage (62.5% vs 31.7%; $p < 0.01$). More patients for whom sepsis order sets were used received antibiotics within 24 hours before or 1 hour after hypotension onset (31.8% vs 24.8%; $p < 0.01$). Although the median duration of initial hypotension did not differ with order set usage (1.5 hr vs 1.5 hr; $p < 0.055$), the median total duration of hypotension was 2.1 hours less in the order set cohort (5.5 hr vs 7.6 hr; $p < 0.01$). More patients were discharged to home in the order set cohort (6.6% more, 61.4% vs 54.8%; $p < 0.01$). Both cohorts had similar rates of readmission within 30 days (8.8% vs 9.5%; $p = 0.05$). Additional process and outcome variables are shown in **Table 2**.

In bivariate analysis, sepsis order set usage was associated with a 6.3% lower hospital mortality (9.7% vs 16.0%; $p < 0.01$). Importantly, across subgroup analyses, order set usage was consistently associated with lower hospital mortality. We found a 3.8% lower hospital mortality in patients with POA sepsis (8.9% vs 12.7%; $p < 0.01$) and an 11.1% lower hospital mortality in non-POA sepsis (28.9% vs 40.0%; $p < 0.01$). Order set usage was associated with 4.0% lower hospital mortality in patients with severe sepsis (6.9% vs 10.9%; $p < 0.01$) and 12.9% lower hospital mortality in patients with septic shock (27.2% vs 40.1%; $p < 0.01$). Order set usage was associated with a 12.2% lower hospital mortality in patients with COVID-19 (19.5% vs 31.7%; $p < 0.01$) despite not including COVID-specific orders. Order set usage was associated with a lower hospital mortality rate across all race/ethnicity groups and ranged from a 4.1% lower hospital mortality rate for patients describing themselves as Native American or Alaska Native (10.4% vs 14.5%; $p = 0.013$) to 8.5% for patients describing themselves as "Other" or whose race/ethnicity was not known (12.6% vs 21.1%; $p < 0.01$). Similarly, order set usage was associated with a 6.0% lower hospital mortality rate across patients listing English as their primary language (15.5% vs 9.5%; $p < 0.01$), an 8.2% lower rate in patients whose primary language was Spanish (9.6% vs 17.8%; $p < 0.01$) and 7.2% lower rate in all other languages (13.5% vs 21.2%; $p < 0.01$). The difference in hospital mortality by order set usage and payer category ranged from 5.2% for Medicaid (7.3% vs 12.5%; $p < 0.01$) to 7.4% for the "other" category (11.1% vs 18.5%; $p < 0.01$), the largest subcomponent of which was "other government payer." Order set usage was also associated with reduced hospital mortality across categories of initial lactate value ranging from 6.4% for lactate less than 2 mmol/L (6.1% vs 12.5%; $p < 0.01$) to 12.0% for lactate greater than or equal to 4 mmol/L (23.5% vs 35.5%; $p < 0.01$). Similarly, order set use was associated with a reduction in hospital mortality across SOFA scores ranging from 3.0% for SOFA scores less than 2 (4.2% vs 7.2%; $p < 0.01$) to 9.9% for a SOFA score of greater than or equal to 6 (24.9% vs 34.8%; $p < 0.01$; **Fig. 2** and **eTables 3** and **4**, http://links.lww.com/CCX/B194).

After multivariable adjustment, order set usage was associated with lower odds of hospital mortality (adjusted odds ratio [OR] 0.70; 95% CI, 0.66–0.73). Other covariates were associated with hospital mortality, including age (adjusted OR 1.02; 95% CI, 1.02–1.02), initial SOFA score (adjusted OR 1.24; 95% CI, 1.22–1.25), initial lactate value (adjusted OR 1.18; 95% CI, 1.17–1.19), COVID-positive status (adjusted OR 2.82; 95% CI, 2.67–2.98), and non-POA sepsis (adjusted OR 5.57; 95% CI, 5.23–5.94). The patient race/ethnicity category "Other/Unknown" (or declined to provide race or ethnicity) was the only race/ethnicity category associated with higher odds of hospital mortality relative to patients identified as white (adjusted OR 1.15; 95% CI, 1.05–1.26). Commercial insurance had lower odds of hospital mortality relative to Medicare (adjusted OR 0.85; 95% CI, 0.79–0.91). Primary language was not associated with hospital mortality, although "other" (non-English, non-Spanish) language had an adjusted OR of hospital mortality of 0.90 (95% CI, 0.81–1.00). The adjusted ORs are shown in Figure 2 and in **eTable 5** (http://links.lww.com/CCX/B194). Sepsis order set usage over time and adjusted hospital mortality by the eight quarters of the study period are shown in **eFigure 1** (http://links.lww.com/CCX/B194).

Mediation Analysis

To test the hypothesis that some of the association between sepsis order set use and hospital mortality is mediated by shorter time to administer antibiotics or shorter duration of hypotension, we conducted a mediation analysis. In regression analysis, order set utilization is associated with the administration of antibiotics 31.0 minutes faster from ED triage (95% CI, 29.4 min–32.7 min), and the number of hours from ED triage to antibiotic administration is inversely associated with hospital mortality (OR 1.03; 95% CI, 1.03–1.04).

TABLE 2.
Patient Treatment and Outcome Characteristics by Order Set Usage

	All Patients, *n* = 104,662	Sepsis Order Set Used, *n* = 58,091	Sepsis Order Set Not Used, *n* = 46,571	*p*
Minutes from emergency department (ED) triage to antibiotics, median (IQR)	141 (76, 263)	125 (68, 221)	179 (98, 379)	< 0.01
Minutes from ED triage to antibiotic order, median (IQR)	98 (36, 207)	82 (27, 171)	134 (60, 304)	< 0.01
Minutes from antibiotic order to administration, med (IQR)	37 (21, 67)	35 (20, 60)	42 (22, 81)	< 0.01
Antibiotics given in 1 hr of triage, *n* (%)	14,925 (14.3)	11,400 (19.6)	3525 (7.6)	< 0.01
Antibiotics given in 3 hr of triage, *n* (%)	51,078 (48.8)	36,295 (62.5)	14,783 (31.7)	< 0.01
Antibiotics given 24 hr before or within 1 hr of hypotension, *n* (%)	30,024 (28.7)	18,488 (31.8)	11,536 (24.8)	< 0.01
Duration initial hypotensive episode (hr), median (IQR)	1.5 (0.6, 3.5)	1.5 (0.7, 3.5)	1.5 (0.6, 3.5)	0.055
Total hypotension duration (hr), SD	6.3 (2.1, 17.6)	5.5 (2.0, 15.0)	7.6 (2.5, 21.8)	< 0.01
Hospital mortality, *n* (%)	13,083 (12.5)	5622 (9.7)	7461 (16.0)	< 0.01
Length of stay (d), median (IQR)	5.4 (3.0, 10.3)	4.9 (2.8, 9.0)	6.0 (3.2, 12.1)	< 0.01
Comfort care, *n* (%)	10,835 (10.4)	5337 (9.2)	5498 (11.8)	< 0.01
Readmitted within 30 d, *n* (%)	9507 (9.1)	5095 (8.8)	4412 (9.5)	0.051
Discharged to home, *n* (%)	61,174 (58.4)	35,661 (61.4)	25,513 (54.8)	< 0.01
Normalized cost (from value-oriented architecture), median (IQR)	8,721 (4884, 17,868)	7,859 (4,603, 15,122)	9,978 (5,293, 21,667)	< 0.01

IQR = interquartile range.

Patients with missing time from emergency department triage to antibiotic administration and patients with no time hypotensive were excluded from those respective analyses.

Mediation testing revealed that time from ED triage to antibiotic administration mediated 2.6% (95% CI, 1.8%–3.4%) of the relationship between order set utilization and lower hospital mortality. Order set utilization was associated with 8.9 fewer hours of overall hypotension (95% CI, 7.8 hr–9.9 hr) and total hypotension (expressed in 10-hr intervals) was associated with hospital mortality (OR 1.05; 95% CI, 1.05–1.06). Mediation testing estimated that total time hypotensive mediated 4.0% (95% CI, 2.8%–5.3%) of the association between order set utilization and lower hospital mortality.

DISCUSSION

In the Donabedian "Structure-Process-Outcome" model of quality improvement, order sets are a structure element of quality (15). Thus, implementing high-quality order sets and increasing their use is a mechanism by which to improve quality structurally, and at scale. Previous observational studies have shown associations between order set implementation and improved process and outcome measures of care in sepsis (16–22). Studies in the United States have shown an association between protocolized care and lower hospital mortality (5, 7–9). Globally, studies in Australia, Germany, Spain and in international registries have shown an association between protocolized sepsis care and improved patient outcomes (6, 23–25). This study adds to the evidence, showing that in a large sepsis cohort, the use of a sepsis order set was associated with substantially lower hospital mortality.

We hypothesized that much of the association of order set use and hospital mortality would be driven by a shorter time to antibiotics and less time hypotensive. Timely antibiotic administration has been associated with lower hospital mortality, is recommended in the 2021 SSC guidelines, and is measured by CMS

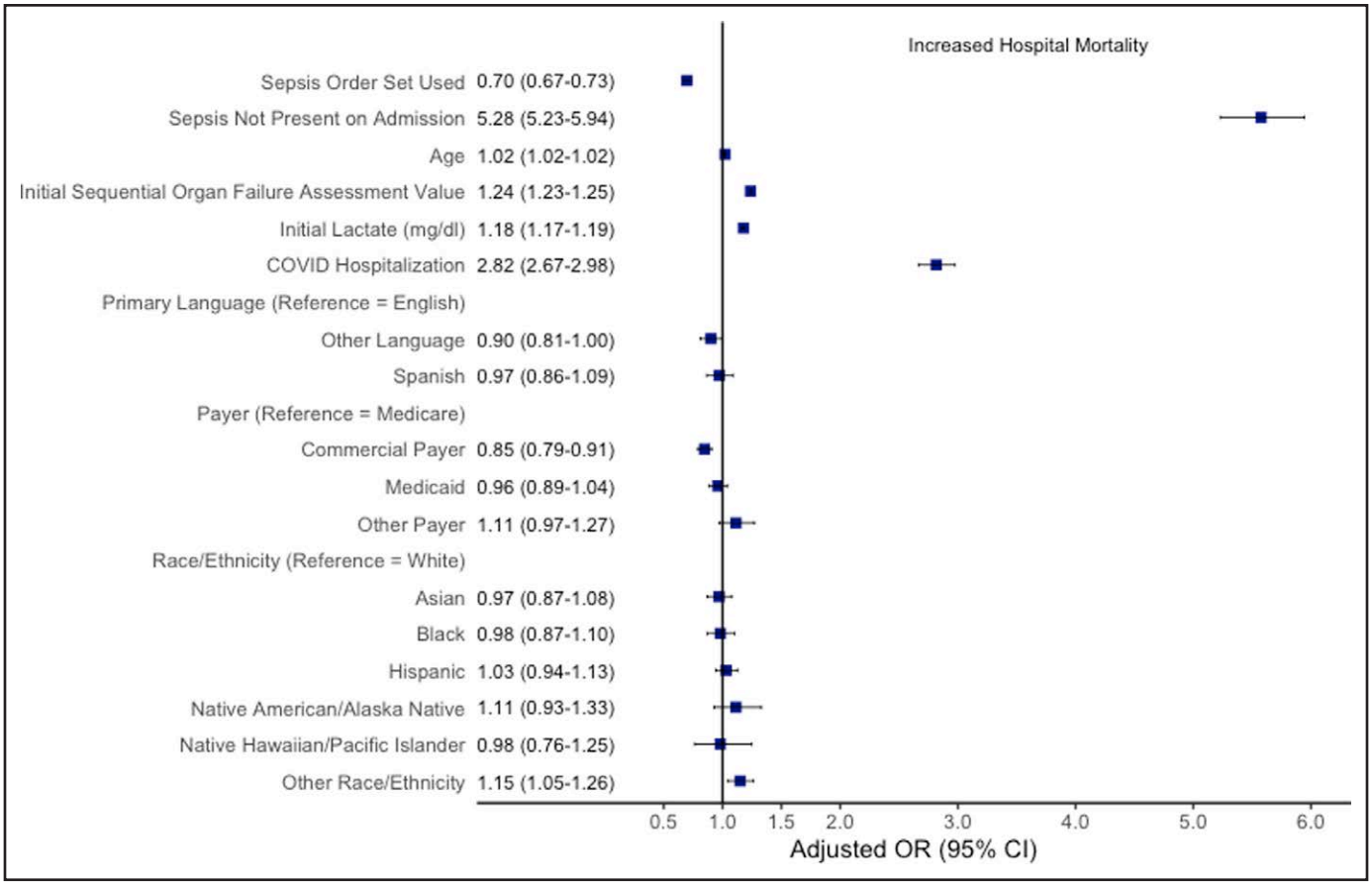

Figure 2. Adjusted odds ratios (OR) and 95% CIs from multivariable model predicting relationship between order set use and hospital mortality in patients hospitalized with sepsis.

(26–30). By including guideline-concordant antibiotics in the sepsis order set and arranging them by site of potential infection, we sought to make it "ridiculously easy to do the right thing." In our study, the use of the sepsis order set was associated with a shorter time to antibiotics; a shorter time to antibiotics was itself associated with lower hospital mortality. Our analysis suggests that 2.4% (95% CI, 1.8%–3.4%) of the association between sepsis order set use and hospital mortality was mediated by a shorter time to antibiotics which aligns with guidelines on the importance of timely antibiotics, but also suggests the importance of other unmeasured factors (13).

Although the evidence base is less robust about the association between time hypotensive and hospital mortality, the avoidance of significant hypotension is recommended by the SSC and is a bedrock principle of clinical medicine (2). Our sepsis order set included fluid boluses, norepinephrine titrated to MAP greater than or equal to 65 mm Hg, and "sepsis vitals"; an order for more frequent vital sign checks to follow up on identified hypotension and to monitor for incident hypotension. Use of the sepsis order set was significantly associated with less total time hypotensive. Less time hypotensive was itself associated with lower hospital mortality and mediation analysis estimated that its effect was 4.0% (95% CI, 2.8%–5.3%) of the association between sepsis order set use and hospital mortality.

Beyond timely antibiotics and normotension, a key component of the order set might be the creation of a shared mental model identifying a septic patient and resulting in unmeasured care team actions, interactions, or processes. Order set effectiveness may be due to communicating a primary diagnosis in a "virtual huddle," helping to create a shared sense of urgency among all members of the care team, as we saw a bivariate mortality association in all subgroups in which we looked (eTable 3, http://links.lww.com/CCX/B194). Declaratively labeling a patient as "septic" may create an "upward spiral" of care team learning and expertise, creating shared experiences and expectations (31).

Order sets are a structural element of quality that could be used to decrease disparities in processes of care and health outcomes (32). In our study, order set usage was associated with improved outcomes in all race/ethnicity categories. We observed that patients without a known race/ethnicity category ("other/unknown") were less likely to have the order set used (45% vs 56% for the other categories combined) and had higher overall mortality (17.3% vs 12.4%). The higher mortality in those for whom no race/ethnicity data was available or who declined to provide data speaks to the importance of improving the quality of race/ethnicity data. Likewise, that patients with commercial insurance had lower adjusted mortality echoes previous findings that groups with lower socioeconomic status have worse sepsis outcomes and speaks to the importance of interventions focused on improving equity (33–35).

LIMITATIONS

Our study has several limitations. Sepsis order set usage was abstracted as a binary variable and data on which specific orders were used are not available. Second, as the order set was part of an organization-wide sepsis quality improvement program, there could be organizational changes outside of the order set that led to increased recognition of sepsis and thereby decreased overall sepsis mortality. For example, some facilities used "sepsis nurses" at various points in time in the study period to ensure that patients flagged by the order set received more timely sepsis care. Third, potentially important information such as time to fluid administration, fluid volume, lactic acid normalization, and vasopressor usage was not included in the study. Fourth, we did not include other patient medical comorbidities in our analysis as they were not available in our study data. Finally, we do not have any data on why the order set was or was not used by the treatment team for a given patient and there could be reasons associated with mortality for which we did not adjust.

Further research is needed to better define the exact mechanism by which sepsis order sets might influence hospital mortality, particularly focusing on team dynamics and the alignment or "virtual huddle" nature of order sets in complex, busy care environments. Significant resources are spent in order set creation and quality improvement collaboratives and understanding which elements of order sets create patient-centered value could free up resources for other quality improvement initiatives. Finally, as computer science advances, our current mental model of static order sets, which is largely based on printed paper order sets common before EMRs, is beginning to evolve. Integration of artificial intelligence into clinical decision support will likely change how order sets function in a more dynamic and patient-specific way.

CONCLUSIONS

In this real-world study of a large cohort of patients hospitalized with sepsis, the use of a sepsis order set was associated with lower hospital mortality. The positive association of order set usage with hospital mortality was demonstrated across multiple racial and ethnic groups. Order sets are a valuable part of quality improvement efforts at scale and more study is needed to define their mechanisms of action.

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