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Variation in Emergency Department Adherence to Treatment **Guidelines for Inpatient Pneumonia and Sepsis: A Retrospective Cohort Study**

Stacy A. Trent, MD, MPH, Zachary J. Jarou, MD, Edward P. Havranek, MD, Adit A. Ginde, MD, MPH, Jason S. Haukoos, MD, MSc

Department of Emergency Medicine (SAT, ZJJ, JSH), Denver Health Medical Center, Denver, CO; the Department of Medicine (EPH), Denver Health Medical Center, Denver, CO; the Department of Emergency Medicine (SAT, AAG, JSH) and the Division of Cardiology (EPH), University of Colorado School of Medicine, Aurora, CO; the Department of Emergency Medicine, University of Chicago School of Medicine (ZJJ), Chicago, IL; and the Department of Epidemiology, Colorado School of Public Health (JSH), Aurora, CO

Abstract

Objectives: Evidence-based clinical practice guidelines (CPGs) for the treatment of pneumonia and sepsis have existed for many years with multiple studies suggesting improved patient outcomes. Despite their importance, little is known about variation in emergency department (ED) adherence to these CPGs. Our objectives were to estimate variation in ED adherence across CPGs for pneumonia and sepsis and identify patient, provider, and environmental factors associated with adherence.

Methods: This was a multicenter retrospective study using standard medical record review methods. The population consisted of consecutive adults hospitalized for pneumonia or sepsis (identified by discharge ICD-9 codes) at five Colorado hospitals (two academic, three community) who were admitted to the hospital from the ED and for whom the ED diagnosed or initiated treatment. The outcome measured was ED adherence to the CPG (primary) and in-hospital mortality (secondary). Hierarchical generalized linear models were used for analysis.

Results: Among 827 patients, ED care was 57% adherence to CPGs with significant variation in adherence across CPGs (sepsis 50%, pneumonia 64%, p < 0.001). Patients were less likely to receive adherent care if they presented with chief complaints that were associated but not typical of the diagnosis (odds ratio [OR] = 0.6, 95% confidence interval [CI] = 0.4-0.8), received an ED diagnosis that was not specific to the CPG (associated diagnosis OR = 0.3 [95% CI = 0.2-0.5]; unrelated diagnosis OR = 0.4 [95% CI = 0.2-0.6]) or presented to a community hospital (OR =

Address for correspondence and reprints: Stacy Trent, MD, MPH; stacy.trent@dhha.org.

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Supporting Information

The following supporting information is available in the online version of this paper available at http://onlinelibrary.wiley.com/doi/ 10.1111/acem.13639/full Data Supplement S1. Supplemental material.

Conclusion: Adherence to ED infectious CPGs for pneumonia and sepsis varies significantly across diseases and types of institutions with significant room for improvement, especially in light of a significant association with in-hospital mortality.

Pneumonia and sepsis are two of the most common reasons for hospital admission and death in the United States, accounting for 2.4 million hospitalizations, 200,000 in-hospital deaths, and \$35.8 billion in aggregate hospital costs annually.¹ Emergency departments (EDs) play a vital role in providing evidence-based care for the management of pneumonia and sepsis as the initial evaluation and treatment is most often initiated in the ED, and both conditions have clinical practice guidelines (CPGs) relevant to ED management that have been shown to improve mortality, hospital length of stay (LOS), and costs.^{2–26}

While ED guidelines for the treatment of pneumonia and sepsis have existed for more than a decade, both have undergone recent updates. For pneumonia, the recommendations to obtain blood cultures on all patients and administered antibiotics within 6 hours of ED arrival have been retired from the Center for Medicare and Medicaid Services (CMS) Pneumonia Core Measure. The Infectious Disease Society of America (IDSA) and the American Thoracic Society (ATS), however, continue to recommend that guideline concordant antibiotics be given in accordance with a patient's risk for atypical organisms.^{27,28} For sepsis, the early management bundles advocated by the Surviving Sepsis Campaign (SSC) have broken down the original 6-hour early resuscitation bundle to two distinct resuscitation bundles with 3- and 6- hour goals, with the 3-hour bundle specifically targeted toward ED management.⁴ Recognizing the importance and need to improve evidence-based care for patients hospitalized with sepsis, CMS introduced a sepsis core measure (SEP-1) in 2016 that parallels the SSC's 3-hour bundle and mandates that hospitals publicly report their adherence to the SEP-1 guideline.²⁹

Previous literature on CPG adherence for pneumonia and sepsis does not reflect current guidelines. In addition, previous literature on sepsis CPG adherence using the SSC registries has largely mixed ED and inpatient care, making it difficult to assess guideline adherence specifically initiated in the ED.^{15,16} Thus, the primary objective of this study was to estimate ED adherence to CPGs for inpatient community acquired pneumonia and sepsis treatment. Secondary objectives were to identify patient, physician, and environmental factors associated with ED adherence and estimate the association between adherence and inhospital patient outcomes including mortality and hospital LOS.

METHODS

Study Design

We performed a retrospective study using standardized medical record review to identify a large, consecutive patient population to determine variation in ED adherence to CPGs for inpatient community acquired pneumonia treatment and early identification and management of sepsis and septic shock. The institutional review boards at each participating hospital approved the study with a waiver of consent.

Study Setting and Population

This study was performed at five hospitals in Colorado with heterogeneous and diverse practice environments that represent the main types of EDs including: 1) urban academic safety-net hospital, 2) suburban academic tertiary care hospital, and 3) urban and rural community hospitals (Table 1). Each ED was staffed by emergency medicine board-certified or board-eligible physicians at all times.

Consecutive patients were identified retrospectively by any hospital discharge ICD-9 codes for pneumonia (481–486.xx) or severe sepsis/septic shock (785.52, 995.92).^{30,31} Starting on January 1, 2013, investigators initially obtained a list of consecutive patients with these ICD-9 codes from the safety-net and tertiary care hospitals. Sufficient sample sizes were obtained from the safety net hospital after reviewing 4 months of consecutive patient charts (i.e., September 2012 to January 1, 2013) and after reviewing 5 months of consecutive charts at the tertiary care hospital (i.e., August 2012 to January 1, 2013). The study was then expanded to the three community hospitals to increase generalizability. Investigators, similarly, obtained a list of consecutive patients from the three community hospitals starting on January 1, 2015. Sufficient sample sizes were obtained from each of the three community hospitals after reviewing 12 months of consecutive patient charts at each hospital from January 2014 to January 1, 2015. From the initial cohort, each chart was screened by a physician abstractor for inclusion using the following criteria: 1) a discharge diagnosis in the medical record of pneumonia, severe sepsis, or septic shock; 2) admission to the hospital from the ED; and 3) diagnosis or initiated treatment of the disease process in the ED. Pneumonia was present in the ED if definitively identified on imaging by a radiologist or treated in the ED based on documentation of clinical suspicion. Pneumonia was not considered to be present if azithromycin was given for the treatment of a chronic obstructive pulmonary disease (COPD) exacerbation alone. Severe sepsis or septic shock was present in the ED if the patient met all criteria for severe sepsis or septic shock as defined by the SSC while in the ED.^{4,32} Exclusion criteria were age < 18 years, repeat visits by the same patients, and patients transferred from another facility as the initial management would not have occurred in the included EDs. Additionally, patients were not included in both the pneumonia and the sepsis cohorts. If the patient met criteria for the sepsis cohort due to pneumonia, the patient was included in the sepsis cohort rather than the pneumonia cohort.

Study Protocol

Once the study cohort was obtained, structured medical record abstraction was performed using established, standard methodology.^{33–35} To maximize validity and reliability of the medical record abstraction process, we used the following established methodologies: 1) physician abstractors, blinded to the purpose of the study, to ensure expert familiarity with medical records and documentation; 2) abstractors trained by the lead author using a set of test cases to standardize approaches; 3) use of a previously developed and refined closed-response data collection instrument (Data Supplement S1, available as supporting information in the online version of this paper, which is available at http:// onlinelibrary.wiley.com/doi/10.1111/acem.13639/full); 4) performance of 10 pilot reviews, using actual cases sampled from each hospital but not included for analysis to gain familiarity with each hospital's medical record system; 5) reabstraction of 15% of randomly

selected included cases to estimate interrater reliability of the primary outcome, with the intention of performing reabstraction with adjudication of 100% of the cases if agreement of the 15% is less than K < 0.8; and 6) routine oversight of the abstractor team by the lead author, who was also available throughout the data collection process to address questions and problems that occurred.^{33,34} Using a structured data abstraction form, abstractors documented the presence of all prespecified variables necessary to assess adherence with each CPG. Using the same data abstraction form, data were collected related to patient, physician, and environmental characteristics that had been shown to be associated with CPG adherence in previous studies on other emergency conditions.^{36–39}

Patient factors included patient demographics, primary health insurance, primary language, infectious disease-related comorbidities, and chief complaint. Patient demographics, insurance, and language were obtained directly from each hospital's administrative database. Missing data were abstracted directly from the patient's medical record when available and when unavailable were recorded as missing. All remaining characteristics were obtained directly from the medical record. Infectious disease-related comorbidities included diabetes, acquired immune deficiency syndrome, and iatrogenic immunosuppression (e.g., chemotherapy or other immunosuppressive medication). Patient chief complaints were stratified into three groups based on how typical the complaint was for the diagnosis. Stratification of chief complaints into three groups was defined by the lead and senior author based on frequency and specificity of the chief complaint for the diagnosis. Typical chief complaints for pneumonia included cough, shortness of breath, and fever. The only typical chief complaint for sepsis was fever. Associated chief complaints for pneumonia included chest pain, abdominal pain, flu, upper respiratory infection, congestion, hemoptysis, chills, myalgias, altered mentation, hypoxia, hypotension, tachycardia, and weakness. Associated chief complaints for sepsis included cough, dysuria, abdominal pain, flank pain, back pain, cellulitis, abscess, wound infection, blood infection, vomiting, diarrhea, altered mentation, chills, myalgias, shortness of breath, hypotension, and tachycardia. All other chief complaints were grouped into an "other" category.

Physician factors included the individual ED physician, ED physician's experience, type of medical degree, and ED diagnosis as well as the admitting hospital unit (i.e., floor vs. intensive care). Patients who were admitted under observation status or admitted to intermediate care units were considered floor admissions. ED physician's experience was determined as the number of years of independent practice at the time the patient was seen (i.e., years following completion of residency training). ED physician's medical degree was categorized into MD or DO. Physician's ED diagnosis was categorized into three groups based on its association with pneumonia or sepsis. If the physician documented pneumonia, sepsis, severe sepsis, or septic shock as the primary ED diagnosis, then the ED diagnosis was designated as "primary." For patients with pneumonia, if the physician documented COPD, hypoxia, pleural effusion, respiratory failure, or sepsis as the primary diagnosis, then the ED diagnosis of pneumonia was designated as "associated" with the primary diagnosis. Similarly, for patients with severe sepsis, if the physician documented a specific type of infection (e.g., pneumonia, cellulitis, and pyelonephritis) as the primary diagnosis, then the ED diagnosis of sepsis was designated as "associated." All other primary ED diagnoses were categorized as "other."

Environmental factors included time of day, day of week, ED occupancy, and hospital. Time of day was categorized into four groups: day (6 AM–11:59 AM), afternoon (12 PM–5:59 PM), evening (6 PM–11:59 PM), and night (12 AM–5:59 AM). Day of week was categorized into two groups: weekday (Monday 7 AM–Friday 4:59 PM) and weekend (Friday 5 PM–Monday 6:59 AM).

Outcome Measures

The primary outcome was ED adherence to the respective CPG for community-acquired pneumonia and severe sepsis/septic shock as written or endorsed by the IDSA/ATS and the SSC.^{4,27,32} Table 2 describes how adherence was determined for each CPG. Secondary outcomes included hospital LOS and all-cause in-hospital mortality. Hospital LOS was measured in days from time of hospital admission order to time of hospital discharge order.

Data Management and Statistical Analyses

All data management and statistical analysis were performed using SAS version 9.4. Descriptive statistics were calculated for all variables. Continuous data were reported as medians with interquartile ranges (IQRs) and categorical variables as percentages with 95% confidence intervals (CIs). Prevalence estimates with 95% CIs were used to report adherence with CPGs, and a chi-square test was used to test the a priori hypothesis that a statistically significant difference in adherence existed between the two CPGs. A p-value of <0.05 was considered statistically significant.

Unadjusted logistic regression was used to estimate the association of each patient, physician, and environmental variable with ED adherence to CPGs within the combined cohort and each disease subgroup. Hierarchical generalized linear models were used to estimate adjusted associations between patient, physician, and environmental factors and ED adherence with CPGs within the combined cohort. Adherence for all CPGs was initially modeled as a composite outcome to evaluate for factors associated with ED adherence to pneumonia and sepsis CPGs. Secondary models for each individual CPG were also developed, incorporating additional disease-specific patient factors. Models were developed by first creating a full model followed by dropping variables found to be collinear. Hospital was included as a random effect. Effect modification, using interaction terms, was assessed for sex, primary language, and race/ethnicity by complaint category and included if they contribute significantly to the model (p < 0.05).

Sample Size Estimation

In an effort to report estimates with reasonable precision, we chose a priori to include numbers of patients based on an upper 95% confidence limit of 5% (10% total CI). This degree of precision allowed for appropriate statistical separation between estimates across institutions with relatively high and relatively low adherence and allowed for separation of all prevalence estimates from our a priori defined 95% adherence threshold. Thus, using estimates for each disease process (700 total patients) to achieve the above stated degree of precision. To provide a more balanced sample between the academic and community hospitals, we increased the sample size needed from the community hospitals as the data

from the academic hospitals had already been collected prior to adding the community hospitals to the study.

RESULTS

Patient Characteristics

Overall, 827 patients were included in the study including 414 patients with pneumonia and 413 patients with severe sepsis or septic shock. Inter-rater reliability of abstraction of the primary outcome exceeded our predefined threshold ($\kappa > 0.8$). Table 3 describes the characteristics of the patients included in the study. The median age was 60 years (IQR = 49–74 years), and 53% were male. Patients were primarily non-Hispanic white (66%), spoke English primarily (91%), and were insured by Medicare (46%). While 60% of pneumonia patients presented with complaints typical of pneumonia, only 14% of sepsis patients presented with complaints typical of sepsis.

Prevalence of Adherence

Overall, the prevalence of adherence to ED infectious CPGs was 57% (95% CI = 54%-61%) (Table 4). Physicians were more adherent to prescribing IDSA-concordant antibiotics to patients with pneumonia (64%, 95% CI = 59%-69%) than completing the SSC's 3-hour bundle (50%, 95% CI = 45%-55%; p < 0.001). Overall adherence to the SSC's 3-hour bundle was no different between patients with severe sepsis and septic shock (p = 0.9; Figure 1). However, while the composite adherence to the SSC's 3-hour bundle was only 50%, completion of individual components of the bundle were markedly better with 92% obtaining a screening lactate, 82% obtaining blood cultures before antibiotics, 72% receiving antibiotics within 3 hours of ED arrival, and 69% of septic shock patients receiving 30 mL/kg IV fluids within 3 hours of ED arrival.

Patient, Physician, and Environmental Variables Associated With Adherence

Table 5 shows the results of our adjusted multivariable analysis for the combined cohort. Patients were more likely to receive adherent care in the ED if they presented with chief complaints that were typical for the diagnoses and if the primary diagnosis in the ED was specific to the CPG. When patients presented with symptoms that were associated but not typical for the disease, the odds of receiving adherent care in the ED were 0.6 (95% CI = 0.4-0.8). When the primary ED diagnosis was associated but not specific to the CPG, the odds of receiving adherent care were 0.3 (95% CI = 0.2-0.5) and 0.4 (95% CI = 0.2-0.6) for other primary diagnoses. Finally, patients, who presented to a community hospital, were less likely to receive adherent care than patients who presented to an academic tertiary care hospital (adjusted odds ratio [AOR] = 0.6, 95% CI = 0.4-0.9).

Table 6 shows the results of our adjusted multivariable analysis for the sepsis cohort. Patients were significantly more likely to receive all components of the SSC's 3-hour bundle in the ED if they presented at night (AOR = 2.5, 95% CI = 1.2-5.3) compared to morning hours. Patients were significantly less likely to receive all components of the SSC's 3-hour bundle in the ED if their infectious source was abdominal (AOR = 0.3, 95% CI = 0.1-0.8) or soft tissue (AOR = 0.4, 95% CI = 0.2-0.9) compared to a respiratory source; if they had

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fluid-sensitive comorbidities such as end-stage renal disease on hemodialysis, congestive heart failure, or end-stage liver disease (AOR = 0.6, 95% CI = 0.3-0.99); were diagnosed by the ED physicians with a specific infection rather than severe sepsis or septic shock (AOR = 0.5, 95% CI = 0.3-0.9); were admitted to a general medical or surgical floor (AOR = 0.5, 95% CI = 0.3-0.9) rather than an intensive care unit; or presented to a community or safety-net hospital (AOR = 0.4, 95% CI = 0.2-0.7, respectively) rather than a quaternary care hospital.

Unadjusted associations between ED adherence to infectious disease CPGs and all patient, provider, and environmental variables for the combined cohort and each disease subgroup are provided in Data Supplement S1 (Tables S1–S3). Adjusted multivariable analysis for the pneumonia cohort is also presented in Data Supplement S1 (Table S4).

Secondary Outcomes

In the combined cohort, 40 (4.8%) patients died during the index hospitalization, 95% of whom were patients in the sepsis cohort. Adjusted for patient age, sex, admitting disease, admitting hospital unit, and ED CPG adherence, the odds of in-hospital mortality were significantly increased in patients who did not receive adherent CPG care in the ED (AOR =2.4, 95% CI = 1.2-4.8; Table 7). The median hospital LOS for pneumonia patients receiving guideline adherent care in the ED was 1 day shorter than pneumonia patients receiving nonadherent care in the ED. In contrast, the median hospital LOS was 1 day longer for sepsis patient receiving guideline adherent ED care than sepsis patients receiving nonadherent care in the ED (Table 8).

DISCUSSION

Our results suggest considerable variation in guideline adherence for two of the most prevalent and deadly infectious diseases encountered in the ED, with only 64% of patients with community-acquired pneumonia and 50% with sepsis receiving recommended therapy in the ED. To our knowledge, this is the only study to examine differences in adherence to contemporaneous guidelines for pneumonia and sepsis treatment in multiple, diverse ED settings in the United States. Similar to our findings among cardiovascular and cerebrovascular ED guideline adherence, chief complaint and primary ED diagnosis were significantly associated with ED adherence, such that the more straightforward the complaint and diagnosis, the more likely ED care was to be adherent to the relevant guideline.⁴⁰ While the random effect of hospital was small, accounting for only 1% of the variability in ED adherence, hospital type was significantly associated with adherence with community EDs less likely to adhere to infectious disease guidelines compared to an academic, tertiary care hospital. Finally, and perhaps most importantly, our results showed a significant association between guideline-adherent care in the ED and in-hospital mortality. After patient age, sex, admitting disease, and acuity of illness were adjusted for, patients who did not receive guideline-adherent care in the ED were 2.4 times more likely to die in the hospital compared to patients who did receive guideline-adherent care.

Since CMS retired its pneumonia core measure in 2014, little has been written on ED adherence to IDSA/ATS recommended antibiotic administration for patients admitted for

community-acquired pneumonia. While the CMS pneumonia core measure was criticized for the lack of evidence related to blood cultures and timing of antibiotics,^{41,42} the recommendation for appropriate antibiotic therapy is supported by the literature, which suggests decreased mortality and hospital LOS when patients are administered guidelinerecommended antibiotics.^{43–45} Additionally, it is important that patients receive appropriate therapy without being exposed to unnecessarily broad therapy, which can result in increased resistance and other adverse effects.^{46,47} This is particularly relevant now that the updated IDSA/ATS guidelines for hospital-acquired and ventilator-associated pneumonia recently removed the concepts of health care-associated pneumonia from the guideline given new evidence that contact with the health care system alone is less important than underlying patient characteristics for predicting risk of multidrug-resistant organisms.^{48–53} Whether health care-associated pneumonia is differentiated from community acquired pneumonia by the IDSA/ATS guidelines for community acquired pneumonia remains unclear at this time. The IDSA and ATS are actively updating their guideline on community-acquired pneumonia with a projected release in the fall 2018. If the concept of health care-associated pneumonia is removed from the guideline, antimicrobial treatment of immunocompetent patients with pneumonia who present to the ED from the community will be greatly simplified, likely leading to improved adherence and antimicrobial stewardship.

For sepsis, most previous literature on adherence to the SSC's resuscitation bundle did not differentiate adherence to components at 3 and 6 hours. While the 3-hour bundle is frequently initiated and completed in the ED, the 6-hour components are more likely completed in the inpatient setting, making it difficult to assess composite guideline adherence from larger studies.^{14–16,21} However, a handful of studies in the past few years have begun to report adherence to the SSC 3-hour bundle and the CMS SEP-1 guideline. The IMPreSS study by Rhodes et al.⁵⁴ showed that adherence to the SSC 3-hour bundle was poor with overall adherence within their multicenter, international cohort being only 19% and rising to only 29% among the subset of North American participating hospitals. Our data are similar to Venkatesh et al.,⁵⁵ who recently showed that among U.S. EDs participating in the American College of Emergency Physician's Emergency Quality Network Sepsis Initiative, overall adherence with the CMS SEP-1 was 54%. Both of these studies as well as ours suggest significant room for improvement in early ED sepsis care. Importantly, the SSC released a new "hour-1" bundle in May 2018, which replaced both the 3-and 6-hour bundles.⁵⁶ The impact of the new SSC recommendation on ED sepsis care is likely to be limited in the United States given its current discordance with the CMS SEP-1 guideline. Moreover, the SSC hour-1 bundle has been highly criticized, particularly within the emergency medicine community, given the low-quality evidence to support these recommendations as well as the risk of over treating some sepsis patients and diverting attention away from nonsepsis patients.⁵⁷

LIMITATIONS

The use of discharge ICD-9 codes to identify ED patients is limited because discharge diagnoses may not be relevant to the reasons for admission from the ED. Consequently, using discharge ICD-9 codes was coupled with direct chart review to ensure that the sample only represented patients with the diagnoses of interest, who were admitted to the hospital

from the ED specifically for these diagnoses. However, we may have missed some sepsis patients who were not coded as such. Additionally, including hospital admission as an inclusion criterion may have excluded patients who died in the ED, had an unknown disposition, or were discharged from the ED. Limiting patients to those who were admitted helped limited chart reviews to patient who were most likely to truly have the disease and in whom the guideline recommended care could actually have been enacted. Missing documentation within the medical chart is a known limitation to medical record abstraction. Missing documentation could have affected our estimates of adherence especially in the pneumonia subgroup where details related to a patient's immune competence could have been missing. Although we abstracted a comprehensive list of potential patient, physician, and environmental factors that have been shown to be associated with CPGs in other studies, additional variables may have been left out of the model, a known limitation of retrospective analyses. We used admitting hospital unit as a proxy for illness severity. The use of a more robust illness severity score may have resulted in a more specific variable for illness severity.

CONCLUSIONS

Adherence to ED infectious clinical practice guidelines for community-acquired pneumonia and sepsis varies significantly across diseases and institutions with significant room for improvement, especially in light of a significant association with in-hospital mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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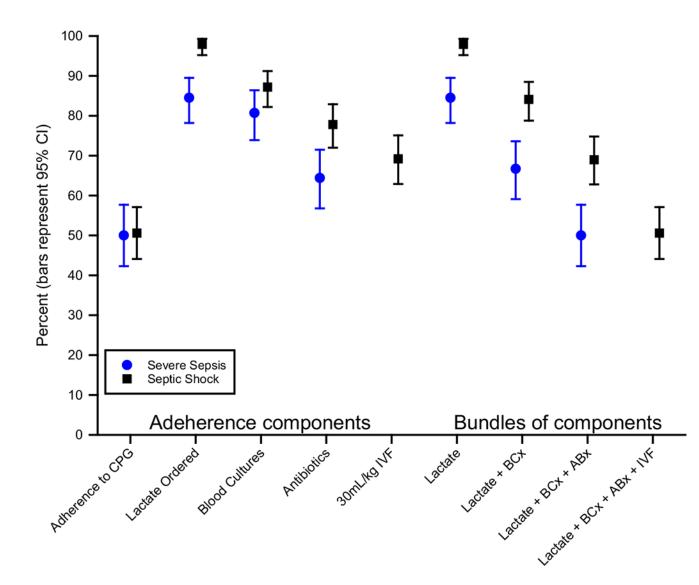


Figure 1.

ED adherence to Surviving Sepsis Campaign's 3-hour bundle and its components. CPG = clinical practice guideline; IVF = intravenous fluids; BCx = blood cultures; ABx = antibiotics.

Table 1

Characteristics of Study Sites in 2014-2015

	Urban Safety Net	Tertiary Care	Rural Community	Urban Safety Net Tertiary Care Rural Community Suburban Community Urban Community	Urban Community
Annual adult ED census	80,000	97,000	25,000	48,000	81,000
% ED patients admitted	15	13	19	16	6
Beds in ED	72	76	20	30	77
% Patients seen by residents	70	55	< 1	< 1	0
% Patients seen by PA/NP	10	30	33	33	11

NP = nurse practitioner; PA = physician assistant.

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Description of CPG Measures

Disease	Quality Measure
Community-acquired pneumonia	Community-acquired pneumonia Guideline-concordant antibiotic selection given risk for atypical infections
Severe sepsis/septic shock	 3-hour bundle 1. Lactate measured 2. Blood cultures prior to antibiotics 3. Antibiotics within 3 hours of ED arrival 4. 30 mL/kg bolus of IVF within 3 hours of ED arrival if sBP < 90 or lactate

CPG = clinical practice guideline; IVF = intravenous fluids.

Table 3

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Patient Characteristics

60 211 203		•	
211 203	(48–76)	61	(49–73)
211 203			
203	(51)	224	(54)
	(49)	189	(46)
281	(68)	262	(63)
65	(16)	96	(23)
46	(11)	36	(6)
22	(5)	19	(5)
382	(92)	366	(68)
23	(9)	41	(10)
6	(2)	9	(2)
197	(48)	186	(45)
71	(17)	68	(22)
96	(23)	62	(15)
42	(10)	68	(17)
8	(2)	8	(2)
16	(4)	4	(1)
47	(11)	54	(13)
85	(21)	113	(27)
3	(1)	17	(4)
1	(0)	19	(5)
34	(8)	35	(6)
34	(8)	· · ·	ŝ
	34		(0) (8)

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Sepsis (n = 413)(14) (71) (15) 56 294 63 Pneumonia (n = 414) (30) (10)249 (60) 125 40 Combined (n = 827)305 (37) 419 (51) 103 (13) Associated with disease Typical for disease Characteristics Other

Data are reported as median (IQR) or n (%).

IQR = interquartile range.

	Overall	Pneumonia*	Sepsis and Septic Shock † p-value	p-value
Adherence to CPG 57.2 (53.7–60.6) 64.0 (59.2–68.6)	57.2 (53.7–60.6)	64.0 (59.2–68.6)	50.4 (45.4–55.3)	<0.001
Hospital type				
Tertiary care	65.4 (58.9–71.5) 68.4 (59.1–76.7)	68.4 (59.1–76.7)	62.4 (53.0–71.2)	
Community	52.9 (47.6–58.2) 56.7 (49.1–64.0)	56.7 (49.1-64.0)	49.2 (41.6–56.7)	
Safety net	55.6 (48.9–62.0) 70.9 (61.8–79.0)	70.9 (61.8–79.0)	40.2 (31.2–49.6)	
Data and month of a 90 (050% CD)	(05% CD			

Data are reported as % (95% CI).

CPGs = clinical practice guidelines.

 $\overset{*}{}$ Infectious Disease Society of America guideline-concordant antibiotics.

 $\dot{\tau}_{\rm Surviving Sepsis Campaign 3-hour bundle.}$

Table 5

Multivariable Model of Adherence to ED Infectious CPGs, Adjusting for Clustering by Hospital

Age (years) 60 $(49-74)$ Sex 53) Male 32 (7) Female 32 (7) Female 32 (7) Female 32 (7) Female 32 (7) Language 748 (90) English 748 (90) Dother 748 (90) Insurance 748 (90) Insurance 15 (2) Insurance 15 (2) Insurance 383 (46) Medicate 383 (40) Medicate 158 (19) Uninsured 158 (19) Other source 158 (19) Uninsured 158 (19) Other source 16 (2) Uninsured 158 (2) Insurance 10 (2) Insurance 10 (2) Insurance 10 (2) Insurance 10 <	60 250 223 223 424 424 38 11 11 11 101	(48-75) (57) (57) (57) (59) (73) (73)	1.00 IR eft	(0.99–1.02)
435 435 392 748 1 748 15 15 15 16 16 178 18 19 10 110 110 15 16 178 170	250 223 223 223 38 424 11 11 11 217 89 89	(57) (57) (57) (59) (73) (57)	IR efi	
435 392 392 392 15 15 16 15 16 16 17 18 19 10 10 110 16 17 18 19 10 10 11 10 11 10 10 103 103 103 103 103 103 103 103 103 103 103 103 103 103 103 103 103 103 103	250 223 223 38 38 38 11 11 217 89 89	(57) (57) (57) (59) (73) (73)	IRefi	
392 n 748 n 64 n 64 n 64 n 15 re 383 re 160 red 150 ource 16 ource 16 plaint 100 for disease 305 for sensis 532	223 424 38 38 11 11 217 89 89	(57) (57) (59) (73) (57)	[1771]	
748 15 15 16 16 17 18 19 red 10 red 110 outce 16 outce 16 outce 16 outce 110 outce 110 outce 110 outce 103 103 D O diagnosis 532	424 38 11 217 89 89	(57) (59) (73) (57)	0.94	(0.70-1.26)
748 1 15 re 16 re 383 red 160 red 170 red 18 19 red 10 red 110 ercial 110 ource 110 ource 110 ource 103 for disease 103 D diagnosis 532	424 38 31 11 11 217 89 89	(57) (59) (73) (57)		
b 64 15 15 re 383 id 160 red 158 red 158 red 158 outce 160 outce 16 outce 305 for disease 305 for disease 305 otagnosis 532	38 11 217 89 101	(59) (73) (57)	[Ref]	
15 re 383 id 160 red 158 red 158 sreial 110 ource 16 plaint 305 for disease 305 ted with disease 305 uid agnosis 532	11 217 89 101	(73) (57)	1.15	(0.64-2.06)
re 383 id 160 red 158 recial 158 ource 16 ource 16 plaint 305 for disease 305 for disease 305 for disease 103 D diagnosis 532	217 89 101	(57)	2.19	(0.63-7.60)
383 160 158 158 110 110 16 868e 305 ith disease 419 ith disease 103 gnosis 532	217 89 101	(57)		
150 158 158 160 110 16 16 16 16 16 16 16 16 16 16 16 16 16 17 18 19 103 205 sensis 532	89 101		[Ref]	
158 110 110 16 8ease 305 103 103 gnosis 532	101	(56)	1.05	(0.65–1.69)
110 16 sease 305 ith disease 419 gnosis 532 sensis 532		(64)	1.19	(0.72-1.97)
16 sease 305 ith disease 419 gnosis 532 sensis 532	57	(12)	0.81	(0.50 - 1.32)
sease 305 ith disease 419 gnosis 103 sensis 532	6	(56)	0.85	(0.29–2.44)
305 ease 419 103				
case 419 103	203	(67)	[Ref]	
103	211	(50)	0.60	(0.42 - 0.84)
532	59	(57)	0.85	(0.52–1.39)
532				
	179	(99)	[Ref]	
Associated with disease 197 (24)	115	(42)	0.34	(0.24 - 0.49)
Other 98 (12)	60	(39)	0.38	(0.23 - 0.60)
Admitting hospital unit				
Floor 508 (61)	293	(56)	[Ref]	
ICU 319 (39)	180	(58)	1.15	(0.84 - 1.59)
Provider experience (years) 9 (5–15)	6	(5–15)	1.01	(0.99 - 1.02)

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Combined Cohort $(N = 827)$	u	(%)	Adher	Adherence, n (%)	Adjusted OR	(95% CI)
MD	682	(82)	396	(58)	[Ref]	
DO	145	(18)	<i>LT</i>	(53)	66.0	(0.64 - 1.51)
Hospital type						
Tertiary care	234	(28)	153	(65)	[Ref]	
Community	359	(43)	190	(53)	0.61	(0.41 - 0.91)
Safety net	234	(28)	130	(56)	0.77	(0.50 - 1.17)
Time of day						
Morning (6 AM-11:59 AM)	245	(30)	150	(61)	[Ref]	
Afternoon (noon-5:59 PM)	300	(36)	160	(53)	0.79	(0.54 - 1.13)
Evening (6 PM-11:59 PM)	190	(30)	108	(57)	0.92	(0.61 - 1.40)
Night (midnight–5:59 AM)	92	(11)	55	(09)	1.10	(0.65 - 1.85)
Day of week						
Weekday	516	(62)	303	(59)	[Ref]	
Weekend (Fri 6 PM to Mon 6 AM)	311	(38)	170	(55)	0.82	(0.60 - 1.11)

Data are reported as median (IQR) or n(%).

CPG = clinical practice guidelines; ICU = intensive care unit; IQR = interquartile range.

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Multivariable Model of ED Adherence to SSC's 3-Hour Bundle, Adjusted for Clustering by Hospital

Sepsis Cohort $(n = 413)$	Ó	Overall	IbA	Adherence	Ad	Adjusted
Age (years)	61	(49–73)	63	(50–75)	1.0	(1.0 - 1.0)
Sex						
Male	224	(54)	116	(52)	[Ref]	(0.6–1.4)
Female	189	(46)	92	(49)	0.9	
Race/ethnicity						
Non-Hispanic white	262	(63)	136	(52)	[Ref]	(0.7 - 2.2)
Hispanic	96	(23)	48	(20)	1.2	(0.3 - 1.7)
Non-Hispanic black	36	(6)	16	(44)	0.8	(0.3–2.5)
Other	19	(2)	8	(42)	0.9	
Comorbidities						
Fluid sensitive *	85	(21)	38	(45)	0.6	(0.3–0.99)
SIRS						
2	136	(33)	61	(45)	[Ref]	
3	198	(48)	103	(52)	1.4	(0.8–2.2)
4	6L	(19)	4	(56)	1.6	(0.8-2.9)
ED source						
Respiratory	137	(33)	78	(57)	[Ref]	
Urinary	110	(27)	54	(49)	0.6	(0.4 - 1.1)
Skin/soft tissue	42	(10)	16	(38)	0.4	(0.2 - 0.9)
Abdominal	34	(8)	12	(35)	0.3	(0.1 - 0.8)
Other	12	(3)	9	(50)	0.5	(0.1 - 1.9)
Unknown	78	(19)	42	(54)	0.6	(0.4 - 1.1)
Primary ED diagnosis						
Sepsis/severe/shock	199	(48)	119	(09)	[Ref]	
Specific infection	161	(39)	99	(41)	0.5	(0.3 - 0.9)
Other	53	(13)	23	(43)	0.6	(0.3 - 1.2)

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Admitting hospital unit 144 (35) 54 (38) [Ref] ICU 144 (35) 54 (38) [Ref] Floor 269 (65) 154 (57) 0.5 (0.3-0.9) Hospital type 2 2 (57) 0.5 (0.3-0.9) Hospital type 2 2 (52) [Fef] (0.3-0.7) Tertiary care 117 (28) 73 (62) [Ref] (0.2-0.7) Safety net 117 (28) 88 (49) 0.4 (0.2-0.7) Safety net 117 (28) 87 (40) 0.4 (0.2-0.7) Time of day 117 (28) 88 (49) 0.4 (0.2-0.7) Time of day 109 (28) 57 (40) 0.4 (0.2-0.7) Morning (6 AM-11:59 AM) 109 (26) 57 (43) 10 (0.6-1.8) Afternoon (noon-5:59 AM) 106 (20) 57 1.2 (0.2-2.3) (0.2-2.3) Night (midnight-5:59 AM) 106 (26) <th>Sepsis Cohort $(n = 413)$</th> <th>Ove</th> <th>Overall</th> <th>Adhe</th> <th>Adherence</th> <th>Υ</th> <th>Adjusted</th>	Sepsis Cohort $(n = 413)$	Ove	Overall	Adhe	Adherence	Υ	Adjusted
144 (35) 54 (38) [Ref] 269 (65) 154 (37) 0.5 e 269 (65) 154 (57) 0.5 are 117 28) 73 (62) [Ref] ty 179 (28) 73 (62) [Ref] ty 179 (28) 47 (40) 0.4 to 117 (28) 47 (40) 0.4 to 117 (28) 47 (40) 0.4 to 109 (26) 52 (48) 10 to 109 (26) 52 (48) 10 to 109 (26) 57 (54) 10 to 106 (26) 57 (55) 12 dot 106 26) 57 (55) 12	Admitting hospital unit						
269 (55) 154 (57) 0.5 e 117 28 57 6.5 18ef are 117 28 73 6.2 18ef ty 179 (43) 88 (49) 0.4 ty 117 28 47 (40) 0.4 t 117 28 47 (40) 0.4 t 117 28 47 (40) 0.4 t 0.3 28 47 0.4 0.4 t 107 28 47 0.4 0.4 t 0.3 0.3 57 48 1.0 t 100 26 57 57 1.0 t 106 26 57 57 1.2 dight-5:59 AM 106 21 31 55 25	ICU	144	(35)	54	(38)	[Ref]	
e 117 (28) 73 (62) [Ref] ty 179 (43) 88 (49) 0.4 ty 117 (28) 47 (40) 0.4 t 109 (26) 52 (48) [Ref] n (noon-5:59 PM) 109 (26) 57 (54) 1.0 6 PM-11:59 PM) 106 (26) 57 (54) 1.0 duight-5:59 AM) 106 (26) 57 (54) 1.2	Floor	269	(65)	154	(57)	0.5	(0.3 - 0.9)
are 117 (28) 73 (62) [Ref] ty 179 (43) 88 (49) 0.4 ty 117 (28) 47 (40) 0.4 th 117 (28) 47 (40) 0.4 th 117 (28) 47 (40) 0.4 th 109 (26) 52 (48) [Ref] th 109 (26) 52 (48) [Ref] th 150 (36) 68 (45) 1.0 th 150 (36) 57 (54) 1.2 th 106 (26) 57 (55) 1.2 db 11:59 PM) 106 260 57 (54) 1.2 db 106 126 31 (65) 2.5 2.5	Hospital type						
ty 179 (43) 88 (49) 0.4 117 (28) 47 (40) 0.4 117 (28) 47 (40) 0.4	Tertiary care	117	(28)	73	(62)	[Ref]	
117 28) 47 (40) 0.4 6 AM-11:59 AM) 109 26) 52 (48) [Ref] 1 (noon-5:59 PM) 150 (36) 68 (45) 1.0 6 PM-11:59 PM) 106 (26) 57 (54) 1.2 dnight-5:59 AM) 48 (12) 31 (65) 2.5	Community	179	(43)	88	(49)	0.4	(0.2 - 0.7)
(6 AM-11:59 AM) 109 (26) 52 (48) [Ref] 1 (noon-5:59 PM) 150 (36) 68 (45) 1.0 6 PM-11:59 PM) 106 (26) 57 (54) 1.2 dnight-5:59 AM) 48 (12) 31 (65) 2.5	Safety net	117	(28)	47	(40)	0.4	(0.2 - 0.7)
109 (26) 52 (48) [Ref] 150 (36) 68 (45) 1.0 106 (26) 57 (54) 1.2 48 (12) 31 (65) 2.5	Time of day						
150 (36) 68 (45) 1.0 106 (26) 57 (54) 1.2 48 (12) 31 (65) 2.5	Morning (6 AM-11:59 AM)	109	(26)	52	(48)	[Ref]	
106 (26) 57 (54) 1.2 48 (12) 31 (65) 2.5	Afternoon (noon-5:59 PM)	150	(36)	68	(45)	1.0	(0.6 - 1.8)
48 (12) 31 (65) 2.5	Evening (6 PM-11:59 PM)	106	(26)	57	(54)	1.2	(0.7 - 2.2)
	Night (midnight-5:59 AM)	48	(12)	31	(65)	2.5	(1.2–5.3)

Data are reported as n (%) or OR (95% CI).

ICU = intensive care unit; IQR = interquartile range; SIRS = systemic inflammatory response syndrome; SSC = Surviving Sepsis Campaign. $\overset{*}{}$ Congestive heart failure, end-stage renal disease on hemodialysis, and end-stage liver disease.

Table 7

Multivariable Model of In-hospital Mortality, Adjusted for Clustering by Hospital

	(%) <i>u</i>	In-hospital Mortality, n (%)	Adjusted OR (95% CI)
Age (years), mean (±SD)	60 (±18)	64 (±13)	1.02 (1.00–1.04)
Sex			
Male	435 (53)	23 (58)	Ref
Female	392 (47)	17 (42)	0.9 (0.5–1.8)
Admitting disease			
Pneumonia	414 (50)	2 (5)	Ref
Severe sepsis/shock	413 (50)	38 (95)	9 (2–38)
Admitting hospital unit			
Floor	508 (61)	5(15)	Ref
ICU	319 (39)	34 (85)	5.4 (2.1–14)
Guideline adherent ED care	e		
Yes	473 (57)	15 (38)	Ref
No	354 (43)	25 (63)	2.4 (1.2-4.8)

ICU = intensive care unit.

Table 8

Hospital LOS and Adherence to ED Infectious Clinical Practice Guideline

	Ove	rall $(N = 827)$	Adhe	rence $(n = 473)$	Nonac	Overall $(N = 827)$ Adherence $(n = 473)$ Nonadherence $(n = 354)$ Median Difference	Med	ian Difference
Hospital LOS (days) 5 (3–9) 5 (3–8)	5	(3-9)	5	(3–8)	5	(3-9)	0	0 (-0.7 to 0.7)
Disease type								
Pneumonia ($n = 414$) 5 (3–7)	5		4	4 (3–6)	5	(3–7)	-1.0	-1.0 (-1.5 to -0.5)
Sepsis $(n = 413)$ 7 $(4-12)$ 7	7	(4–12)	7	(4–13)	9	(4-11) 1.0 (0.3 to 1.7)	1.0	(0.3 to 1.7)

Data are reported as median (95% CI).