

# Epidemiology and Predictors of 30-Day Readmission in Patients With Sepsis



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**BACKGROUND:** Patients with sepsis are particularly vulnerable to readmissions. We describe the associated etiology and risk factors for readmission in patients with sepsis using a large administrative database inclusive of patients of all ages and insurance status.

**METHODS:** Our study cohort was derived from the Healthcare Cost and Utilization Project's National Readmission Data from 2013 to 2014 by identifying patients admitted with sepsis. The primary outcome was 30-day readmission with etiology identified by using International Classification of Diseases, Ninth Revision, Clinical Modification, codes.

**RESULTS:** From a total 1,030,335 index admissions; mean age,  $66.8 \pm 17.4$  years (60% age  $\geq 65$  years), 898,257 patients (87.2%) survived to discharge. A total of 157,235 (17.5%) patients had a 30-day readmission; median time to readmission was 11 days (interquartile range, 5-19). Infectious etiology (42.16%; including sepsis, 22.86%) was the most commonly associated cause for 30-day readmission followed by gastrointestinal (9.6%), cardiovascular (8.73%), pulmonary (7.82%), and renal causes (4.99%). Significant predictors associated with increased 30-day readmission included diabetes (OR, 1.07; 95% CI, 1.06-1.08;  $P < .001$ ), chronic kidney disease (1.12; 1.10-1.14,  $P < .001$ ), congestive heart failure (OR, 1.16; 95% CI, 1.14-1.18;  $P < .001$ ), discharge to short-/long-term facility (OR, 1.13; 95% CI, 1.11-1.14;  $P < .001$ ), Charlson comorbidity index  $\geq 2$ , and length of stay  $\geq 3$  days during the index admission. The mean cost per readmission was \$16,852; annual cost was  $> \$3.5$  billion within the United States.

**CONCLUSION:** We describe that readmission after a sepsis hospitalization is common and costly. The majority of readmissions were associated with infectious etiologies. The striking rate of readmission demands efforts to further clarify the determinants of readmission and develop strategies in terms of quality of care and care transitions to prevent this outcome.

CHEST 2019; 155(3):483-490

**KEY WORDS:** predictors; readmission; sepsis

**ABBREVIATIONS:** ACSC = ambulatory care sensitive conditions; AMI = acute myocardial infarction; CCI = Charlson comorbidity index; CHF = congestive heart failure; CMS = Centers for Medicare & Medicaid Services; ICD = International Classification of Diseases; LOS = length of stay; NRD = National Readmission Data

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This article was presented in abstract form at the annual CHEST meeting, November 1, 2017, Toronto, ON, Canada.

**FUNDING/SUPPORT:** The authors have reported to CHEST that no funding was received for this study.

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**DOI:** <https://doi.org/10.1016/j.chest.2018.12.008>

Rehospitalizations after hospital discharge are common, costly, and have far-reaching implications for patients and the society. Approximately one-fifth of Medicare beneficiaries are readmitted within 30 days of a hospital discharge. These unplanned admissions are associated with a projected cost of \$17.4 billion.<sup>1</sup> The Centers for Medicare & Medicaid Services (CMS) uses 30-day readmission rates to measure quality of care and as a guide for pay-for-performance. CMS tracks and publically reports readmissions following index hospitalizations for acute myocardial infarction (AMI), congestive heart failure (CHF), COPD, and pneumonia because these conditions account for a large proportion of hospital admissions and readmissions.<sup>2</sup>

The hospital length of stay (LOS) and cost of hospitalization for unplanned admission after sepsis

are higher than readmissions following AMI, heart failure, COPD, and pneumonia.<sup>3</sup> The epidemiology, risk factors, and targets for preventive strategies for sepsis readmissions have focused on selective patient cohorts, however.<sup>4,5</sup> Studies have described system-based differences among academic medical centers, Veterans Administration hospitals, or individual hospital cohorts<sup>6-8</sup>; yet, the epidemiology and predictors of unplanned readmissions following sepsis hospitalizations at a national level in policy relevant populations is lacking. Accordingly, the primary objective of our study was to evaluate the epidemiology and predictors of 30-day readmission in patients admitted with sepsis at a national level from one of the largest nationwide databases.

## Methods

The study cohort was derived from Healthcare Cost and Utilization Project's National Readmission Database (NRD) of 2013 and 2014, sponsored by the Agency for Healthcare Research and Quality. NRD is one of the largest publicly available all-payer inpatient databases in the United States, estimating roughly 36 million discharges from 21 states with reliable, verified linkage numbers. NRD represents 49.1% of total US hospitalizations.<sup>9</sup> Because the NRD database is publicly available and contains deidentified patient information, the study was labeled as exempt from institutional board review by the authors.

Patients were tracked using variable "NRD\_visitlink"; time between two admissions was calculated by subtracting the variable "NRD\_DaysToEvent." Time to readmission was calculated by subtracting LOS of index admissions from time between two admissions. National estimates were produced for estimated cost impact using sampling weights provided by the sponsor. The details regarding the NRD data are available online.<sup>10</sup>

We queried the NRD database using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes for sepsis (ICD-9-CM codes 038, 785.52, 995.9x; e-Table 1). We excluded patients age < 18 years, with missing data for age, sex, or mortality. We also excluded index admissions done in December because we did not have 30-day follow-up data. The primary outcome was 30-day readmission. Readmission causes were identified

by using ICD-9-CM codes in the primary diagnosis and combining those with similar diagnoses to make clinically important groups.

NRD variables were used to identify patients' demographic characteristics including age, sex, primary payer, and discharge disposition.<sup>11</sup> "CM\_" variables identified different comorbidities by using ICD-9-CM diagnoses and the diagnosis-related groups in effect on the discharge date (e-Table 2). These comorbidities are not directly related to the principal diagnosis or the main reason for admission and are likely to have originated before the hospital stay.<sup>12</sup> Severity of comorbid conditions defined using Deyo modification of Charlson comorbidity index (CCI), which contains 17 comorbid conditions with differential weights. The score ranges from 0 to 33, with higher scores corresponding to greater burden of comorbid diseases.<sup>13</sup>

SPSS 23.0 (IBM) was used for analysis. Differences between categorical variables were tested using the  $\chi^2$  test and continuous variables by using the Student *t* test. A multivariable regression model with the hospital identification as random effect was used to evaluate predictors of readmission. The model included patient level variables such as age groups (50-64, 65-79,  $\geq 80$  vs 18-49), sex, CCI ( $\geq 3$ , 2 vs 1), primary payer (private insurance and self-pay vs Medicaid/Medicare); comorbidities; disposition after index admission (long- or short-term facility vs home); LOS of index admission ( $\leq 2$  as reference, 3-4, 5-8, and  $> 8$ ). Multivariate model for readmission was run only among patients who survived index admission.

## Results

### Baseline Characteristics at Index Admission

Our analysis included 1,030,335 index admissions for sepsis in the United States during the study period. The mean age was  $66.8 \pm 17.4$  years (60% aged  $\geq 65$  years); 51.7% were women (e-Table 3). The in-hospital mortality rate during the index admission was 12.8%. Among the 898,257 who survived, 157,235 (17.5%) patients were readmitted within 30 days

(Table 1, e-Table 3). Forty-eight percent of the patients who were readmitted had significant comorbidities at baseline, with a CCI  $\geq 3$ . A total of 59.9% of the readmitted patients were from large hospitals. Medicare/Medicaid was the primary insurance payer in 82.1% of these patients. A greater proportion of patients that were readmitted belonged to lower socioeconomic strata on the median household income by ZIP code (Table 1). Our analysis suggested that patients who were readmitted had a

**TABLE 1 ]** Baseline Characteristics of Patients Who Survived Index Admission

Characteristics	Overall (N = 898,257)	30-d Readmission		P
		Yes (n = 157,235)	No (n = 741,022)	
Age, y, mean ± SD	66.0 ± 17.6	66.9 ± 16.3	65.7 ± 17.9	< .001
Age, y				< .001
18-49	17.7	14.6	18.4	
50-64	24.3	25.5	24.0	
65-79	31.2	33.6	30.7	
≥ 80	26.8	26.3	26.9	
Women	51.8	50.3	52.1	< .001
Payer information				< .001
Medicare	64.6	69.2	63.6	
Medicaid	11.9	12.9	11.7	
Private	16.8	13.3	17.5	
Self-pay	3.8	2.3	4.1	
No charge	0.5	0.3	0.5	
Other	2.4	1.9	2.6	
Cost of hospitalization in US\$, mean	19,612	24,291	18,611	< .001
LOS, mean ± SD	8.1 ± 10.0	9.9 ± 11.2	7.7 ± 9.7	< .001
LOS categories, d				< .001
≤ 2	13.9	8.2	15.1	
3-4	26.7	20.1	28.1	
5-7	25.5	26.2	25.4	
≥ 8	34.0	45.5	31.5	
LOS ≥ 31 d	2.6	3.9	2.3	< .001
Median household income category for patient's ZIP code, percentile <sup>a</sup>				< .001
0-25	26.5	27.9	26.2	
26-50	26.1	26.1	26.1	
51-75	24.7	24.0	24.8	
76-100	22.7	22.0	22.8	
CCI				< .001
≤ 1	44.1	32.9	46.5	
2	18.8	19.2	18.7	
≥ 3	37.1	47.9	34.9	
Hospital bed size <sup>b</sup>				< .001
Small	13.6	12.6	13.8	
Medium	28.0	27.5	28.1	
Large	58.4	59.9	58.1	
Hypertension with and without complications	59.4	62.0	58.8	< .001
Diabetes with and without complications	34.7	38.8	33.9	< .001
Chronic pulmonary disease	26.6	29.4	26.0	< .001
Congestive heart failure	20.2	26.0	19.0	< .001
Obesity	15.1	14.8	15.1	< .001
Acute kidney injury	36.1	40.1	35.2	< .001
Chronic kidney disease	23.3	29.6	22.0	< .001

(Continued)

**TABLE 1 ] (Continued)**

Characteristics	Overall (N = 898,257)	30-d Readmission		P
		Yes (n = 157,235)	No (n = 741,022)	
Shock	17.4	20.9	16.7	< .001
Vasopressor use	1.8	2.2	1.7	< .001
Acute cardiorespiratory failure	28.1	32.0	27.3	< .001
Ventilator use	10.3	13.2	9.7	< .001
Lymphoma	1.8	2.6	1.6	< .001
Metastatic cancer	4.1	5.5	3.8	< .001
Solid tumor without metastasis	3.8	5.0	3.6	< .001
Discharge disposition				< .001
Home	44.7	33.9	47.0	
Short-term hospital	1.8	2.0	1.8	
SNF	32.1	39.0	30.6	
Home with HHC	20.0	23.2	19.3	
Other	1.4	1.9	1.2	

Data are presented as % unless otherwise indicated. CCI = Deyo modification of Charlson comorbidity index; HHC = home health care; LOS = length of stay.

<sup>a</sup>Quartile classification of the estimated median household income of residents in the patient's ZIP code, derived from ZIP code demographic data obtained from Claritas. The quartiles are identified by values of 1 to 4, indicating the poorest to wealthiest populations. Because these estimates are updated annually, the value ranges vary by year.

<sup>b</sup>The bed size cutoff points were divided into small, medium, and large so that approximately one-third of the hospitals in a given region, location, and teaching status combination would fall within each bed size category. *State and County QuickFacts*. Washington, DC: US Census Bureau; 2012.

longer LOS ( $9.9 \pm 11.2$  vs  $7.7 \pm 10.3$  days,  $P < .001$ ), a higher cost of hospitalization (\$24,291 vs \$18,611,  $P < .001$ ), and a greater likelihood of discharge to a skilled nursing facility or home with home health care during their index admission (Table 1).

### At 30-Day Readmission

There were 179,253 readmissions in total, with 137,191 (87.2%) patients readmitted once and the rest readmitted at least twice within 30 days from discharge. A total of 157,235 unique patient admissions were included in the analysis, and 9.2% of the patients died during the rehospitalization within 30 days. Figure 1 represents the time to first 30-day readmission among survivors of the index hospitalization. The median time to readmission was 11 days (interquartile range, 5-19 days).

Infectious causes (42.16%) were the most commonly identified ICD-9-CM codes for the readmissions with new-onset sepsis accounting for 22.86% of the readmissions (Table 2). In most cases, the causal organism was not specified in the coding (unspecified septicemia) (18.38%). Staphylococcal species (1.45%), *Escherichia coli* (1.16%), and *Pseudomonas* (0.42%) were the most commonly identified bacteria. Organ-specific infections were classified under the infectious etiology and not the organ system involved. Pneumonia (6.75%),

urinary tract infection and pyelonephritis (2.94%), skin and soft-tissue infections (2.25%), catheter-related infections (1.51%), and *Clostridium difficile* colitis (1.77%) were the most commonly identified organ-specific infections. Among noninfectious etiologies, gastrointestinal diagnoses accounted for 9.6% of the readmissions; 8.73% of the readmissions were attributed to cardiovascular causes (primarily heart failure, 4.22%); 7.82% were attributed to pulmonary diagnosis (primarily respiratory failure followed by obstructive lung diseases); and 4.99% were due to renal causes (primarily acute kidney injury, 3.48%) (e-Table 4).

### Predictors Associated With 30-Day Readmission

Predictors associated with increased 30-day readmission (e-Table 5) included diabetes (OR, 1.07; 95% CI, 1.06-1.08;  $P < .001$ ), chronic lung disease (OR, 1.09; 95% CI, 1.07-1.10;  $P < .001$ ), chronic kidney disease (OR, 1.12; 95% CI, 1.10-1.14;  $P < .001$ ), CHF (OR, 1.16; 95% CI, 1.14-1.18;  $P < .001$ ), discharge to short-/long-term facility (OR, 1.13; 95% CI, 1.11-1.14;  $P < .001$ ), higher CCI (OR, 1.27; 95% CI, 1.24-1.29;  $P < .001$ ), and longer LOS during the index admission ( $> 3$  days). Factors associated with reduced 30-day readmission were obesity (OR, 0.91; 95% CI, 0.89-0.92;  $P < .001$ ), higher socioeconomic status (51th-75th percentile, 0.95;

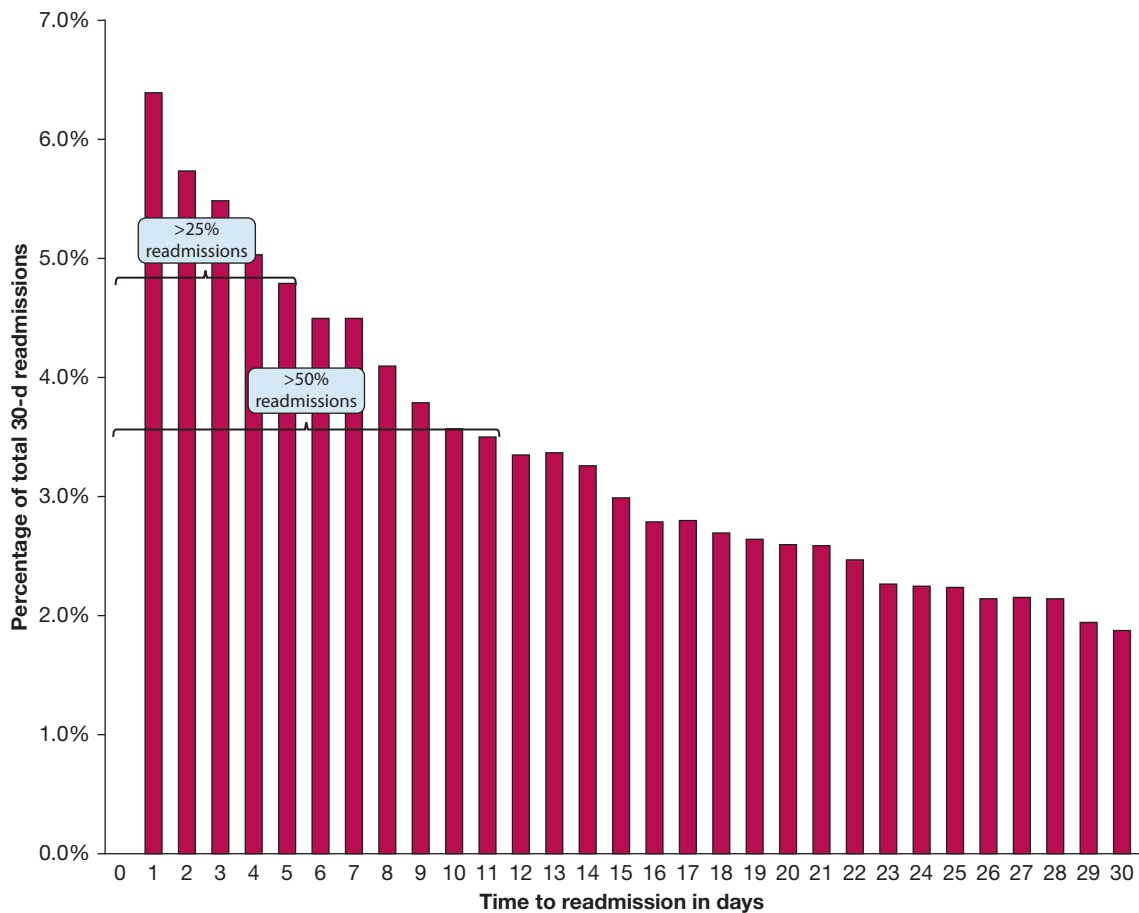


Figure 1 – Time to first 30-d readmission following a sepsis admission.

95% CI, 0.93-0.96;  $P < .001$ ; and 76th-100th percentile, 0.96; 95% CI, 0.95-0.98;  $P < .001$ ), private insurance/self-pay (private insurance OR, 0.77; 95% CI, 0.76-0.79;  $P < .001$ ; and self-pay OR, 0.61; 95% CI, 0.58-0.63;  $P < .001$ ), female sex (OR, 0.97; 95% CI, 0.96-0.98;  $P < .001$ ), and age  $> 80$  years (OR, 0.82; 95% CI, 0.80-0.84;  $P < .001$ ) (e-Table 5). There was no statistically significant association between the presence of shock (OR, 1.009; 95% CI, 0.99-1.02;  $P = .2$ ), need for vasopressors (OR, 0.98; 95% CI, 0.94-1.02;  $P = .4$ ), or need for mechanical ventilation (OR, 1.001; 95% CI, 0.98-1.02;  $P = .9$ ) at the times of index admission and 30-day readmission.

### Economic Impact

The national estimate for cost related to index admission for sepsis was calculated to be  $> \$23.3$  billion annually within the United States. The mean cost per readmission within 30 days was calculated to be  $\$16,852$ , amounting to an annual cost of  $> \$3.5$  billion within the United States. In our analysis, therefore, 30-day readmission following index admission for sepsis accounted for 13% of all sepsis-related hospitalization costs (total cost

of readmissions/total cost for index admissions and readmissions).

### Discussion

We report contemporary data from a large nationwide database on the epidemiology and predictors of 30-day readmission for patients with sepsis. Our study confirms and complements the findings of previous studies.<sup>4,5,14-17</sup> In this large national database, we observed that readmissions after sepsis hospitalization are common, costly, and occur early after discharge. In our study, the estimated annual cost of sepsis readmissions amounted to  $> \$3.5$  billion within the United States. When compared with  $\$7.0$  billion<sup>18</sup> for the four conditions (AMI, CHF, COPD, and pneumonia) targeted by the Hospital Readmissions Reduction Program, this accounts for a significant underrecognized burden on the US health-care system.

Our study suggests that the risk of readmission was highest during the first 2 weeks after discharge from the hospital. We observed a 17.5% rate of 30-day

**TABLE 2 ] Etiologies for 30-d Readmission Following Primary Admission for Sepsis**

Etiology for Readmission	No. (%)
<b>Infectious etiologies</b>	<b>75,433 (42.16)</b>
Sepsis	35,944 (22.86)
Unspecified septicemia	32,779 (18.38)
Staphylococcal septicemia	2,601 (1.45)
<i>Escherichia coli</i> septicemia	1,908 (1.16)
<i>Pseudomonas</i> septicemia	758 (0.42)
Other gram-negative septicemia	1,923 (1.07)
Anaerobic septicemia	692 (0.38)
Pneumonia/pneumonitis	12,107 (6.75)
UTI or pyelonephritis	5,281 (2.94)
Infections of skin and subcutaneous tissue	4,050 (2.25)
UTI from indwelling catheter	1,485 (0.82)
Central venous catheter-related infection	1,249 (0.69)
<i>Clostridium difficile</i> colitis	3,189 (1.77)
Intestinal infections	365 (0.2)
Acute and subacute bacterial endocarditis	609 (0.33)
Meningitis	94 (0.05)
Central nervous system abscess	240 (0.13)
<b>Gastrointestinal/hepatic and pancreatic etiologies</b>	<b>17,252 (9.6)</b>
<b>Cardiovascular etiologies</b>	<b>15,737 (8.73)</b>
Heart failure <sup>a</sup>	7,571 (4.22)
<b>Respiratory etiologies</b>	<b>14,063 (7.82)</b>
Respiratory failure	5,268 (2.94)
Obstructive lung disease	3,358 (1.87)
<b>Kidney/genitourinary etiologies</b>	<b>8,958 (4.99)</b>
Acute or acute on chronic kidney failure	6,249 (3.48)

All percentages were rounded off to the closest second decimal point; total may not equal 100%. Boldface type indicates broad subcategories of etiology of readmission.

<sup>a</sup>Includes systolic, diastolic, combined, acute, chronic, unspecified, and volume overload.

readmissions for all patients with sepsis. The readmission rate in our study was lower than the reported 30-day readmission rate for patients with severe sepsis (26%-32%)<sup>5,15</sup> and in sepsis irrespective of severity (20%-29%).<sup>14,16</sup> Prescott et al<sup>4</sup> reported a much higher 90-day readmission rate of 42.6% in their study of older Medicare patients with severe sepsis. These differences are explained because our study included all levels of severity of sepsis and our population included Medicaid, private/health maintenance organization, and self-pay patients, besides Medicare. This readmission

rate is comparable to other conditions (COPD, CHF, pneumonia, and AMI) targeted by the Centers for Medicare & Medicaid Services Hospital Readmissions Reduction Program.<sup>18,19</sup>

In our study, sepsis readmission was associated with a lower socioeconomic status or having Medicare/Medicaid as the primary payer. This aligns with the findings of Chang et al,<sup>14</sup> who described lower income as a risk factor for readmissions in a study of 240,198 patients with sepsis at nonfederal hospitals in California. Similarly, Donnelly et al<sup>6</sup> reported Medicaid/Medicare beneficiaries exhibited a higher risk of unplanned readmissions after discharge for severe sepsis in a cohort from 213 academic medical centers and affiliates. These findings may be related to the variation in access to care, chronic disease management skills, social support, and health literacy in these patients.

In our study, 60% of the patients were > 65 years of age. Yet, age > 80 years was associated with reduced 30-day readmission. Goodwin et al<sup>5</sup> described readmissions in 43,452 patients with severe sepsis in nonfederal hospitals in California, Florida, and New York using claims-based data. They reported a similar decreased risk of readmission in older patients with severe sepsis. It is likely that greater utilization of hospice and palliative services in the critically ill older population may be associated with decreased risk for readmission.<sup>20</sup> Notably, as described by others,<sup>5,7,21</sup> the presence of malignancy was associated with in a 30% to 50% increase in the risk of readmission. This highlights the need for targeted discussions and timely access to palliative care and hospice services in patients with active malignancies presenting with sepsis.

We observed that a longer LOS during the index admission was associated with greater odds of 30-day readmission. Liu et al<sup>17</sup> observed a similar trend in a study using claims-based approach to identify readmission in patients with sepsis at community hospitals. Prolonged hospital stays likely expose patients to nosocomial infections, in-hospital complications, and further deconditioning, ultimately contributing to higher readmission risk.

Our analysis suggested that 42% of the readmissions were due to infectious causes. Our study supports the findings of the single center study by Ortego et al,<sup>7</sup> in which 46% of patients who survived hospitalization for septic shock were readmitted within 30 days for an infection-related cause. Similarly, Chang et al<sup>14</sup> reported that infections accounted for 59.3% of the primary

diagnoses on readmission at 30 days. Further research is required to determine if the increased rate of infection after sepsis hospitalization is attributable to the immunosuppressive effects of sepsis<sup>22</sup> vs related to hospital interventions such as instrumentation, antibiotic, and catheter use; or microbiome disruption during index admission.<sup>23</sup> Interestingly, Sun et al<sup>24</sup> have reported that more than one-half of the infection-related sepsis readmissions may be due to recurrent or unresolved infection; hence, it is important to exercise antibiotic stewardship both during and after a sepsis hospitalization. An active surveillance for new or recurrent infections, ensuring removal/discontinuation of indwelling catheters (which can be potential nidus for infections) with a strong push toward completion of therapy, and follow-up with appropriate specialists might be important variables to be addressed at the time of discharge for these patients.

Consistent with previous sepsis readmission studies,<sup>7,14,25</sup> our study suggests that sepsis survivors are at risk for readmissions from pulmonary complications and cardiovascular events, including exacerbation of heart failure and acute renal failure. Krumholz et al<sup>26</sup> have elegantly explained this physiologic impairment as posthospital syndrome. Patients who were recently hospitalized are not only recovering from their acute illness, but also experience a transient period of generalized risk for a wide range of adverse health events. Polypharmacy, nutritional deficits, disturbances in circadian rhythm, and deconditioning could be some of the factors contributing to this state.

Postacute care is an important target for intervention to reduce sepsis readmissions. Our analysis suggested that nearly 40% of patients who had a readmission were discharged to a facility at the time of the index admission; moreover, discharge to a facility was associated with increased 30-day readmission. This supports the finding by Goodwin et al,<sup>5</sup> who described that survivors who were discharged to a care facility were 48% more likely to be readmitted than those who were discharged to home. It is therefore prudent to undertake collaborative efforts with postacute care providers to mitigate readmission risk.

Ambulatory care of the patient with sepsis is another domain of interest in reducing readmissions. Prescott et al<sup>4</sup> noted that readmission for ambulatory care-sensitive conditions (ACSCs) was more common after severe sepsis than other acute medical diagnoses. ACSCs are a group of diagnoses including hypertension,

diabetes, and CHF, for which effective outpatient management may prevent hospitalization.<sup>4,27</sup> Our study suggests that patients with sepsis have significant ACSCs and are rehospitalized often for conditions that are potentially treatable in the outpatient setting.<sup>25</sup> Complementary to the findings of Jones et al,<sup>21</sup> we noted that most readmissions occurred early after discharge. As a result, early surveillance and focused management of medical problems in the outpatient setting is needed to minimize the risk of readmission.

We acknowledge that our study has limitations. First, by using an administrative database, our ability to adjust all possible confounders is limited; however, the NRD has a validated robust and rigorous methodology to collect a large number of variables. Second, the database reported readmissions between 2013 and 2014; hence, we lack data regarding ICD-10 codes. Moreover, the effect of changes in the coding for severe sepsis during the study period is not known. We lacked data on peridischARGE practices, including transition of care to the outpatient setting; we are unable to determine the relative roles of these variables on readmission rates. Finally, the retrospective nature of the study prohibited us from establishing causality for any of the risk factors identified in the study. The results of the study reflect associations only, and firm conclusions regarding cause and effect cannot be made. Despite the limitations, our study describes real-world experience in a large, diverse all-payer population and complements and validates the findings of previous studies regarding predictors of readmissions in patients with sepsis.

## Conclusions

This exploration of a national database with a large sample of patients hospitalized with sepsis confirms the results seen in many smaller studies. Our analysis points out that many modifiable system-based factors are associated with readmissions after an episode of sepsis, but, more importantly, we also identified a number of patient-based characteristics associated with readmission after an episode of sepsis. Our findings serve to create awareness among clinicians, administrators, and policy makers alike regarding patient populations that are vulnerable to sepsis readmission and thus increased utilization of resources. Although it may be necessary to readmit some patients, the striking rate of readmission demands efforts to further clarify the determinants of readmission and develop strategies in terms of quality of care and care transitions to prevent this adverse outcome. To this

extent, we believe that better definition of the epidemiology of postsepsis readmissions would allow

the design of risk-stratified interventional clinical trials to mitigate the risk for sepsis readmissions.

## Acknowledgments

**Author contributions:** S. G. and M. S. take responsibility for (are the guarantors of) the content of the manuscript, including the data and analysis. S. K. G. participated in the design of the study, data collection, interpretation of the results and critical revision of the manuscript for important intellectual content, and final approval of the manuscript submitted. M. S. participated in the design of the study, data collection, statistical analysis, interpretation of the results and critical revision of the manuscript for important intellectual content, and final approval of the manuscript submitted. E. M.-C. participated in the design of the study, interpretation of the results and critical revision of the manuscript for important intellectual content, and final approval of the manuscript submitted. B. P. participated in the design of the study, data collection, statistical analysis, interpretation of the results, revision of the manuscript, and final approval of the manuscript submitted. A. D. participated in the design of the study, data collection, statistical analysis, interpretation of the results, writing and critical revision of the manuscript for important intellectual content, and final approval of the manuscript submitted.

**Financial/nonfinancial disclosures:** None declared.

**Role of sponsors:** The sponsor had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

**Additional information:** The e-Tables can be found in the Supplemental Materials section of the online article.

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