Readmission to a Different Hospital and Worse Outcomes Following Sepsis: A Nationwide Cohort Study

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Research

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**Abstract**

**Background**

In the United States (U.S.), sepsis accounts for 13% of total hospital expenses and more than 50% of hospital deaths. People with sepsis are more likely to be readmitted. Little is known about the prevalence and outcomes of different hospital readmissions (DHR) in sepsis patients, and the factors associated with DHR have not been well studied.

**Methods**

We used data during 2010 to 2017 from the Nationwide Readmissions Database of the U.S. 2010 to 2017 to identify the patients with admission for sepsis. Multivariable logistic regression analysis was used to evaluate the associated factors for DHR, and five models were constructed to elucidate the relationship between DHR and in-hospital outcomes.

**Results**

From 2010 to 2017, 450,560 (19.65%) of all readmitted sepsis patients in the U.S. were readmitted to a different hospital within 30 days. The prevalence of DHR increased from 18.45% in 2010 to 22.07% in 2017 (P for trend < 0.001). The factors associated with DHR included elective admission, diabetes, drug abuse, alcohol abuse, psychoses, and depression. The most common reason for readmission was infections irrespective of hospital status. DHR was associated with higher hospitalization costs [$4,909, 95% confidence interval (CI), $4,542-$5,276, P<0.001], longer length of stay (LOS) (0.97 days, 95% CI, 0.87 days-1.08 days, P<0.001), and higher risk of in-hospital mortality (odds ratio,1.08, 95% CI, 1.04-1.12, P < 0.001).

**Conclusions**

DHR occurred for one fifth of sepsis patients in the U.S. Our findings suggest that patients readmitted to a different hospital within 30 days may experience higher in-hospital mortality, longer LOS, and higher hospitalization costs. Future studies need to examine whether continuity of care can improve the prognosis of patients with sepsis.

**Introduction**

Sepsis management remains a major challenge for healthcare systems worldwide. Over one million cases of sepsis are diagnosed in the United States (U.S.) each year, and the number is still increasing.\(^1\) A study based on a nationally representative sample showed an 8.7% increase in the annualized incidence of sepsis, while a decrease in total in-hospital mortality.\(^1\) In the U.S., sepsis accounts for 13% of total hospital expenses and more than 50% of hospital deaths, with an average length of hospital stay (LOS) approximately 75% longer than those in most other cases.\(^2\) With the high mortality, it is important to improve the post-hospital prognosis of patients with sepsis.

Readmission increases medical costs and places a huge burden on medical resources, which has raised concerns of healthcare stakeholders and health decision and/or policy makers.\(^3\) People with sepsis are more likely to be readmitted. Previous studies have shown that 30-day readmission rates for sepsis range from 17% to 26%.\(^4\)\(^-\)\(^7\) For a variety of reasons, many patients are redirected to a different hospital instead of the initial one, which leads to fragmentation of care. Poorer outcomes due to different hospital readmissions (DHR) have been found in patients with stroke\(^8\), cirrhosis\(^9\), and heart failure\(^10\).

Little is known about the prevalence and outcomes of DHR following in sepsis patients, and the factors associated with DHR have not been well studied. We tried to study these issues using the National Readmission Database (NRD) of the U.S., which allows us to track patients' readmissions in the same calendar year. In this study, we sought to: (1) determine the rate of DHR following sepsis; (2) identify the factors associated with DHR; (3) evaluate the associations of DHR with hospitalization cost, LOS, and in-hospital mortality.
Methods

Data source

As part of a set of database and software tools developed by the Healthcare Cost and Utilization Project (HCUP), the NRD provides nationally representative information on readmissions. With a coverage of 36 million discharges every year from more than 20 states in the U.S, the NRD is a unique and powerful database that can be used to analyze national readmission rates for different types of patients. The NRD has previously been used to describe the outcomes of DHR in different patient populations. The NRD is publicly available, thus this study was exempt from the formal institutional review board approval.

Study population

We obtained data between 2010 and 2017 of the NRD, and identified the patients with admission for sepsis using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and ICD-10-CM diagnosis codes. The NRD variable “NRD_visitlink” was used to track patients. DHR was defined as readmission to a different hospital by using the NRD variable “HOSP_NRD”. We excluded patients younger than 18 years or with missing data for LOS. We also excluded patients who died in the index hospitalization. Because the NRD does not provide cross-year follow-up data, we further excluded the patients who were discharged in December. Finally, we excluded planned readmissions. The details regarding inclusion and exclusion are showed in Figure 1.

Covariates

Demographic characteristics and hospital characteristics of patients are available in the NRD. The demographic characteristics included age, gender, income by postal code, weekend admission, elective admission, payer information, and resident of the same state. We used the “APRDRG_Severity” to subdivide the degree of loss of function and the “APRDRG_Risk_Mortality” to subdivide the risk of mortality. The hospital characteristics included ownership of hospital, bed size, urban–rural designation, location, and teaching status. The Elixhauser Comorbidity Index (ECI) was used to account for the burden of 29 common comorbidities. We used the ICD-9-CM and ICD-10-CM codes to identify the comorbidities related to sepsis (e-Table 1).

Primary and secondary outcomes

The primary outcome was in-hospital mortality rate during readmission within 30 days. Our secondary outcomes of interest included hospitalization cost, LOS during readmission within 30 days, differences of readmission causes between patients with same hospital readmission (SHR) vs DHR, temporal trend of DHR, and in-hospital outcomes during the 60-day and 90-day readmission. The hospitalization cost was recalculated by cost-to-charge ratios, which was provided by the HCUP.

Statistical analysis

All analyses were using the survey analytical methods recommended by the HCUP for national estimates. The readmissions were divided into SHR group and DHR group. The t-test was used to compare the continuous variables, and the chi-squared test was used to compare categorical variables.

We conducted a multivariable logistic regression analysis to evaluate factors associated with DHR. The demographic characteristics, hospital characteristics, and comorbidities were incorporated into the regression models. In total five models were constructed to elucidate the relationship between DHR and in-hospital outcomes. Model 1 was a bivariate regression model. In model 2, we included the demographic characteristics and hospital characteristics variables from the index admission. Model 3 was adjusted for comorbidities from the index admission based on model 2. In addition to adjusting for the variables at the index admission, we also considered the variables at readmission. In model 4, we included
the demographic characteristics and hospital characteristics variables measured during the readmission. Model 5 was adjusted for comorbidities from the readmission based on model 4.

We further conducted three sensitivity analyses to validate the results for the primary outcome. First, we performed a propensity-matched model (PSM) to match patients of SHR and DHR. The two groups were 1:1 matched using a caliper of 0.1. Second, we assessed the outcomes of 60-day and 90-day readmissions. Third, we evaluated the outcomes of patients readmitted for different reasons.

Two-sided P-values ≤ 0.05 were considered statistically significant. All statistical analyses were performed in SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

Baseline characteristics

From 2010 to 2017, 450,560 (19.65%) of all readmitted sepsis patients in the U.S. were readmitted to a different hospital within 30-day, while 1,873,462 (80.35%) patients readmitted to the same hospitals. The prevalence of DHR increased from 18.45% in 2010 to 22.07% in 2017 (P for trend < 0.001) (Figure 2). Differences in patient characteristics during index admissions between SHR and DHR were presented in Table 1. Patients of DHR were more likely to be younger, male, smoker, and obesity. They also had higher prevalence for drug abuse, alcohol abuse, psychoses, and ventilator use. In addition, they were less likely to have Medicare, metastatic cancer, viral or bacterial pneumonia, and atrial fibrillation. E-Table 2 shows the characteristics of patients in both groups during readmission. The DHR patients were more likely to be readmitted to smaller hospitals, urban teaching hospitals, or hospitals located at large metropolitan areas with at least one million residents.

Reasons for 30-day unplanned readmissions

Figure 3 shows the top 15 reasons for 30-day readmission to the same or a different hospital. The most common reason was infections irrespective of hospital status, while the proportion was smaller in the DHR patients (30.82% vs 43.23%, P < 0.001) followed by gastrointestinal, respiratory, neuropsychiatric, and hematological causes. The top 15 reasons contributed to more than 80% of all the readmissions.

Factors associated with DHR

The results of multivariable logistic regression analysis to identify factors associated with DHR are shown in Table 2. The factors with statistically significantly positive association with DHR included elective admission (odds ratio [OR], 1.90; 95% confidence interval [CI], 1.83-1.97), admitted to private and invest-own hospital (OR, 1.11; 95% CI, 1.06-1.15), hypertension (OR, 1.02; 95% CI, 1.01-1.03), diabetes (OR, 1.04; 95% CI, 1.03-1.06), drug abuse (OR, 1.26; 95% CI, 1.22-1.29), alcohol abuse (OR, 1.13; 95% CI, 1.10-1.16), psychoses (OR, 1.13; 95% CI, 1.10-1.15), depression (OR, 1.02; 95% CI, 1.00-1.04), acute kidney injury (OR, 1.07; 95% CI, 1.06-1.09), ventilator use (OR, 1.13; 95% CI, 1.10-1.15), acute myocardial infarction (OR, 1.23; 95% CI, 1.20-1.27), ischemic stroke/TIA (OR, 1.23; 95% CI, 1.18-1.28), higher degree of loss of function (OR, 1.67; 95% CI, 1.57-1.77), and higher risk of mortality (OR, 1.17; 95% CI, 1.13-1.21). In contrast, female sex, higher income, lymphoma, viral or bacterial pneumonia, and clostridium difficile gastroenteritis were inversely associated with DHR. The patients who were initially admitted to private, nonprofit, or urban teaching hospitals, or hospitals with more beds were less likely to be DHR.

Impact of DHR on outcomes

After adjusting for index admission variables (model 3), DHR was associated with higher hospitalization costs ($2,019, 95% CI, $1,804-$2,235, P<0.001), longer LOS (0.50 days, 95% CI, 0.43 days-0.57 days, P<0.001), and higher risk of in-hospital mortality (OR, 1.70, 95% CI, 1.66-1.74, P<0.001). The analysis adjusting for readmission variables (model 5) showed similar results, with higher hospitalization costs ($1,894, 95% CI, $1,710-$2,079, P<0.001), longer LOS (0.51 days, 95% CI, 0.46 days-0.57 days, P<0.001), and higher risk of in-hospital mortality (OR, 1.79, 95% CI, 1.74-1.83, P<0.001) (Table 3).
Sensitivity analyses

In the three sensitivity analyses, similar results were seen in PSM, and 60- and 90-day readmissions, i.e. DHR was associated with higher hospitalization costs, longer LOS, and higher risk of in-hospital mortality. The same results were observed in patients who were readmitted for infection, gastrointestinal, respiratory, and neuropsychiatric causes (Table 4).

Discussion

In this 8-year register-based cohort study, we evaluated the outcomes after SHR and DHR following sepsis using the current real-world data. Our study reveals statistically significant associations between DHR and poorer outcomes for sepsis patients, and the robustness of the results was validated by three sensitivity analyses. Our findings also reveal that: 1) the prevalence of DHR in the U.S. increased from 18.45% in 2010 to 22.07% in 2017; 2) the factors associated with DHR include elective admission, diabetes, drug abuse, alcohol abuse, psychoses, depression, acute kidney injury, ventilator use, acute myocardial infarction, ischemic stroke/TIA, higher degree of loss of function, and higher risk of mortality; 3) the most common reason for readmission is infections irrespective of hospital status; 4) the DHR patients had higher risk of in-hospital mortality, higher hospitalization costs, and longer LOS.

As an incentive to improve the quality of healthcare, the Centers for Medicare & Medicaid Services (CMS) of the U.S. began publicly reporting standardized readmission rates for 30-day risks of heart failure (HF), acute myocardial infarction (AMI), and pneumonia to reduce preventable readmissions. While the LOS and hospitalization costs in sepsis patients after readmission were higher than those with AMI, HF, and pneumonia. We therefore believe that focusing on the readmission of sepsis patients might facilitate to improve current intervention strategies for reducing unplanned health care costs. Current studies on sepsis readmission have focused on the prediction of the readmission rate of sepsis or the risk factors for readmission, while studies on the relationship between readmission and outcomes at the national level have been lacking. Our evaluation about the adverse effects of sepsis DHR may provide new evidence for the development of medical policy focusing on sepsis patients.

Evidence on the factors associated with DHR in sepsis patients is lacking. We found that acute kidney injury, ventilator use, acute myocardial infarction, and ischemic stroke were associated with DHR. Sepsis patients complicated by myocardial infarction or stroke are more likely to have an acute emergency and be sent to the nearest hospital instead of the index hospital. The study by Sun et al. also showed that 77% of sepsis patients were readmitted through the emergency department, and 39% of them required ICU care. In case of emergency, the ambulance will send the patient to the nearest hospital. These patients often require early stabilization, and moving to the nearest hospital may be the most appropriate measure in this situation. As a result, healthcare workers will face the challenge of deciding whether to divert patients to the nearest emergency department of a different hospital or to the index hospital. A study based on the Danish population reported that low socioeconomic status was associated with higher risk of bacteremia and increased mortality, compared to high socioeconomic status. In this study, low-income patients were more likely to be DHR. One possible reason is that income may influence patients’ treatment choices.

Hospital factors can also have impacts on DHR. Patients initially admitted to a smaller or non-teaching hospital are more likely to be subsequently readmitted to a different hospital, thus affecting the continuity of care after discharge. We also found that patients who admitted to a profit-making hospital are more likely to be DHR. It suggests that readmission rates of profit-making hospitals are underestimated compared to those of government-nonfederal hospitals or private-nonprofit hospitals. The CMS penalizes hospitals based on their readmission rate, which affects government-nonfederal and private-nonprofit hospitals even more. These hospitals treat most sepsis patients and are more dependent on government funding.

We found that the DHR patients had higher risk of in-hospital mortality, higher hospitalization costs, and longer LOS. May et al. reported the outcomes of DHR in patients with critical illness, and they believed that care fragmentation was a possible cause of the poorer outcomes. Sepsis is a complex disease, and sepsis patients are more likely to experience fragmentation
of care. As a high-risk group with high in-hospital mortality rate, diagnosis and treatment for sepsis patients may be delayed due to incomplete knowledge of the patients. Fragmented care is also closely related to hospitalization costs, which were increased when unnecessarily repeated tests were used. These tests are primarily diagnostic laboratory, radiological, and cardiology tests. Continuity of care can improve survival, reduce readmission, and conserve the use of health care resources. It has been believed that health care providers may be more responsible for the patients whom they have previously cared for, and that doctors may be more attentive to their care when the patients were readmitted.

Previous study have shown that accidental readmission after sepsis is common, and most of them are due to infection, which is consistent with our findings. A half of infection-related readmissions were due to recurrent or unresolved infections, and the others were due to new infections. For patients who were readmitted to the same hospital, doctors can quickly identify resistance-related pathogens and select the appropriate type of antibiotic. Therefore, post-discharge follow-up for monitoring and early intervention can reduce infection-related readmission. For patients with low income who discharged from hospital after sepsis, their rehabilitation and follow-up plan also require further attention. We should encourage patients who experience complications and need readmission return to the same hospital. In addition, sharing electronic medical records between hospitals can mitigate or offset some of the negative consequences of medical interruptions. By sharing electronic medical records, different doctors may think outside the box and offer more treatment ideas for the same patient, which may lead to fewer missed diagnoses and medical errors.

This study has several limitations. First, because we used an administrative database, although we adjusted for some covariates, we could not excluded other confounders that might have influence on the outcomes. Second, the inability of NRD to track patients across states and years might understate the readmission rate for sepsis. Our study did not include planned readmissions, nor did it include key factors associated with post-discharge outcomes, such as functional status and health literacy. Due to the inherent limitations in the database, we can only evaluate the in-hospital mortality rate, but cannot track the post-hospital mortality rate, thus the mortality of DHR might be underestimated. Although our primary findings were limited to a limited time frame, the results of 60 - and 90-day readmission were also analyzed in the sensitivity analysis. Third, different definitions of sepsis may lead to different estimates of readmission rates, in-hospital mortality, and hospitalization costs. The definition of sepsis in this study was based on the study of Gadre et al. In addition, limited by the data available and statistical analysis methods, our results reflect only associations rather than causalities.

**Conclusions**

This study explored a national database containing an 8-year sample of sepsis inpatients. DHR occurred in one fifth survivors of sepsis patients. Our findings suggest that patients readmitted to a different hospital within 30 days may experience higher in-hospital mortality, longer LOS, and higher hospitalization costs. These patients should be identified and intervened. At the same time, our analysis reveals factors associated with DHR. Our findings help clinicians and healthcare policy makers have a better understanding of DHR in sepsis patients, thereby optimize the utilization of resources. Further studies are needed to examine whether continuity of care can improve the prognosis of sepsis patients.

**Abbreviations**

U.S., United States

DHR, different hospital readmission

CI, confidence interval

LOS, length of stay

NRD, National Readmission Database
Declarations

Ethics approval and consent to participate The NRD is publicly available, so this study was exempt from formal institutional review board approval.

Consent for publication Not applicable.

Availability of data and materials The datasets generated and/or analysed during the current study are available in the https://www.hcup-us.ahrq.gov/nisoverview.jsp.

Competing interests The authors declare that they have no competing interests.

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Contributors: Zhen Lin, Hedong Han, Jiangfang Xu, and Jia He designed the research. Zhen Lin, Hedong Han and Yang Cao had full access to the data and conducted all analyses. Zhen Lin, Hedong Han, Jiangfang Xu, and Yang Cao wrote the article draft. Yingyi Qin, Xin Wei, Cheng Wu, Yang Cao, and Jia He critically reviewed and revised the article. All authors contributed to the writing of the manuscript and read and approved the final manuscript. He Jia acted as the guarantor.

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**Tables**

**Table 1.** Comparison baseline characteristics during index admissions of the same vs a different readmission
|                          | SHR            | DHR            | P-value |
|--------------------------|----------------|----------------|---------|
| **Age, year (mean±SE)**  |                |                | <0.001  |
| ≤49                      | 346,690 (18.51)| 92,635 (20.56)|         |
| 50–64                    | 495,037 (26.42)| 128,990 (28.63)|        |
| 65–79                    | 603,608 (32.22)| 144,035 (31.97)|        |
| ≥80                      | 428,128 (22.85)| 84,900 (18.84)|         |
| **Female sex**           |                |                | <0.001  |
|                         | 945,595 (50.47)| 218,829 (48.57)|         |
| **Weekend admission**    |                |                | 0.077   |
|                         | 473,866 (25.29)| 113,005 (25.08)|         |
| **Elective admission**   |                |                | <0.001  |
|                         | 54,123 (2.89)  | 23,616 (5.25)  |         |
| **Payer information**    |                |                | <0.001  |
| Medicare                 | 1,237,357 (66.14)| 290,409 (64.55)|         |
| Medicaid                 | 263,572 (14.09)| 78,541 (17.46)|         |
| Private insurance        | 279,943 (14.96)| 58,879 (13.09)|         |
| Self-pay                 | 43,466 (2.32)  | 11,323 (2.52)  |         |
| Other                    | 46,519 (2.49)  | 10,734 (2.39)  |         |
| **Resident of same state**| 1,806,646 (96.43)| 441,128 (97.91)| <0.001  |
| **Patient zip code income quartile** |                |                | <0.001  |
| 0–25th percentile        | 575,989 (31.19)| 151,979 (34.25)|         |
| 26th–50th percentile     | 474,337 (25.69)| 114,177 (25.73)|         |
| 51st–75th percentile     | 434,877 (23.55)| 100,308 (22.61)|         |
| 76th–100th percentile    | 361,288 (19.57)| 77,239 (17.41)|         |
| **APR-DRG severity**     |                |                | <0.001  |
| Minor (or no) loss of function | 55,386 (2.96)  | 5,955 (1.32)  |         |
| Moderate loss of function | 257,344 (13.74)| 54,226 (12.04)|         |
| Major loss of function   | 772,716 (41.25)| 180,565 (40.08)|         |
| Extreme loss of function | 787,334 (42.03)| 209,620 (46.52)|         |
| **APR-DRG Risk of Mortality** |                |                | <0.001  |
| Minor likelihood of dying | 160,541 (8.57)| 28,708 (6.37)  |         |
| Moderate likelihood of dying | 292,699 (15.62)| 65,871 (14.62)|         |
| Major likelihood of dying | 726,083 (38.76)| 170,291 (37.80)|         |
| Extreme likelihood of dying | 693,458 (37.01)| 185,497 (41.17)|         |
| **Hospital Characteristics** |                |                | <0.001  |
| Control or ownership of hospital |          |                |         |
| Category                              | Government, nonfederal | Private, nonprofit       | Private, invest-own      |
|---------------------------------------|------------------------|-------------------------|--------------------------|
|                                       | 207,156 (11.06)        | 1,419,615 (75.77)       | 246,692 (13.17)          |
|                                       | 52,235 (11.59)         | 320,546 (71.14)         | 77,780 (17.26)           |
| Hospital bed size, <0.001             |                        |                         |                          |
| Small                                 | 228,010 (12.17)        | 76,515 (16.98)          |                          |
| Medium                                | 474,494 (25.33)        | 121,122 (26.88)         |                          |
| Large                                 | 1,170,958 (62.50)      | 252,924 (56.14)         |                          |
| Hospital urban–rural designation, <0.001 |                      |                         |                          |
| Large metro area >1 million residents | 1,061,221 (56.64)      | 282,481 (62.70)         |                          |
| Small metro area <1 million residents | 645,967 (34.48)        | 125,703 (27.90)         |                          |
| Micropolitan area                     | 132,419 (7.07)         | 30,367 (6.74)           |                          |
| Not metropolitan or micropolitan      | 33,856 (1.81)          | 12,009 (2.67)           |                          |
| Location/teaching status of hospital, <0.001 |                     |                         |                          |
| Urban nonteaching                     | 604,604 (32.27)        | 156,264 (34.68)         |                          |
| Urban teaching                        | 1,102,584 (58.85)      | 251,920 (55.91)         |                          |
| Rural                                 | 166,275 (8.88)         | 42,376 (9.41)           |                          |
| **Comorbidities**                     |                        |                         |                          |
| Elixhauser comorbidity index, <0.001  |                        |                         |                          |
| 0                                     | 52,592 (2.81)          | 7,014 (1.56)            |                          |
| 1                                     | 116,688 (6.23)         | 22,688 (5.04)           |                          |
| 2                                     | 219,989 (11.74)        | 47,261 (10.49)          |                          |
| 3                                     | 1,484,194 (79.22)      | 373,597 (82.92)         |                          |
| Hypertension                          | 1,132,254 (60.44)      | 274,177 (60.85)         | 0.006                    |
| Diabetes                              | 696,970 (37.20)        | 177,120 (39.31)         | 0.001                    |
| Chronic pulmonary disease             | 537,440 (28.69)        | 132,473 (29.40)         | 0.001                    |
| History of stroke or TIA              | 110,771 (5.91)         | 27,266 (6.05)           | 0.030                    |
| History of myocardial infarction      | 104,033 (5.55)         | 25,005 (5.55)           | 0.960                    |
| Drug abuse                            | 90,005 (4.80)          | 33,991 (7.54)           | 0.001                    |
| Alcohol abuse                         | 84,673 (4.52)          | 27,469 (6.10)           | 0.001                    |
| Current or past smoker                | 388,697 (20.75)        | 100,415 (22.29)         | 0.001                    |
| Peripheral vascular disorders         | 190,419 (10.16)        | 46,808 (10.39)          | 0.021                    |
| Congestive heart failure              | 450,171 (24.03)        | 112,697 (25.01)         | 0.001                    |
| Liver disease                         | 121,927 (6.51)         | 36,249 (8.05)           | 0.001                    |
| Fluid and electrolytes disorders      | 1,030,533 (55.01)      | 269,631 (59.84)         | 0.001                    |
| Obesity                               | 277,591 (14.82)        | 72,405 (16.07)          | 0.001                    |
| Condition                                      | SHR         | DHR         | p-value   |
|------------------------------------------------|-------------|-------------|-----------|
| Acute kidney injury                            | 651,137 (34.76) | 173,665 (38.54) | <0.001    |
| Chronic kidney disease                         | 549,503 (29.33) | 137,182 (30.45) | <0.001    |
| Depression                                     | 256,612 (13.70) | 64,156 (14.24) | <0.001    |
| Psychoses                                      | 117,966 (6.30)  | 36,719 (8.15)  | <0.001    |
| Valvular heart disease                         | 134,433 (7.18)  | 34,104 (7.57)  | <0.001    |
| Shock                                          | 332,278 (17.74) | 93,954 (20.85) | <0.001    |
| Vasopressor use                                 | 24,467 (1.31)   | 6,501 (1.44)    | 0.001     |
| Acute cardiorespiratory failure                | 450,839 (24.06) | 121,536 (26.97) | <0.001    |
| Ventilator use                                 | 165,349 (8.83)   | 53,272 (11.82)  | <0.001    |
| Lymphoma                                       | 39,969 (2.13)    | 8,276 (1.84)     | <0.001    |
| Metastatic cancer                              | 96,735 (5.16)    | 19,874 (4.41)    | <0.001    |
| Solid tumor without metastasis                 | 81,203 (4.33)    | 18,461 (4.10)    | 0.001     |
| Gastrointestinal bleeding                      | 60,795 (3.25)    | 17,376 (3.86)    | <0.001    |
| Acute myocardial infarction                    | 82,866 (4.42)    | 25,672 (5.70)    | <0.001    |
| Atrial fibrillation or flutter                 | 319,289 (17.04)  | 74,007 (16.43)   | <0.001    |
| Endocarditis                                   | 33,551 (1.79)    | 11,110 (2.47)    | <0.001    |
| Viral or bacterial pneumonia                   | 1,819,049 (97.10)| 430,513 (95.55)  | <0.001    |
| Meningitis                                     | 4,494 (0.24)     | 1,390 (0.31)     | <0.001    |
| Urinary tract infection or pyelonephritis      | 44,645 (2.38)    | 11,654 (2.59)    | <0.001    |
| Clostridium difficile gastroenteritis          | 88,665 (4.73)    | 19,942 (4.43)    | <0.001    |
| Ischemic stroke/TIA                            | 30,809 (1.64)    | 10,077 (2.24)    | <0.001    |
| Systemic thromboembolic event                  | 48,158 (2.57)    | 12,905 (2.86)    | <0.001    |

**In-hospital outcomes**

| Outcome                                      | SHR         | DHR         | p-value   |
|----------------------------------------------|-------------|-------------|-----------|
| Length of stay, day                          | 6.44(3.52-11.90) | 7.32(3.87-14.24) | <0.001    |
| Cost, $,                                     | 14,666(8,150-28,324) | 17,231(9,263-34,850) | <0.001    |

**Disposition**

| Disposition                                 | SHR         | DHR         | p-value   |
|---------------------------------------------|-------------|-------------|-----------|
| Routine: home or self-care                  | 669,017 (35.71) | 143,793 (31.91) | <0.001    |
| Transfer to Short-term Hospital             | 24,652 (1.32)   | 17,922 (3.98)   |          |
| Transfer to SNF, ICF, or other facility     | 699,605 (37.34) | 181,177 (40.21) |          |
| Home health care                            | 450,782 (24.06) | 899,22 (19.96)  |          |
| Against medical advice                     | 28,250 (1.51)    | 17,458 (3.87)    |          |
| Discharged alive, destination unknown       | 1,157 (0.06)     | 289 (0.06)       |          |

Abbreviation: SHR, same hospital readmission; DHR, different hospital readmission; SE, standard error; APR-DRG, All Patient Refined Diagnosis Related Groups; TIA, transient ischemic attacks; SNF, skilled nursing facility; ICF, intermediate care facility.

**Table 2. Factors associated with DHR**

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| Variable                        | OR (95% CI)     | P-value |
|--------------------------------|-----------------|---------|
| Age, per 1-year increase       | 0.99 (0.99,0.99) | <0.001  |
| Female                         | 0.95 (0.94,0.96) | <0.001  |
| Weekend admission              | 1.00 (0.99,1.02) | 0.696   |
| Elective admission             | 1.90 (1.83,1.97) | <0.001  |
| Insurance                      |                 |         |
| Medicare                       | Reference       |         |
| Medicaid                       | 1.02 (1.00,1.04) | 0.063   |
| Private                        | 0.88 (0.87,0.90) | <0.001  |
| Self-pay                       | 0.92 (0.89,0.96) | <0.001  |
| Others                         | 0.85 (0.82,0.89) | <0.001  |
| Resident of same state         | 1.77 (1.65,1.91) | <0.001  |
| Income quartile                |                 |         |
| 1<sup>st</sup>–25<sup>th</sup> | Reference       |         |
| 26<sup>th</sup>–50<sup>th</sup>| 0.94 (0.92,0.95) | <0.001  |
| 51<sup>st</sup>–75<sup>th</sup>| 0.88 (0.87,0.90) | <0.001  |
| 76<sup>th</sup>–100<sup>th</sup>| 0.80 (0.78,0.82) | <0.001  |
| APR-DRG severity               |                 |         |
| Minor loss of function         | Reference       |         |
| Moderate loss of function      | 1.73 (1.64,1.82) | <0.001  |
| Major loss of function         | 1.75 (1.66,1.85) | <0.001  |
| Extreme loss of function       | 1.67 (1.57,1.77) | <0.001  |
| APR-DRG Risk of Mortality      |                 |         |
| Minor likelihood of dying      | Reference       |         |
| Moderate likelihood of dying   | 1.15 (1.11,1.18) | <0.001  |
| Major likelihood of dying      | 1.18 (1.14,1.22) | <0.001  |
| Extreme likelihood of dying    | 1.17 (1.13,1.21) | <0.001  |
| Hospital Characteristics       |                 |         |
| Control or ownership of hospital| Reference     |         |
| Government, nonfederal        | Reference       |         |
| Private, nonprofit             | 0.90 (0.86,0.93) | <0.001  |
| Private, invest-own            | 1.11 (1.06,1.15) | <0.001  |
| Hospital bed size              |                 |         |
| Small                          | Reference       |         |

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| Hospital urban–rural designation                  | 0.73 (0.71,0.75) | <0.001 |
|-------------------------------------------------|------------------|--------|
| Large                                           | 0.61 (0.60,0.63) | <0.001 |

| Reference                                       |                  |        |
| Large metro area >1 million residents           | Reference        |        |
| Small metro area <1 million residents           | 0.71 (0.69,0.73) | <0.001 |
| Micropolitan area                                | 0.80 (0.77,0.84) | <0.001 |

| Not metropolitan or micropolitan                | 1.05 (0.99,1.12) | 0.129  |

| Location/teaching status of hospital            |                  |        |
| Urban nonteaching                               | Reference        |        |
| Urban teaching                                  | 0.84 (0.82,0.86) | <0.001 |

| Comorbidities                                   |                  |        |
| Elixhauser comorbidity index                    |                  |        |
| 0                                               | Reference        |        |
| 1                                               | 1.24 (1.17,1.32) | <0.001 |
| 2                                               | 1.29 (1.21,1.37) | <0.001 |
| 3                                               | 1.32 (1.24,1.41) | <0.001 |

| Hypertension                                    | 1.02 (1.01,1.03) | 0.006  |
| Diabetes                                        | 1.04 (1.03,1.06) | <0.001 |

| Chronic pulmonary disease                       | 0.99 (0.98,1.01) | 0.466  |
| History of stroke or TIA                        | 1.00 (0.98,1.02) | 0.918  |
| History of myocardial infarction                | 1.02 (0.99,1.04) | 0.204  |
| Drug abuse                                      | 1.26 (1.22,1.29) | <0.001 |
| Alcohol abuse                                   | 1.13 (1.10,1.16) | <0.001 |
| Current or past smoker                          | 1.03 (1.01,1.05) | 0.0004 |
| Peripheral vascular disorders                   | 0.98 (0.96,1.00) | 0.035  |
| Congestive heart failure                        | 1.01 (0.99,1.02) | 0.263  |
| Liver disease                                   | 1.09 (1.06,1.11) | <0.001 |
| Fluid and electrolytes disorders                | 1.08 (1.07,1.10) | <0.001 |
| Obesity                                         | 1.03 (1.02,1.05) | 0.0001 |
| Acute kidney injury                             | 1.07 (1.06,1.09) | <0.001 |
| Chronic kidney disease                          | 0.99 (0.98,1.01) | 0.237  |
| Depression                                      | 1.02 (1.00,1.04) | 0.035  |
| Psychoses                                       | 1.13 (1.10,1.15) | <0.001 |
| Valvular heart disease                          | 1.05 (1.03,1.07) | <0.001 |
| Shock                                           | 1.06 (1.05,1.08) | <0.001 |
| Condition                                      | Odds Ratio (95% CI) | p-value |
|------------------------------------------------|---------------------|---------|
| Vasopressor use                                | 0.97 (0.92,1.03)    | 0.341   |
| Acute cardiorespiratory failure                | 1.03 (1.01,1.04)    | 0.002   |
| Ventilator use                                 | 1.13 (1.10,1.15)    | <0.001  |
| Lymphoma                                       | 0.95 (0.91,0.99)    | 0.008   |
| Metastatic cancer                              | 0.93 (0.90,0.96)    | <0.001  |
| Solid tumor without metastasis                 | 1.01 (0.98,1.04)    | 0.367   |
| Gastrointestinal bleeding                      | 1.06 (1.03,1.09)    | 0.0001  |
| Acute myocardial infarction                    | 1.23 (1.20,1.27)    | <0.001  |
| Atrial fibrillation or flutter                 | 0.99 (0.97,1.00)    | 0.1101  |
| Endocarditis                                   | 1.04 (1.00,1.08)    | 0.050   |
| Viral or bacterial pneumonia                   | 0.77 (0.74,0.80)    | <0.001  |
| Meningitis                                     | 1.13 (1.03,1.25)    | 0.014   |
| Urinary tract infection or pyelonephritis      | 1.14 (1.10,1.18)    | <0.001  |
| Clostridium difficile gastroenteritis          | 0.88 (0.86,0.91)    | <0.001  |
| Ischemic stroke/TIA                            | 1.23 (1.18,1.28)    | <0.001  |
| Systemic thromboembolic event                  | 1.05 (1.01,1.08)    | 0.015   |
| **Length of stay**                             | **1.01 (1.01,1.01)**| **<0.001**|

### Disposition

| Disposition                                     | Odds Ratio (95% CI) | p-value |
|-------------------------------------------------|---------------------|---------|
| Routine: home or self-care                       | Reference           |         |
| Transfer to Short-term Hospital                  | 2.96 (2.82,3.10)    | <0.001  |
| Transfer to SNF, ICF, or other facility          | 1.13 (1.11,1.15)    | <0.001  |
| Home health care                                | 0.90 (0.88,0.91)    | <0.001  |
| Against medical advice                          | 2.35 (2.27,2.43)    | <0.001  |
| Discharged alive, destination unknown            | 1.11 (0.93,1.33)    | 0.262   |

Abbreviation: SE, standard error; APR-DRG, All Patient Refined Diagnosis Related Groups; TIA, transient ischemic attacks; SNF, skilled nursing facility; ICF, intermediate care facility.

Adjusting for: demographic characteristics, hospital characteristics, comorbidities, in-hospital procedures, and in-hospital complications at the time of index admission

**Table 3: Impact of DHR on outcomes**
| Model       | Hospitalization costs, $ | Length of stay, d | In-hospital mortality |
|-------------|--------------------------|-------------------|-----------------------|
|             | Difference | 95% CI         | P-value | Difference | 95% CI         | P-value | OR        | 95% CI    | P-value |
| Model 1     | 2773       | 2559,2987      | <0.001  | 0.77       | 0.71,0.84      | <0.001  | 1.67      | 1.63,1.71 | <0.001  |
| Model 2     | 2249       | 2037,2461      | <0.001  | 0.58       | 0.52,0.64      | <0.001  | 1.69      | 1.65,1.72 | <0.001  |
| Model 3     | 2019       | 1804,2235      | <0.001  | 0.50       | 0.43,0.57      | <0.001  | 1.70      | 1.66,1.74 | <0.001  |
| Model 4     | 2537       | 2350,2724      | <0.001  | 0.69       | 0.64,0.75      | <0.001  | 1.84      | 1.79,1.88 | <0.001  |
| Model 5     | 1894       | 1710,2079      | <0.001  | 0.51       | 0.46,0.57      | <0.001  | 1.79      | 1.74,1.83 | <0.001  |

Model 1: unadjusted model

Model 2: adjusting for demographic characteristics, hospital characteristics at the time of index admission

Model 3: adjusting for demographic characteristics, hospital characteristics, comorbidities, in-hospital procedures, and in-hospital complications at the time of index admission

Model 4: adjusting for demographic characteristics, hospital characteristics at the time of readmission

Model 5: adjusting for demographic characteristics, hospital characteristics, comorbidities, and in-hospital complications at the time of readmission

Table 4: Sensitivity analyses

| Sensitivity analyses | Hospitalization costs, $ | Length of stay, d | In-hospital mortality |
|---------------------|--------------------------|-------------------|-----------------------|
|                     | Difference | 95% CI         | P-value | Difference | 95% CI         | P-value | OR        | 95% CI    | P-value |
| Propensity-matched model | 1726       | 1500,1953      | <0.001  | 0.24       | 0.16,0.31      | <0.001  | 1.66      | 1.61,1.71 | <0.001  |
| 60-d readmission    | 1638       | 1448,1830      | <0.001  | 0.39       | 0.33,0.44      | <0.001  | 1.72      | 1.68,1.75 | <0.001  |
| 90-d readmission    | 1429       | 1246,1612      | <0.001  | 0.32       | 0.27,0.37      | <0.001  | 1.72      | 1.68,1.75 | <0.001  |

Cause-specific readmission

|                     | Hospitalization costs, $ | Length of stay, d | In-hospital mortality |
|---------------------|--------------------------|-------------------|-----------------------|
|                     | Difference | 95% CI         | P-value | Difference | 95% CI         | P-value | OR        | 95% CI    | P-value |
| Infection           | 1629       | 1293,1966      | <0.001  | 0.19       | 0.08,0.29      | 0.001   | 2.22      | 2.14,2.30 | <0.001  |
| Gastrointestinal    | 2543       | 2283,2803      | <0.001  | 0.71       | 0.62,0.79      | <0.001  | 1.40      | 1.24,1.57 | <0.001  |
| Respiratory         | 3079       | 2560,3598      | <0.001  | 0.79       | 0.61,0.97      | <0.001  | 1.54      | 1.43,1.65 | <0.001  |
| Neuropsychiatric    | 2218       | 1899,2537      | <0.001  | 1.35       | 1.24,1.47      | <0.001  | 1.28      | 1.10,1.48 | 0.001   |
| Hematological       | 3299       | 2899,3700      | <0.001  | 0.78       | 0.65,0.90      | <0.001  | 1.25      | 1.15,1.36 | <0.001  |
All models were adjusting for variables at the time of index admission.

**Figures**

![Selection flow diagram of target population.](image)

**Figure 1**

Selection flow diagram of target population.
Figure 2

The prevalence of different hospital readmission in sepsis.
Figure 3

Reasons for 30-day unplanned readmissions in sepsis.

Supplementary Files

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