Rural Patients With Severe Sepsis or Septic Shock Who Bypass Rural Hospitals Have Increased Mortality: An Instrumental Variables Approach*

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Objective: To identify factors associated with rural sepsis patients' bypassing rural emergency departments to seek emergency care in larger hospitals, and to measure the association between rural hospital bypass and sepsis survival.

Design: Observational cohort study.

Setting: Emergency departments of a rural Midwestern state.

Patients: All adults treated with severe sepsis or septic shock between 2005 and 2014, using administrative claims data.

Interventions: Patients bypassing local rural hospitals to seek care in larger hospitals.

Measurements and Main Results: A total of 13,461 patients were included, and only 5.4% (n = 731) bypassed a rural hospital for their emergency department care. Patients who initially chose a top-decile sepsis volume hospital were younger (64.7 vs 72.7 yr; $p < 0.001$) and were more likely to have commercial insurance (19.6% vs 10.6%; $p < 0.001$) than those who were seen initially at a local rural hospital. They were also more likely to have significant medical comorbidities, such as liver failure (9.9% vs 4.2%; $p < 0.001$), metastatic cancer (5.9% vs 3.2%; $p < 0.001$), and diabetes with complications (25.2% vs 21.6%; $p = 0.024$). Using an instrumental variables approach, rural hospital bypass was associated with a 5.6% increase (95% CI, 2.2–8.9%) in mortality.

Conclusions: Most rural patients with sepsis seek care in local emergency departments, but demographic and disease-oriented

factors are associated with rural hospital bypass. Rural hospital bypass is independently associated with increased mortality. (*Crit Care Med* 2017; 45:85–93)

Key Words: emergency medical services; emergency service, hospital; hospitals, rural; rural health services; sepsis

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S evere sepsis is responsible for 390,000 emergency department (ED) visits annually (1) and has a mortality rate of over 24% (2). Early targeted therapy, provided in the ED, can improve survival (3), but this care is not provided consistently across community EDs (2, 4). There is poor adherence to Surviving Sepsis Campaign guidelines (5) in sepsis patients treated in low-volume hospitals, which may explain the increased mortality risk for these patients (6). This increased mortality remains true even for patients transferred from rural hospitals to high-volume centers (7). Rural hospitals have unique challenges in providing high-quality critical care (8), yet patients value proximity to home when deciding where they seek inpatient care (9). This suggests that improving care delivery for sepsis patients presenting to rural community hospitals is an urgent need.

Financial factors, transportation factors, perceived quality, and convenient access to care are all influential factors for patients in choosing the hospital where they seek care (10–13). With respect to emergency care, perceived quality of care, wait times, comorbidities, and severity of illness all have been shown to contribute to the choices patients make in choosing an ED (14–16), and some of these factors also contribute to clinical outcomes (17, 18). Previously, investigators have shown that rural patients bypass local rural hospitals in up to 30–50% of cases (19–25), but this has not been studied for critically ill patients with severe sepsis. As delays in sepsis care are associated with mortality (3, 26, 27) and are more frequent in rural sepsis patients (4), defining influential factors related to bypass are vital in order to devise systems to improve care of rural sepsis patients.

The objective of this study is to describe where rural patients with severe sepsis or septic shock seek emergency care. The secondary objective is to define factors that contribute to patients bypassing rural EDs, to elucidate how these factors influence the probability of interhospital transfer, and to measure the association between rural hospital bypass and clinical outcomes.

MATERIALS AND METHODS

This study is a cohort analysis of administrative billing claims of all adults (≥ 18 yr old) treated in Iowa EDs for severe sepsis or septic shock from 2005 to 2014. The Iowa Hospital Association Inpatient and Outpatient datasets were used to create a linkage across interhospital transfer using a probabilistic linkage algorithm that used date of birth, sex, patient zip code, county of residence, and date of visit through a sequential matching algorithm, using social security number to break nonmatching linkages. Social security numbers were maintained on a secure server accessible only to the study statistician and were used only for the purposes of the linkage; this variable was removed from the analysis dataset for security. Ten percent of records were manually verified to confirm appropriate linkages. This study was approved by the local institutional review board under waiver of informed consent.

Definitions

Severe sepsis was identified using a previously validated definition based on inpatient diagnosis codes from the *International Classification of Diseases*, 9th Edition, Clinical Modification (ICD-9-CM) (28), while having a qualifying infection diagnosis at the time of the ED evaluation. Comorbidities were defined using the Elixhauser methodology, a set of 30 comorbid conditions defined by ICD-9-CM codes that have been shown to predict mortality, hospitalization, and healthcare utilization (29, 30). Rurality was defined using Rural Urban Commuting Area codes (31), which is an accepted form of classifying census tracts by population density, urbanization, and daily commuting (32).

"Top-decile sepsis volume hospitals" were defined as hospitals in the top decile of inpatient sepsis volume. The "rural choice cohort" was defined as patients who had a local hospital within 20 miles of their residence, but that hospital was not a top-decile sepsis volume hospital, and there was no top-decile hospital within 20 miles of the patient residence. These patients were felt to have a choice of where they would receive their emergency care.

Driving Distances

Driving distances were estimated using geocoded hospital locations from each hospital street address to the centroid of the zip code of residence, using the GoogleMaps Application Programming Interface (33).

Outcomes

The primary analysis was to describe the proportion of rural choice cohort patients who bypass a local hospital and to identify factors associated with rural hospital bypass. The primary outcome was hospital mortality, and secondary outcomes included subsequent interhospital transfer, and the association between rural hospital bypass and hospital length of stay.

Analysis

Patients in the rural choice cohort were divided into 1) those who sought care at their local hospital and 2) those who bypassed their local hospital. Bypass rate was calculated as a proportion, and demographics, insurance status, comorbidities, and clinical outcomes were compared in univariate analysis using the *t* test, Wilcoxon signed rank test, and the chi-square test, as appropriate.

Multivariable Regression Model

To determine factors associated with rural hospital bypass, a multivariable explanatory logistic regression model was

created, including factors from the univariate analysis. Variables were selected for inclusion based on statistical criteria ($p < 0.20$), then screened for clinical relevance prior to inclusion (because statistical significance can be misleading in large populations). Nonsignificant covariates were retained in the model if two investigators agreed they were of clinical importance. Collinearity and interactions were evaluated with each variable. Using the same analysis approach, a second multivariable logistic regression model was developed to measure the effect of rural hospital bypass on hospital mortality.

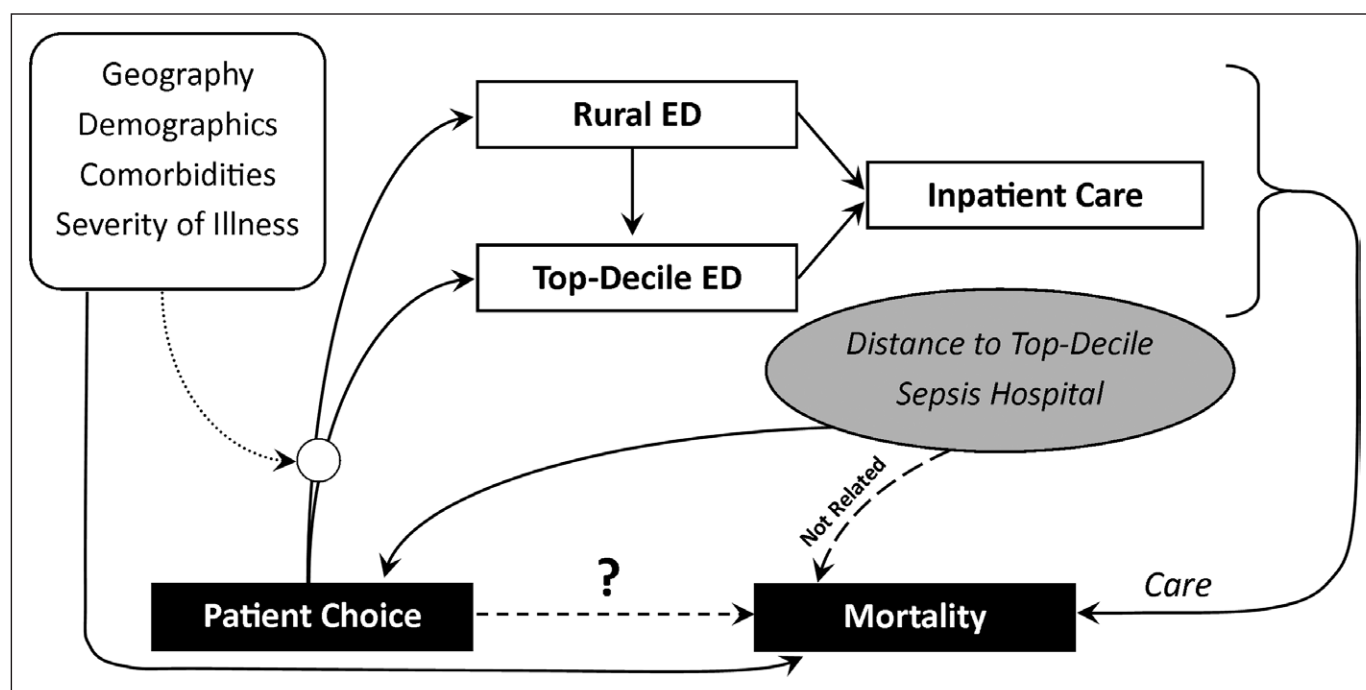### Instrumental Variables Model

Because no physiologic severity of illness indices were available in the administrative dataset, sepsis severity could have been a significant unmeasured confounder in explaining mortality. To account for this missing variable, an instrumental variables approach was used. Distance to a top-decile sepsis volume hospital was used as the instrument to predict rural hospital bypass. This variable meets the assumptions of an instrumental variable because of the following: 1) increasing distance from residence to a top-decile hospital is inversely associated with rural hospital bypass (F-statistic, 623.5) and 2) the exclusion restriction applies because no other plausible relationship exists between distance and death, except through access to care. This model assumes that severity of illness is uniformly distributed over geography, and there exists no theoretic or empiric basis upon which to refute that assumption (**Fig. 1**).

Driving Distance Sensitivity Analysis

Sensitivity analysis was conducted to determine the effect of driving distance on hospital choice. To do so, a series of rural choice cohorts were defined iteratively using alternative distance thresholds (e.g., 25 and 30 miles). For instance, patients were identified who live within 30 miles of a local hospital, but not within 30 miles of a top-decile sepsis volume hospital and a rate of rural hospital bypass was calculated. This analysis was reported graphically by the proportion of patients bypassing rural hospitals using each cohort definition. All statistical analyses were completed using SAS v.9.2 (SAS Institute, Cary, NC) or Stata v.13.1 (StataCorp LP, College Station, TX), and this study is reported in accordance with the Strengthening The Reporting of OBservational Studies in Epidemiology statement (34).

RESULTS

Over the 10-year period, 13,461 comprised the rural choice cohort (**Supplemental Fig. 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/C162; legend, Flow chart of study subjects; ED). Most patients (94.6%) sought care initially in their local hospital. We are unable to determine why patients chose to bypass their local hospital, and many may have chosen to seek care in a tertiary hospital because of health insurance or prior care for chronic medical conditions. Most patients (60%) were transferred, even among those who bypassed rural hospitals (52%). Bypass patients were more frequently transferred

Figure 1. Conceptual model including instrumental variables analysis. Patients choose whether to be treated in a rural emergency department (ED) or a top-decile sepsis volume ED, but that decision is influenced by several factors, including geography, demographics, comorbid conditions, and illness severity. After arriving to their ED of choice, patients may be admitted directly to the hospital or transferred to another hospital for admission. The care provided during the ED and inpatient stay influences mortality, but measurable and unmeasurable variables that influenced patient choice also influence mortality. Distance to a top-decile sepsis volume hospital is proposed as an instrumental variable because it is clearly associated with patient choice, but should not be associated with mortality except through the care and choices that patients make in where they receive their care. In that way, the instrument can be used to understand the role of patient choice in influencing care and ultimately the causal relationship between patient choice and mortality.

after hospital admission as part of their inpatient stay rather than directly from the ED (65% vs 30%; $p < 0.001$).

In this cohort, top-decile hospitals included the 12 hospitals that averaged more than 25 inpatient severe sepsis admissions annually.

Factors Associated With Rural Bypass

Patients who bypassed local rural hospitals were younger ($p < 0.001$), more likely to have commercial insurance ($p < 0.001$), and had more medical comorbidities than those initially seen in a local hospital (**Table 1**). Even restricting to patients younger than 65 (who would not be categorically eligible for Medicare), rural bypass patients were still more likely to have commercial insurance (37% vs 32%; $p < 0.001$). Using a multivariable logistic regression model, the following factors were associated with increased rural hospital bypass: decreasing age; commercial insurance (relative to Medicare or uninsured); a source of infection other than pneumonia, urinary infection, or cellulitis; comorbidities; and decreasing distance to a top-decile sepsis volume hospital (**Table 2**).

Mortality Analysis

Rural patients who presented to their local hospital were more likely to survive their sepsis hospitalization than those who presented initially to a tertiary care center (Table 2). In the instrumental variables model, patients who bypassed their local rural hospital continued to have 5.6% higher mortality than those who initially visited the local ED. The instrumental variables model did not adjust the effect of rural hospital bypass significantly from the naive linear regression model (**Table 3**).

Driving Distance Sensitivity Analysis

As driving distance to a top-decile sepsis volume hospital increases, the proportion of patients who bypass local hospitals falls rapidly, with the greatest proportion of patients willing to bypass local hospitals with a threshold defined at 20 miles. Interestingly, older patients are less likely to bypass rural hospitals, and those with comorbid medical conditions are much more likely (**Fig. 2**).

Inpatient Transfer

Although the transfer rate for sepsis patients who bypassed rural hospitals was lower than those who sought care in rural hospitals (52.1% vs 60.8%; $p < 0.001$), more of these transferred patients were transferred from inpatient status after hospital admission (65.4% vs 30.0%; $p < 0.001$). Those transferred from inpatient status had higher mortality than those transferred from the ED (22.8% vs 18.9%; $p < 0.001$).

DISCUSSION

Multiple studies have detailed how rural patients experience delays or limitations in accessing healthcare (4, 36), and prior studies have examined the issue of patient choice in rural patients' receipt of care in rural hospitals (15, 21–23, 37–40). Much of the data describing rural hospital bypass focuses on elective and scheduled healthcare (20, 24, 41) rather than unscheduled emergent care. This report is the first to detail issues of patient choice and hospital selection specifically among the critically ill, and it suggests that in this population the rural hospital bypass rate is much lower than the 30–50% rate reported in rural bypass studies previously (19–25).

Our data identified that 95% of rural patients being admitted with severe sepsis or septic shock received care in local hospitals. The majority of these hospitals were critical access hospitals, a federal designation for small hospitals with 24-hour emergency services, but without many of the resources that larger urban hospitals have. From our data, it is not possible to determine whether patients sought local care because 1) it was most rapidly available and they perceived that they had a time-sensitive condition, 2) they were transported by ambulance, and emergency medical personnel selected a local hospital for treatment, 3) they anticipated transfer to a tertiary center because of their perceived severity of illness, or 4) because they preferred to receive care from their personal physician. We have reported previously that rural patients value strongly both proximity to home and the comprehensive medical capabilities of the hospital where they receive their care (9), but balancing these factors with their perceived severity of illness and the capabilities of local hospitals can be challenging (42).

Despite the low rate of rural hospital bypass, patients who bypassed local hospitals had characteristics that differed from rural hospital patients in very important ways. First, they were more likely to have commercial insurance. This could be because of differences in transportation availability (for which health insurance is functioning as a surrogate measure), because commercial health insurance carriers required participants to travel to preferred hospitals or health systems, or because rural bypass patients are younger and less likely to be qualified for Medicare coverage (unlikely, because these differences persist in those younger than 65). This factor has importance for rural hospital systems, for whom payer mix is critical to maintaining financial viability (43–45), and also for case-mix risk adjustment models, because health insurance has been associated with clinical outcomes (46, 47).

Second, using a multivariable model to adjust for potential confounders, rural hospital bypass is associated with higher mortality. A mortality difference could have one of two possible explanations: 1) either rural hospital bypass "causes" worse clinical outcomes because of delays in sepsis care or 2) the observed differences come from inadequate risk adjustment for the factors that differ between rural bypass and nonbypass patients. The instrumental variables model attempts to adjust for unmeasured differences in severity of illness, and despite the adjustment, mortality is still higher in those who bypass rural hospitals. This finding suggests that the association may be causal, and that timely resuscitation provided in rural hospitals may be better than the delay during which patients are traveling to tertiary centers. Notably, the instrumental variables model is only slightly different from the naive linear regression model, so although the effect remains significant, the adjustment provided by the instrumental variables approach was small. The 5.6% increased mortality associated with rural

TABLE 1. Demographics, Comorbidities, and Clinical Outcomes Stratified by Rural Bypass Status

Factor	Treated in Local Hospital (*n* = 12,730)	Bypassed Local Hospital (*n* = 731)	*p*
Age, yr (mean, sd)	72.7 (15.4)	64.7 (15.9)	< 0.001
18–50, *n* (%)	1,245 (10)	146 (20)	< 0.001
51–69, *n* (%)	3,502 (28)	291 (40)	
70–81, *n* (%)	3,903 (31)	178 (24)	
Over 82, *n* (%)	4,080 (32)	116 (16)	
Non-White, *n* (%)	167 (1)	14 (2)	0.179
Male, *n* (%)	6,337 (50)	389 (53)	0.071
Rural residence (31), *n* (%)	11,660 (92)	604 (83)	< 0.001
Primary source of health insurance, *n* (%)			< 0.001
Medicare	10,251 (81)	458 (63)	
Medicaid	656 (5)	85 (12)	
Commercial	1,351 (11)	143 (20)	
Uninsured	404 (3)	23 (3)	
Source of infection (28), *n* (%)			
Pneumonia	4,790 (38)	210 (29)	< 0.001
Urinary tract infection	3,150 (25)	106 (15)	< 0.001
Cellulitis and soft tissue infection	884 (7)	61 (8)	0.150
Other	4,296 (34)	369 (51)	< 0.001
Surgery during hospitalization (broad definition) (35), *n* (%)	805 (6)	69 (9)	0.001
Comorbidities[a] (Elixhauser methodology) (30), *n* (%)			
Congestive heart failure	3,243 (25)	192 (26)	0.634
Valvular heart disease	897 (7)	82 (11)	< 0.001
Peripheral vascular disease	1,233 (10)	94 (13)	0.005
Hypertension	6,880 (54)	421 (58)	0.061
Neurologic disorders	1,638 (13)	87 (12)	0.447
Chronic pulmonary disease	3,539 (28)	208 (28)	0.701
Diabetes mellitus with complications	3,381 (27)	202 (28)	0.024
Renal failure	3,313 (26)	194 (27)	0.758
Liver disease	539 (4)	72 (10)	< 0.001
Metastatic cancer	404 (3)	43 (6)	< 0.001
Interhospital transfer, *n* (%)	7,739 (61)	381 (52)	< 0.001
Inpatient transfer, *n* (% among transfers)	2,321 (30)	249 (65)	< 0.001
Distance, miles (sd)			
First hospital	7.3 (11.6)	58.7 (36.4)	< 0.001
Admitting hospital	40.9 (39.2)	50.7 (43.4)	< 0.001
Top-decile sepsis volume hospital	55.1 (25.1)	41.1 (18.3)	< 0.001
Transfer distance	40.2 (46.7)	42.1 (54.0)	0.286
Critical access hospital, *n* (%)	10,413 (82)	0 (0)	< 0.001
Outcomes			
Hospital length of stay, median (IQR)	6 (3–11)	10 (5–18)	< 0.001
Died, *n* (%)	2,123 (17)	153 (21)	0.003

IQR = interquartile range.

[a]For brevity, not all Elixhauser comorbidity variables are listed. The remaining variables either had very low prevalence or had no significant differences between cohorts.

TABLE 2. Multivariable Models Predicting Rural Hospital Bypass and Mortality

Factor	Rural Hospital Bypass		Mortality	
	Adjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
Age (per decade)	0.804 (0.753–0.857)	< 0.001	1.121 (1.074–1.170)	< 0.001
Non-White	0.855 (0.482–1.517)	0.593	1.171 (0.793–1.731)	0.427
Male	1.036 (0.880–1.220)	0.669	0.873 (0.792–0.963)	0.007
Rural residence (31)	0.597 (0.476–0.749)	< 0.001	1.159 (0.964–1.392)	0.116
Primary source of health insurance		< 0.001		0.061
Medicare	0.691 (0.546–0.877)		1.042 (0.872–1.245)	
Medicaid	1.060 (0.781–1.437)		1.167 (0.906–1.503)	
Commercial	1.0 (ref)		1.0 (reference)	
Uninsured	0.485 (0.299–0.788)		1.489 (1.100–2.015)	
Source of infection (28)				
Pneumonia	0.686 (0.569–0.828)	< 0.001	0.647 (0.580–0.721)	< 0.001
Urinary tract infection	0.554 (0.436–0.706)	< 0.001	0.320 (0.277–0.371)	< 0.001
Cellulitis and soft tissue infection	0.876 (0.646–1.187)	0.392	0.353 (0.277–0.453)	< 0.001
Comorbidities (Elixhauser methodology) (30)				
Congestive heart failure	1.170 (0.963–1.420)	0.114	1.315 (1.177–1.470)	< 0.001
Valvular heart disease	1.555 (1.190–2.034)	0.001	1.012 (0.844–1.215)	0.894
Peripheral vascular disease	1.359 (1.066–1.733)	0.013	1.427 (1.227–1.659)	< 0.001
Hypertension	1.246 (1.050–1.479)	0.012	0.736 (0.666–0.814)	< 0.001
Neurologic disorders	0.983 (0.767–1.260)	0.891	1.138 (0.988–1.312)	0.074
Chronic pulmonary disease	1.035 (0.862–1.243)	0.710	1.128 (1.012–1.257)	0.029
Diabetes mellitus with complications	0.995 (0.821–1.207)	0.962	0.800 (0.706–0.907)	< 0.001
Renal failure	1.019 (0.838–1.239)	0.852	0.956 (0.850–1.074)	0.445
Liver disease	1.689 (1.273–2.241)	< 0.001	1.848 (1.505–2.268)	< 0.001
Metastatic cancer	2.275 (1.607–3.220)	< 0.001	2.052 (1.630–2.583)	0.045
Top-decile sepsis volume hospital (per 10 miles)	0.756 (0.722–0.793)	< 0.001	0.979 (0.960–0.999)	0.045
Rural hospital bypass	NA	NA	1.255 (1.027–1.535)	0.027

NA = not applicable, OR = odds ratio.

hospital bypass approximates the 7.6% per hour increased mortality associated with antibiotic delays previously reported by Kumar et al (26) With an average additional distance to first hospital of 51 miles in rural bypass patients, it seems possible that delays in antimicrobial therapy and resuscitation could explain much of the mortality decrement in patients who bypass rural EDs.

Third, the differences in transfer patterns between those who bypass rural hospitals are interesting and may inform our understanding of rural sepsis networks. Those patients who present to rural hospitals are often transferred from the ED to a high-volume tertiary center. Interestingly, though, many who drive to a top-decile sepsis volume hospital are also transferred to a higher volume center. The difference in these groups is that those who bypassed rural hospitals and sought care at larger hospitals were typically admitted to the hospital and were subsequently transferred from inpatient status, whereas those who presented to rural hospitals were transferred from the ED. That is an important distinction, because even among transferred patients, mortality is 21% higher in those transferred from inpatient status than those transferred from the ED. Presenting to a rural ED and receiving timely sepsis therapy prior to being transferred may be preferable to presenting to a larger hospital that still may ultimately require transfer, but for which the transfer may be delayed for inpatient admission. In this way, commercial insurance may actually be associated with delays in care, similar to that observed in the trauma literature (48).

TABLE 3. Instrumental Variables Model Predicting Hospital Mortality, Using an Instrument of Distance to a Top-Decile Sepsis Volume Hospital

| Factor	Naive Model (Ordinary Least Squares)		Instrumental Variable: Two-Stage Least Squares[a] (Linear)	
	β (95% CI)	p	β (95% CI)	p
Rural hospital bypass	0.061 (0.032–0.090)	< 0.001	0.056 (0.022–0.089)	0.001
Interhospital transfer	0.097 (0.082–0.112)	< 0.001	0.075 (0.005–0.144)	0.034
Age, per decade increase	0.023 (0.018–0.029)	< 0.001	0.022 (0.013–0.030)	< 0.001
Non-White	0.018 (−0.036 to 0.071)	0.523	0.018 (−0.035 to 0.072)	0.503
Male	−0.019 (−0.032 to −0.006)	0.004	−0.019 (−0.032 to −0.006)	0.004
Rural residence (31)	0.021 (−0.002 to 0.045)	0.073	0.020 (−0.003 to 0.044)	0.094
Insurance type				0.101
Medicare	0.014 (−0.009 to 0.037)	0.100	0.012 (−0.012 to 0.036)	
Medicaid	0.024 (−0.009 to 0.057)		0.023 (−0.012 to 0.036)	
Commercial	0 (reference)		0 (reference)	
Uninsured	0.050 (0.008–0.091)		0.051 (0.009–0.093)	
Source of infection (28)				
Pneumonia	−0.044 (−0.059 to −0.029)	< 0.001	−0.048 (−0.068 to −0.028)	< 0.001
Urinary tract infection	−0.118 (−0.135 to −0.101)	< 0.001	−0.123 (−0.144 to −0.101)	< 0.001
Cellulitis and soft tissue infection	−0.110 (−0.136 to −0.084)	< 0.001	−0.113 (−0.140 to −0.085)	< 0.001
Comorbidities (Elixhauser methodology) (30)				
Congestive heart failure	0.032 (0.017–0.047)	< 0.001	0.033 (0.018–0.049)	< 0.001
Valvular heart disease	−0.007 (−0.033 to 0.018)	0.571	−0.005 (−0.031 to 0.022)	0.727
Peripheral vascular disease	0.039 (0.017–0.061)	< 0.001	0.042 (0.018–0.066)	< 0.001
Hypertension	−0.051 (−0.064 to −0.037)	< 0.001	−0.048 (−0.063 to −0.033)	< 0.001
Neurologic disorders	0.019 (0.001 to −0.038)	0.045	0.019 (−0.001 to 0.038)	0.052
Chronic pulmonary disease	0.004 (−0.010 to 0.019)	0.565	0.007 (−0.010 to 0.024)	0.407
Diabetes mellitus with complications	−0.032 (−0.047 to −0.016)	< 0.001	−0.031 (−0.47 to −0.015)	< 0.001
Renal failure	−0.015 (−0.030 to 0.001)	0.054	−0.013 (−0.029 to 0.003)	0.119
Liver disease	0.091 (0.060–0.123)	< 0.001	0.093 (0.061–0.124)	< 0.001
Metastatic cancer	0.102 (0.067–0.138)	< 0.001	0.105 (0.068–0.141)	< 0.001

OR = odds ratio.

[a]Instrumental variables model F-statistic = 623.5.

The naive model is the linear regression model without using the instrumental variables approach.

So how can these findings be used to improve sepsis care? First, this study is the first to observe how low the rate of rural hospital bypass is among patients with sepsis. This finding is important, because it suggests that rural critical access hospitals are an important consideration in developing rural sepsis networks. Most patients in rural America receive sepsis care in these hospitals, so the need for rural sepsis protocols and rural hospitals' influence on clinical outcomes cannot be discounted. It also raises important questions on how rural care can be substituted in areas where rural hospitals are closing. Second, although many regionalization systems have been designed to bypass rural hospitals to achieve rapid regionalization for patients with trauma and ST-elevation myocardial infarction (8, 49, 50), these regionalization strategies may be inappropriate for sepsis care. In contrast to conditions where specific interventions are only available in tertiary hospitals, sepsis care can be delivered in rural EDs, and these interventions appear to be important. Finally, these data highlight the importance of accurate risk stratification among patients who are not immediately transferred. Many patients admitted to even a top-decile hospital are ultimately transferred, but they are often admitted to inpatient status first. Those patients admitted as
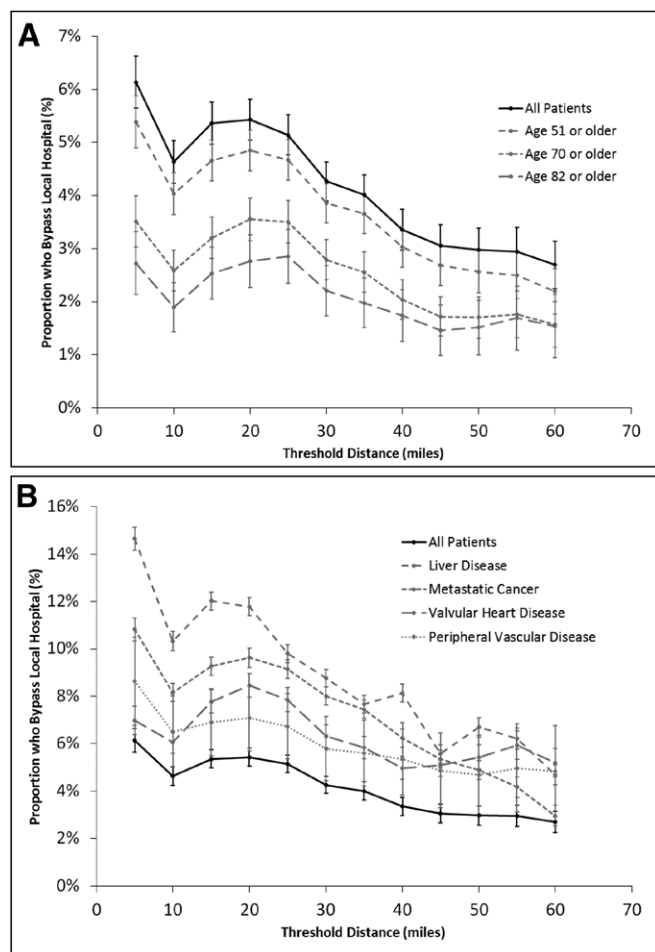
Figure 2. Rate of rural hospital bypass in severe sepsis or septic shock, stratified by additional travel distance. **A,** Older patients are less likely to bypass local rural hospitals than younger patients. **B,** Patients with significant comorbidities were more likely to bypass local rural hospitals.

inpatients and subsequently transferred have higher mortality than those transferred immediately, so the ability to accurately identify patients who benefit from tertiary care early may also improve sepsis survival.

This study has several limitations. The administrative data employed for the study are retrospective data and are subject to error in classifying and coding the information. Specifically, part of the increased prevalence of sepsis over this time period is related to improvements in medical coding, and initiatives to improve the coding of major comorbid conditions over this period could have increased the apparent prevalence of these conditions over time. We do not expect, however, that those changes in coding sepsis or comorbid diagnoses introduced bias, because these efforts have been in place nationally over the same period. We are unable to determine why patients chose to bypass their local hospital, and many may have chosen to seek care in a tertiary hospital because of health insurance or prior care for chronic medical conditions. In addition, we do not know the transportation mode used by patients to arrive at their particular hospital. Patients arriving by ambulance may not have participated in destination decision-making, and EMS services may have had preselected receiving hospitals

within their emergency response area. Although we are using comparative effectiveness techniques to understand how decision-making influences outcomes, our observational design only allows us to identify association rather than causation. Finally, we used objective covariates as part of the data analysis, but we do not have any data regarding patients' subjective thoughts and impressions, which may influence not only the hospitals where they choose to seek care, but also the reasons why they choose to be seen in those hospitals.

CONCLUSION

Rural hospital bypass is rare among those presenting to EDs with severe sepsis or septic shock. Patients who bypass rural EDs are younger, more likely to have commercial insurance, and have more medical comorbidities than those who present to rural hospitals. Distance to a top-decile sepsis volume hospital strongly predicts whether patients will bypass local hospitals to seek care in a larger hospital. Even when adjusting for measured and unmeasured confounders using an instrumental variable model, rural hospital bypass continues to be associated with higher mortality. Future research should better elucidate the role of rural EDs in caring for patients with sepsis, defining prospective criteria for transfer to regional sepsis centers, and providing prehospital providers guidance on centers most appropriate for caring for patients with severe sepsis prospectively.

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