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TITLE: Rural-urban differences in in-hospital mortality among admissions for end-stage liver disease in the United States

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Abstract (Word count: 250)

Background: Access to quality hospital care is a persistent problem for rural patients. Little is known about rural-urban disparities in in-hospital outcomes for end-stage liver disease (ESLD) patients. We aimed to determine whether rural ESLD patients experienced higher in-hospital mortality than urban patients, and whether disparities were attributable to the rurality of the patient or the center.

Methods: This was a retrospective study of admissions in the National Inpatient Sample, a population - based sample of hospitals in the United States. Admissions were included if they were from adult patients that had an ESLD-related admission defined from ICD-9 codes between January 2012 and December 2014. The primary exposures of interest were patient-level rurality and hospital-level rurality. The main outcome was in-hospital mortality. We stratified our analysis by disease severity score.

Results: After accounting for patient- and hospital-level covariates, ESLD admissions to rural hospitals in every category of disease severity had significantly higher odds of in-hospital mortality than admissions to urban hospitals; those with moderate or major risk of dying had more than twice the odds of in-hospital mortality (OR for moderate: 2.41, 95% CI: 1.62, 3.59; OR for major: 2.49, 95% CI: 1.97, 3.14). There was no association between patient-level rurality and mortality in adjusted models.

Conclusions: ESLD patients admitted to rural hospitals had an increased odds of in-hospital mortality compared to those admitted to urban hospitals; differences were not attributable to patient-level rurality. Our results suggest that interventions to improve outcomes in this population should focus on the health systems level.

Keywords: rural; ESLD; mortality; hospital

Introduction:

Patients with end-stage liver disease (ESLD) are often critically ill and require hospital admission for the management of complications. Consistent with a general trend of improvement in outcomes across other common chronic conditions[1-3], there has been a substantial reduction in in-hospital mortality among cirrhotic patients over the past decade[4,5]. This trend has been attributed to improved medical care aimed at prolonging life among cirrhotic patients and increased attention to health care delivery, including quality improvement initiatives[6].

Characteristics of the treating hospital play a large role in the outcomes of cirrhotic patients. In-patient mortality varies substantially among hospitals[7], and is partially attributable to differences in resource intensity at the hospital level[8]. Little is known about treatment outcomes in rural hospitals, where outcomes for other conditions – such as acute myocardial infarction and congestive heart failure - are known to be inferior[9]. The quality of rural hospital care is particularly relevant for patients with ESLD, as rural areas experience a disproportionate burden of ESLD mortality[10]. Improving outcomes for these patients requires consideration of both the patient- and health systems-level factors that affect care in rural areas.

To clarify the role of hospital setting on outcomes among ESLD patients, we used national-level hospital admissions data to examine whether rural ESLD patients experienced higher in-hospital mortality than urban patients. We also sought to discern whether observed disparities were primarily attributable to the rurality of the patient or to the center. Finally, we examined patterns of intensity of care that may potentially explain observed differences in outcomes.

Methods:

Data Source

This study was a secondary analysis of the 2012-2014 National Inpatient Sample (NIS), collected as a part of the Healthcare Cost and Utilization Project (HCUP) at the Agency for Healthcare Research and Quality. The NIS is a 20-percent stratified random sample of discharge records from general, community, and academic medical centers in the U.S. from 46 participating states; patients admitted to long-term care or rehabilitation facilities are not represented in the NIS. NIS data can be weighted to represent national estimates of health care utilization, access, charges, quality, and outcomes[11].

Study Population

The unit of analysis was hospital admission. Admissions were classified on the basis of ICD-9 diagnosis codes into three groups: cirrhosis (571.2, 571.5), portal hypertensive complications (portal hypertension [572.3], ascites [78959], hepatic encephalopathy [572.2], upper gastrointestinal bleed [456.0, 456.2, 578.0, 578.1, 578.9], or hepatorenal syndrome [572.4]), or primary liver tumor (155.0). Admissions were considered ESLD-related if they met one of three criteria: 1) primary diagnosis of cirrhosis, with a secondary diagnosis of portal hypertensive complications, 2) primary diagnosis of portal hypertensive complications, with a secondary diagnosis of cirrhosis, or 3) primary liver tumor as either the primary or secondary diagnosis. This algorithm has been previously shown to have a high positive predictive value for identifying ESLD patients[12]. Admissions were included if they were from adult patients (over 18 years of age) that had an ESLD-related admission between January 1st, 2012 and December 31st, 2014.

Study Variables

The primary outcome was in-hospital mortality, obtained from the discharge disposition of the patient. Patients with the outcome were those who died while admitted to the hospital. Patients without the outcome were alive at the time of discharge, even if they died outside of the hospital later. As a secondary outcome, we used ICD-9 procedural codes to determine whether an admission had a paracentesis (549.1) or endoscopy (451.3, 441.3, 422.3, 423.3) performed. Paracentesis and endoscopy serve diagnostic and therapeutic roles in ESLD patients with suspected peritonitis and gastrointestinal bleeding.

The primary exposures of interest were patient-level rurality, assessed using the county of patient residence, and hospital-level rurality. Patient rurality was assessed using the National Center for Health Statistics classification scheme for counties, and dichotomized to rural counties (micropolitan or non-core counties) and urban counties (counties in metropolitan areas of greater than 50,000). Hospital rurality was based on the Core Based Statistical Area (CBSA) of the hospital. Hospitals with a CBSA type of micropolitan or non-core were considered rural, while urban non-teaching and teaching hospitals were collapsed into one urban category. We assessed whether this affected results in a sensitivity analysis that compared rural hospitals and urban, non-teaching hospitals to urban teaching hospitals.

As patients with more severe disease tend both have a higher risk of mortality and to self-select or be transferred into hospitals with more resources, we stratified our analysis by disease severity in order to account for this potential bias. Disease severity was classified according to the All Patient Refined diagnosis-related group (APR-DRG) risk of mortality scheme, developed for HCUP databases and previously found to be the strongest predictors of in-hospital mortality among cirrhosis admissions[13]. The APR-DRG is a four-category scale (1 = "Minor risk of dying", 2 = "Moderate risk of dying", 3 = "Major risk of dying", 4 = "Extreme risk of dying"). Patient-level covariates collected at the time of hospital admission included age, sex, race, primary payer, zip-code level income, Elixhauser comorbidity index, and whether the patient was transferred into the hospital. Hospital-level covariates included region and number of beds.

Statistical Analyses

We used the provided survey weights for NIS to account for the stratified sampling. Descriptive statistics for our population, including means, medians, and proportions, were calculated. Bivariate analyses were used to compare discharge-level categorical variables by patient-level and hospital-level rurality. We used multivariable logistic regression to estimate the association between rurality and in-hospital mortality, accounting for patient-level and hospital-level factors. Generalized estimating equations (GEE) were used to account for correlations between patients in the same hospitals. We chose to use GEE since it is considered an appropriate method to obtain the average effect of both patient- and hospital-level covariates on an outcome in a population in the presence of correlated data[14]. All models were stratified by APR-DRG mortality risk group. Due to our interest in identifying the relative importance of patient-level and hospital-level rurality, we examined effects one at a time. First, we separately estimated the crude association between hospital rurality (Model 1A) and patient rurality (Model 1B) with in-hospital mortality. Second, we included both hospital rurality and patient rurality in the model (Model 2). Finally, we included all identified patient- and hospital-level covariates in a fully adjusted model (Model 3). To accomplish our secondary aim, we used Chi-square tests to compare the frequency of receiving paracentesis, endoscopy, or either by hospital rurality. We then included paracentesis and endoscopy into the fully-adjusted model above to determine whether their inclusion explained the association between rurality and in-hospital mortality (Model 4). We conducted a complete case analysis; 8,685 patients (7.8%) were excluded for missing covariate or outcome information. All analyses were conducted in SAS 9.4.

Results:

We identified 111,044 ESLD-related admissions between January 1st, 2012 and December 31st, 2014. Demographic characteristics are provided in Table 1. Approximately 16% of ESLD admissions resided in a rural area (N = 17,559), while 8% of admissions were at a rural hospital (N = 8,992). Admissions were predominantly male (66%, N = 7372,839) and white (64%, N = 67,815), with a mean age of 60 (SD = 26 years). Medicare was the most frequent primary payer (43%, N = 47,478), followed by Medicaid (23%, N = 25,2089) and private insurance (22%, N = 24,332). Approximately one-third of ESLD admissions were patients who lived in zip codes in the lowest income quartile (33%, N = 36,073). The South was the most common hospital region of admissions (40%, N = 44,737), and most admissions were to large hospitals (61%, N = 67,596). Approximately 7% of ESLD admissions resulted in an in-hospital death (N = 7,178), and over half of the sample was at a major or extreme risk of dying as measured by the APR-DRG mortality risk classification (60%, N = 66,434) (Table 1).

Demographic characteristics varied by both hospital-level and patient-level rurality (Table 2). Over 90% of admissions to rural hospitals were patients that lived in rural areas, but over half of admissions among patients who lived in rural areas were to urban hospitals. Admissions to rural hospitals were more likely to be white (82% vs. 62%), have Medicare as the primary payer (51% vs. 42%), and live in zip codes in the lowest income quartile (54% vs. 32%). Over half of admissions to rural hospitals were in the South (52% vs. 39%). Admissions to rural hospitals were less likely to be at an extreme risk of dying (12% vs. 17%) or major risk of dying (38% vs. 43%). The crude difference in in-hospital mortality among admissions to rural hospitals was small (7% vs. 6%). Admissions to rural hospitals were more likely to be transferred to another short-term facility (7.8% vs. 2.7%) or to a skilled nursing facility (15.9% vs. 14.6%) than admissions to rural hospitals. Admissions to rural hospitals less likely than admissions to urban hospitals to have portal hypertension (27.7% vs. 37.8%) or a primary liver tumor (18.1% vs. 28.9%) but more likely to have hepatic encephalopathy (43.4% vs. 33.9%). Admissions to rural hospitals had a shorter mean length of stay than admissions to urban hospitals (4.4 days vs. 5.6 days). Demographic and clinical characteristics among patients living in rural areas were essentially identical to admissions to rural hospitals with the exception of disease severity, comorbidity score, and portal hypertensive complications; the distribution of these characteristics was similar between rural and urban patients.

Among rural patients, 47.6% were admitted to a rural hospital, and 52.4% were admitted to an urban hospital. Among rural patients, admissions to rural hospitals were more likely to have Medicaid (50.8% vs. 44.2%), to live in a zip code in the lowest quartile of income (56.0% vs. 53.3%) and to live in the Northeast (12.4% vs. 6.1%) than admissions to urban hospitals. There were substantial differences in admission location among rural patients by disease severity, with admissions to rural hosptials less likely to be at extreme (11.9% vs. 21.4%) or major (39.5% vs. 43.2%) risk of dying. Similar to the overall population, among rural patients those admitted to rural hospitals were less likely to have portal hypertension (27.5% vs. 41.7%) or a primary liver tumor (18.2% vs. 26.7%) but more likely to have hepatic encephalopathy (43.6% vs. 34.0%). While there was not a meaningful difference in length of stay between rural and urban patients (5.2 days vs. 5.6 days), among rural patients, those in rural hospitals had a shorter length of stay than those in urban hospitals (4.4 days vs. 5.9 days). Rural patients seen in rural hospitals had a lower comorbidity score than rural patients seen in urban hospitals (11.8 vs. 13.3).

In stratified bivariate analyses (Figure 2), hospital rurality was significantly associated with in-hospital mortality among every category of disease severity. Among admissions at minor, moderate, or major risk of dying, admissions to rural hospitals had double the proportion of in-hospital mortality (2% vs. 1%, 2% vs. 1%, 6% vs. 3%, respectively). Patient rurality was significantly associated with in-hospital mortality among every category of disease severity with the exception of those at extreme risk of mortality ($p = 0.86$). When limited to admissions to urban hospitals, there were no statistically significant differences in in-hospital mortality between rural and urban patients in any category of disease severity.

The multivariable logistic regression analyses examining the association between rurality and in-hospital mortality, accounting for other patient- and hospital-level covariates, are presented in Table 3. Model 1 presents the crude association of both hospital-level and patient-level rurality with in-hospital mortality. Rural admissions of either classification had significantly increased odds of in-hospital mortality than urban patients, with the exception of rural patients at an extreme risk of dying (OR: 0.99, 95% CI: 0.91, 1.08). In Model 2, we examined the association of hospital-level and patient-level rurality on in-hospital mortality together. Among patients at a minor risk of dying, there were no significant associations between rurality and in-hospital mortality. Among patients at a moderate or major risk of dying, admissions to rural hospitals had over twice the odds of experiencing in-hospital mortality as patients in urban hospitals (Moderate OR: 2.12; 95% CI: 1.47, 3.05; Major OR: 2.16, 95% CI: 1.75, 2.66); the association between patient-level rurality and in-hospital mortality was not significant (Moderate OR: 1.14, 95% CI: 0.82, 1.58; Major OR: 0.97, 95% CI: 0.82, 1.17).

In Model 3, after adjustment for age, race, sex, comorbidity index, insurance, zip code-level income, transfer status, region, and hospital bed size, there was a significant association between hospital rurality and in-hospital mortality in every stratum of disease severity. The strength of the association decreased as disease severity increased; admissions among patients with a minor risk of dying had nearly three times the odds of in-hospital mortality at rural hospitals than at urban hospitals (OR: 2.73, 95% CI: 1.20, 6.22). Admissions at rural hospitals at a moderate or major risk of dying had more than twice the odds of experiencing in-hospital mortality as admissions to urban hospitals (OR for moderate risk: 2.41, 95% CI: 1.62, 3.59; OR for major risk: 2.49, 95% CI: 1.97, 3.14). Among patients who were at an extreme risk of dying, admissions to rural hospitals had a 32% increased odds of in-hospital mortality compared to urban hospitals (95% CI: 1.11, 1.58), even after adjustment for patient- and hospital-level covariates. There were no significant associations between patient-level rurality and likelihood of in-patient hospital mortality in any strata of disease severity.

Table 4 presents the frequency of access to liver-disease specific procedures including paracentesis and endoscopy by hospital-level rurality, stratified by disease severity. For each procedure and in every strata of disease severity, with the exception of admissions at a minor risk of death, admissions to urban hospitals were statistically significantly more likely to have the procedure than admissions to rural hospitals. Inclusion of paracentesis and endoscopy to the fully-adjusted model only partially attenuated the association between hospital rurality and in-hospital mortality (Table 3, Model 4).

The attenuation was strongest for patients in the moderate (OR: 2.15, 95% CI: 1.43, 3.23) and major (OR: 2.29, 95% CI: 1.81, 2.89) risk categories.

In a sensitivity analysis, we compared rural admissions and urban non-teaching admissions to urban teaching hospitals, accounting for the covariates described above. In every strata of disease severity except for severe disease, admissions to rural hospitals were significantly more likely to experience in-hospital mortality than admissions to urban teaching hospitals (OR for minor risk: 2.82, 95% CI: 1.18, 6.74; OR for moderate risk: 2.73, 95% CI: 1.78, 4.19; OR for major risk: 2.39, 95% CI: 1.88, 3.04; OR for extreme risk: 1.15, 95% CI: 0.96, 1.38). Admissions to urban non-teaching hospitals also had a significantly higher likelihood of in-hospital mortality among patients at a moderate or major risk of dying, although the magnitude of the association was lower (OR for moderate risk: 1.89, 95% CI: 1.49, 2.42; OR for major risk: 1.28, 95% CI: 1.14, 1.45). We also conducted a sensitivity analysis to evaluate whether results differed among the Medicare population or after adjustment for portal hypertensive complications or primary liver tumor, and found no significant differences (data not shown).

To explore whether the effect of hospital location on mortality among rural patients could be explained by differences in referral patterns to urban hospitals (for example, if patients retained in rural hospitals were sicker or had lower socioeconomic status), we compared demographic and clinical characteristics between rural patients admitted to rural hospitals and rural patients admitted to urban hospitals (Supplementary Table 1). Rural patients admitted to rural hospitals were more likely to live in the lowest income zip codes (56.7% vs. 53.3%), have Medicare (50.8% vs. 44.2%), and be at minor (9.3% vs. 5.0%) or moderate (39.3% vs. 30.5%) risk of dying compared to rural patients admitted to urban hospitals. On average, rural patients admitted to rural hospitals were older (60.7 years vs. 58.8 years) but had a lower comorbidity index (11.8 vs. 13.3) compared to those admitted to urban hospitals. Based on these findings, it does not appear that rural patients in rural hospitals are not being referred to urban hospitals because of futility, as patients in rural hospitals have less severe disease (based on APR-DRG mortality risk) and similar comorbidity scores. Socioeconomic status could play a role in referral, as rural patients in rural hospitals had a higher proportion of patients in the lowest income zip codes, but the absolute difference between the two groups appears to be small and not likely to explain our findings.

Discussion:

In this analysis of a representative sample of ESLD admissions in the United States, we found that admission to a rural hospital, compared to an urban hospital, was associated with increased in-hospital mortality, independent of patient-level rurality and other covariates. This association was strongest among patients with moderate or major disease-severity scores on admission, who had more than twice the odds of experiencing in-hospital mortality as their urban counterparts, and was not explained by receipt of paracentesis or endoscopy. After accounting for hospital-level rurality, patient-level rurality was not significantly associated with in-hospital mortality in any strata of disease severity. Our findings are relevant to the 1,800 rural community hospitals in the United States[15], and imply that interventions to improve outcomes among rural ESLD patients may need to focus on intensity or quality of care at the health system level. As nearly half of the ESLD admissions in our study were covered by Medicare, and similar associations between hospital rurality and mortality were observed in the Medicare population, our findings may also be relevant to the Centers for Medicare and Medicaid Services.

Rural areas in the U.S. have experienced higher mortality rates and excess death for the past two decades[16]. While prevalence estimates for ESLD are unavailable, rural areas have higher age-adjusted ESLD mortality rates than urban areas[10]. However, in our study, rural patients made up 15.3% of ESLD admissions despite making up 19.3% of the U.S. population. This underrepresentation in admissions, combined with an overrepresentation in mortality, signals that that there may be a disparity in access to care for rural ESLD patients that contributes to poor outcomes in this population.

Our results offer an important insight into care and outcomes for patients with cirrhosis. Potential reasons for excess mortality in rural hospitals include low volume of invasive procedures[17,18] and less access to subspecialists such as gastroenterologists, which has been associated with poor outcomes for liver disease patients.[19-21] One immediate implication of our findings is that liver disease patients benefit from care at urban centers, either due to resources or personnel which are more commonly available than in rural settings. Previous studies have shown that rural patients prefer hospitals with greater service capacity[22], and are more likely to “bypass” closer, rural hospitals for urban hospitals if they have acute medical conditions[23], such as decompensated cirrhosis. While expedited transfer of ESLD patients to urban centers could potentially reduce mortality risks in the short term, such a policy would be costly and risk further partitioning quality care away from rural communities where hospital closures already threaten access to care[24]. A more inclusive and ultimately effective approach would be to leverage technologies such as telemedicine, which has been applied to other facets of rural healthcare delivery including preventing emergency room transfers[25], providing pediatric subspecialty care[26], and providing time-sensitive care to stroke patients[27]. Clinical decision support systems[28] and regional collaborations and support networks[29] have also been successfully implemented to improve quality of care and in rural hospitals. One such pilot program using Veterans Health Administration referrals to a central subspecialty service found similar survival with telepresence consultations and in-person visits, and a marked reduction in patient mortality across early and late stage liver disease in propensity-matched cohorts without any visit, particularly for rural patients[30]. Subspecialty care through dispersed networks have shown telemedicine and spoke-and-hub referral systems to be highly cost effective in other disease settings[31-33]. Another strategy to contain costs and facilitate patient referral and follow-up would be the employment of patient navigators, who have been proven to reduce unnecessary emergency department visits and readmissions in other settings[34,35].

Our findings support those of previous studies that demonstrated the importance of hospital-level characteristics to outcomes among cirrhosis patients[7,8]. Mellinger et al. found that admissions to rural hospitals had 27% higher odds of in-hospital mortality than admissions to urban hospitals after accounting for patient-level factors, although in their cohort, this was effect not statistically significant.[7] However, this analysis was restricted to one year of data from a "high volume cohort" of hospitals, potentially skewing the association between rurality and mortality due to differential exclusion of rural hospitals with less experience treating cirrhotic patients and higher in-hospital mortality rates. Our results are also consistent with findings from other diseases, including rural-urban disparities in the quality of care and mortality rates for cardiopulmonary conditions including acute myocardial infarction, pneumonia and congestive heart failure.[9,36] Disparities in inpatient care quality in the rural setting reflect environmental considerations that extend beyond the hospital itself[37], but key contributors within the health system framework are lesser engagement of multidisciplinary teams outside of teaching and high-volume centers[38], less timely access to procedural specialists such as interventional radiologists[39], and even structural considerations such as the size and experience of health care informatics and administrative staff[40,41]. Although the manifold drivers of rural disparity are challenging, they represent numerous domains in which quality improvement projects may identify and ameliorate excess risks in this population.

This analysis is constrained by limitations common to retrospective review of administrative data. Patient-specific risks are not captured in registry data, so that considerations such as clinical stability for transfer and proximity of the admitting hospital to a tertiary referral center cannot be adjusted for in models. As a sample of admissions, the NIS lacks any patient identifier to follow patients across admissions. The re-design of the NIS after 2011 does not allow for hospital identification or linkage to other datasets. This lack of hospital identifiers restricts our ability to explore hospital-specific characteristics such as care processes that might differ between rural and urban hospitals and account for the observed disparity, as well as factors that occur before the admission (such as access to primary or specialty care). Because of these limitations, NIS data must be taken as a stand-alone depiction of hospitalization, with limited context and no ability to imply causality. Despite these constraints, however, NIS represents the largest all-payer inpatient care database in the United States, containing data on more than seven million hospital stays. As a result, our nationally representative sample of patients with end stage liver disease offers insights into patterns of disease and care at a level not obtainable through other data sources.

In conclusion, end-stage liver disease patients admitted to rural hospitals had an increased odds of in-hospital mortality compared to those admitted to urban hospitals, particularly among patients with lower APR-DRG expected mortality scores. After accounting for hospital rurality, patient-level rurality was not associated with increased in-hospital mortality. These findings suggest that excess mortality associated with rural hospitals may not be due to patient-level factors, but rather features of the admitting center. Further research is needed to identify potential hospital-level mediators and targets for improved care of liver disease patients in rural settings.

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Table 1. Demographic characteristics of end-stage liver disease (ESLD) hospital admissions in the National Inpatient Sample, United States, 2012 – 2014.

	Frequency (N = 111,044)	Weighted Frequency (N = 555,220)	%
Hospital rurality			
Rural	8,992	44,960	8.1
Urban	102,052	510,260	91.9
Patient rurality			
Rural	17,559	87,795	15.9
Urban	92,657	463,285	84.1
Missing	828		
Sex			
Male	72,839	364,195	65.6
Female	38,191	190,955	34.4
Missing	14		
Race			
White	67,815	339,075	63.8
Black	11,142	55,710	10.5
Hispanic	18,776	93,880	17.7
Asian/Pacific Islander	3,274	16,370	3.1
Native American	1,476	7,380	1.4
Other	3,820	19,100	3.6
Missing	4,741		
Primary payer			
Medicare	47,478	237,390	42.9
Medicaid	25,089	125,445	22.6
Private insurance	24,332	121,660	22.0
Self-pay	8,591	42,955	7.8
No charge	796	3,980	0.7
Other	4,464	22,320	4.0
Missing	294		
Median household income			

$1 - 38,999	36,073	180,365	33.5
$39,000 - 47,999	28,388	141,940	26.4
$48,000 - 63,999	24,389	121,945	22.6
$64,000+	18,884	94,420	17.5
Missing	3,310		
Hospital region			
Northeast	20,600	103,000	18.6
Midwest	20,491	102,455	18.5
South	44,737	223,685	40.3
West	25,216	126,080	22.7
Hospital bed size			
Small	14,136	70,680	12.7
Medium	29,312	146,560	26.4
Large	67,596	337,980	60.9
APR-DRG mortality risk			
Minor risk of dying	7,122	35,610	6.4
Moderate risk of dying	37,477	187,385	33.8
Major risk of dying	47,565	237,825	42.8
Severe risk of dying	18,869	94,345	17.0
Missing	11		
Died in hospital			
Yes	7,178	35,890	6.5
No	103,823	519,115	93.5
Missing	43		
	Mean	**Standard Deviation**	
Age	59.5	26.6	
Einhauser index	12.9	25.0	

Table 2. Demographic characteristics of end-stage liver disease admissions stratified by hospital-level and patient-level rurality, National Inpatient Sample, United States, 2012 – 2014.

	Hospital rurality					Patient rurality					Among rural patients				
	Rural Hospital		Urban Hospital			Rural Patient		Urban Patient			Rural Hospital		Urban Hospital		
	N	%	N	%	p	N	%	N	%	p	N	%	N	%	p
Hospital rurality										<0.01					
Rural						8,356	47.6	623	0.7						
Urban						9,203	52.4	92,034	99.3						
Patient rurality					<0.01										
Rural	8,356	93.1	9,203	9.1											
Urban	623	6.9	92,034	90.9											
Sex					<0.01					<0.01					<0.01
Male	5,626	62.6	67,203	65.9		11,269	64.2	60,928	65.8		5,224	62.5	6,045	65.7	
Female	3,356	37.4	34,835	34.1		6,289	35.8	31,717	34.2		3,132	37.5	3,157	34.3	
Race					<0.01					<0.01					<0.01
White	6,853	82.2	60,962	62.2		13,028	80.4	54,424	61.0		6,330	82.0	6,698	78.9	
Black	479	5.7	10,663	10.9		892	5.5	10,115	11.3		442	5.7	450	5.3	
Hispanic	566	6.8	18,210	18.6		1,262	7.8	17,324	19.4		528	6.8	734	8.7	
Asian/Pacific Islander	65	0.8	3,209	3.3		114	0.7	3,134	3.5		63	0.8	51	0.6	
Native American	237	2.8	1,239	1.3		589	3.6	886	1.0		222	2.9	367	4.3	
Other	142	1.7	3,678	3.8		319	2.0	3,403	3.8		133	1.7	186	2.2	
Primary payer					<0.01					<0.01					<0.01
Medicare	4,516	50.4	42,962	42.2		8,283	47.4	38,996	42.2		4,230	50.8	4,053	44.2	

Medicaid	1,852	20.7	23,237	22.8		3,524	20.2	21,271	23.0		1,724	20.7	1,800	19.7	
Private insurance	1,552	17.3	22,780	22.4		3,405	19.5	20,804	22.5		1,426	17.1	1,979	21.6	
Self-pay	652	7.3	7,939	7.8		1,344	7.7	7,120	7.7		594	7.1	750	8.2	
No charge	41	0.5	755	0.7		80	0.5	704	0.8		41	0.5	39	0.4	
Other	344	3.8	4,120	4.0		848	4.9	3,545	3.8		307	3.7	541	5.9	
Median household income					<0.01					<0.01					0.01
$1 - 38,999	4,697	54.2	31,376	31.7		9,251	54.6	26,822	29.5		4,520	56.0	4,731	53.3	
$39,000 - 47,999	2,921	33.7	25,467	25.7		5,733	33.8	22,655	25.0		2,688	33.3	3,045	34.3	
$48,000 - 63,999	859	9.9	23,530	23.8		1,687	10.0	22,702	25.0		738	9.2	949	10.7	
$64,000+	195	2.2	18,689	18.9		271	1.6	18,613	20.5		120	1.5	151	1.7	
Hospital region					<0.01					<0.01					<0.01
Northeast	1,161	12.9	19,439	19.0		1,594	9.1	18,674	20.2		1,032	12.4	562	6.1	
Midwest	1,912	21.3	18,579	18.2		4,234	24.1	16,221	17.5		1,829	21.9	2,405	26.1	
South	4,706	52.3	40,031	39.2		9,338	53.2	35,146	37.9		4,330	51.8	5,008	54.4	
West	1,213	13.5	24,003	23.5		2,393	13.6	22,616	24.4		1,165	13.9	1,228	13.3	
Hospital bed size					<0.01										<0.01
Small	995	11.1	13,141	12.9		1,735	9.9	12,336	13.3		917	11.0	818	8.9	
Medium	1,798	20.0	27,514	27.0		3,884	22.1	25,243	27.2		1,664	19.9	2,220	24.1	
Large	6,199	68.9	61,397	60.2		11,940	68.0	55,078	59.4		5,775	69.1	6,165	67.0	
APR-DRG mortality risk					<0.01					<0.01					<0.01
Minor risk of dying	830	9.2	6,292	6.2		1,237	7.0	5,825	6.3		781	9.4	456	5.0	
Moderate risk of dying	3,525	39.2	33,952	33.3		6,089	34.7	31,106	33.6		3,283	39.3	2,806	30.5	
Major risk of dying	3,570	39.7	43,995	43.1		7,272	41.4	39,945	43.1		3,300	39.5	3,972	43.2	
Severe risk of dying	1,067	11.9	17,802	17.4		2,957	16.8	15,774	17.0		992	11.9	1,965	21.4	

Died in hospital					0.02					<0.01					0.86
Yes	635	7.1	6,543	6.4		1,248	7.1	5,862	6.3		591	92.9	657	92.9	
No	8,353	92.9	95,470	93.6		16,302	92.9	86,761	93.7		7,761	7.1	8,541	7.1	
Discharge location					<0.01					<0.01					<0.01
Routine	4,763	53.0	60,768	59.6		10,104	57.6	54,914	59.3		4,409	52.8	5,695	61.9	
Transfer to short-term	702	7.8	2,760	2.7		884	5.0	2,561	2.8		649	7.8	235	2.6	
Transfer to SNF, ICF, other	1,427	15.9	14,933	14.6		2,525	14.4	13,748	14.8		1,353	16.2	1,172	12.7	
Home health	1,298	14.4	14,827	14.5		2,523	14.4	13,502	14.6		1,197	14.3	1,327	14.4	
AMA	148	1.7	2,032	2.0		248	1.4	1,888	2.0		140	1.7	108	1.2	
Died	635	7.1	6,543	6.4		1,248	7.1	5,862	6.3		591	7.1	657	7.1	
Portal hypertensive complication															
Portal hypertension	2,489	27.7	38,598	37.8	<0.01	6,139	35.0	34,645	37.4	<0.01	2,301	27.5	3,838	41.7	<0.01
Ascites	4,177	46.5	50,464	49.5	<0.01	8,593	48.9	45,654	49.3	0.42	3,860	46.2	4,733	51.4	<0.01
Hepatic encephalopathy	3,901	43.4	34,557	33.9	<0.01	6,775	38.6	31,476	34.0	<0.01	3,645	43.6	3,130	34.0	<0.01
Upper gastrointestinal bleed	1,652	18.4	17,347	17.0	0.01	3,212	18.3	15,627	16.9	<0.01	1,534	18.4	1,678	18.2	0.83
Hepatorenal syndrome	518	5.8	6,609	6.5	0.01	1,188	6.8	5,893	6.4	0.04	486	5.8	702	7.6	<0.01
Primary liver tumor	1,631	18.1	29,490	28.9	<0.01	3,984	22.7	26,839	29.0	<0.01	1,524	18.2	2,460	26.7	<0.01
	Mean	SD	Mean	SD	p	Mean	SD	Mean	SD	p	Mean	SD	Mean	SD	p
Length of stay, in days	4.4	4.5	5.6	6.9	<0.01	5.2	5.8	5.6	6.9	<0.01	4.4	4.4	5.9	6.7	<0.01
Age, in years	60.7	11.8	59.4	11.9	<0.01	59.7	11.8	59.5	11.9	0.04	60.7	11.8	58.8	11.8	<0.01
Comorbidity score	11.7	10.8	13.0	11.2	<0.01	12.6	11.0	12.9	11.2	<0.01	11.8	10.8	13.3	11.1	<0.01

Figure 1. Proportion of admissions for ESLD patients that died in the hospital, stratified by disease severity, hospital rurality, and patient rurality, National Inpatient Sample, 2012 – 2014.

	Model 1A/B [1]		Model 2[2]		Model 3[3]		Model 4[4]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Minor risk of dying								
Rural hospital	2.47	1.44, 4.22	1.35	0.63, 2.91	2.73	1.20, 6.20	2.67	1.18, 6.07
Urban hospital	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Rural patient	2.44	1.50, 3.96	1.99	1.00, 4.00	1.36	0.64, 2.92	1.36	0.64, 2.90
Urban patient	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Moderate risk of dying								
Rural hospital	2.34	1.82, 3.00	2.12	1.47, 3.05	2.39	1.61, 3.58	2.15	1.43, 3.23
Urban hospital	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Rural patient	1.8	1.44, 2.26	1.14	0.82, 1.58	1.05	0.72, 1.54	1.05	0.71, 1.55
Urban patient	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Major risk of dying								
Rural hospital	2.11	1.82, 2.44	2.16	1.75, 2.66	2.48	1.97, 3.14	2.29	1.81, 2.89
Urban hospital	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Rural patient	1.47	1.29, 1.66	0.97	0.82, 1.17	0.89	0.73, 1.10	0.91	0.74, 1.12
Urban patient	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Extreme risk of dying								
Rural hospital	1.15	1.00, 1.31	1.23	1.05, 1.45	1.32	1.01, 1.57	1.23	1.03, 1.47
Urban hospital	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Rural patient	0.99	0.91, 1.08	0.92	0.83, 1.02	0.91	0.81, 1.03	0.92	0.82, 1.05
Urban patient	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref

Table 3. Multivariable logistic regression examining effect of rurality on in-hospital mortality among admissions for end-stage liver disease, 2012 – 2014.

[1] Model includes either hospital-level or patient-level rurality.

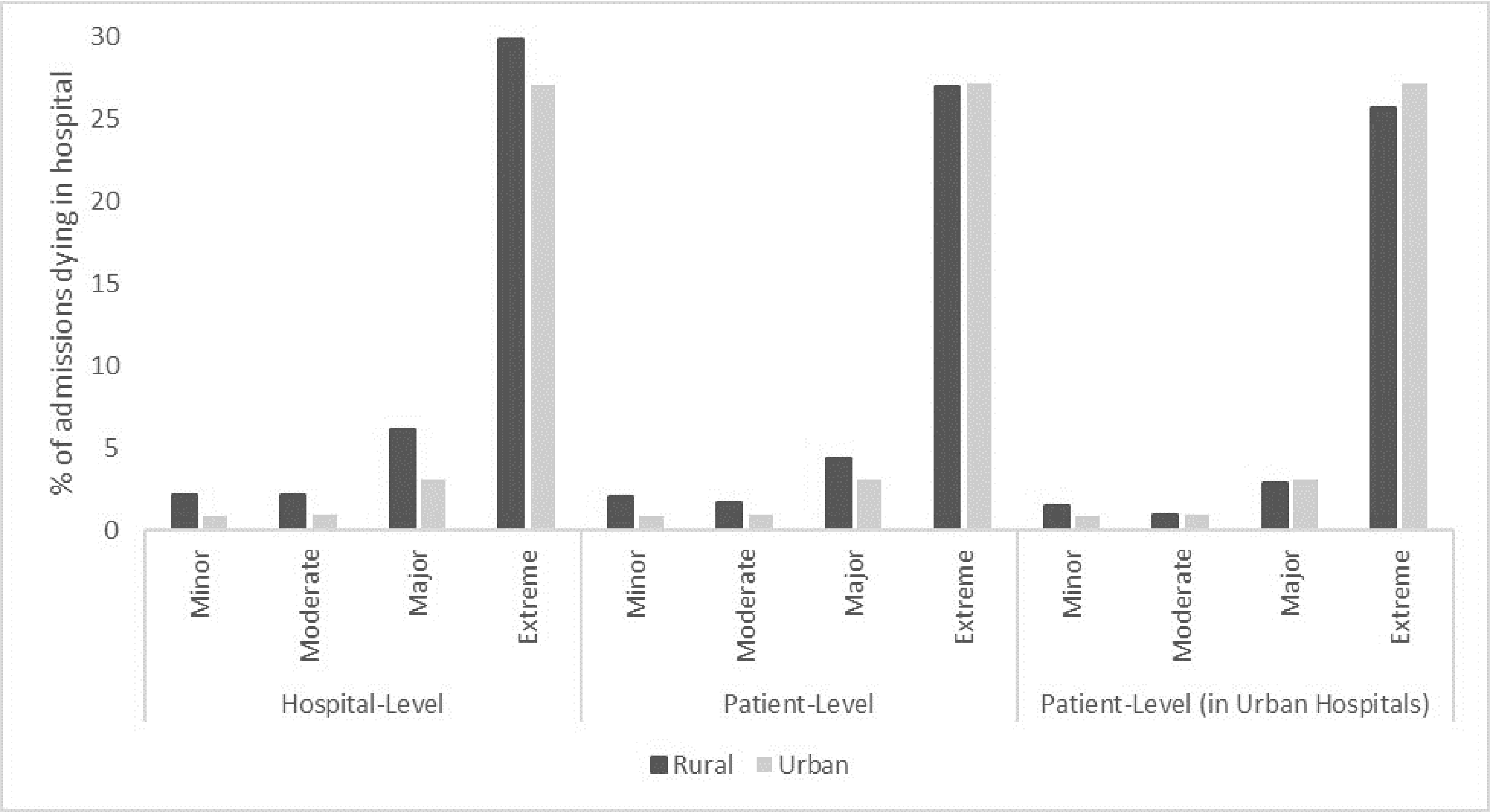
[2] Model includes both hospital-level and patient-level rurality.

[3] Model includes hospital-level rurality, patient-level rurality, age, gender, race, primary payer, income quartile, comorbidity score, transfer status, hospital bedsize, and hospital region.

[4] Model includes hospital-level rurality, patient-level rurality, age, gender, race, primary payer, income quartile, comorbidity score, transfer status, hospital bedsize, hospital region, receipt of paracentesis, and receipt of endoscopy.

Table 4. Receipt of procedures among admissions for end-stage liver disease by hospital rurality in the National Inpatient Sample, 2012 – 2014.

	Paracentesis					Endoscopy					Either				
	Rural		Urban			Rural		Urban			Rural		Urban		
	N	%	N	%	p-value	N	%	N	%	p-value	N	%	N	%	p-value
Minor risk of dying					0.50					0.02					0.06
Procedure	109	13.1	880	14.0		40	4.8	434	6.9		148	17.8	1300	20.7	
No procedure	721	86.9	5412	86.0		790	95.2	5858	93.1		682	82.2	4992	79.3	
Moderate risk of dying					<0.001					<0.001					<0.001
Procedure	957	27.1	11343	33.4		329	9.3	5545	16.3		1217	34.5	15703	46.3	
No procedure	2568	72.9	22609	66.6		3196	90.7	28407	83.7		2308	65.5	18249	53.7	
Major risk of dying					<0.001					<0.001					<0.001
Procedure	979	27.4	14634	33.3		662	18.5	10771	24.5		1516	42.5	22608	51.4	
No procedure	2591	72.6	29361	66.7		2908	81.5	33224	75.5		2054	57.5	21387	48.6	
Extreme risk of dying					<0.001					<0.001					<0.001
Procedure	361	33.8	7492	42.1		183	17.2	4622	26.0		498	46.7	10229	57.5	
No procedure	706	66.2	10310	57.9		884	82.8	13180	74.0		569	53.3	7573	42.5	



% of admissions dying in hospital
30
25
20
15
10
5
0
Minor
Moderate
Major
Extreme
Hospital-Level
Patient-Level
Patient-Level (in Urban Hospitals)
Rural
Urban