



Superior Performance of Teaching and Transplant Hospitals in the Management of Hepatic Encephalopathy from 2007 to 2014

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Abstract

Background and Aims: Hepatic encephalopathy is a liver disease complication with significant mortality and costs. The aim of this study was to evaluate the relative performance of facilities based on their teaching status and transplant capability by correlating their connections to mortality, cost, and length of stay from 2007 to 2014. **Methods:** The Nationwide Inpatient Sample database was utilized to collect information on (USA) American patients admitted with a primary diagnosis of hepatic encephalopathy from 2007–2014. Hospitals were placed into one of four categories using their teaching and transplant status. Using regression analysis, mortality, length of stay and cost adjusted rate ratios were calculated. **Results:** The study revealed that teaching transplant centers had a mortality risk ratio of 0.783 (95% confidence interval (CI): 0.750–0.819, $p < 0.001$). Blacks had the highest mortality risk ratio, of 1.273 (95%CI: 1.217–1.331, $p < 0.001$). Furthermore, teaching transplant hospitals had a cost rate ratio of 1.226 (95%CI: 1.214–1.238, $p < 0.001$) and a length of stay rate ratio of 1.104 (95%CI: 1.093–1.115, $p < 0.001$). **Conclusions:** It appears that admission to transplant facilities for hepatic encephalopathy is associated with reduced mortality but increased costs and longer stay independent of transplantation. Moreover, factors impacting black mortality should also be examined more closely. **Citation of this article:** Bodek D, Patel P, Ahlawat S, Orosz E, Nasereddin T, Pylsopoulos N. Superior performance of teaching and transplant hospitals in the management of hepatic encephalopathy from 2007 to 2014. *J Clin Transl Hepatol* 2018;6(4): 362–371. doi: 10.14218/JCTH.2017.00078.

Introduction

Hepatic encephalopathy is a debilitating condition that occurs in patients with decompensated cirrhosis, among other liver diseases. It is a neuropsychiatric syndrome for which symptoms may begin with subtle psychomotor changes and progress to confusion, somnolence, coma, and death.¹

Keywords: Disparities; Mortality; Cost; Length of stay; Hepatic encephalopathy. **Abbreviations:** CI, confidence interval.

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The admission and readmissions of these patients is known to have a substantial economic impact. Yearly expenditures related to chronic liver disease have risen to greater than 2 billion dollars annually, even as length of stay is in decline.^{2–4}

Given the pressures to provide more cost effective care in tandem with improved patient outcomes, we sought to further elucidate trends underlying admissions for which the primary diagnosis was hepatic encephalopathy and what affects costs, lengths of stay, and mortality in the USA. We explored the performance of centers based on their teaching status and transplant capabilities, grouping them into four categories with nontransplant nonteaching hospitals as the reference, while controlling for a number of additional demographic and clinical factors to assess whether teaching and transplant centers offer superior outcomes.

Methods

The National Inpatient Sample database⁵ captures about 20% of all admissions annually across the USA. It provides diagnosis codes, procedure codes, and demographic data along with a number of other variables, including length of stay, charges, and hospital-specific data. The *International Classification of Diseases, Ninth Edition, Clinical Modification* codes⁶ were utilized to identify procedures and diagnoses.

Inclusion criteria

Only patients aged 18 or older with a primary diagnosis of either hepatic encephalopathy or hepatitis with coma (572.2, 70.0, 70.6, 70.20–23, 70.41–44, 70.49, 70.71) were selected.

Exclusion criteria

Patients with primary hepatic malignancy (155.0), metastatic disease to the liver (197.7), or cholangiocarcinoma (155.1, 156.1) were excluded. For mortality analysis, those with missing information on death were excluded.

Other included variables

The other factors utilized in logistic regression analysis included a hospital's teaching and transplant status (capability was defined as a center having performed at least one documented transplant in that year), receipt of a liver transplant (50.5, 50.51, 50.59), race, age, gender, region, income

quartile by zip code, each Elixhauser comorbidity marker (as seen in Table 1),⁷ excluding liver issues (added via Statistical Analysis Software, University Edition⁸), transfer status, hospital size, and payer.

For those categorical variables, the reference or baseline variables were as follows: nonteaching nontransplant hospitals; Caucasian; age 18 to 35 years; female; Northeast region; bottom income quartile based on zip code; nontransfer patient; small hospital size; and insured by Medicare.

Additional acute issues were also utilized including hepatorenal syndrome (572.4), variceal bleeding (456.0 and 456.20), spontaneous bacterial peritonitis (567.23), and pneumonia (480.xx–486.xx and 487.0). Sepsis (995.91 and 995.92) and septic shock (785.52) were also included as a categorical variable. Weighting as provided by the Healthcare Cost and Utilization Project was utilized. A full listing of the prevalence of these independent variables in each hospital subtype can be seen in Table 2. Independent variables with less than 20 results are not shown as per the data use agreement in order to avoid identification of any patients.

Statistical analysis

To assess impact on cost and length of stay, negative binomial regression was performed. Disposition was utilized as a categorical variable. Length of stay, paracentesis (54.91), esophagogastroduodenoscopy without biopsy (45.13), and transjugular intrahepatic portosystemic shunt (39.1) were also included in cost analysis. Cost was calculated from charge data as provided by the Healthcare Cost and Utilization Project and adjusted for inflation.⁹

For statistical analysis, a p value <0.05 was considered significant. Pearson correlation tables were utilized to avoid significant collinearity.

Etiologies of cirrhosis

Diagnosis of hepatitis C (070.44, 070.51, 070.71, V0262, 070.7, 07054, 070.41, 070.51), hepatitis B (070.21, 070.2, 070.21–23, 070.3–33, V0261), hepatitis A (070.0–1), hepatitis E (070.43, 070.53), nonalcoholic steatohepatitis (571.8), Wilson's disease (275.1), hemochromatosis (275, 275.01–03, 275.09), autoimmune hepatitis (571.42), primary sclerosing cholangitis (576.1), primary biliary cholangitis (571.6), evidence of alcohol abuse (291.0–5, 291.8–82, 281.89–90, 303.0, 303.9–93, 571.0–3), cryptogenic cirrhosis (571.5), and other viral hepatitis (573.1, 573.3) were also noted. To identify nonalcoholic steatohepatitis as the definitive cause, only those cases lacking any of the other aforementioned markers were utilized. For alcohol- and hepatitis C-related admissions, overlapping potential causes were allowed.

Results

The most notable finding was the lower mortality risk ratio for teaching transplant centers of 0.783 (95% confidence interval (CI): 0.750–0.819, $p < 0.001$) as seen in Fig. 1. Nontransplant teaching centers had a ratio suggestive of lower mortality, at 0.959 (95%CI: 0.929–0.991, $p < 0.001$), while transplant nonteaching status had the lowest ratio at 0.698 (95%CI: 0.542–0.899, $p < 0.001$). Granted, the number of cases present at these nonteaching transplant facilities were limited, at only 1,771 out of the total of 547,177. It should be noted that those who received a liver transplant had a

Table 1. Elixhauser comorbidity variables

Diagnosis	ICD-9 Codes
Congestive heart failure	398.91, 428.0–428.9
Valvular disease	093.20–093.24, 394.0–397.1, 397.9, 424.0–424.99, 746.3–746.6, V42.2, V43.3
Pulmonary circulation disease	415.11–415.19, 416.0–416.9, 417.9
Peripheral vascular disease	440.0–440.9, 441.00–441.9, 442.0–442.9, 443.1–443.9, 444.21–444.22, 447.1, 449, 557.1, 557.9, V43.4
Arterial hypertension	401.1, 401.9, 642.00–642.04
Arterial hypertension with complications	401.0, 437.2
Paralysis	342.0–344.9, 438.20–438.53, 780.72
Other neurologic disease	330.0–331.9, 332.0, 333.4, 333.5, 333.7, 333.71, 333.72, 333.79, 333.85, 333.94, 334.0–335.9, 338.0, 340, 341.1–341.9, 3450.0–345.11, 345.2–345.3, 345.40–345.91, 347.00–347.01, 347.10–347.11, 649.40–649.44, 768.7, 768.70–768.73, 780.3, 780.31, 780.32, 780.33, 780.39, 780.97, 784.3
Chronic pulmonary disease	490–492.8, 493.00–493.92, 494–494.1, 495.0–505, 506.4
Diabetes without complications	250.00–250.33, 648.00–648.04, 249.00–249.31
Diabetes with complications	250.40–250.93, 775.1, 249.40–249.91
Hypothyroidism	243–244.2, 244.8, 244.9
Renal failure	585.3, 585.4, 585.5, 585.6, 585.9, 586, V42.0, V45.1, V56.0–V56.32, V56.8, V45.11–V45.12
Liver disease (excluded)	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 456.0, 456.1, 456.20, 456.21, 571.0, 571.2, 571.3, 571.40–571.49, 571.5, 571.6, 571.8, 571.9, 572.3, 572.8, 573.5, V42.7
Peptic ulcer without bleeding	531.41, 531.51, 531.61, 531.70, 531.71, 531.91, 532.41, 532.51, 532.61, 532.70, 532.71, 532.91, 533.41, 533.51, 533.61, 533.70, 533.71, 533.91, 534.41, 534.51, 534.61, 534.70, 534.71, 534.91
AIDS	042–044.9
Lymphoma	200.00–202.38, 202.50–203.01, 238.6, 273.3, 203.02–203.82

(continued)

Table 1. (continued)

Diagnosis	ICD-9 Codes
Cancer with metastatic disease	196.0–199.1, 209.70–209.75, 209.79, 789.51
Tumor	140.0–172.9, 174.0–175.9, 179–195.8, 209.00–209.24, 209.25–209.3, 209.30–209.36, 258.01–258.03
Rheumatic disease	701.0, 710.0–710.9, 714.0–714.9, 720.0–720.9, 725
Coagulopathy	286.0–286.9, 287.1, 287.3–287.5, 649.30–649.34, 289.84
Obesity	278.0, 278.00, 278.01, 278.03, 649.10–649.14, V85.30–V85.39, V85.41–V85.45, V85.54, 793.91
Weight loss	260–263.9, 783.21–783.22
Electrolyte imbalance	276.0–276.9
Acute blood loss	280.0, 648.20–648.24
Iron deficiency anemia	280.1–281.9, 285.21–285.29, 285.9
Alcohol abuse	291.0–291.3, 2915, 291.8, 291.81, 291.82, 291.89, 291.9, 303.00–303.93, 305.00–305.03
Drug abuse	292.0, 2928.2–2928.9, 292.9, 304.00–3049.3, 30520–30593, 648.30–648.34
Psychosis	2950.0–298.9, 299.10, 299.11
Depression	300.4, 301.12, 309.0, 309.1, 311

particularly low mortality risk ratio of 0.112 (95%CI: 0.093–0.137, $p < 0.001$). Overall, however, transplant centers had 7.3% mortality rate compared to the 5.6% of nontransplant centers.

Additionally, those of African American ethnicity also had a higher risk of mortality, with a mortality risk ratio of 1.273 (95%CI: 1.217–1.331, $p < 0.001$). However, all other minority groups actually had lower ratios relative to the reference population—whites. Hispanics had a mortality risk ratio of 0.837 (95%CI: 0.084–0.873, $p < 0.001$).

In regards to other important factors, self-payers and those not charged were correlated with higher mortality rates with ratios of 2.104 (95%CI: 1.985–2.230, $p < 0.001$) and 1.842 (95%CI: 1.563–2.170, $p < 0.001$). Age became a significant factor for patients over the age of 65, with a ratio of 1.540 (95%CI: 1.388–1.708, $p < 0.001$). Income level by zip code showed a decremental decline in the ratio, with those facilities in the highest (4th) income quartile having a mortality risk ratio of 0.865 (95%CI: 0.828–0.904, $p < 0.001$) relative to those in the 1st. Also evident was the significant mortality associated with the additional acute issues, especially septic shock [mortality risk ratio: 28.439 (95%CI: 26.686–30.307, $p < 0.001$)].

Costs among transplant hospitals were highest, with teaching transplant facilities averaging \$22,395.48 per admission, as compared to \$16,571.67 at nonteaching transplant facilities. Costs at nontransplant centers averaged

\$10,781.20 at teaching institutions and \$9,538.20 at nonteaching facilities. After adjustment, as seen in Table 3, we found that teaching and nonteaching transplant hospitals had cost ratios of 1.226 (95%CI: 1.214–1.238, $p < 0.001$) and 1.179 (95%CI: 1.12–1.24, $p < 0.001$) respectively. It was western USA-based hospitals notably though that were associated with greatest cost [cost ratio: 1.148 (95%CI, 1.137–1.160, $p < 0.001$)], followed by the reference region—the northeast.

Procedures were associated with greater cost, with ratios of 2.867 (95%CI: 2.755–2.984, $p < 0.001$) for orthotopic liver transplantation, of 1.793 (95%CI: 1.706–1.883, $p < 0.001$) for transjugular intrahepatic portosystemic shunt placement, and of 1.327 (95%CI: 1.307–1.346, $p < 0.001$) for esophagogastroduodenoscopy. Of particular importance was also degree of illness, with additional acute conditions besides hepatic encephalopathy having elevated cost ratios, such as variceal bleed [1.458 (95%CI: 1.432–1.485, $p < 0.001$)] and septic shock [1.364 (95%CI: 1.326–1.403, $p < 0.001$)].

Investigation of the length of stay (Table 4) demonstrated liver transplantation had the single highest length of stay rate ratio, of 3.383 (95%CI: 3.254–3.517, $p < 0.001$). The length of stay was found to be longer at teaching facilities compared to nonteaching facilities, with transplant teaching hospitals having the longest length of stay at 7.5 days compared to 6.4 days at nonteaching transplant hospitals. Comparatively, teaching and nonteaching facilities without transplant capabilities had averages of 5.5 and 5.0 days each. Adjusting for transplantation, teaching transplant facility status was predictive of the greatest increase, with a ratio of 1.104 (95%CI: 1.093–1.115, $p < 0.001$), while nonteaching transplant facilities actually were associated with shorter stays, with a ratio of 0.923 (95%CI: 0.873–0.976, $p < 0.001$).

The patient's insurance coverage also had significant impact, with lack of insurance having the largest length of stay ratios relative to Medicare coverage, at 1.153 (95%CI: 1.135–1.172, $p < 0.001$) and no charge with a ratio of 1.197 (95%CI: 1.144–1.253, $p < 0.001$). In a similar manner, regression analysis suggested the significant effect of disposition, with death and discharge to skilled nursing, long-term acute care hospitals, or in-patient rehabilitation centers having the two highest ratios, at 1.152 (95%CI: 1.130–1.173, $p < 0.001$) and 1.711 (95%CI: 1.696–1.726, $p < 0.001$) respectively.

Those with illness markers also had significantly elevated length of stay ratios, namely for pneumonia at 2.078 (95%CI: 1.998–2.160, $p < 0.001$), septic shock at 1.808 (95%CI: 1.757–1.859, $p < 0.001$), and variceal bleeding at 1.399 (95%CI: 1.373–1.425, $p < 0.001$).

To study the trends of hepatic encephalopathy admissions, we utilized a quadratic trend rather than a linear trend. While the rate of all-cause, and alcohol- and hepatitis C-related admissions are slowing, nonalcoholic steatohepatitis-related admissions were observed to be rising consistently, as can be observed in Fig. 3, with 573 (1.2%) associated admissions in 2007 compared to 2,190 (2.9%) in 2014.

Discussion

In prior studies of large-scale administrative data, a focus has often been comparing the quality of care between facilities based on their teaching status and their presumed expertise in management of particular disease states. In this study, significant survival benefits were provided to patients

Table 2. Characteristics of cases at each hospital subtype

Independent variable	Nontransplant nonteaching hospitals (249,222 cases)	Nontransplant teaching hospitals (177,620 cases)	Transplant nonteaching hospitals (1,617 cases)	Transplant teaching hospitals (83,290 cases)
Deaths	13,419 (5.4%)	10,523 (5.9%)	94 (5.8%)	6,066 (7.3%)
Age in years				
18–35	4,032 (1.6%)	3,284 (1.8%)	25 (1.5%)	2,168 (2.6%)
36–50	44,070 (17.7%)	32,224 (18.1%)	373 (23.1%)	15,971 (19.2%)
51–64	124,027 (49.8%)	91,982 (51.8%)	913 (56.5%)	48,038 (57.7%)
65 and up	77,093 (30.9%)	50,129 (28.2%)	306 (18.9%)	17,113 (20.5%)
Male	148,017 (59.4%)	108,094 (60.9%)	994 (61.5%)	51,093 (61.3%)
Female	101,187 (40.6%)	69,521 (39.1%)	623 (38.5%)	32,177 (38.6%)
Ethnicity				
White	154,257 (61.9%)	94,134 (53%)	934 (57.8%)	46,780 (56.2%)
Black	16,352 (6.6%)	20,871 (11.8%)	106 (6.6%)	10,307 (12.4%)
Hispanic	42,614 (17.1%)	34,159 (19.2%)	258 (15.9%)	12,784 (15.3%)
Asian or Pacific Islander	3,661 (1.5%)	2,946 (1.7%)	<i>withheld due to case count < 20</i>	1,511 (1.8%)
Native American	4,410 (1.8%)	2,520 (1.4%)	<i>withheld due to case count < 20</i>	834 (1.0%)
Other	5,528 (2.2%)	5,149 (2.9%)	258 (15.9%)	3,047 (3.7%)
Missing	22,400 (9.0%)	17,841 (10.0%)	61 (3.8%)	8,027 (9.6%)
Transferred from outside facility	3,939 (1.6%)	6,920 (3.9%)	29 (1.8%)	14,892 (17.9)
Sepsis	4,807 (1.9%)	4,101 (2.3%)	54 (3.3%)	2,608 (3.1%)
Septic shock	1,947 (0.8%)	2,113 (1.2%)	25 (1.5%)	2,486 (3.0%)
Hepatorenal syndrome	12,284 (4.9%)	9,613 (5.4%)	182 (11.3%)	8,539 (10.3%)
Variceal bleeding	7,209 (2.9%)	5,683 (3.2%)	40 (2.5%)	2,797 (3.4%)
Spontaneous bacterial peritonitis	4,059 (1.6%)	3,777 (2.1%)	39 (2.4%)	3,142 (3.8%)
Pneumonia	1,208 (0.5%)	1,117 (0.6%)	<i>withheld due to case count < 20</i>	986 (1.2%)
Medicare	122,821 (49.3%)	78,560 (44.2%)	666 (41.2%)	33,211 (39.9%)
Medicaid	53,793 (21.6%)	45,526 (25.6%)	314 (19.4%)	19,082 (22.9%)
Private insurance	47,594 (19.1%)	33,982 (19.1%)	527 (32.6%)	24,551 (29.5%)
Self-pay	12,773 (5.1%)	10,542 (5.9%)	79 (4.9%)	2,755 (3.3%)
No charge	1,174 (0.5%)	736 (0.4%)	20 (1.2%)	607 (0.7%)
Income quartile by zip code				
1st	81,384 (32.7%)	59,604 (33.6%)	356 (22.0%)	27,721 (33.3%)
2nd	69,268 (27.8%)	43,604 (24.5%)	367 (22.7%)	19,689 (23.6%)
3rd	55,037 (22.1%)	38,603 (21.7%)	557 (34.4%)	18,807 (22.6%)
4th	36,407 (14.6%)	29,046 (16.4%)	299 (18.5%)	14,979 (18.0%)
Missing	7,127 (2.9%)	6,763 (3.8%)	38 (2.4%)	2,095 (2.5%)
Received orthotopic liver transplantation	N/A	N/A	33 (2.1%)	3,204 (3.8%)

N/A, not available.

admitted to transplant hospitals, specifically those with training programs, as compared to hospitals without trainees or transplant capability. These findings help support the argument for proper referral of patients with decompensated liver

disease to a specialty center, which may have higher hepatic encephalopathy admission volume. Moreover, through the accounting for a number of possible confounders, such as comorbidities, concomitant acute illnesses and demographics,

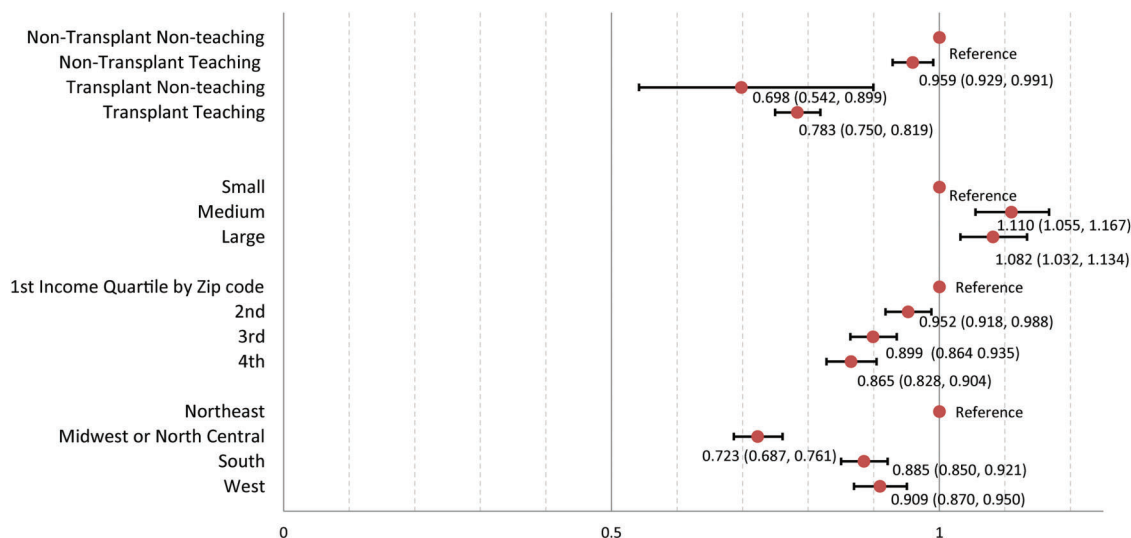


Fig. 1. Adjusted mortality risk ratios related to hospital characteristics.

the analysis was able to at least partially isolate the mortality risk reduction provided by teaching transplant centers despite an unadjusted higher mortality rate. From this analysis, it can be inferred that those patients admitted to teaching centers with transplant capabilities have poorer prognostic indicators, which more specialized care is not able to completely offset, resulting in a raw increase of approximately 2% in mortality.

These findings are in line with those of Ananthakrishnan *et al.*,¹⁰ who found that in cases of acute liver failure, high-volume centers had the lowest adjusted mortality rates. Another study dealing with a wider swath of liver disease diagnoses, however, showed the greatest correlation between

mortality and severity of illness rather than the type of hospital to which a patient was admitted.¹¹

The question is the means by which these transplant facilities provided better care beyond transplantation. One possibility is more readily available specialty and interdisciplinary care. As Mellinger *et al.*,¹² has previously discussed, there is potentially an increased benefit created by enhancing multidisciplinary care for cirrhotic patients. Specifically, those authors reference a USA Veterans' Affairs-based study on patients with ascites that provided evidence that involvement of gastroenterologists in hospitalized patients' management was associated with greater adherence to standards of care.¹³ It was also quite notable that, in our analysis, these same

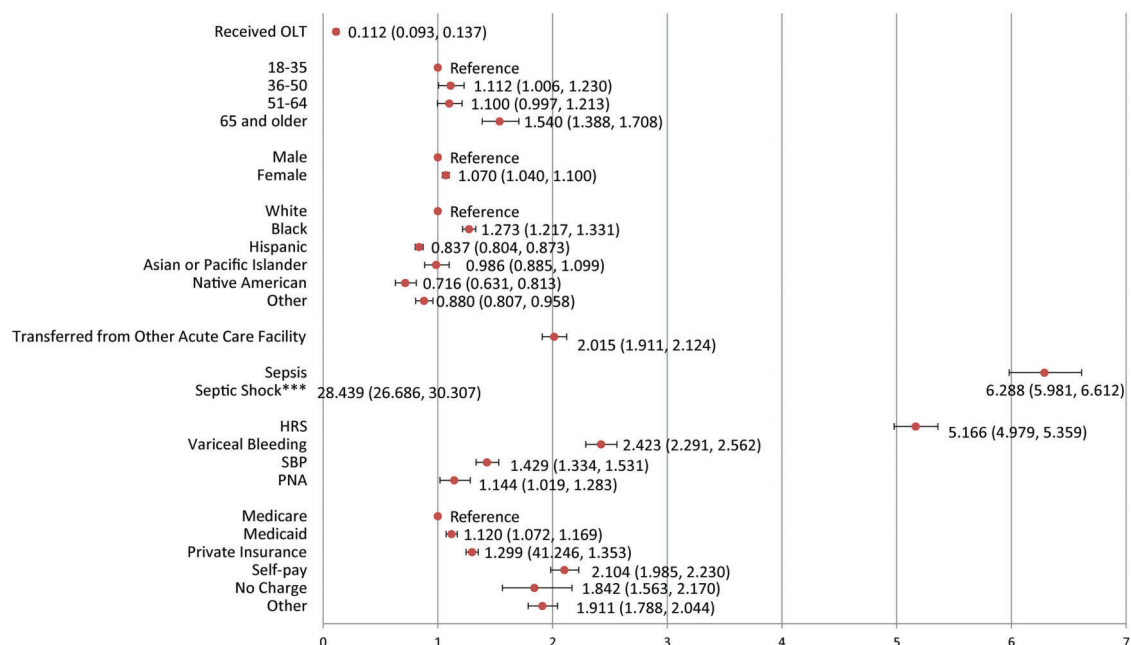


Fig. 2. Adjusted mortality risk ratios related to patient characteristics.

Table 3. Multivariate negative binomial regression for cost.

Independent variable	p	RR	95% CI	
			Lower	Upper
Nontransplant nonteaching		1.00		
Nontransplant teaching	<0.01	1.02	1.01	1.02
Transplant nonteaching	<0.01	1.18	1.12	1.24
Transplant teaching	<0.01	1.23	1.21	1.24
OLT	<0.01	2.87	2.76	2.98
EGD	<0.01	1.33	1.31	1.35
Paracentesis				
TIPS	<0.01	1.79	1.71	1.88
18–35 years old		1.00		
36–50 years old	<0.01	0.93	0.91	0.95
51–64 years old	<0.01	0.92	0.90	0.94
65 and older	<0.01	0.89	0.87	0.91
Male		1.00		
Female	<0.01	1.01	1.01	1.02
White		1.00		
Black	<0.01	1.07	1.06	1.08
Hispanic	<0.01	1.02	1.01	1.03
Asian or Pacific Islander	<0.01	1.09	1.06	1.11
Native American	0.03	0.97	0.95	1.00
Other	<0.01	1.08	1.06	1.10
Northeast		1.00		
Midwest or North Central	<0.01	0.92	0.91	0.93
South	<0.01	0.87	0.86	0.88
West	<0.01	1.15	1.14	1.16
Transferred in from another acute care facility	<0.01	1.02	1.01	1.04
Length of stay	<0.01	1.10	1.10	1.10
Sepsis	<0.01	1.26	1.23	1.28
Septic shock	<0.01	1.36	1.33	1.40
Variceal bleed	<0.01	1.46	1.43	1.49
HRS	<0.01	1.10	1.09	1.12
SBP	<0.01	1.16	1.14	1.19
PNA	<0.01	1.17	1.13	1.22
Routine		1.00		
Short term hospital	<0.01	1.22	1.20	1.24
Another type of facility	<0.01	1.14	1.13	1.15
Home health care	<0.01	1.09	1.08	1.10

(continued)

Table 3. (continued)

Independent variable	p	RR	95% CI	
			Lower	Upper
Against medical advice	<0.01	0.96	0.94	0.98
Died	<0.01	1.40	1.38	1.42
Medicare		1.00		
Medicaid	<0.01	0.98	0.97	0.99
Private insurance	0.20	1.01	1.00	1.02
Self-pay	<0.01	1.04	1.03	1.06
No charge	<0.01	1.09	1.05	1.14
Other	<0.01	0.97	0.95	0.99
1st income quartile		1.00		
2nd income quartile	<0.01	1.02	1.01	1.03
3rd income quartile	<0.01	1.06	1.05	1.07
4th income quartile	<0.01	1.14	1.13	1.15
Small		1.00		
Medium	<0.01	0.94	0.93	0.95
Large	<0.01	0.93	0.92	0.93

teaching transplant capable centers, had significantly worse lengths of stay and greater costs per admission. The question arising from these findings is what connection longer length of stays and costs may have to the actual quality of care being provided to our study population.

As discussed by Neff *et al.*,¹⁴ along with spontaneous bacterial peritonitis, hepatic encephalopathy has been rising as the root cause of cirrhosis admissions. Over this period, the study estimates, based on Healthcare Cost and Utilization Project data, charges (not costs) of about \$11,000 per admission related to hepatic encephalopathy in 1993 rose to \$35,875 in 2009, with increasing percentage discharged to rehab centers or long-term nursing home care rising from 2% to 25%. Whether this is indicative of more aggressive and expensive therapy that is warranted is clearly an important question.

It is possible that nonteaching nontransplant centers, in particular, are failing to offer the same level of guideline-directed care. Given that care guidelines' cost effectiveness is based at least in part on reducing readmissions—which are not categorized in the National Inpatient Sample database—there exists the possibility that while those admissions at transplant and teaching centers may have higher costs and longer stays, that there are lower readmission rates resulting in substantial savings. That said, in a study by Volk *et al.*,¹⁵ proper titration of lactulose and diuretics along with failure to plan out-patient paracenteses were the greatest drivers of “preventable” readmissions. Of interest though, there have been multiple studies that have shown correlation between spending and improved morality, including cirrhosis,^{16–20} which is in line with this study's results. However, another study by Fisher *et al.*²¹ demonstrated that greater spending driven by more specialists' involvement and therapeutic interventions were not correlated with improved outcomes. It is important, however, to acknowledge that their study focused on colorectal cancer, myocardial infarctions, and hip fractures.

Table 4. Multivariate negative binomial regression for length of stay

Independent variable	<i>p</i>	RR	95% CI	
			Lower	Upper
Nontransplant nonteaching		1.00		
Nontransplant teaching	<0.01	1.03	1.03	1.04
Transplant nonteaching	<0.01	0.92	0.87	0.98
Transplant teaching	<0.01	1.10	1.09	1.11
OLT	<0.01	3.38	3.25	3.52
18–35 years old		1.00		
36–50 years old	<0.01	0.95	0.93	0.98
51–64 years old	<0.01	0.91	0.89	0.94
65 and older	<0.01	0.90	0.88	0.92
Male		1.00		
Female	<0.01	1.03	1.02	1.03
White		1.00		
Black	<0.01	1.08	1.07	1.09
Hispanic	0.85	1.00	0.99	1.01
Asian or Pacific Islander	<0.01	1.04	1.02	1.07
Native American	<0.01	0.90	0.88	0.92
Other	<0.01	1.05	1.03	1.07
Transferred in from another acute care facility	<0.001	1.26	1.24	1.28
Northeast		1.00		
Midwest or North Central	<0.01	0.82	0.82	0.83
South	<0.01	0.89	0.89	0.90
West	<0.01	0.87	0.86	0.88
Sepsis	<0.01	1.78	1.74	1.82
Septic shock	<0.01	1.81	1.76	1.86
HRS	<0.01	1.28	1.26	1.30
Variceal bleed	<0.01	1.40	1.37	1.42
SBP	<0.01	1.22	1.20	1.25
PNA	<0.01	2.08	2.00	2.16
Routine		1.00		
Short term hospital	<0.01	1.15	1.13	1.17
Another type of facility	<0.01	1.71	1.70	1.73
Home health care	<0.01	1.36	1.34	1.37
Against medical advice	<0.01	0.84	0.82	0.87
Died	<0.01	1.46	1.44	1.49
Medicare		1.00		
Medicaid	<0.01	1.10	1.09	1.11

(continued)

Table 4. (continued)

Independent variable	<i>p</i>	RR	95% CI	
			Lower	Upper
Private insurance	<0.01	1.03	1.02	1.04
Self-pay	<0.01	1.15	1.14	1.17
No charge	<0.01	1.20	1.14	1.25
Other	<0.01	1.11	1.09	1.13
Small		1.00		
Medium	<0.01	1.05	1.03	1.06
Large	<0.01	1.11	1.10	1.12
1st income quartile		1.00		
2nd income quartile	0.90	1.00	0.99	1.01
3rd income quartile	0.88	1.00	0.99	1.01
4th income quartile	<0.01	1.02	1.01	1.03

In our analysis, poverty and black ethnicity were associated with reduced survival. With a greater than 27% increased mortality risk among blacks relative to the white population, whose outcomes were worse than any race. However, in contrast to teaching transplant facilities, which had longer lengths of stay and higher costs but a lower mortality risk, black ethnicity was associated with 8% longer admissions and 6.6% higher admission costs in spite of higher mortality. This indicates that the deficiencies in care may not be restricted to the outpatient side, as clearly resources are dedicated at a higher rate once these patients are admitted. Those patients in hospitals located in poorer zip codes, however, exhibited lower costs per admission, with those in the wealthiest quartile of zip codes demonstrating a 15% increased risk ratio for cost, with minimal difference in length of stay. This, perhaps, helps indicate that different factors may be affecting the worse outcomes in blacks and the poor. One relevant study, however, regarding ethnic differences in cirrhosis mortality suggested that the issue was admittance to facilities with reduced resources.²²

Given that it is well documented that African Americans and Hispanics are more likely to be poor and less likely to have health insurance relative to White and Asian populations,^{23,24} further efforts to ensure that this correlation was not having excessive confounding influence over the results were taken. The Cramer's V for the association between race and both payer and zip code income quartile were derived. In both cases though, the association was weak, with a value of 0.122 in relation to income quartile and a value of 0.070 in relation to payer, inadequate to disregard the observations as a function of poverty alone.

One possible issue that likely is affecting the black population and resulting in these poor associations with mortality, spending, and length of stay is reduced transplantation rates. Significant discrepancy between liver disease prevalence among African Americans and placement on waiting lists has been seen,²⁵ but perhaps most troubling are delayed referrals^{26–28} for African Americans.²⁹ They have also been noted to be less likely to receive hepatitis C virus therapy, independent of comorbidities or income level.³⁰ The problem, however, may be more complex though, as a study of heart transplant listings found that multiple state

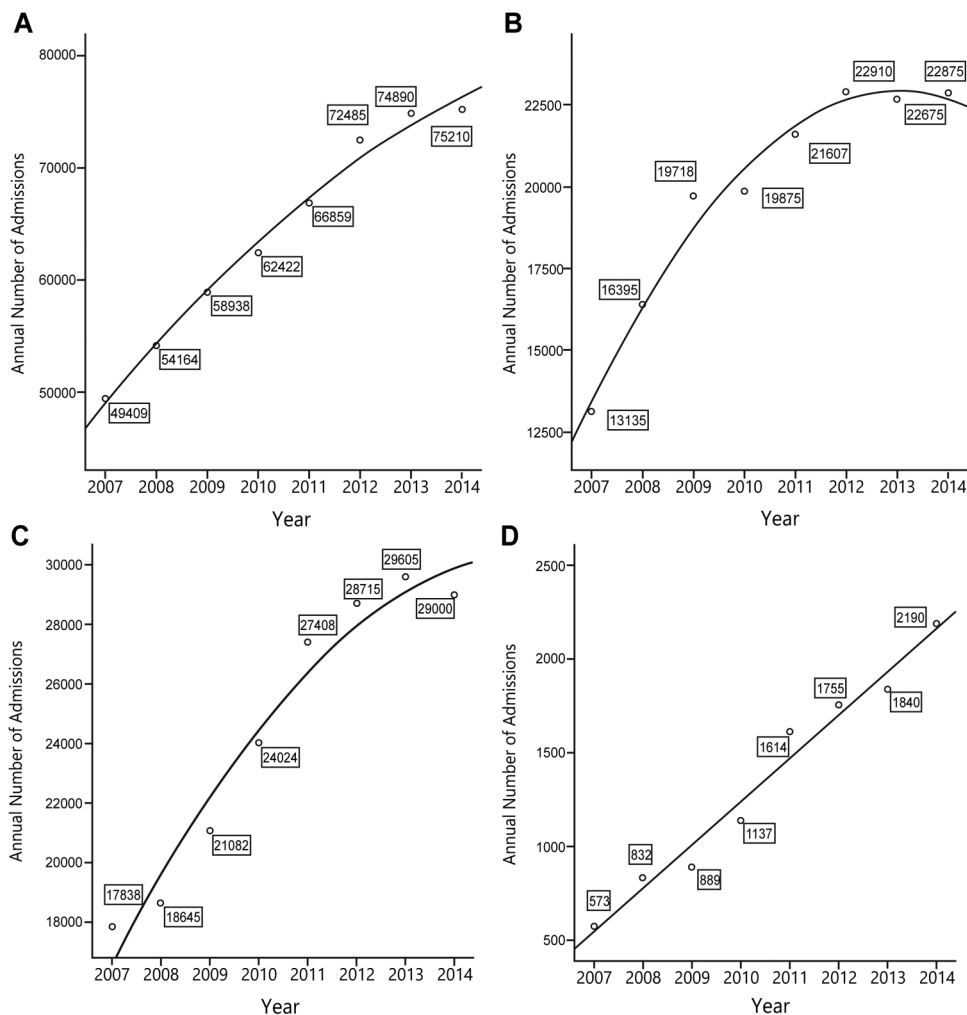


Fig. 3. Findings for our patient population. (A) Overall admissions. (B) Hepatitis C-related admissions (C) Alcohol-related admissions. (D) Nonalcoholic steatohepatitis-related admissions.

listed candidates were more likely white, privately insured, and from wealthier areas.³¹ While physicians cannot control larger socioeconomic forces, aggressive early referral to specialty care will likely be a cornerstone of improved outcomes, specifically in the black population moving forward.

In considering further trends, admissions primarily for hepatic encephalopathy continue to rise, with 51,456 admissions (weighted) identified in 2007 compared to 80,460 in 2014. Given increasing costs such a trend presents a challenge for the ability to adequately allocate resources to the issue. However, more reassuring was that the trend line best fits a quadratic model with deceleration of this increase as opposed to a linear yearly increase, which may be a sign that a peaking in admissions may be on the horizon. A similar trend was seen in HCV admissions, which is appropriate given the reduction in new diagnoses of HCV by year since 1992³⁰ and new curative modalities.³² Also demonstrated was a similar pattern in alcohol-related admissions, with an increase of 50%, similar to a previous study of those being transplanted which revealed an increase in the proportion of alcoholic liver disease-related cases.³³ Nonalcoholic fatty liver disease, while

accounting for a smaller overall share compared to these other etiologies in this analysis, was rapidly rising as a cause of liver disease. We cannot comment on how much of this can be attributed to increased awareness and subsequent physician coding versus pathological prevalence,^{33,34} especially considering attribution was limited to only those patients without other diagnoses capable of explaining their liver disease and subsequent encephalopathy. However, given this trend, it will be important to continue to develop improved management techniques and therapies to curb the increasing rate of these admissions.

In spite of the large volume of data available from the National Inpatient Sample database, there were certain limitations of the study based upon its data source. The database was created from coding and insurance data, which is subject to multiple issues.³⁵⁻³⁷ Poor coding practices, such as incorrect ICD-9 codes or improper categorization of the primary diagnosis code, certainly would affect our findings. Additionally, greater awareness and therefore resultant increase in coding for given diagnoses is an important confounder. Moreover, case level data on income, medications received, and lab values are

missing. This limits our ability to properly assess the accuracy of coding or stratifying by model of end-stage liver disease-Na scoring, which in one study showed better predictive value for mortality than Elixhauser.³⁸ Also, conversion of charges to cost does not allow for absolute accuracy, as not all hospitals had specific conversion multipliers. Moreover, we are not able to categorize those patients readmitted within 30 days, which could potentially be a valuable data point in regards to cost effective care.

Conclusions

It is encouraging to observe that transplant and teaching center clinical practice is associated with reduced mortality, and hopefully improved management strategies can be expanded to other facilities that lack such resources. However, the fact that such care is associated with higher costs continues to present an issue moving forward with healthcare cost ballooning. The question that will need to be addressed in further studies, though, should not be limited to merely mortality rates, but whether such improved standards of care and expanded resources are able to reduce readmission rates. A reduction in readmissions would likely allow for more comprehensive care and expensive interventions to actually be cost effective.

Greater emphasis, though, will also need to be placed on mortality reduction among economically disadvantaged groups and minorities. Some of these changes may involve changing clinical practice patterns via standardization and training, even among hospitals with less resources or a lower degree of specialization. On a much wider scale, higher governmental spending may be required in order to ensure a larger share of the population has access to health insurance, thereby allowing for increased eligibility for transplantation and access to donor livers across socioeconomic backgrounds.

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Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Conception of study objectives and design (DB, PP, SA, EO, NP), collection of data (DB), analysis of data (DB), drafting of the article (DB, PP, TN, NP), revising the article for important intellectual content (DB, PP, NP).

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