American Journal of Transplantation 2009; 9: 2092–2101
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2009.02737.x

Sociodemographic Differences in Early Access to Liver Transplantation Services

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The question of whether health care inequities occur before patients with end-stage liver disease (ESLD) are waitlisted for transplantation has not previously been assessed. To determine the impact of gender, race and insurance on access to transplantation, we linked Pennsylvania sources of data regarding adult patients discharged from nongovernmental hospitals from 1994 to 2001. We followed the patients through 2003 and linked information to records from five centers responsible for 95% of liver transplants in Pennsylvania during this period. Using multinomial logistic regressions, we estimated probabilities that patients would undergo transplant evaluation, transplant waitlisting and transplantation itself. Of the 144 507 patients in the study, 4361 (3.0%) underwent transplant evaluation. Of those evaluated, 3071 (70.4%) were waitlisted. Of those waitlisted, 1537 (50.0%) received a transplant. Overall, 57 020 (39.5%) died during the study period. Patients were less likely to undergo evaluation, waitlisting and transplantation if they were women, black and lacked commercial insurance ($p < 0.001$ each). Differences were more pronounced for early stages (evaluation and listing) than for the transplantation stage (in which national oversight and review occur). For early management and treatment decisions of patients with ESLD to be better understood, more comprehensive data concerning referral and listing practices are needed.

Key words: Access to transplantation, equity, liver disease

Received 14 March 2009, revised 14 March 2009 and accepted for publication 07 May 2009

Introduction

Policies for the allocation of donated organs to patients who need them have been scrutinized and revised repeatedly in an effort to both enhance the public health benefits of transplantation and improve the process's equity and fairness (1–7). These changes, however, can only have minimal impact, as the allocation of organs is simply the last step in transplantation, and potential barriers can be encountered at the diagnostic, referral or listing stages as well. Indeed, as Alexander and Sehgal observed in their study of end-stage renal disease, gender- and race-based barriers to care are found at all stages of management, from diagnosis of end-organ disease through the actual receipt of an organ (8).

What allowed Alexander and Sehgal to examine access in the entire system was the availability of information from the US Renal Data System (USRDS), a population-based registry created by Medicare to track the management of patients with end-stage renal disease from diagnosis/dialysis through death and/or transplantation (9). No similar registry exists for patients with liver disease. Once patients progress to end-stage liver disease (ESLD) and are placed on the United Network for Organ Sharing (UNOS) liver transplant waiting list, access- and equity-related issues can be monitored. However, the UNOS waitlist includes only those individuals who were listed by transplant centers (10), and it fails to account for potential inequities associated with diagnosis, referral or evaluated-but-not-listed decisions. The Institute of Medicine (IOM) agrees with this analysis, indicating that 'the larger problems of equitable access to transplantation occur prior to a patient being put on a waiting list for a transplant; they take the form of inadequate health insurance coverage and inadequate access to primary care, proper diagnosis and treatment, and referral for transplant evaluation' (11).

Previous evaluation of the early stages of the process leading to liver transplantation has been survey based or limited to descriptions of center-specific practices (12–15).

A survey conducted by the American Society of Transplant Physicians reported on practice variation across centers, including both patient factors (e.g. age, compliance and medical condition) and center factors (academic vs. nonacademic medical centers) (12). Trotter et al. described early practices and determinants of successful transplantation in North Carolina, noting that evaluation of candidates included subjective assessments by the team and that exclusionary criteria often varied across centers (e.g. patient age) (13).

Eckhoff et al. provided a more systematic examination of patients referred to the center for liver transplantation and tested explicitly for racial differences (14). The authors reported that although blacks were referred to their center less often than appropriate given their prevalence of liver disease and were sicker at referral than whites, once evaluated, blacks and whites were equally likely to be listed for transplantation, to receive a transplant and had similar 1- and 3-year posttransplant survival rates.

More recently, Julapalli et al. examined liver-related encounters for a large VA Medical Center, following patients for 1 year to analyze referral patterns for transplantation services (15). The mention of liver transplantation in the medical record or other evidence of arranging for referral to a transplant center occurred in only 21% of all cases and was discussed less often if the patient was black or had alcoholic liver disease.

To our knowledge, the only population-based study of early access to transplantation services used discharge data for the state of North Carolina to estimate the prevalence of ESLD and the covariates associated with the likelihood of liver transplantation. Although several nonmedical factors (e.g. source of payment, distance to transplant center) were associated with the likelihood of transplantation, the authors were not able to link hospitalization data to other sources or to follow patients over time (16).

This study follows patients with liver disease who might potentially need a liver transplant in the future, allowing us to examine the early barriers to access and the impact of sociodemographic factors (i.e. gender, race or insurance status) on variation in referrals to and listings by transplant centers. It uses hospitalization data for liver-related discharges as a means of flagging patients who either have or may be 'at risk' for ESLD and may eventually require transplantation. We treat the earliest instance for each patient as the index hospitalization and then link discharge records to other data sources that allow us to follow these 'transplant-potential' patients over time, using information about subsequent hospitalizations, transplant evaluation, transplant-related care and death. We compare sociodemographics observed prior to listing with those observed after listing, as a way of assessing whether later stages provide an accurate picture in describing the overall equity of the current liver transplantation process.

Methods

We used several linked secondary data sources to identify patients who were hospitalized between 1994 and 2001 for liver-related 'transplant-potential' conditions and followed them through 2003. We estimated the likelihood that patients would move through various stages of the disease management process, including evaluation/referral, listing and transplantation, and examined variation in likelihoods after adjusting for clinical and nonclinical factors. The main hypothesis of this study is that gender, race and insurance status affect early access to liver transplantation services (namely, referral to transplant centers and listing by transplant centers) differently than they affect access after patients are placed on the transplant waiting list.

Model development and data collection

We defined six stages that a patient with liver disease must pass through prior to transplantation (Figure 1): disease occurrence (incidence), disease progression (natural history), disease diagnosis, referral/evaluation for transplantation, listing for transplantation and organ receipt (transplantation). Patients may not complete all of these stages for myriad reasons, including recovery of liver function, medical unsuitability for a transplant, refusal of treatment, disparities/bias and death.

Using the 9th edition of the International Classification of Diseases (ICD-9) (17), we developed a list of diagnostic and procedural codes that are available through a discharge data set and indicative of conditions that could eventually require liver transplantation (Table 1). The list of codes was deliberately created to be overly sensitive so as not to exclude any potential patients who might benefit from transplant. After gastroenterologists and critical care physicians at the University of Pittsburgh Medical Center (UPMC) reviewed the list, we pretested its usefulness and applicability by searching the UPMC medical record system for patients with liver transplant-potential conditions. We first searched all available data fields in the medical record, including diagnostic and procedural codes and physician notes; we then compared this to searching only the smaller subset diagnostic and procedural codes that UPMC (and all nongovernmental hospitals in Pennsylvania) is required by state law to submit clinically abstracted data to the Pennsylvania Health Care Cost Containment Council (PHC4) for all hospital discharges; its accuracy has been validated against chart reviews (18). In this way, we were able to verify that the standard data fields in PHC4 data could reliably identify patients with transplant-potential conditions.

We assumed that most people who become sufficiently ill to be considered for transplantation are hospitalized at some point in their illness and that, in turn, we could identify much of the liver transplant-potential population through hospital discharge summary data available in PHC4 data. The PHC4 discharge database includes nine diagnostic and six procedural data fields, and we requested that all 15 fields be searched for codes on our list in patients who were $\geq$18 years old and were discharged between 1994 and 2001. The PHC4 provided us with the following variables: the patient's age, gender, race and county and ZIP code of residence; type of admission; admission and discharge diagnoses, procedures and diagnosis-related group (DRG) codes; discharge destination; total charges; Uniform Billing Form (UB-92) revenue charges and unit categories; and Medical Illness Severity Grouping System (MEDISGRPS) disease category (mortality risk) and severity score.

In an effort to limit our study to a cohort of patients hospitalized between 1995 and 2001 for newly diagnosed liver disease (a cohort of patients with incident disease), we excluded patients who had been hospitalized for a liver-related condition in the previous year (1994). For this group of patients,

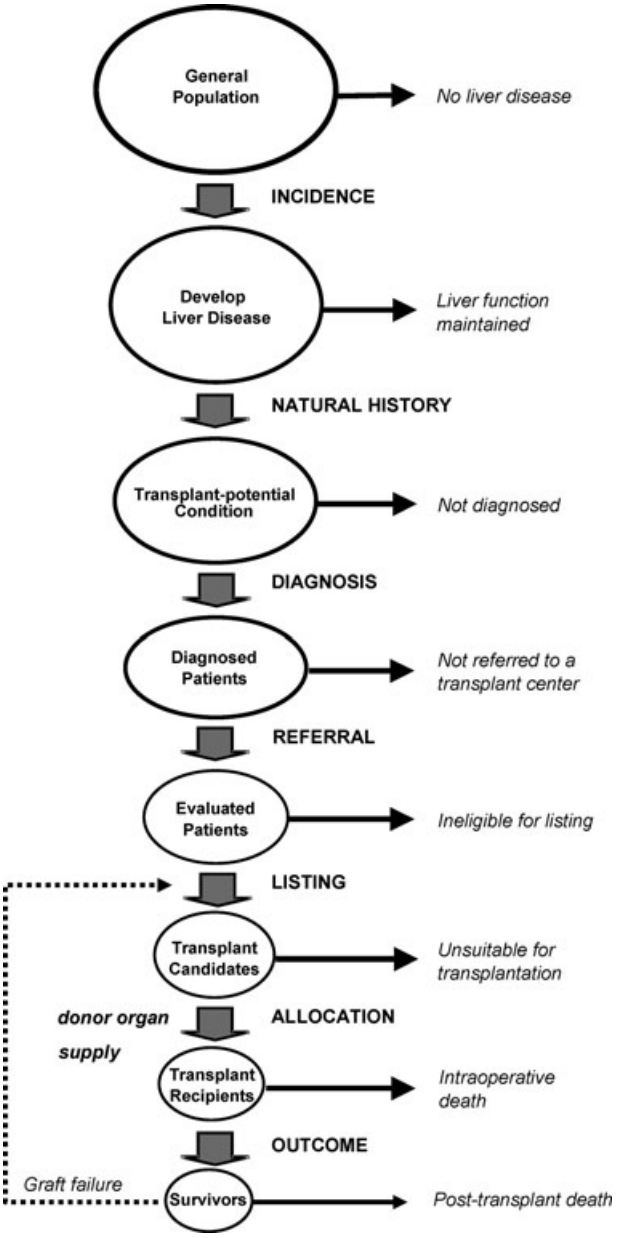

Figure 1: Conceptual model of the (liver) transplantation process. The conceptual model illustrates six stages of the transplantation process (incidence, natural history, disease diagnosis, patient referral to a transplant center, listing for transplantation and allocation of organ to a recipient). It also describes several reasons that patients may not receive a transplant; patient-related reasons (e.g. patient refusal, geographic access to centers) may occur throughout the process.

PHC4 provided additional data on all other hospitalizations (liver related or otherwise) through December 2003.

We then followed the cohort longitudinally by linking the data from this 'index' admission—which refers to patients at the 'diagnosis' stage of our conceptual model (Figure 1)—to data sources that contain data on the subsequent stages of the liver transplantation process. We obtained evaluation data from five transplant centers, which together performed 95% of the adult liver transplants in Pennsylvania during the study period (19): Albert Einstein Medical Center, Hospital University of Pennsylvania, Thomas Jefferson University Hospital, UPMC and the VA Pittsburgh Healthcare System (VAPHS). We obtained Organ Procurement and Transplantation Network (OPTN) data from UNOS, enabling us to track everyone in the cohort who was listed or transplanted. Therefore, for patients obtaining care outside of Pennsylvania, we had no information about evaluated-but-not-listed cases but we did know instances where the evaluation resulted in placement

Table 1: Selection criteria for identifying liver-related hospitalizations

Procedure episodes (1 principal, 5 secondary)	
Procedure code	Description
39.1	Transjugular intrahepatic portosystemic shunt
42.33	Variceal sclerotherapy
42.91	Variceal ligation
43.41	Variceal ligation
44.91	Variceal ligation
50.11	Closed liver biopsy
50.12	Open liver biopsy
51.87	Endolns sten biliary
54.91	Paracentesis
87.51	Perc hepat cholangiogram
87.52	i.v. cholangiogram
87.53	Cholangiogram, intraoperative
87.54	Cholangiogram, NEC
Diagnosis codes (1 principal, 8 secondary)	
Diagnosis code	Description
070.x	Viral hepatitis
155.x	Malignant neoplasm of liver and intrahepatic bile ducts
211.5	Benign neoplasm, liver and biliary passages
230.8	Carcinoma *in situ*, liver and biliary system
235.3	Neoplasm of uncertain behavior, liver/biliary passages
270.x	Disorders of amino-acid transport and metabolism
271.x	Disorders of carbohydrate transport and metabolism
272.x	Disorders of lipoid metabolism
275.0	Disorders of iron metabolism
275.1	Disorders of copper metabolism
277.4	Disorders of bilirubin excretion
277.6	Other deficiencies of circulating enzymes
279.12	Wiskott–Aldrich syndrome
444.89	Thrombosis, hepatic artery
452	Portal vein thrombosis
453.0	Budd–Chiari syndrome
456.0	Esophageal varices with bleeding
456.1	Esophageal varices without mention of bleeding
456.2x	Esophageal varices in diseases classified elsewhere
570	Acute and subacute necrosis of liver
571.xx	Chronic liver disease and cirrhosis
572.x	Liver abscess and sequelae of chronic liver disease
573.x	Other disorders of the liver
576.x	Other disorders of the biliary tract
751.6x	Anomalies of gallbladder, bile duct and liver
794.8	Abnormal liver scan

The suffix 'x' is a wildcard, indicating that the search should include the full range of numeric values plus a blank field (e.g. '155.x' includes 155.1 through 155.9, plus 155).

on the transplant waiting list. We received death data from the Bureau of Health Statistics and Research of the Pennsylvania Department of Health.

Our study was funded by the National Institute of Diabetes and Digestive and Kidney Diseases and approved by the Institutional Review Boards at the University of Pittsburgh and all of the participating transplant centers. The PHC4 acted as an honest broker to protect patient confidentiality, by linking records across the various data sources and providing the study team with deidentified versions of the files.

Statistical analyses

To characterize patients in terms of sociodemographic and clinical characteristics, we used descriptive statistics.

To compare these characteristics in subsets of patients who reached specific stages of the disease management process (diagnosis, listing by a transplant center and receiving a transplant), we used univariable and multivariable survival models that included the following covariates: age; gender; race/ethnicity (white, black, other, unknown); insurance status (commercial, Medicare, Medicaid, combined commercial/Medicare, combined Medicare/Medicaid and none); illness severity at the time of diagnosis, ranging from 0 (none) to 4 (maximal) on the 5-point MediQual severity score (20) and type of liver disease, based on diagnostic categories that we have used elsewhere (viral hepatitis, alcoholic liver disease, autoimmune disorder, metabolic disease, primary sclerosing cholangitis, cancer, primary biliary cirrhosis, other chronic diseases and acute liver failure) (21,22) (if more than one diagnosis was coded, we used the primary diagnosis field if it was liver related; otherwise, we used the more definitive diagnosis to avoid classifying the patient into the miscellaneous 'other chronic disease' category whenever possible). Although the cohort was identified using Pennsylvania discharges, we did include location of transplant center (Pennsylvania vs. non-Pennsylvania) as a covariate in the model to account for Pennsylvania residents who were listed and/or transplanted at other centers. We included year of index hospitalization and also tested for interaction variables (e.g. diagnosis and gender; diagnosis and race).

To test for differences in early access to liver transplantation services, we estimated the likelihood that patients in our cohort with a liver transplant-potential diagnosis would be referred to and evaluated by a transplant center. We then proceeded to estimate the likelihood that evaluated patients would be listed by a transplant center, and last we estimated the likelihood that listed patients would be transplanted. For each of these likelihoods, we used multinomial logistic regression and defined three possible outcomes: proceed to the subsequent stage of the process, remain at the current stage (censor) or die. We compared differences in the magnitude and significance of our primary covariates (gender, race and insurance status) while adjusting for the other patient- and disease-related covariates.

Results

A total of 192 243 patients were hospitalized in Pennsylvania for liver-related conditions between 1994 and 2001. We excluded 42 482 individuals (22.1%) who were admitted before 1995 and 4216 (2.2%) who were younger than 18 years. We also excluded 1038 (0.5%) individuals who were already liver transplant recipients or candidates.

Of the 144 507 adults in our final cohort, a total of 4361 patients (3.0%) were evaluated for liver transplantation during the study period. Of those who were evaluated, 3071 patients (70.4%) were placed on the transplant waiting list and 1537 (50.0%) went on to receive a liver transplant by December 2003. A total of 57 020 (39.5%) patients died during the study period (Table 2).

The characteristics of patients in the full cohort (diagnosis) compared to those who reached the evaluation, listing and transplantation stages are presented in Table 2. Due to sample size, all of the differences were statistically significant; yet the demographics and clinical characteristics of patients reaching different stages of the transplantation process were most dissimilar in moving from diagnosis to evaluation. For example, the proportion of women declined between diagnosis (46.1%) and evaluation (39%) stages and then remained stable through listing and transplantation. Similarly, 40.1% of the cohort was $\geq$65 years of age, but older patients comprised less than 10% of those who were referred and evaluated for transplant. There were similar declines at the evaluation stage for black race and patients insured by Medicare.

Adjusted likelihoods of obtaining transplant-related services

The Appendix provides coefficient estimates for three multinomial logistic regression models estimating: (1) probability of evaluation, (2) probability of listing, given evaluation and (3) probability of transplantation, given listing. In addition to the main variables of interest (gender, race/ethnicity and insurance status) and the covariates listed above, we included interaction terms for both gender and race with diagnosis. Because of the small numbers for some of the interactions, we aggregated our 10 disease groups to five combined groups, based on prior work (23). Interactions between insurance status and diagnosis were not significant and therefore excluded from the models.

The relationship of major sociodemographic factors (gender, race/ethnicity and insurance status) to access to transplantation services is presented in Table 3, which represents a summary of the analyses. These results demonstrate that sociodemographic differences are more significant early in the transplantation process, in terms of both referral to a transplant center and listing by a transplant center. There are far fewer sociodemographic differences in the latter stage (from listing to receipt of a transplant), where there is national oversight of liver transplant candidates and information is systematically collected and reviewed. Complete reports of the multinomial logistic regressions estimating the probability of evaluation, the probability of listing, given evaluation and the probability of transplantation, given listing, are provided in the Appendix.

Gender: The probability of being evaluated, listed or transplanted was consistently lower for women than for men (Table 3), except among patients with acute liver failure where women were more likely to progress through the various stages (see the Appendix).

Table 2: Characteristics of liver'transplant-potential' patient cohort (N = 144 507)*

Characteristic, n (%)	Diagnosed (all patients) N = 144 507	Evaluated N = 4361	Listed N = 3071	Transplanted N = 1537
Gender				
Male	77 885 (53.9)	2662 (61.0)	1880 (61.2)	987 (64.2)
Female	66 622 (46.1)	1699 (39.0)	1191 (38.8)	550 (35.8)
Age				
18–< 40 years	25 779 (17.8)	658 (15.1)	493 (16.1)	225 (14.6)
40–< 65 years	60 856 (42.1)	3290 (75.4)	2365 (77.0)	1219 (79.3)
≥65 years	57 872 (40.1)	413 (9.5)	213 (6.9)	93 (6.1)
Race/ethnicity				
White	103 969 (72.0)	3218 (73.8)	2267 (73.8)	1165 (75.8)
Black	19 791 (13.7)	374 (8.6)	260 (8.5)	114 (7.4)
Other	6363 (4.4)	248 (5.7)	185 (6.0)	87 (5.7)
Unknown	14 384 (10.0)	521 (12.0)	359 (11.7)	171 (11.1)
Insurance status				
Commercial only	51 711 (35.8)	2706 (62.0)	2043 (66.5)	1049 (68.2)
Medicaid only	24 214 (16.8)	743 (17.0)	475 (15.5)	219 (14.2)
Medicare only	14 315 (9.9)	207 (4.7)	123 (4.0)	64 (4.2)
Medicare + Commercial	40 137 (27.8)	383 (8.8)	229 (7.5)	107 (7.0)
Medicare + Medicaid	7721 (5.3)	110 (2.5)	61 (2.0)	24 (1.6)
Uninsured (incl. self-pay)	4915 (3.4)	170 (3.9)	109 (3.5)	59 (3.8)
Unknown	1494 (1.0)	42 (1.0)	31 (1.0)	15 (1.0)
Liver disease categories				
Viral hepatitis	28 392 (19.6)	638 (14.6)	448 (14.6)	211 (13.7)
Alcoholic liver disease	16 301 (11.3)	1102 (25.3)	763 (24.9)	391 (25.4)
Autoimmune disorder	15 652 (10.8)	1351 (31.0)	966 (31.5)	518 (33.7)
Metabolic disease	14 344 (9.9)	27 (0.6)	15 (0.5)	9 (0.6)
Primary sclerosing cholangitis	6635 (4.6)	152 (3.5)	118 (3.8)	56 (3.6)
Cancer	4754 (3.3)	110 (2.5)	54 (1.8)	29 (1.9)
Primary biliary cirrhosis	864 (0.6)	114 (2.6)	80 (2.6)	53 (3.5)
Other chronic disease	46 096 (31.9)	483 (11.1)	349 (11.4)	156 (10.2)
Acute liver failure	11 469 (7.9)	384 (8.8)	278 (9.1)	114 (7.4)
Severity of illness at diagnosis				
None	11 985 (8.3)	236 (5.4)	179 (5.8)	85 (5.5)
Minimal	33 284 (23.0)	780 (17.9)	509 (16.6)	246 (16.0)
Moderate	39 719 (27.5)	1575 (36.1)	1142 (37.2)	564 (36.7)
Severe	27 508 (19.0)	1082 (24.8)	746 (24.3)	367 (23.9)
Maximal	3615 (2.5)	71 (1.6)	45 (1.5)	16 (1.0)
Unknown	28 396 (19.7)	617 (14.1)	450 (14.7)	259 (16.9)
Pennsylvania transplant center	N/A	2758 (63.2)	2758 (89.8)	1416 (92.1)
Died during study period	57 020 (39.5)	1678 (38.5)	1027 (33.4)	374 (24.3)

N/A = not applicable for patients at the diagnosis stage.
*p-values < 0.001 (for Pennsylvania transplant center, p = 0.01) because of sample size.

Race/ethnicity: Relative to white patients, black patients were less likely to be referred and evaluated for liver transplantation, even though they had similar overall risks of dying without a transplant (Table 3). For those who reached the evaluation stage, blacks were equally as likely as whites to be listed and transplanted; among cancer patients, blacks were more likely than whites to reach these stages. Among candidates listed for transplant, blacks showed a higher likelihood of dying on the waiting list than did white transplant candidates.

Throughout the process, patients in the other race/ethnicity category experienced lower probabilities both for progressing to the next stage of the process and for death. The only disease-specific exception to this pattern was found in patients being evaluated with hepatitis or acute liver failure, where they had increased likelihoods of being listed by transplant centers relative to white patients with these conditions (see the Appendix).

Patients whose race/ethnicity was classified as unknown (missing from the data set) were more likely to be referred for evaluation, but were similar to white patients in our cohort at later stages (Table 3).

Insurance status: Insurance status is strongly associated with the likelihood of being referred and evaluated for liver transplantation (Table 3). Compared to those insured by Medicare only, patients with commercial insurance were much more likely to be referred and evaluated and much

Table 3: Effect of sociodemographic factors on likelihood of progressing through transplant process

	Diagnosis to evaluation		Evaluation to listing		Listing to transplantation	
	Coefficient estimate for:		Coefficient estimate for:		Coefficient estimate for:	
	Evaluation (p-value)	Death (p-value)	Listing (p-value)	Death (p-value)	Transplantation (p-value)	Death (p-value)
Women (men omitted)	**−0.113**	**−0.437**	**−0.323**	**−0.499**	**−0.319**	−0.092
	(0.010)	**(<0.001)**	**(0.007)**	**(0.001)**	**(0.006)**	(0.513)
Race/ethnicity (white omitted)						
Black	**−0.602**	**0.180**	0.127	0.293	0.170	**0.625**
	(<0.001)	**(<0.001)**	(0.621)	(0.335)	(0.498)	**(0.024)**
Other	−0.047	**−0.317**	**−0.653**	**−1.226**	−0.333	−0.272
	(0.633)	**(<0.001)**	**(0.004)**	**(0.001)**	(0.170)	(0.376)
Unknown	**0.219**	0.068	−0.167	−0.292	−0.294	−0.290
	(0.001)	(0.086)	(0.325)	(0.188)	(0.078)	(0.171)
Insurance status (Medicare-only omitted)						
Commercial only	**0.919**	**−0.304**	**0.580**	0.042	−0.211	−0.284
	(<0.001)	**(<0.001)**	**(0.004)**	(0.866)	(0.371)	(0.301)
Medicaid only	**−0.346**	**0.096**	0.175	**0.625**	−0.240	0.046
	(<0.001)	**(0.001)**	(0.437)	**(0.022)**	(0.354)	(0.879)
Medicare + Commercial	**−0.233**	**−0.073**	0.335	0.318	−0.220	−0.023
	(0.009)	**(0.001)**	(0.178)	(0.269)	(0.438)	(0.944)
Medicare + Medicaid	0.022	**0.286**	0.163	**0.958**	−0.703	−0.439
	(0.859)	**(<0.001)**	(0.628)	**(0.013)**	(0.061)	(0.323)
Uninsured (incl. self-pay)	**0.238**	**−0.371**	−0.234	−0.026	−0.159	0.215
	(0.033)	**(<0.001)**	(0.411)	(0.942)	(0.629)	(0.590)

Bold indicates covariates that were statistically significant ($p < 0.05$).

less likely to die. Once evaluated, they were also more likely to be placed on the waiting list by a transplant center. There was no difference, however, in their likelihood for receiving a transplant.

Similarly, uninsured patients in our cohort (where the numbers are small but do include self-pay patients and, in the case of organ transplant services, may actually be wealthier than uninsured more commonly) had an increased likelihood of being evaluated, despite lower risks of dying. Once they were evaluated, they experienced similar chances for listing and transplantation as the Medicare patients (Table 3).

In contrast, patients covered by Medicaid or by a combination of Medicare and commercial insurance were less likely to be evaluated for liver transplant and more likely to die than Medicare patients in our cohort. Yet once seen by a transplant center, they were equally likely as Medicare patients to be listed and ultimately to receive a transplant (Table 3).

Finally, patients with a combination of Medicare and Medicaid had similar likelihoods for being evaluated, listed and transplanted as Medicare patients, but they also had higher risks of dying early in the process (Table 3).

Discussion

Because donated organs are limited, equitable access to transplant services is of utmost concern. UNOS, which oversees organ allocation in the United States, claims that access will not be based on 'political influence, race, gender, religion, or financial or social status' (23). Moreover, in the case of liver transplants, use of the model for end-stage liver disease (MELD) score (24) for allocating deceased donor livers has emphasized medical urgency (subject to some geographic/regional restrictions) over other criteria, thereby reducing the number of deaths on the waiting list since its adoption (25).

Yet, both UNOS and the MELD scoring system focus on the transplant waiting list, requiring that individuals be referred to, evaluated by and ultimately listed by transplant centers. The decisions that either help or hinder individuals through these earlier stages are largely invisible and take place without governance or oversight. As a result, the total demand for liver transplant services, the equity surrounding transplant decisions and the true cost of donor organ shortages are unknown because the appropriate denominator—all persons with ESLD who are potentially eligible for transplant—is not directly measured.

Our study illustrates the importance of this problem through a retrospective analysis of Pennsylvania-specific data. First, our findings indicate that early management of liver disease varies substantially by gender, race and insurance. Women were less likely than men to move through stages of the transplantation process. Blacks were less likely to be referred and evaluated for transplantation, while patients in our 'other race/ethnicity' classification were less likely to be listed or transplanted. Insurance

status was particularly important in explaining early access to evaluation/referral, whereas it played no role once candidates were placed on the transplant waiting list.

Second, the associations among sociodemographics and progressing through early stages of the process differed substantially from associations at the later stages—when data from UNOS become available. The analysis reported here is the most comprehensive analysis of early access for a population-based cohort of transplant-potential patients, and in that context, the key finding is simple but important: controlling for disease and other important factors, who proceeds through the process to transplantation is significantly determined by gender, race and insurance. In other words, however critical it may be to monitor the national transplant waiting list and ensure fairness in the actual allocation of donor organs, it is equally important to understand prior decisions that exclude many more people from having the opportunity of even being considered for transplantation in the first place.

Our study had several limitations. First, although Pennsylvania is a major provider of liver transplants and had completed 9% of the adult liver transplants performed during the 9-year study period (19), the data were limited to hospitalizations only in this state. Second, we had no information on patients who may have been referred but never evaluated, nor did we have information about patients evaluated at non-Pennsylvania transplant centers but never listed. These are important omissions that available data sources could not address, despite the fact that we did examine access much earlier and fill in many stages of the transplantation process not previously studied. 'Referred but not evaluated' includes patients who refuse to consider transplantation, but it also includes those who cannot afford to travel to a transplant center, even in their own state. As a result, the impact of socioeconomic factors (namely, insurance status and race/ethnicity) is likely to be underestimated here. On the other hand, similar speculation about patients who are evaluated outside Pennsylvania but not placed on the waiting list suggests that this group is more likely to be wealthier and have the economic means to travel to distant centers for consultation.

Third, the retrospective nature of the study prevents us from inferring causality in explaining the differences we observed. Fourth, the study period predates the MELD scoring system, although it is important to reiterate that MELD affects the organ allocation process for patients on the waiting list and the lack of oversight early in the process is as true today as it was prior to MELD.

Despite these limitations, our findings provide statewide population-based evidence about the role of sociodemographics in referral/evaluation, listing and transplant practices for patients with ESLD. The findings underscore the importance of understanding earlier stages of the transplantation process, rather than focusing only on the more visible events after the patient is listed for transplant. Given the persistent shortage of donor organs, it is critical that the process leading to transplantation be both transparent and equitable. Fairness in allocation of organs requires a deliberate effort by policymakers and the transplant community to identify all potential candidates who might benefit from liver transplant services.

Acknowledgments

This publication was made possible by Grant Number K25 DK002903 from the National Institute for Diabetes and Digestive and Kidney Disorders, which supported Dr. Bryce's Career Development Award during the study period, and Grant Number UL1 RR024153 from the National Center for Research Resources and NIH Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NIDDK, NCRR or NIH. Information on NCRR is available at http://www.ncrr.nih.gov/.

The authors also acknowledge assistance from the staff at Pennsylvania Health Care Cost Containment Council; Maureen McBride and Sarah Taranto (the United Network for Organ Sharing); Craig Edelman (the Pennsylvania Department of Health); Howard Nathan (Gift of Life Donor Program); Mical S. Campbell, MD (Coastal Digestive Diseases, New London, CT); Elliot Kozin (University of Pennsylvania); Joe Donaldson (Starzl Transplant Institute); and D. Renae Geraci (University of Pittsburgh).

The contributing authors have no conflicts of interest, including financial interests and relationships and affiliations relevant to the subject of the manuscript.

PHC4 Disclaimer

The Pennsylvania Health Care Cost Containment Council (PHC4) is an independent state agency and has provided data to this entity in an effort to further PHC4's missions of educating the public and containing health care costs in Pennsylvania.

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UNOS Disclaimer

The data reported here have been supplied by the United Network for Organ Sharing (UNOS) as the contractor for the Organ Procurement and Transplantation Network (OPTN). The interpretation are reporting of these data are the responsibility of the author(s) and in no way should be

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Appendix: Coefficient estimates for multinomial regression models

	Diagnosis to evaluation		Evaluation to listing		Listing to transplantation	
	Coefficient estimate for:		Coefficient estimate for:		Coefficient estimate for:	
	Evaluation (p-value)	Death (p-value)	Listing (p-value)	Death (p-value)	Transplantation (p-value)	Death (p-value)
Constant	−2.148 (<0.001)	−3.147 (<0.001)	2.053 (<0.001)	−2.517 (<0.001)	0.937 (0.015)	−1.019 (0.030)
Women (men omitted)	−0.113 (0.010)	−0.437 (<0.001)	−0.323 (0.007)	−0.499 (0.001)	−0.319 (0.006)	−0.092 (0.513)
Race/ethnicity (white omitted)						
Black	−0.602 (<0.001)	0.180 (<0.001)	0.127 (0.621)	0.293 (0.335)	0.170 (0.498)	0.625 (0.024)
Other	0.047 (0.633)	−0.317 (<0.001)	−0.653 (0.004)	−1.226 (0.001)	−0.333 (0.170)	−0.272 (0.376)
Unknown	0.219 (0.001)	0.068 (0.086)	−0.167 (0.325)	−0.292 (0.188)	−0.294 (0.078)	−0.290 (0.171)
Insurance status (Medicare omitted)						
Commercial only	0.919 (<0.001)	−0.304 (<0.001)	0.580 (0.004)	0.042 (0.866)	−0.211 (0.371)	−0.284 (0.301)
Medicaid only	0.346 (<0.001)	0.096 (0.001)	0.175 (0.437)	0.625 (0.022)	−0.240 (0.354)	0.046 (0.879)
Medicare + commercial	−0.233 (0.009)	−0.073 (0.001)	0.335 (0.178)	0.318 (0.269)	−0.220 (0.438)	−0.023 (0.944)
Medicare + Medicaid	0.022 (0.859)	0.286 (<0.001)	0.163 (0.628)	0.958 (0.013)	−0.703 (0.061)	−0.439 (0.323)
Uninsured (self-pay)	0.238 (0.033)	−0.371 (<0.001)	−0.234 (0.411)	−0.026 (0.942)	−0.159 (0.629)	−0.215 (0.590)
Age	−0.019 (<0.001)	0.039 (<0.001)	−0.003 (0.553)	0.044 (<0.001)	0.005 (0.287)	0.021 (<0.001)
Diagnosis (primary biliary cirrhosis omitted)						
Hepatitis (HBV and HCV infection)	−1.353 (<0.001)	−0.599 (<0.001)	−0.265 (0.150)	−0.038 (0.874)	−0.358 (0.041)	−0.168 (0.443)
Acute liver failure	−1.607 (<0.001)	−0.253 (<0.001)	−0.327 (0.210)	−0.137 (0.674)	−0.866 (<0.001)	−0.326 (0.232)
Cancer	−0.685 (<0.001)	0.469 (<0.001)	−1.321 (<0.001)	−0.413 (0.297)	−0.483 (0.305)	−0.155 (0.794)
Metabolic disorders (Met dis), other chronic liver disease	−2.64 (<0.001)	−0.420 (<0.001)	−0.419 (0.040)	−0.637 (0.025)	−0.298 (0.138)	−0.065 (0.790)
Severity of illness at diagnosis ('none' omitted)						
Minimal	0.502 (<0.001)	0.615 (<0.001)	0.003 (0.989)	0.816 (0.019)	0.047 (0.820)	−0.049 (0.848)
Moderate	1.317 (<0.001)	1.296 (<0.001)	0.416 (0.033)	0.905 (0.008)	0.129 (0.498)	0.067 (0.778)
Severe	1.910 (<0.001)	2.220 (<0.001)	0.546 (0.009)	1.370 (<0.001)	0.204 (0.312)	0.270 (0.277)
Maximal	1.662 (<0.001)	2.910 (<0.001)	1.482 (0.018)	3.080 (<0.001)	0.224 (0.626)	1.151 (0.014)
Unknown	0.322 (<0.001)	0.933 (<0.001)	0.010 (0.963)	0.494 (0.176)	0.327 (0.129)	−0.093 (0.732)
Year of index admission (1995 omitted)						
1996	0.145 (0.014)	0.044 (0.055)	−0.236 (0.236)	0.122 (0.960)	0.106 (0.511)	0.252 (0.196)
1997	−0.479 (0.412)	−0.248 (<0.001)	−0.404 (0.036)	−0.355 (0.140)	−0.093 (0.545)	0.094 (0.613)
1998	−0.034 (0.559)	−0.323 (<0.001)	−1.028 (<0.001)	−0.688 (0.002)	−0.290 (0.066)	−0.071 (0.708)
1999	−0.199 (0.001)	−0.501 (<0.001)	−1.097 (<0.001)	−0.730 (0.002)	−0.488 (0.002)	−0.253 (0.196)
2000	−0.250	−0.604	−1.191	−0.979	−0.788	−0.400

Continued.

Appendix: Continued

	Diagnosis to evaluation		Evaluation to listing		Listing to transplantation	
	Coefficient estimate for:		Coefficient estimate for:		Coefficient estimate for:	
	Evaluation (p-value)	Death (p-value)	Listing (p-value)	Death (p-value)	Transplantation (p-value)	Death (p-value)
	(<0.001)	(<0.001)	(<0.001)	(<0.001)	(<0.001)	(0.039)
2001	−0.447	−0.848	−1.413	−1.028	−0.522	−0.812
	(<0.001)	(<0.001)	(<0.001)	(<0.001)	(0.002)	(<0.001)
Interaction: sex and diagnosis						
Female* (HCV, HBV)	−0.238	0.129	0.322	−0.140	0.862	0.215
	(0.015)	(0.002)	(0.244)	(0.703)	(0.745)	(0.498)
Female* (Acute liver failure)	0.736	0.358	−0.044	−0.262	0.791	0.389
	(<0.001)	(<0.001)	(0.895)	(0.553)	(0.011)	(0.277)
Female* (Cancer)	−1.243	−0.236	0.475	0.502	1.192	1.405
	(<0.001)	(0.001)	(0.424)	(0.500)	(0.191)	(0.219)
Female* (Met dis, other chronic)	−0.194	0.089	0.155	0.284	−0.089	−0.277
	(0.053)	(0.004)	(0.566)	(0.456)	(0.744)	(0.404)
Interaction: race and diagnosis						
Black* (HCV, HBV)	−0.130	0.985	0.222	0.449	−0.255	−0.265
	(0.352)	(0.065)	(0.603)	(0.376)	(0.531)	(0.555)
Black* (Acute liver failure)	0.554	−0.169	1.942	1.804	−0.512	−0.444
	(0.783)	(0.020)	(0.069)	(0.118)	(0.351)	(0.445)
Black* (Cancer)	0.882	0.204	21.195	21.738	22.101	20.919
	(0.013)	(0.119)	(<0.001)	(.)	(<0.001)	(.)
Black* (Met dis, other chronic)	0.535	0.107	−0.090	0.230	−0.634	−0.334
	(0.002)	(0.038)	(0.856)	(0.719)	(0.210)	(0.544)
Other* (HCV, HBV)	−0.443	0.149	1.204	0.443	0.427	−0.132
	(0.016)	(0.109)	(0.021)	(0.592)	(0.350)	(0.829)
Other* (Acute liver failure)	0.002	0.051	23.080	23.155	0.765	1.369
	(0.996)	(0.712)	(<0.001)	(.)	(0.327)	(0.093)
Other* (Cancer)	0.210	−0.290	1.057	−0.140	0.247	−33.412
	(0.509)	(0.072)	(0.136)	(0.910)	(0.762)	(1.000)
Other* (Met dis, other chronic)	0.106	0.103	0.997	1.266	−0.418	1.039
	(0.650)	(0.252)	(0.147)	(0.212)	(0.536)	(0.111)
Unknown* (HCV, HBV)	−0.626	−0.090	0.473	0.719	0.766	−0.178
	(<0.001)	(0.201)	(0.292)	(0.208)	(0.066)	(0.781)
Unknown* (Acute liver failure)	0.432	0.073	0.512	0.455	0.196	0.652
	(0.008)	(0.397)	(0.226)	(0.450)	(0.645)	(0.175)
Unknown* (Cancer)	0.018	−0.979	0.022	0.480	−0.472	−33.681
	(0.953)	(0.415)	(0.975)	(0.549)	(0.637)	(1.000)
Unknown* (Met dis, other chronic)	−0.093	0.033	0.452	0.530	0.310	0.084
	(0.566)	(0.525)	(0.300)	(0.394)	(0.464)	(0.883)

*Indicates insufficient sample size to calculate p-value.