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Increase in Mortality Rate of Liver Transplant Candidates Residing in Specific Geographic Areas: Analysis of UNOS Data

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Abstract

We sought to evaluate survival of liver transplant candidates living in geographic areas with limited access to specialized transplant centers (T×C). We analyzed survival outcome among candidates listed for liver transplant in United Network of Organ Sharing (UNOS) Region 4 from 2004 to 2010. Candidates were stratified into three groups according to the distance from the patient's residence to the closest hospital with a liver transplant program: Group 1 (Gr1) <30 miles (m), Group 2 (Gr2) 30–60 m, and Group 3 (Gr3) >60 m. Of the 5673 patients included in the study, 49% resided >30 m from a T×C. Eight percent of the cohort experienced death or dropped out of the list due to medical condition deterioration, with worse outcomes for Gr2 and Gr3 (8.5% and 9.9%, respectively, vs. 6.5% for Gr1 [p<0.001]). Among patients with a MELD score <20, mortality was higher in Gr2 and Gr3 compared to Gr1 (p<0.001). We conclude that for Region 4, the mortality risk in patients living >30 m from a T×C is higher. We suggest that the variable “distance from a T×C” should be used to improve the estimate of the mortality risk for patients on the waiting list.

Keywords

MELD score; waiting list mortality; distance transplant center; geographic residence; UNOS liver transplant

INTRODUCTION

The liver is the second most commonly transplanted solid organ after the kidney. Currently, more than 17,000 people in the United States are waiting for orthotopic liver transplants (OLT) (unos.org). According to the United Network for Organ Sharing (UNOS), approximately 6,100 liver transplantations were performed in the United States in 2009 and approximately 6,300 were performed in 2010 (www.unos.org).

The Model for End-Stage Liver Disease (MELD) system was implemented in 2002 to prioritize patients waiting for OLT and is based on the risk of death within three months

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from listing. The score is objective and calculated using the most recent laboratory data. Variables playing a role in this mortality rate include the severity of liver disease, the rate of organ donation, and criteria used for organ allocation. Since 2002, the MELD score has been used as an objective tool for allocation of organs (1, 2). Worsening of the clinical condition is associated with an increase in MELD score for listed patients, with a consequent higher priority in organ allocation. This often sudden and dramatic deterioration requires specialized medical care not available in all medical centers. From our clinical experience, it has been observed that this suboptimal management of acute clinical deterioration of patients residing in locations distant from the transplant center (TxC) can lead to fatal outcomes.

When considering distance, it is important to look at differences in various regions. In fact, each region might have peculiar differences based on the geographic morphology. According to UNOS, the United States is divided into 11 regions. Among them, there is a huge variability in terms of land area, population density, distribution between urban and rural areas within a single region, socioeconomic disparities, and distribution of TxC (www.census.gov; www.unos.org). Our UNOS Region 4 (Texas and Oklahoma) is a relatively unique geographic area. Texas encompasses 268,580 square miles and Oklahoma totals 69,899 square miles (www.census.gov). These two states rank number 2 and 19 respectively in the US for surface extension, and number 26 and 35 for population density; in addition, they are among the states with the nation's largest rural population (10% of the total population) (www.census.gov). In our region, all liver TxC are located in the largest metropolitan areas: Houston/Galveston, Dallas/Fort Worth, San Antonio, and Oklahoma City. Consequently, many large rural settings and thus a large percentage of the population lives a great distance from a specialized liver TxC.

A recent study by Axelrod et al. highlights the issues faced by candidates living in rural areas (3). Rural residents are less likely to be wait-listed for transplant and up to 20% less likely to get a liver transplant than urban dwellers; these differences were noticed in all 11 UNOS regions (3). Distance to the TxC plays a pivotal role in the disparity of access to the transplant network, as reported by other authors (4–6). However, whether the distance to a TxC may play a pivotal role in waiting list mortality once the patients are listed has never been investigated.

The present study was designed with the specific aim to assess the impact of the geographic area of residence and distance from a specialized TxC on mortality risk of patients with end-stage liver disease waiting for cadaveric OLT in Region 4. Based on our clinical experience, we hypothesize that specialized health care access might play a significant role on mortality in addition to liver disease severity. Individual regional analyses should be performed to investigate their specific significance, as geographical variations in the different UNOS regions might affect the impact of distance.

METHODS

Study design

A retrospective analysis of the UNOS database for patients listed for OLT from January 2004 – July 2010 for any disease in Region 4 was conducted.

The primary objective was to assess overall mortality rate while waiting for OLT. Secondary objectives included analyzing variables such as gender, age, and MELD as predictor of mortality.

The predictor, distance from a T×C, was based on the patient's zip code of residence. Distance from a T×C was considered both as a continuous variable and divided into groups to simplify interpretation. Possible groupings included tertiles, quartiles, and 30–60-mile intervals. Distance under 30 miles is close to a T×C, 30 to 60 miles is within an hour of a T×C and more than 60 miles is at least an hour's drive from a T×C. The decision as to which distance grouping depended on minimizing Akaike's Information Criterion (AIC) (7). This was computed for proportional hazards models with all variables included before statistical testing. The results are shown in Appendix 1. The AIC for the four models indicates the best model for the study would be the 30–60-mile model. The 30–60-mile grouping showed the lowest AIC (Appendix 1), (smaller number indicates that there is less entropy in the study model), hence analysis focused on the 30–60-mile grouping.

Candidates were stratified into three groups according to the distance from the patient's residence to the closest T×C:

- Group 1 (Gr 1) within 30 miles,
- Group 2 (Gr 2) between 30 and 60 miles,
- Group 3 (Gr 3) over 60 miles.

Data collection and analysis

Data were prospectively collected by UNOS. Sociodemographic variables included gender, age at time of listing, and zip code of the listed location of residence. Clinical variables included MELD score at the time of listing, MELD score at the time of removal from the waiting list, diagnosis at the time of listing, reason for removal from listing, date of listing, and date of removal. The distance of candidate's residence from a liver T×C and nearest 300-bed hospital were calculated as distance between zip codes using Geographic Information software (www.zip-codes.com). The follow-up period lasted until November 5, 2010 date of obtaining the database.

Outcome status was defined as death or removal from waiting list due to being deemed too sick to undergo OLT (failure outcome), deceased donor OLT, or survival on waiting list on the follow-up date (still waiting). The censoring event was either transplant or end of follow-up.

The patient's MELD score, gender, and age at baseline were treated as confounding variables. In addition, we recognize that health and distance from a T×C may be associated with socioeconomic characteristics (8). Therefore, we used several zip code level characteristics from the 2000 census to adjust for these effects, as shown in Table 2. Distance to the nearest hospital with at least 300 beds that was not a T×C was also a confounding variable included in the analysis.

Inclusion and exclusion criteria

For the statistical analysis, all adult patients listed for OLT by UNOS were included. Patients younger than 18 years or with acute liver failure as diagnosis at listing were excluded as well as patients who underwent a living donor liver transplant. Patients with incomplete data (missing or invalid zip codes, missing MELD scores, or patients listed as temporarily inactive at the end of follow-up) or with a listed zip code of residence outside Region 4 were also excluded (Figure 1).

Statistical analysis

Demographic characteristics of the subjects were compared using chi-square or a t-test. The MELD score at baseline was treated as a confounding variable. The summaries included

frequency distributions for categorical variables and univariate statistics and plots for continuous variables. Analysis relied on contingency tables and Pearson chi-square statistics for categorical variables (9), and one-way ANOVA to compare groups (10). The primary analysis used Kaplan Meier nonparametric survival curve estimates with log-rank tests (11) to compare the distances for the selected model based on the AIC criterion. This analysis was then adjusted for the confounding variables (patient's MELD score, diagnosis, gender, age at baseline, percent Hispanic population in home zip code, zip code median household income, percentage of households below federal poverty line, and distance to the nearest hospital with at least 300 beds) using Cox's proportional hazards model (11). Because of the large and growing Hispanic population in Texas, we selected proportion of population self identified as Hispanic in the patient's zip code to represent the effect of ethnicity in our statistical models.

To overcome the bias of informative censoring by transplantation, we also estimated models with transplanted patients removed.

All computations were conducted with SAS version 9.2 (*SAS Institute Inc., Cary, NC*). Statistical significance required a p-value 0.05.

RESULTS

Study group demographics

A total of 8250 patients were identified in the OPTN/UNOS data set for Region 4 between 2004 and 2010. After excluding patients according to the study criteria, the final cohort included 5673 patients listed for deceased donor liver transplant (Figure 1). Baseline characteristics of the final population divided into the three groups are summarized in Table 1. Sixty-three percent of the 5673 wait-list patients were male, with significantly different distribution in the three groups. The mean age of the cohort was 53 years old, with significantly younger patients in Gr 3. Mean MELD score at listing was 16 for all groups, and MELD score distribution was comparable among the three groups (Table 1). A total of 49% of the entire population resided over 30 miles from a TxC (Figure 1).

Table 2 shows the socioeconomic status (SES) of the population in UNOS Region 4. Areas of residence at more than 60 miles from a liver TxC are characterized by a higher percentage of non-Hispanic white and Hispanic population, higher percentage of poverty, lower median household income, and lower educational level. Distance to the closest non-TxC hospital did not differ significantly across the groups ($p < 0.0001$) (Table 2). Table 3 summarizes the primary pathological indications for OLT in the three groups of patients. Overall, the most prevalent cause of chronic liver disease was viral hepatitis C infection (HCV), which was the primary indication for OLT in 39% of patients. Cholestatic liver disease, defined as patients affected by primary sclerosing cholangitis (PSC) or primary biliary cirrhosis (PBC), was the primary indication for OLT in 28% of the population, while 10% of the cohort had hepatocellular carcinoma. We observed a significantly different distribution of each primary indication among the groups, with the only exception for alcoholic-related cirrhosis, which was approximately 14% in all groups (Table 3).

Waiting-list mortality

Of the 5673 patients included in the analysis, 456 experienced death or were dropped from the list for medical condition deterioration, i.e. 8% of the entire cohort. The breakdown of the failure rate (dead or too sick) on the waiting list for the three groups showed a significantly better outcome for Gr 1 (6.5%) versus Gr 2 (8.5%) and Gr 3 (9.9%); $p < 0.001$ (Table 1).

Patients residing farther away from a liver TxC also had significantly less chance of transplantation, with 56% and 57% for Gr 2 and Gr 3, respectively, compared to 61% for Gr 1, despite the fact that they were likely listed in more than one TxC (Gr 3 multiple listing 10% versus 8% per Gr 1; $p=0.007$) (Table 1).

At the end of the follow-up, 3352 (59%) were transplanted and 1865 (33%) were still awaiting OLT.

To avoid possible bias from the excluded patients, outcome was analyzed for those with available distance. For the 1777 excluded patients, we had distance available for 1452 patients (325 had missing or invalid zip codes). The excluded patients analyzed had similar distribution as the study cohort (51% in Gr1, 9% in Gr2 and 41% in Gr3). When these patients were added to the study cohort for a total of 7125 (1452 + 5673) and outcome analysis was performed, we did not find differences in our findings (failure outcome: Gr1 15.2%; Gr2 17.2%; Gr3; 19.3%; $p=0.0002$).

Figure 2 shows the Kaplan Meyer (K-M) overall survival curve of the study population adjusted by MELD score stratified per distance; Gr 2 and Gr 3 were combined considering the similarity in the previous shown data (Log-rank $p=0.0002$).

As previously stated, MELD score distribution was not different among groups. We then considered a subpopulation of the entire cohort with less severe liver dysfunction, e.g. the patients with a MELD score at listing less than 20. Among this subgroup, we observed the same trend of significantly worse outcomes for patients residing farther away from a TxC; with 9.9% mortality rate for Gr 3 compared to 5.9% for Gr 1; $p<0.001$. (Table 1) Figure 3 shows the K-M overall survival of the subpopulation with MELD score <20 stratified per distance (Log-rank $p=0.0028$).

Risk factors for waiting-list mortality

We next estimated a proportional hazards model with the data from the study cohort. The results are shown in Table 4. These results clarify the findings based on the K-M analysis, because they were adjusted for personal characteristics. We found that whether a subject was 30–60 miles or more than 60 miles from a TxC, did not change the corresponding hazard ratio, so these groups were combined for the final reporting. The multivariate Cox regression analyses incorporating various confounding factors demonstrated that liver candidates have significantly higher adjusted hazard for more than 30 miles distance from a TxC (HR 1.4892; $p<0.0001$). Additional risk factors associated with increased wait-list mortality were MELD score and age at listing (Table 4). The candidate's gender had no effect on wait-list mortality ($p=0.5838$). To adjust for differences in patient socioeconomic status and education attainment, which may contribute to limited access to specialized medical care, we included these factors in the Cox regression analysis. They did not materially change the association with the distance (Table 4); education, income, poverty, and distance to a 300-bed hospital were not associated with risk of death or being too sick for transplant ($p > 0.18$). Residing in a neighborhood with a higher proportion of Hispanics (surrogate for social status) was associated with a higher risk ($p=0.0042$); however, it is important to emphasize that after adjusting for the confounders (social status, age, underlying illness, and MELD) distance from a TxC remains a significant predictor of outcome (Table 4). When proportional hazard models between censored for transplant and transplant removed were compared, the statistical significance of the distance finding changed from <0.0001 to 0.0002 and the hazard ratio was slightly reduced (Table 4). Therefore we believe the censoring mechanism is not invalidating our findings.

The same analysis was also repeated for the pediatric population (n=371) excluded from the study group (data not shown). For the pediatric population, the association between distance from a liver TxC ($p=0.0165$), PELD score at listing ($p=0.0492$), and the failure outcome was statistically significant (data not shown).

DISCUSSION

This study showed that increased distance from a specialized liver TxC is associated with increased likelihood of death in patients listed for OLT in our region (UNOS Region 4). At equal MELD score, the likelihood of wait list drop out for death or worsening medical condition is significantly higher for patients residing in geographic areas more than 30 miles from a liver TxC (with a 49% increased chance of failure outcome). Therefore, distance from a TxC will improve the predictivity obtained with the MELD score.

A Canadian group has recently shown that geographical factors could have an impact on mortality risk of patients with end-stage liver disease waiting for OLT (12). The authors concluded that residence over 500 Km (approximately 310 miles) from a TxC was an independent predictor of waiting-list mortality (HR 2.1) (12). In our analysis, we observed that living over 30 miles from a liver TxC was an independent predictor of waiting-list mortality for UNOS Region 4 (HR 1.49). The Canadian study focused on a very peculiar geographic area, Atlantic Canada, with 46% of the population living in rural settings. The authors reported a remarkably high waiting-list mortality in Atlantic Canada (35%), which exceed published data (13). In our analysis, we did not observe higher waiting-list mortality compared to the reported literature. Our overall waiting-list mortality was 8%, which was comparable to the reported rate in the literature of 10–24% (14, 15). Our region is also a relatively unique geographic area, including states with large land areas, low population density, large rural populations, and urban settings located at distances exceeding 30–60 miles from a TxC. In our analysis, regardless of the possible rural or urban setting in which this population may live, what appears to be primarily important is the distance (over 30 miles) from a liver TxC.

Due to distance when facing clinical deterioration, this population has delayed access to specialized healthcare or is directed to local medical facilities lacking transplant and hepatology expertise. In our clinical experience, when these patients are hospitalized elsewhere, we observed delay or lack of communication from families and physicians about patient condition changes so that MELD score updates are often delayed or missing in these circumstances.

Increasing the number of transplant-trained gastroenterologists/hepatologists in remote areas and opening satellite transplant clinics are potentially useful but limited options due to the considerable economic impact associated. Also, offering transportation plans to facilitate access to a TxC or using telemedicine-based transplant support for local hospitals could be utilized. Additional areas of improvement are increasing families' and physicians' education about the need of promptly transferring and referring these patients to specialized TxCs and providing real-time updates of laboratory values from the electronic medical record to the TxC to upgrade the MELD score. This can be accomplished by providing patients and their families with identification devices (bracelets) or information cards with instructions to follow in case of emergency and hospitalization in non-TxC. These strategies are partially adopted in our region and if optimized could improve access to OLT and reduce mortality for those on the waiting list who reside far from a TxC.

Patient SES and education attainment might also contribute to limited access to specialized medical care; therefore, to adjust for these differences we included such factors in the

analysis. They did not materially change the association with the distance (Table 4). In addition, in the attempt to overcome all the possible confounding bias, we estimated whether it is the access to a specialized TxC or rather the access to a large hospital itself which contributes to the outcome. OLT candidates living over 30 miles from a TxC lived an average of 30 miles away from a large hospital both in Gr2 and Gr3 (Table 2); the multivariate analysis (Table 4) showed that the distance from these hospitals was not a predictor of outcome ($p=0.8$), while the distance to a specialized TxC was (<0.001).

It is well described how access to care impacts the pre-OLT evaluation and consequently lowers the rate of wait-list registration (3, 16, 17). Rural residents are less likely to be wait listed for transplant, up to 20% less likely to get an OLT than urban dwellers, and have a very high mortality (4–6). These differences are described in all 11 UNOS regions (3). Our study emphasizes the risk for these patients, as we showed increased mortality for patients who overcame the limitation of access to care. We focused on patients who already had initial access to a TxC since they were already listed for OLT and provided evidence that geographic access to a specialized liver TxC correlates with a better outcome. Not only did patients living far away have a significantly higher death rate while on the waiting list (10% vs. 6%; $p<0.001$), they also had a reduced chance of transplantation (57% vs. 61%; $p=0.004$) despite the fact that they were often listed in multiple centers (10% vs. 8%; $p=0.005$). Increased waiting-list mortality was also observed for not necessarily sick patients (i.e. MELD <20) when residing over 30 miles from a specialized TxC (Table 1). High mortality with such low MELD is not expected and it appears that patients living at farther distance from a TxC die with a low MELD almost twice as frequently. This cannot be explained by disease distribution. For example, hepatocellular carcinoma, which in our analysis is associated with higher mortality ($p=0.03$), is more frequent in patients living within 30 miles from a TxC (<30 miles 12% vs. >30 miles 8%). This data seems to support that there are management issues in these patients when mortality is seen.

Our study did not focus on the post-transplant outcome specifically for Region 4, however as reported by Axerlod et al. (3), there was no difference in the post-transplant outcomes between patients residing in urban or rural areas in all 11 UNOS regions. The concept of distance as a factor in limiting accessibility, utilization of healthcare, and worsening outcome has also been described in cancer patients (18–20). Geographic factors were an important consideration in the National Cancer Institute's initial deliberations about where cancer centers should be developed in the attempt to optimize access for the US population. The fall in use with increased distance is apparently geometric, and it is not surprising that proximity is the major determinant of where cancer patients are diagnosed and whether they are referred after diagnosis (19–21). An attempt to apply this concept to the transplant population was described in one study focused on the need to maximize geographic access to liver TxC for liver-disease patients in the US (22). The authors of this study concluded that 100 optimally placed satellite clinics in the US would increase accessibility to a liver TxC from 64% to 93% for liver disease patients (22). However, in our opinion, this solution is associated with a significant cost and is not always practical in all areas.

This study shows that in Region 4 there are geographically pervasive disparities in patient survival for OLT candidates living over 30 miles from a specialized TxC. We suggest that corrective measures to balance the mortality risk in this population be adopted. When considering distance, it is important to consider differences in various regions. In fact, each region might have peculiar differences based on the geographic morphology. A straight-line distance between residence and a TxC provides only a crude measure of the travel time, and other factors such as actual driving mileage, traffic, and seasonal road conditions might be also important. Among the 11 UNOS regions, we would expect to find similar association of distance from a TxC and outcome observed in Region 4 in regions with similar geographic

characteristics (i.e. low density and vast land area). Meanwhile, in regions with high population density and small land area this phenomenon could be attenuated or absent.

The idea of distance is embedded in the philosophy of organ allocation. In fact, it has been stated by Malinchoc et al. in his initial work on MELD that the ideal model “should use commonly available determinants, be easily calculated, and be widely applicable to geographically diverse patient.” (23) Further studies focusing on other UNOS regions are necessary to confirm our observations in order to nationally validate the conclusions or to identify local variables.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Flow diagram representing the study population

The total number of patients listed for liver transplantation in UNOS Region 4 (Texas-Oklahoma) over a period of 6 years (Jan 2004-July 2010) was 8250. Among them, patients with acute liver disease diagnosis (153), with incomplete data (1777), with a zip code of residence outside Region 4 (276), and pediatric patients (<18 years of age) (371) were excluded from the analysis because they did not meet the inclusion criteria. The final study population of 5673 patients was divided into three groups according to the distance from patient's residence to the closest hospital with a liver transplant program: Group 1 (Gr 1)—within 30 miles, Group 2 (Gr 2)—between 30 and 60 miles, and Group 3 (Gr 3)—over 60 miles.

Time point (days)	0	90	500	1000	1500	2000
Gr1 – N	2890	1801	794	322	122	42
Gr2+3 – N	2783	1786	807	345	113	37

Figure 2. Overall waiting list survival rate adjusted per MELD and stratified per distance
 Comparison of Kaplan-Meier curves for patients waiting for liver transplantation (OLT) in UNOS Region 4 stratified per distance from the liver transplant center (T×C). Solid line: Group 1 (Gr 1), <30 miles from T×C. Interrupted line: Group 2 (Gr 2) and Group 3 (Gr 3) combined, ≥ 30 miles from T×C. The difference in survival between the patients residing at less than 30 miles and over 30 miles from a T×C was statistically significant ($p= 0.0002$).

Time point (days)	0	90	500	1000	1500	2000
Gr1 – N	2161	1659	757	316	117	41
Gr2+3 – N	2139	1663	786	337	112	36

Figure 3. Waiting list survival rate for the subpopulation of MELD score <20, adjusted per MELD and stratified per distance

Comparison of Kaplan-Meier curves for patients with MELD score less than 20 waiting for liver transplantation (OLT) in UNOS Region 4 stratified per distance from the liver transplant center (T×C). Solid line: Group 1 (Gr 1), <30 miles from T×C. Interrupted line: Group 2 (Gr 2) and Group 3 (Gr 3) combined, ≥30 miles from T×C. The difference in survival between the patients with MELD <20 residing at less than 30 miles and over 30 miles from a T×C was statistically significant ($p=0.0028$).

Table 1

Demographic and clinical characteristic of study population (Total no. 5673 patients)

Variable	Statistic	Gr1	Gr2	Gr3	p-value
Sample Size		2890	573	2210	
Age	mean	53.16	53.18	52.50	0.0374**
	SD	9.59	8.76	9.68	
Gender male	%	63.36	67.19	60.54	0.0072*
	n	1831	385	1338	
Days in listing	Mean	373.95	402.50	393.1	0.2869**
	SD	475.76	494.35	478.60	
MELD Score at listing	Mean	15.76	15.83	16.04	0.4143**
	SD	7.66	7.44	7.60	
	n	2890	573	2210	
MELD < 20 (4300 tot)	%	75.92	76.96	75.34	0.8731*
	n	2194	441	1665	
MELD 20 to 30 (954 tot)	%	17.66	15.96	16.76	
	n	485	88	381	
MELD > 30 (419 tot)	%	7.3	7.68	7.42	
	n	211	44	164	
Failure outcome	%	6.5	8.55	9.9	<0.0001*
	n	188	49	219	
OLT	%	61.04	55.67	57.42	0.004*
	n	1764	319	1269	
Multiple Listing	%	8.1	8.2	10	0.007*
	n	233	47	222	
Still waiting	%	32.46	35.78	32.67	0.5945*
	N	938	205	722	
Mortality per MELD <20 (4300 tot)	%	5.9	6.3	9.9	<0.001*
	n	129/2161	30/479	165/1660	

TxC: transplant center; Gr1=group 1, within 30 miles, Gr2=group 2, between 30 and 60 miles, and Gr3=group 3, over 60 miles; SD: standard deviation; n: number of patients; tot: total; Failure outcome: death or dropped from the list; OLT: orthotopic liver transplantation.

* Pearson Chi-Square
** One-way ANOVA F-test

Table 2

Socio-economic status of UNOS region 4 population based on zip code level characteristics from the 2000 census

Variable	Statistic	Distance from liver TxC			p-value*
		Gr1	Gr2	Gr3	
Percent NH White	Mean	55.94	75.51	59.53	<0.0001
	SD	25.56	15.79	27.43	
Percent NH Black	Mean	12.16	5.29	7.70	<0.0001
	SD	15.62	7.66	10.67	
Percent Hispanic	Mean	25.87	15.65	28.42	<0.0001
	SD	22.38	13.58	29.66	
Percent Other	Mean	6.03	3.55	4.35	<0.0001
	SD	4.56	4.19	5.60	
Percent of all households are single-parent households with children	Mean	9.65	7.84	9.19	<0.0001
	SD	3.58	2.07	3.18	
Percent of adults have at least high school diploma	Mean	79.66	78.16	74.79	<0.0001
	SD	14.92	7.86	13.53	
Median Household Income (000s)	Mean	49.58	41.78	36.15	<0.0001
	SD	17.68	11.53	13.36	
Percent of persons in households in poverty	Mean	11.35	12.05	17.04	<0.0001
	SD	8.36	4.86	9.67	
Closest TxC (miles)	Mean	12.90	42.14	153.60	<0.0001
	SD	7.07	8.78	105.95	
Closest 300 Bed Hospital (miles)	Mean	30.21	27.58	29.99	0.7353
	SD	82.01	40.12	69.83	

NH: non Hispanic; TxC: transplant center; Gr1=group 1, within 30 miles, Gr2=group 2, between 30 and 60 miles, and Gr3=group 3, over 60 miles; SD: standard deviation.

* One-way ANOVA F-test

Table 3
Primary indication for liver transplantation (OLT) in the study population (Total no. 5673 patients)

Primary indication	Statistic	Total	Distance from TxC			p-value
			< 30	30 –60	>60	
HCV	%	39.27	37.85	43.98	39.91	0.0369*
Cholestatic Liver Disease (PSC, PBC)	N	2228	1094	252	882	
	%	27.55	26.71	23.91	29.59	0.0193*
Alcohol-related cirrhosis	N	1563	772	137	654	
	%	13.62	13.15	13.96	14.16	0.4891*
HCC	N	773	380	80	313	
	%	10.1	11.87	8.38	8.24	0.0008*
Others	N	573	343	48	182	
	%	9.45	10.42	9.77	8.1	0.0139*
	N	536	301	56	179	

TxC: transplant center; Gr1=group 1, within 30 miles, Gr2=group 2, between 30 and 60 miles, and Gr3=group 3, over 60 miles; N: number of patients; HCV: Hepatitis C virus infection; PSC: primary sclerosing cholangitis; PBC: primary biliary cirrhosis; HCC: Hepatocellular Carcinoma.

* Pearson Chi-Square

Table 4

Proportional hazards model for distance effect on failure outcome (mortality or being dropped because too sick). Multivariate analysis of risk factors predicting overall wait-list mortality in patients with end stage liver disease listed for liver transplantation (OLT) in UNOS Region 4. Results are presented for patients censored for transplant and for transplant removed.

Parameter	Censored for Transplant				Transplant Removed			
	p-value	Hazard Ratio	Lower	Upper	p-value	Hazard Ratio	Lower	Upper
MELD at Listing	<.0001	1.1402	1.1257	1.1548	<.0001	1.1663	1.1520	1.1808
Age in decades	<.0001	1.4417	1.2869	1.6150	<.0001	1.3043	1.1671	1.4576
Gender (Male is referent)	0.5838	1.0565	0.8678	1.2863	0.0089	1.3065	1.0695	1.5960
Diagnosis (Alcohol disease is referent)	0.0138							
Cholestatic Liver Disease	0.4043	1.1429	0.8349	1.5645	0.0081	1.5325	1.1172	2.1022
HCV	0.0245	1.3870	1.0430	1.8445	0.0012	1.6077	1.2069	2.1415
cancer	0.0347	1.7042	1.0390	2.7953	<.0001	3.6840	2.2461	6.0426
others	0.0052	1.7370	1.1797	2.5577	<.0001	2.2177	1.5034	3.2715
Proportion Hispanic (0.01)	0.0042	2.0227	1.2489	3.2760	0.0114	1.9024	1.1557	3.1315
Median Household Income ('000s)	0.1822	1.0064	0.9970	1.0158	0.4978	1.0034	0.9935	1.0135
Proportion of persons living in households < federal poverty line (0.01)	0.6250	1.6124	0.2374	10.9520	0.9083	0.8885	0.1188	6.6459
Nearest 300 Bed Hospital (/100 miles)	0.8417	1.0143	0.8822	1.1662	0.4964	1.0546	0.9047	1.2293
< 30m vs 30m (<30m is referent)	0.0001	1.4892	1.2136	1.8272	0.0020	1.3913	1.1286	1.7152

Censored for Transplant		Transplant Removed
Number of Observations	5673	2321
Non censored	456	456
Censored values	5217	1865