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Racial and spatial disparities in liver transplant acceptance in the United States

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2019

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An abstract of
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Rollins School of Public Health of Emory University
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Abstract

Racial and spatial disparities in liver transplant acceptance in the United States

By Haley Tailor

Little is known about how transplant center behaviors are associated with liver transplant offer acceptance rates and whether this may result in racial and spatial disparities in acceptance. Liver transplant offer acceptance refers to a transplant center's acceptance of a given donor organ on a candidate's behalf. Recent OPTN organ allocation policies have shifted transplant center behaviors, specifically in organ offer practices. We examined the association between transplant center behaviors and liver transplant acceptance in the United States from 2020-2021 upon implementation of updated OPTN organ allocation policies. We obtained data from the Scientific Registry of Transplant Recipients (SRTR) and performed a multiple linear regression model to assess the association between the racial and spatial distribution of a transplant center's patient population and that center's liver acceptance rate. Candidate demographics and center-level characteristics were described to ascertain variation across centers. Rates of offer acceptance responses were represented visually by race and distance to a transplant center. Rates of acceptance within racial groups remained consistent across all groups. Distance to a transplant center did not prove significant in liver transplant acceptance. While no significant association between transplant center behaviors and liver transplant acceptance was found, there was substantial variation in liver transplant acceptance across individual centers. Examination of transplant center behaviors and how they may play a role in transplant outcomes is imperative to ensuring equitable transplant outcomes.

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BACKGROUND

Introduction

Liver transplantation is the leading curative treatment for end-stage liver disease and has become the standard therapy for acute and chronic liver failure of all etiologies (1). More than 80,000 liver transplantation procedures were performed as of 2016 (1). By definition, liver transplantation is a surgery that replaces non-functioning livers and with a healthy liver from a deceased donor or a portion of a healthy liver from a living donor (2). As the body's largest internal organ with several critical functions, liver transplants are a treatment method reserved for individuals with complications such as end-stage chronic liver disease, cirrhosis, or sudden liver failures (2). According to the Mayo Clinic, the number of people waiting for a liver transplant greatly exceeds the number of deceased-donor livers (2).

History of liver transplantation

In 1963, the first liver transplantation was performed by Starz (8). Of the first five liver transplantations, no patient survived more than 23 days (9). Infection complications and chronic rejection in liver transplantation were known causes of death (9). Since then, considerable progress has been made in the care of liver transplant candidates and recipients with immunosuppressants and anti-infection agents to increase the success of transplantation (8,9).

The National Institute of Health (NIH) declared liver transplantation as an accepted therapy for end-stage liver disease in 1983 (10). Currently, the one- and five-year patient survival rates are approximately 85 and 75% (11). Liver transplantation is a highly successful treatment method commonly used in patients with viral hepatitis (24%), alcoholic liver disease (20%),

cholestatic liver diseases (18%) and hepatocellular carcinoma (10%) (7). The versatility of this treatment method has led to over 10,000,000 liver transplantations in the world.

History of MELD scores

Prior to 2002, the Child-Pugh-Turcotte scoring classification system was used to prioritize patients in need of liver transplants (1). Priority for those on the waitlist was based on waiting time and severity of liver disease (1). Since then, the Model of End-Stage Liver Disease (MELD) scoring system was developed and is validated as an accurate predictor of survival among different populations of patients with advanced liver disease (12). Initially, MELD was used to determine short-term prognoses and predicting 3-month mortality in patients with end-stage liver disease (1). The rationale behind using the MELD score is the 'sickest first' policy in which mortality risk determines organ allocation, instead of time on the waitlist (12). After the introduction of MELD scoring in the United States, waitlist morality has dropped substantially (16). Advancements in MELD scoring have also made it possible to predict survival in patients with cirrhosis who have infections, variceal bleeding, fulminant hepatic failure, and alcoholic hepatitis (12).

MELD score mechanics

MELD incorporates 3 widely available laboratory variables including the international normalized ratio (INR), serum creatinine, and serum bilirubin. The INR is used to measure the time for the blood to clot or whether a blood clotting problem exists in the patient. An INR of 1 is considered normal and each increase of 0.1 represents slightly thinner blood, or a longer time to clot (13). The MELD score was updated recently to incorporate serum sodium and estimates survival probability and disease severity in patients with cirrhosis (17). However, numerous

studies question its predictive power and claim it does not resolve the disparity in the allocation of organs between various organ procurement organizations (17,18).

US organ allocation system

UNOS, the United Network for Organ Sharing, manages the organ transplantation system in the United States (19). There are 56 Organ Procurement Organizations (OPOS) responsible for recovering organs from deceased donors for transplantation and mandated by federal law to perform transplantations in donation service areas (DSA) (3). After an OPO receives consent for an organ donation, medical data is entered into a secure web-based transplant platform that is used to link all OPOs and transplant hospitals (3). Thus, the data for potential match-runs is made available and ready for use.

Match run mechanics

For every deceased-donor liver, UNOS ranks all all-eligible patients based on blood type, recipients' geographic location, most recent MELD score, and their willingness to accept based on donor characteristics (19). Once rankings are identified, the organ is then offered to the center with the highest-ranked patient on the waitlist (19). This match run is defined as a rank-order list of candidates to be offered each organ using a combination of donor and candidate information (4). A match is considered unique to each donor and each organ (4). Rankings for match runs appear where the highest rank represents urgent need or most likely to survive a transplant whereas the lowest rank represents low priority or low chance of survival (4). To account for new patients and changing MELD scores, rank lists for each organ are constantly changing.

While the rank system is a sequential and effective process in liver matching, transplant centers may also make exceptions.

Transplant center behaviors

There is marked variability in center practices regarding accepting livers allocated to the highest-priority patients (19). Center-level decisions to decline a liver substantially increased patients' odds of dying on the waitlist on a transplant (19). Variation in practice between units also impacts waitlist mortality (20). Center-level acceptance rates were associated with wait-list mortality, with a >10% increase in risk of waitlist mortality for every 1% decrease in a center's adjusted liver offer acceptance rate (20). Additionally, transplant center incentives for liver transplantation vary greatly. While there is differential utilization of available organs, high volume centers and centers with more local competition often use higher-risk organs (19).

Despite an allocation system strategically designed to expedite donor livers to the sickest patients, a vast number of transplantable livers are declined by transplant centers leaving many patients to die without transplantation (19). When a liver is offered to a transplant center, the center could decline an organ due to donor quality (e.g. donor age), recipient clinical status, donor-recipient size mismatch or because a patient ranked as low priority has a seemingly greater risk of death (19). Upon decline, the patient is subject to future offers or dies without being transplanted (19).

In 2020, the liver distribution policy was modified to replace donation service areas and regions with circles for distribution livers (5). The new prioritization system ensures that livers from all deceased donors are offered to candidates at transplant hospitals within a radius of 500

nautical miles of the donor hospital (5). After that, livers are distributed depending on the donor's age and mechanism of death (5).

Race-specific trends in liver transplantation

Racial disparities in liver transplant acceptance rates are only marginally understood. In an expanded MELD-era analysis, Black, Asian, and patients classified as other race had similar adjusted liver transplant rates to White patients. Hispanic patients had an 8% lower rate of liver transplant compared with White patients (hazard ratio [HR], 0.92; P=0.011). Other studies have examined the role that transplant centers may play in perpetuating racial disparities in liver transplant outcomes and identified significant racial disparities in survival after transplant (21).

Geographic trends in liver transplantation

Geographic patterns in liver transplantation depend strongly on disparities in burden of care and access to transplantation services. Regional disparities in allocation are a result of the distance between a patient's home and the transplant center and its policy (22). Moreover, visualizations of transplant registrations revealed geographic disparities in organ allocation (22). Upon identifying geographic disparities, it has been suggested that the distance from the transplant center should be included to improve the estimate of the mortality risk for patients on the waitlist (22). A larger distance from a liver transplant center is associated with a higher likelihood of mortality and a lower likelihood of transplantation, giving an advantage to individuals living in urban areas over rural areas (23). Local transplant center density was significantly associated with organ offer acceptance patterns (19).

Public health implications and study purpose

In this study, we will estimate variation in liver transplant offer acceptance rates in the United States and identify and describe racial and spatial trends in liver transplantation acceptance. Upon recent policy changes in 2020, it is imperative to understand how the new allocation system may perpetuate disparities in liver transplant acceptance. Examining spatial trends in liver transplant acceptance allows us to identify geographic heterogeneity among distances to a transplant center, which could inform future center-level transplant policy. Furthermore, examining racial trends in liver transplantation acceptance informs us of how transplant center behaviors may contribute to racial inequities in access. There is an increasing need to understand how acceptance patterns vary across the United States as this may inform organ allocation policy and targeted interventions among centers to reduce or prevent inequities in liver transplant acceptance.

INTRODUCTION

Liver transplantation, the only curative treatment for end-stage liver disease, is becoming the standard therapy for acute and chronic liver failure of all etiologies, with more than 80,000 procedures performed as of 2016 (1). In the past, donated livers were generally offered first to the sickest candidates in donation service areas (6). However, after the implementation of the Organ Procurement and Transplantation Network's liver allocation policy in 2017 and 2020, livers are now generally offered first to the sickest candidates based on distance (6). Previous literature suggests that there is marked variability in center practices regarding accepting livers allocated to the highest priority patients (19). Center-level decisions to decline organs substantially increased patients' odds of dying on the waitlist without a transplant (19). With a scarcity of donor organs relative to the high number of patients on the waitlist, it is important to focus on organ utilization and allocation as it is critical in ensuring optimal outcomes for all candidates in need.

Patients face unique barriers to referral and acceptance for organ transplant based on social determinants of health (24). Prior research examining disparities in patients receiving liver transplants noted that compared to Whites, Blacks and Native Americans had decreased transplant rates (25). According to a study by Epstein et al., Black patients are less likely than White patients to be rated as appropriate candidates for transplantation according to appropriateness criteria based on expert opinion, (71 blacks [9.0 percent] vs. 152 whites [20.9 percent]) and were more likely to have had incomplete evaluations (368 [46.5 percent] vs. 282 [38.8 percent] (25), among patients considered to be appropriate candidates for transplantation, Blacks were less likely than Whites to be referred for evaluation, placed on a waiting list, or to undergo transplantation (25). This knowledge suggests there are racial disparities at many steps

in the transplant process, but further research is needed to examine differences in acceptance rates for racial minorities. Moreover, less is known about the role of transplant centers in perpetuating racial and spatial disparities in liver acceptance. While policy changes have been implemented to create equitable transplant outcomes, little is known about how transplant center behaviors contribute to liver transplant acceptance rates and whether variation in acceptance exists across racial groups and distance to a transplant center.

In addition, geographic heterogeneity in liver transplantation is strongly impacted by OPTN policy mechanisms. Recent organ allocation policy has shifted liver transplant allocations to a radius of donor hospitals (5). Prior studies have examined and suggested that distance from a transplant center be examined to understand mortality risk and organ offer acceptance patterns (19, 22). One study suggests that local transplant center density was significantly associated with organ offer acceptance patterns (19). However, the available evidence of geographic heterogeneity in liver transplantation is limited in examining differences since recent organ allocation policy changes in 2020.

Understanding how center-level behaviors contribute to racial and spatial disparities in liver transplant acceptance rates is imperative to reducing waitlist mortality for racial minorities and ensuring equitable transplant outcomes. Further, this can effectively inform policy efforts and center-level interventions to improve liver transplant outcomes. The purpose of this study was to examine the association between transplant center behaviors and liver transplant acceptance rates among centers across the United States, and whether transplant center behaviors perpetuate racial and spatial disparities in this relationship.

METHODS

Data Source

Liver transplant recipient data from SRTR, the Scientific Registry of Transplant Recipients were obtained. Briefly, SRTR is a database that collects transplant data directly from the OPTN and supplemented by data from the Centers for Medicare and Medicaid Services (14). We included data from 2020-2021 of 12,624,574 match runs across 142 transplant centers across the United States. A match run is defined as a rank-order list of candidates to be offered each organ using a combination of donor and candidate information (4). Match runs include candidates who were offered livers and registered on the OPTN waitlist and candidates who received a living donor liver transplant, even if they were never placed on the waitlist. We examined the match run data to estimate variation in offer response based on distance to a transplant center. For distance analysis, offer data of 114 transplant centers across the United States were included (excluding Hawaii and Alaska). In addition, the match run data were similarly examined to estimate variation in offer response based on reported candidate race status. Patients with missing offer response, race or zip code data were excluded from the analysis.

Variables

For further analysis, race and candidate zip codes were included. Race was categorized as White, Black, Asian, Native Pacific Islander, and multi. Offer response rates were calculated across each racial group. Candidate zip codes were also examined alongside center zip codes to assess distance (in miles) between the candidates place of residence and center at which offers were made. Upon initial examination of the distribution in candidate distances from a transplant center, distance bands were identified in miles as 0-20, 20-50, 50-100, and 100+. Furthermore, the distance bands were created as intervals to categorically examine variation in offer

acceptance response by distance from a transplant center. Offer response rates were also calculated across each distance band. Geographic heterogeneity and racial heterogeneity in offer acceptance responses were represented visually by stacked bar graphs created in R-Studio.

Outcome and Analysis

Our primary outcome of interest was liver transplant offer acceptance rates, specifically, accepted offers. Offer acceptance information was categorized as “yes”, “no”, “provisional yes” “bypass”, where response types “provisional yes” and “yes” were categorized as “yes”. Current OPTN policy defines “provisional yes” as when the transplant hospital notifies OPTN or the host Organ Procurement Organization indicates interest in accepting the organ or receiving more information about the organ (15). Because we were interested in understanding variation in center organ utilization, we considered a provisional yes to also indicate acceptance as it has been used to express interest in accepting an organ (4). While “provisional yes” is useful in managing organ offers, it is not always effectively used and thus was categorized as a single “yes” response (15). Offer data were aggregated by transplant centers and offer acceptance response for primary analysis. Rates of offer acceptance response were calculated.

To explore whether transplant center behaviors were associated with liver transplant offer acceptance rates, we performed a multiple linear regression model in R-Studio. Center characteristics such as center codes and center zip codes were included in the analysis alongside offer data. In addition, general center-level and candidate characteristics were examined in Table 1.

RESULTS

As presented in Table 1, the study sample includes transplant candidates who received offers across 142 transplant centers. 337,224 adult patients who were identified as candidates for a liver transplant between January 1,2020 and December 31,2021 were included. Demographic and transplant center characteristics are noted in Table 1. In this sample, an average of nearly 200 offers were made to each candidate (interquartile range, 26.0 - 262.0). Approximately 7% of candidates in this study were Black whereas 86% were White. On average, there are nearly 200 liver transplant offers made per candidate (interquartile range: 26.0-262.0). The mean age of transplant candidates at listing was 52.83 with the youngest candidate being 47 years and the eldest being 63 years. Table 2 presents results from a linear regression model estimating the effects of transplant center behaviors on offer acceptance. Figure 3 highlights variation in offer response types by transplant center with a range of offer acceptance rates from 7.3-38.1%.

Racial Variation in Offer Acceptance

Our findings indicate that the proportion of accepted transplant offers did not vary substantially by race. While Black candidates had a 16.2% offer acceptance rate, White candidates had a 15.5% offer acceptance rate. This difference in offer acceptance is marginal. Subsequently, Asian candidates and Native American/Pacific Islander candidates also had 14.5% and 15.0% acceptance rates, respectively. Though there is a large difference in racial distributions across the sample, rates of acceptance within racial groups remain fairly consistent. For every one percent increase in overall rate of accepted liver transplant offers, there is a decrease in offer acceptance by racial group (Whites, Blacks, Asians and Native American/Pacific Islanders) when distance bands are held constant (-0.082, p=0.66; -0.079, p=0.69; -0.089, p=0.73; -0.141, p=0.63).

Geographic Variation in Offer Acceptance

Similarly, variation in the proportion of accepted transplant offers did not vary by distance to a transplant center. Figure 1 visualizes differences in offer response by distance bands and indicates no substantial variation. Results from the multiple linear regression analysis also suggest that for every one percent increase in overall rate of accepted liver transplant offers, there is no significant increase in offer acceptance by distance band (0.020, p=0.78; 0.099, p=0.05, -0.029, p=0.50).

DISCUSSION

There is little heterogeneity in offer acceptance by race and distance from a transplant center. As found in our study, the proportion of accepted transplant offers only varied marginally across racial groups. Similarly, distance to a transplant center is not a significant predictor of offer acceptance. However, variation in offer acceptance across transplant centers in the United States is substantial and highlights how center-level decisions impact offer acceptance.

We built on previous research that suggests that transplant center decisions to decline organs increases a patient's odds of dying on the waitlist without a transplant (19). Upon OPTN transplant policy changes in 2020, we sought to understand whether transplant center behaviors contribute to racial and spatial disparities in liver transplant acceptance. In contrast to previous studies that have examined transplant center behaviors (21), we did not observe a significant association between transplant center behaviors and liver transplant outcomes. It is possible these findings are attributed to limitations in substantial center-level characteristics. Our findings indicate there is little geographic and racial heterogeneity in liver transplant offer responses across the United States. While center-level acceptance rates were associated with wait-list mortality (19), results of this study indicate that there are no known racial and spatial disparities in liver transplant offer acceptance.

Results of the multiple linear regression model suggest a negative association between predictors in the model and rate of offer acceptance. Using this model, we sought to examine geographic patterns in liver transplant acceptance. In a study conducted by Ghaoui et al., it was suggested that distance from the transplant center should be included in future studies to improve estimates of mortality risk (22). In our study, we examined offer acceptance rates by distance from a transplant center using distance bands. Our findings suggest that that there is no

statistically significant association between transplant center behaviors and offer acceptance variation across distance bands 20-50 and only marginal significance for candidates 50-100 miles away from the transplant center. Furthermore, our linear regression analysis also suggests that transplant center behaviors do not perpetuate disparities in offer acceptance by race (Table 2). While there appears to be substantial variation across transplant centers in offer response (Figure 3), transplant center behaviors that contribute to this are not well explained. Further research would need to examine center-specific offer practices, outside of adhering to organ allocation policies, that contribute to variation in candidate offer acceptance.

Limitations

Despite a robust and representative sample of liver transplant candidates in the US, the present study has a few limitations. The present analysis examines the association of transplant center behaviors using subsamples of existing offer data. While the sample size is quite large, it is possible that the racial distribution of the existing sample may have impacted regression results. A vast majority of the sample used to examine the association by race includes White candidates. This may limit our understanding of the true effects on racial minority groups who are offered liver transplants. In addition, including offer data of transplant centers outside of the contiguous United States (e.g. Hawaii and Alaska) may appropriately demonstrate the effects for Native American and Pacific Islander groups. Furthermore, it is important to note that distance band categories were arbitrarily assigned upon initial examination of the distribution of candidate distances from a transplant center.

Future research should consider incorporating further transplant center characteristics to explore broader transplant center level behaviors that may impact transplant offer acceptance. Including multiple years of SRTR data may also improve potential to detect candidate patterns in

offer response. This may be useful in examining candidate preferences for transplant centers. Additionally, future studies may consider understanding between center effects through further multilevel analysis. Lasty, while the present study seeks to understand transplant center behaviors after recent changes in OPTN allocation policy, center-specific operations that may contribute to organ acceptance were not accounted for. This analysis serves as the first initial examination of offer variation across transplant centers in the United States after updated OPTN policies in 2020.

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TABLES AND FIGURES

Table 1: Characteristics of U.S. Transplant Center Organ Offers and Candidate Demographics (2020-2021)

	Total (N=142) **N (%) / Mean [IQR]**
Descriptive	
Center Total	142
Offers per candidate	199.5 [26.0 - 262.0]
Offers per center	52,776 [8,274-7,9223]
Gender	
Female	14,645 (39.0%)
Male	22,915 (61.0%)
Age	52.83 [47-63]
Race	
White	32,466 (86.9%)
Black or African American	2,764 (7.4%)
Asian	1,630 (4.4%)
Alaska Native or Other Pacific Islander	450 (1.20%)
Multi-racial	52 (0.1%)
Ethnicity	
Latino	6,872
Non-Latino	30,688
Previous Liver Transplant	
Yes	1,343 (3.6%)
No	36,217 (96.4**%)**
Offer Response by Center	
Yes or Provisional Yes	7,584 (14.9%)
No	33,002 (62.5%)
Bypass	11,919 (22.6%)

Table 2: Linear Regression Model of U.S. Transplant Center Organ Offers and Candidates (2020-2021)

Model	***B***	**Std. Error**	**T**	**Significance**
Variables				
Percent of White candidates	-0.082	0.188	-0.438	0.662
Percent of Black candidates	-0.079	0.195	-0.403	0.688
Percent of Asian candidates	-0.089	0.254	-0.351	0.727
Percent of Native Am./ Pacific Islander candidates	-0.141	0.293	-0.483	0.630
Percent of candidates 20-50 miles from TC	0.020	0.074	0.277	0.782
Percent of candidates 50-100 miles from TC	0.099	0.051	1.951	0.054
Percent of candidates 100+ miles from TC	-0.029	0.042	-0.681	0.497

Figure 1: Liver transplant offer responses by distance (in miles) from transplant center across the United States. All percentages are calculated as rates; SRTR, Scientific Registry Transplant Recipient 2020-2021.

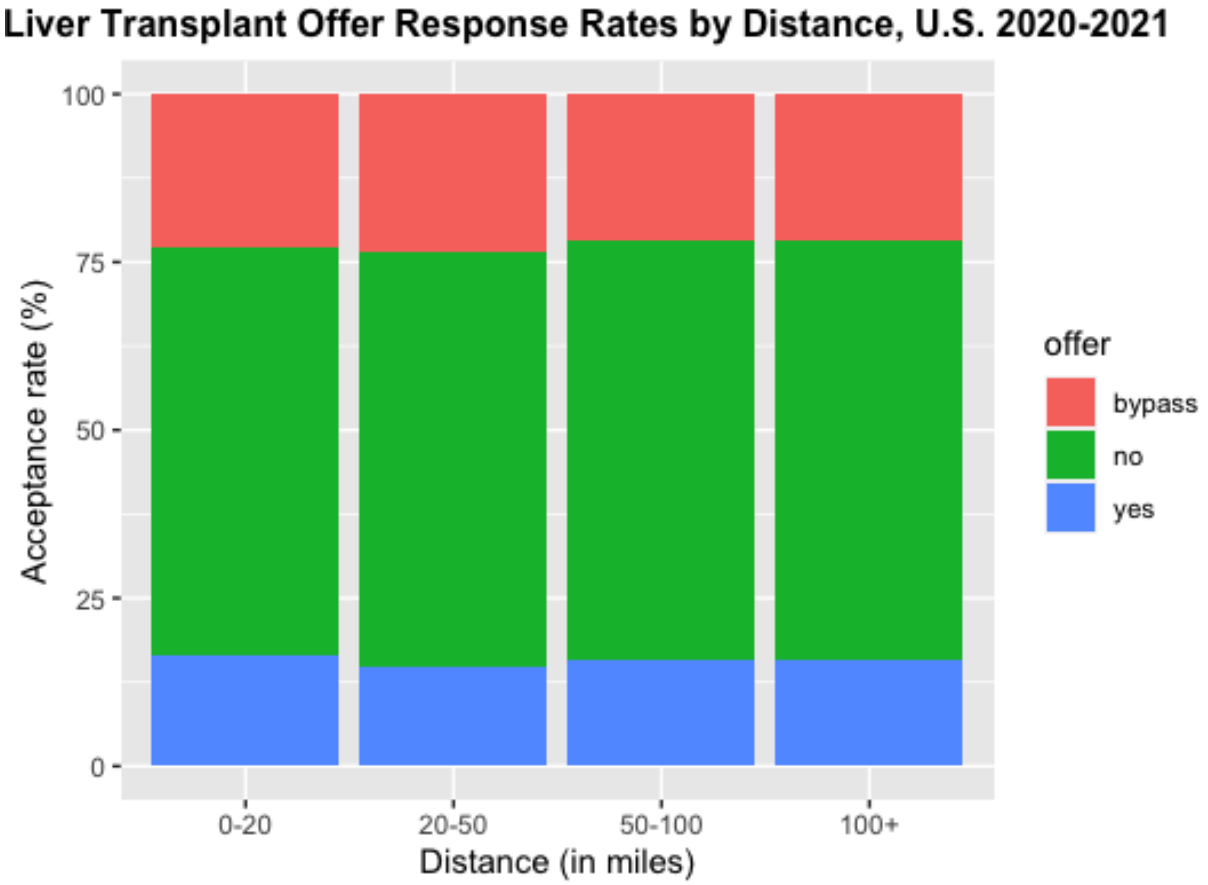

Figure 2: Liver transplant offer responses by race across the United States. All percentages are calculated as rates; SRTR, Scientific Registry Transplant Recipient 2020-2021.

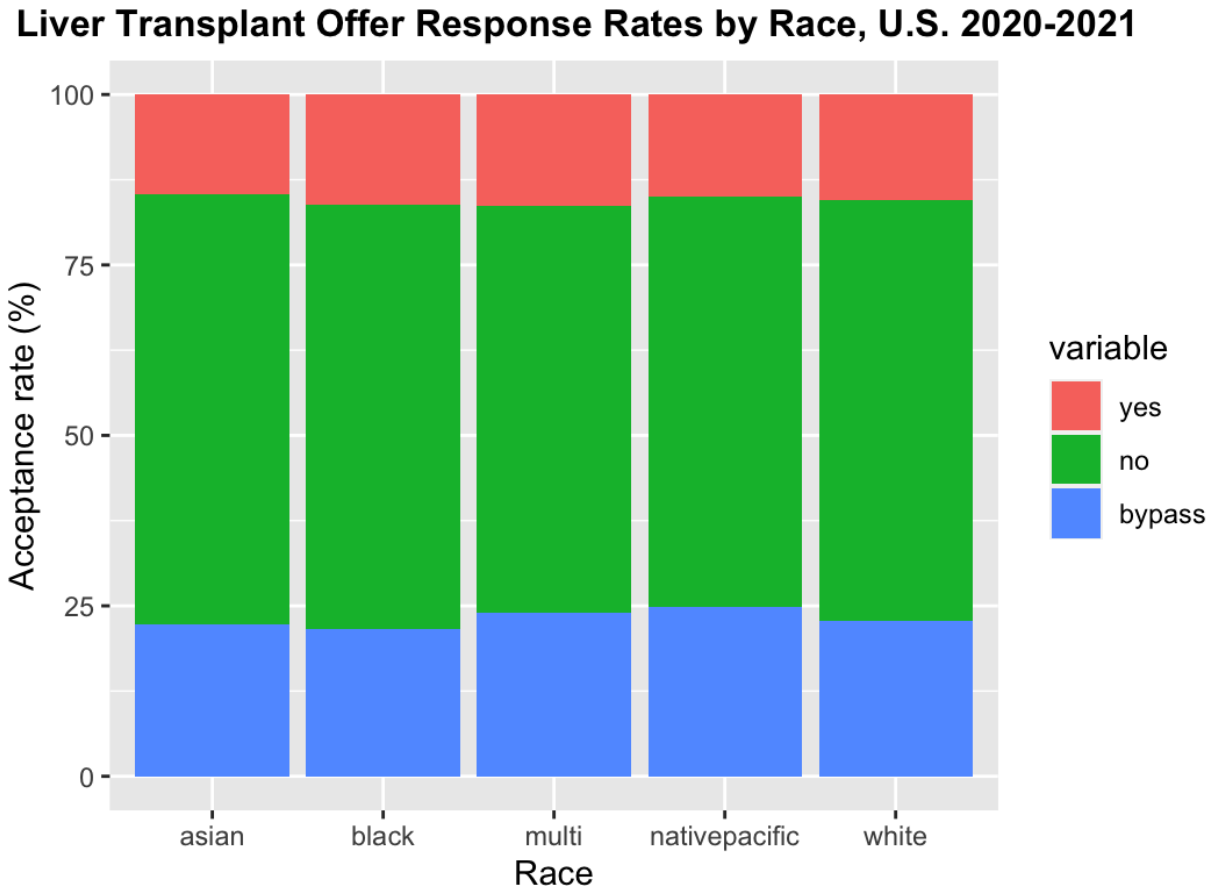

Figure 3: Liver transplant offer responses by transplant center, United States. All percentages are calculated as rates; SRTR, Scientific Registry Transplant Recipient 2020-2021.