Title

Implications of Liver Transplant Allocation Policy for Healthcare Resource Utilization: An Analysis of United Network for Organ Sharing Share 35 Policy

Author

Russell, Tara Anastasia

Publication Date

2018

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

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A dissertation submitted in partial satisfaction of the requirements for the degree

Doctor of Philosophy in Health Policy and Management

by

Tara Anastasia Russell

2018

ABSTRACT OF THE DISSERTATION

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by

Tara A Russell

Doctor of Philosophy in Health Policy and Management

University of California, Los Angeles, 2018

Professor Susan Louise Ettner, Chair

Since its evolution, organ allocation in liver transplantation has been based upon the 'rule of rescue', where patients are prioritized for transplantation based on their medical need and acuity. As the system has evolved, arbitrary geographic boundaries and variations in the supply and demand for organs have created a system marked by geographic inequities. Share 35, the most recent of the United Network for Organ Sharing liver transplant allocation policies, aimed to reduce these inequities at the regional level by instituting intra-regional organ sharing for the sickest patients (defined as allocation Model for End Stage Liver Disease (MELD) scores of ≥35). Similar to other organ allocation policies, evaluations of Share 35 have been limited to traditional markers of quality in transplantation, namely pre- and post-transplant survival. Acknowledging that these policies have far reaching effects, beyond patient survival alone, this

dissertation assessed the potential impacts of the Share 35 policy on both inpatient utilization and post-transplant disability. Utilizing a novel database linkage between six state inpatient datasets (Agency for Healthcare Research and Quality – Healthcare Cost and Utilization Project and California Office for Statewide Hospital Planning and Development) and the liver transplant registry, a stepwise analysis of the potential causal pathways through which the policy may have affected each outcome was completed. Prior to assessing the impact of Share 35 directly, potential drivers of post-transplant utilization prior to policy implementation were evaluated, indicating that both patient acuity at the time of transplant and donor organ quality are strongly associated with post-transplantation inpatient utilization within the six months following transplantation. These findings build upon previous single-institution studies and prior reports which were limited to only 30-days of post-transplant follow-up. This dissertation then assesses Share 35 and demonstrates that by increasing organ availability to patients in the greatest need of transplantation, Share 35 resulted in substantial decreases in post-transplant inpatient utilization as well as modest improvements in post-transplant disability. These findings suggest that continued efforts to expand organ sharing across geographic boundaries will lead to improved patient outcomes and reduced health resource utilization.

The dissertation of Tara A Russell is approved.

Jack Needleman

Thomas H. Rice

David Scott Zingmond

Susan Louise Ettner, Committee Chair

University of California, Los Angeles

2018

Table of Contents

Tables

Figures

Appendices

Vita

Education and Training

8/2002 – 5/2006	**Dickinson College** Carlisle, Pennsylvania Bachelor of Science, Biology and Sociology
9/2007 – 5/2009	**Tufts University School of Medicine, Public Health & Professional Degree Program** Boston, Massachusetts Masters of Public Health, Epidemiology & Biostatistics
8/2009 – 5/2013	**New York University School of Medicine** New York, New York Doctor of Medicine
6/2013 – Present	**UCLA – David Geffen School of Medicine, Department of General Surgery** Los Angeles, California General Surgery Resident
7/2015 – 6/2017	**Robert Wood Johnson Clinical Scholars Program - UCLA** Los Angeles, California Robert Wood Johnson/Veterans Affairs Clinical Scholar

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1. Introduction

The field of liver transplantation has evolved significantly over the last fifteen years, in terms of both the science of transplantation and the associated organ allocation policy. In 1998, in the setting of expanded use of liver transplantation across the country, but marked disparities in the availability of organs, the U.S. Department of Health and Human Services issued 'The Final Rule,' which is now the guiding principle of organ allocation. The Final Rule dictates that donated organs should be distributed over as broad a geographic area as feasible and allocated to patients in order of decreasing medical urgency. This rule has ultimately been interpreted by the transplant community as a "sickest first" policy, in which those with the greatest immediate need are given priority in receiving available organs.

Over the last two decades the organ allocation system has undergone many iterations and adjustments with the aim of meeting the standards of The Final Rule. The most pivotal of these changes was the transition to the MELD (Model for End Stage Liver Disease) score in 2002 which prioritized patients based solely on objective measures of liver disease severity, and no longer on wait list time or patient location. Initial evaluations of the MELD score relied heavily on traditional markers of quality in liver transplant, namely waitlist mortality (deaths amongst those patients awaiting transplantation) and patient and graft (transplanted organ) survival. While there have been striking successes in these measures, increasing attention has been paid to the economic and health resource impact of MELD allocation. Evaluations of the 2002 MELD transition indicated a significant trend towards increased health resource utilization, specifically longer intensive care unit (ICU) stays, longer post-transplant length of stay (LOS), a higher rate of complications and an overall increase in costs.[1-7]

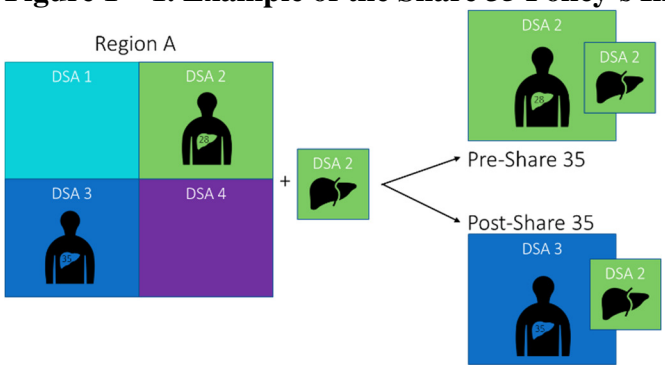
Assessments of health care utilization among liver transplant patients in the post-MELD period have attempted to identify primary drivers of these increased costs associated with treating higher acuity patients. Work by Buchanan et al. (2009) found that approximately 58% of orthotopic liver transplantation (OLT) costs occur during the transplant period (2 days pre-transplant to 90 days post-transplant), 27% during the pre-transplant period (1 year prior to transplant) and 15% in the extended post-transplant period (90 days to 1 year post-transplant).[8] Costs incurred following discharge from the index (transplantation) admissions are attributable to the extended post-transplant period, and a component of the transplant period. The primary drivers of these post-discharge costs are readmission and emergency room utilization, markers of quality that have been poorly assessed in the transplant literature. To date there are only three studies that specifically evaluate post-transplant readmissions, two of which are single-center studies and the third of which only accounts for readmissions within the first 30 days.[7,9,10] Among these studies, readmission rates are projected to be almost twice those of general surgical procedures, ranging from 26.3% to 50.8% within 30 days and 69% within 1 year. Within these studies, the risk of readmission has been correlated with a higher MELD score at the time of transplant, and is associated with poorer traditional outcomes, including graft and patient survival.[9]

Although there have been early indications that the "sickest first" policies have trended towards increasing utilization and costs associated with transplantation, they remain the guiding principle of organ allocation policy. In June 2013, the United Network for Organ Sharing (UNOS) implemented another policy to promote the transplantation of the highest-acuity patients with the Share 35 policy. Share 35 was projected to decrease waitlist mortality and reduce regional disparities in patient acuity, by altering the order of deceased donor allocation by

placing all recipients with a MELD score greater than 35 onto a regional, rather than local waitlist. Under this new system, organs that would have previously been offered first to patients within a local area of distribution (donor service area) with a lower MELD score, are now first offered to any patients within the regional area of distribution with a MELD score of 35 of higher.

Figure 1-1 provides an example of how Share 35 has changed the allocation of organs. In this example, the patient in donor service area (DSA) 2 has a MELD of 28 and the patient in DSA 3 has a MELD of 35. With the regional sharing that occurs under the Share 35 policy, an available organ in DSA 2 that would have previously gone to a patient in that DSA prior to Share 35 is now moved to a higher acuity patient in another DSA post-Share 35.

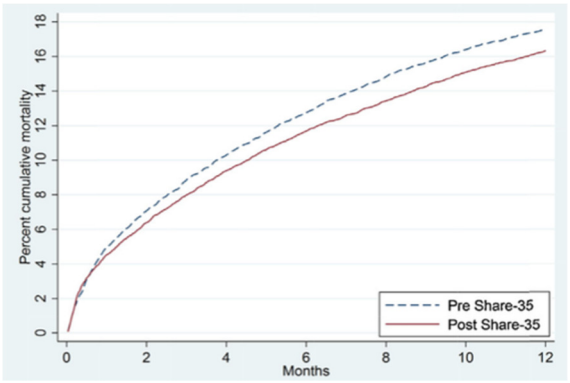
Figure 1 – 1. Example of the Share 35 Policy's Impact on Organ Allocation.

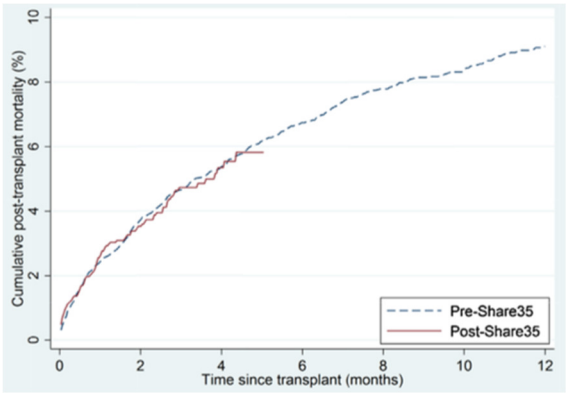


Share 35 has undergone a handful of evaluations in the literature utilizing both single-center data as well as national datasets provided by the Scientific Registry of Transplant Recipients (SRTR). The most robust of these studies was done by Massie et al., who demonstrated that there was an increase in the proportion of patients transplanted with a MELD ≥35, that wait list mortality declined and that graft and patient survival remained stable in the first year after policy implementation (Figure 1 – 2)[11]. Other studies have demonstrated some variation in outcomes across the UNOS regions, such that some regions have experienced a

decrease in graft and patient survival where others have had modest improvements.[12] Overall, the majority of reports have relied on the traditional markers of quality (graft and patient survival), and have failed to evaluate the potential economic and health resource impact of this policy change. Specifically, there have been very limited evaluations of non-traditional markers of quality or patient-related outcomes, such as readmission rates, hospitalization burden or complications.

Figure 1 - 2. Share 35 resulted in improved waitlist mortality (A) and stable post-transplant patient survival (B)

A. 

B. 

Within the transplant literature and within the evaluations of Share 35, there remains a need for more in-depth evaluation of non-traditional markers of quality in transplantation. Previous studies of health care utilization have relied heavily on single institution reports or upon utilization exclusive to the index transplant center, which is likely a gross underestimate of the total health care utilization by this population. Overall, these underestimates arise for a variety of reasons, including that patients do not exclusively receive that care at a single site due to the great distances traveled to receive transplants, the large geographic areas that are not covered by transplant centers, and the often urgent/emergent nature of follow-up care. Overall, to understand health care utilization in this population, it is important to assess the totality of this utilization, patterns related to where patients seek care, and the outcomes related to these factors. As well, in

the context of Share 35 it is important to assess how this policy has impacted utilization for individual patients, as well as how different centers and regions have responded to the implementation of this policy.

1.1 Research Questions

Q1. What are the factors associated with inpatient utilization among liver transplant patients in the post-transplant period prior to Share 35?

Q2. How did Share 35 impact post-transplant inpatient utilization?

Q3. How did Share 35 impact post-transplant disability?

1.2 Overview of Methods

In order to assess patterns related to inpatient utilization, waitlist time and post-transplant health-related quality of life, a nationally representative database will be constructed from administrative state inpatient databases and transplant-specific registries to include information related to: (1) liver transplant waiting list information, (2) recipient medical condition, (3) transplantation-related factors, (4) insurance status and payer information, (5) hospital information, and (6) inpatient post-transplant utilization (available for patients in six states). Utilization will be assessed through cross-sectional analysis of a six-state cohort of transplanted patients from 2010-2014, and post-transplant disability will be assessed using a complete national cohort of transplanted patients from 2010-2016 respectively. The effect of Share 35 on utilization and disability will be assessed using generalized linear regression. The models allow for the impact of Share 35 to vary with MELD score.

2. Background

2.1 Liver Transplantation in the United States

2.1.1 Indications for Liver Transplantation

Liver transplantation is considered the only curative therapy for end stage liver disease (ESLD), a condition that is noted to be the 12th leading cause of death in the United States overall, and the 4th leading cause of death among adults between the ages of 45 and 54.[13] Yet, more than any other health resource in the United States, liver transplantation is a procedure that is limited and challenged by issues of organ supply and demand. In 2014 alone, while 6,729 patients were able to be transplanted, more than 10,500 were added to the already saturated waiting list for transplantation, which held 14,632 patients at the end of 2014.[14,15] This marked imbalance in the number of patients needing and receiving a transplant accounted for a total of 1,673 deaths while awaiting transplant and 1,227 removals from the transplant list due to progression of liver disease in 2015 alone.[16] In the setting of this marked disparity, determining who is eligible for, and who should receive organs, is shrouded by ethical, political, economic and medical issues.

Chronic liver disease affects more than 45 million adults in the United States, and annually 25,000 – 45,000 individuals die due to complications related to ESLD.[17,18] The etiology of liver disease varies, with the most common causes of cirrhosis (irreversible fibrosis of the liver) within the U.S. being non-alcoholic steatohepatitis (NASH, infiltration of fat, causing fibrosis and scarring of the liver), alcoholic hepatitis (fibrosis and scarring of the liver caused by alcohol use), hepatitis C, hepatitis B, biliary duct disease and genetic disorders. Regardless of the etiology, as liver function diminishes, all types of cirrhosis culminate with the same manifestations of liver failure. The sequela of liver failure is marked by progressive organ

dysfunction which manifests most poignantly with complications such as altered mental status (hepatic encephalopathy) due to an inability to clear ammonia from the blood stream, coagulopathy due to an inability of the liver to produce essential proteins for hemostasis (synthetic dysfunction), and complications of portal hypertension including variceal bleeding (venous bleeding most commonly from esophageal or rectal veins), renal failure (hepatorenal syndrome), fluid overload (ascites and anasarca). Unlike many other end stage organ diseases, there is yet to be any reliable or efficient system for organ replacement therapy, such as dialysis for kidney failure. In this way, patients with end stage liver disease and its associated complications have very few options for treatment as disease continues to progress, with liver transplant being the only therapy that offers a cure.

In current practice, there are a wide variety of indications for liver transplantation, which are divided into four categories: acute liver failure, end stage liver disease with complications, liver-based metabolic conditions and oncologic conditions. A list of indications for liver transplantation is included in Appendix 1. Acute liver failure, which occurs in 2,000 patients in the U.S. annually, is defined as 'a severe liver injury, potentially reversible in nature and with onset of hepatic encephalopathy within 8 weeks of the first symptoms in the absence of pre-existing liver disease.'[19] In the U.S., acute liver failure (ALF) is most commonly caused by acetaminophen (Tylenol) overdose, other drug-induced hepatotoxicity, acute viral infection and acute ischemic injury.[20] As discussed above, ESLD is commonly due to progressive cirrhosis. In addition to the above-mentioned causes for ESLD, liver cancer, and specifically hepatocellular carcinoma and cholangiocarcinoma (cancer of the biliary ductal system adjacent to or within the liver), is also an indication for liver transplantation. The guidelines for transplantation among patients with intrahepatic malignancies has been defined by multiple different studies, with the

overarching aim of assuring that transplantation maximized the chance of cure from the malignancy and improves disease-free (cancer-free) survival. At present, the Milan Criteria are used to determine if a patient's disease burden is low enough to assure acceptable outcomes with >50% 5-year survival after transplantation (Milan Criteria are listed within Appendix 1.1). Finally, liver-based metabolic conditions include those genetic conditions and diseases with a progressive and inevitable prognosis resulting in liver failure.

2.1.2 An Overview of the Transplant System

The process for attaining liver transplantation in the United States requires multiple steps. Patients with an indication for liver transplantation must be evaluated by a liver transplant center to determine if they are medically eligible for transplantation. This evaluation includes a thorough evaluation of the patient's liver disease as well as any comorbid conditions that would ultimately interfere with their ability to undergo and recover from transplantation. Patients who are deemed medically suitable for transplant then undergo a psychosocial evaluation to ensure they can comply with care following transplantation, have adequate social support and have a stable source of income and health insurance to support their care for the pre- and post-transplant period. An overview of the transplant evaluation process as outlined by the American Association for the Study of Liver Diseases (AASLD) is contained in Appendix 1.2. Once the evaluation process is completed, transplant centers convene a multidisciplinary selection committee which reviews each patient's candidacy to determine if they are suitable for placement on the transplant center's waiting list.

Once a patient has been approved by an individual transplant center, transplant centers then provide documentation to UNOS to place the patient on the liver transplant waiting list. At present, the waiting list is organized by severity of liver disease, as measured by the Model for

End Stage Liver Disease (MELD) score. A patient's MELD score is calculated at the time of listing and can be updated by the transplant center up to once per week, allowing the patient's position on the list to reflect their current disease state. Patients remain on the waiting list until they receive an organ or are removed from the waiting list. Patients can be removed from the waiting list for a variety of reasons, which are at the discretion of the transplant center. Reasons for removal, when reported to UNOS, are classified as either death, medically unstable, or too sick to transplant. Other reasons for removal that are classified under miscellaneous by UNOS may include: non-compliance, loss to follow-up, removal for psychosocial reasons (drug or alcohol use), refusal of transplant, or medical condition improved. The ordering and organization of the waiting lists is discussed in more detail in the section on organ allocation.

2.2 History of the Organ Allocation System

2.2.1 Early Organ Allocation – From an Experimental Operation to Standard of Care

The field of liver transplantation and the corresponding organ allocation system have evolved within the United States in parallel. As the science of transplantation advanced from mere experiments to a broadly accepted standard of care over the past 50 years, hospitals, organizations and ultimately the federal government came to play a role in discerning how this health care service and donor organs would be delivered.

The first liver transplant occurred in the United States in 1963 at the University of Colorado.[21] During this early period, liver transplantation was considered experimental in nature, and was marked by very low overall patient survival. Yet as the science of transplantation advanced, and survival improved, the procedure became more common and the need for donor organs increased. In the early 1980s, as the number of transplants reached just over 30 per year

and techniques in organ preservation advanced, mechanisms for organ sharing developed. Specifically, through academic networks and by reliance on previously developed networks for cadaveric kidney donation, liver procurement was incorporated into the newly established organ procurement organizations.[21]

This early exchange of organs spurred the first legislative acts surrounding organ transplantation, and in 1968 the Uniform Anatomical Gift Act was passed. This act unified state laws regarding the exchange and donation of organs and tissues. Specifically, it outlined legal methods for the donation of organs and tissues post-mortem by identifying what organs and tissues could be donated, how they could be donated, the role of the decedent and their next of kin in decisions regarding donation as well as the role of the physician in organ donation. This act marked the first legislation legalizing organ exchange, and has since provided the foundation for organ donation in the US.

As organ donation increased and transplant centers gained more experience with organ transplantation, patient survival improved. In 1983, the National Institutes of Health (NIH) declared that liver transplantation was no longer an "experimental" therapy, and was the only known cure for end stage liver disease. This designation spurred the spread and adoption of liver transplant services throughout the country.

2.2.2 Development of a National Organ Allocation System

With rising frequency of liver transplantation, the need for organs, and in turn fair and equitable organ donation and allocation, arose. The dawn of organized allocation began in 1984 with the enactment of the National Organ Transplant Act (NOTA) which called for the development of the Organ Procurement and Transplantation Network (OPTN). In 1986, the United Network for Organ Sharing (UNOS) was granted the contract for the OPTN, managing

and incorporating organ procurement organizations (OPOs) across the country into a unified organ transplant and procurement network. Each OPO serves a distinct geographic area, providing services related to the evaluation of donors, organ procurement and allocation. As OPOs developed, there were no specific regulations on how service areas were defined. Regulation guiding the formation of OPOs, which was passed in 1990, set a loose framework, stating that OPOs must be of sufficient size to maximize effectiveness, yet did not delineate the exact geographic area or population that needed to be covered by each OPO. Therefore, OPO service areas varied drastically in the populations and geographic regions they served, with populations varying from 70,000 to 11,000,000, and geographic areas varying from small clusters of counties to large multistate organizations, as is demonstrated in Figure 2 – 1 below. OPOs were further organized into regions, of which there were 11, again with great size variation, with their coverage ranging from a single to multiple-state area (Figure 2 – 2).

Figure 2 - 1. Organ Procurement Organization Service Areas, 1999.
There were a total of 62 OPO service areas which provided service to geographic areas that varied from a few counties to multiple states[22]

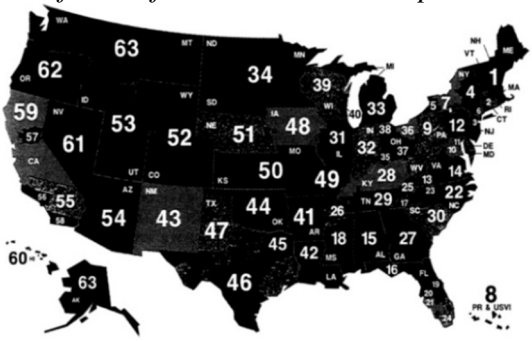
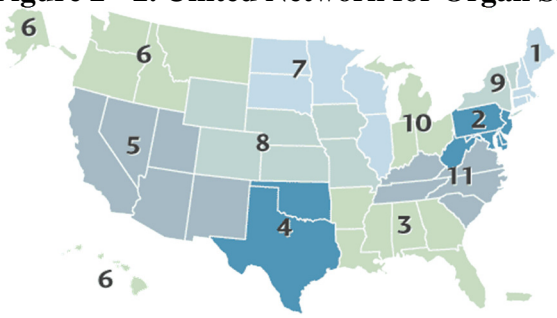


Figure 2 - 2. United Network for Organ Sharing Allocation Regions.



These regions and OPOs comprised the basis for organ distribution, defining geographic parameters for organ procurement. Yet the decision on how organs would be allocated within and amongst these organizations and regions was still to be determined.

In parallel with the distribution system developed in cadaveric kidney transplantation, the initial allocation system in liver transplantation was developed such that priority was provided to patients who had been waiting the longest. While such a system is equitable in terms of wait time, this system did not differentiate patients based on their imminent need for an organ, or the degree of their organ failure.

It was not until 1998 that the allocation system first incorporated disease severity, the driving factor for organ allocation today. This system, termed the 'medical urgency status system,' categorized patients based on their emergent versus non-emergent transplant need, and further by their in-hospital or outpatient location. The system, as it was defined in January 1998, is included in Table 2 – 1 below. Status 1 patients required emergent transplantation, Status 2 were non-emergent but currently receiving intensive care unit (ICU) level care, Status 3 were non-ICU hospitalized inpatients and Status 4 were outpatient.[23]

This system underwent many modifications, including the integration of the Child-Turcotte-Pugh (CTP) score, which added more objective measures of illness severity to the medical urgency status system. By definition the CTP score included five clinical variables

(serum albumin, total bilirubin, international normalized ratio, ascites and hepatic encephalopathy), each with 3 possible points, with a maximum score of 15. All five clinical variables are markers of liver disease severity, therefore higher scores indicated more severe disease.

Even with the addition of the CTP score in 1998, which added a somewhat objective measure of disease severity to the medical urgency system, a patient's position on the waitlist still relied heavily on wait list time. Within this system, all patients with a particular status rating (of which there were only 4 active levels) were ranked by their blood type and wait list time, ultimately making wait list time one of the greatest predictors of a patient's position on the list and probability of receiving a donated organ.[23]

Table 2 - 1. Medical Urgency System for Deceased Donor Liver Donation

Medical Urgency Status	Description
Status I	Fulminant hepatic failure with life expectancy <7 days Primary graft non-function <7 days after live transplantation Acute decompensated Wilson's disease
Status 2A	Chronic hepatic failure, hospitalized in ICU with life expectancy <7 days; CTP score ≥10; and at least one of the following: acute unrelenting variceal hemorrhage, hepatorenal syndrome, refractory ascites or hepatic hydrothorax, Stage 3 or 4 (poorly controlled) hepatic encephalopathy
Status 2B	Chronic hepatic failure, requiring inpatient medical care; CTP score ≥ 10; or CTP ≥7 and at least one of the following: acute unrelenting variceal hemorrhage, hepatorenal syndrome, spontaneous bacterial peritonitis, refractory ascites or hepatic hydrothorax
Status 3	Chronic hepatic failure; CTP ≥ 7, but not meeting criteria for status 2B
Status 7	Temporarily inactive on the waiting list

While the incorporation of the CTP score aided in creating greater equity in allocation and distribution of donated organs, great disparities arose within and between regions due to geographic imbalances in supply and demand. These disparities were accentuated due to the fact that organs were procured and allocated within individual OPOs, and there was no organ sharing between OPOs (within regions) or between regions. This lack of reciprocity between OPOs and

regions, in conjunction with the wide variability in both geographic size as well as regional organ supply and demand, led to significant disparities.

As well, during this era concerns arose that waitlist time and patient location were not well correlated with a patient's medical acuity or their relative need for a transplant. Much of the literature published at this time demonstrated the unrest within the field about appropriate and adequate allocation rules. Papers in the Lancet, New England Journal of Medicine and other major publications urged the transplant community to implement a more equitable system, one that focused on reducing disparities in outcomes between geographic areas, that was guided by more objective parameters for selecting patients for transplantation, and that assessed transplant center quality.[24-27]

2.2.3 Developing a More Equitable System: The Final Rule

As concerns continued to rise, the modern guiding principle of organ allocation, commonly referred to as the Final Rule, was set forth by the United States Department of Health and Human Services (US-DHHS) in April 1998. With the intent of assuring allocation "was based on common medical criteria, not accidents of geography," the Final Rule defined three performance standards for allocation policies including: 1. Place of residence and place of listing could not be a major factor determining who receives an organ, 2. Uniform listing criteria must be developed, and 3. A system must be devised so that medical urgency could be given greater weight.[28] Collectively these three goals have been interpreted to indicate that the overall goal of allocation under The Final Rule is "distributing organs over as broad a geographic area as feasible … and in order of decreasing medical urgency".[22,29] Additional components of the Final Rule included a call for improved data collection on patient, transplant center and OPO outcomes in order to assure the allocation goals were met.

The Final Rule was met with mixed sentiment within the transplant community. While proponents of the rule felt it was a step towards equity, opponents expressed concern that expansion of organ sharing would increase the costs associated with transplantation, discourage donation and result in fewer lives saved. As it was unclear exactly how the rule would be implemented, and what the effects of the rule would be, in October 1998, the implementation of The Final Rule was suspended until January 2000, by the US-DHHS. In this announcement, US-DHHS called for an evaluation of the potential impact of the Final Rule, with specific attention to: access to services among low socioeconomic status patients and racial minorities, organ donation rates across regions/states, waiting times for organs, patient survival rates, organ failure rates and the cost of organ transplantation services.[22]

In response to this call for further evaluation of the potential impact of the Final Rule, there were multiple reports issued by proponents and opponents of the DHHS policy. The most well-respected and largest review was developed by the Institute of Medicine (IOM). The report broadly found that the Final Rule would likely increase the cost of procurement, have an unclear impact on racial and financial disparities (as these were felt to be secondary to access to health insurance), and had the potential to aid in decreasing the distribution and allocation disparities between regions. Specifically, the IOM's report made multiple recommendations in regards to the implementation of the Final Rule, including:

- *Establishment of larger organ allocation areas (OAAs) to facilitate broader and more equitable sharing arrangements among OPOs*
- *Discontinuation of the use of waiting time as an allocation criterion*
- *Timely evaluation of transplant center, OPO and patient outcomes to improve quality and reliability of the analyses used to set policy*

The IOM's report was well received within the medical community as a whole, but was met with some opposition by both the United Network for Organ Sharing (UNOS) and the OPTN.[28] The major concerns from UNOS relied on the concern that major changes to the OAAs would negatively impact small or low volume centers and OPOs. Such arguments by UNOS against broader sharing were countered by multiple organizations which emphasized the ethical argument set forth by the American Medical Association in 1977, indicating that "organs should be considered a national, rather than local or regional resource".[28]

During this same era, there was increasing pressure to assess and evaluate potential disparities in patient outcomes between geographic regions and centers. In response, UNOS as well as other organizations evaluated outcomes between transplant centers, uncovering great disparities. In particular, one-year mortality between low- and high-volume centers differed by greater than 8 percentage points (28.3% versus 20.1% mortality and low- and high-volume centers), with an adjusted odds ratio for death of 2.04 at lower volume centers. Furthermore, transplant centers that were identified as having an exceptionally high one-year mortality rate, >40%, were all also classified as low volume.[30] Such results pushed UNOS and the OPTN to reconsider their position on the Final Rule, and eventually led to their acceptance and support of the rule in 2000.

2.2.4 The MELD Era

Following acceptance of the Final Rule, UNOS and the transplantation community were faced with designing and implementing an allocation system that would resolve geographic disparities and eliminate the use of wait time from allocation criteria. Given concerns about the difficulty in changing OPOs and OAAs due to political and organizational challenges, the first major steps towards achieving the final rule were made through changes in the definition of

medical acuity. In a landmark article published in 2001, Kamath et al. demonstrated that the Model for End Stage Liver Disease (MELD) score (initially designed to estimate survival for patients undergoing the transjugular intrahepatic portosystemic shunt (TIPS) procedure) performed well as a predictor of death from liver disease within 3 months across ambulatory and hospitalized patients of varying disease etiologies and severities.[31,32] This score is calculated from laboratory values for serum bilirubin, international normalized ratio for prothrombin time (INR), and creatinine[i] and was viewed as a more specific and objective measure of disease severity than the CTP score which had previously been used in the medical urgency status system(Figure 2 – 3).[32] In particular, the score was more granular, providing a more gradated system for evaluating disease severity. As the first stride towards achieving the goals of the Final Rule, the MELD score was implemented as the primary mechanism for allocation within each OPO and region in February 2002.[33] Under the OPTN/UNOS guidelines MELD scores had a minimum of 6 and a maximum of 40, arbitrarily drawn parameters based on limited differentiation of disease acuity at the upper and lower margins of the MELD score. In addition to the MELD score, which was used for the majority of allocation, the MELD system also carried over medical urgency status for the most acute patients, maintaining the Status 1A and Status 1B criteria for patients with acute liver failure. The MELD Distribution schema is outlined below in Figure 2 – 4.

[i] MELD Score is calculated using the equation indicated below. All values are entered in US units (creatinine and bilirubin in mg/dL). Creatinine has a minimum value of 1.0 when entered into the equation. Serum creatinine should be replaced with a value of 4.0 if the patient has a value >4.0, has received ≥2 dialysis treatments or has received ≥24 hours of continuous hemodialysis within 7 days.

$$MELD = 3.78\ln(serum\ bilirubin) + 11.2\ln(INR) + 9.57\ln(serum\ creatinine) + 6.43$$

Figure 2 - 3. Comparison of MELD and CTP ROC Curve[31] .

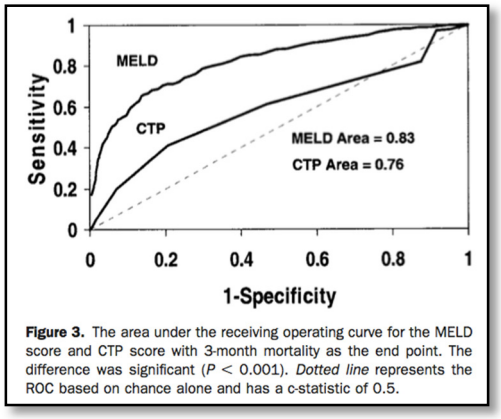


Figure 3. The area under the receiving operating curve for the MELD score and CTP score with 3-month mortality as the end point. The difference was significant ($P < 0.001$). *Dotted line* represents the ROC based on chance alone and has a c-statistic of 0.5.

Figure 2 - 4. 2002 MELD Distribution Schema. Allocation priority was ranked by patient location and status; first to receive an organ would be Local Status 1A, followed by regional status 1A, etc

MELD Distribution
Local status 1A
Regional status 1A
Local status 1B
Regional status 1B
Local MELD allocation
Regional MELD allocation
National MELD allocation

The MELD allocation and distribution system set into motion a new mechanism for prioritizing patients within individual OPOs and regions, such that patients were ranked from highest to lowest MELD scores. In addition to the implementation of MELD as the guiding score for wait list order, the MELD system also ushered in the first rules for regional sharing of donated organs. Under the MELD system, high-acuity patients (status 1A and 1B, with criteria carried over from the medical urgency status system), were eligible for organs outside of their own OPO area. Specifically, patients with a medical urgency status of 1A were placed at the top of both their local waitlist as well as at the top of a regional waitlist. Status 1B patients were ranked just below 1As on both the local and regional lists. Organs therefore were offered to all

local and then regional 1A and 1B candidates respectively, before they were then offered to patients at the top of a local waitlist ranked according to MELD score.

Within the field of liver transplantation, the transition to the MELD score marked a new era in organ transplant allocation. The new system focused on prioritizing allocation by objective measures of acuity and was held to a new standard of regional equity set by The Final Rule. Yet, issues of organ shortage, imbalances in supply and demand, and variable transplant center behavior in regard to patient listing and risk aversion led to persistent and challenging inequities between regions, which have created new challenges and barriers to fulfilling the standards set forth by the Final Rule.

2.3 Liver Transplant Allocation Policy

2.3.1 Organ Allocation Policy: Development & Implementation

Within the United States, organ allocation policy is developed and implemented by the United Network for Organ Sharing (UNOS), which derives its authority from the 1984 National Organ Transplantation Act (NOTA) and the Final Rule. As previously discussed, NOTA established a national system for organ allocation and granted UNOS a contract for managing the OPTN through the authority of the Health Resources and Service Administration (HRSA). Hospitals and liver transplant providers who wish to provide organ transplantation services are mandated to be a part of the OPTN, and abide by the policies, rules and requirements of the OPTN, as stipulated under the Social Security Act. The Final Rule further enhanced the authority of the OPTN by establishing the Secretary of Health and Human Services with the responsibility to enforce OPTN requirements. Therefore, while UNOS remains a private entity, it is supported contractually by the United States Federal Government.

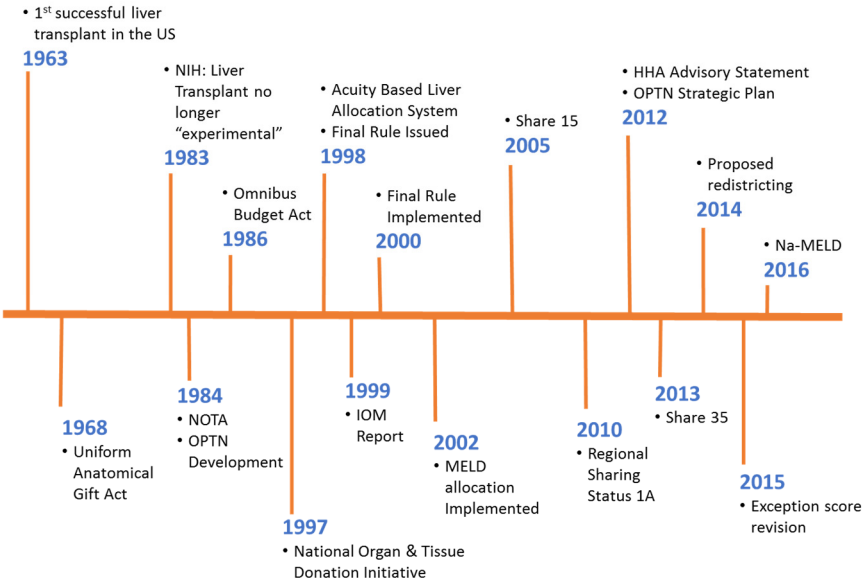
Organ allocation policies are set by UNOS through a standardized process that integrates both public opinion and consensus amongst transplant providers. Under this process there are five major steps: (1) identification of an allocation policy issue, (2) policy investigation and proposal development, (3) proposal open for comments, (4) proposal revision, (5) UNOS Board of Directors vote, and (6) notification of the transplant community and policy implementation.[34] When proposals are open for comment, they are posted to the OPTN website and open for public comment for a period of 60 days. Additionally, new proposals are discussed by regional OPTN committees to obtain comment and feedback from the transplant community. The UNOS Board of Directors is composed of physicians, nurses, procurement organization staff, legal staff and representatives of the general public. The Board meets twice annually and is responsible for approving or rejecting policy proposals. Once a policy is approved, it is integrated into the electronic allocation system which is directly managed by UNOS. This system for policy development and implementation has allowed UNOS to make timely updates to the allocation system, through a mechanism that is touted as inclusive, responsive, equitable and evidence-based.[35]

2.3.2 Modern Changes to the Organ Allocation System – Modifications to the MELD System

The implementation of the MELD score was the first step towards achieving the standards set by The Final Rule. Inherently, the MELD score put forth a new objective measure of liver disease severity as the guiding principle for allocation. Yet, the score was ultimately designed for other purposes, and therefore close attention was given to its performance as a metric for organ allocation. The results of this close attention led to many adjustments to the allocation system, which have continued into the modern era (Figure 2 – 5). With each

adjustment, the transplant community has made an attempt to more closely align the allocation system with The Final Rule, aiming for equity in terms of both patient needs and geography.

Figure 2 - 5. Timeline of the history of organ allocation & UNOS policy changes



MELD Exception Points

In conjunction with the use of the MELD score as the principal mechanism for organizing the liver transplant wait list, the MELD system included provisions for patients with disease processes that were indications for transplantation, but did not result in progressive liver dysfunction as measured by the MELD. In order to provide these patients with a fair opportunity for transplantation under the MELD system, MELD exception points were created which provided additional points which could then be added to the original, physiologic MELD score.[ii] Under the system put in place in 2002, MELD exception points were provided for a variety of conditions including hepatocellular carcinoma (HCC), familial amyloidosis, hepatopulmonary

[ii] Physiologic MELD score is the score defined by the lab values. This differs from the exception MELD score which is the physiologic score + exception points.

syndrome, and metabolic disorders. The most common and most debated indication for MELD exception points, since 2002 and through the present, is HCC.

HCC is one of the leading causes of cancer-related morbidity and mortality, and within the U.S. is the 5th and 9th most common cause of cancer mortality among men and women respectively.[36] HCC is noted to have a low 5-year survival rate, estimated to be less than 20%.[36] Given this poor prognosis, liver transplantation was evaluated as an option for treatment of HCC as early as the 1960s. Yet during this early period, transplantation for HCC was associated with very high mortality and recurrence rates, which led the DHHS to specifically identify HCC as a contraindication for liver transplant in 1989.[37-39] In 1996, a series of studies arose in Europe that demonstrated success in liver transplantation for HCC when tumor burden was limited.[40] In response to these findings, DHHS removed the restriction on liver transplantation for HCC in 2001. The criteria, set forth by Mazzaferro et al. (1996) and commonly referred to as the Milan Criteria, have since been broadly implemented, and were utilized as the first guidelines for the use of MELD exception points for HCC in 2002 (see Appendix 1).[40]

In association with the MELD allocation system implementation, MELD exception point criteria were issued by OPTN based on the Milan criteria and the risk of progression beyond Stage II/T2 (a level of cancer progression for which patients are no longer considered eligible for transplantation). In this first iteration of the system, Stage I/T1 lesions (1 nodule <2cm) were considered to have a risk of progression of 15% and Stage II/T2 (1 nodule 2-5cm or 2-3 nodules each ≤3cm) a risk of 30%, which corresponded to MELD estimated mortality risks (while awaiting transplant) similar to a score of 24 and 29 respectively.[41] Additionally, the new policy provided the option for centers to apply to a regional board for an additional point every 3 months (corresponding to a 10% increased risk of progression beyond Stage II) if the patient's

tumor had not progressed beyond Stage II criteria. In the first year after its implementation, this policy contributed to a dramatic increase in the proportion of organs allocated to patients with HCC, increasing from 7% in the pre-MELD era to 22% in the first year post-MELD.[42] In light of such a dramatic increase, which was seen to provide patients with HCC an unfair advantage, MELD exception points were readjusted by the OPTN in 2003, decreasing the MELD exception points to 20 for Stage I/T1 and 24 for Stage II/T2. In response to these adjustments, the proportion of transplants for HCC declined from 22% to 14%.[42] Since the 2003 MELD exception point adjustment, there have been a series of minor adjustments to the exception point policy, which ultimately resulted in the 2005 policy which set the exception points to 22 for T2 lesions (1 tumor 2-5cm or 2-3 cm with the largest tumor <3cm) and no exception points for T1 lesions (1 tumor <2cm).[43]

There is wide variability in the use of MELD exception points nationwide, with a general trend towards greater use of MELD exception points over time.[44,45] It is likely that this trend towards increasing use of exception points is propagated by the patient's higher likelihood of transplant, and lower likelihood of waitlist mortality associated with the use of these points.[44] There is varying literature on whether or not patients with HCC have better outcomes. While the recent annual reports from SRTR have both cited equivalent 5-year survival between HCC and non-HCC recipients, there are multiple studies which have indicated differences in outcomes in terms of disease recurrence and utilization.[14,15] A single center study found that pre-transplant inpatient utilization was higher amongst patients awaiting transplant with a diagnosis of HCC.[46] Conversely, a study by Krishnan et al, found that HCC patients had a significantly lower transplantation length of stay.[47] Overall, it is clear that outcomes differ between patients listed with and without exception points, particularly with regard to utilization.

It is also important to note that the use of MELD exception points varies nationwide. In a study by Massie et al, use of MELD exception points for transplant recipients by individual OPO's varied from 0-21.4%.[44] Such variability may be attributable to differences in transplant center experiences or preferences, or due to the prevalence of HCC in different regions.

Share 15

During the first few years after implementation of the MELD score, a variety of studies sought to evaluate the MELD as a predictor of post-transplant outcomes such as patient and graft survival. Among these, the most critical was the work by Merion et al (2005), which compared the relative benefit of transplantation to that of progressive liver disease while awaiting transplant.[48] In their analysis of approximately 13,000 patients on the liver transplantation waitlist from 2001-2003, the authors demonstrated that for patients transplanted with a MELD of 6-11 and 12-14, the hazard ratios for death with transplantation as compared to death while awaiting transplantation (waitlist mortality) were 3.64 and 2.35 respectively, indicating a greater risk of death with transplantation than with continued waitlist status.[48] In light of these findings, it was felt that patients with a MELD score under 15 did not have a relative benefit of undergoing transplantation.

Acknowledging there is untoward risk associated with transplantation when the patient's MELD is less than 15, the OPTN and UNOS developed the Share 15 policy, which was implemented in January 2005. Under Share 15, within each region donor livers were diverted away from patients with a MELD <15 to provide them to patients with a MELD >15, who could attain benefit from transplantation. Due to regional variability, such redistribution required exchange of organs beyond the local donor service area (DSA), and to other DSAs within the same region. When a donor organ became available, it would first be offered within the local

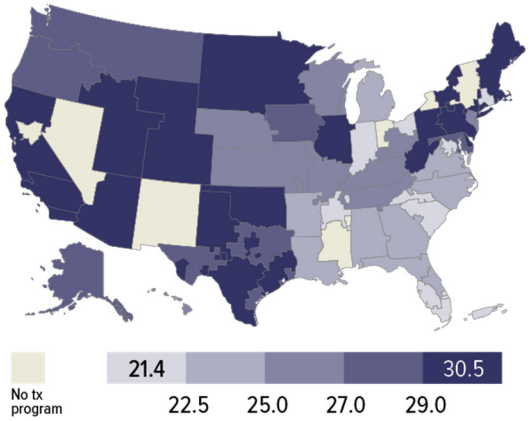
DSA sequentially to all waitlist candidates in order of decreasing MELD score down to a minimum MELD score of 15. If the organ was not accepted within the local DSA, it would then be offered within the region (at other DSAs) sequentially to all waitlist candidates with a MELD >15.[29,49] This policy marked the first shift away from local use and towards regional sharing.

In the years that followed the Share 15 policy, evaluations indicated that the policy had in fact lowered the wait-list mortality rate and improved organ distribution.[29] Due to the success of this policy, it was amended to allow for national sharing if a recipient with a MELD >15 was not available within the region (see Table 2 – 2 for updated allocation schema). Both the regional Share 15 and national Share 15 policies demonstrated the ability of OPOs within DSA networks to carry out organ sharing. Therefore, as the medical community looked for further advances in allocation, principles from Share 15, such as regional and local sharing, were considered to be highly feasible.

Share 35

While Share 15 improved organ distribution by increasing regional sharing and prioritizing patients who would benefit from transplantation, it did not eliminate the disparities in acuity between regions. In particular, the median MELD at transplantation varied widely between regions, as demonstrated in Figure 2 – 6 below. In addition to this variation by MELD score, there were also significant differences in wait list time and wait list mortality that remained. Such regional inequities led to the transplant community to propose additional changes in allocation policy in 2009, which built upon the principles of broader sharing that were at the foundation of the Share 15 policy.

Figure 2 - 6. Variation in median MELD at transplantation by OPO, 2012.[15] As indicated in the legend, OPOs with a higher median MELD at transplantation are shaded darker than those with a lower median MELD at transplantation.



While regional sharing had demonstrated positive outcomes in the Share 15 model, there was opposition to applying broader sharing guidelines.[29] In particular, there were concerns related to the cost associated with such broader sharing, as well as to the added burden of extended cold ischemia time (the time an organ remains without perfusion, a factor that is associated with poorer graft function). Due to these concerns, additional models with the Liver Simulated Allocation Modeling System (LSAMS) were completed and presented to both UNOS and OPTN boards as well as through a public forum. In an evaluation of regional sharing for high acuity patients (defined as a high MELD score), Washburn et al. demonstrated that in a model with sharing provided only for high acuity patients, the costs of shares would be limited to a subset of available livers, yet would also provide the opportunity for the available organs to serve those patients in greatest need of transplantation.[50-52] Within the Washburn study, models were designed for a variety of high acuity cut points, including MELDs of 29, 32 and 35. Sharing at the highest acuity, only for those with a MELD ≥35, demonstrated a benefit of approximately 80 waitlist lives saved annually.[50] The various allocations models with differing cut points were discussed amongst UNOS and OPTN as well as within a public forum, with an ultimate decision

to move forward with broader sharing only for the highest acuity patients, in a policy that would be referred to as Share 35.

Implemented in June 2013, Share 35 relied on some of the same principles as the Share 15 model, in which organ distribution was shifted away from local sharing, and towards regional sharing. In this model, organs are first offered locally to regionally to Status 1A and 1B recipients, then to all patients locally and regionally with a MELD >35, ultimately prioritizing those patients with the greatest need for a liver based on the liver disease severity. If the liver could not be regionally distributed to a high acuity patient, the organ would then be offered locally in sequential order (based on decreasing MELD score) to patients with a MELD <35 and >15. The new distribution model is demonstrated below in Table 2 – 2, in which OPOs work down through each level of distribution until an appropriate recipient is identified. Figure 1 – 1 also demonstrates an example of the change in distribution following Share 35 policy implementation.

Table 2 - 2. Allocation Policy Pre- and Post-Share 35 Implementation in June 2013. The allocation priority list below indicates the order in which patients were prioritized on the wait list from top to bottom. Once an organ becomes available in a local area it is offered down the list sequentially to each patient according to the allocation priority list. The italicized text indicates changes in the post-Share 35 period.

Pre-Share 35	Post-Share 35
Status 1A – Local	Status 1A – Local
Status 1A – Regional	Status 1A – Regional
Local distribution by highest MELD score (minimum score 15)	*Regional distribution by highest MELD for all patients with MELD ≥35*
Regional distribution by highest MELD score (minimum score 15)	*Local distribution by highest MELD score (<35 and >15)*
Status 1A – National	*Regional distribution by highest MELD score (<35 and >15)*
National distribution by highest MELD score (minimum score 15)	Status 1A – National
Local distribution by highest MELD score <15	National distribution by highest MELD score (<35 and >15)
Regional distribution by highest MELD score <15	Local distribution by highest MELD score <15
National distribution by highest MELD score <15	Regional distribution by highest MELD score <15
	National distribution by highest MELD score <15

The success of this most recent policy change has been evaluated in many ways. National assessments of the policy, have noted its success in 1. reducing the number of discarded organs (reduction of 16% within the first year of the policy), 2. increasing the rate of transplantation for the highest acuity recipients (rate of transplantation for MELD ≥35 increased from 22.3% to 30.5%), and 3. decreasing overall waitlist mortality for patients with MELD >30.[11] But there have also been reports of potential adverse consequences. In particular, a report by Halazun et al. indicated that although there have been national improvements, individual regions were affected differently, some of which saw worse patient outcomes. In an analysis of the individual regional impacts of Share 35, Halazun noted that regions 4 and 10 had significantly worse post-transplantation survival.[12] Additionally, one of the major concerns in the setting of broader sharing is the added cost of procurement, a fact that was referenced in the original IOM report in 1999. Fernandez et al. evaluated this concern in a brief report published in 2015, which indicated that post-Share 35, the costs of organ imports (bringing a regionally or nationally shared organ into an OPO that is different from the OPO in which it was procured) increased across all nine OPOs evaluated, and that this increase varied dramatically between regions, ranging from a 7.1% to a 240.7% increase.[53] Similar increases were also seen in export costs, with an estimated total increase, across all 9 OPOs evaluated of $11 million.

While early analyses have demonstrated both positive and negative effects of this policy, given its relative youth, being implemented just over three years ago, it remains unclear as to how it will impact disparities within and between regions. While broader sharing has assured that higher acuity patients receive priority, it has not changed the overall problem of inadequate supply for increasing demand, which rests at the crux of the issues in equitable organ allocation.

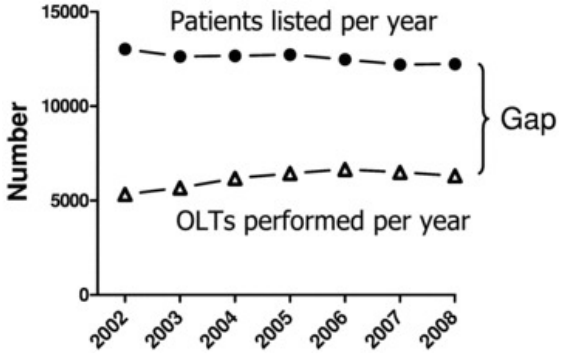
2.4 Modern Issues in Liver Transplantation & Organ Allocation

2.4.1 Implications of Organ Shortage

Among all types of organ transplantation, liver transplantation has been the most fraught by an imbalance between supply and demand. During the debates over the development of a national, standardized organ allocation system in 1998, the marked disparity between available organs and the need for transplants was considered to be the greatest for liver transplantation, and therefore put deceased donor liver graft allocation at the center of the debate over The Final Rule. Yet, unfortunately, even after designation of UNOS regions and the MELD allocation policy, disparities between organ supply and demand persist.

Although MELD allocation was thought to improve utilization of supplied organs, there continues to be a gap between overall supply and demand. As indicated in the figure below (Figure 2 – 7), while over 5,000 liver transplants are done annually, more than twice as many patients are waitlisted for transplantation.[54] Over the past decade, the annual number of patients added to the list has stabilized at approximately 10,500 new patients per year, yet in 2014, only 6,449 deceased donor adult transplants were performed.[55] This gap between those listed and transplanted, resulted in over 3,000 deaths in 2014, with a resultant waitlist mortality of 12.3 per 100 waitlist years (a number that has steadily climbed from 11.1 in 2009).[55] This shortage, combined with the current allocation paradigm of sickest first, has contributed to waitlist mortality and resulted in a population of patients undergoing transplant who inherently require greater health resources both as they await transplant and in the time immediately following transplantation.

Figure 2 - 7. Gap between supply and demand for useable donor livers [54]



2.4.2 Increasing Patient Acuity

Organ shortages paired with the current allocation paradigm have led to increasing patient acuity amongst transplanted patients. Over the past decade, from 2004 to 2014, a greater proportion of patients have been transplanted at the highest acuity (MELD >30), increasing from 20.4% to 40.4%. As well, more patients have been hospitalized at the time of transplantation, 28.7% versus 35.7%.[55] Patients are also more likely to be older (number of recipients ≥65 years of age has increased from 11% to 21% from 2004 to 2014) and are more likely to have multiple comorbidities (Table 2 – 3). As indicated in the table below, the rates of obesity, diabetes and renal insufficiency have increased over time.[55,56] The collective effect of both increasing acuity of liver disease and increased proportion of patients with comorbidities has in turn led to a much higher acuity liver transplant population.

Table 2 - 3. Increasing Rates of Comorbidities Among Transplant Patients Over Time[56]

Table 4: Incidence of comorbidities among liver recipients by year of transplant

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Number of patients	4498	4595	4672	4969	5351	5848	6121	6363	6228	6069
Obesity (BMI ≥ 35 kg/m^2; %)	7.8	8.5	8.3	6.9	8.2	8.9	8.3	8.4	9.8	11.0
Diabetes (%)	14.9	15.6	17.8	16.8	18.1	18.9	18.9	21.6	22.0	21.5
Renal insufficiency (Cr ≥ 1.5 mg/dL; %)	–	–	–	26.1	29.1	30.8	32.5	30.2	31.1	29.8

2.3.3 Regional Variability

One of the pivotal mandates within the Final Rule stated that allograft allocation "[s]hall not be based on the candidate's place of residence or place of listing," yet it remains clear that

dramatic disparities of geography still exist.[29,33,57-59] In particular, the mean MELD at the time of transplant varies considerably both within and between regions. In the figures below, mean MELD at the time of transplant (match MELD) is graphed by donation service area (Figures 2 – 8 and 2 - 9). As indicated in the figures, the match MELD can vary by up to ten points within a single UNOS region. When looking at inter-regional comparisons, this variability is even more striking, such that the median MELD at transplant by region varied by 20 points in the 2014 SRTR Annual Report, with region 3 having a median MELD of 18 and region 5, 38.[55]

Figure 2 – 8. Mean match MELD scores at the time of transplantation for deceased donor liver transplants in 2009 (only adults and no exception points) by donation service area (local region of distribution). Vertical bars represent 1 standard deviation from the mean[29].

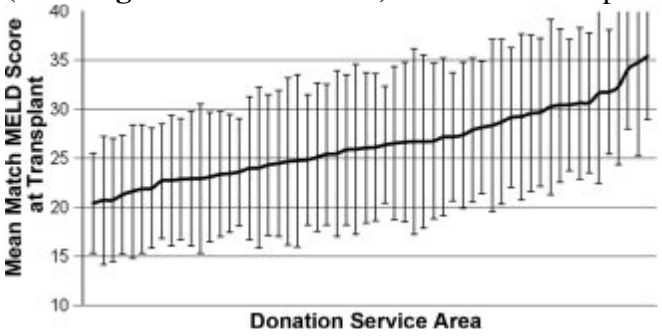
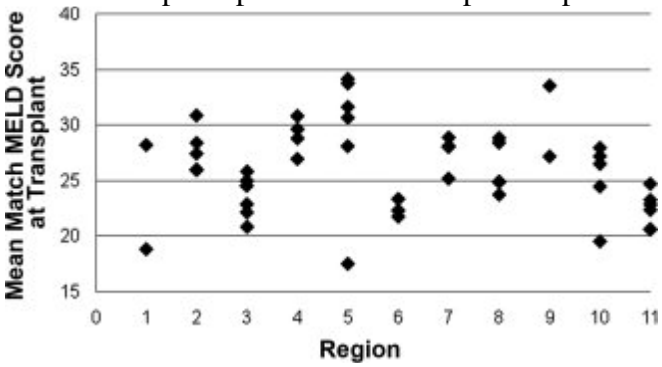


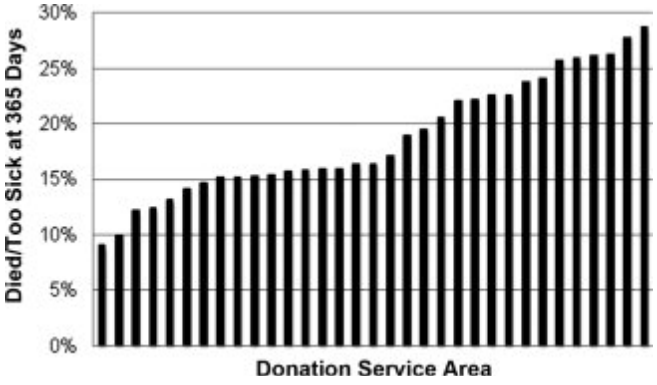
Figure 2 - 9. Mean match MELD scores at the time of transplantation for deceased donor liver transplants in 2009. Graph includes only adults, and excludes those patients who received MELD exception points. Each data point represents an individual donation service area[29].



This variability in acuity translates directly into differences in likelihood of receiving a transplant, survival on the waitlist and post-transplant survival. In an assessment of intra-regional variations, a study by Barshes et al. (2007) found that the likelihood of transplantation between

DSAs within region 4 varied dramatically, with certain DSAs conferring a 23-55% lower likelihood of undergoing transplantation.[57] This difference in likelihood of transplant is likely to be even greater if more disparate regions or DSAs had been compared. Such disparities translate directly into lower waitlist and post-transplant survival for areas with a lower likelihood of transplant. During the period of time patients await an organ, their MELD score, and in turn their risk of 3-month mortality, continues to increase. Such increasing acuity can ultimately lead to patients being removed from the transplant waitlist, secondary either to advanced disease, severity of their overall medical condition or death. Therefore in parallel with the variability in acuity at the time of transplant, there is similar variability in the rate at which patients are removed from the waitlist, as seen in Figure 2 – 10.[29]

Figure 2 - 10. Variation in the Rate of Waitlist Removals for Death or "Too Sick to Transplant" by Donor Service Area. Percentage of patients that died or were removed from the waitlist because they were too sick for transplant at 365 days for all candidates listed for deceased donor liver transplantation between January 1, 2008 and June 30, 2009 by donation service area.[29]

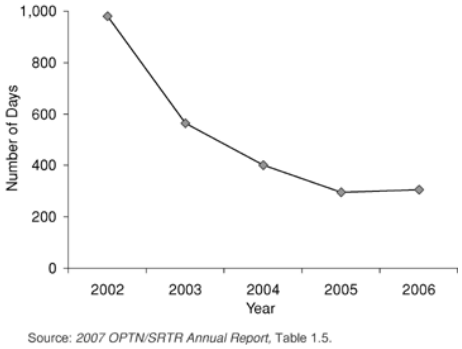


Regional disparities are one of the major concerns within UNOS and the transplant community. It is well understood that disparities between and within regions have developed due to differences in organ supply and demand.[33,41] In recent years, steps have been taken to reduce these disparities, through allocation policy changes, which are discussed below.

2.4.4 Waitlist Dynamics

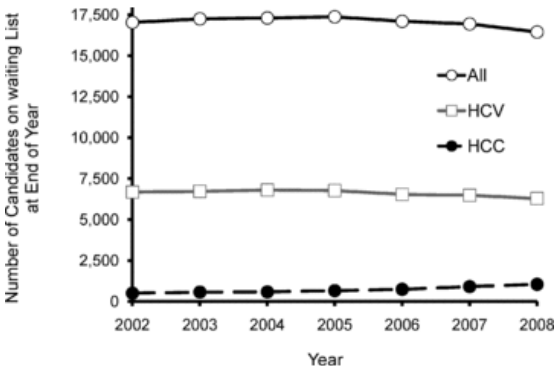
Waitlist dynamics include trends in both patient additions and removals from the waitlist, as well as trends in outcomes for patients on the waitlist. Following implementation of the MELD allocation system, which deprioritized wait list time, there was a dramatic decrease in the median time new liver transplant candidates waited for transplantation (Figure 2 – 11).[60] In addition to this trend, the early post-MELD period also saw a gradual decline in the number of patients on the waitlist at the end of each calendar year (Figure 2 – 12).[56] In the last few years, this trend has begun to stabilize, with a relatively constant number of patients added to and remaining on the waitlist annually, approximately 15,000 and 10,000 patients respectively.[55] Yet while these numbers have been stable, waitlist mortality has increased dramatically. Comparing 2004 to 2014, 2400 versus 3111 patients were removed from the waitlist due to death or being too sick to transplant over the course of a 1 year period, corresponding to a 30% increase in waitlist removals.[55] As well, waitlist mortality has continued to increase with a rate of 11.1 per 100 waitlist years in 2009 to 12.3 in 2014.[55] The overall increase in mortality and wait list removals is attributed to a variety of causes including: fewer patients listed at low acuity (MELD <15), greater number of patients listed at high acuity (MELD >30), geographic disparities and organ shortages.

Figure 2 - 11: **Median time in days to transplant for new liver waiting list registrations, 2002–6.** [60]



Source: *2007 OPTN/SRTR Annual Report*, Table 1.5.

Figure 2 - 12. Number of patients on waitlist at the end of each calendar year. HCV – Hepatitis C Virus as primary diagnosis, HCC – Hepatocellular carcinoma as primary diagnosis.[56]



In addition to these overall trends, it is important to note that additions and removals from the waitlist are likely to vary by UNOS regions and transplant centers. In particular, it is acknowledged by UNOS that transplant centers have discretion over patient selection for entering the waitlist as well as discretion in determining who is no longer eligible due to illness severity or changes in a patient's social, financial or economic status. While there is very little research focused on evaluating these variations in transplant program or regional differences in waitlist behavior, there is some literature to suggest such variation does exist. In an early post-MELD era report of the new allocation system implementation, Schaffer et al. noted distinct variation in the number of patients added to the list over the 6 month period after MELD implementation between derived transplantation service areas as well as variation in the number of patients removed due to death or becoming too sick for transplantation.[61] Other findings within this same study that suggest transplant center variation in waitlist behavior indicate variation in the number of patients listed with MELD exception points, and in particular with a diagnosis of HCC, as well as variation in MELD score at the time of listing.[61]

2.4.5 Sociodemographic Disparities

Gender

Although the MELD system led to a more equitable system in terms of objective disease severity, inherent disparities arose between genders. Early work in the post-MELD era demonstrated that following MELD implementation, the odds of death or removal from the transplant waiting list due to severe disease increased by 30% for women when compared to men.[59] As well, other reports indicated that women were less likely to be evaluated, listed or transplanted and more likely to die following transplantation.[62-64] Various reports have proposed potential explanations for such disparities, such as differences in serum creatinine values (a variable included in the MELD score calculation) and severity of renal disease by gender or difficulties in organ size matching. Evidence has mounted on both sides of the creatinine argument, with some studies suggesting that an average of 3 points should be added to the MELD scores of females, while others have demonstrated no significant difference in creatinine levels and renal disease severity between genders.[65] Although such disparities persist, particularly in waitlist mortality and the risk of becoming too sick for transplantation, there have been no changes to the organ allocation system to control for gender differences.[66,67]

Race

With the transition to the MELD score, UNOS and the OPTN were optimistic that this more objective measure would eliminate many of the racial and ethnic disparities in transplantation. In a series of studies comparing rates of transplantation between racial groups, the transition to the MELD score appears to have reduced or eliminated many of these disparities. In a study of UNOS and OPTN data, Moylan et al. indicated that the disparities present prior to the MELD score between blacks and whites were nearly eliminated, such that the

odds of death or removal from the waiting list due to advanced disease between blacks and whites dropped from a pre-MELD OR of 1.51 to a post-MELD OR of 0.96.[59] As well, the study found that while black patients listed for transplant were less likely than whites to be transplanted in the pre-MELD era (OR 0.75), in the post-MELD period they were slightly more likely (OR 1.04).[59]

Yet while these studies have demonstrated improved equity after transplantation, it is important to note that these results only pertain to patients who are able to attain access to a transplant center and undergo evaluation for liver transplantation. Multiple studies have demonstrated that it is at this juncture where much of the disparity between racial minorities and whites still exists.[64,68,69] In particular, a study by Reid et al. demonstrated that overall, blacks are underrepresented on the OPTN waitlists in comparison to both the proportion of blacks in the U.S. as well as the proportion of blacks with end stage liver disease.[68] Similarly, a study within the Veterans Affairs system has also demonstrated significant racial disparities in access to liver transplantation. Julapalli et al. (2005) indicated that in comparison to white veterans, blacks had a decreased likelihood of referral for liver transplantation.[69]

Finally, there are differences in the time of listing, which may ultimately impact waitlist mortality and overall outcomes from liver transplantation. In both the Reid and Moylan studies, the MELD score at listing was significantly higher amongst blacks as compared to whites, with Moylan reporting at least at 2 points difference.[59,68]

Issues of access, both in ability to achieve a position on the waitlist and to do so in a timely manner, likely impact some of the difference seen between racial groups in terms of both attaining and surviving liver transplantation.

Location

Due to the location of transplant centers across the country, there are large areas both within and across states that have limited access to transplant services. Furthermore, transplant centers are more likely to be in more urban areas, commonly at large academic medical centers, which may in turn limit access to patients from more rural areas. While these geographic barriers have been shown to have a significant impact on a patient's likelihood of attaining a referral for transplantation, there is very little research on how these geographic disparities impact patient outcomes post-transplant.

Analysis of the likelihood of transplant waitlist entry, transplantation and time to transplant have demonstrated significant disparities due to geography. In a study by Axelrod et al, when adjusted for demographic characteristics, patients living in rural regions were significantly less likely to be listed for liver transplant (relative risk (RR) = 0.86, $p<0.001$), less like to undergo transplantation (RR = 0.80, $p<0.001$), but no more likely to wait longer for an organ once listed for transplant (hazard ratio (HR) = 0.96, $p=0.24$) than patients in urban areas.[70] These differences extended to the micropolitan regions as well, as this population was also less likely to be listed for transplant (HR = 0.90, $p<0.001$) and less likely to undergo transplantation (HR = 0.80, $p<0.001$). In a similar study, done within the Veterans Affairs system, Goldberg et al. found that distance from a VA transplant center or any transplant center was associated with a decreased likelihood of being evaluated and listed for transplantation, as well as a decreased likelihood of undergoing transplant.[71] Collectively, these studies indicate that there are unintended consequences to the centralization of transplantation services, such that centralization has limited access to these services, and therefore may influence the patient population that is listed for transplantation.

While location and distance from a transplant center may hinder the ability of a patient to attain access to transplantation, for those who do undergo evaluation and ultimately receive a transplant, there is very little literature on the impact this distance has on their post-transplant outcomes, in particular survival, graft function, and utilization. To date, the only study that addresses this issue is the previously mentioned Axelrod study, which demonstrated that rural residence was not associated with time to death (HR 1.01, p=0.92) after transplant when compared to urban residents.[70] There are no studies that have focused more closely on utilization and how patient location may impact both where patients seek services as well as the volume of services they may require.

Insurance Status

Insurance status and type of insurer have been associated with differences in outcomes across the course of transplantation. In particular, Bryce et al. (2009) noted that insurance status is strongly associated with the likelihood of undergoing evaluation, as well as ultimately being listed for transplantation.[64] These differences indicate clear disparities in access to transplantation services for patients with Medicare, Medicaid or no insurance coverage when compared to the privately insured. For patients who are able to attain referral, evaluation and listing, there is substantial evidence, again, that patients without private health insurance are at greater risk for poor transplant outcomes. Multiple studies have demonstrated lower overall survival amongst patients with public insurance or charity care (uninsured).[72,73] As well, a study by Glueckert et al. demonstrated that patients without private insurance had a higher rate of missed clinic appointments and a high rate of complications after transplantation. Collectively, these studies suggest that insurance status is a major predictor of both access and outcomes in liver transplantation.

2.5 Prior Literature on Share 35: Impact on Listing Behavior and Patient Acuity

Share 35, implemented in June 2013, was aimed at reducing wait list mortality and regional variability. In general, initial evaluations of the policy highlighted many of its successes, in particular increasing the transplantation rate for patients at higher MELD scores (proportion of patients transplanted in the 1st year of the policy change with a MELD ≥35 increased from 22.3% to 30.5%).[11] In the year immediately following its implementation, there were a series of evaluations completed by both UNOS and independent academic centers which evaluated different components of the policy's effects. The effects, in terms of patient acuity, listing behavior, waitlist times, waitlist mortality and overall transplant survival, will be discussed in detail below.

2.5.1 Patient Acuity

Consistent with the Share 35 policy, which prioritized patients with MELD scores greater than 35 for regional distribution of organs, most studies demonstrate a parallel increase in overall patient acuity. Preliminary studies indicated that overall, more patients with a MELD of 35 or higher were on the waitlist over time (Figure 2 – 13).[74] As well, a study by Massie et al (2015), which utilized SRTR data from June 2012 – June 2014 in a 1-year pre/post design, reported a significant increase in MELD score at transplant, as well as an increased proportion of recipients receiving an organ at a MELD ≥35 (increased from 22.3% to 30.5%, $p<0.001$) (Figure 2 – 14).[11] This increase in patients with a MELD ≥35, likely contributes to the overall increase in MELD at transplant seen in multiple studies, which indicated an increase from a MELD of 27 to 28 when comparing 1 year pre/post periods.[49,74] When looking more closely within regions, in a study by Halazun et al., which utilized UNOS data and the Social Security Death File, they found that MELD scores increased in 3 out of the 11 regions, while remaining stable in the others.[12]

Figure 2 – 13. Number of MELD/PELD 35+ candidates on the waiting list at month's end from June 2011 to June 2015 [74].

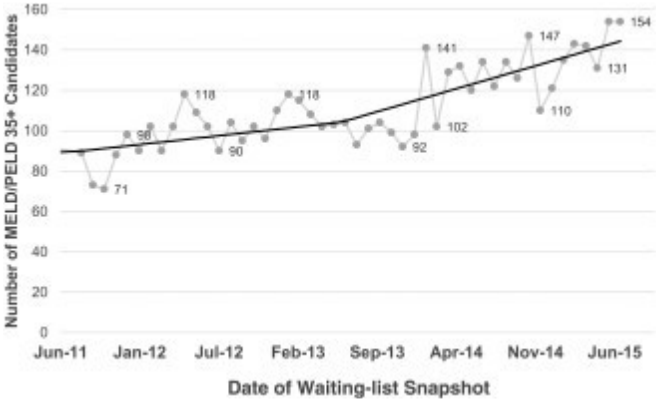
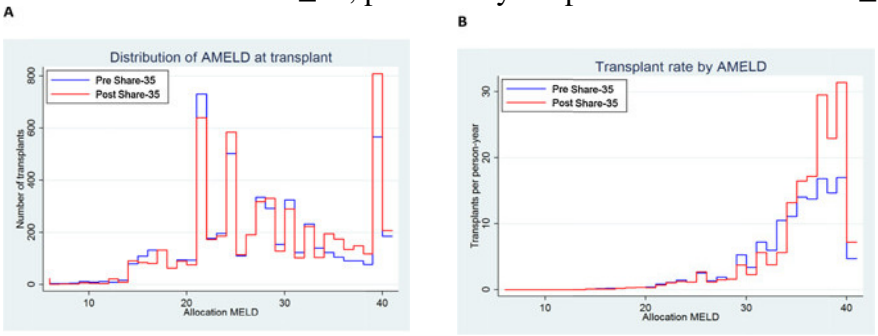


Figure 2 - 14. Distribution of AMELD (allocation priority based on MELD or exception points) at transplantation, before and after implementation of Share 35. Status 1 recipients are categorized as AMELD = 41. (A) Number of transplants at each AMELD. Post-Share35, there were more total transplants, and more transplants with AMELD ≥ 35. AMELD at transplant increased under Share 35 (Wilcoxson rank-sum p = < 0.001). The proportion of transplants with AMELD ≥35 increased from 22.3% to 30.5% ($\chi 2$ p = < 0.001). (B) Rate of transplants for waitlist registrants at each AMELD score. Under Share 35, the transplant rate increased for AMELD ≥35, particularly for patients with AMELD ≥38.[11]



When looking beyond the MELD score, Halazun found that there were also increases in other markers of acuity, such that there was an increase in the likelihood of patients being in the intensive care unit (3/11 regions), requiring mechanical ventilation or vasopressor support (3/11 regions), and having low functional status (Karnofsky scores <30%) (3/11 regions) prior to transplant in the post-Share 35 period.[12]

Initial evaluations of Share 35 demonstrated that there was likely an increase in patient acuity, but that the degree to which this has changed is likely dependent on region. Furthermore

it is clear that acuity has increased both in terms of MELD and by other markers such as markers of physical debility and severity of illness at transplant.

2.5.2 Listing Behavior

Collectively, listing behavior encompasses both patient selection (placement on the waitlist) and removal from the waitlist. It is well known that patient selection varies by transplant center, as individual centers are able to set specific criteria (for example: disease state, compliance with drug and alcohol abstinence, age, comorbidities) as to who may be eligible for transplantation at their center. Similarly, it is well-known that patterns of delisting also vary by center, in that the threshold for removing a patient because they have become "too sick" for transplantation may vary center to center. There is unfortunately very little literature on how these practices vary by center.

Although there are no studies amongst those evaluating Share 35 that have specifically evaluated center or regional differences in patient selection before or after policy implementation, some studies have assessed proxy measures of such behavior. In particular, Massie et al. (2015) assessed changes in the listing MELD in the pre/post Share period and found it to be relatively unchanged, with a median MELD of 17 (IQR 12-23) pre-Share to 18 (IQR 12-23) post-Share ($p=0.6$).[11] Looking at more granular differences, the study by Halazun et al (2015), which assessed regional variations in patient acuity by region, found that, as previously stated, 3 out of the 11 regions had an increase in MELD score (Regions 2, 4, 5), although the overall national MELD at transplant was relatively unchanged.[12] As well, Halazun identified that in certain regions there was an increase in the percentage of patients in the ICU prior to transplant (Regions 3, 4, 5), percentage of patients requiring ventilator or vasopressor support (Regions 3, 4, 11) and percentage of patients with a Karnofsky score <30% (Regions 4, 5, 11).

These markers of increased acuity may represent changes in patient selection in these regions, as centers may have been more likely to list patients at a higher acuity and less likely to remove them as their disease progressed.

Patient selection also encompasses the selection of patients who are eligible for MELD exception points. In an analysis of the impact of Share 35 on patients with HCC (and therefore eligible for MELD exception points), a study by Croome et al., which utilized UNOS STAR data from 2011-2015, found that there was no difference in the proportion of patients transplanted for HCC pre/post Share 35 (23.0% and 22.4% respectively).[75] Furthermore, they found no difference in wait times for patients with HCC (185 versus 195 days). Interestingly, they did find differences in the utilization of regional sharing (instituted under the Share 35 policy) for HCC patients between regions, such that while 6 regions had no shares for HCC, regions 1, 2, 5, 8, and 9 did share organs for HCC patients under the new policy. In each of the regions, 1, 2, 8 and 9, these shares composed less than 2% of grafts shared in their region, but in region 5 (a high acuity region), 33 organs were shared for HCC, accounting for 8.3% of the grafts shared.

With regard to delisting behaviors, removals from the waitlist, there is very sparse literature, both before and after the implementation of Share 35. Studies by Barshes et al. and Schaffer et al, completed prior to Share 35, attempted to elucidate differences in delisting behavior through evaluation of delisting by DSA and by transplant service area (defined by the authors as a geographic segment of a UNOS region).[57,61] Barshes gave a more cursory evaluation, indicating that during the 4-year study period 12.8% of patients were delisted and that delisting rates, even after controlling for patient and disease characteristics, varied by DSA. Their group further assessed risk factors associated with delisting, and found that the following characteristics were significant: increasing MELD score (HR 1.10), status 1 designation (HR 8.59), increasing age

(HR 1.01), race (African Americans having a lower likelihood of being delisted (HR 0.62)), presence of MELD exception points (HR 0.36) and multiple organ transplant (HR 0.59). Schaffer et al. (2003) provided more specific statistics from their comparison between 3 transplant service areas within a single UNOS region. Amongst these service areas, there was notable variation in the rate of non-death removals from the transplant waiting list, such that the 3 transplant service areas accounted for 71%, 22% and 7% of the removals respectively. The median MELD within each of these areas also varied, ranging from 23-30.[61] Collectively these studies demonstrate that there was wide variation in delisting behaviors even prior to Share 35.

Amongst the studies evaluating Share 35, none addressed patient removals from the waitlist for reasons other than death. In the single study that did address delisting, Annamali et al. reported no change in the overall rate of waitlist removals due to death, which was remained stable at 13% in the 1-year pre and post-Share 35 periods evaluated within their study.[49] In subgroup analyses, when patients were grouped by MELD score, there was a statistically significant increase in the rate of removals due to death amongst patients with a MELD 15-34, which increased from 2.6% to 3.2%. No other groups, either the MELD <15 or MELD ≥35 subgroups, had statistically significant changes.

Overall, listing behavior is not well evaluated in the transplant literature. From the handful of studies that are available, it is clear that there is variation in patient selection and removal from the waitlist. Outside of HCC, for which it appears there was no change, it is not clear whether or not there have been changes in listing behavior due to the Share 35 policy.

2.5.3 Waitlist Mortality

Waitlist mortality, the rate of deaths while awaiting transplantation, was expected to decrease with the implementation of Share 35, due to an expected increase in the rate of

transplants for the patients with the highest probability of death while awaiting transplant. Amongst those studies that have evaluated changes in waitlist mortality after Share 35, the majority have found that there was no change in waitlist mortality.[49,74] Alternatively, Massie et al. indicated that when accounting for the competing risk of transplantation and adjusting for allocation MELD score, Share 35 was associated with an 8% overall decrease in waitlist mortality. This difference in results is likely due to the fact that their model appropriately controlled for competing risk, and also utilized physiologic MELD (not including exception points). In sub-analyses, their study found that the decreased mortality was solely attributable to the change in mortality for the highest acuity patient, MELD >30, who experienced a decrease in waitlist mortality of 30%, whereas all other groups were noted to have no significant change. The findings of the Massie study are in line with the expected results of the Share 35 policy, in that only those at the highest acuity ultimately benefit.

The impact of Share 35 of waitlist mortality has varying results in the literature, yet when accounting for competing risk of death without transplantation, it is likely that Share 35 has improved waitlist mortality for those at the highest acuity. These studies are limited to very short-term follow-up, with the longest follow-up 1.5 years after implementation of Share 35. Further evaluations of waitlist mortality are important as greater follow-up becomes available. As well, no study has yet evaluated the impact of Share 35 on waitlist mortality at a more granular level, particularly by DSA, center or region.

2.5.4 Survival

Initial proposals for Share 35 did not directly hypothesize the impact of the policy on overall patient survival after transplantation. One may theorize that the transplantation of sicker patients may result in lower overall survival, yet the impact of lower survival amongst a small

group of patients may not impact the survival of the overall transplant population. Alternatively, the policy may result in improved post-transplant survival due to the prioritized transplantation of the highest acuity patients that could potentially be offset by the increased waitlist mortality amongst patients who are less sick, but waiting longer. Amongst the studies that evaluated 1-year survival amongst patient transplanted after the implementation of Share 35, the majority demonstrated that there was no overall change in patient survival.[11,12,74,76] Edwards et al, further found that there was no difference in survival in patients transplanted at a MELD ≥35. This finding somewhat contradicts the conclusions of a study by Nekrosav et al, which analyzed patients with a MELD ≥40 and did find an improvement in both graft and patient survival in the post-Share 35 periods, with improvements from 77% to 80% and 79% to 82% at 1-year respectively.[77] The differences between these two study populations, MELD ≥35 and MELD ≥40, may indicate that the improvements in graft and patient survival are only seen amongst those with the highest of MELD scores. In the Halazun study, which compared regional outcomes, there were again differences between regions, such that Region 4 and 10 were noted to have significantly decreased 1-year survival after the implementation of Share 35, whereas there were no significant changes in any of the other 9 regions.[12]

The results of the studies to date present conflicting results of the impact of Share 35 on patient survival. Further work is needed to assess if the policy resulted in the transplantation of patients with poorer 1-year outcomes, and to assess how differences in survival vary by patient acuity prior to transplant and by region, DSA and center.

3. Focused Literature Review

In this section, I review the prior literature addressing my dissertation research questions and discuss the contributions of my dissertation to this existing literature.

3.1 What are the factors associated with inpatient utilization among liver transplant patients? (Q1, Q2)

Inpatient utilization for transplant patients can be divided into three phases of care: pre-transplant, transplant, and post-transplant. Pre-transplant care includes utilization leading up to the transplant admission; transplant care is solely the utilization during the transplantation admission; post-transplant care is all utilization that occurs after transplant discharge. The window for pre-transplant care is poorly defined in the literature, and can broadly include any care ever provided to patients with end stage liver disease to more succinctly include only care provided within one year or six months prior to transplant. Due to the ambiguity of this time period and difficulties in clearly defining this patient population, pre-transplant utilization will not be directly addressed in this dissertation. The transplant period, for the purpose of this discussion, is defined as the index hospitalization related to liver transplantation, and the post-transplant period will be defined as all utilization that occurs from the transplantation date up and 180 days post-transplant (six months post-transplantation).

Evaluations of inpatient utilization among transplant patients have indicated an overall trend in increased utilization amongst the sickest patients. In particular, work by Buchanan et al, Axelrod et al, and others have demonstrated a clear correlation between increasing MELD score and increased utilization.[4,8,78] In many ways, this association is logical. Sicker patients require more care, utilize more services and ultimately result in greater overall costs. Studies have also

demonstrated that donor characteristics, in particular higher risk donor organs, are associated with increased costs of care, which may be a proxy for utilization by the recipient.[79] At the population level, this is supported through trends within the biannual Milliman reports, which demonstrate that costs have continued to increase over time, in parallel with the increasing acuity of transplant patients nationwide.[80-82]

Previous literature, published prior to the implementation of Share 35, with regard transplant and post-transplant utilization is discussed below.

3.1.1 Transplant Utilization

The index hospitalization for liver transplantation is the greatest contributor to the overall cost of care within one year of transplant.[8] This admission, which encompasses both the transplantation as well as immediate post-transplant care, has been the focus of the majority of utilization research that exists in the field of liver transplantation. In particular, research demonstrated that over time the overall length of stay and ICU length of stay both increased, resulting in increases in overall utilization as well as costs.[8,83]

The majority of studies have focused on the index hospitalization, in particular, assessing clinical risk factors for prolonged length of stay. Across these studies, risk factors can be grouped into patient, donor or utilization factors. The factors that have been associated with increased length of stay at each level are compiled in Table 3 – 1. In one of the most thorough studies to date, Krishnan et al, utilized UNOS-STAR data from 2003-2010 to assess clinical, patient and payer characteristics to develop the HALOS-ND score for predicting length of stay.[47] This model identified 25 factors associated with increased length of stay and three factors associated with decreased length of stay (Table 3 – 2).

Table 3 - 1. Factors Associated with Increased Transplant Length of Stay

Category	Risk Factors	
Patient Factors	Age[6,84]	Sex [84,85]
	BMI [6,86]	MELD score at transplant [4,6,8,83,87]
	Redo transplantation [6]	Post-transplant complications[85,88]
Donor Factors	Age[6,84]	Weight[6]
	Donor risk index [6]	Cold ischemia time [6]
Utilization Factors	ICU care required prior to transplant [84,88]	
	Ward care required prior to transplant [84,88]	

Table 3 – 2. HALOS-ND Model for Predicting Post-Transplant Length of Stay – Multivariable analysis. Only statistically significant factors are shown.[47]

Category	Variable	Estimate	p-value
Recipient Factors	Age: >55, <65	0.04	<0.0001
	Age: >65	0.08	<0.0001
	Gender: male	- 0.05	<0.0001
	BMI: <22	0.03	<0.0001
	BMI: >40	0.05	<0.0001
	Diagnosis: Acute hepatic necrosis	- 0.06	<0.0001
	Diagnosis: Cholestatic disease	- 0.03	<0.01
	Medical condition at transplant: Hospital bound	0.11	<0.0001
	Medical condition at transplant: ICU bound	0.14	<0.0001
	Medical condition at transplant: dialysis within 1 wk of transplant	0.07	<0.0001
	Encephalopathy: Grade 3-4	0.09	<0.0001
	Ascites: Moderate	0.03	<0.01
	Any life support	0.14	<0.0001
	Diabetes	0.03	<0.0001
	Portal vein thrombosis, history of	0.05	<0.0001
	Previous abdominal surgery, history of	0.02	0.01
	TIPS present at transplant	0.03	<0.001
	Albumin, <3 mg/dL	0.02	<0.001
	MELD score: 22-30	0.06	<0.0001
	MELD score: >30	0.08	<0.0001
	Exception MELD points for HCC	- 0.07	<0.0001
	Previous liver transplant, 1	0.07	<0.0001
	Previous liver transplant, >1	0.15	<0.0001
	Living donor	0.08	<0.001
Payment Factors	Primary payment: Medicare/Medicaid	0.03	<0.001
	Primary payment: VA	0.09	<0.001
	Secondary payment: Medicare/Medicaid	0.04	<0.01
Donor Factors	Age: >55	0.02	<0.001
	Non-heart beating donor	0.07	<0.0001
	Share type: national	0.03	<0.01
	Cold ischemia time: >6 to 9 hours	0.06	<0.0001
	Cold ischemia time: >9 to 12 hours	0.10	<0.0001
	Cold ischemia time: >12 hours	0.12	<0.0001
	Transplant type: Left lobe only	0.13	<0.001
Post-Transplant Factors	ACR during transplant admission: Yes, no treatment given	0.17	<0.001
	ACR during transplant admission: Yes, treatment given	0.18	<0.001
	Re-transplant during transplant admission	0.30	<0.001

In addition to assessing patient and clinical characteristics associated with length of stay, two additional studies identified variation in length of stay by transplant center. In particular, a study by Washburn et al, which utilized data from two different transplant centers, noted that center was one of the strongest predictors of length of stay.[6] As well, center was shown to be a significant factor in a study by Showstack et al. which assessed variation in utilization across 4 different centers included in the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Liver Transplantation Database.[84]

One of the major components of utilization during the transplant admission is the duration of stay in the intensive care unit following transplantation. Amongst the handful of studies that have assessed ICU length of stay, MELD remains one of the greatest predictors of increased utilization.[83,87,89] Additional factors which have also been found to be significantly associated with ICU length of stay include: marginal/high risk graft, development of renal failure, development of respiratory failure, transfusion of >10 units of fresh frozen plasma, transfusion of >7 units of packed red blood cells, sepsis, BMI, ICU care required prior to transplant.[86,89]

Finally, there are very few studies that have evaluated the pre-transplant length of stay. As stated above, patient location within the hospital is associated with longer post-transplant length of stay, but, to date, there is little research on the predictors of pre-transplant length of stay within the transplant admission. Research on this topic has primarily evaluated the impact of pre-transplant hospitalization on post-transplant survival, such as the work of Nekrosav et al. which indicated that prolonged pre-transplant length of stay was associated with decreased graft and patient survival.[77] Additionally, patterns of hospitalization have been evaluated in the pre- and post-transplant periods, by Schaubel et al, indicating that transplantation results in decreased

hospital utilization.[90] Yet, this study did not isolate the transplant admission length of stay, or segregate that admission into a pre- and post-transplant period, therefore it is unclear how these two periods of utilization are related.

Collectively these studies indicate that there are a wide variety of factors that contribute to differences in transplant length of stay and utilization of the ICU. The majority of the studies to date have focused primarily on clinical variables, and indicate that patients at higher acuity or with multiple comorbidities are at higher risk for prolonged length of stay. Unfortunately, to date, there are very few studies that have looked beyond clinical factors and evaluated the impact of patient sociodemographics, insurance status, or location.

3.1.2 Post-Transplant Utilization

While there is substantial literature evaluating factors contributing to transplant length of stay and ICU utilization, there is very little work focused on utilization after transplant discharge. In Buchanan's evaluation of costs during the entire first year after transplant, the post-transplant period account for >20% of the annual costs, much of which is likely attributable to post-transplant readmissions.[8] Yet, to date there is very little work evaluating these readmissions, and among those studies that have evaluated this period of utilization, they are either small single center series or national studies with limited follow up.

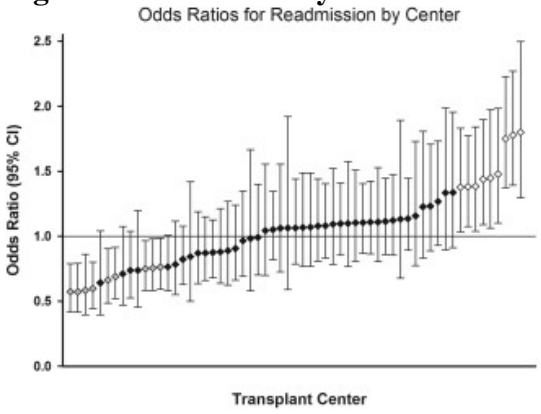
Evaluations of readmissions following transplantation have primarily been done at a single transplant center. To date, very few reports have been published, with the two most recent and generalizable studies being published out of the University of Cincinnati and University of Washington.[9,10] It is important to note that both centers represent low to moderate acuity centers, with average MELD scores reported as 21.6 in the Cincinnati study and as 39% of patients with a MELD >19 in the Washington study. The remaining studies included those that were completed

outside the U.S. or only focused on a subset of readmissions.[91,92] Amongst single center studies evaluating post-transplant discharges, the rate of readmissions within 30 days and 1 year ranged from 41-45% and 69-70%, respectively.[9,10] The Cincinnati study demonstrated that the majority of transplant readmissions occurred within the first two months after transplant discharge, but continued to occur throughout the first year post-transplant, plateauing at a rate of about 11% at 4 months after transplantation.[9] Furthermore, the authors provided details regarding the most common causes for readmission, by time period. The most common causes for readmission within 30 days included: infection (19.5%), renal failure (9.3%), gastrointestinal disorder (8.5%) and pulmonary edema or effusion (7.6%). Readmissions occurring after the first 30 days had similar reasons for readmission, including: infection (24.8%), acute cellular rejection (8.5%), pulmonary edema or effusion (7.1%) and biliary complications (7.1%). Amongst readmissions, the median length of stay was 4 days. As well, the authors identified a subset of patients within their cohort with a high rate of recurrent readmissions, with 18% with ≥4 readmissions. The results of the Cincinnati study provide insight into the overall causes and types of readmissions that may occur and indicate that a subgroup of patients may have a high volume of readmissions. The Washington study did not provide further details in regard to the reasons for, or characteristics of, their readmissions.[10] The Canadian study done by Shankar et al. reported their most common causes of readmission as due to surgical complications (28.4%) and malnutrition (13.9%), yet their study period included only those readmission within 90 days of transplant.[92]

The only multicenter study on readmissions in liver transplant patients is by Wilson et al, which utilized both the SRTR and University Health System Consortium databases in order to determine the incidence and risk factors associated with 30-day readmissions.[7] The UHC dataset captures 63 of the 135 transplant centers across the U.S. and accounts for 43.1% of all liver

transplants that were performed in the U.S. during the study period (2007-2011). This study highlights the high rate of readmissions and associated costs, but is limited by its short follow-up period (30-days following discharge). Within their sample, Wilson et al., reports a 30-day readmission rate of 37.9% with 51.7% of the readmitted patients presenting within 7 days of discharge. Furthermore, this study demonstrated that readmissions rates, and in turn inpatient utilization post-transplant, varies by transplant center, with center-specific adjusted ORs for readmission ranging from 0.53 to 1.90 (Figure 3 – 1). Unfortunately, the study does not provide information on transplant center characteristics that differentiate these low- and high-rate readmission hospitals.

Figure 3 – 1. Variability in Readmission Rates by Transplant Center[7]



In both Wilson's study as well as single center evaluations, risk factors for readmission have been evaluated. The factors that were significant across multiple studies included: diabetes, hypoalbuminemia, dialysis dependence, hospitalization prior to transplant, MELD at transplantation, transplant length of stay, high risk donor characteristics (DCD donor or elevated DRI), and post-operative complications.[7,9,10,91] Additional contributing factors, identified as significant in only one of the studies, included: dependent functional status, proximity to the transplant center, race, high school education or less, BMI >32, pre-transplant portal vein

thrombosis, malignancy as an indication for transplant, discharge to a rehabilitation facility.[7,9,10,91] Collectively, these risk factors indicate that acuity at the time of transplant, functional status at transplant and at discharge, comorbidities and post-transplant complications are all associated with an increased risk of readmission following transplantation.

The present literature provides foundational work in understanding inpatient utilization following transplantation, but there remain significant gaps. None of the studies have adequately addressed issues of sociodemographics, payer source, or transplant center level factors (hospital size, location, resources). Additionally, to date, there have been no evaluations of inpatient or emergency room utilization that occurs outside of the patient's index hospital. Given that transplant patients often travel long distances for transplant, it is likely that a component of utilization after transplant discharge may occur at hospitals other than this index location.

3.2 How did Share 35 impact post-transplant disability? (Q3)

As previously discussed, policy evaluations, to date, have focused primarily on traditional metrics such as post-transplant patient and graft survival. To date, there are no specific evaluations of how changes in allocation policy have affected alternative health-related metrics which could be measured through a patient's ability to return to work, or functional status. These metrics are of particular interest when assessing the benefit of transplantation, and are essential in assessing the balance between the potential costs associated with allocation policy changes. Furthermore, previous studies have demonstrated that such metrics are often more important to patients than longevity.[93,94]

While these factors have not been directly addressed in allocation policy evaluations, there is a substantial literature addressing post-transplant outcomes. In a 1999 meta-analysis of

quality of life studies after liver transplantation, Bravata et al, details the wide variety of metrics that have been utilized in order to assess health-related quality of life (HRQL).[95] The most common scales utilized amongst this patient population include: the Karnofsky Performance Status Scale, Sickness Impact Profile, Stait-Tait Anxiety Inventory, and the Medical Outcomes Survey Short Form 36 (SF-36). Amongst these studies, the most common design included cross-sectional assessments of post-transplant HRQL, comparisons of pre- to post-transplant HRQL and the comparison of a post-transplant cohort to a control group. Aggregate findings from the meta-analysis demonstrated that patients have significant impairments across a variety of domains in the pre-transplant period, with the most profound deficits in physical functioning. In the subset of studies which included pre- and post-transplant metrics there is demonstrable improvement in the domains of physical health, sexual functioning, daily activities, and overall quality of life; yet less significant improvements are seen in psychosocial and social functioning.

In addition to studies utilizing HRQL scales to assess post-transplant health outcomes, there is also a small subset of literature which has assessing other metrics of disability, such as the ability to return to work after transplantation. The ability to return to work demonstrates the ability to attain an independent functional status and additionally supports the argument for societal cost-utility benefit. Literature on return to work within liver transplant has identified a relatively low rate of transplant recipients returning to work, with Huda et al reporting a rate of less than 25% at two years post-transplant amongst U.S. liver transplant recipients.[96,97] As well, rates of unemployment after liver transplant have been found to be substantially higher than those amongst kidney or lung transplant recipients, and furthermore, rates of voluntary work have also been noted to be lower in comparison to the general population.[98] There are a variety of reasons for unemployment following transplantation, which were highlighted in a review by

Huda et al., and included: poor functional status, continued health concerns, and risk of losing disability or Medicaid insurance.[96] In assessing the impact of pre-transplant medical, social and demographic factors associated with post-transplant employment, previous research has demonstrated that patients with lower pre-transplant functional status, liver disease secondary to alcohol use, and older age were less likely to return to work following transplantation.[96] It is particularly important to note that these studies have not found a significant correlation between patient's MELD score at allocation and employment post-transplant.[96] This lack of correlation may indicate that patient factors outside of the MELD score are greater predictors of employment, and may also indicate that policy changes based on the MELD score alone may not substantially impact employment.

A small subgroup of studies have also evaluated the association between pre-transplant functional status and post-transplant mortality, providing a logical link between these non-traditional and traditional metrics of policy evaluation. In particular, a study of the UK and Ireland liver transplant population, including all patients transplanted between 1994 to 2003, identified pre-transplant functional status (graded on a 5 point scale) to be a significant predictor of 90-day post-transplant mortality.[99] Results of this study demonstrated that in comparison to the reference group (those who could move freely and complete self-care, but were unable to work), those who had no restrictions were 44% less likely, and those who were completely reliant on nursing/medical care were 3.3 times more likely to die within 90 days. A similar study completed in the U.S. using data from SRTR identified patients with a severe functional status (>80% impaired at the time of transplant) as having 2.5 times the odds of 30-day mortality when compared to those with a normal functional status (able to complete independent activities of daily living).[100] This correlation is important, such that if allocation policy leads to a greater

number of patients with poor pre-transplant functional status being transplanted, it may have a subsequent effect on patient survival.

While such health-related metrics (HRQL, return to work and functional status) have not yet been utilized in the assessment of liver transplant allocation policy, the previous literature sets a framework for considering the potential impact of the Share 35 policy. In particular, previous findings suggest a potential correlation between pre- and post-transplant functional status as well as the impact of functional status on survival. When considering that patients with an elevated MELD score are more likely to have a lower pre-transplant functional status, it is plausible to hypothesize that the transplantation of sicker patients may result in a greater proportion of patients with a lower post-transplant functional status. In the single study evaluating the impact of allocation MELD score on return to work, there is no demonstrable association, and therefore it is plausible that policy changes that are specific to allocation MELD will have no effect on post-transplant employment.

3.3 Contributions to the Literature

There is a significant gap in the liver transplant literature regarding the evaluation of allocation policy in the context of non-traditional markers of quality, such as inpatient utilization and post-transplant health outcomes. In the ever-changing landscape of the American health care system, it is essential to recognize factors that predict high utilization and poor outcomes amongst liver transplant patients, as well as critical to understand the spectrum of utilization from the time of transplant and through the recovery period. Such markers of quality and utilization have yet to be applied to evaluations of allocation policy, in particular those policies

that continue to propagate “sickest first” allocation and therefore may theoretically result in both increased utilization and poorer health outcomes.

In order to fill this significant gap in the literature, and to more fully inform future policy changes in the field of liver transplantation, this dissertation has two aims. First, this dissertation will define clinical, social and economic factors that are associated with variations in post-transplant inpatient utilization. To date, evaluations of utilization have been limited to the immediate post-transplant period, individual transplant centers, or Medicare-insured patients. By employing a novel database linkage that captures utilization both at and beyond the patient’s transplant center, this dissertation will be the first to capture the full spectrum of utilization inclusive of all insurance types and services received both within and outside the transplant center. Capturing utilization beyond the index hospital is of particular importance in transplantation as patients often travel great distances for transplant and therefore much of their utilization after transplantation may occur at other centers.

Second, it will evaluate the impact of a recent policy change, Share 35, which further prioritized the sickest patients for transplantation, in terms of waitlist time, inpatient utilization and post-transplant health outcomes. To date, policy evaluations have been limited to assessments of national pre- and post-transplant mortality, and therefore have not evaluated the differences that occur at the regional, DSA or transplant center level. This dissertation intends to take a more granular approach, assessing outcomes at both the national and intra-regional level. This is particularly warranted given that the Share 35 policy only affects intra-regional organ sharing and therefore is more likely to have an intra-regional rather than national level effects. As well, previously policy evaluations have not evaluated the impact of such policy changes on

both the health care system, in terms of utilization, and transplant patients, in terms of both the time spent awaiting transplantation and post-transplant disability.

Collectively, this dissertation will suggest new metrics for assessing liver transplant allocation policy which will inform the true impact and tradeoffs of such policies on both liver transplant patients and the health care system.

4. Conceptual Model

4.1 Primary Outcome - Inpatient Utilization

Throughout health care policy evaluations, it is essential to define the primary outcome measure, whether it be the financial costs induced by the policy or relative changes in patient outcomes such as morbidity or mortality. In assessments of transplant allocation policy, evaluations have primarily focused on the latter, e.g., changes in patient mortality either while awaiting an organ (waitlist mortality) or after transplantation (patient mortality), or even more specifically the survival of the transplanted organ itself (graft survival). While each of these measures holds great merit in the field of transplantation, where the goal is to utilize the limited supply of available organs to optimize the number of lives saved, the literature is relatively devoid of policy evaluations addressing issues of cost and health care outcomes. Evaluating changes in healthcare utilization, in particular, is essential for assessing the impact of health care policies. Such evaluations provide powerful insight into how policy changes impact the delivery of health services at the patient-, hospital- and health system-level. For this reason, one of the aims of this dissertation is to assess and evaluate health care utilization amongst liver transplant patients.

Healthcare utilization can be broadly defined to include any services used or consumed by patients within the health care sector. Such utilization can be further segregated into inpatient utilization, occurring during hospital admission, and outpatient utilization, occurring outside of the hospital setting. In prior evaluations of costs related to liver transplantation, it has been demonstrated that the majority of costs occur in the inpatient setting.[80] As well, inpatient utilization, primarily in the post-surgical period, has been the focus of many recent payment policies directed at reducing costs and improving hospital quality amongst surgical patients.

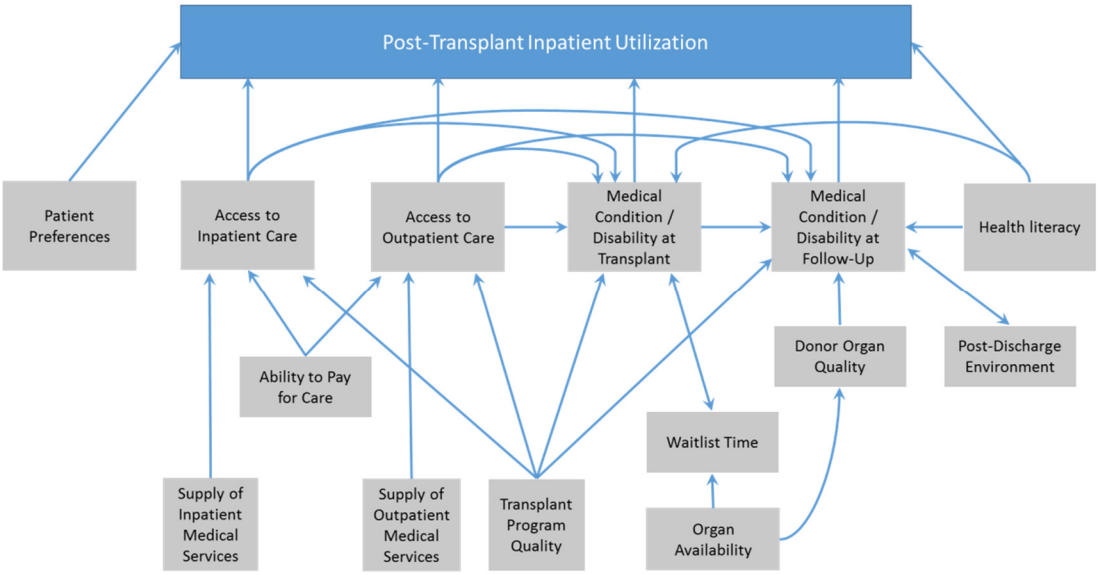
Given the collective impact that inpatient utilization has on the overall cost of care for liver transplant patients as well as its relevance in terms of health policy and payment models, it is the focus of this dissertation.

Like other surgical patients, utilization amongst liver transplant patients can be divided into two phases of care, the pre-operative / pre-transplant phase and the post-operative / post-transplant phase. Utilization during the post-operative / post-transplant phase is the focus of this dissertation. For transplant patients, in particular, health states during each of these phases are distinct. During the pre-transplant phase, patients are facing increasing disease severity as liver disease progresses. In many ways, during this phase patients are suffering from a chronic, debilitating and progressive disease. Alternatively, during the post-transplant phase, transplant patients are more similar to other surgical patients, in that they enter a phase of recovery from their surgical procedure, as well as from their chronic disease. Given the different disease states, there are distinct factors that drive utilization amongst patients within these two phases. For this dissertation, the focus will be on post-transplant utilization, which is discussed in detail below.

4.1.1 Post-Transplant Inpatient Utilization

Basic economic theory defines utilization of goods as the intersection of supply and demand. The conceptual model presented above depicts post-transplant inpatient utilization through this lens, with a focus on the individual patient-level factors that contribute to post-transplant inpatient utilization as well as transplant center-level factors which influence patient-level outcomes and the supply of medical services (Figure 4 – 1). In discussing this model, I will begin with post-transplant inpatient utilization and then work through the remaining concepts in a counterclockwise fashion.

Figure 4 – 1. Predictors of Post-Transplant Inpatient Utilization



Conceptually, *post-transplant inpatient utilization* is defined by the use of inpatient services following liver transplantation. As discussed in the following section, this utilization can be defined both in terms of total number of days spent hospitalized after transplantation (both during the index hospitalization and in the time after transplant) or by the number of admissions (inclusive of both the index admission and any subsequent readmissions post-transplant). *Post-transplant inpatient utilization*, is directly affected by six factors: patient preferences, access to inpatient care, access to outpatient care, medical condition/disability at the transplant, medical condition/disability at follow-up and health literacy.

Patient preferences encompass a patient's individual desire to use health services. Throughout economics, it is well understood that preferences drive variations in utilization. In particular, some patients may seek health care services more often than others or may wish to remain in the hospital longer due to individual preferences

Access to care in both the inpatient and outpatient setting defines a patient's ability to get necessary medical services, and encompasses both geographic and financial access. Inpatient and

outpatient services are separated in this model as they have opposite effects on the utilization of inpatient care. *Access to inpatient care* will increase inpatient utilization as patients will attain needed services resulting in inpatient hospitalization. Alternatively, *access to outpatient care* will likely decrease inpatient utilization. The ability for patients to obtain both routine care and preventative services in the outpatient setting ultimately decreases the likelihood that they will require inpatient hospitalization.[101]

Access to care, in both the inpatient and outpatient setting, is directly influenced by the *supply of services* (either in the inpatient or outpatient setting), the *ability to pay for care* and by *transplant program quality*. A patient's geographic location likely defines the *supply of both inpatient and outpatient medical services*. Increased *supply of outpatient medical services* will increase patient access to preventative care, resulting in decreased inpatient utilization. Alternatively, poor *supply of outpatient services* can result in delays in care and ultimately result in increases in inpatient utilization. The *supply of inpatient medical care* directly influences patient inpatient utilization, as limited supply constrains a patient's ability to obtain inpatient services; with increased supply, patients are more able to utilize these services. It is also important to note that a patient's location relative to their transplant center also contributes to their access and therefore supply of inpatient care. Previous work looking at distance between index hospitals and post-surgical complications have indicated that this distance can be predictive of utilization and risk of additional complications, likely due to patient seeking services at hospitals or with providers unfamiliar with their care or disease process.[102] *Transplant program quality* may also influence a patient's ability to obtain necessary medical services. Transplant program factors, such as the ability to provide services, connect patients to services, assure adequate care and refer patients for inpatient care when necessary are all factors that

influence a patient's ability to obtain necessary medical services. In this manner a low-quality program may not provide appropriate outpatient care, which will decrease the patient's ability to attain needed care and in turn impact inpatient utilization. The *ability to pay for care* also greatly impacts the ability to attain care. Conceptually, *the ability to pay for care* defines a patient's economic resources to pay for healthcare services. This includes economic resources for out-of-pocket payments as well as health insurance coverage. Lack of health insurance, poor insurance coverage, and lower socioeconomic status are demonstrated barriers to the receipt of medical care.[103-105]

Medical condition / disability at transplant defines a patient's overall health state including chronic diseases, liver disease severity, functional status and age. Patients listed for liver transplant represent a diverse cohort of patients with varying disease etiologies. As discussed previously, different types of liver disease are associated with different rates of inpatient utilization. In particular, patients with hepatocellular carcinoma may have a different pattern or volume of utilization in comparison to patients with decompensated cirrhosis, as patients with progressive end stage liver disease (ESLD) secondary to cirrhosis are at elevated risk for gastrointestinal bleeding, ascites, pulmonary effusions, spontaneous bacterial peritonitis, renal failure and hepatic encephalopathy. As well medical comorbidities will directly increase a patient's use of inpatient services, in particular, patients with chronic diseases (such as renal insufficiency or cardiac disease) are more likely to require inpatient medical care as they may require care not only for transplant-related conditions, but also for care of their other chronic diseases.[86,92] A patient's medical condition will also place them at increased risk for pre-operative complications such as infections related to uncontrolled diabetes or exacerbations of renal failure. Complications ultimately create a need for healthcare services due to a change in

health status, which in turn increases a patient's demand for and utilization of inpatient care.[91,106] In turn, the *medical condition / disability at transplant* has a direct impact on the patient's *medical condition / disability at follow-up.* It is well documented that elevated pre-transplant acuity, as defined by MELD score, patient location prior to transplant (home versus hospital ward bed versus ICU), and ventilator or vasopressor requirements, result in a poorer *medical condition / disability at follow-up.*[2,4,87,92]

Medical condition / disability at follow-up encompasses a patient's overall medical condition following transplantation, including chronic medical conditions as well as any medical or surgical complications that occur following transplantation. Complications ultimately create a need for healthcare services due to a change in health status, which in turn increases a patient's demand for and utilization of inpatient care.[91,106] The rate of post-operative complications is directly influenced by a number of factors including the patient's pre-transplant medical condition, transplant program quality, donor organ quality, post-discharge environment and health literacy.

A patient's *post-transplant medical condition / disability* impacts their *post-discharge environment*, influencing whether a patient is discharged to their home or to a rehabilitation facility. The *post-discharge environment* is a critical factor influencing the risk of post-operative complications, and in turn a need for inpatient care.[70,73,107] This concept defines both the patient's medical support in the immediate post-operative period, whether that be familial support when a patient is discharged home or nursing support at a rehabilitation facility, as well as the physical environment. Lack of support or an unsafe environment likely increase a patient's likelihood of post-operative complications, in turn resulting in increased inpatient utilization. This concept

also considers the geographic distance between the patient and the transplant center following discharge.

Medical condition / disability at both transplant and *follow-up* are influenced by a patient's *access to care*. Patients who are unable to attain care are likely to have both acute and chronic conditions go untreated, resulting in worsening medical comorbidities, which will ultimately result in a greater need for health services and increased inpatient utilization.

Waitlist time indicates the amount of time a patient has been listed for and awaiting transplantation. Longer waitlist times are associated with increased patient debility and a higher MELD score at the time of transplant. Waitlist time is a direct product of *organ availability*, such that when there are more organs available, there is less of an imbalance between supply and demand for donated organs and patients are able to receive an organ more rapidly. *Organ availability* under the current organ allocation system is determined by a patient's geographic location.[108] Under the current system, patients become eligible for donated organs within their own geographic area, with the highest priority being given to patients with the greatest need (highest MELD score). In turn, the supply of organs is determined by the number of donors in the same geographic space.

Another major predictor of *medical condition / disability at follow-up* is *donor organ quality*. It is well documented that organs of poorer quality, specifically those from older donors or those that have undergone a longer period of time without perfusion (referred to as cold ischemia time), increase a patient's risk for post-operative complications.[47,79,109] As such, *donor organ quality* has a direct impact on *medical condition / disability at follow-up*. It is important to note that transplant programs may differ in their donor selection, informed by experience and preferences. Such preferences may manifest such that specific programs may feel more

comfortable with the use of lower-quality donors, while other programs may not share this preference. Differences in donor organ selection by transplant center are well documented in the literature.[50,79,108,110]

Health literacy describes a patient's understanding of the medical system and medical conditions. Lower health literacy has been associated with increased health care costs, unplanned readmissions and increased utilization of inpatient services.[111-114] Amongst surgical literature health literacy has a demonstrated impact on hospital length of stay, such that lower literacy leads to longer inpatient stays.[115] Additionally, lower health literacy directly influences a patient's overall *medical condition / disability at transplant* and due to either a lack of understanding of the signs and symptoms of disease, or a decreased ability to complete or maintain self-care by taking prescribed medications or participating in positive health behaviors such as a healthy diet or exercise.[116-118]

Finally, in a similar manner to *medical condition / disability at transplant*, *health literacy* will have an impact on *medical condition / disability at follow-up* through a patient's ability to manage their medical condition, be adherent to anti-rejection medications, and provide self-care.

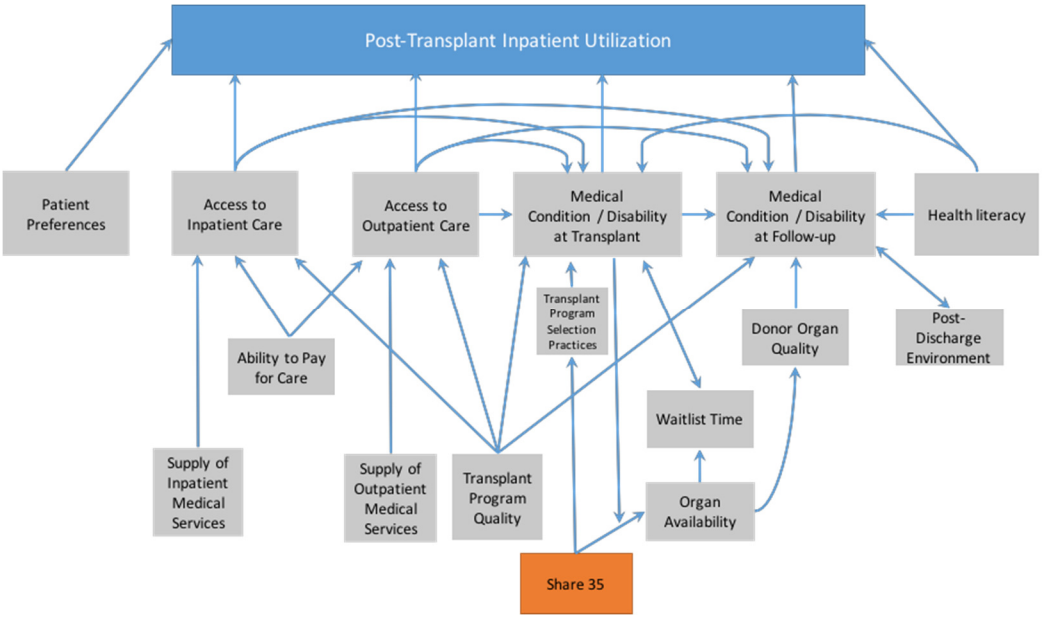
4.2 Share 35: Impact on Inpatient Utilization

The Share 35 policy had two points of impact on inpatient utilization: *medical condition/disability at transplant* (mediated through transplant program selection practices), and *organ availability* (Figure 4 – 2). The first effect of the Share 35 policy is that it increases organ availability for patients with an allocation MELD score of ≥35, which in turn alters the amount of time spent on the waitlist. For patients who reach an allocation MELD of 35, this should reduce the waitlist time, and for those who do not reach an allocation MELD of 35 the policy

may in turn increase their waitlist time. The net effect of this change on the entire population is difficult to predict, yet overall increased time spent on the waitlist allows greater time for disease progression and ultimately leads to more patients being transplanted at a higher acuity. Within the conceptual model the relationship between Share 35 and organ availability is indicated by an arrow that is transected by and arrow going from medical condition / disability at transplant (where MELD score is a measurement proxy) to indicate that the effect on organ availability is moderated by allocation MELD score.

The second effect of Share 35 is that the policy likely influenced *transplant program selection practices,* which in turn affected the *medical condition / disability* of patients at the time of transplantation. For example, through the policy's aim of prioritizing high acuity patients for transplant this incentivizes centers to list high acuity patients as they have a higher likelihood of transplantation. Therefore, higher acuity patients being listed/selected for the transplant waitlist leads to patients with a poorer *medical condition / disability at transplant*.

Figure 4 – 2. Predictors of Post-Transplant Inpatient Utilization Account for the Impact of Share 35



4.3 Share 35: Impact on Post-Transplant Disability

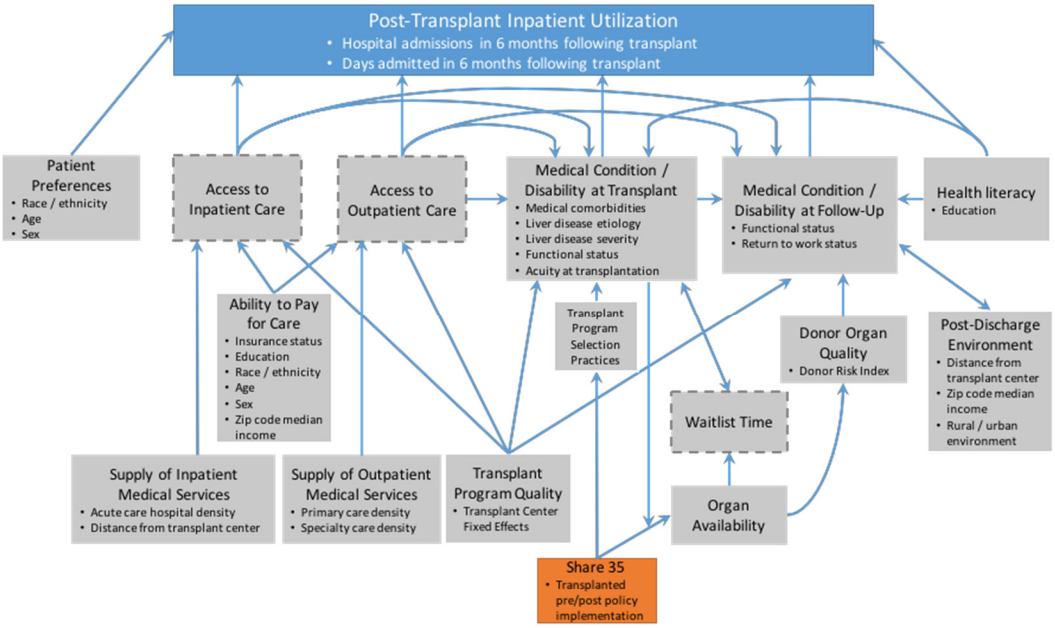
Post-transplant medical condition / disability, as previously defined, is inclusive of a patient's chronic medical condition following transplantation as well as functional status. Factors directly influencing *post-transplant medical condition / disability* include *access to inpatient care, access to outpatient care, medical condition / disability at transplant, transplant program quality, donor organ quality, post-discharge environment, and health literacy.* Each of these constructs has been previously defined.

Similar to the model for post-transplant inpatient utilization, the effect of *Share 35* is conceptually related to *post-transplant medical condition / disability* through the policy's impact on *pre-transplant medical condition / disability* as well as on *organ availability* through its impact in turn on *donor organ quality*. Poorer *pre-transplant medical condition / disability*, inclusive of a poorer health status and less functional independence, is associated with a poorer *post-transplant medical condition / disability*. The remaining effects of waitlist time and organ availability are in parallel with those presented in the previous conceptual model.

5. Measurement Model

The measurement model for post-transplant inpatient utilization defines the proxy measures for each of the concepts introduced in the previous chapter. In some cases, the models are estimated in reduced-form with regard to certain conceptual variables; that is, the regression model controls for the exogenous precursors to those concepts instead of including empirical proxies for the concepts themselves; all other concepts are measured by the empirical proxies indicated in bullets and discussed below. Within the discussion it will be noted that in measuring the effect of Share 35, multiple concepts are included or excluded based upon the causal pathway that is tested. Similar to the discussion of the conceptual model, we will work counter-clockwise through each concept beginning with *post-transplant inpatient utilization* (Figure 5 – 1).

Figure 5 – 1. Measurement Model for Post-Transplant Inpatient Utilization. Each concept is contained within a separate box. Relationships between concepts are indicated by arrows, where the arrowhead indicates the direction of effect. Note that not all arrows are shown (i.e. we do not show arrows representing all of the possible collinearity between predictors). Moderating relationships are indicated by the intersection of an arrowhead along the pathway between two concepts (i.e. the effect of medical condition/disability at transplant on the relationship between Share 35 and organ availability). Measurement proxies are indicated beneath each concept in bullet points. Concepts that are unmeasured are indicated by a dashed border.



Post-transplant inpatient utilization is the primary outcome measure for this model and is measured in terms of the total number of admissions to inpatient facilities, and as the total number of admitted days during the six months following liver transplantation.

Patient preferences encompass individual patient preferences in the use of health care services. Such preferences are informed by a patient's age, culture and beliefs about the health system as well as individual desire or need to use health services. Because there are no specific measures available in the current databases for culture or beliefs about the health system, race/ethnicity, age and sex were used as crude proxy measures. Race and ethnicity have been documented as predictors of health care use across patient settings, findings that may be due to individual patient preferences or secondary to other social and environmental factors which contributing to health care utilization (financial resources, discrimination, differences in care delivery).[119-122] Additionally, sex and age are also associated with health care utilization, with many previous studies suggesting that that women and older adults are more likely to use services as compared to men, findings that again may be secondary to preferences or due to social and environmental factors contributing to health care utilization practices.[123-125]

Instead of controlling directly for *access to inpatient and outpatient care*, the models include their exogenous precursors, *supply of medical services* and *ability to pay for care*. *Supply of inpatient care* was measured by the density of acute care hospitals per 1,000 population within the patient's geographic area (defined as the core based statistical area), and the patient's distance to the transplant center. The geographic distance from the transplant defines the patient's relative travel distance to the transplant center after transplantation, and informs their ability to maintain consistent follow-up and access to experienced transplant providers. *Supply of outpatient care* was measured by two variables, the density of primary care providers and the

density of outpatient gastroenterology providers. The density of primary care providers provided a measure of supply of physicians who provide routine preventative care, while the measure of gastroenterology providers provided a measure of the supply of physicians who provide care specific to liver disease. *Ability to pay for care* was proxied by six variables: insurance status, education, race/ethnicity, age, sex and median income by patient zip code. The ability to pay for care was defined in this way in order to account for both the ability to pay for services through insurance coverage and out-of-pocket expenses. Insurance status provided a measure of the type of insurance coverage, and additionally defined the types of providers and hospitals a patient can access. Education, which served as a proxy for permanent income, informs an individual's highest level of academic achievement and therefore measures potential income based on the degree of education a patient has attained. Education therefore serves as a proxy for ability to pay out-of-pocket medical expenses. Sex and age are also predictors of a patient's economic income and therefore are also included. Finally, median income by home zip code serves to provide a measure of the relative wealth of the patient's environment and in combination with education achievement will provide a more informed measure of a patient's ability to pay for care.

Transplant program quality can be measured in terms of experience, available resources, program size and patient outcomes. Given the wide variation in transplant programs that is both measured and unmeasured, heterogeneity across transplant programs was controlled for by using fixed effects for transplant program in the regression models. All characteristics of transplant programs, both observed and unobserved, that do not vary across patients within the program are subsumed into these fixed effects.

Share 35 indicated the timing of a patient's transplant in relation to the implementation of the Share 35 policy. In evaluating the impact of Share 35 on post-transplant utilization and post-transplant disability, Share 35 was measured as a dichotomous indicator for whether the patient was transplanted in the pre- or post-Share 35 period. It is important to note that the impact of Share 35 is moderated by a patient's allocation MELD score, which is defined as the physiologic MELD score plus an additional MELD points which are awarded for malignancy or other causes (exception points). The allocation MELD score is that score at which the patient is ranked on the waiting list and the score at which the patient is allocated their donor organ.

Waitlist time is an indicator of time spent awaiting transplantation. This concept lies along the causal pathway for the effect of Share 35 through organ availability and therefore is never directly measured or included within the regression models.

Pre-transplant medical condition / disability encompasses the patient's chronic medical condition, liver disease, functional status, and medical acuity at the time of transplantation. A patient's overall medical condition, inclusive of medical comorbidities, informs a patient's need for inpatient medical care due to diseases and conditions which may or may not be related to their liver disease, such as diabetes, pulmonary or cardiac disease. Liver disease etiology was defined by the type of liver disease for which the patient is listed for transplant. This is an important measure as patients with hepatitis and genetic diseases are at risk for recurrent disease following transplantation. Functional status served as a measure of overall fitness. With lower functional status at the time of transplantation, patients are more severely debilitated and are therefore at elevated risk for post-transplant complications and may require a greater degree of post-transplant inpatient care. Like functional status, acuity at the time of transplantation informs the medical condition of a patient immediately prior to transplantation and has a significant and

well-documented impact on post-transplant utilization and post-transplant medical condition, such that patients at higher acuity have a worse overall post-transplant medical condition and in turn have greater need for, and use of, inpatient medical services. Acuity can be measured in part by patient's liver disease severity. Liver disease acuity was measured by patient's physiologic MELD score, which quantifies the degree of liver disease at the time of transplant.

Donor Organ Quality is a measure of the quality of the donor liver, which is commonly measured by both donor factors (age, cause of death) and factors related to the procurement of the organ (time between removal of the organ from the donor and implantation into the recipient). Collectively these factors were measured through the Donor Risk Index, a well-validated measure of donor organ quality that is predictive of both graft failure and graft-related complications.[109] It is important to note that donor organ quality is only included in the evaluation of inpatient utilization for research question 1, which assesses utilization exclusive of the Share 35 policy. For research questions assessing the impact of Share 35, donor organ quality is excluded from the analysis as it lies along the causal pathway for the impact of Share 35 on inpatient utilization through organ availability.

Post-transplant medical condition / disability encompasses the degree to which a patient recovers from transplant and is measured by two empirical proxies, functional status and work status. Similar to functional status prior to transplant, post-transplant functional status indicates the degree of functional independence and the degree of illness burden that remains post-transplant. The ability to return to work is a secondary proxy, which informs the degree of functional independence and recovery from transplantation. Both measures have been used previously as methods to assess post-transplant health-related quality of life, and serve as a summary measure for disability after transplantation.

Post-discharge environment is defined by the patient's physical and social environment after transplantation. There are two empirical proxies for *post-discharge environment*, relative wealth of the patient's home zip code, and rural / urban environment. Relative wealth of the patient's home zip code has previously been discussed as a proxy measure of ability to pay for care. This measure also contributes to the patient's home environment as higher income areas are more likely to be able to provide additional support through the ability of family or a social support system to take time off to care for an ill family member, and may also be indicative of the ability to provide ancillary support services that aid in the patient's recovery after transplant. Rural / urban environment also indicates the relative resources of a patient's surrounding area, such as the potential density of support services, and distance between the patient and necessary post-operative and rehabilitation services.

Health literacy was measured by the empirical proxy of educational achievement. Higher education is associated with greater health literacy and therefore appropriately served as a measure of one's understanding of the health care system, health conditions and ability to complete self-care.

It is of note that there are multiple empirical measures that serve as proxies for more than one construct. In interpreting the effect of these measures, I take into account that these could be proxying for multiple constructs, such that they may offset each other in terms of sign and magnitude but may also jointly contribute to the same direction of effect.

6. Questions & Hypotheses

6.1 Inpatient Utilization

Q1. What are the factors associated with inpatient utilization among liver transplant patients in the post-transplant period?

Hypotheses H1a-H1d below assume that the models for inpatient utilization in the post-transplant period control for the following predictors: patient preferences, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality), medical condition / disability at transplant, health literacy and other exogenous determinants of medical condition / disability at follow-up (donor organ quality and post-discharge environment).

H1a: Patients with a higher physiologic MELD score at transplant will have greater inpatient utilization in the post-transplant period, ceteris paribus.

Patients at a higher acuity will require a longer in-patient stay following transplantation and will be at greater risk for complications in the post-transplant period, which could lead to greater in-patient utilization.

H1b: Patients who are transplanted for malignancy will have less post-transplant inpatient utilization as compared to patients suffering from liver failure secondary to cirrhosis (steatohepatitis), ceteris paribus.

Patients who are transplanted for diseases causing cirrhosis and subsequent liver failure reach their allocation MELD score due to disease severity, whereas patients with malignancy reach their allocation MELD score due to the allotment of exception points. These two systems result in two populations of patients who are at differing degrees of illness at the time of transplantation. Patients with HCC are less physiologically ill at the

time of transplant and therefore will have shorter post-transplant lengths of stay and are less likely to have complications in the post-transplant period.

H1c: Patients with a lower ability to pay for care will have greater post-transplant inpatient utilization than patients with a greater ability to pay for care, ceteris paribus.

A lower ability to pay for care will have two effects on inpatient utilization, a direct effect in which patients who have a lower ability to pay seek fewer inpatient services, and an indirect effect where a lower ability to pay results in a delay in seeking outpatient care and ultimately increases inpatient utilization. Given the acuity of illness related to liver transplantation, I hypothesize that the indirect effect will dominate and therefore patients with a lower ability to pay, such as those without insurance or with Medicaid, or with a low income, may have decreased access to necessary outpatient care, resulting in care delays and ultimately greater inpatient utilization and more post-transplant complications. Note that there is a competing hypothesis that patients with a lower ability to pay will have lower post-transplant inpatient utilization because the direct effect (reductions in inpatient care) will be larger than the indirect effect (increases in inpatient care due to lower use of outpatient care).

H1d: Patients who receive a poorer quality organ will have higher inpatient utilization in the post-transplant period, ceteris paribus.

Donor organs with specific characteristics (older age, longer time between removal and transplant, and cardiac death) are associated with a greater number of post-operative complications, which in turn results in increased inpatient utilization.

6.2 Share 35: Impact on Utilization

Q2. How did Share 35 impact post-transplant inpatient utilization?

H2a: Share 35 increased inpatient utilization in the post-transplant period, when not controlling for medical condition / disability at transplant, but controlling for patient preferences, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality) and health literacy.

Hypothesis 2a test both causal pathways through which Share 35 can impact post-transplant inpatient utilization, through medical condition / disability at transplant and organ availability. Share 35 led to more patients being transplanted at high MELD scores (MELD ≥35) leading to increased acuity and greater debility at the time of transplant. This increased debility will lead to a greater need for post-operative rehabilitation and a higher risk of post-operative complications, leading to higher inpatient utilization through both longer index hospitalization length of stay and higher readmission rates. Conversely, Share 35 also increased organ availability to high acuity patients, which likely decreased their wait times, ultimately decreasing their relative debility and acuity at transplant (as compared to the Pre-Share 35 period), and in turn decreased inpatient utilization. These two pathways work in opposing manners. Under H2a, when medical condition is not controlled, we hypothesize that there is greater inpatient utilization because the pathway through medical condition / disability outweighs that of increased organ availability. These causal pathways are diagramed in Figure 7 – 4 A.

H2b: Share 35 decreased inpatient utilization in the post-transplant period when controlling for medical condition / disability at transplant in addition to controlling for patient preferences, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality) and health literacy.

Share 35 affects post-transplant inpatient utilization through its impact on both patient acuity as well as organ availability. When controlling for patient acuity at the time of transplant, only the pathway through organ availability is tested. Share 35 results in increased organ availability for high acuity patients and decreased organ availability for lower acuity patients. Therefore sicker patients are likely to achieve transplantation earlier, resulting in less disability post-transplant, and lower acuity patients may ultimately wait longer (due to decreased organ availability) and therefore have a greater degree of disability post-transplant. I hypothesize that the balance of these opposing effects will favor decreased disability post-transplant and therefore result in less post-transplant utilization. The counter hypotheses are that these opposing effects will either favor greater disability and result in greater post-transplant utilization, or that these effects balance each other and there is no difference in utilization after Share 35. Causal pathways tested in H2b are diagrammed in Figure 7 – 4 B.

H2c: The negative effect of Share 35 on inpatient utilization in the post-transplant period will be larger amongst patients with high allocation MELD scores, when controlling for medical condition / disability at transplant, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality) and health literacy.

The Share 35 policy is designed to increase organ availability amongst patients with allocation MELD scores ≥35. Increased organ availability within this cohort likely resulted in decreased disability and medical acuity prior to transplantation which in turn provided a greater propensity for recovery post-transplant and decreased need for medical

services. Patients with allocation MELD scores less than 35 did not benefit from this policy in the same manner, and may alternatively experience increased wait times. I therefore hypothesize that the effect of Share 35 on inpatient utilization is dependent on allocation MELD score, such that the patients with a high allocation MELD scores are likely to have decreased inpatient utilization in the Post-Share 35 period and patients with allocation MELD scores <35 will experience no change or a slight increase in inpatient utilization, when controlling for medical condition / disability at transplant. Causal pathways tested in H2c are diagrammed in Figure 7 – 4 C.

6.3 Share 35: Impact on Post-Transplant Disability

Q3. How did Share 35 impact post-transplant disability?

H3a. Share 35 resulted in less post-transplant disability, when controlling for medical status / disability at transplant, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality), health literacy and post-discharge environment.

Under Share 35, the sickest patients are likely to be less debilitated at the time of transplant due to increased organ availability and reduced wait times. Therefore, it is likely that the sickest patients are more likely to fully recover, and have improved post-transplant health outcomes. Again, given that the policy may also lead to longer wait times for patients who are less sick (allocation MELD scores <35) there may be an opposing effect where less sick patients become more debilitated in the post-Share 35 period. I hypothesize that these two opposing effects will result in less disability on average for the transplant population.

H3b. The effect of Share 35 in reducing post-transplant disability will be greater amongst patients transplanted with a high allocation MELD score, when controlling for medical status / disability at transplant, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality), health literacy and post-discharge environment.

Given that Share 35 should increase organ availability to patients with allocation MELD scores ≥35, patients with high allocation MELD scores should spend less time at such high acuity and ultimately be less debilitated prior to transplantation. When controlling for medical status and disability prior to transplantation, patients with high allocation MELD scores should therefore have a greater ability to recover post-transplant than they would have in the Pre-Share 35 era, resulting in less post-transplant disability. Again the competing effect is that patients with lower allocation MELD scores may have to wait longer due to the diversion of organs to higher acuity patients. This increased wait time may result in either no discernable change in disability at transplant or increased disability at transplant for patients with lower allocation MELD scores.

7. Methods

7.1 Data Sources

In order to assess patterns related to listing, transplantation, and utilization, a database was constructed to include information related to: (1) liver transplant waiting list information, (2) recipient medical condition, (3) transplantation-related factors, (4) insurance status and payer information, (5) hospital information, and (6) utilization in the pre- and post-transplant period. For transplanted patients, listing, transplant and follow-up information is contained in the Scientific Registry of Transplant Recipients (SRTR). This dataset was linked with hospital utilization data attained from the Agency for Healthcare Resource and Quality (AHRQ) Hospital Cost and Utilization Project (HCUP) State Inpatient Databases (SIDs) and the California Office of Statewide Hospital Planning and Development (OSHPD) Patient Discharge Data (PDD).

In addition to these databases, the Area Health Resource File (AHRF) as used to attain regional level data on health resource availability.

7.1.1 Scientific Registry of Transplant Recipients (SRTR)

The SRTR database is maintained by the Chronic Disease Research Group at the Minneapolis Medical Research Foundation. The SRTR database is compiled from various sources including the Organ Procurement and Transplantation Network (OPTN), organ procurement organizations (OPOs), Centers for Medicare & Medicaid Services (CMS), and the National Technical Information Service's (NTIS) Death Master File. The data supplied within the SRTR database includes information on every transplant and organ donation that has occurred in the U.S. from October 1, 1987 to December 1, 2017. The unit of observation for the SRTR dataset is the individual transplant. Patients who underwent multiple transplants will have multiple entries, linked by a unique patient identifier.

For each liver transplant, there is information available related to the: recipient demographics, limited social history, overall medical condition and comorbidities, liver disease, disease acuity at the time of transplantation, surgical details, donor information, post-transplant complications, graft and patient survival.

7.1.2 Agency for Health Resource and Quality (AHRQ) Hospital Cost and Utilization Project (HCUP) State Inpatient Databases (SIDs)

The AHRQ-HCUP-SIDs are publicly available administrative hospital discharge data collected from the participating states and then standardized to allow inter-state analyses or consolidation of data across multiple states. Individual discharge records are collected by state organizations from community hospitals. At present 48 states participate in the SIDs, accounting for approximately 97% of all U.S. community hospital discharges. Data availability varies by year and by state, with the most recent year of available data being 2014. Within the AHRQ-HCUP-SIDs, the unit of observation is an individual hospital discharge record. Each record contains administrative data including: admitting diagnosis, discharge diagnosis, procedures, length of stay, demographics, payers and charges.

Amongst participating states, a subgroup of states provide unique patient identifiers (visit-link) which allow researchers to track patients longitudinally across visits and hospitals.

For the purpose of this study, AHRQ-HCUP-SIDs from states which contain both transplant centers and visit-link variable were eligible for inclusion. Based on these two criteria, eight states had available data, including: Florida, Georgia, Iowa, Massachusetts, Nebraska, New York, Utah and Washington. The visit link variable does not carry over between calendar years in the state of Washington and therefore Washington was excluded. Amongst the seven

remaining states, data were obtained from five: Florida, Georgia, Massachusetts, Nebraska and New York. Data for each of these states were available from 2010 – 2014.

7.1.3 California Office of Statewide Hospital Planning and Development (OSHPD) Patient Discharge Data (PDD)

The OSHPD-PDD database contains information similar to the AHRQ-HCUP-SIDS for the state of California. The PDD is similarly constructed from administrative hospital discharge records, and is obtained by the state of California for all hospitals licensed within the state. The unit of observation is the hospital admission including: admitting diagnosis, discharge diagnosis, procedures, length of stay, demographics, payers and charges. Similar to the visit-link variable, the OSPHD file contains an encrypted social security number that allows researchers to track patients longitudinally across visits and hospitals. OSHPD data were available from 2010-2015.

7.1.4 Area Health Resource File (AHRF)

The AHRF is a publicly available resource provided by the Health Resource & Service Administration that provides county, state and national-level information related to health care professions, health care facilities, population characteristics, economics, health professions training, hospital utilization, hospital expenditures and environment. Inclusive within the AHRF is the American Hospital Association (AHA) survey and American Medical Association (AMA) Physician Master File, which details the density of health care facilities and health care service providers in each geographic area. For this dissertation, the 2010 AHA and AMA data was abstracted from the AHRF to provide information related to health professional and hospital density for a given geographic area. These data were linked to patient-level data by patient core-based statistical area (CBSA) or zip code, which are available in the AHRQ-HCUP and OSHPD databases respectively.

7.2 Data Linkage

The datasets are classified as utilization (OSHPD, AHRQ-HCUP-SIDS) or transplant databases (SRTR). To address research questions regarding utilization, the utilization and transplant databases were linked. For details on linkage methodology and management of unlinked cases see Appendix 3.

For the research questions regarding post-transplant disability, the SRTR database was utilized independent of the utilization datasets.

7.3 Patient Cohorts

For this dissertation, two separate patient cohorts were utilized to address the stated research questions.

7.3.1 National Cohort: Transplanted Patients

The complete national cohort of transplanted patients was derived from the SRTR dataset, and included all adult patients who underwent deceased donor liver transplantation between January 2010 and November 2016 (truncated at this date to assure the potential for at least one year of follow-up after transplantation). Patients were excluded from analysis if they met any of the following exclusion criteria:

- Age <18 at the time of transplantation
- Transplanted at a pediatric hospital
- History of prior organ transplantation
- Donor organ was provided through living donation
- Received organ outside of MELD-based allocation (Status 1A recipients)

- Receipt of a multi-visceral transplant (with the exclusion of simultaneous liver and kidney transplants)

7.3.2 Utilization Cohort

The utilization cohort (UC) is a subset of the national cohort that included patients who underwent transplantation within 6 states that had available utilization data allowing for longitudinal tracking of patients across hospitals over time. Utilization data were derived from the AHRQ-HCUP and California OSHPD inpatient utilization files. These six states included: California, Florida, Georgia, Massachusetts, Nebraska, and New York. The end date for the UC was limited by data availability; specifically, the last year of available inpatient data for Georgia, Massachusetts and New York was 2014. Therefore to ensure complete 6-month follow up on all transplanted patients, this cohort was limited to patients who underwent transplantation between January 1, 2010 and June 30, 2014.

The same exclusion criteria were applied to the UC as the national cohort of transplanted patients.

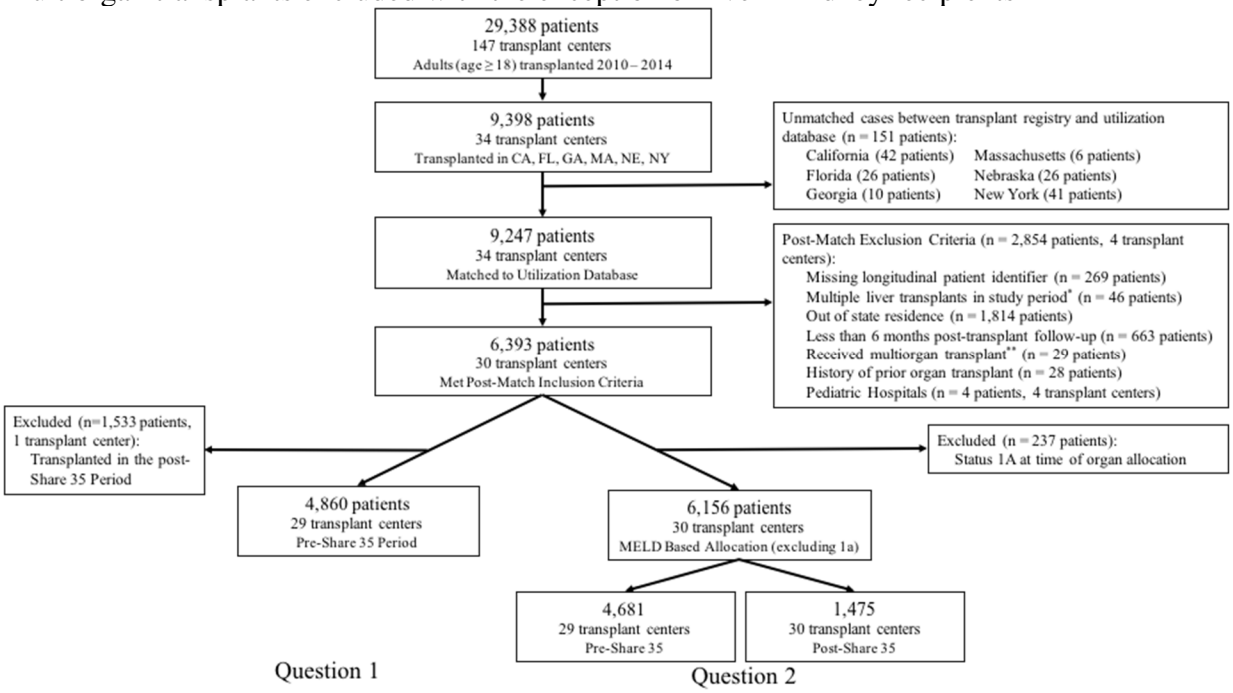
7.3.3 Cohorts by Research Question

Research question 1, which assessed post-transplant inpatient utilization, was addressed using the UC, inclusive of patients transplanted prior to the implementation of the Share 35 policy. The final sample size for the Pre-Share 35 cohort was 4,860 (Figure 7 – 1). This cohort, inclusive of 6 states and 29 transplant centers, accounts for 27.6% (4,860/17,635)[iii] of the

[iii] When study exclusion criteria are applied to all patients within the SRTR database who underwent liver transplantation between January 1, 2010 and June 1, 2013, a total of 17,635 underwent transplantation. This number does not appear in the sample size flow chart, as patients were excluded due to state of transplantation prior to database merging.

patients and 24.2% (29/120) of the centers included in the national cohort meeting the same exclusion criteria.

Figure 7 – 1. Sample Size Flow Diagram for Utilization Cohorts. Diagram indicates number of patients meeting each inclusion/exclusion criterion for the utilization cohorts used to address research questions 1 and 2. *: Excluded only 2nd transplant per patient within study period. **: Multiorgan transplants excluded with the exception of liver + kidney recipients



For research question 2, which addressed post-transplant inpatient utilization in both the pre- and post-Share 35 period, the UC was again employed. In contrast to the cohort utilized for question 1, in question 3 all patients in both the pre- and post-Share 35 period were included. Patients who received their transplant as a Status 1A recipient were excluded as these patients receive priority in allocation over those recipients listed by MELD score, and therefore were not affected by Share 35. The final cohort size is 6,156, with 4,681 in the Pre- and 1,475 in the Post-Share 35 cohorts (Figure 7 – 1). This cohort represents approximately 27.0% of the total number of liver transplants done in the U.S. during the same period meeting the same exclusion criteria (22,793). Five out of the eleven UNOS regions were represented in the UC, Regions 1, 3, 5, 8

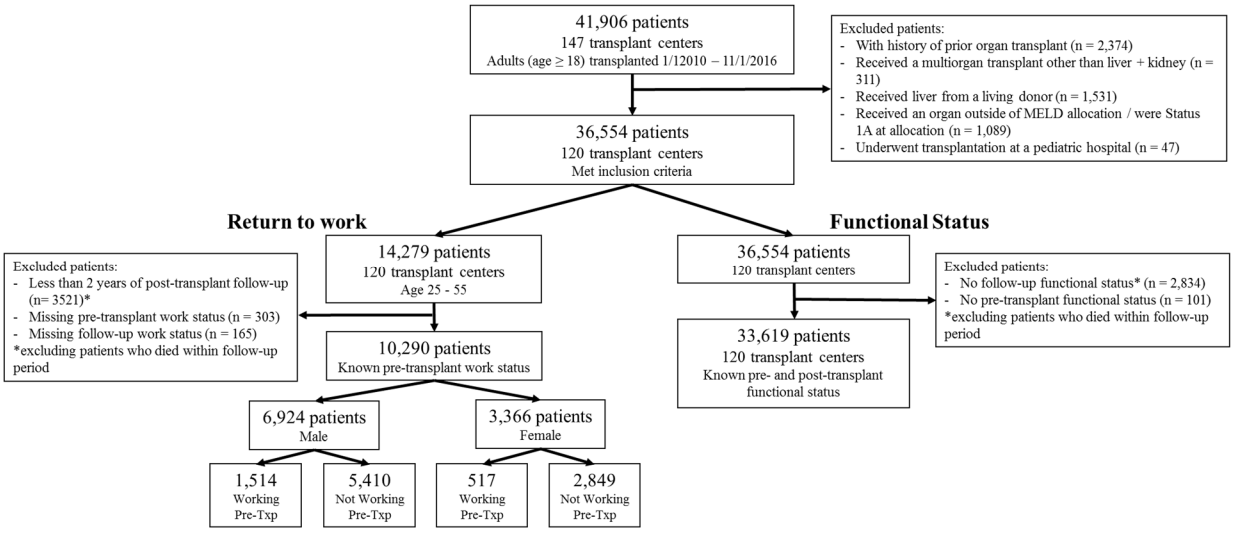
and 9. Collectively these regions account for 30 transplant centers, which is 25% of all adult transplant centers in the U.S. (30/120). The Region 1 UC included 75.6% (517 / 684) of the patients who underwent transplant within the region during the same time period that met study inclusion criteria, the Region 3 UC included 69.3% (2310 / 3335), the Region 5 UC included 77.4% (2273 / 2936), the Region 8 UC included 11.3% (126 / 1116) and the Region 9 UC included 100%.

Comparisons between the six-state cohort and the remaining patients transplanted in the U.S. during that same time period indicated only small differences between the two groups. Amongst those differences, it is important to note that the six-state cohort was of slightly higher acuity with regard to the rate of overall allocation to patients with an allocation MELD score ≥30 or ≥35. With regard to factors that were unmeasured in the regression models discussed below, patients also were of higher acuity by the rate of ventilator dependence, dialysis dependence and life support measures utilized at the time of transplant. These differences between the UC and the remaining transplants are likely due to the selection of states within regions that have higher acuity patients, and therefore may suggest that the sample utilized for our model may overestimate the effects of the policy. A detailed discussion of the differences between the UC and the remaining patients transplanted during the same time period is included in Appendix 2A. Comparisons between the UC and remaining cases within each region indicated that overall the UCs were very similar to the remaining patients within each region. While the UC from region 1 and 3 were similar, there were notable differences in the region 5 and 8 cohorts as compared to the remaining region. In particular the UC for region 5 was at higher acuity as compared to the remaining patients within the region, and the UC for region 8 was of lower acuity as compared to

the remaining patients within the region. A detailed discussion the differences between the UC and remaining transplanted patients for each region is included in Appendix 2B.

For research question three, which addresses changes in post-transplant disability, the national cohort of transplanted patients was utilized. The primary post-transplant outcomes that were measured were post-transplant functional status and return to work. Both of these measures are first assessed at six and twelve months post-transplant follow-up and therefore at least twelve months of post-transplant follow-up was required for all patients. The study population therefore included all adult patients who underwent deceased donor liver transplantation in the U.S. between January 1, 2010 and November 30, 2016. In parallel with the previous research questions on utilization, exclusion criteria included: age <18, history of prior organ transplantation, receipt of a multi-visceral transplant (with the exception of simultaneous liver and kidney transplant), receipt of an organ from a living donor, receipt of an organ outside of the MELD allocation process (exclusion of status 1A recipients), and those patients who underwent transplantation at a pediatric hospital. For the work outcome, the patient cohort was further limited by exclusion of patients <25 years of age or >55 years of age, and also patients with inadequate follow-up (less than two years post-transplant, excluding those patients who died prior to this time point) or missing information on their pre-transplant (baseline) work status. For the functional status outcome there were no additional age restrictions, but patients missing data for pre-transplant (baseline) functional status were excluded. The final cohort included 10,290 patients for the work outcome, and 33,619 for the functional status outcome; both cohorts included patients from 120 transplant centers (Figure 7 – 2).

Figure 7 – 2. Sample Size Flow Diagram for National Cohort of Transplanted Patients. Diagram indicates number of patients meeting each inclusion/exclusion criteria for the national cohort of transplanted patients utilized for research question 3.



7.4 Variable Definitions

Utilizing the framework set forth in the discussion of the measurement models, the following section outlines the variables discussed for each measure. This section outlines the two primary outcomes (post-transplant inpatient utilization, post-transplant health outcomes) followed by a discussion of each of the variables utilized to assess these concepts.

7.4.1 Outcome Measure: Post-Transplant Inpatient Utilization

The first outcome of interest is the inpatient utilization in the post-transplant period. For the purposes of this research question, post-transplant utilization was assessed through two measures: (1) total number of admitted days from the date of transplantation to 6-months post-transplant and (2) total number of admissions, inclusive of the index transplant admission within the 6-months post-transplant.

- Total number of admitted days includes all admitted days from the day of transplantation and through six months following the date of transplantation.

- Total number of admissions includes a count of the number of inpatient admissions that occur within six months of the date of transplantation, including the index admission.

The first of these measures assesses the total burden of hospitalization on both the patient and the health care system, whereas the second is a total count of admissions, which compares event rates.

Utilization data for all patients were obtained through the six-state inpatient databases. Within the HCUP-SIDs and OSHPD, individual patients were uniquely identified by a patient identifier. Utilizing the patient identifier, all associated visits with the same unique ID across all study years within an individual state were abstracted. All rehospitalizations for each individual patient were then organized in chronological order. All visits occurring within 180 days following transplantation were counted within the post-transplant period. A limitation of the available datasets is that only hospitalizations that occurred within state borders were included, therefore rehospitalizations that occurred outside the state of the original transplantation were not included.

The number of post-transplant admitted days was then calculated as the sum of the length of stay (LOS) for all visits that occurred within the post-transplant period. LOS was calculated at the difference between the discharge and admission date plus 1, such that a patient admitted and discharged within the same day had a LOS of 1, and patients admitted and discharged on consecutive days had a LOS of 2. This count is inclusive of the days spent hospitalized following transplantation during the index admission. The total number of admitted days during the post-transplant period was truncated at 180. For rehospitalizations that spanned the 180-day period, the LOS for that visit was censored at the day corresponding to the 180^{th} day post-transplant.

The number of post-transplant admissions was defined as a count of hospital admissions that occurred within the post-transplant period. All patients had at least one admission as the index admission was counted within the total number of admissions in the post-transplant period.

7.4.2 Outcome Measure: Post-Transplant Medical Condition / Disability

The second conceptual outcome is post-transplant disability, which was measured by two empirical proxies, *functional status* and *work status*.

Functional status defines the patient's degree of disability and is collected by individual transplant centers and reported to UNOS and SRTR at specific intervals following transplantation, the first of which occurs at six months post-operatively, and annually thereafter beginning at one-year post-transplant. Functional status is measured by the Karnofsky scale, which categorizes function by the decile of disability. The categorical responses were recoded to utilize the decile of disability as a continuous variable. The table below demonstrates the associated definitions for each decile of disability (Table 7 – 1). As an outcome measure, for Question 3, functional status was defined as the difference in functional status between transplantation and approximately six months (defined as the visit closest to six months post-transplant that is greater than three months and less than nine months after the transplantation date) and 1-year post-transplant (defined as the follow-up closest to 1-year post-transplant that is greater than eight months and less than sixteen months after the transplantation date). Patients who have died in the interval six or twelve month period post-transplant period have a functional status of zero assigned at follow-up.

Table 7 – 1. Karnofsky Scale for Functional Status

Karnofsky Functional Status Scale
10% - Moribund, fatal processes progressing rapidly
20% - Very sick, hospitalization necessary, active treatment necessary
30% - Severely disabled, hospitalization is indicated, death is not imminent
40% - Disabled, requires special care and assistance
50% - Requires considerable assistance and frequent medical care
60% - Requires occasional assistance but is able to care for needs
70% - Cares for self, unable to carry on normal activity or active work
80% - Normal activity with effort, some symptoms of disease
90% - Able to carry on normal activity, minor symptoms of disease
100% - Normal, no complaints, no evidence of disease
Unknown

In parallel with the report of functional status, individual transplant centers report patient work status both prior to transplantation and at specific intervals following transplantation. These data are collected both as a binary response, indicating whether a patient is working for income, and in further detail indicating why or why not a patient is or is not working (i.e. not working due to retirement, disability, insurance conflict) and to what degree they are working (i.e. full-time, part-time). In assessing post-transplant disability, we quantified work status as a binary outcome representing post-transplant work-status (work at any time during post-transplant follow-up). Working at any time within two years of transplantation was selected over using a single follow-up time period as work status was inconsistently recorded at each follow-up visit, but was typically recorded at least once during the patient's entire follow-up period (i.e. patient may be reported as working at six months and then no additional work status is available at 12, 18 or 24 months). By utilizing work at any time as an outcome, the measure assesses the ability to return to work and is likely to capture the greatest number of patients reaching a functional status allowing them to return to work. Patients were stratified for analysis by their pre-transplant work status and sex. Patients missing either pre- or post-transplant work status were excluded

from the analysis, and sensitivity analyses were completed to assess for systematic differences between those patients who were missing work status data. Patients who died during their transplant admission or prior to the initial six-month follow-up were considered not to be working at follow-up.

7.4.3 Primary Regressor: Share 35

Share 35, the primary regressor of interest, was defined as an indicator variable equal to zero if the patient was transplanted prior to June 1, 2013 (i.e., the reference value was defined as transplantation occurring in the pre-Share 35 period) and equal to one for patients transplanted after this date (post-Share 35 period).

Of note, the impact of Share 35 on the outcomes is mediated by the patient's allocation MELD score, which is defined as the MELD score, inclusive of MELD exception points, for which the patient was allocated their donor organ. The allocation MELD score is an ordinal value ranging from 6 – 40 and will be treated as a continuous variable.

7.4.4 Patient Preferences

Patient preferences were measured by the empirical proxies *race/ethnicity, age* and *sex.*

Race/Ethnicity was defined by a categorical variable derived from the SRTR database. The variable race from the SRTR dataset categorizes race/ethnicity into 6 categories: White, Black, Asian, Native American, Pacific Islander, and Multiracial. In addition, the ethnicity variable was used to categorize Latinos. Within the SRTR dataset, less than 0.5% of Latinos were non-white, therefore non-white Latinos were categorized by race alone, and White-Latinos were categorized separately from White, Non-Latinos. Due to data use restrictions requiring that within any tables, the reported cell size is >10, the race/ethnicity variable was then collapsed to five categories: White Non-Latino, White Latino, Black, Asian and Other. When collapsed, the

"Other" category is inclusive of: Native American, Pacific Islander and Multiracial groups. These values were used to generate a set of mutually exclusive and exhaustive binary indicator variables, with an omitted reference category of "White Non-Latino".

Age was defined as a continuous variable representing the patient's age at the time of transplant derived from the SRTR database.

Sex was defined as an indicator variable where female served as the reference value. Patient sex was abstracted from the SRTR database which categorizes all candidates as male, female or unknown. If sex was unknown in the SRTR database, sex from the AHRQ-HCUP or OSHPD database was used based upon reported gender recorded from the index (transplant) hospitalization.

7.4.5 Supply of inpatient medical services

Supply of inpatient medical services was measured by *density of short-term hospital beds* and *travel distance from the transplant center.* Collectively these measures summarize the overall supply of hospitals (density of short-term hospital beds) as well as their access to specific transplant-related inpatient care (travel distance from the transplant center).

Density of short-term hospital beds within the patient's core based statistical area (CBSA), calculated as the number of hospital beds divided by the population per 1,000 census population. Both the population and number of short-term hospital beds within a CBSA were derived from the AHRF. As previously stated, the AHA 2010 survey data was utilized as this represents the number of beds available at the beginning of the study period.

Travel distance from the transplant center was defined by the estimated travel time between the patient's home 5-digit zip code (determined by the center point within the zip by latitude and longitude) and the address of their transplant center (defined in latitude and

longitude). In the state of Massachusetts, this was defined by the distance between the patient's home 3-digit zip code and latitude and longitude of the transplant center, as the HCUP-SID for Massachusetts only provides 3-digit zip codes. Travel time was calculated by the georoute function within STATA which utilizes optimal travel/driving time between two points based upon the HERE API (https://develop.here.com). Travel time calculations through similar methods have been demonstrated to provide reasonable estimates of travel time for epidemiologic and health services research.[126]

7.4.6 Supply of outpatient medical services

Supply of outpatient medical services conceptually refers to the supply of providers in the outpatient setting to treat both chronic conditions and liver disease, and was therefore measured by two empirical proxies, *density of primary care physicians* and *gastroenterologists*. Similar to the supply of inpatient medical services, data related to physician density was abstracted from the AHRF using the 2010 AMA Physician Master File. The density of primary care physicians was measured by the number of primary care physicians participating in patient care, excluding hospital residents and physicians over the age of 75 divided by the CBSA population per 1,000 census population, as defined by the 2010 AMA Physician Master File. Similarly, the total number of gastroenterologists participating in patient care as measured in the 2010 AMA Physician Master File was divided by the CBSA population per 1,000 census population as a measure of density of gastroenterologists.

7.4.7 Ability to pay for care

The ability to pay for care was defined by four empiric measures: insurance status, education, race/ethnicity, age, sex, and zip code median income.

Insurance status was defined by the categorical variable for primary payer, defined by SRTR. Payer data is collected by the transplant center and reported to UNOS/SRTR both at the time of listing and at the time of transplant. Given that our primary outcome is concerned with utilization during the transplant admissions and in the six months following, we used insurance status at the time of transplant, as this was the most proximal and relevant measure. SRTR defines the primary payer as a categorical variable including the following values: private insurance, public insurance – Medicaid, public insurance – Medicare Fee for Service (FFS), public insurance – Medicare & Choice, public insurance – Department of Veterans Affairs (VA), public insurance – other government, self, donation, free care, and foreign government. These values were then collapsed to create a categorical variable with the following values: Private, Medicaid, Medicare (inclusive of Medicare FFS, Medicare & Choice), and Other (inclusive of public insurance – other government, foreign government, VA, Free Care (inclusive of donation, free care), Self-Pay). This variable was coded as a series of mutually exclusive and exhaustive dummy variables, with Private Insurance as the reference value.

Education as defined as a categorical variable for highest educational achievement, attained from the SRTR dataset. The information for the SRTR variable for education is obtained at the time a patient is listed for transplantation. This categorical variable contains the following values: no education, grade school, high school or GED, attended college or technical school, associate/bachelor degree, post-college graduate degree, and unknown. No education and grade school were condensed to a variable indicating “less than a high school education”. Utilizing these 6 categories: less than a high school education, high school/GED, college or technical school, associate or bachelors degree, post-college graduate degree and unknown, this variable

was coded as a series of dummy variables, where less than a high school education served as the reference value.

Race/ethnicity, age and *sex* have been defined previously under the subheading Patient Preferences.

Median income by zip code was defined by the quartile classification of the estimated median household income of residents within the patient's home zip code. These data are provided for all patients within the AHRQ HCUP SIDs and were calculated for all patients within the OSHPD data set based on home zip code and the American Community Survey (US Census Bureau).

7.4.8 Pre-Transplant Medical Condition / Disability

Pre-transplant medical condition encompasses both the patient's chronic and liver related medical condition and was empirically defined by four factors: medical comorbidities, liver disease etiology, liver disease severity, and functional status.

Medical comorbidities represent other medical conditions that may lead to increased inpatient utilization prior to liver transplantation. Data reported to SRTR by the transplant center is abstracted directly from the patient record, indicating the presence of specific disease comorbidities. Six of these comorbidities were included, each as a binary variable indicating a positive personal medical history of the following conditions: *hypertension, chronic obstructive pulmonary disease, vascular disease, diabetes and renal failure.*

Liver disease etiology was defined by the primary diagnosis of liver disease at the time of listing for transplantation. This value is obtained from the SRTR database and is originally reported by the transplant center at the time of listing. The SRTR variable is initially coded into specific diagnoses, which were collapsed into nine groups, resulting in a categorical variable

which contained the following categories: acute liver failure, autoimmune hepatitis, cholestatic liver disease, cryptogenic cirrhosis, genetic/metabolic disease, hepatitis C, malignancy, steatohepatitis and other. This variable was coded as a series of dummy variables where steatohepatitis (inclusive of non-alcoholic and alcoholic steatohepatitis) is the reference category.

Liver disease severity was empirically defined by the physiologic MELD score at the time of allocation/transplantation. The physiologic MELD score is collected by both UNOS and SRTR, and is defined as the calculated MELD score based solely on lab values, and not accounting for exception points, at the time of organ allocation. The physiologic score therefore directly quantifies the severity of liver disease. This variable was defined by ordinal values ranging from 6 – 40. Physiologic MELD score is used as a predictor in the analysis of inpatient utilization for question 1. For research questions 2 and 3, which include an interaction term between Share 35 and the allocation MELD score, the physiologic score is replaced by allocation MELD score and a MELD difference variable. MELD difference indicates difference in a patient's physiologic and allocation MELD score. It is important that allocation MELD score is used in the interaction term as the impact of Share 35 is dependent on the score for which the patient was allocated the organ, and therefore must be inclusive of any additional points awarded for malignancy or other disease process. In regression analysis the allocation MELD score is de-meaned in order to assure that the null value of the interaction term is set at the mean allocation MELD score rather than a MELD score of 0.

Functional status, as discussed above, defines the patient's degree of disability and is collected by individual transplant centers and reported to UNOS and SRTR. As a proxy for pre-transplant medical condition, the functional status at the time of transplantation was utilized.

Again, the Karnofksy score was used and quantified as a continuous variable, corresponding to the percent of disability.

7.4.9 Donor Organ Quality

Donor organ quality was measured by the Donor Risk Index (DRI) which is a validated index utilized throughout the transplant community as a measure of objective donor organ quality.[109] DRI has been associated with the risk of post-transplant complications and graft failure.[109] The factors considered in the calculation of DRI are: donor age, donor cause of death (COD), donor race, donor height, donation type (full organ or partial/split organ), duration of cold ischemia time (time between donor and recipient operations), and type of organ share (another proxy for distance the organ must travel). The equation is included below:

> DRI = exp[(0.154 if age 40 ≤ age <50) + (0.274 if age 50 ≤ age <60) + (0.424 if 60 ≤ age <70) + (0.501 if 70 ≤ age) + (0.079 if COD = anoxia) + (0.145 if COD = cerebral vascular event) + (0.184 if COD = other) + (0.176 if race = African American) + (0.126 if race = other) + (0.411 if donor after cardiac death) + (0.422 if partial/split) + (0.66((170-height)/10)) + (0.105 if regional share) + (0.244 if national share) + (0.010 x cold time)]

All of the factors included in the DRI equation are available within the SRTR dataset. These variables were used to calculate a DRI for each organ utilized for transplantation during the study period.

7.4.10 Post-Discharge Environment

Post-discharge environment has three empirical proxies: distance from the transplant center, median income of the patient's home zip code, and rural/urban classification.

Distance from the transplant center was discussed previously under *supply of inpatient care.*

Median income by zip code was discussed previously under *ability to pay for care.*

Rural / urban classification was defined by the estimated population of the patient's county. These data are provided for all U.S. counties within the AHRF. The rural/urban classification was grouped into six categories: completely rural or < 2,500 urban population, 2,500 – 20,0000 urban population, >20,000 urban population, metropolitan <250,000 population, metropolitan 250,000 – 1 million population, metropolitan >1 million population.

Each of these empirical proxies were only available for patients within the utilization cohort as the data were derived from the utilization databases. The data source for the evaluation of post-transplant disability (Q3) included only the transplant data set, so post-discharge environment had no empirical proxies and therefore was unmeasured in the Q3 analysis.

7.4.11 Health literacy

Education level, discussed previously as a proxy measure for ability to pay for care, was also utilized as a proxy for health literacy.

7.5 Descriptive Statistics

7.5.1 Characterizing Regional Variability & Likely Response to Share 35

The Share 35 policy was intended to improve organ availability for patients at the highest medical acuity (allocation MELD score ≥35) through increasing intra-regional organ sharing. While the policy was enacted across all regions at the same time, the effect of the policy occurs within regional borders. Because regions differ in size, population, acuity and other factors, it would be expected that the policy is likely to have differing effects within different regions. To describe these potential differences, and characterize the likely response to Share 35, the Pre-Share 35 period was assessed for both the UC and national cohort. By design, if effective, the Share 35 policy should result in an increase in patient acuity by transplanting more high acuity

patients. This is outcome most likely to occur when (1) there are patients within the region with allocation MELD scores ≥35 and (2) there are disparities in the rate or number of these patients between DSAs within regions that would cause organs to be shared. For the purpose of quantifying these two factors, the rates of allocation to patients with very high (≥35) allocation MELD scores, and the variability in this rate between DSAs was compared within each region. Rates of allocation were terms low, moderate and high if <10%, 10-20% or >20% of patients were allocated organs at very high allocation MELDs. Variability was defined as low, moderate or high if the greatest difference between the rates of very high MELD allocation between DSAs within a single region was <10%, 10-20%, or >20%, amongst DSAs with a minimum volume of 30 transplants per year. The likelihood of a region responding to Share 35 was then ranked a high, moderate and low to allow for regional assessment of the disability outcomes in research question 3, and to assist with interpretation of regional analysis in question 2.

Secondarily, each region was also assessed to determine if there was a change in patient acuity following Share 35 implementation by comparing the rate of very high (≥35) allocation MELD allocation within the time periods utilized for the utilization and national cohort evaluations.

7.5.2 National, Regional & DSA Level Changes Associated with Share 35

Descriptive comparisons between the Pre- and Post-Share 35 periods were completed to assess differences within the patient populations, with the primary aim of assessing changes in patient acuity at the time of transplant, patient functional status, and mortality (post-transplant). Comparisons were made utilizing the national cohort of transplanted patients, with additional subgroup comparisons made at the regional, and DSA level. A secondary analysis was completed utilizing the regions and time period for the two utilization questions (Q1 and Q2) to

aid in understanding whether part of the impact of Share 35 was mediated through changes in medical condition / disability at transplant which were unmeasured in the regression analysis due to collinearity with the outcome of inpatient utilization. Variables utilized for comparisons are listed in Table 7 – 2. Binary and categorical variables were compared with chi-squared analysis, ordinal and continuous variables with independent samples t-tests.

Table 7 – 2. Variables for Comparison between Pre- and Post-Share 35 Periods

Variable	Definition	Type
Patient Acuity at the Time of Transplant		
Physiologic MELD	MELD score at the time of transplant	Ordinal
Allocation MELD	MELD score, inclusive of MELD exception points, at the time of transplant	Ordinal
Allocation MELD ≥ 30	MELD score, inclusive of MELD exception points, at the time of transplant ≥ 30. Indicator of a high acuity transplantation.	Binary
Allocation MELD ≥ 35	MELD score, inclusive of MELD exception points, at the time of transplant ≥ 35. Indicator of a high acuity transplantation.	Binary
Dialysis dependence	Hemodialysis required at the time of transplant	Binary
Ventilator dependence	Life support with mechanical ventilations required at the time of transplant	Binary
Life support	Life support required at the time of transplant	Binary
Location at the time of transplant	Indicator of whether the patient was hospitalized within the ICU, hospitalized on the ward or not hospitalized prior to transplant	Categorical
Mortality		
Post-transplant death	Death following transplantation	Survival / Binary

7.6 Study Design and Regression Models by Research Question

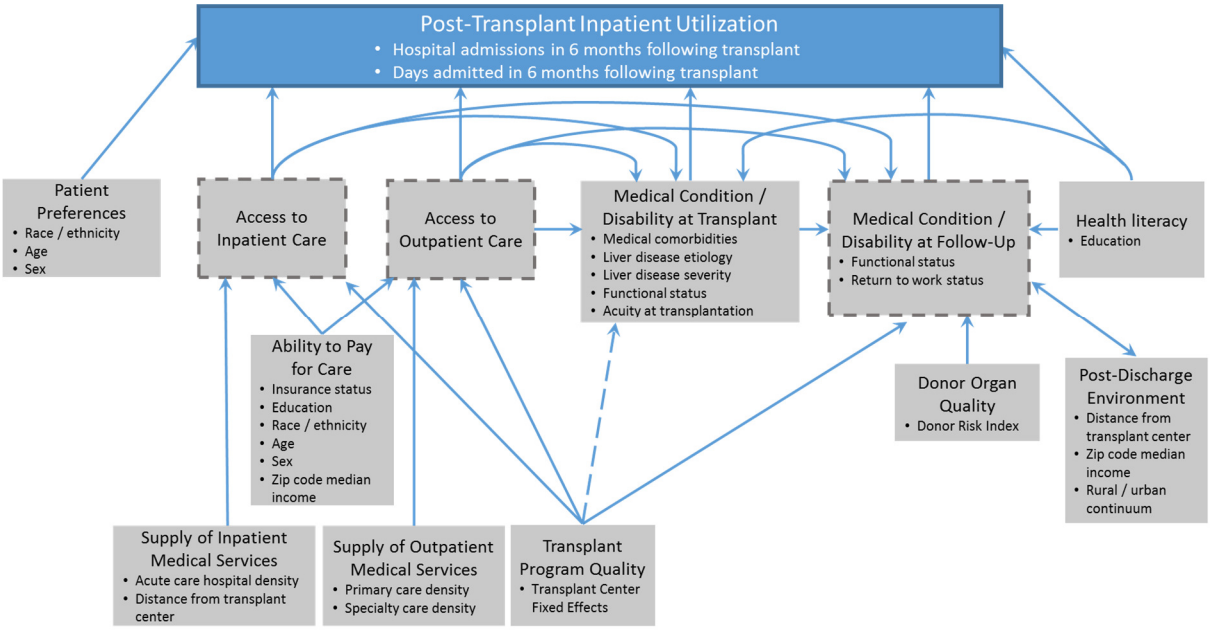
7.6.1 Question 1: What are the factors associated with post-transplant inpatient utilization among liver transplant patients in the pre-Share 35 period?

This question is aimed at understanding the factors associated with inpatient utilization following liver transplantation. This was assessed through a cross-sectional study of patients who underwent liver transplantation in the pre-Share 35 period, defined as January 1, 2010 to May 31,

2013. Restricting the time period to patients transplanted prior to Share 35 eliminates the effect of the policy, and allowed for an isolated evaluation of factors contributing to inpatient utilization.

To address this question, the reduced-form model for post-transplant inpatient utilization was utilized (Figure 7 – 3). Within the reduced-form model, the direct predictors of post-transplant inpatient utilization are patient preferences, access to inpatient care, access to outpatient care, medical condition / disability at transplant, medical condition / disability at follow-up and health literacy. To assess the influence of both donor organ quality and post-discharge environment on post-transplant inpatient utilization, the endogenous mediator, medical condition / disability post-transplant, was omitted (as indicated by the dashed border). Access to inpatient and outpatient care were replaced by their exogenous precursors, ability to pay for care, supply of inpatient and outpatient medical services and transplant program quality. Transplant program quality, which influences multiple constructs on the causal pathway (access to inpatient and outpatient care, medical condition / disability) was controlled for through transplant center dummy variables.

Figure 7 – 3. Reduced Form Model for Post-Transplant Inpatient Utilization. Each construct is included as an individual box. Measurement proxies are listed in bullets. The primary outcome is indicated by the solid border. Constructs that are intentionally omitted are indicated by a dashed border. Fixed effects are indicated by a dotted arrow.



The regression model for Question 1 was modeled as indicated below, where Y_{ij} represents post-transplant inpatient utilization for individual i at transplant center j, f represents the link function appropriate to the distribution of the outcome.

$$Y_{ij} = f[\beta_0 + \beta_1(\text{Patient Preferences})_i + \beta_2(\text{Supply of Inpatient Medical Services})_i + \beta_3(\text{Supply of Outpatient Medical Services})_i + \beta_4(\text{Ability to Pay})_i + \beta_5(\text{Medical Condition / Disability at Transplant})_i + \beta_6(\text{Donor organ quality})_i + \beta_7(\text{Post-Discharge Environment})_i + \beta_8(\text{Health Literacy})_i + \beta_9(\text{Transplant Center})_j + \varepsilon_{ij}]$$

Post-transplant inpatient utilization, defined as inpatient utilization within the six months following transplantation, was evaluated in terms of number of admissions and admitted days. The post-transplant period began the day of transplantation and therefore all patients had at least one admitted day and at least one admission following transplantation, resulting in a zero-truncated distribution of the outcome. The mean and variance for each outcome were calculated

to discern the appropriate count distribution for regression analysis. The link function *f* was defined as a zero-truncated negative binomial distribution for admitted days, and a zero-truncated Poisson distribution for admissions. Patients who died during the first six months following transplantation were included in the analysis, and an exposure option was utilized to account for truncated follow-up time secondary to death.

Results of the regression analysis are presented as marginal effects. Marginal effects are the predicted change in the outcome based on a single unit change in the covariate of interest (for continuous variables), or in comparison to the reference value (for categorical variables) averaged over the study cohort when all other covariates are held equal.

As discussed previously, this research question aimed to assess factors which were predictive of post-transplant inpatient utilization. Individual hypotheses were assessed by testing individual covariates as discussed below.

H1a: Patients with a higher physiologic MELD score at transplant will have greater inpatient utilization in the post-transplant period, ceteris paribus.

Physiologic MELD score is a measure of liver disease severity (higher score = greater severity) and is a continuous variable included in the regression model for post-transplant inpatient utilization as component of pre-transplant medical condition. This hypothesis defines the expected effect of physiologic MELD to be positive, such that a higher physiologic MELD score correlates with higher utilization. This hypothesis was tested by assessing the marginal effect of physiologic MELD at transplant within the final model for post-transplant inpatient utilization. We will have found support for hypothesis H1a if the marginal effect of MELD at transplant is positive and statistically significant with a p-value < 0.05.

H1b: Patients who are transplanted for malignancy with have less post-transplant inpatient utilization as compared to patients suffering from liver failure secondary to cirrhosis (steatohepatitis), ceteris paribus.

Patients with liver failure secondary to cirrhosis and those with malignancy are less physiologically ill at the time of transplantation and therefore would be expected to recover more rapidly, have less complications and overall utilize fewer services in the post-transplant period. To assess this difference in post-transplant inpatient utilization, the categorical variable for *liver disease etiology* was assessed. Hypothesis 1b specifies that patients with malignancy will have less utilization in comparison to patients with cirrhosis (steatohepatitis). Cirrhosis was defined as the reference value for *liver disease etiology*, and therefore we would predict that hepatic malignancy would have a negative marginal effect. Support for H1b will be defined by a negative and statistically significant ($p<0.05$) marginal effect for the dummy variable for hepatic malignancy.

H1c. Patients with a lower ability to pay for care will have greater post-transplant inpatient utilization than patients with a greater ability to pay for care, ceteris paribus.

The ability to pay for care is defined by six measures: insurance status, education, race/ethnicity, age, sex and median income by patient zip code. To assess the relationship between ability to pay and utilization, we utilized two measures (those expected to be the best proxies for ability to pay): insurance status and education. Under hypothesis 1c, a higher ability to pay is associated with lower inpatient utilization, such that private insurance and higher educational achievement should be associated with lower utilization. Given that there are multiple measures, a negative marginal effect associated with each of these would independently support H1c. For insurance, private insurance is the reference value, therefore a negative

marginal effect associated with any of the following dummy variables would support the H1c: Medicare or Medicaid. For education, the reference value is less than a high school education, therefore a negative marginal effect associated with any of the following dummy variables would support H1c: attended high school or attained GED, attended college or technical school, associate/bachelor degree, post-college graduate degree. After assessing each independent variable, these variables were collectively assessed by testing them jointly. A significance level of <0.05 was used for all measures.

H1d: Patients who receive a poorer quality organ will have higher inpatient utilization in the post-transplant period, ceteris paribus.

Donor organ quality, as measured by the DRI, is included within the conceptual model for post-transplant inpatient utilization. A higher DRI score implies a higher risk, and therefore poorer quality organ. Hypothesis 1d predicts a direct relationship between inpatient utilization in the post-transplant period and donor organ quality. Therefore, support will be found for this hypothesis if the marginal effect of DRI was positive and statistically significant at a p-value <0.05.

Sensitivity Analyses

Six sensitivity analyses were completed utilizing the six-state cohort included in question 1. These sensitivity analyses pertain to: (1) definition of HCC, (2) use of three versus nine diagnostic groups, (3) model comparisons, (4) definition of state residence, (5) inclusion of patients who have truncated follow-up due to death within six months of transplant, and (6) inclusion of patients who underwent simultaneous liver and kidney transplant.

Definition of HCC

Due to variable definitions within the SRTR database, there were multiple ways to define the diagnosis of HCC. Therefore, a sensitivity analysis was completed to compare the three different definitions of HCC. This analysis was completed prior to multiple imputation, utilizing only complete data to compare different diagnostic definitions. The three definitions of HCC compared included: (1) malignancy only if malignancy was the primary or secondary diagnosis listed at the time of transplantation, (2) malignancy if diagnosis codes included malignancy as the primary or secondary diagnosis and if the physiologic MELD score was less than the allocation MELD score (indicating additional exception points which are awarded for HCC), or (3) malignancy if diagnosis codes included malignancy or if the patient was ever approved for exception points due to HCC (binary variable available in the SRTR database). Overall model significance, and the magnitude, direction and significance of marginal effects of interest were compared using each of the three definitions of HCC.

Use of Three versus Nine Diagnostic Groups

A sensitivity analysis was completed comparing the use of nine diagnostic groups (steatohepatitis, malignancy, acute liver failure, hepatitis C, cholestatic liver disease, cryptogenic cirrhosis, genetic/metabolic disease, autoimmune and other) to three diagnostic groups (chronic liver disease, acute liver failure and malignancy). When three diagnostic groups were used, chronic liver disease was inclusive of steatohepatitis, hepatitis C, cholestatic liver disease, cryptogenic cirrhosis, genetic/metabolic disease, autoimmune and other. The acute liver failure and malignancy categories were the same whether three or nine diagnostics groups were used. The sign and significance of the malignancy and acute liver failure covariates were compared between regression models using three or nine diagnostic groups. If the signs and significance of the covariates were similar, then the nine diagnostic group definition was preferred.

Model Comparisons

Comparisons between potential regression distributions and alternative models were completed for each outcome. For the admissions outcome, the stability of marginal effects was compared between ordinary least squares (OLS), Poisson, zero-truncated Poisson (final model), mixed effects Poisson, and Poisson with transplant center fixed effects. In all models, except Poisson with transplant center fixed effects, transplant center was included as a covariate. For the admitted days outcome, the stability of marginal effects was compared between the OLS regression, negative binomial regression, zero-truncated negative binomial regression (final model), mixed effects negative binomial regression, and negative binominal regression with fixed effects by transplant center. In all models, except the negative binomial with transplant center fixed effects, transplant center was included as a covariate. The significance and direction of marginal effects of interest, and overall model significance were assessed across all models.

Definition of state residence

Patient state of residence was available in both the utilization (OSHPD or HCUP) and transplantation datasets. While the datasets were concordant for the majority of cases, there were 45 cases (0.9%) in which the patient was classified as an in-state resident by SRTR but as an out-of-state resident by HCUP or OSHPD, and 53 cases (1.1%) in which the utilization database classified the patient as in-state, but SRTR classified them as out-of-state, collectively accounting for 98 cases (2.0%) of patients who may ultimately be inappropriately included within the sample for analysis. State residence is an important inclusion criterion as state utilization databases can only account for utilization within their geographic borders, therefore out-of-state patients may bias the results towards the null as they may be more likely to seek care within their home state. The patients who were classified by a single database as out-of-state had an admission rate >1 in 56.12% of patients, which was similar to the rate amongst patients who

were classified as in-state in both datasets (56.47%, p = 0.946 by Pearson chi-squared). For the admitted days outcome, there was no difference in the mean number of admitted days between patients who were classified as in-state by both datasets and those classified as out-of-state by one dataset (mean 27.97 days (SE 0.42) and mean 26.88 days (SE = 2.44) respectively, with p = 0.710 by two-sample t-test). Although there were no clear differences in preliminary evaluations, to further assess if the results of the regression analysis changed with exclusion of the 101 cases that may be out-of-state, a sensitivity analysis was completed comparing the overall model as well as the significance, direction and magnitude of marginal effects for covariates of interest.

Inclusion of Patients who Died within Six months of Transplantation

Within the six-state cohort there are 342 patients (7.04%) who died before completion of six-month follow-up. Amongst those patients who died prior to six month follow-up, the mean follow-up time was 1.93 months (range 0.03 – 6 months). To account for the differential follow-up, the total months of follow-up were used as an exposure in regression modeling. To assess whether the results of the regression change with exclusion of these 342 patients, a sensitivity analysis was completed comparing overall model significance and the significance, direction and magnitude of marginal effects for the covariates of interest. If no difference was detected, then inclusion of the patients who died within six months of transplant is preferred.

Inclusion of Patients who Underwent Simultaneous Liver and Kidney Transplant

Within the six-state cohort there are 330 patients (6.79%) who underwent simultaneous liver and kidney transplant, while 4530 underwent liver transplant alone. To assess whether the results of the regression change with inclusion of these 330 patients, a sensitivity analysis was completed comparing the significance, direction and magnitude of marginal effects for the covariates of interest with the inclusion and exclusion of liver + kidney recipients. Additionally, when these patients were included, the need for an additional covariate for simultaneous liver

and kidney transplant was assessed. If no difference was detected between models, then inclusion of the patients who underwent simultaneous liver and kidney transplant is preferred.

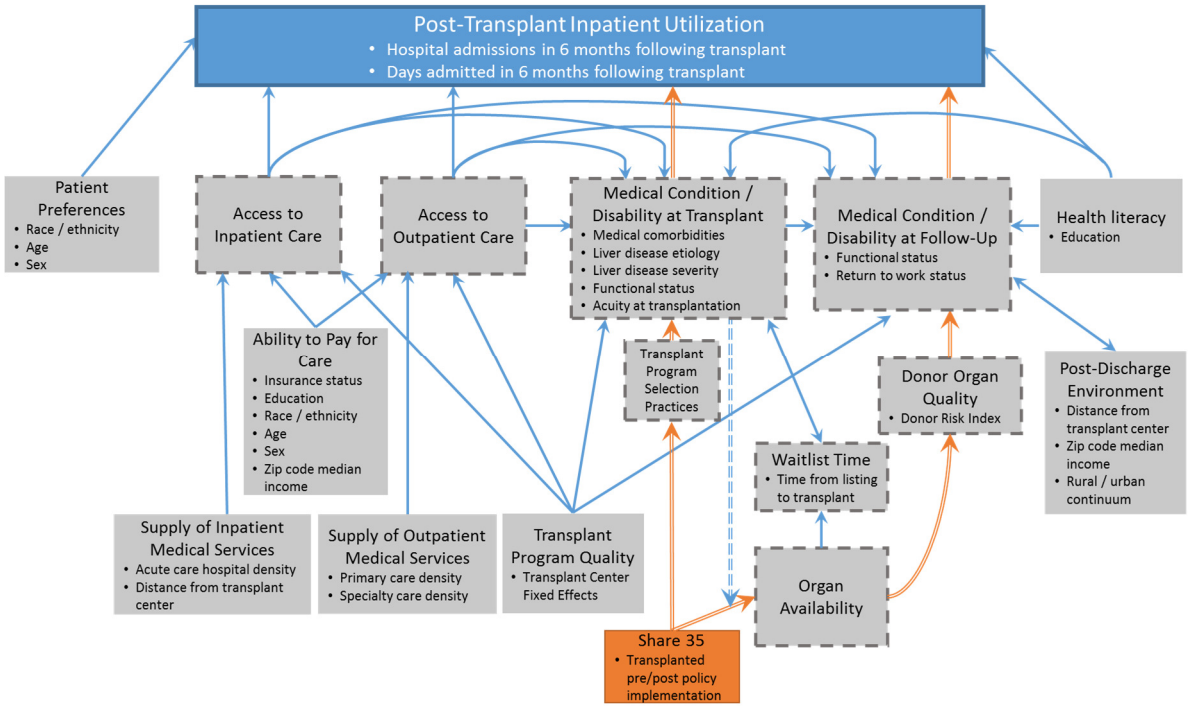
7.6.2 Question 2: How did Share 35 impact post-transplant inpatient utilization?

Question 2 builds upon the initial cross-sectional study done in Question 1, which assessed post-transplant inpatient utilization. In order to assess the effect of Share 35, a pre-/post-study design was utilized. The study sample included patients in the utilization cohort, who underwent liver transplantation between January 1, 2010 and June 1, 2014, with the exclusion of patients who received transplants under a Status 1A designation. The regression analysis was informed by the reduced-form model for post-transplant inpatient utilization, accounting for Share 35.

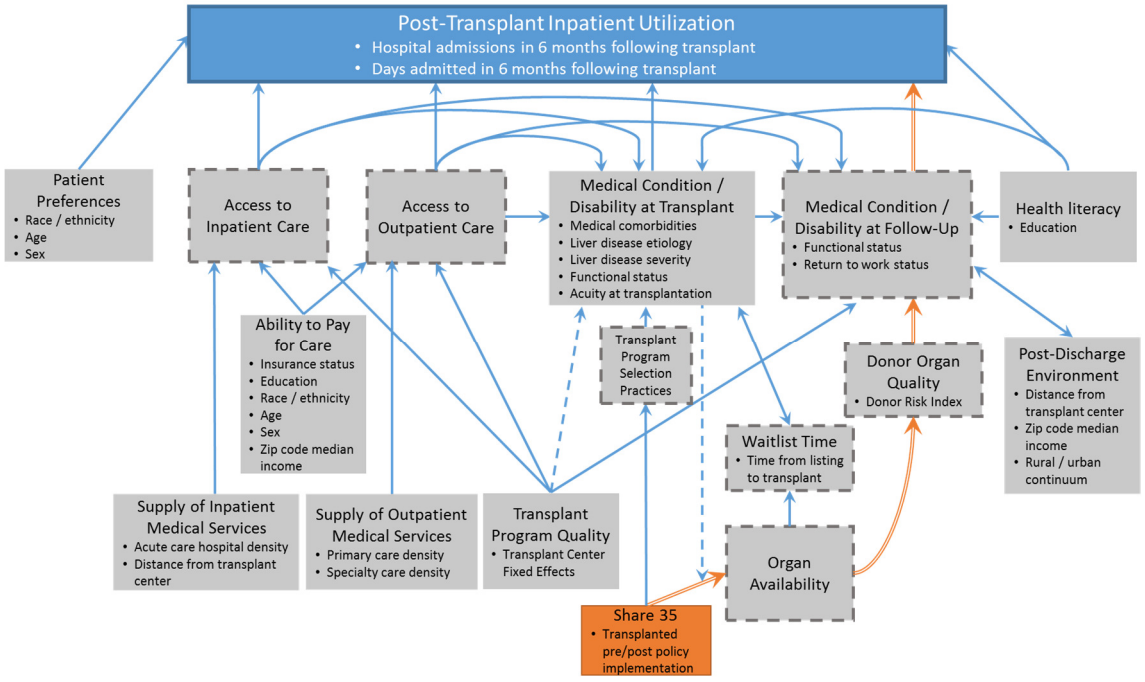
As demonstrated in the conceptual model below, the effect of Share 35 on post-transplant inpatient utilization is mediated through both pre-transplant medical condition and organ availability (which in turn affects waitlist time, donor organ quality and post-transplant medical condition). To assess these two causal pathways, the reduced-form model was utilized in two forms. First, the full effect of Share 35 was evaluated by omitting mediating factors along both causal pathways, which is demonstrated in Figure 7 – 4A. In this reduced-form model, transplant program selection practices, and medical condition / disability at transplant are omitted (1st causal pathway), as well as medical condition / disability at follow up, donor organ quality and organ availability (2nd causal pathway). Second, the reduced-form model was modified by controlling for medical condition / disability at transplant, which therefore isolates the effect of Share 35 through organ availability and subsequent mediators (2nd causal pathway). In this model the effect of the policy, through organ availability, will be assessed by inclusion of a Share 35 covariate, as well as an interaction term between Share 35 and allocation MELD score, as the

effect of Share 35 is mediated by the allocation MELD score. The moderating effect of allocation MELD score on Share 35 will be assessed through comparisons of the mean effect of Share 35, excluding the interaction term (H2b), and the allocation MELD dependent effect, with inclusion of the interaction term (H2c). The second model is indicated in Figure 7 – 4B. In both reduced-form models, and in parallel with the model utilized for Question 1, transplant program quality is controlled through transplant center fixed effects (through the use of dummy variables).

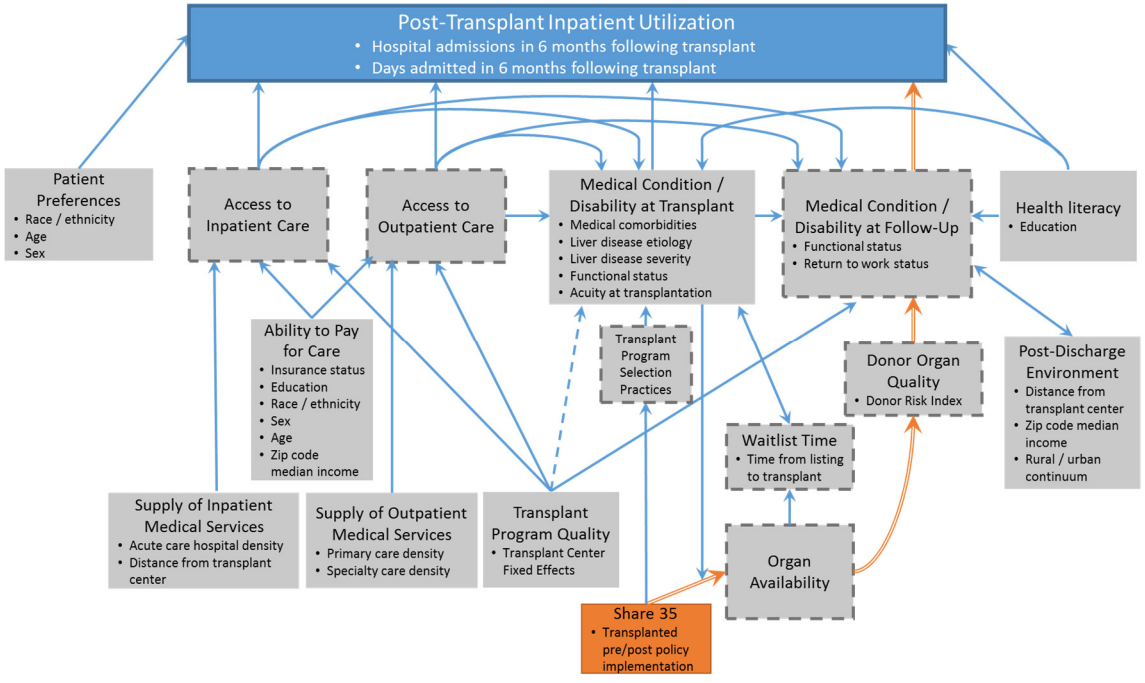
Figure 7 – 4. Reduced Form Models and Casual Pathways for Post-Transplant Inpatient Utilization Accounting for Share 35. Each construct is indicated by an individual box and measurement proxies are indicated in bullets below each concept. Omitted constructs are indicated by dashed borders. The causal pathways tested are highlighted in orange with double lines in the diagram below. (A) both pathways through both medical condition / disability at transplant and organ availability are tested. Note that the moderating effect of allocation MELD score on Share 35 is excluded (dashed arrow between medical condition / disability at transplant and the line between Share 35 and organ availability). (B) Only the pathway through organ availability is tested. Of note, the moderating effect between medical condition / disability at transplant (by allocation MELD score) on the relationship between Share 35 and organ availability is not tested (dashed arrow). (C) Only the pathway through organ availability is tested, but the moderating effect between medical condition / disability at transplant (by allocation MELD score) on the relationship between Share 35 and organ availability is tested (solid arrow).



A.



B.



C.

The regression model for Question 2, when assessing the full effect of Share 35, is expressed as follows, where Y_{ij} represents post-transplant inpatient utilization for patient i at

transplant center *j*, and *f* represents the link function selected based on the distribution of the outcome, and θ_j represents transplant center fixed effects.

A. $Y_{ij} = f\,[\beta_0 + \beta_1(\text{Patient Preferences})_i + \beta_2(\text{Supply of Inpatient Medical Services})_i + \beta_3(\text{Supply of Outpatient Medical Services})_i + \beta_4(\text{Ability to Pay})_i + \beta_5(\text{Health literacy})_i \beta_6(\text{Post-Discharge Environment})_i + \mathbf{\beta_6(Share\ 35)_i} + \beta_7(\text{Transplant Center})_j + \varepsilon_{ij}]$

When controlling for medical condition / disability at transplant, the regression model was adjusted to account for this additional construct, and is expressed as follows.

B. $Y_{ij} = f\,[\beta_0 + \beta_1(\text{Patient Preferences})_i + \beta_2(\text{Supply of Inpatient Medical Services})_i + \beta_3(\text{Supply of Outpatient Medical Services})_i + \beta_4(\text{Ability to Pay})_i + \beta_5(\text{Health literacy})_i + \mathbf{\beta_6(Share\ 35)_i} + \beta_8(\text{Medical Condition / Disability at Transplant})_i + \beta_9(\text{Post-Discharge Environment})_i + \beta_{10}(\text{Transplant Center})_j + \varepsilon_{ij}]$

Of note, the construct for medical condition / disability at transplant includes physiologic MELD score. In order to create symmetry between models B and C, physiologic MELD score is replaced with two terms, allocation MELD score and MELD difference, which indicates the number of MELD exception points awarded to the patient.[iv] Allocation MELD score will be de-meaned in order to assure that when Share 35 and allocation MELD score are interacted (model C below) that the interpretation of the effect of Share 35 is meaningful at a null value for allocation MELD score. When controlling for medical condition / disability at transplant, and accounting for the moderating effect of the patient's allocation MELD score on the relationship between Share 35 and organ availability, the regression model is expressed as follows:

[iv] Allocation MELD score = physiologic MELD score + MELD exception points. MELD exception points are discussed in section 2.3.2. Given that allocation MELD score moderates the effect of Share 35 (model C), and therefore will be included in the model, allocation MELD score and MELD difference will be used in place of physiologic MELD score for the construct medical condition / disability at transplant.

C. $Y_{ij} = f\,[\beta_0 + \beta_1(\text{Patient Preferences})_i + \beta_2(\text{Supply of Inpatient Medical Services})_i + \beta_3(\text{Supply of Outpatient Medical Services})_i + \beta_4(\text{Ability to Pay})_i + \beta_5(\text{Health literacy})_i + \mathbf{\beta_6(Share\ 35)_i + \beta_7(Share\ 35)_i*(Allocation\ MELD\ Score)} + \beta_8(\text{Medical Condition / Disability at Transplant})_i + \beta_9(\text{Post-Discharge Environment})_i + \beta_{10}(\text{Transplant Center})_j + \varepsilon_{ij}]$

Similar to Question 1, post-transplant inpatient utilization was assessed both as the number of admissions and admitted days within the six months following transplantation, which resulted in a zero-truncated count distributions. Therefore function, *f,* was informed by a zero-truncated Poisson distribution for number of admissions and zero-truncated negative binomial function for admitted days.

The Share 35 policy most directly impacted regional distribution of organs, therefore in addition to the full analysis, inclusive of all 6 states, an additional sub-analysis was completed by region to assess if there are regional differences in the effect of Share 35. The six states are from 5 different UNOS regions: California (region 5), Florida (region 3), Georgia (region 3), Massachusetts (region 1), Nebraska (region 8) and New York (region 9). Of note, due to a small sample size and the potential for overfitting (<10 cases per covariate) the region 8 analysis was excluded.

Results of the regression analysis are presented as marginal effects. Margins indicate difference in the predicted number of admissions or admitted days between the Pre- and Post-Share 35 period averaged over the study cohort when all other covariates are held equal. For hypotheses H2c, the margins indicate the difference for a specified allocation MELD score.

H2a: Share 35 increased inpatient utilization in the post-transplant period, when not controlling for medical condition / disability at transplant, but controlling for patient preferences, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality) and health literacy

Hypothesis 2a indicates that Share 35 lead to increased utilization due to the effects mediated through both medical condition / disability at transplant and organ availability. This hypothesis will be supported by a positive and statistically significant marginal effect, at an alpha level of 0.05, for the primary regressor, Share 35, in model A demonstrated above.

H2b: Share 35 decreased inpatient utilization in the post-transplant period when controlling for medical condition / disability at transplant in addition to controlling for patient preferences, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality) and health literacy.

Hypothesis 2b indicates that the mean effect of Share 35 led to decreased inpatient utilization in the post-transplant period when controlling for medical condition / disability at transplant, therefore indicating that the effect mediated through organ availability has a significant effect. This hypothesis will be supported by a negative and statistically significant marginal effect of Share 35 on post-transplant inpatient utilization when the covariates for medical condition / disability at transplant are included within the model, but the interaction term between Share 35 and the patient's allocation MELD score is excluded (model B above).

H2c: The negative effect of Share 35 on inpatient utilization in the post-transplant period will be larger amongst patients with high allocation MELD scores, when controlling for medical condition / disability at transplant, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality) and health literacy.

Hypothesis 2c indicates that the effect of Share 35, through organ availability, is dependent on a patient's allocation MELD score; such that patients with higher allocation MELD scores will have a larger decrease in post-transplant disability (negative effect) of Share 35, whereas patients with lower allocation MELD scores will have less of an effect or no effect. This hypothesis will be supported by a negative and statistically significant marginal effect of the interaction between Share 35 and allocation MELD scores at allocation MELD scores of 35 or higher when the covariates for medical condition / disability at transplant are included within the model (model C above).

Sensitivity Analyses

Four sensitivity analyses were completed addressing: (1) definition of state residence, (2) inclusion of patients who died within six months of transplantation, (3) inclusion of patients who underwent simultaneous liver and kidney transplant, and (4) use of a categorical or continuous interaction term for allocation MELD score. All sensitivity analyses were completed utilizing the main model (not subdivided by UNOS region) for H2a – H2c for both the admissions and admitted days models. If sensitivity analyses detected a difference, further analysis was completed to assess possible explanations for the detected effect.

State Residence

As discussed above for question 1, the definition of state residence was evaluated by sensitivity analysis. While the utilization and transplantation datasets were concordant in classification of patients as in-state or out-of-state residents for the majority of cases, there were 66 cases (1.1%) in which the patient was classified as an in-state resident by SRTR but as an out-of-state resident by HCUP or OSHPD, and 119 cases (1.9%) in which the utilization database classified the patient as in-state, but SRTR classified them as out-of-state, collectively accounting for 185 cases (3.0%) of patients who may be misclassified as in-state residence. Ninety-four of the cases that were potentially misclassified were from the pre-Share 35 period and 91 from the post-Share 35 period. The sensitivity analysis was completed by comparing marginal effects estimates for covariates of interest with the inclusion or exclusion of patients who were only classified as in-state residents by one of the two databases (utilization or transplantation). If estimates were robust, inclusion of these patients was preferred.

Inclusion of Patients who Died within Six months of Transplantation

In parallel with the analysis done for question 1, a sensitivity analysis was completed comparing the inclusion or exclusion of patients who died within six months of transplantation, and therefore had truncated follow-up. Comparisons were made between the two samples by regression analysis using the main models for H2a – H2c marginal effects for covariates of interest were assessed. If the estimates were robust, inclusion of patients who died within six months of transplantation was preferred.

Inclusion of Patients who Underwent Simultaneous Liver and Kidney Transplant

Within the six-state cohort there are 454 patients (7.4%) who underwent simultaneous liver and kidney transplant, while 5702 underwent liver transplant alone. In the pre- and post-Share 35 period liver + kidney recipients accounted for 7.0% (329 / 4681) and 8.5% (125 / 1475)

of liver transplant recipients. To assess whether the results of the regression change with inclusion of these 454 patients, a sensitivity analysis was completed comparing the significance, direction and magnitude of marginal effects for the covariates of interest with the inclusion and exclusion of liver + kidney recipients. Additionally, when these patients were included, the need for an additional covariate for simultaneous liver and kidney transplant was assessed. If no difference was detected between models, then inclusion of the patients who underwent simultaneous liver and kidney transplant is preferred.

Allocation MELD Score as a Categorical Predictor

Allocation MELD score moderates the effect of Share 35, as those patients with higher MELD scores are more likely to benefit from Share 35 than those with lower scores. Given that Share 35's effect may not be linear, such that it provides a specific advantage to allocation MELD scores of 35 or higher that is different from that provided to lower scores, a sensitivity analysis was completed using binary and categorical definitions of allocation MELD score.

Dummy variables combining a patient's allocation MELD score and their Pre- or Post-Share 35 status were created for both binary and categorical definitions of allocation MELD score. The binary definition of allocation MELD score created a cut point at an allocation MELD score of 35. The four indicator variables utilized for the binary sensitivity analysis included: Pre-Share 35 with allocation MELD <35, Pre-Share 35 with allocation MELD ≥35, Post-Share 35 with allocation MELD <35, Post-Share 35 with allocation MELD≥35. The reference value was defined as Pre-Share 35 with an allocation MELD ≥35. For the categorical analysis, 3 levels of allocation MELD score were defined: <20, 20-29 and >30. Dummy variables were constructed in the same manner as for the binary analysis, and Pre-Share 35 with allocation MELD >30 was used as the reference value.

The direction and significance for the marginal effect associated with the Post-Share 35 high allocation MELD score dummy variable (Post-Share 35 with allocation MELD≥35 for the binary construction and Pre-Share 35 with allocation MELD >30 for the categorical construction) will be compared to the marginal effect of Share 35 at increasing allocation MELD scores with the use of a continuous allocation MELD score covariate. If no difference is detected between models, use of allocation MELD score as a continuous variable is preferred.

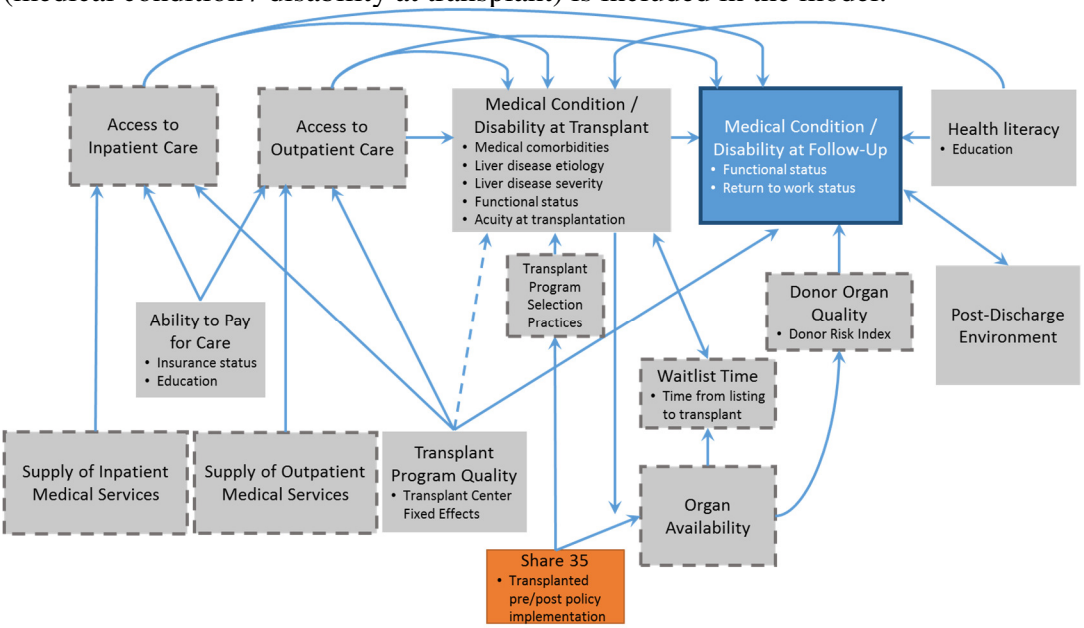
7.6.3 Question 3: How did Share 35 impact post-transplant disability?

Question 3 was aimed at assessing the impact of Share 35 on post-transplant disability as measured by functional status and return to work post-transplant. Similar to the study designs employed for question 2, this question was addressed utilizing a cross-sectional analysis of patients who underwent liver transplantation. Given that this study addresses post-transplant outcomes (and not utilization) the sample was extended to include all patients transplanted between January 2010 and November 1, 2016 included within the national cohort of transplanted patients. The sample was truncated at a transplantation date of November 1, 2016 to ensure patients had at least 1-year of potential follow-up time within the available dataset (last available follow-up December 1, 2017).

The reduced-form model for medical condition / disability at follow-up was utilized to inform regression analysis (Figure 7 – 5). Within the model, Share 35 has an impact on medical condition / disability at follow-up through two causal pathways, one through transplant program selection and medical condition / disability at transplant and a second through organ availability. In addressing Question 3, only the causal pathway through organ availability was tested, so that medical condition / disability at transplant could be controlled within the model. As indicated within the reduced-form model below, the direct predictors of medical condition / disability at

follow-up are: access to inpatient care, access to outpatient care, medical condition / disability at transplant, health literacy, post-discharge environment, Share 35 and transplant program quality. Similar to previous reduced-form models, access to inpatient and outpatient care were omitted and replaced by exogenous precursors, including ability to pay for care and supply of inpatient and outpatient medical services. In contrast to the models used for questions one and two, this model excludes the supply constructs as the measurement proxies were derived from data available only in the utilization databases and not within the transplantation database which is the sole source of data for this research question. Transplant program quality was measured through transplant center fixed effects. Post-discharge environment had no measurement proxies available within the national databases and therefore was excluded from this regression analysis.

Figure 7 – 5. Reduced Form Model for Post-Transplant Disability Accounting for Share 35. Each concept is indicated by an individual box and relationships between concepts are indicated by arrows. Note that not all arrows are shown in the graph (for example, we do not show arrows representing all of the possible collinearity between predictors). Omitted concepts which will be measured by exogenous precursors are indicated by a dashed border. The primary outcome is indicated by a solid border. The dashed arrow between transplant program quality and medical condition disability at transplant indicates that the relationship is unmeasured since the mediator (medical condition / disability at transplant) is included in the model.



Based upon the reduced-form conceptual model, the regression model for Question 3 can be expressed as follows, where Y_{ij} represents the medical condition / disability at follow-up for individual *i* at transplant center *j*, *f* represents the link function appropriate to the distribution of the outcome, and θ_j represents transplant center fixed effects. Similar to previous models, physiologic MELD score was replaced with the demeaned allocation MELD score and the MELD difference when used as a measurement proxy for Medical Condition / Disability at Transplant[v].

$$Y_{ij} = f\ [\ \beta_0 + \beta_1(\text{Ability to Pay})_i + \beta_2(\text{Medical Condition / Disability at Transplant})_i + \beta_3(\text{Health Literacy})_i + \beta_4(\text{Share 35})_i + \beta_5(\text{Share 35*Allocation MELD})_i + \theta_j + \varepsilon_{ij}\ ]$$

There were two measures of Medical Condition / Disability at Follow-Up, which were assessed in the evaluation of Question 3, work status and functional status, which will each be discussed separately below.

Work Status

Work status is collected prior to transplantation and at interval follow-up visits, and is reported as a binary outcome indicating if a patient is working for an income (yes / no). Pre-transplant work status was defined as a patient's work status within 90 days of transplantation (either at the time of transplantation or at the time of listing if the patient was listed <90 days prior to transplantation). Post-transplant work status was defined as any return to work within two years of transplantation. In evaluating work status there are many considerations: (1) given

[v] Given that allocation MELD score and physiologic MELD score are collinear, such that the allocation MELD score = physiologic MELD score + MELD exception points, when the interaction term was included within the model the physiologic MELD score was substituted with a term indicating the difference between the two scores (MELD difference = allocation MELD score – physiologic MELD score).

that population includes a subset of patients who are unlikely to be contributing to the workforce either prior to transplant or after transplantation, we limited this analysis to patients who are age 25-55 at the time of listing, (2) given the difference in workforce contributions by males and females, we stratified the cohort by sex, (3) patients who died during their transplant visit or prior to their six month follow-up were considered to have not returned to work. The subset of patients who have died were included due to the fact that increases in transplant-related mortality have an impact on the overall disability of the transplant population.

Based on these considerations, work status was assessed in four stratified samples: males working before transplant, males not working before transplant, females working before transplant and females not working before transplant. The outcome for the model was binary indicating a return to work after transplant, and therefore the link function for the regression model specified above was a logit model, with dichotomous indicators for transplant center.

Patients who were missing work status in the pre-transplant period were excluded from the analysis as this was required for sample stratification. Comparisons between patients with and without a documented pre-transplant work status were completed to assess differences between patients included and excluded from the analysis.

When considering the outcome in terms of work at any time within two years of transplantation, it was important to control for the number of times the patient was evaluated/measured, as patients with more measured time points had an increased likelihood that their work status was recorded. Therefore, the regression model for working at any time was expressed as follows:

$$P(\text{Working at any time post-transplant})_{ij} = f[\beta_0 + \beta_1(\text{Ability to Pay})_i + \beta_2(\text{Pre-Transplant Medical Condition / Disability})_i + \beta_3(\text{Health Literacy})_i + \mathbf{\beta_4(Share\ 35)_i} + \mathbf{\beta_5(Share}$$

35*Allocation MELD)$_i$ + + β_6(Number of Follow-Up Visits)$_i$ + β_7(Transplant Center)$_j$ + ε_{ij}]

Similar to question 2, all analyses were completed with the inclusion and exclusion of the interaction term between Share 35 and allocation MELD. Inclusion of this term provided the opportunity to evaluate the allocation MELD score-dependent effect of Share 35 (H3b), while exclusion provided the mean effect of Share 35 across the population (H3a).

Functional Status

Similar to work status, functional status is assessed both prior to transplantation and at interval follow-up visits. Functional status was conceptualized as the change in pre- to post-transplant functional status. For the ease of interpretation, this difference was defined as the post-transplant functional status minus the pre-transplant status, such that a positive difference corresponds to an improvement in functional status after transplantation. Pre-transplant functional status was defined by the Karnofsky score (percent of independent function) at the time of transplantation, and post-transplant functional status was defined as the Karnofsky score at 6-months and 1 year post-transplant. For all analyses, patients who died following transplantation were assumed to have a post-transplant functional status equal to 0%. Unlike the sample for work status, there were no restrictions on age or stratification by sex for this outcome.

Patients who were missing functional status in both the pre- and post-transplant period were excluded from the analysis.

The distribution of change in functional status was assessed to determine the appropriate regression model. Given that the distribution approached normal, ordinary least squares (OLS) regression was utilized. The regression model was expressed as follows, where Y_{ij} is the mean change in functional status pre- to post-transplant for patient *i* at transplant center *j* at time *t*

(defined as either six months or one year post-transplant) and θ_j represents transplant center fixed effects:

$$\mu(Y_{ijt}) = \beta_0 + \beta_1(\text{Ability to Pay})_i + \beta_2(\text{Pre-Transplant Medical Condition / Disability})_i + \beta_3(\text{Health Literacy})_i + \mathbf{\beta_4(Share\ 35)_i} + \mathbf{\beta_5(Share\ 35*Allocation\ MELD)_i} + \theta_j + \varepsilon_{ijt}$$

In parallel with the assessment of work status, all analyses were completed with the inclusion and exclusion of the Share 35 and allocation MELD score interaction term. Inclusion of this term provided the opportunity to evaluate the allocation MELD score-dependent effect of Share 35 (H3b), while exclusion provided the mean effect of Share 35 across the population (H3a).

Results of the hypotheses tests are reported as marginal effects. The marginal effects for the logistic regression model utilized for the work status outcome indicated the change in the predicted probability of returning to work between the Pre- and Post- Share 35 period averaged over the sample, when all else is equal. For the functional status outcome the marginal effects indicated the difference in the change in functional status from transplantation to the follow-up period between the Pre- and Post-Share 35 periods averaged over the sample, when all else is equal.

H3a. Share 35 resulted in less post-transplant disability, when controlling for medical status / disability at transplant, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality), health literacy and post-discharge environment.

Hypothesis 3a states that when controlling for medical condition / disability at transplant, Share 35 is likely to result in less post-transplant disability. As both outcomes (work status and functional status) are defined such that a higher value means less disability, the hypothesis will

be supported if the marginal effects of Share 35 on these outcomes are positive and statistically significant at a p-value of <0.05.

H3b. The effect of Share 35 in reducing post-transplant disability will be greater amongst patients transplanted with a high allocation MELD score, when controlling for medical status / disability at transplant, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality), health literacy and post-discharge environment.

Hypothesis 3c indicates that the effect of Share 35 is dependent on a patient's allocation MELD score; such that patients with higher allocation MELD scores will have a greater decrease in post-transplant disability associated with Share 35, whereas patients with lower allocation MELD scores will have less of an effect or no effect. For either outcome (work status or functional status), this hypothesis will be supported by a positive and statistically significant marginal effect of the interaction between Share 35 and allocation MELD scores at allocation MELD scores of 35 or higher.

Sensitivity Analyses

Two sensitivity analyses were completed addressing inclusion of patients who underwent simultaneous liver and kidney transplant and the use of a categorical or continuous interaction term for allocation MELD score. All sensitivity analyses were completed utilizing the main model (not subdivided by UNOS region) for both the admissions and admitted days models. The allocation MELD sensitivity analysis was only completed for H3b because the interaction term is not included in the models for H3a. If sensitivity analyses detected a difference, further analysis was completed to assess possible explanations for the detected effect.

Inclusion of Patients who Underwent Simultaneous Liver and Kidney Transplant

Within the work and functional status cohorts approximately 8% of patients underwent simultaneous liver and kidney transplant. To assess whether the results of the regression change with inclusion of these patients, a sensitivity analysis was completed comparing the significance, direction and magnitude of marginal effects for the covariates of interest with the inclusion and exclusion of liver + kidney recipients. If no difference was detected between models, then inclusion of the patients who underwent simultaneous liver and kidney transplant is preferred.

Allocation MELD Score as a Categorical Predictor

In parallel with the sensitivity analysis done for Question 2, allocation MELD score was tested as both a binary and categorical predictor in the interaction term utilized for H3b. Dummy variables were constructed as previously discussed. If no difference was detected between models, use of allocation MELD score as a continuous variable is preferred.

7.7 Missing Data

For the six-state cohort (utilized for question one and two), there were no missing data amongst the outcomes of interest (admissions and admitted days). There was a small degree of missingness amongst the covariates of interest within both the Pre-Share 35 and Post-Share 35 cohorts (Table 7 – 3). Given the desire to preserve case inclusion, imputation was utilized for missing values. Although multiple imputation is the gold standard, in order to report results in terms of marginal effects, a single imputed dataset was required for the final analysis, as marginal effects cannot be produced from a multiply imputed dataset. Current literature supports using multiple imputation to create multiple imputed datasets and then selecting the imputed dataset with the best fit statistics for final modeling when marginal effects are desired.[127] To assure that single imputation did not produce different results as compared to multiple

imputation, a sensitivity analysis was completed, comparing coefficient estimates between the multiply imputed and single imputation datasets. Due to limitations of multiple imputation software, models were completed using Poisson and negative binomial regression rather than zero-truncated Poisson and zero-truncated negative binomial. The sensitivity analyses, comparing the model results for covariates of interest with single and multiple imputation are included in Appendix 4A for question one and in Appendix 5A for question two. All four sensitivity analyses demonstrated consistent results across coefficient estimates, standard error and statistical significance. Therefore for both questions one and two, single imputation with the imputed model with the best overall fit statistics was used for the reported analysis.

Table 7 – 3. Missing Data within the Pre- and Post-Share 35 Cohorts

	Question 1 Pre-Share 35 n = 4860		**Question 3** Pre-Share 35 n = 4681		Post-Share 35 n = 1475	
Covariate	**Missing**	**%**	**Missing**	**%**	**Missing**	**%**
Education	434	8.93%	411	8.78%	70	4.75%
Income by zip code	55	1.13%				
Rural / Urban Continuum	11	0.23%				
Hospital Density	11	0.23%	11	0.23%	4	0.27%
Primary care density	47	0.97%	11	0.23%	4	0.27%
Specialty care density	47	0.97%	11	0.23%	4	0.27%
Functional status at transplant	2	0.04%	1	0.02%	1	0.07%
Donor Risk Index	28	0.58%				
Distance from transplant center	60	1.23%				

	Question 4 - Work Status Pre-Share 35 n = 6887		Post-Share 35 n = 7089		**Question 4 - Functional Status** Pre-Share 35 n = 16,526		Post-Share 35 n = 18,664	
Covariate	**Missing**	**%**	**Missing**	**%**	**Missing**	**%**	**Missing**	**%**
Education	588	8.50%	340	4.80%	1549	9.40%	1000	5.36%
Functional status at transplant	44	0.64%	60	0.85%	55	0.30%	127	0.68%
Functional status at listing					502	3.04%	395	2.11%

8. Results

8.1 Descriptive Comparisons

8.1.1 Characterizing Regional Variability & Likely Response to Share 35

In order to characterize the regions, the median allocation MELD scores and the rate of MELD score ≥35 were calculated for each region utilizing only the Pre-Share 35 time period. The variability by region is indicated in Figure 8 – 1. Additionally, within-region variability was assessed by comparing median allocation MELD scores and the rate of allocation MELD scores ≥35 for each DSA within a region (Figures 8 – 2). As defined in the methods section, both acuity and variability for each region were ranked as high, moderate or low, based on the rate of very high MELD allocation and the greatest difference between any two DSAs within a single region. These differences are summarized in Table 8 – 1. Considering both regional acuity and intra-regional variability, the regions were grouped into high, moderate or low predicted response groups based on their likelihood of a response to Share 35. The high predicted response group included regions 1, 5, 7 and 9; moderate predicted response included regions 2, 3, 4, and 10; low predicted response included regions 6, 8, and 11. These groups are utilized during evaluation of hypothesis three and are referenced in the discussion.

Figure 8 – 1. Regional Variability by (A) Median Allocation MELD Score and (B) Proportion of Patients with an Allocation MELD Score ≥ 35. (A) indicates the median allocation MELD score within each UNOS region in the Pre-Share 35 period (January 2010 – May 2013), and (B) indicates the proportion of patients within each UNOS region with an allocation MELD score ≥35 in the Pre-Share 35 period

(A) **(B)**

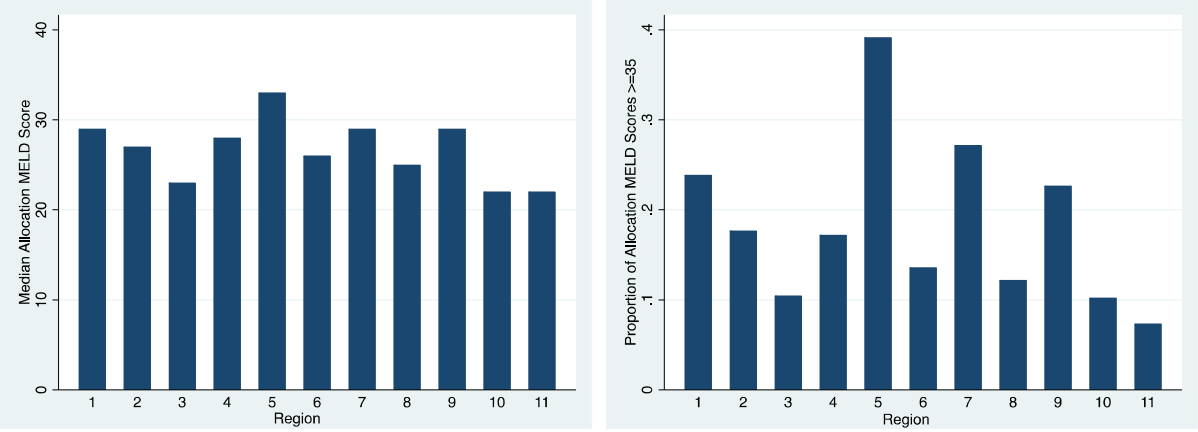
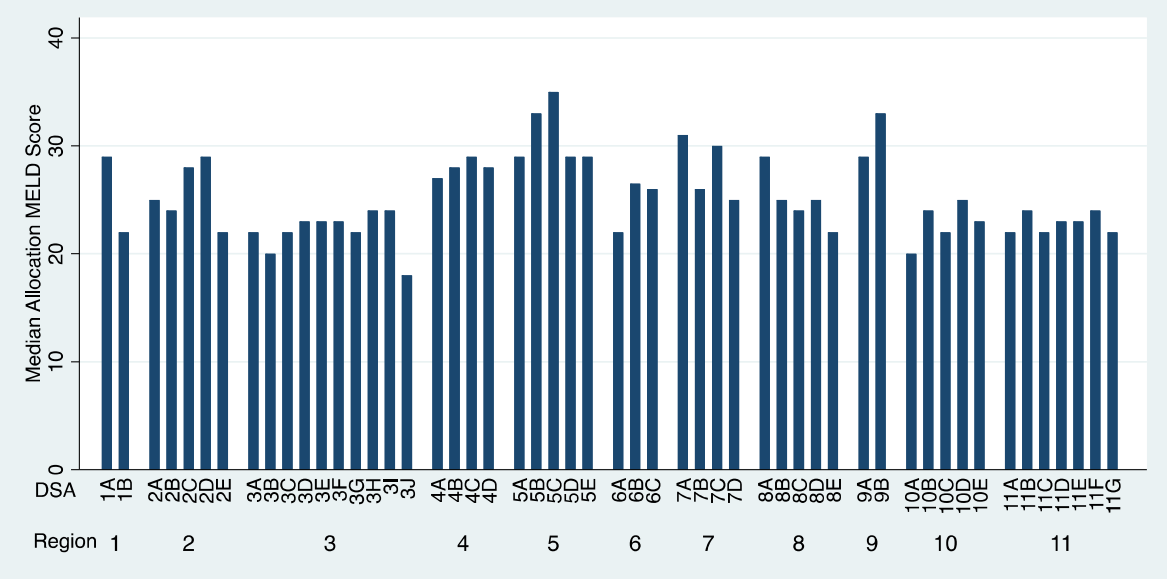


Figure 8 – 2. Intra-Regional Variability in (A) Median Allocation MELD Score and (B) Proportion of Patients with an Allocation MELD Score ≥ 35 by DSA. Graphs indicates the median allocation MELD score (A) and proportion of patients with an allocation MELD score ≥35 (B) within each DSA, grouped by UNOS region, in the Pre-Share 35 period (January 2010 – May 2013).

(A)



(B)

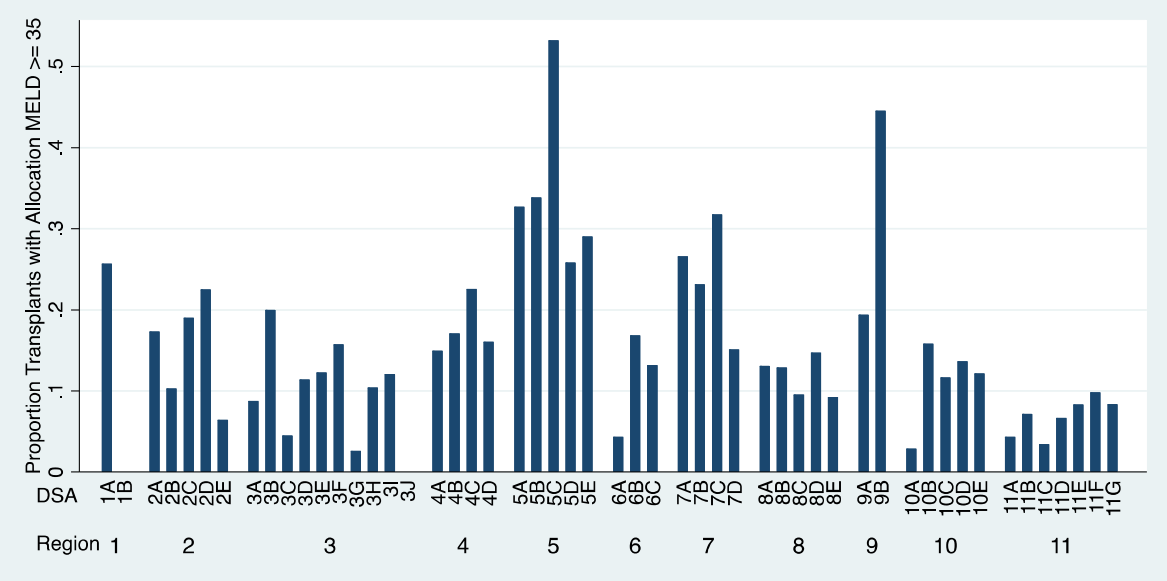

Proportion Transplants with Allocation MELD >= 35
0
.1
.2
.3
.4
.5
DSA
1A 1B 2A 2B 2C 2D 2E 3A 3B 3C 3D 3E 3F 3G 3H 3I 3J 4A 4B 4C 4D 5A 5B 5C 5D 5E 6A 6B 6C 7A 7B 7C 7D 8A 8B 8C 8D 8E 9A 9B 10A 10B 10C 10D 10E 11A 11B 11C 11D 11E 11F 11G
Region 1 2 3 4 5 6 7 8 9 10 11

Table 8 – 1. Summary of Regional Acuity & Intra-Regional Variability by Region and Predicted Effect of Share 35.

	Pre-Share 35 Acuity	Pre-Share 35 Intra-regional Variability	Likelihood of Responding to Share 35	Change in Acuity Post-Share 35 (UC)	Change in Acuity Post-Share 35 (NC)
Region 1	↑ 23.9%	*	High	--	--
Region 2	-- 17.7%	-- 16.1%	Moderate		+ 10.1%
Region 3	-- 10.4%	-- 11.3%	Moderate	+ 6.4%	+ 6.4%
Region 4	-- 17.2%%	↓ 7.6%	Moderate		+ 13.5%
Region 5	↑ 39.1%	↑ 39.1%	High	+ 11.5%	+ 11.2%
Region 6	-- 13.6%	↓ 3.7%	Low		+ 9.0%
Region 7	↑ 27.2%	-- 16.7%	High		+ 3.5%
Region 8	-- 12.2%	↓ 5.5%	Low	+ 6.4%	+ 6.9%
Region 9	↑ 22.7%%	↑ 25.2%	High	--	--
Region 10	-- 10.2%	-- 13.0%	Moderate		+ 2.4%
Region 11	↓ 7.3%	↓ 6.4%	Low		+ 5.1%

↑ = High (>20% acuity or variability), -- = Moderate (10-20%), ↓ = Low (<10%). Pre-Share 35 acuity indicates the rate of very high (allocation MELD ≥35) MELD allocation in the Pre-Share 35 period (1/2010 - 5/2013). Pre-Share 35 Intra-Regional Variability indicates the greatest difference in rate of very high MELD allocation between any two DSAs within the region. Likelihood of Responding to Share 35 indicates the predicted effect of Share 35 within the region based on the Pre-Share 35 acuity and intra-regional variability (? = unclear effect). Change in Acuity Post-Share 35 indicates the change in the rate of very high MELD allocation between the Pre-Share 35 period and Post-Share 35 period for the Utilization Cohort (UC), where the Post-Share 35 period is inclusive of transplants from 6/1/2013 - 12/1/2014 (cross-hatched boxes indicate regions not included within the UC), and for the National Cohort (NC) is inclusive of transplants from 6/1/2013 - 11/1/2016. Only statistically significant differences in acuity in the Post-Share 35 period are included in the figure. *Region1 includes only 2 DSAs, and 1 DSA does <30 transplants per years, therefore no intra-regional comparisons based on variability could be made.

8.1.2 National, Regional & DSA Level Changes Associated with Share 35

National Cohort

From January 1, 2010 to November 1, 2016, 36,601 patients underwent liver transplantation and met the inclusion criteria for the national cohort (age ≥18, no history of prior organ transplantation, underwent liver or liver + kidney transplantation only, recipient of a deceased donor transplant, received an organ through MELD based allocation); 17,059 prior to and 19,542 following Share 35 implementation.

To assess differences that occurred following policy implementation, a national analysis comparing the Pre- and Post-Share 35 patient cohorts was completed. Analysis at the national level indicated that patients undergoing transplantation after Share 35 implementation were older (56.4 versus 55.6 years, $p<0.001$), more likely to have significant medical comorbidities (diabetes (28.7% versus 26.1%, $p<0.001$) or renal failure (16.8% versus 14.0%)) (Appendix 3A). Patients were also more acute by both physiologic and allocation MELD scores at listing and at transplant ($p<0.001$ for all), more likely to require life support measures, be ventilator dependent or dialysis dependent, and more likely to be in the ICU at the time of transplant. Overall functional status was also lower at both listing and transplant in the Post-Share 35 period ($p<0.001$ for both). Overall, at the national level, the Post-Share 35 cohort was more acutely and chronically ill and had a slightly lower functional status at the time of transplant.

Analysis at the regional level indicates that these changes in acuity are not consistent across the regions, but that overall, most regions saw an increase in patient acuity following Share 35 (Appendix 3B). Table 8 – 2 summarizes the different markers for acuity by region. All regions, except Regions 1 and 8, saw an increase in mean allocation MELD score, and all

regions, except Region 7, saw an increase in the rate of high MELD allocation (allocation MELD ≥30). All regions, except Regions 1 and 9, saw an increase in the rate of very high MELD allocation (allocation MELD ≥35), likely secondary to the Share 35 policy. Regions 2 – 6 and 11 saw the most increases in patient acuity across most markers of acuity, with the majority of these regions experiencing increases in the rate of ICU or hospital admissions prior to transplantation, need for life support measures prior to transplant, ventilator and hemodialysis dependence.

Table 8 – 2. Changes in Patients Acuity after Implementation of Share 35 by UNOS Regions. Statistically significant decreases in acuity are indicated in green with a downward arrow and increases in acuity in orange with an upward arrow. The difference in the rate or mean MELD score between the Pre- and Post-Share 35 period (Post – Pre) is indicated for each statistically significant change. Pre-Share 35 period inclusive of patients transplanted 1/2010 – 5/2013, and the Post-Share 35 period is inclusive of patients transplant 6/2013 – 11/1/2016.

Region	Physiologic MELD (mean)	Allocation MELD (mean)	Allocation MELD • 30 (%)	Allocation MELD • 35 (%)	Hospitalized or ICU prior to Transplant (%)	Life Support Measures (%)	Ventilator Dependent (%)	HD Dependent (%)	Mortality, 30 days (%)	Mortality, 90 days (%)
National	↑ 0.516 **	↑ 1.344 **	↑ 8.4% **	↑ 7.2% **	↑ 3.4% **	↑ 2.1% **	↑ 0.5% *	↑ 3.2% **	--	↓ 0.6% *
1	↓ -1.865 *	--	↑ 10.4% **	--	--	--	↓ 2.1% *	↑ 1.9% *	--	--
2	↑ 1.250 **	↑ 1.877 **	↑ 11.3% **	↑ 10.1% **	↑ 6.2% **	↑ 2.6 % **	↑ 1.7% *	↑ 4.5% **	--	--
3	--	↑ 1.682 **	↑ 7.6% **	↑ 6.4% **	↑ 3.5% **	↑ 2.3% **	↑ 1.2% *	↑ 4.6% **	--	--
4	↑ 1.536 **	↑ 1.415 **	↑ 13.9% **	↑ 13.5% **	↑ 6.9% **	↑ 4.5% **	↑ 2.8% *	↑ 5.0% **	--	--
5	↑ 0.691 *	↑ 0.824 **	↑ 5.4% **	↑ 11.2% **	↑ 3.5% **	↑ 4.4% **	--	↑ 5.2% **	--	--
6	--	↑ 2.410 **	↑ 15.7% **	↑ 9.0% **	↑ 9.4% *	--	--	↑ 5.5% *	--	--
7	--	↑ 0.713 *	--	↑ 3.5% *	--	↑ 2.9% *	--	--	--	--
8	--	--	↑ 4.2% *	↑ 6.9% **	--	↓ 1.5% *	--	--	--	↓ 1.6% *
9	--	↑ 1.308 **	↑ 12.5% **	--	--	--	--	--	↓ 2.9% *	↓ 3.8% *
10	↑ 0.728 *	↑ 0.982 **	↑ 4.9% **	↑ 2.4% *	--	--	--	↑ 3.0% *	--	--
11	↑ 1.148 **	↑ 2.096 **	↑ 9.4% **	↑ 5.1% **	↑ 5.8% **	↑ 2.0% *	--	↑ 2.3% *	--	--

-- no statistically signficant change, * p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, HD - hemodialysis.

Further analysis at the DSA level also indicates that Share 35 had a variable effect on markers of patient acuity (Table 8 – 3). In particular DSAs within Region 2, 4, 5, 10, and 11

almost universally saw an increase in patient acuity. DSAs within Region 9 saw a decrease across many parameters, most notably mortality. It is also of note that some regions, such as Region 1, 5, 7 and 9 had a single DSA with a decrease in acuity while the remaining DSAs almost universally increased in acuity. This difference in response to Share 35 may be seen in these regions due to the baseline variability, where a single DSA was lower in acuity as compared to other DSAs within the region.

Table 8 – 3. Changes in Patient Acuity after Implementation of Share 35 by Donor Service Areas (DSA). Statistically significant decreases in acuity are indicated in green with a downward arrow and increases in acuity in orange with an upward arrow. The Pre-Share 35 period inclusive of patients transplanted 1/2010 – 5/2013, and the Post-Share 35 period is inclusive of patients transplant 6/2013 – 11/1/2016.

	Physiologic MELD	Allocation MELD	Allocation MELD • 30	Allocation MELD • 35	Hospitalized or ICU prior to Transplant	Life Support Measures	Ventilator Dependent	HD Dependent	Mortality, 30 days	Mortality, 90 days
Region 1										
1A	↓	--	↑	--	↓	--	↓	↓	--	--
1B	--	↑	--	--	--	--	--	--	--	--
Region 2										
2A	↑	↑	↑	↑	↑	↑	↑	↑	--	--
2B	↑	↑	--	↑	↑	--	--	↑	--	--
2C	--	↑	↑	↑	--	--	--	↑	--	--
2D	--	--	--	--	--	--	--	--	--	--
2E	↑	↑	↑	↑	↑	↑	↑	↑	--	--
Region 3										
3A	--	↑	--	↑	--	--	--	--	--	--
3B	--	--	--	--	--	--	--	--	--	--
3C	↑	↑	↑	↑	↑	↑	↑	↑	--	--
3D	↓	--	--	--	↑	↑	--	--	--	--
3E	↓	--	--	--	↓	--	--	--	--	--
3F	--	--	--	--	--	--	--	--	--	--
3G	↑	↑	↑	↑	↑	--	--	↑	--	--
3H	↑	↑	↑	↑	↑	--	--	↑	--	--
3I	--	↑	↑	↑	↑	--	--	--	--	--
3J	--	--	--	--	--	--	--	--	--	--
Region 4										
4A	↑	↑	↑	↑	--	--	--	--	--	--
4B	↑	↑	↑	↑	↑	↑	↑	↑	--	--
4C	--	--	--	↑	↑	--	--	--	--	--
4D	--	--	↑	↑	--	--	--	--	--	--
Region 5										
5D	↓	↓	--	--	↓	--	--	--	--	--
5A	--	↑	↑	↑	--	--	--	--	--	--
5B	--	↑	↑	↑	↑	--	--	--	--	--
5C	↑	↑	↑	↑	↑	--	--	↑	--	--
5E	--	↑	↑	↑	--	--	--	↑	--	--
Region 6										
6A	--	↑	↑	--	--	--	--	--	--	--
6B	--	--	--	--	--	--	--	--	--	--
6C	↑	↑	↑	↑	↑	--	--	↑	--	--
Region 7										
7A	--	--	--	--	--	--	--	--	--	--
7B	--	↓	↑	↑	--	↑	--	--	--	--
7C	↓	--	↓	--	--	↓	↓	↓	--	--
7D	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑
Region 8										
8A	--	↑	↑	↑	--	--	--	--	--	--
8B	--	--	--	--	--	--	--	--	--	--
8C	--	--	--	--	--	--	--	--	--	--
8D	↓	--	--	--	--	--	↓	--	--	--
8E	--	--	--	↑	--	--	--	--	--	--
Region 9										
9A	↓	↑	↑	↑	--	↓	--	--	--	↓
9B	↓	--	↑	--	--	--	--	--	↓	↓
Region 10										
10A	↑	--	↑	↑	--	--	--	↑	--	--
10B	--	--	--	--	--	--	--	--	--	--
10C	↑	↑	↑	↑	--	↑	--	--	--	--
10D	↓	↓	--	--	--	--	--	--	--	--
10E	--	↑	--	--	--	--	--	↑	--	--
Region 11										
11A	--	↑	↑	↑	--	--	--	--	--	--
11B	↑	↑	↑	↑	↑	--	--	↑	--	--
11C	--	↑	↑	↑	↑	--	--	--	--	--
11D	--	↑	--	--	--	--	--	--	--	--
11E	--	↑	↑	--	--	--	--	--	--	--
11F	↑	↑	↑	↑	--	--	--	↑	--	--
11G	↑	↑	↑	↑	↑	↑	↑	↑	--	--

Utilization Cohort

Similar findings were identified when the cohort was truncated to meet the study period for the UC. A detailed description of the regional analysis for the UC is included in Appendix 3C.

8.1.2 Comparison Between Pre- and Post-Share 35 within the 5 Regions Included in the Utilization Analysis

From January 1, 2010 until June 30, 2014, 8,307 patients underwent transplantation within the regions (1, 3, 5, 8 and 9) included in the utilization analysis (research question 1 and 2). To assess potential changes within regions in response to Share 35, MELD scores (physiologic and allocation), patient acuity and mortality were assessed across the regions and DSAs between the Pre- and Post-Share 35 periods. Summary findings are discussed for each Region below, and a detailed description of each region is included in Appendix 3D – 3G.

Region 1

Within Region 1, 866 patients underwent liver transplantation during the study period, 666 and 200 patients in the Pre- and Post-Share 35 periods respectively. There are 2 DSAs within this Region 1, yet DSA 1A performs the majority of transplants (DSA 1A performed 93.0% of the transplants over the entire study period, 600 Pre-Share 35 and 186 Post-Share 35).

Changes in patient acuity across Region 1 and within each DSA are summarized in Table 8 – 4 and detailed in Appendix 3D. Overall, there was a substantial increase in the rate of transplantation to patients with allocation MELD scores ≥30, but no change in the allocation to patients with allocation MELD scores ≥35. Additionally, decreases were seen in physiologic MELD at transplant and the rate of ICU prior to transplant. All changes identified occurred primarily within DSA1A, which were then reflected at the regional level due to the predominance of transplants done within this DSA.

Table 8 – 4. Changes in Patients Acuity after Implementation of Share 35 for Region 1 by Donor Service Area (DSA). Statistically significant decreases in acuity are indicated in green with a downward arrow and increases in acuity in orange with an upward arrow. The difference in the rate or mean MELD score between the Pre- and Post-Share 35 period (Post – Pre) is indicated for each statistically significant change.

	Physiologic MELD (mean)	Allocation MELD (mean)	Allocation MELD • 30 (%)	Allocation MELD • 35 (%)	Hospitalized prior to Transplant (%)	ICU prior to Transplant (%)	Life Support Measures (%)	Ventilator Dependent (%)	HD Dependent (%)	Mortality, 30 days (%)	Mortality, 90 days (%)
Region 1	• -2.10 *	--	• 10.4% *	--	--	• 6.0% *	--	--	--	--	--
DSA 1A	• -2.02 *	--	• 13.7% *	--	--	• 6.4% *	--	--	--	--	--
DSA 1B	--	--	--	--	--	--	--	--	--	--	--

-- no statistically signficant change, * p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, HD - hemodialysis.

Region 3

Within Region 3, 4,147 patients underwent liver transplantation during the study period, 3,130 Pre-Share 35 and 1,017 Post-Share 35. There are 10 DSAs within Region 3, there are 3 larger DSAs (3E, 3H, and 3I), each conducting approximately 20% of the transplants, 3 medium DSAs (3A, 3C, and 3D) which each conduct approximately 10% of the transplants, and 4 smaller DSAs (3B, 3F, 3G, and 3J) which each conduct <10% of the transplants.

Changes in patient acuity across Region 3 and within each DSA are summarized in Table 8 – 5 and detailed in Appendix 3E. Overall, the region had significant increases in acuity across all measures, with an increase in the rate of allocation to high and very high allocation MELD scores of 7.4% and 6.4% respectively. The majority of the changes occurred in 4 DSAs (3A, 3C, 3G and 3H), while 6 DSAs saw little to no change associated with the policy.

Table 8 – 5. Changes in Patients Acuity after Implementation of Share 35 for Region 3 by Donor Service Area (DSA). Statistically significant decreases in acuity are indicated in green with a downward arrow and increases in acuity in orange with an upward arrow. The difference in the rate or mean MELD score between the Pre- and Post-Share 35 period (Post – Pre) is indicated for each statistically significant change.

	Physiologic MELD (mean)	Allocation MELD (mean)	Allocation MELD • 30 (%)	Allocation MELD • 35 (%)	Hospitalized prior to Transplant (%)	ICU prior to Transplant (%)	Life Support Measures (%)	Ventilator Dependent (%)	HD Dependent (%)	Mortality, 30 days (%)	Mortality, 90 days (%)
Region 3	• 0.661 *	• 1.743 **	• 7.4% **	• 6.4% **	• 4.4% *	• 3.9% **	• 6.4% **	• 2.3% **	• 2.7% *	--	--
DSA 3A	--	• 2.754 *	--	• 10.9% **	• 11.4% *	• 10.9% *	--	--	--	--	--
DSA 3B	--	--	--	--	--	• -20.0% *	--	--	--	--	--
DSA 3C	• 1.857 *	• 3.835 **	• 11.4% *	• 12.4% *	• 10.5% *	• 10.1% **	• 5.4% **	• 5.4% **	--	--	--
DSA 3D	--	--	--	--	--	--	• 3.4% *	--	--	--	--
DSA 3E	--	--	--	--	--	--	--	--	--	--	--
DSA 3F	--	--	--	--	--	• 17.6% *	--	--	--	--	--
DSA 3G	--	• 3.385 *	• 21.5% *	• 13.0% *	--	• 5.7% *	• 6.3% *	• 6.3% *	--	--	--
DSA 3H	• 0.620 **	• 2.695 **	• 15.6% *	• 9.7% *	• 11.6% *	• 7.0% *	• 5.6% *	• 4.1% *	• 9.3% **	--	--
DSA 3I	--	• 3.051 **	• 10.7% *	--	--	--	--	--	--	--	--
DSA 3J	--	--	--	--	--	--	--	--	--	--	--

-- no statistically signficant change, * p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, HD - hemodialysis.

Region 5

There were 3,170 patients who underwent liver transplantation in Region 5 during the study period, 2,410 prior to Share 35, and 760 following implementation of Share 35. Within Region 5 there are 5 DSAs, two large DSAs (5B and 5C) which each complete more than 30% of the region's transplants, one moderate sized DSA (5D) which makes up 16% and then two smaller DSAs which each complete less than 10% of the region's transplants (DSAs 5A and 5E).

Changes in patient acuity across Region 5 and within each DSA are summarized in Table 8 – 6 and Appendix 3F. Overall the region saw significant increases across all markers of acuity, except ventilator dependence, with an increase in the rate of very high MELD allocation by

11.5%. The majority of changes occurred within the two largest DSAs (5B and 5C) and the smallest DSA (5E).

Table 8 – 6. Changes in Patients Acuity after Implementation of Share 35 for Region 5 by Donor Service Area (DSA). Statistically significant decreases in acuity are indicated in green with a downward arrow and increases in acuity in orange with an upward arrow. The difference in the rate or mean MELD score between the Pre- and Post-Share 35 period (Post – Pre) is indicated for each statistically significant change.

	Physiologic MELD (mean)	Allocation MELD (mean)	Allocation MELD • 30 (%)	Allocation MELD • 35 (%)	Hospitalized prior to Transplant (%)	ICU prior to Transplant (%)	Life Support Measures (%)	Ventilator Dependent (%)	HD Dependent (%)	Mortality, 30 days (%)	Mortality, 90 days (%)
Region 5	• 1.142 *	• 0.954 **	• 4.9% *	• 11.5% **	• 5.0% *	• 8.9% **	• 3.1% **	--	• 6.4% *	--	--
DSA 5A	--	--	• 16.9% *	--	--	--	--	--	--	--	--
DSA 5B	--	• 1.203 *	--	• 15.3% **	• 7.6% *	• 13.1% **	--	• 2.6% *	--	--	--
DSA 5C	--	• 1.124 *	--	• 10.0% *	--	--	--	--	• 10.7% *	--	--
DSA 5D	--	• 1.992 *	--	--	--	--	--	--	--	--	--
DSA 5E	• 5.714 *	• 3.384 **	• 28.5% **	• 24.9% **	• 16.9% *	• 18.0% *	• 7.5% *	• 6.2% *	• 20.2% **	--	--

-- no statistically signficant change, * p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, HD - hemodialysis.

Region 8

Within Region 8, 1,635 patients underwent transplantation during the study period, 1,254 Pre-Share 35 and 381 Post-Share 35. There are 5 DSAs within Region 8, 4 larger DSAs which each account for 17-29% of the region's transplants, and 1 smaller DSA which accounts for 8.5% of the region's transplants.

Changes in patient acuity across Region 8 and within each DSA are summarized in Table 8 – 7 and Appendix 3G. While there was a significant increase in the rate of allocation to very high MELD scores (6.4%), there was no additional indications of an increase in patient acuity. This increase in very high MELD allocation occurred primarily in DSAs 8A and 8E that saw greater than 10% increases. Of note, this region had a small decrease in 90 day mortality after the implementation of Share 35, a trend that was not seen in other regions during this time.

Table 8 – 7. Changes in Patients Acuity after Implementation of Share 35 for Region 8 by Donor Service Area (DSA). Statistically significant decreases in acuity are indicated in green with a downward arrow and increases in acuity in orange with an upward arrow. The difference in the rate or mean MELD score between the Pre- and Post-Share 35 period (Post – Pre) is indicated for each statistically significant change.

	Physiologic MELD (mean)	Allocation MELD (mean)	Allocation MELD • 30 (%)	Allocation MELD • 35 (%)	Hospitalized prior to Transplant (%)	ICU prior to Transplant (%)	Life Support Measures (%)	Ventilator Dependent (%)	HD Dependent (%)	Mortality, 30 days (%)	Mortality, 90 days (%)
Region 8	--	--	--	• 6.4% **	--	--	• -2.3% *	--	--	--	• -2.4% *
DSA 8A	• 3.378 *	--	• 13.7% *	• 17.8% **	• 11.9% *	--	--	--	--	--	--
DSA 8B	--	--	--	--	--	--	--	--	--	--	--
DSA 8C	--	--	--	• 7.6% *	--	--	• -3.9% *	--	--	--	--
DSA 8D	• -4.169 *	• -3.278 *	• 19.0% *	--	--	--	--	--	--	--	--
DSA 8E	--	--	--	• 13.3% *	--	--	--	--	--	--	--

-- no statistically signficant change, * p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, HD - hemodialysis.

Region 9

A total of 1,107 patients underwent liver transplantation in Region 9 during the study period, 847 prior to Share 35 and 260 after Share 35 implementation. There are 2 DSAs within Region 9, DSA 9A contains the majority of transplants (88.1%), while DSA 9B only completes a minority (12.0%).

Changes in patient acuity across Region 9 and within each DSA are summarized in Table 8 – 8 and Appendix 3H. A small increase was seen in the mean allocation MELD score and rate of high MELD allocation for the region which are reflective of changes within the largest DSA (9A). There were not statistically significant changes notes within the smaller DSA (9B).

Table 8 – 8. Changes in Patients Acuity after Implementation of Share 35 for Region 9 by Donor Service Area (DSA). Statistically significant decreases in acuity are indicated in green with a downward arrow and increases in acuity in orange with an upward arrow. The difference in the rate or mean MELD score between the Pre- and Post-Share 35 period (Post – Pre) is indicated for each statistically significant change.

	Physiologic MELD (mean)	Allocation MELD (mean)	Allocation MELD • 30 (%)	Allocation MELD • 35 (%)	Hospitalized prior to Transplant (%)	ICU prior to Transplant (%)	Life Support Measures (%)	Ventilator Dependent (%)	HD Dependent (%)	Mortality, 30 days (%)	Mortality, 90 days (%)
Region 9	--	• 1.359 *	• 11.8% *	--	--	--	--	--	--	--	--
DSA 9A	--	• 1.682 *	• 13.7% **	• 6.4% *	--	--	--	--	--	--	--
DSA 9B	--	--	--	--	--	--	--	--	--	--	--

-- no statistically signficant change, * p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, HD - hemodialysis.

8.2 Question 1: Factors associated with inpatient utilization among liver transplant patients in the post-transplant period.

8.2.1 Descriptive Statistics

A total of 4,860 patients in the six-state cohort underwent primary liver transplantation in the Pre-Share 35 period (January 1, 2010 and May 31, 2013). Patient demographics and covariate descriptive statistics are included in Table 8 – 9. Patients ranged in age from 18-80, with a mean of 55.7 years; two-thirds of the patients were male and over 60% were white, non-Latino. Patients are clustered within transplant centers, of which there are 29. Transplant volume by state and center are included in Appendix 4B. Transplant center annual volumes were relatively stable over the study period.

The primary outcomes for question 1 are the total number of admissions and total admitted days following transplantation. Both outcomes have non-normal distributions given that each represent count data with long right tails (Figure 8 – 3). The median number of admissions was 2 (range 1 – 15), and the median admitted days was 17 (range 1 – 180). The mean and

variance for each distribution were calculated, indicating that the variance approximates the mean for number of admissions (mean 2.21, variance 2.45), and that the variance is much greater than the mean for number of admitted days (mean 27.95, variance 832.07), supporting the use of Poisson and negative binomial distributions respectively. Both outcomes were inclusive of the index transplant admission, and therefore took on only positive values, as such, zero-truncated distributions were preferred.

Table 8 – 9. Descriptive Statistics of Pre-Share 35 Utilization Cohort. (A) Categorical covariates, (B) Continuous covariates, (C) Outcome variables by entire cohort and regions.
A.

Patient Preferences	**n**	%
Race / Ethnicity		
White, non-latino	2,931	60.31
White, latino	1,058	21.77
Black	427	8.79
Asian	408	8.40
Native American	19	0.39
Other	17	0.35
Sex		
Male	3212	66.09
Female	1648	33.91
Medical Condition / Disability at Transplant		
Medical Comorbidities		
COPD	1064	21.89
Diabetes	1217	25.04
Hypertension	1650	33.95
Renal failure	1311	26.98
Vascular disease	487	10.02
Liver Disease Etiology		
Acute liver failure	232	4.77
Autoimmune hepatitis	100	2.06
Cholestatic liver disease	292	6.01
Cryptogenic cirrhosis	208	4.28
Genetic/metabolic	87	1.79
Hepatitis C	839	17.26
Malignancy	1753	36.07
Steatohepatitis	1179	24.26
Other	170	3.50

Ability to Pay for Care	n	%
Primary Insurance Coverage		
Private insurance	2,583	53.15
Medicare	1,248	25.68
Medicaid	952	19.59
Veterans Affairs	20	0.41
Self-Pay	12	0.25
Other	45	0.93
Education		
Less than High School / GED	360	7.41
High School / GED	1,815	37.35
Some college or technical school	1,153	23.72
Associate or bachelors degree	779	16.03
Post-college graduate degree	319	6.56
Unknown/missing	434	8.93
Zip Code Median Income		
1st Quartile	906	18.64
2nd Quartile	1086	22.35
3rd Quartile	1331	27.39
4th Quartile	1482	30.49
Unknown/missing	55	1.13
Post-Discharge Environment		
Rural / Urban Continuum		
Completely rural or <2500 urban pop.	17	0.35
Urban 2500 - 20,000 pop.	109	2.24
Urban >20,000 pop.	114	2.35
Metropolitan <250,000 pop.	244	5.02
Metropolitan 250,000 - 1 mill. Pop.	958	19.71
Metropolitan >1 mill. Pop.	3407	70.10
Unknown/missing	11	0.23

Primary insurance coverage indicates the patient's primary payer at the time of transplantation. Steatohepatitis is inclusive of non-alcoholic steatohepatitis and alcoholic steatohepatitis. Zip code median income is the median income of the patient's home zip code as it corresponds to the national quartiles for income during the calendar year the patient underwent transplantation. Rural / Urban Continuum is based on the patient's county classification by the 2013 Rural-Urban Continuum codes. Abbreviations: GED - General equivalency diploma, COPD - chronic obstructive pulmonary disease, mill. – million, pop. – population.

B.

Patient Preferences	n	Mean	Range	Std Dev.
Age (years)	4860	55.67	(18 - 80)	9.83
Supply of Inpatient Medical Services				
Acute Care Hospital Density	4849	2.39	(0 - 13.08)	1.19
Supply of Outpatient Medical Services				
Primary Care Density	4849	0.03	(0 - 0.21)	0.02
Specialty Care Density	4849	0.05	(0 - 0.18)	0.03
Medical Condition / Disability at Transplant				
Liver Disease Severity				
Physiologic MELD at Transplant	4860	22.56	(6 - 40)	10.74
Functional Status				
Karnofsky Score at Transplant	4858	50.49	(10 - 100)	24.99
Donor Organ Quality				
Donor Risk Index	4832	1.63	(0.95 - 3.65)	0.39
Post-Discharge Environment				
Distance from Transplant Center				
Minutes	4800	66.20	(0 - 483.52)	61.09

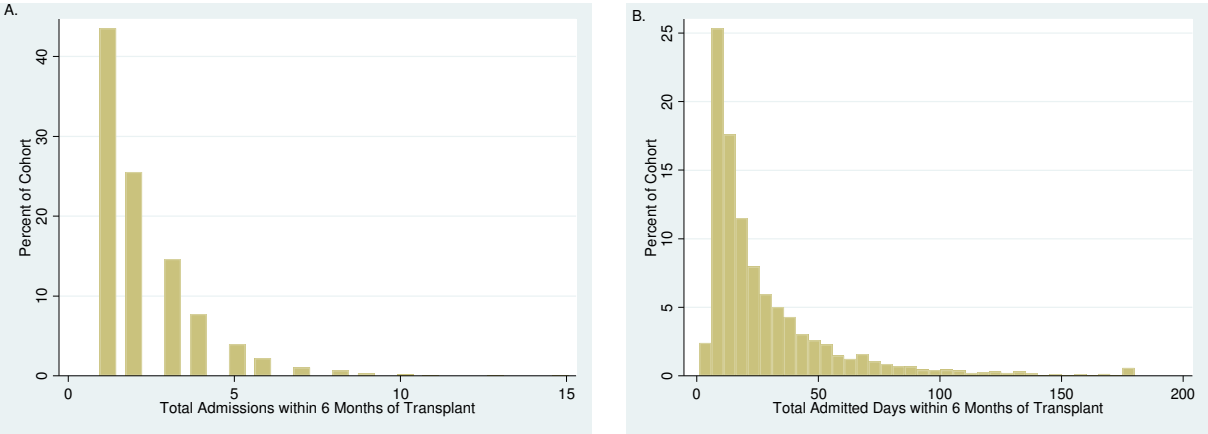
Acute care hospital density is the number of hospital beds per 1,000 census population for patient's home county; PCP density is the number of practicing primary care providers per 1,000 census population for patient's home county; Specialty care density is the number of practicing outpatient gastroenterologists per 1,000 census population for patient's home county. Travel distance to the transplant center was calculated from the patient's home zip code or if zip was unavailable their county centroid.
Abbreviations: MELD - model for end stage liver disease.

C.

	All Patients n = 4860		Region 1 n = 412		Region 3 n = 1798		Region 5 n = 1814		Region 8 n = 96		Region 9 n = 740	
Admissions	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
1	2,116	43.5%	153	37.1%	836	46.5%	731	40.3%	64	66.7%	332	44.9%
2	1,242	25.6%	90	21.8%	483	26.9%	473	26.1%	14	14.6%	182	24.6%
3	712	14.7%	68	16.5%	235	13.1%	297	16.4%	8	8.3%	104	14.1%
4	377	7.8%	47	11.4%	125	7.0%	128	7.1%	8	8.3%	69	9.3%
5	193	4.0%	24	5.8%	54	3.0%	87	4.8%	1	1.0%	27	3.6%
≥ 6	220	4.5%	30	7.3%	65	3.6%	98	5.4%	1	1.0%	26	3.5%
Admitted Days												
<= 14 days	2,084	42.9%	142	34.5%	928	51.6%	687	37.9%	45	46.9%	282	38.1%
15 - 30 days	1,356	27.9%	133	32.3%	492	27.4%	502	27.7%	27	28.1%	202	27.3%
31 - 60 days	908	18.7%	99	24.0%	256	14.2%	380	20.9%	16	16.7%	157	21.2%
61 - 90 days	297	6.1%	27	6.6%	67	3.7%	134	7.4%	7	7.3%	62	8.4%
>90 days	215	4.4%	11	2.7%	55	3.1%	111	6.1%	1	1.0%	37	5.0%

Number of admissions is inclusive of the transplant admission, and admitted days is inclusive of all days admitted during the index admission following transplantation.

Figure 8 – 3. Distribution of Cumulative Visits and Length of Stay within Six Months of Liver Transplantation. (A) distribution of individual admissions within six months of transplantation and (B) distribution of total inpatient length of stay within six months of transplantation.



8.2.2 Regression Analysis

Amongst the covariates included in the conceptual model, five (physiologic MELD, liver disease etiology / diagnosis, education, insurance and donor risk index) were the specific focus of hypotheses 1A – 1D. The regression model statistics and marginal effects for the complete model, inclusive of all covariates, are included in Appendix 4C and 4D for admissions and admitted days respectively.

Hypothesis 1A: Patients with a higher physiologic MELD score at transplant will have greater inpatient utilization in the post-transplant period, ceteris paribus.

Physiologic MELD score is a statistically significant predictor of both the number of admissions and total number of admitted days, such that each additional MELD point is associated with a 0.02 increase in the number of admissions and a 0.57 increase in the number of admitted days within the first six months following transplantation (Table 8 – 10). As such, the predicted number of admissions and admitted days for a patient with a physiologic MELD score of 15 is 1.69 and 25.85, compared to 2.14 and 40.91 for a patient with a physiologic MELD score of 40 at the time of transplantation (Table 8 – 10). This increase in predicted number of

admissions and admitted days is demonstrated in Figure 8 – 4. Based on both outcomes (admissions and admitted days), we reject the null hypothesis and conclude that patients with higher physiologic MELD scores at transplant will have greater inpatient utilization in the post-transplant period when all else is equal.

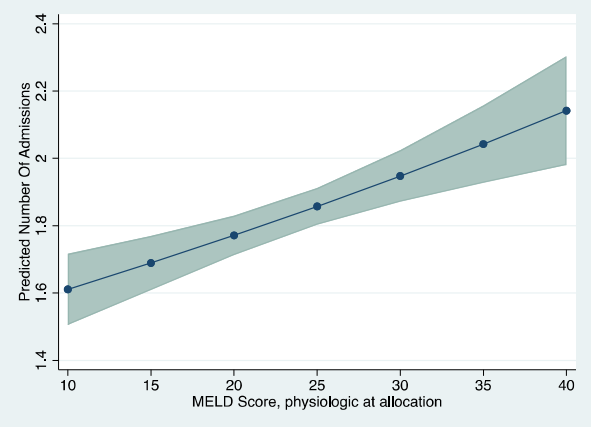
Table 8 – 10. Predicted Number of Admissions and Admitted Days by MELD Scores

	Increase in Admissions per physiologic MELD point increase	**SE**	**p-value**	**Increase in Admitted Days per physiologic MELD point increase**	**SE**	**p-value**
MELD	0.017	0.004	<0.001 **	0.573	0.077	<0.001 **
By Physiologic MELD Score	**Predicted Number of Admissions**	**SE**	**p-value**	**Predicted Number of Admitted Days**	**SE**	**p-value**
10	1.611	0.054	<0.001 **	23.577	0.979	<0.001 **
15	1.689	0.041	<0.001 **	25.845	0.795	<0.001 **
20	1.771	0.030	<0.001 **	28.331	0.616	<0.001 **
25	1.857	0.028	<0.001 **	31.055	0.538	<0.001 **
30	1.948	0.039	<0.001 **	34.042	0.707	<0.001 **
35	2.042	0.058	<0.001 **	37.316	1.097	<0.001 **
40	2.142	0.082	<0.001 **	40.905	1.637	<0.001 **

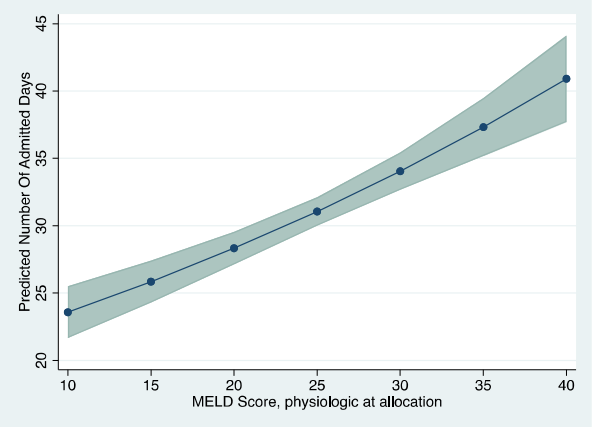
Marginal effects by zero-truncated Poisson regression for admissions and zero-truncated negative binomial for admitted days controlling for functional status, liver disease etiology, medical comorbidities, insurance, education, donor risk index, age, sex, race/ethnicity, access to care, post-discharge environment and transplant center. Increase in admissions per physiologic MELD point indicates linear change in number of admissions or admitted days for each additional physiologic MELD point. Predicted admissions or admitted days indicates the estimated number of admissions or days for the physiologic MELD score listed. Abbreviations: MELD - model for end stage liver disease, SE - standard error, CI - confidence interval

Figure 8 – 4. Predicted Number of Admissions and Admitted Days within Six months of Transplant by MELD Score. Point estimates plotted with shaded area of 95% confidence intervals. (A) Admissions, (B) Admitted Days.

A.



B.



Hypothesis 1B: Patients who are transplanted for malignancy will have less post-transplant inpatient utilization as compared to patients suffering from liver failure secondary to cirrhosis (steatohepatitis), ceteris paribus.

A primary liver diagnosis of malignancy was associated with an increased rate of admissions, such that malignancy was associated with 0.22 more predicted admissions as compared to steatohepatitis (Table 8 – 11). However, there was no statistically significant difference in admitted days between patients with cirrhosis and malignancy (Table 8 – 11). Given that the only difference in utilization between patients with malignancy and cirrhosis is in the number of admissions and not number of admitted days, we conclude that patients with malignancy have a greater likelihood of readmission after transplantation than those with cirrhosis, but that overall the number of admitted days is not significantly different between the two groups when all else is equal.

Table 8 – 11. Predicted Number of Admissions and Admitted Days by Liver Diagnosis

	Admissions			Admitted Days		
Liver Diagnosis	**Predicted number of admissions**	**Difference compared to steatohepatitis**	**p-value**	**Predicted number of admitted days**	**Difference compared to steatohepatitis**	**p-value**
Steatohepatitis	1.718			30.814		
Malignancy	1.934	0.216	0.011*	31.804	0.991	0.544

Predicted number of events by zero-truncated Poisson regression for admissions and zero-truncated negative binomial for admitted days controlling for physiologic model for end stage liver disease score at allocation, functional status, medical comorbidities, insurance, education, donor risk index, age, sex, race/ethnicity, access to care, post-discharge environment and transplant center. Differences indicate the difference in predicted mean number of admissions or admitted days as compared to the predicted number for patients with a primary diagnosis of steatohepatitis (non-alcoholic steatohepatitis or alcoholic steatohepatitis), p-value corresponds to differences as compared to steatohepatitis. * indicates $p<0.05$, ** $p<0.001$.

Hypothesis 1C: Patients with a lower ability to pay for care will have greater post-transplant inpatient utilization than patients with a greater ability to pay for care, ceteris paribus.

The ability to pay for care is defined by two measurement proxies, education and insurance status. Education, at any level, was not a significant predictor of either total number of admissions or admitted days (Table 8 – 12). Private insurance, when compared to Medicare or Medicaid was not a significant predictor of total number of admitted days, but Medicaid did approach statistical significance for total number of admissions, such that Medicaid insurance was associated with 0.15 more admissions than private insurance (Table 8 – 12). There was no significant difference between privately insured and Medicare for number of admissions. Test of joint significance indicate that there are no combinations of insurance status and education that are jointly significant ($p = 0.168$ and $p = 0.888$ for admissions and admitted days respectively).

Given that neither educational achievement (as compared to less than high school) or insurance status (Private versus Medicare or Medicaid) was a significant predictor, we fail to

reject the null hypothesis that there is no association between a lower ability to pay for care and inpatient utilization when all else is equal.

Table 8 – 12. Predicted Number of Admissions and Admitted Days by Insurance Status and Educational Achievement

	Admissions			Admitted Days		
Insurance	**Predicted number of admissions**	**Difference compared to Private Insurance**	**p-value**	**Predicted number of admitted days**	**Difference compared to Private Insurance**	**p-value**
Private Insurance	1.793	ref.		30.623	ref.	
Medicare	1.843	0.049	0.458	31.252	0.629	0.606
Medicaid	1.945	0.152	0.051	32.674	2.051	0.170
Education	**Predicted number of admissions**	**Difference compared to Less than HS**	**p-value**	**Predicted number of admitted days**	**Difference compared to Less than HS**	**p-value**
Less than High School/GED	1.814	ref.		33.480	ref.	
High School/GED	1.820	0.007	0.951	31.146	-2.301	0.415
Some college or tech. school	1.894	0.082	0.477	31.356	-2.102	0.482
Associate or bachelors degree	1.777	-0.036	0.762	30.448	-3.010	0.331
Post-college graduate degree	1.859	0.045	0.763	29.789	-3.669	0.258

Predicted number of events by zero-truncated Poisson regression for admissions and zero-truncated negative binomial for admitted days controlling for physiologic model for end stage liver disease score at allocation, functional status, medical comorbidities, insurance, education, donor risk index, age, sex, race/ethnicity, access to care, post-discharge environment and transplant center. Differences indicate the difference in predicted mean number of admissions or admitted days for each group as compared to the predicted number for patients from the reference group (indicated by ref.), p-value corresponds to differences as compared to the reference group * indicates $p<0.05$, ** $p<0.001$. Abbreviations: tech. – technical

Hypothesis 1D: Patients who receive a poorer quality organ will have higher inpatient utilization in the post-transplant period, ceteris paribus.

The Donor Risk Index (DRI) is a statistically significant predictor of post-transplant inpatient utilization, such that a higher DRI (poorer quality organ) is associated with increased utilization. Specifically, a one-point increase in DRI is associated with 0.23 greater admissions and 5.68 more admitted days in the first six months following liver transplantation (Table 8 – 13). The linear increase in utilization by both admissions and days is outlined in Table 8 – 13 and visually demonstrated in Figure 8 – 5.

In terms of both admissions and total admitted days, we reject the null hypothesis and conclude that patients who receive a poorer quality organ (higher DRI) will have greater inpatient utilization in the post-transplant period as compared to those with higher quality organs (lower DRI) when all else is equal.

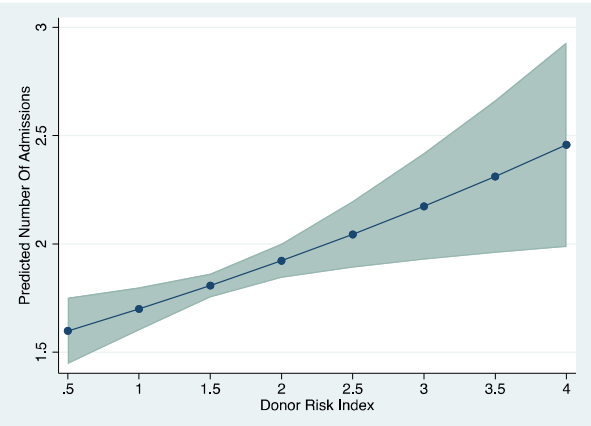
Table 8 – 13. Marginal Predicted Number of Admissions and Admitted Days by Donor Risk Index (DRI)

	Increase in Admissions per DRI point	SE	p-value	Increase in Admitted Days per DRI point	SE	p-value
DRI	0.225	0.075	0.003 *	5.684	1.394	<0.001 **
DRI	**Predicted Admissions**	**SE**	**p-value**	**Predicted Admitted Days**	**SE**	**p-value**
1	1.598	0.078	<0.001 **	25.411	1.358	<0.001 **
2	1.807	0.028	<0.001 **	30.490	0.562	<0.001 **
3	2.044	0.078	<0.001 **	36.585	1.551	<0.001 **
4	2.311	0.180	<0.001 **	43.897	3.733	<0.001 **

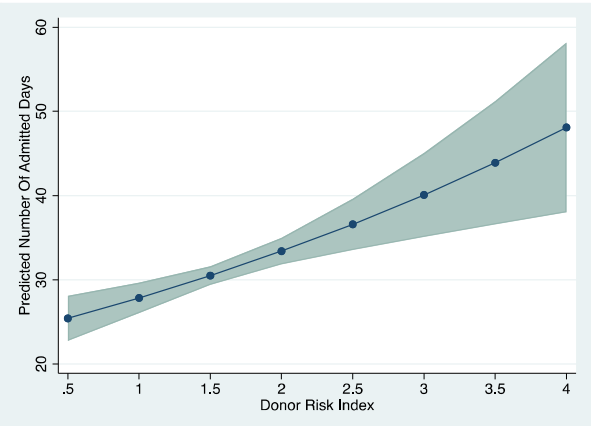
Marginal effects by zero-truncated Poisson regression for admissions and zero-truncated negative binomial for admitted days. Increase in admissions per DRI point indicates linear change in number of admissions or admitted days for each additional DRI point. Predicted admissions or admitted days indicates the estimated number of admissions or days for the DRI score listed. * p<0.05, ** p<0.001. Abbreviations: DRI - donor risk index, SE - standard error.

Figure 8 – 5. Predicted Number of Admissions and Admitted Days within Six months of Transplant by Donor Risk Index. Point estimates plotted with shaded area indicating the 95% confidence intervals. (A) Admissions, (B) Admitted Days.

A.



B.



8.2.3 Sensitivity Analyses

Definition of HCC / Malignancy

A sensitivity analysis comparing three different definitions of HCC/malignancy was completed. Comparison of the marginal effects for the covariates of interest indicated there was no difference in direction, magnitude or significance between the three definitions (Appendix 4E). In order to include all patients with possible diagnosis of malignancy within the malignancy category, malignancy was defined as either a primary diagnosis of malignancy or any previous approval by UNOS for MELD exception points due to malignancy for all analyses.

Number of Diagnostic Groups

A sensitivity analysis comparing the use of 3 versus 9 diagnostic groups was completed. Comparison of the marginal effects for the covariates of interest indicated there was no difference in direction, magnitude or significance for the covariates of interest (Appendix 4F). Given the potential audience for future publications of this research, the more granular diagnostic groups were preferred.

Modeling Comparisons

A sensitivity analysis comparing potential regression distributions and alternative models was also completed for each outcome. The significance and direction of marginal effects of interest, and overall model significance were stable across all models for both the admissions (Appendix 4G) and admitted days (Appendix 4H) outcomes. The zero-truncated Poisson and zero-truncated negative binomial distributions were selected as the final models for admissions and admitted days respectively, as they were most appropriate given the zero-truncation of the data and stability of marginal effects.

Loss of Follow-Up Secondary to Death

A sensitivity analysis was completed to assess the inclusion of patients who died during the six months following transplantation. Marginal effects for the covariates of interest for hypotheses H1a – H1d with inclusion and exclusion of patients who died within six months of transplant are included in Appendix 4I. Across covariates for H1a, H1b and H1d the marginal effects are robust for both admissions and admitted days across both samples (all patients and excluding patients who died before six months of follow-up). For H1c, which included insurance status and education as measures of the ability to pay for care, the marginal effects are stable for the admissions model, but for the admitted days model the marginal effect for Medicare crosses the threshold for statistical significance. Amongst those patients who survived at least six months post-transplant, Medicare patients (as compared to privately insured) had a predicted 2.01 day increase in total admitted days. This effect is not age-dependent, as when marginal effects are evaluated at age intervals there is no loss of effect with younger patients. Given that Medicare provides more extensive hospice and end-of-life care benefits in comparison to private insurances, the location of death was compared between the two groups, as it may be plausible that terminal patients with Medicare had shorter lengths of stay due to better out-of-hospital end-of-life care options. When location of death was compared between Medicare and privately insured patients there were no differences, such that regardless of insurance type, approximately 40% of patients died within the hospital and 60% of patients died after discharge.

State Residence

In a comparison of patients defined as in-state residents by both SRTR and their state utilization database (OSHPD or HCUP) and those defined as instate in only one of the two databases, marginal effects for covariates of interest were robust for both the admissions and

admitted days outcomes (Appendix 4J). Given that inclusion of patients classified as in-state within a single database did not alter the results of the regression analysis, these patients remained in the sample and were included in the results presented for the hypothesis tests.

Simultaneous Liver and Kidney Transplant Recipients

There were no significant differences in marginal effects for covariates of interest with the inclusion or exclusion or patients who received a simultaneous liver and kidney transplant, therefore inclusion of these patients was preferred (Appendix 4K). When these patients were included, the addition of a liver-kidney covariate did not change the marginal effects of the covariates of interest and was not statistically significant in either the admissions or admitted days model (Appendix 4K). Given that the inclusion of liver-kidney recipients did not alter the results, and there was not a significant effect of a liver-kidney covariate, these patients remained in the model, and the liver-kidney covariate was not included in the final model.

8.3 Question 2: How did Share 35 affect post-transplant inpatient utilization

8.3.1 Descriptive Statistics

A total of 6,156 patients are included in the analysis of the impact of Share 35 on post-transplant inpatient utilization; 4,681 who underwent transplantation prior to the implementation of Share 35 (January 1, 2010 – May 31, 2013) and 1,475 after implementation of Share 35 (June 1, 2013 – June 1, 2014). The number of Pre-Share 35 patients is smaller as compared to question one due to exclusion of patients who were granted Status 1A designation, which ultimately prioritized them above MELD based organ allocation, a system that was unchanged by the Share 35 policy.

The Pre- and Post-Share 35 cohorts were similar in terms of race/ethnicity, sex, medical comorbidities, liver disease etiology, and supply of in- and out-patient medical services. The two

cohorts differed by insurance status, age and liver disease severity. Within the post-Share35 cohort patients were more likely to have Medicare insurance and less likely to be privately insured, be slightly older (mean 56.2 years and 57.0 years Pre- and Post-Share 35), and at higher medical acuity (mean physiologic MELD score was on average 1.1 points higher Post-Share 35, and functional status was on average 2.1% lower (indicating less functional independence)). Descriptive statistics are included in Table 8 – 14.

Table 8 – 14. Descriptive Statistics for the Pre- and Post-Share 35 Cohorts. (A) Categorical variables, p-values indicate results of comparisons between the Pre- and Post-Share 35 cohorts by chi-squared statistics. (B) Continuous variables, p-values indicate results of comparisons between Pre- and Post-Share 35 cohorts by independent samples t-tests.

A.

Categorical Predictors	Pre-Share 35 n = 4681		Post-Share 35 n = 1475		p-value
Patient Preferences					
Race / Ethnicity					
White, non-latino	2831	60.5%	909	61.6%	
White, latino	1034	22.1%	328	22.2%	
Black	396	8.5%	115	7.8%	0.845
Asian	387	8.3%	114	7.7%	
Other	33	0.7%	9	0.6%	
Sex					
Male	3166	67.6%	976	66.2%	0.295
Female	1515	32.4%	499	33.8%	
Ability to Pay for Care					
Insurance Status					
Private insurance	2483	53.0%	722	48.9%	
Medicare	1229	26.3%	460	31.2%	0.003 *
Medicaid	897	19.2%	272	18.4%	
Other	72	1.5%	21	1.4%	
Education					
Less than High School/GED	355	7.6%	116	7.9%	
High School / GED	1752	37.4%	588	39.9%	
Some college or technical school	1098	23.5%	376	25.5%	<0.001 **
Associate or bachelors degree	757	16.2%	231	15.7%	
Post-college graduate degree	308	6.6%	94	6.4%	
Unknown	411	8.8%	70	4.7%	
Zip Code Median Income					
1st Quartile	868	18.5%	249	16.9%	
2nd Quartile	1057	22.6%	392	26.6%	
3rd Quartile	1294	27.6%	410	27.8%	0.017*
4th Quartile	1407	30.1%	420	28.5%	
Unknown/missing	55	1.2%	4	0.3%	

Medical Condition / Disability at Transplant					
Medical Comorbidities					
Chronic obstructive pulmonary disease	1040	22.2%	348	23.6%	0.27
Diabetes	1213	25.9%	398	27.0%	0.415
Hypertension	1624	34.7%	504	34.2%	0.712
Renal failure	1272	27.2%	437	29.6%	0.067
Vascular disease	468	10.0%	155	10.5%	0.571
Liver Disease Etiology					
Acute liver failure	81	1.7%	13	0.9%	
Autoimmune hepatitis	96	2.1%	42	2.8%	
Cholestatic liver disease	292	6.2%	77	5.2%	
Cryptogenic cirrhosis	206	4.4%	51	3.5%	
Genetic/metabolic	72	1.5%	25	1.7%	0.064
Hepatitis C	839	17.9%	257	17.4%	
Malignancy	1753	37.4%	572	38.8%	
Steatohepatitis	1178	25.2%	391	26.5%	
Other	164	3.5%	47	3.2%	
Post-Discharge Environment					
Completely rural or <2500 urban population	3274	69.9%	1056	71.6%	
Urban 2500 - 20,000 population	931	19.9%	244	16.5%	
Urban >20,000 population	236	5.0%	88	6.0%	
Metropolitan <250,000 population	110	2.4%	41	2.8%	0.119
Metropolitan 250,000 - 1 million population	102	2.2%	36	2.4%	
Metropolitan >1 million population	17	0.4%	6	0.4%	
Unknown/missing	11	0.2%	4	0.3%	

Steatohepatitis is inclusive of non-alcoholic steatohepatitis (NASH) and alcoholic steatohepatitis. Primary insurance coverage indicates the patient's primary payer at the time of transplantation. Zip code median income is the median income of the patient's home zip code as it corresponds to the national quartiles for income during the calendar year the patient underwent transplantation. Rural / Urban Continuum is based on the patient's county classification by the 2013 Rural-Urban Continuum codes. P-value indicates comparison between Pre- and Post-Share 35 cohorts by chi-squared. * indicates $p < 0.05$, ** $p < 0.001$. Abbreviations: GED - General equivalency diploma, COPD - chronic obstructive pulmonary disease.

B.

Continuous Predictors	Pre-Share 35	Post-Share 35
Patient Preferences		
Age (years), n	4681	1475
mean	56.209	56.953
range	18 - 80	18 - 81
Mean difference, p-value	-0.744	0.010 *
Supply of Inpatient Medical Services		
Acute Care Hospital Beds per 1000, n	4670	1471
mean	2.391	2.345
range	0 - 13.08	0 - 13.48
Mean difference, p-value	0.046	0.199
Distance to Transplant Center, hours	4642	1354
mean	1.107	1.203
range	0 - 8.11	0 - 8.28
Mean difference, p-value	-0.097	0.002*
Supply of Outpatient Medical Services		
Primary Care Density, n	4670	1471
mean	0.027	0.026
range	0 - 0.21	0 - 0.23
Mean difference, p-value	0.000	0.581
Specialty Care Density, n	4670	1471
mean	0.046	0.045
range	0 - 0.18	0 - 0.18
Mean difference, p-value	0.000	0.691
Medical Condition / Disability at Transplant		
Liver Disease Severity		
Physiologic MELD at Transplant, n	4681	1475
mean	22.140	23.193
range	6 - 40	6 - 40
Mean difference, p-value	-1.053	0.001 *
Functional Status		
Karnofsky Score at Transplant, n	4680	1474
mean	51.786	49.715
range	10 - 100	10 - 100
Mean difference, p-value	2.071	0.005 *

Acute care hospital density = number of hospital beds per 100,000 census population for patient's home county; PCP density = number of practicing primary care providers per 100,000 census population for patient's home county; Distance to Transplant Center = estimated travel time, in hours, between patient's home zip code centroid (or 3-digit zip centroid for patients from the state of Massachusetts) to their transplant center; Specialty care density = number of practicing outpatient gastroenterologists per 100,000 census population for patient's home county. P-value indicates comparison between Pre- and Post-Share 35 cohorts by independent samples t-tests. * indicates $p < 0.05$, ** $p < 0.001$. Abbreviations: MELD - model for end stage liver disease.

8.3.2 Regression Analysis

Similar to question one, question two defined post-transplant inpatient utilization in terms of both counts of admissions and counts of admitted days. The distribution of each outcome was evaluated and various models were tested to assure the best fit for the given distribution. Both models were zero-truncated count distributions and were found to have the best fit with the zero-truncated Poisson and negative binomial models for the admissions and admitted days outcomes respectively. Model comparisons for each outcome are included in Appendix 5B and 5C respectively.

Hypothesis 2A assessed the full effect of Share 35 through both medical condition / disability at transplant and organ availability, as such the primary regressor of interest was the Share 35 covariate. Complete regression model results for 2A are included in Appendix 5D. Hypotheses 2B and 2C assessed only the effect of Share 35 through organ availability (by controlling for medical condition / disability at transplant). The primary regressor of interest for hypothesis 2B was the Share 35 covariate (modeled without the interaction term between Share 35 and allocation MELD score) and for 2C, it was the interaction between Share 35 and the patient's allocation MELD score. The allocation score is the score at which the patient is eligible for transplantation and is inclusive of both the physiologic MELD score and any MELD exception points. It is expected that the allocation MELD score moderates the effect of the policy, given that once a patient reached an allocation MELD score of 35 or higher they became eligible for all regional organs, as compared to only local organs when allocation MELD scores are less than 35. The complete regression model results for 2B and 2C are included in Appendices 5E and 5F.

For both outcomes, admissions and admitted days, the marginal effects for Share 35 and Share 35 at increasing allocation MELD scores are discussed by hypothesis below. Given that

the policy is ultimately implemented at the regional level, sub-analysis by UNOS region was completed. Sub-analysis within region 8 was excluded due to small sample size (<10 cases per included covariate).

Hypothesis 2A: Share 35 increased inpatient utilization in the post-transplant period, when not controlling for medical condition / disability at transplant, but controlling for patient preferences, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality) and health literacy

When not controlling for medical condition / disability at transplant, Share 35 unexpectedly resulted in 0.11 fewer admissions in the post-Share 35 period as compared to the pre-Share 35 period, but did not result in a significant change in the number of admitted days (Table 8 – 15), suggesting that post-Share 35, longer hospital lengths of stay were offsetting reductions in readmissions for a net non-significant overall impact on inpatient days.

In a sub-analysis by UNOS region, Share 35 again was unexpectedly found to be a significant predictor of decreased admissions within Region 1, with an average reduction of 0.75 admissions (p-value <0.001) (Table 8 – 15). There was no statistically significant reductions in admissions in regions 3, 5, or 9. Furthermore, there was no significant reduction in admitted days for any region (Table 8 – 15). Based on regional analysis, we conclude that across the six-state cohort there was not a consistent effect of Share 35 when considering the full effect of the policy.

In summary, we find that Share 35 resulted in decreased admissions both on the national analysis and within Region 1, but no difference in admitted days (both nationally and regionally). Therefore, we reject the null hypothesis and conclude that Share 35 was associated with an increase in inpatient utilization. This finding supports the competing hypothesis, such that the

balance between increased organ availability and increased medical acuity / disability at transplant, favors increased organ availability (rather than medical acuity as hypothesized), resulting in a net decrease in inpatient utilization.

Table 8 – 15. Marginal Effects of Share 35 through Medical Condition / Disability at Transplant and Organ Availability on Number of Admissions and Admitted Days within the Six months Following Liver Transplantation (H2a)

		Admissions			Admitted Days		
Cohort	**n**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
National	6156	-0.113	0.056	0.044*	-0.325	1.104	0.769
Region 1	517	-0.751	0.179	<0.001**	-4.308	2.722	0.114
Region 3	2310	0.084	0.099	0.271	-0.744	1.219	0.542
Region 5	2273	-0.157	0.092	0.088	2.133	1.588	0.179
Region 9	930	-0.092	0.141	0.516	-2.681	2.696	0.320

For H2a the full effect of Share 35 is through both organ availability and medical condition/ disability at transplant. The admissions model was completed with zero-truncated Poisson and the admitted days model by zero-truncated negative binomial regression. Only Share 35 marginal effects displayed. For H2a, covariates not displayed include: sex, age, race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, distance to transplant center, rural urban continuum and transplant center. Outcomes, admissions and total admitted days, are inclusive of the index admission and days admitted following transplantation during the index admission, respectively. Margin indicates the difference in predicted number of admissions or admitted days between the pre- and post-Share 35 periods for all patients. * p<0.05, **p<0.001. Abbreviations: SE - standard error.

Hypothesis 2B: Share 35 decreased inpatient utilization in the post-transplant period when controlling for medical condition / disability at transplant in addition to controlling for patient preferences, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality) and health literacy.

When controlling for medical condition / disability at the time of transplant and therefore evaluating the mean effect of Share 35 through organ availability, Share 35 is associated with a significant reduction in the total number of admissions and admitted days. In comparing the Pre- to Post-Share 35 periods, when all else is equal, patients had, on average, 0.14 fewer admissions and were admitted 2.0 fewer days (Table 8 – 16).

On regional sub-analysis, significant reductions in admissions were seen in Region 1 and Region 5 (Table 8 – 16), but no significant changes in the rate of admissions were identified in Regions 3 or 9, or in any region for admitted days.

Overall these results suggest that Share 35 is associated with decreased inpatient utilization with regard to admissions both within the entire cohort, and within regions 1 and 5. Given that the policy's effect, of increasing organ availability, is aimed at patients with high allocation MELD scores, it is likely that mean effect, exhibited here, is dampened by the subset of patients who did not benefit from increased organ availability after the implementation of the policy. This moderating effect of allocation MELD score will be explored in the next section (H2c).

At the national level the regression analysis provides support for the hypothesis and therefore we conclude that, on average, when controlling for medical condition and disability at transplant, Share 35 resulted in decreased in-patient utilization. Alternatively, we must note that in regional sub-analyses, this difference was only detected within the admissions outcome, suggesting that Share 35 may have had a greater effect in reducing readmissions than decreasing hospital length of stay.

Table 8 – 16. Marginal Effects of Share 35 through Organ Availability on Number of Admissions and Admitted Days within the Six months Following Liver Transplantation (H2b)

		Admissions			Admitted Days		
Cohort	**n**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
National	6156	-0.139	0.055	0.012*	-1.974	0.971	0.042*
Region 1	517	-0.625	0.182	0.001*	-2.862	3.234	0.376
Region 3	2310	0.044	0.100	0.662	-0.823	1.377	0.550
Region 5	2273	-0.205	0.090	0.024*	-2.446	1.588	0.124
Region 9	930	-0.091	0.134	0.498	-4.389	3.006	0.144

For H2b the partial effect of Share 35 is only through organ availability as medical condition/disability are controlled in the model. The admissions model was completed with zero-truncated Poisson and the admitted days model by zero-truncated negative binomial regression. Only Share 35 marginal effects displayed. Covariates not displayed include: sex, age, race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, distance from the transplant center, liver disease etiology, demeaned allocation MELD score at transplantation, difference between physiologic and allocation MELD score, functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease) and transplant center. Outcomes, admissions and total admitted days, are inclusive of the index admission and days admitted following transplantation during the index admission, respectively. Margin indicates the difference in predicted number of admissions or admitted days between the pre- and post-Share 35 periods for all patients. * $p<0.05$, ** $p<0.001$. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease score.

Hypothesis 2C: The negative effect of Share 35 on inpatient utilization in the post-transplant period will be larger amongst patients with high allocation MELD scores, when controlling for medical condition / disability at transplant, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality) and health literacy.

When controlling for medical condition / disability at the time of transplant and accounting for the moderating effect of allocation MELD score on organ availability, amongst patients with high allocation MELD scores, Share 35 resulted in a reduction in both admissions and admitted days in the six months following liver transplantation (Table 8 – 17). As indicated in Table 8 – 17, the threshold for incurring a benefit from Share 35 is at an allocation MELD score of 30, and the marginal effect increases (larger reductions in admissions and admitted days) with increasing allocation MELD scores. When all else is held equal, patients with an

allocation MELD score of 35 and 40 are predicted to have 0.21 and 0.31 fewer admissions and 3.1 and 4.3 fewer admitted days in the Post-Share 35 period respectively. In contrast, patients with low allocation MELD scores do not have significantly different utilization in the pre- and post-Share 35 periods.

Table 8 – 17. Marginal Effect of Share 35 through Organ Availability on Number of Admissions and Admitted Days Accounting for the Moderating Effect of Allocation MELD Score on Share 35 – Complete Utilization Cohort

	Admissions			Admitted Days		
	Margin	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD = 10	0.180	0.151	0.234	1.014	2.063	0.623
Share 35 at aMELD = 15	0.112	0.123	0.361	0.453	1.769	0.798
Share 35 at aMELD = 20	0.039	0.095	0.679	-0.218	1.443	0.880
Share 35 at aMELD = 25	-0.039	0.071	0.585	-1.014	1.127	0.369
Share 35 at aMELD = 30	-0.122	0.056	0.030*	-1.952	0.960	0.042*
Share 35 at aMELD = 35	-0.212	0.063	0.001*	-3.051	1.165	0.009*
Share 35 at aMELD = 40	-0.308	0.087	<0.001**	-4.334	1.741	0.013*

For H2c the effect of Share 35 is tested only through organ availability as medical condition/disability are controlled in the model. H2c differs from H2b in that H2c includes an interaction term for the moderating effect of allocation MELD score on Share 35. The admissions model was completed with zero-truncated Poisson and the admitted days model by zero-truncated negative binomial regression. Only Share 35 marginal effects displayed. Covariates not displayed include: sex, age, race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, distance from the transplant center, liver disease etiology, demeaned allocation MELD score at transplantation, difference between physiologic and allocation MELD score, functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease) and transplant center. Outcomes, admissions and total admitted days, are inclusive of the index admission and days admitted following transplantation during the index admission, respectively. Margin indicates the difference in predicted number of admissions or admitted days between the pre- and post-Share 35 periods for patients at a given allocation MELD score. * $p<0.05$, ** $p<0.001$. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease score, aMELD – allocation MELD score.

On sub-analysis by UNOS region, Share 35 had varying effects across the regions with respect to both admissions and admitted days (Tables 8 – 18, 8 – 19). There were statistically significant decreases in the predicted number of admissions for patients with high allocation MELD scores within regions 1, 5, and 9. Although the individual threshold for a significant effect and the magnitude of the effect varies between these regions, the direction of the effect is consistent (greater decreases in admissions with increasing allocation MELD scores). The

individual threshold for the effect of Share 35 varies by region, such that the effect is found within Region 1 between allocation MELD scores 15 to 39, Region 5 between 31 and 40 and within Region 9 at a score of 40 (Appendix 5G).

With regard to admitted days, significant effects were only identified within Region 1 and Region 5 which both demonstrated a reduction in admitted days amongst patients with the highest allocation MELD scores. Again, while the magnitude differs, within both regions the direction of the effect is the same, such that with increasing allocation MELD scores, greater reductions in admitted days were identified.

Table 8 – 18. Marginal Effect of Share 35 through Organ Availability on Number of Admissions Accounting for the Moderating Effect of Allocation MELD Score on Share 35 – Regional Cohorts

	Admissions							
	Region 1 n = 517		Region 3 n = 2310		Region 5 n = 2273		Region 9 n = 930	
	Margin	p-value	Margin	p-value	Margin	p-value	Margin	p-value
Share 35 at aMELD 10	-0.591	0.079	0.407	0.032*	-0.055	0.848	0.500	0.180
Share 35 at aMELD 15	-0.602	0.028*	0.314	0.033*	-0.083	0.722	0.361	0.208
Share 35 at aMELD 20	-0.612	0.004*	0.213	0.050	-0.113	0.539	0.218	0.296
Share 35 at aMELD 25	-0.622	<0.001**	0.103	0.213	-0.143	0.287	0.073	0.617
Share 35 at aMELD 30	-0.631	<0.001**	-0.017	0.840	-0.175	0.060	-0.075	0.521
Share 35 at aMELD 35	-0.641	0.006*	-0.149	0.218	-0.207	0.007*	-0.228	0.102
Share 35 at aMELD 40	-0.650	0.046*	-0.292	0.089	-0.241	0.017*	-0.384	0.048*

For H2c the effect of Share 35 is tested only through organ availability as medical condition/disability are controlled in the model. H2c differs from H2b in that H2c includes an interaction term for the moderating effect of allocation MELD score on Share 35. The admissions model was completed with zero-truncated Poisson regression. Only Share 35 marginal effects displayed. Covariates not displayed include: sex, age, race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, distance from the transplant center, liver disease etiology, demeaned allocation MELD score at transplantation, difference between physiologic and allocation MELD score, functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease) and transplant center. Admissions are inclusive of the index admission. Margin indicates the difference in predicted number of admissions between the pre- and post-Share 35 periods for patients at a given allocation MELD score. * p<0.05, **p<0.001. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease score, aMELD - allocation MELD score.

Table 8 – 19. Marginal Effect of Share 35 through Organ Availability on Number of Admissions Accounting for the Moderating Effect of Allocation MELD Score on Share 35 – Regional Cohorts

	Admitted Days							
	Region 1 n = 517		Region 3 n = 2310		Region 5 n = 2273		Region 9 n = 930	
	Margin	p-value	Margin	p-value	Margin	p-value	Margin	p-value
Share 35 at aMELD 10	12.453	0.076	-0.183	0.927	1.019	0.768	-6.835	0.135
Share 35 at aMELD 15	8.008	0.123	-0.337	0.842	0.501	0.868	-6.528	0.106
Share 35 at aMELD 20	3.624	0.335	-0.522	0.698	-0.110	0.965	-6.059	0.074
Share 35 at aMELD 25	-0.723	0.799	-0.746	0.508	-0.825	0.670	-5.396	0.049*
Share 35 at aMELD 30	-5.055	0.060	-1.015	0.450	-1.659	0.250	-4.498	0.072
Share 35 at aMELD 35	-9.396	0.004*	-1.334	0.520	-2.625	0.051	-3.320	0.315
Share 35 at aMELD 40	-13.769	0.001*	-1.714	0.589	-3.741	0.055	-1.807	0.727

For H2c the effect of Share 35 is tested only through organ availability as medical condition/disability are controlled in the model. H2c differs from H2b in that H2c includes an interaction term for the moderating effect of allocation MELD score on Share 35. The admitted days model was completed by zero-truncated negative binomial regression. Only Share 35 marginal effects displayed. Covariates not displayed include: sex, age, race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, distance from the transplant center, liver disease etiology, demeaned allocation MELD score at transplantation, difference between physiologic and allocation MELD score, functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease) and transplant center. Outcome, total admitted days, is inclusive of the days admitted following transplantation during the index admission. Margin indicates the difference in predicted number of admitted days between the pre- and post-Share 35 periods for patients at a given allocation MELD score. * $p<0.05$, ** $p<0.001$. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease score, aMELD - allocation MELD score.

Based upon both the evaluation of the entire cohort, and regional sub-analysis we reject the null hypothesis and conclude that Share 35 decreased inpatient utilization, through decreases in both admissions and admitted days, amongst patients with high allocation MELD scores. This effect is seen across the six-state cohort when analyzed collectively, but upon subgroup analysis the effect is most pronounced within regions 1, 5 and 9.

8.3.3. Sensitivity Analyses

Exclusion of Patients who Died within Six months of Transplant

A sensitivity analysis was completed excluding patients who died within six months of transplant. For hypotheses 2A – 2C, marginal effects were similar across the admissions outcomes with inclusion or exclusion of the patients who died within six months of transplant

(Appendix 5H). For the admitted days outcome, when patients who died were excluded statistically significant effects for H2a and H2b were no longer identified, and within H2c the effect is only seen at a higher allocation MELD score. This difference is likely due to longer lengths of stay during between patients who died within the first six months of transplant and those that survived. Given the desire to account for differences across the patient population, and account for increased utilization that may be attributable to increased mortality, it is preferred to include these patients within the main analysis. We therefore included these patients as it is important to include the utilization of these patients when assessing overall changes to utilization due to the policy change.

State Residence

To assess if the inclusion of patients who were possibly misclassified as in-state would affect the results of the regression analysis, a sensitivity analysis was completed. Marginal effects and for hypotheses 2A – 2C for both outcomes are included in Appendix 5I. For both outcomes, exclusion of possible out-of-state patients results in the marginal effect for Share 35 to cross the threshold for non-significance for both H2A and H2B, yet the estimates are robust for H2C. For H2A and H2B the significant marginal effects found with inclusion of possible out-of-state patients are close to the alpha value and therefore the transition to a non-significant result with exclusion of possible out-of-state patients likely represent small differences amongst patients excluded from the analysis. Bivariate comparisons of these two groups indicate that the possible out-of-state patients have lower physiologic and allocation MELD scores, on average, and higher functional status at transplant, and therefore represent a slightly healthier cohort of patients. Although these differences are present, the incremental changes are small, and the estimates are robust for H2C, which fully adjusts for the effect of Share 35 by allocation MELD

score. We therefore proceeded with inclusion of the 189 patients, who were classified as in-state within only one of the two datasets, for the regression analyses presented for the hypothesis tests.

Inclusion of Patients Who Underwent Simultaneous Liver + Kidney Transplantation

Patients who undergo simultaneous liver and kidney transplantation may differ from those patients undergoing a liver transplantation alone. In order to assess the relative impact of these patients on the overall regression model, two sensitivity analyses were completed: (1) excluding patients who underwent simultaneous liver and kidney transplantation and (2) including a liver-kidney covariate. For hypotheses 2A – 2C, marginal effects were similar across the admissions outcome with inclusion or exclusion of the patients who underwent simultaneous liver and kidney transplantation (Appendix 5J). Addition of the liver-kidney covariate was only significant in hypothesis 2A, likely due to the fact that under this hypothesis medical condition is not controlled and therefore the liver-kidney covariate is proxying for medical condition. Given that the admissions models are stable with inclusion of patients undergoing liver-kidney transplantation, they remained in the cohort for hypothesis testing. Similar results were seen for the admitted days outcome, with the exception that with exclusion of liver-kidney patients under hypothesis 2A, the marginal effect crossed the threshold for statistical significance. The difference is small given that with inclusion of these patients, the effect was of borderline statistical significance with a p-value of 0.048 (Appendix 5J). Given that the results are robust with inclusion of these patients, similar to the admissions model, patients who underwent liver-kidney transplant remained in the cohort for hypothesis testing.

Categorical Interaction Term for Allocation MELD Score and Share 35

Share 35 was expected to have a different effect on inpatient utilization based on allocation MELD score. In the main model for H2c allocation MELD score is used as a

continuous variable, but given that there is an expected cut-point in the effect at an allocation MELD score of 35, two different categorical variables (binary and three groups based on allocation MELD score) were also tested in the interaction term (Appendix 5K). For the admissions outcome, both the binary and three group categorical variables were consistent with the continuous allocation MELD model, such that the effect of Share 35 which results in fewer inpatient admissions is seen in patients with the highest allocation MELD scores in the post-Share 35 period. For the admitted days outcome, the binary outcome did not demonstrate a statistically significant effect within the high allocation MELD score group, but the direction of the effect is consistent with the continuous allocation MELD model. In the 3 group categorical variable the effect is similar to that seen in the continuous model such both of the higher allocation MELD score groups in the post-Share 35 period had fewer predicted admitted days as compared to the patients with an allocation MELD score >30 in the pre-Share 35 period. The lack of statistical significance in the binary model for admitted days may be due to the fact that the effect of Share 35 is not as finite as an allocation MELD score of 35, and that rather there is an effect that spans this threshold (which is seen in the continuous model). The continuous allocation MELD score model is preferred as it provides more granular information about the effect of Share 35.

8.4 Question 3: How did Share 35 affect post-transplant disability

8.4.1 Descriptive Statistics

Question three addresses the effect of Share 35 on post-transplant disability, which is defined as a patient's ability to return to work and the change in functional status pre- to post-transplant. Throughout the discussion of the results, these two outcomes will be addressed separately, as different inclusion criteria were applied to the patient populations for each

question. The patient cohort for this question was derived from the SRTR database and was inclusive of patients who underwent transplant from 1/1/2010 – 11/1/2016, resulting in an initial cohort size of 41,960 patients. After imposing the exclusion criteria utilized across all three research questions, 36,554 patients met inclusion criteria for this question (Figure 7 – 2).

Work Status

The cohort for analysis of work status was limited to patients between the ages of 25-55 with at least 24 months of post-transplant follow-up, and to those patients who had pre- and post-transplant work status recorded, resulting in a cohort size of 10,290 patients. Within this cohort, 6,587 (64.0%) were transplanted prior to Share 35 and 3,703 (36.0%) after policy implementation. Only 19.7% (n=2,031) were working prior to transplantation (defined as working within 90 days prior to, or at the time of transplant), with nearly equal rates in the pre- and post-Share 35 cohorts (20.2% versus 19.0%, p=0.17 by univariate logistic regression). Given known differences in likelihood of working both pre- and post-transplant based on sex, an a priori decision was made to analyze this cohort by sex subgroups. To ensure that this known difference held true within this cohort, univariate analysis of work status was completed by sex. Within both the pre- and post-Share 35 periods, women were at least 33% less likely to be working prior to transplant (OR 0.67 for the pre-Share 35 period and OR 0.62 for the post-Share 35 period, $p<0.001$ for both by univariate logistic regression), and at least 33% less likely to be working post-transplant in both the pre- and post-Share 35 period (OR 0.59 and 0.65, $p<0.001$ for each period respectively). Given that this difference held within this patient cohort, the analysis for work status was completed as planned, subdividing the analysis by sex.

Bivariate comparisons of the pre- and post-Share 35 cohorts indicated that the post-Share 35 cohort was composed of slightly more females (34.6% versus 31.6%, p=0.002), had fewer

patients with a missing educational status (5.3% versus 8.6%) and was slightly younger (mean age 47.3 versus 48.1, $p<0.001$) (Table 8 – 20). In terms of medical condition and disability, the post-Share 35 cohort was slightly more ill/disabled with a higher physiologic MELD score (25.4 versus 23.5, $p<0.001$) and a lower functional status (46.7% versus 50.5%, $p<0.001$) at transplant. Patients were also more likely to have a diagnosis of renal failure (24.0% versus 7.8%, $p<0.001$), undergo a combined liver and kidney transplant (7.8% versus 6.5%, $p=0.011$) and have a diagnosis of steatohepatitis (37.8% versus 29.9%, $p<0.001$) in the post-Share 35 period.

Table 8 – 20. Descriptive Statistics for the Work Status Cohort by Share 35 Cohorts. (A) Categorical variables. (B) Continuous variables. (C). Outcomes

A.

Categorical Predictors	Pre-Share 35 n = 6,587		Post-Share 35 n = 3,703		
Patient Preferences	n	%	n	%	p-value
Sex					
Male	4503	68.4%	2421	65.4%	0.002*
Female	2084	31.6%	1282	34.6%	
Ability to Pay for Care					
Insurance Status					
Private insurance	3845	58.4%	2140	57.8%	0.881
Medicare	1123	17.1%	664	17.9%	
Medicaid	1371	20.8%	760	20.5%	
Veterans Affairs	89	1.4%	46	1.2%	
Self-Pay	27	0.4%	14	0.4%	
Other	132	2.0%	79	2.1%	
Education					
Less than High School/GED	325	4.9%	178	4.8%	<0.001**
High School / GED	2894	43.9%	1636	44.2%	
Some college or technical school	1491	22.6%	894	24.1%	
Associate or bachelors degree	1003	15.2%	585	15.8%	
Post-college graduate degree	306	65.0%	214	5.8%	
Unknown	568	8.6%	196	5.3%	
Medical Condition / Disability at Transplant					
Medical Comorbidities					
COPD	108	2.2%	74	2.6%	0.236
Diabetes	1304	19.9%	759	20.5%	0.459
Hypertension	1162	23.3%	670	23.3%	0.945
Renal failure	975	7.8%	744	24.0%	<0.001**
Vascular disease	77	1.5%	53	1.8%	0.251
Liver Disease Etiology					
Acute liver failure	103	1.6%	72	1.9%	<0.001**
Autoimmune hepatitis	185	2.8%	136	3.7%	
Cholestatic liver disease	582	8.8%	347	9.4%	
Cryptogenic cirrhosis	257	3.9%	147	4.0%	
Genetic/metabolic	211	3.2%	113	3.1%	
Hepatitis C	1394	21.2%	598	16.2%	
Malignancy	1598	24.3%	736	19.9%	
Steatohepatitis	1966	29.9%	1398	37.8%	
Other	291	4.4%	156	4.2%	
Type of Transplant					
Liver only	6159	93.5%	3413	92.2%	0.011*
Liver + Kidney	428	6.5%	290	7.8%	

Steatohepatitis is inclusive of non-alcoholic steatohepatitis (NASH) and alcoholic steatohepatitis. Primary insurance coverage indicates the patient's primary payer at the time of transplantation. P-value indicates comparison between Pre- and Post-Share 35 cohorts by chi-squared. * indicates $p < 0.05$, ** $p < 0.001$. Abbreviations: GED - General equivalency diploma, COPD - chronic obstructive pulmonary disease.

B.

Continuous Predictors	Pre-Share 35	Post-Share 35
Patient Preferences		
Age (years), n	6587	3703
mean	48.072	47.308
range	25 - 55	25 - 55
Mean difference, p-value	0.765	<0.001**
Medical Condition / Disability		
Liver Disease Severity		
Physiologic MELD at Transplant, n	6587	3703
mean	23.480	25.362
range	6 - 40	6 - 40
Mean difference, p-value	-1.882	<0.001**
Functional Status		
Karnofsky Score at Transplant, n	6546	3679
mean	50.516	46.738
range	10 - 100	10 - 100
Mean difference, p-value	3.778	<0.001**

P-value indicates comparison between Pre- and Post-Share 35 cohorts by independent samples t-tests. * indicates $p < 0.05$, ** $p < 0.001$. Abbreviations: MELD - model for end stage liver disease.

C.

Work Status	Pre-Share 35 n = 6,587		Post-Share 35 n = 3,703		
	n	%	n	%	p-value
Working prior to transplant					
Male	995	22.1%	519	21.4%	0.527
Female	332	15.9%	185	14.4%	0.241
Working within 2 years post-transplant					
Male	1567	34.8%	853	35.2%	0.718
Female	497	23.9%	334	26.1%	0.150

Working prior to transplant indicates work status at transplant admission or at the time of listing if patients was listed <90 days prior to transplant. Working post-transplant indicates if patient worked at any time during their 2-year post-transplant follow-up. P-value indicates comparison between Pre- and Post-Share 35 cohorts by chi-squared analysis. * indicates $p < 0.05$, ** $p < 0.001$.

Functional Status

Unlike the cohort utilized for analysis of work status, the functional status cohort was not limited by age. This cohort was therefore inclusive of all patients with functional status recorded at the time of transplantation and at six and/or twelve months post-transplant, who underwent transplantation between January 1, 2010 and November 1, 2016, and met study inclusion criteria, resulting in a sample size of 33,619 patients (Figure 7 – 2).

Within the functional status cohort, 46.9% (n = 15,772) underwent transplantation prior to, and 53.1% (n = 17,847) after, implementation of Share 35. Overall the cohorts were very similar, with small but statistically significant differences in covariates which are discussed below. The post-Share 35 cohort has slightly more patients with Medicare insurance (29.4% versus 25.8% pre-Share 35) and fewer privately insured (52.3% versus 55.6% Pre-Share 35). The post-Share 35 cohort also had higher proportion of patients with higher educational achievement, although this may be secondary to a greater percentage of patients with unknown educational status in the pre-Share 35 cohort. The post-Share 35 cohort also had a higher rate of medical comorbidities (diabetes, hypertension and renal failure) and a higher rate of simultaneous liver-kidney transplants. Additionally, the post-Share 35 cohort was at slightly higher acuity in terms of physiologic MELD score, allocation MELD score, and functional status. Descriptive statistics for the functional status cohort are included in Table 8 – 21.

Table 8 – 21. Descriptive Statistics for the Functional Status Cohort by Share 35 Cohorts.
(A) Categorical variables. (B) Continuous variables. (C) Outcomes
A.

Categorical Predictors	Pre-Share 35 n = 15,772		Post-Share 35 n = 17,847		p-value
Patient Preferences					
Sex					
Male	10822	68.6%	12052	67.5%	0.033*
Female	4950	31.4%	5795	32.5%	
Ability to Pay for Care					
Insurance Status					
Private insurance	8773	55.6%	9329	52.3%	<0.001**
Medicare	4074	25.8%	5253	29.4%	
Medicaid	2203	14.0%	2489	14.0%	
Veterans Affairs	393	2.5%	418	2.3%	
Self-Pay	58	0.4%	54	0.3%	
Other	271	1.7%	304	1.7%	
Education					
Less than High School/GED	784	5.0%	940	5.3%	<0.001**
High School / GED	6419	40.7%	7290	40.9%	
Some college or technical school	3596	22.8%	4356	24.4%	
Associate or bachelors degree	2496	15.8%	3054	17.1%	
Post-college graduate degree	1018	6.5%	1271	7.1%	
Unknown	1459	9.3%	936	5.2%	
Medical Condition / Disability at Transplant					
Medical Comorbidities					
COPD	324	2.7%	258	2.7%	0.826
Diabetes	4115	26.3%	5124	28.8%	<0.001**
Hypertension	3579	29.8%	3100	32.7%	<0.001**
Renal failure	2100	16.0%	2954	26.2%	<0.001**
Vascular disease	268	2.2%	227	2.4%	0.271
Liver Disease Etiology					
Acute liver failure	186	1.2%	212	1.2%	<0.001**
Autoimmune hepatitis	338	2.1%	396	2.2%	
Cholestatic liver disease	1140	7.2%	1209	6.8%	
Cryptogenic cirrhosis	732	4.6%	672	3.8%	
Genetic/metabolic	358	2.3%	376	2.1%	
Hepatitis C	2912	18.5%	2542	14.2%	
Malignancy	5630	5.7%	6128	34.3%	
Steatohepatitis	3985	25.3%	5777	32.4%	
Other	491	3.1%	535	3.0%	
Type of Transplant					
Liver only	14680	93.1%	16207	90.8%	<0.001**
Liver + Kidney	1092	6.9%	1640	9.2%	

Steatohepatitis is inclusive of non-alcoholic steatohepatitis (NASH) and alcoholic steatohepatitis. Primary insurance coverage indicates the patient's primary payer at the time of transplantation. P-value indicates comparison between Pre- and Post-Share 35 cohorts by chi-squared. * indicates $p < 0.05$, ** $p < 0.001$.
Abbreviations: GED - General equivalency diploma, COPD - chronic obstructive pulmonary disease

B.

Continuous Predictors	Pre-Share 35	Post-Share 35
Patient Preferences		
Age (years), n	15,772	17847
mean	55.582	56.384
Mean difference, p-value	-0.802	<0.001**
Medical Condition / Disability at Transplant		
Liver Disease Severity		
Physiologic MELD at Transplant, n	15772	17847
mean	21.578	22.202
Mean difference, p-value	-0.624	<0.001**
Allocation MELD at Transplant, n	15772	17847
mean	27.058	28.48
Mean difference, p-value	-1.431	<0.001**
Functional Status		
Karnofsky Score at Transplant, n	15772	17847
Mean	53.448	50.764
Mean difference, p-value	2.684	<0.001**
Karnofsky Score at 6 months follow-up, n	15772	17847
Mean	79.869	79.685
Mean difference, p-value	0.185	0.4278
Karnofsky Score at 12 month follow-up, n	15772	17847
Mean	79.273	80.071
Mean difference, p-value	-0.798	0.003*

P-value indicates comparison between Pre- and Post-Share 35 cohorts by independent samples t-tests. * indicates $p < 0.05$, ** $p < 0.001$. Abbreviations: MELD - model for end stage liver disease.

C.

Outcomes	Pre-Share 35	Post-Share 35
Functional Status Difference - 6 months, n	15772	17847
Mean	26.422	28.921
Standard deviation	29.298	28.398
Mean difference, p-value	-2.499	<0.001**
Functional Status Difference - 12 months, n	15722	17847
Mean	25.825	29.307
Standard deviation	31.900	30.679
Mean difference, p-value	-3.848	<0.001**

Functional status difference = (follow-up Karnofsky score - transplant Karnofsky score). P-value indicates comparison between Pre- and Post-Share 35 cohorts by independent samples t-tests. * indicates $p < 0.05$, ** $p < 0.001$.

8.4.2 Regression Analysis

Work Status

Logistic regression was utilized to assess the likelihood of a patient returning to work following transplantation; patients were segregated into cohorts by their pre-transplant work status and sex as discussed previously. Post-transplant work status was defined as working at any time within two years of transplantation. The primary regressors of interest were the Share 35 covariate (H3a) and the interaction term between Share 35 and allocation MELD score (H3b). H3a differed from H3b in that H3a assessed the mean effect of Share 35 across all patients, while H3b assessed the effect of Share 35 by allocation MELD score, accounting for the moderating effect of allocation MELD score on Share 35 through the use of an interaction term. Analysis was carried out at the national level and by grouped regions. Individual regional analysis was precluded due to small cohort sizes, and therefore regions were grouped by their predicted response to Share 35, previously discussed in section 8.1.1. The groupings are as follows: high likelihood of response (regions 1, 5, 7, and 9), moderate likelihood of response (regions 2, 3, 4, and 10) and low likelihood of response (regions 6, 8 and 11). Small sample size, and the risk of overfitting, precluded analysis of females working prior to transplant (national and regional subanalysis) and regional subanalysis of men working prior to transplant.

Functional Status

Ordinary least squares (OLS) regression was utilized to assess if the Share 35 policy impacted the change in functional status (Karnofsky score, ranges from 0 – 100%) between transplantation and interval follow-up at six months and twelve months post-transplant. The outcome was defined as the difference in the Karnofsky score between transplantation and the follow-up time period, such that an improvement in functional status at follow-up was defined as

a positive change. The distribution of the change in functional status for both six months and twelve months post-transplant approached normal and therefore OLS regression was determined to be appropriate. In parallel with the evaluation of work status, the impact of Share 35 was assessed independent of allocation MELD score (H3a) and accounting for the moderating effect of allocation MELD score (H3b). Regional sub-analyses were also completed, again grouping regions by likelihood of their response to Share 35, as discussed above.

H3a. Share 35 resulted in less post-transplant disability, when controlling for medical status / disability at transplant, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality), health literacy and post-discharge environment.

For each hypothesis the two outcomes are discussed separately (work status and functional status) and then the findings from both are summarized in response to the stated hypothesis.

Work Status

Share 35 was not associated with a change in the predicted probability of returning to work across all three subgroups (males not working prior to transplant, females not working prior to transplant and males working prior to transplant) (Table 8 – 22).

Results of the regional analysis demonstrate a statistically significant increase amongst men not working prior to transplant in regions with a high likelihood of response to Share 35 Such that within regions with a high probability of response to Share 35, men not working prior to transplant had a 4.6 percentage point increase in their predicted probability of returning to work in the post-Share 35 period as compared to the pre-Share 35 period. (Table 8 – 23), but did not demonstrate statistically significant differences in any other subgroup.

Table 8 – 22. Marginal Effect of Share 35 on Predicted Probability of Returning to Work at Any Time During Follow-Up by Pre-Transplant Work Status & Sex – National Cohort

	Not Working Pre-Transplant				Working Pre-Transplant	
	Males n = 5371		Females n = 2,754		Males n = 1,408	
	Margin	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Share 35	0.010	0.524	0.006	0.6874	-0.020	0.4974
	Pred. Prob.	**SE**	**Pred. Prob.**	**SE**	**Pred. Prob.**	**SE**
Pre-Share 35	0.239	0.005	0.173	0.006	0.726	0.010
Post-Share 35	0.249	0.010	0.179	0.009	0.707	0.019

Logistic regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, physiologic MELD score, functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), follow-up time and transplant center. Margin indicates the change in the predicted probability of returning to work post-transplant. Predicted probabilities indicates the probability of returning to work in the Pre- or Post-Share 35 periods. *p<0.05, **p<0.001. Abbreviations: Pred. Prob. - predicted probability, SE - standard error.

Table 8 – 23. Marginal Effect of Share 35 on Predicted Probability of Returning to Work at Any Time During Follow-Up by Pre-Transplant Work Status & Sex – Regional Analysis

	Not Working Pre-Transplant					
	Low Likelihood of Response		**Moderate Likelihood of Response**		**High Likelihood of Response**	
	Males n = 1121	**Females** n = 609	**Males** n = 2544	**Females** n = 1289	**Males** n = 1689	**Females** n = 852
	Margin	**Margin**	**Margin**	**Margin**	**Margin**	**Margin**
Share 35	0.010	0.037	-0.012	-0.002	0.046*	-0.007

Logistic regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, allocation MELD score, MELD difference (allocation - physiologic MELD score), functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), count of follow-up visits, and transplant center. Margin indicates the change in the predicted probability of returning to work post-transplant. UNOS regions grouped by likelihood of response to Share 35, such that low, moderate and high likelihood groups include regions: 6, 8 and 11; 2, 3, 4 and 10; 1, 5, 7 and 9. *p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease.

Functional Status

Share 35 was associated with a 1.5 point greater difference in the change in functional status between transplantation and twelve months post-transplant, but no statistically significant difference at six months post-transplant (Table 8 – 24). Given that the Karnofsky scale grades functional status in 10 point increments (see section 7.4.2), the change in overall functional improvement is very small, and may not be clinically significant.

In subanalyses, across all three regional subgroups at both six and twelve months follow-up, Share 35 was not associated with a significant change in functional status (Table 8 – 25).

Table 8 – 24. Marginal Effect of Share 35 on Change in Functional Status at Six months & Twelve months Post-Transplant

	6 Months Post-Transplant n = 33,619			12 Months Post-Transplant n = 33,619		
	Margin	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35	0.272	0.703	0.698	1.534	0.694	0.027*

Ordinary least squares regression with fixed effects for transplant center. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, difference between physiologic and allocation MELD, functional status at transplant, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), and follow-up time. Margin indicates the difference between the Pre- and Post-Share 35 periods in the change in functional status score (Karnofsky Score, %) between transplant and 6 or 12 month follow-up. *p<0.05, **p<0.001. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease.

Table 8 – 25. Marginal Effect of Share 35 on Change in Functional Status at Six months & Twelve months Post-Transplant – Regional Analysis

	Low Likelihood of Response		Moderate Likelihood of Response		High Likelihood of Response	
	n = 7,120		**n = 16,478**		**n = 10,021**	
6 months post-transplant	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Share 35	0.039	0.964	0.946	0.369	-0.761	0.598
12 months post-transplant	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Share 35	0.462	0.693	1.819	0.084	1.474	0.261

Ordinary least squares regression with fixed effects for transplant center. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, MELD difference (allocation MELD - physiologic MELD), functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), and follow-up time. Margin indicates change in the functional status score (Karnofsky Score, %) between transplantation and either 6 or 12 month post-transplant follow-up contrasted between the Pre- and Post-Share 35 period. Regions with a low, moderate and high likelihood of response to Share 35 include: 6, 8 and 11; 2, 3, 4, and 10; 1, 5, 7 and 9. *p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease.

Post-Transplant Disability

Overall, with regard to post-transplant disability, at the national level there was no difference in the predicted probability of returning to work after implementation of Share 35, and only a small (but likely clinically insignificant) improvement in the change in functional status between transplantation and twelve months post-transplant. Alternatively, on regional

subanalysis findings within work status suggest that there is an increase in the predicted probability of returning to work amongst men not working prior to transplant in regions with a high likelihood of response to Share 35, but that such an effect was not seen in any other subgroup by sex, pre-transplant work status or likelihood of response to Share 35. There were no differences in functional status on regional subanalysis. Given the mixed findings, we conclude that Share 35 was not associated with decreased disability with regards to work status or functional status across the population of transplanted patients (fail to reject the null hypothesis), but that there are some indications of improved return to work within patient subgroups.

H3b. The effect of Share 35 in reducing post-transplant disability will be greater amongst patients transplanted with a high allocation MELD score, when controlling for medical status / disability at transplant, exogenous determinants of access to inpatient and outpatient care (supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality), health literacy and post-discharge environment.

Work Status

When accounting for the moderating effect of allocation MELD score on Share 35's impact on work status there were no significant effects identified across all 3 subgroups (males not working prior to transplant, females not working prior to transplant, or males working prior to transplant) (Table 8 – 26, predicted probabilities for each group by allocation MELD score are included in Appendix 6A).

In subanalyses stratifying the groups of regions defined by likelihood of response to Share 35, the effect of Share 35 varied between groups (Table 8 – 27). Within regions with a low likelihood of response, Share 35 was associated with an increase in the predicted probability of

returning to work in the Post-Share 35 period amongst females with high allocation MELD scores; such that patients with an allocation MELD score of 35 had a 10.3 percentage point increase and patients with an allocation MELD score of 40 had a 16.2 percentage point increase in the predicted probability of returning to work after Share 35 implementation. Within high likelihood regions, men not working prior to transplant with high allocation MELD scores also had an increased in the predicted probability of working after transplantation in the Post-Share 35 period (Table 8-27). There was no statistically significant effect within moderate likelihood regions.

Table 8 – 26. Marginal Effect of Share 35 by Allocation MELD Score on Predicted Probability of Returning to Work at Any Time During Follow-Up by Pre-Transplant Work Status & Sex – National Cohort

	Not Working Pre-Transplant				Working Pre-Transplant	
	Males n = 5371		Females n = 2,754		Males n = 1,408	
	Margin	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Share 35 at aMELD 10	-0.036	0.243	-0.018	0.529	-0.065	0.293
Share 35 at aMELD 15	-0.026	0.329	-0.014	0.580	-0.049	0.285
Share 35 at aMELD 20	-0.014	0.508	-0.009	0.675	-0.035	0.312
Share 35 at aMELD 25	-0.002	0.903	-0.003	0.879	-0.021	0.473
Share 35 at aMELD 30	0.010	0.499	0.005	0.734	-0.007	0.816
Share 35 at aMELD 35	0.023	0.169	0.014	0.440	0.005	0.897
Share 35 at aMELD 40	0.036	0.091	0.024	0.368	0.017	0.735

Logistic regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, difference between physiologic and allocation MELD score, functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), number of follow-up visits and transplant center. Margin indicates the change in the predicted probability of returning to work post-transplant for a given allocation MELD score. *p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, aMELD = allocation MELD score.

Table 8 – 27. Marginal Effect of Share 35 by Allocation MELD Score on Predicted Probability of Returning to Work at Any Time During Follow-Up by Pre-Transplant Work Status & Sex – Regional Analysis

	Not Working Pre-Transplant					
	Low Likelihood of Response		Moderate Likelihood of Response		High Likelihood of Response	
	Males n = 1121	Females n = 609	Males n = 2544	Females n = 1289	Males n = 1689	Females n = 852
	Margin	**Margin**	**Margin**	**Margin**	**Margin**	**Margin**
Share 35 at aMELD 10	0.010	-0.137	-0.075	0.073	0.031	-0.080
Share 35 at aMELD 15	0.010	-0.097	-0.059	0.055	0.034	-0.070
Share 35 at aMELD 20	0.010	-0.054	-0.042	0.036	0.037	-0.057
Share 35 at aMELD 25	0.010	-0.006	-0.026	0.017	0.041	-0.040
Share 35 at aMELD 30	0.010	0.047	-0.008	-0.003	0.044	-0.019
Share 35 at aMELD 35	0.010	0.103*	0.009	-0.022	0.048*	0.007
Share 35 at aMELD 40	0.010	0.162*	0.027	-0.043	0.052	0.037

Logistic regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, allocation MELD score, MELD difference (allocation MELD - physiologic MELD score), functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), count of follow-up visits, and transplant center. Margin indicates the change in the predicted probability of returning to work post-transplant. UNOS regions grouped by likelihood of response to Share 35, such that low, moderate and high likelihood groups include regions: 6, 8 and 11; 2, 3, 4 and 10; 1, 5, 7 and 9. *p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, aMELD - allocation MELD score.

Functional Status

When accounting for the moderating effect of allocation MELD score on Share 35, small, but statistically significant improvements in the change in functional status at twelve months post-transplant were identified amongst patients with high allocation MELD scores (Table 8 – 28). Amongst patients with allocation MELD scores >25, there was an approximate 1.5 point increase in the change in functional status from transplant to 12 months post-transplant when comparing the pre- and post-Share 35 periods. There were no statistically significant differences identified at six months post-transplant.

In regional subanalyses, there were no statistically significant changes in functional status identified within any regional subgroup at either six months or twelve months post-transplant (Table 8 – 29).

Table 8 – 28. Marginal Effect of Share 35 by Allocation MELD Score on Change in Functional Status at Six months & Twelve months Post-Transplant

	6 Months Post-Transplant n = 33,619			12 Months Post-Transplant n = 33,619		
	Margin	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD 10	1.601	1.190	0.179	1.117	1.163	0.337
Share 35 at aMELD 15	1.226	0.957	0.201	1.235	0.959	0.198
Share 35 at aMELD 20	0.850	0.776	0.273	1.353	0.796	0.089
Share 35 at aMELD 25	0.475	0.687	0.489	1.471	0.705	0.037*
Share 35 at aMELD 30	0.100	0.726	0.891	1.589	0.713	0.026*
Share 35 at aMELD 35	-0.276	0.877	0.753	1.706	0.817	0.037*
Share 35 at aMELD 40	-0.651	1.093	0.552	1.824	0.987	0.065

Ordinary least squares regression with fixed effects for transplant center. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, MELD difference (allocation MELD - physiologic MELD), functional status at baseline, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), and follow-up time. Margin indicates the difference between the Pre- and Post-Share 35 periods in the change in functional status score (Karnofsky Score, %) between transplant and 6 or 12 month follow-up at the stated allocation MELD score. *p<0.05, **p<0.001. Abbreviations: SE - Standard Error, MELD - Model for End Stage Liver Disease, aMELD - allocation MELD.

Table 8 – 29. Marginal Effect of Share 35 by Allocation MELD Score on Change in Functional Status at Six months & Twelve months Post-Transplant by Regional Subgroups. (A) Six Months Post-Transplant, (B) Twelve Months Post-Transplant

A.

	6 Months Post-Transplant					
	Low Likelihood of Response n = 7,120		**Moderate Likelihood of Response n = 16,478**		**High Likelihood of Response n = 10,021**	
	Margin	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Share 35 at aMELD 10	-1.238	0.573	2.253	0.185	1.417	0.259
Share 35 at aMELD 15	-0.836	0.630	1.857	0.189	0.896	0.433
Share 35 at aMELD 20	-0.435	0.738	1.462	0.218	0.374	0.740
Share 35 at aMELD 25	-0.034	0.971	1.066	0.312	-0.147	0.904
Share 35 at aMELD 30	0.367	0.606	0.671	0.523	-0.669	0.629
Share 35 at aMELD 35	0.768	0.335	0.275	0.815	-1.190	0.460
Share 35 at aMELD 40	1.169	0.296	-0.121	0.932	-1.712	0.361

Ordinary least squares regression with fixed effects for transplant center. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, MELD difference (allocation - physiologic MELD score), functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), and follow-up time. Margins indicates the change in the functional status score (Karnofsky Score, %) between transplantation and 12 month follow-up contrasted between the Pre- and Post-Share 35 period. Regions with a low, moderate and high likelihood of response to Share 35 include: 6, 8 and 11; 2, 3, 4, and 10; 1, 5, 7 and 9. *p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, aMELD - allocation MELD.

B.

	12 Months Post-Transplant					
	Low Likelihood of Response n = 7,120		**Moderate Likelihood of Response n = 16,478**		**High Likelihood of Response n = 10,021**	
	Margin	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Share 35 at aMELD 10	-1.845	0.442	2.633	0.085	0.772	0.601
Share 35 at aMELD 15	-1.120	0.565	2.386	0.067	0.940	0.484
Share 35 at aMELD 20	-0.395	0.798	2.140	0.059	1.108	0.381
Share 35 at aMELD 25	0.330	0.786	1.894	0.071	1.277	0.307
Share 35 at aMELD 30	1.055	0.319	1.647	0.122	1.445	0.266
Share 35 at aMELD 35	1.780	0.118	1.401	0.237	1.613	0.252
Share 35 at aMELD 40	2.505	0.077	1.154	0.401	1.782	0.254

Ordinary least squares regression with fixed effects for transplant center. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, MELD difference (allocation - physiologic MELD score), functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), and follow-up time. Margins indicates the change in the functional status score (Karnofsky Score, %) between transplantation and 12 month follow-up contrasted between the Pre- and Post-Share 35 period. Regions with a low, moderate and high likelihood of response to Share 35 include: 6, 8 and 11; 2, 3, 4, and 10; 1, 5, 7 and 9. *p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, aMELD - allocation MELD.

Post-Transplant Disability

Overall, with regards to post-transplant disability, the moderating effect of allocation MELD score on Share 35 was found in each of the outcomes, but to a varying degree of statistical significance and only within particular subgroups. For the work status outcome, the trend of an increasing effect of Share 35 with increasing allocation MELD score is seen across groups in both the national and regional analysis (with the exception of females not working prior to transplant in regions with a moderate likelihood of response to Share 35), yet this moderating effect only reached statistical significance amongst females not working prior to transplant in regions with a low likelihood of response to Share 35 and men not working prior to transplant in regions with a high likelihood of response to Share 35. For the functional status outcome, the results were less consistent. At six months post-transplant, none of the trends reached statistical significance and the majority of the six month analyses demonstrated a trend

in the opposite direction of the hypothesized effect. Alternatively, at twelve months post-transplant the national evaluation demonstrated the hypothesized effect and reached statistical significance. On regional analysis this trend was again demonstrated in regions with low and high likelihood of response to Share 35, but it did not reach statistical significance. Given the mixed findings we conclude that effect of Share 35 in reducing post-transplant disability was not consistently greater amongst patients transplanted with a high allocation MELD scores (fail to reject the null hypothesis).

8.4.3 Sensitivity Analyses

Comparison Between Patients Missing a Pre-Transplant Work Status

Patients missing a pre-transplant work status were excluded from the analysis of work status, given that patients were stratified by this status for analysis. Of the 10,593 patients that met inclusion criteria for the work-status evaluation, 303 (2.9%) were missing a pre-transplant work status. Descriptive comparisons are included in Appendix 6B. These comparisons indicate that patients missing pre-transplant work status were more likely to be have Veterans Affairs insurance (9.9% versus 1.3% in the cohort with completed work status) and an unknown educational status (24.4% versus 7.4%). In terms of medical condition patients with a missing work status were more likely to have hypertension (32.1% versus 23.3%), but less likely to have renal failure (9.4% versus 20.0%). Patients missing work status were also more likely to have a diagnosis of malignancy, which is concordant with findings of a lower physiologic MELD score and higher functional status at the time of transplant. Overall patients missing work status are slightly healthier, and have an improved functional status as compared to those not missing pre-transplant work status.

Inclusion of Simultaneous Liver + Kidney Transplants

A sensitivity analysis was completed excluding patients who underwent simultaneous liver and kidney transplantation. For hypotheses 3A and 3B, marginal effects were similar across the all outcomes for work and functional status, with inclusion or exclusion of the patients who underwent liver and kidney transplantation (Appendix 6C and 6D). We therefore included these patients in assessments of work and functional status for hypothesis testing.

Use of a Categorical Allocation MELD Score Variable

A sensitivity analysis was completed comparing the use of a continuous, binary or categorical variable for allocation MELD score within the interaction term for H3b. For the work status outcome, the binary allocation MELD score covariate demonstrated the expected trend, such that there was a positive margin associated with the Post-Share 35 high allocation MELD (≥35) covariate as compared to the reference category (Pre-Share 35 high allocation MELD), yet it did not reach statistical significance. A similar effect was seen in when allocation MELD score was subdivided into 3 categories, such that the Post-Share 35 high allocation MELD (≥30) had a positive marginal effect, yet again this didn't reach statistical significance. These findings are consistent with the trend within the continuous allocation MELD score covariate used in the main regression model. For the functional status outcome, the direction of effect seen for each dummy variable within the binary and 3 group allocation MELD score covariates is similar to that seen in the continuous allocation MELD score covariate. Across both the work status and functional status outcomes the findings with the use of a continuous, binary or 3 group allocation MELD covariate are consistent, we therefore preferred the use of the continuous allocation MELD score variable for hypothesis testing (Appendix 6E and 6F).

9. Discussion

Liver transplant allocation policy within the United States is guided by the principle of 'sickest first allocation'. As such, the evolution of allocation policy is marked by the continued aim of transplanting those patients in the greatest medical need of transplantation, which has been defined by a patient's MELD score since the current allocation policy's implementation in 2002. Modifications to MELD-based allocation have occurred incrementally over time, with the same overarching principle, prioritizing those patients who are 'the sickest' and have the greatest 'immediate need' for transplantation. Share 35, implemented in 2013, is one of these incremental changes to MELD-based allocation. Evaluation of policies such as Share 35 have relied, almost universally, on assessments of mortality amongst patients who are awaiting or have undergone transplantation. Unfortunately, these evaluations only address one aspect of the relative costs and benefits of such policy changes. In particular, very little attention has been paid to the potential economic impact of these policies in terms of inpatient utilization, or the potential impacts on patient disability (outside of mortality).

Given these notable gaps in current policy evaluations, this dissertation aimed to assess the potential impacts of Share 35, on post-transplant inpatient utilization and disability. Implemented in June 2013, Share 35 imposed greater intra-regional sharing, shifting organs to the sickest patients within each region. This shift altered the order of deceased donor allocation by placing all recipients with an allocation MELD score ≥35 onto a regional, rather than local waitlist. Under this policy, organs that would have previously been offered first to patients within a local area of distribution (donor service areas, DSAs) with a lower allocation MELD score, were instead offered to patients within the regional area of distribution with an allocation MELD score ≥35. Advocates of the policy suggested that by diverting organs to the sickest patients first,

there would be subsequent decreases in wait time and in turn decreases in both pre- and post-transplant mortality. Previous studies, which focused on mortality, have found that on a national level there have been small improvements in waitlist mortality, but no improvements in post-transplant outcomes[74]. Yet, to date, outcomes beyond mortality have yet to be fully evaluated.

Utilizing both the SRTR database and a novel database linkage between state inpatient datasets and SRTR, a comparative analysis of the post-transplant disability and inpatient utilization was completed. These results shed light on the potential economic and quality of life impacts of the Share 35 policy. Additionally, this dissertation evaluated the policy not only at the national level, but assessed the regional impact. Such evaluation is essential given that while the policy was implemented nationwide, it is truly a regional policy and is likely to have differing effects based on regional characteristics.

9.1 Interpretation of Results

This dissertation specifically explored factors associated with inpatient utilization in the transplant period and the effects of Share 35 on both inpatient utilization and post-transplant disability. Overall this analysis demonstrates that both physiologic MELD score and donor organ quality are strong predictors of inpatient utilization following transplantation, indicating that both poorer physiologic condition of the patient and poorer quality of the donor organ lead to increased admissions and admitted days in the post-transplant period. Given that both of these factors are commonly considered in the development of allocation policy, this finding is important in assessing the potential impact of future policies.

In the assessment of the Share 35 policy, our findings suggest that the policy was associated with a decrease in inpatient utilization both in terms of admissions and admitted days (when controlling for patient medical condition / disability at transplant), and that this effect is greatest amongst patients with the highest allocation MELD sores. This result suggests that

amongst patients who were most likely to benefit from this policy, there was a substantial decrease in utilization. The effect of the policy on disability was less robust, with very small changes noted in functional status at 12 months post-transplant, and a trend of increased likelihood of return to work in the Post-Share 35 period. Overall this analysis indicates that the Share 35 policy resulted in decreased inpatient utilization and likely some improvement in post-transplant disability amongst patients transplanted following policy implementation. A summary of all findings, at the national level, are included by research question and hypothesis below.

Table 9 – 1. Summary of Findings by Research Question and Hypothesis

Questions & Hypotheses	Hypothesized direction of effect	Actual direction of effect
Q1. What are the factors associated with inpatient utilization among liver transplant patients in the post-transplant period?		
H1a. Patients with a higher physiologic MELD score at transplant will have greater inpatient utilization in the post-transplant period, ceteris paribus	↑	↑
H1b. Patients who are transplanted for malignancy will have less post-transplant inpatient utilization as compared to patients suffering from liver failure secondary to cirrhosis (steatohepatitis), ceteris paribus	↓	↑
H1c. Patients with a lower ability to pay for care will have greater post-transplant inpatient utilization than patients with a greater ability to pay for care, ceteris paribus	↑	NS
H1d. Patients who receive a poorer quality organ will have higher inpatient utilization in the post-transplant period, ceteris paribus	↑	↑
Q2. How did Share 35 impact post-transplant inpatient utilization?		
H2a. Share 35 increased inpatient utilization in the post-transplant period, when not controlling for medical condition / disability at transplant, but controlling for other exogenous predictors of inpatient utilization.	↑	↓
H2b. Share 35 decreased inpatient utilization in the post-transplant period when controlling for medical condition / disability at transplant and other exogenous predictors of inpatient utilization	↓	↓
H2c. The negative effect of Share 35 on inpatient utilization in the post-transplant period will be larger amongst patients with high allocation MELD scores when controlling for medical condition / disability at transplant and other exogenous predictors of inpatient utilization	↑ with increasing allocation MELD score	↑ with increasing allocation MELD score
Q3. How did Share 35 impact post-transplant disability?		
H3a. Share 35 resulted in less post-transplant disability, when controlling for medical status / disability at transplant, exogenous determinants of access to care, health literacy and post-discharge environment	↓	↑ for functional status, NS for work status
H3b. The effect of Share 35 in reducing post-transplant disability will be greater amongst patients transplanted with a high allocation MELD score, when controlling for medical condition / disability at transplant, exogenous determinants of access to care, health literacy and post-discharge environment	↑ with increasing allocation MELD score	↑ with increasing allocation MELD score

Direction of effect indicated by upward or downward arrow indicating an increase or decrease in the outcome respectively. For question 1, across all hypothesis the following factors are controlled: patient preferences, supply of inpatient and outpatient medical services, ability to pay for care, transplant program quality, medical condition / disability at transplant, donor organ quality, health literacy and post-discharge environment. For question 2, the additional exogenous predictors of inpatient utilization include all factors included in question 1, with the exception of donor organ quality. Abbreviations: NS – not significant, Q – research questions, H – hypothesis.

9.1.1 Factors Associated with Inpatient Utilization

Prior literature on inpatient utilization in the post-transplant period was primarily single center in nature, restricted to the 90 days post-transplant, and limited to only utilization at the transplant center. Our study expands upon previous work by both including utilization outside of the index hospital (transplant center) and extending the follow-up period to include utilization up until six months after transplantation. Results of this study demonstrate a relatively high rate of both inpatient utilization and readmissions in the Pre-Share 35 period, with over 50% of patients experiencing at least one readmissions and approximately 30% of patients experiencing more than two readmissions within six months of transplantation. Similarly, greater than 50% of patients were admitted for more than two weeks and approximately 30% admitted for more than 30 days during the six months following transplantation. Such high rates of utilization highlight the overall acuity of these patients as well as the significant burden of care this patient population places on the healthcare system. As such, policies that are able to reduce utilization are likely to have a substantial impact on the overall cost of the healthcare system. It is also important to note that rates of readmission and admitted days varied by region and transplant center, with higher acuity regions having higher rates of readmissions and admitted days. This again suggests that it is the highest acuity patients (and regions) which must be targeted in order to make a substantial and durable impact on health resource utilization by this population. The variability seen between centers and regions is consistent with previous reports in the literature, yet this work further explains a component of this variability due to regional acuity.[7]

Individual patient factors associated with post-transplant inpatient utilization found in this study highlight the importance of disease acuity and donor organ quality. Specifically a patient's physiologic MELD score at the time of transplant was associated with both increased number of

admission and admitted days. Patients with low physiologic MELD scores (<20) were predicted to have between 1.6 and 1.8 admissions and 23 – 28 admitted days, whereas patients with physiologic MELD scores >35 were predicted to have slightly greater than 2 admissions and 37 to 41 admitted days. This finding is consistent with previous work, which has demonstrated correlation between physiologic MELD score and utilization at the index hospital and within 30 days of transplantation. This work builds upon these findings and further supports the strong correlation between physiologic MELD score and inpatient utilization up to six months after transplantation and beyond the index hospital. Similarly the DRI, which quantifies the quality of the donor organ, was also highly associated with post-transplant utilization in terms of admitted days and admissions, such that each additional DRI point (range 1-4) was associated with a 0.22 increase in the number of admissions and a 5.7 day increase in the predicted number of admitted days. In comparison to other factors assessed, DRI demonstrated one of the strongest effects, likely due to the association of factors which contribute to high DRI scores (donation after cardiac death, warm ischemia time, older age donors, etc.) with the rates of post-operative complications and delayed graft function which may extend the duration of the transplant admission[7,10]. DRI has previously been associated with increased risk of readmissions within 30 days in a single center study, but has not previously been shown to be associated with total inpatient utilization[7]. This finding highlights the importance of donor quality in predicting utilization in terms of both readmissions as well as total admitted days. This is particularly important in the context of ongoing efforts within the transplant community to increase utilization of higher risk donor organs (discussed below).

Interestingly, patients transplanted for malignancy had a greater number of admissions when compared to patients with steatohepatitis (inclusive of non-alcoholic and alcoholic

steatohepatitis), but there was no statistically significant difference in the total number of admitted days between these two groups. Patients with malignancy are physiologically less ill at the time of transplantation, as they are awarded MELD exception points which inflate their allocation MELD score, granting them greater priority for transplantation. The finding that they have increased admissions, but no increase in admitted days, suggests that they have a higher rate of readmissions, but may have shorter post-transplant lengths of stay (during the index admission). Potential causes for this difference in readmissions may be due to the increased rate of acute cellular rejection amongst this patient population, due to their more robust immune systems (secondary to less physiologic illness). Alternatively given that the difference in admissions is relatively small (difference of 0.21 predicted admissions) and that there is no difference in admitted days, one may also consider that the current allocation system (which provides MELD exception points to patients with malignancy in order to expedite their transplantation) adequately reaches a degree of equality between patients with malignancy and physiologic liver disease, such that these two distinct groups of patients have almost equivalent outcomes with regards to post-transplant utilization.

In contrast to the medical factors assessed as risk factors for increased inpatient utilization, a patient's ability to pay for care was not associated with post-transplant inpatient utilization, which is in contrast to findings in other fields of medicine.[122,128] One potential explanation for this finding, which is in contrast to the relationship between decreased access and increased inpatient utilization, is that the relative access to inpatient care within this population differs in comparison to other populations. Patients who receive a transplant undergo arduous pre-transplant evaluations which assess a patient's insurance coverage, financial resources and other social support factors, all which must reach particular standards in order to be considered a

candidate for transplantation. Patient selection may therefore heavily contribute to this finding, as such selection may diminish the relative economic barriers to access to care seen in other patient populations.

Overall, the evaluation of factors associated with inpatient utilization provides a foundation for evaluating the potential impacts of liver transplant allocation policy changes. At present policies rely on providing greater access to the sickest patients. Based on these results such policies are likely to lead to increased utilization, as patients with higher physiologic MELD scores utilize more resources. As well, these results indicate the potential effects of increasing use of high risk donor organs, such that increased use of such donor organs may also lead to increased inpatient utilization.

9.1.2 Impact of Share 35 – Nationally & Regionally

The Share 35 policy prioritized patients for transplantation based on their allocation MELD score, which inherently led to an increase in the rate of patients transplanted at MELD scores ≥35 which is seen both in this study and within the previous literature[11,74]. Nationally, following implementation of Share 35, the rate of allocation to patients with allocation MELD scores >30 increased by 8.4 percentage points and to patients with allocation MELD score ≥35 by 7.2 percentage points. Given that approximately 6,400 adults undergo transplantation annually, this increase is associated with approximately 538 more patients transplanted each year with an allocation MELD score >30 and 461 with an allocation MELD score ≥35. This trend in higher MELD allocation is also associated with other increases in patient acuity, including an increase in the mean physiologic MELD score, rate of patients hospitalized or within the ICU prior to transplant, need for various life support measures prior to transplantation, and decreased functional status at the time of transplant. Overall these trends indicate that following Share 35

patient acuity increased not only by allocation MELD score, but in terms of various markers beyond MELD score alone.

These changes in acuity were also present on regional evaluation. While almost all regions saw an increase in the rate of allocation to patients with allocation MELD score ≥35, this increase ranged dramatically from 2.4% to 13.5%. Similarly, there is wide variability in the other markers of patient acuity, with the majority of regions seeing an increase in the rate of hospitalized or ICU bound patients at the time of transplant (6/11 regions) the need for life support measures prior to transplant (6/11 regions), and dialysis dependence (8/11 regions), yet only a minority with increased rates of ventilator dependence (3/11 regions). These changes likely indicate that regions varied in how they responded to Share 35, with many transplanting sicker patients than they did prior to policy implementation. Yet it also indicates that many regions maintained particular selection policies, for example, with many regions still maintaining low rates of transplantation amongst patients requiring ventilator and life support measures[vi]. Additionally, it is important to note that while the mean allocation MELD scores increased in 9 regions, the physiologic MELD scores increased within only 5, likely indicating that many regions saw increases in high MELD allocation due to increased transplantation to patients who had been awarded MELD exception points; again indicating probable changes in patient selection following policy implementation.

In assessing Share 35, it is important to note that while it is advertised as a national policy, the policy impacted organ availability and distribution within regional borders. In

[vi] It is important to note that these changes are only amongst transplanted patients. The current data analysis is limited in that we are unable to assess how selection changed across the entire population of patients with end stage liver disease, including those patients who were not listed for transplant, and those who were listed but never underwent transplantation.

particular, the policy was aimed at shifting organs to patients with allocation MELD scores ≥35 and away from local areas where patients were receiving organs at lower allocation MELD scores. In predicting a particular region's response to Share 35, one would expect that regions would need a pool of patients with allocation MELD scores ≥35 that could benefit from greater organ availability and a local area (DSA) from which organs could be shifted. Within this dissertation, it was proposed that regions with high rates of high MELD allocation and high variability between DSAs within regions would have the greatest response to Share 35. The predicted responses of different regions were categorized as low, moderate and high based upon these characteristics. The magnitude of changes seen within regions following Share 35 approximated the predictions for regional response, yet indicated that there were likely other predictors that were not initially considered. Overall, almost all regions saw an increase in acuity following Share 35 implementation. The regions with the greatest relative change in very high MELD allocation (allocation to patients with allocation MELD scores of ≥35) were within the high and moderate groups, and similarly regions within these groups also had the greatest increases in the patients requiring life support prior to transplantation and dialysis dependence. Interestingly, two of the regions in the low likelihood of response group also saw substantial changes in both very high MELD allocation and the rate of patients hospitalized or within the ICU prior to transplant. This is contrasted by two of the high acuity regions which has very little change in very high MELD allocation (regions 1 and 7). There are a variety of potential explanations for why these changes did not match the predicted responses. In particular regions with lower relative responses were more likely to have fewer DSAs within the region and also had high rates of very high MELD prior to policy implementation. The latter may indicate that these regions had a lower ability to change their patient selection in response to the policy, as

they were already listing and transplanting very sick patients prior to Share 35 implementation. Alternatively, larger changes may have been seen in regions with a lower predicted degree of response for the opposite reason, as these regions may have had a greater ability to change patient selection because prior to Share 35 they were not listing the sickest patients for transplantation. Additionally a high degree of change was also seen in regions where there was the potential for greater DSA competition, for example within region 11. Within this region all DSAs had relative similar acuity prior to Share 35, but after implementation of the policy some DSAs saw significant changes indicating that they may have seen the opportunity to increase their rate of transplantation by changing selection practices and listing sicker patients. Overall, it appears that regional responses to Share 35 were influenced by both pre-policy rates of very high MELD allocation and intra-regional variability in acuity between DSAs, but that other factors such as regional competition, DSA density and capacity for change in patient selection may have also contributed.

Overall, evaluation of changes following Share 35 at the national level indicates mild increases in acuity both in terms of physiologic and allocation MELD scores as well as other markers of acuity. Yet when these changes are further evaluated at the regional level it is clear that regions responded and were affected very differently. Understanding these varying trends between regions is essential in evaluating the impact of Share 35. As presented within the conceptual models within this dissertation, the two causal pathways for the impact of Share 35 on utilization act in opposing manners through increased medical acuity and increased organ availability. Within regions which altered selection practices, leading to the transplantation of patients who were much sicker Post-Share 35 as compared to Pre-Share 35, one would expected increase in utilization and post-transplant disability. In contrast, regions which benefited from the

change in organ availability, which ultimately began transplanting sick patients more rapidly may conversely see a decrease in utilization and disability. Overall, the analysis of these trends and the documented variability between regions substantiates the need to analyze policy changes at their level of intervention, rather than at the national level where the mean effect may not adequately capture the true impact of the policy.

9.1.3 Impact of Share 35 on Inpatient Utilization

Conceptually the Share 35 policy further prioritized the sickest patients for liver transplantation, which was theorized to have two potential opposing effects on inpatient utilization. By transplanting more sick patients, and incentivizing transplant centers to list sick patients, the policy could have led to increased inpatient utilization. Alternatively, by increasing organ availability to the sickest patients and therefore transplanting sick patients more quickly (and in turn earlier in the course of their illness), the policy could have led to decreased inpatient utilization, Through stepwise analysis of each of these potential causal pathways, this study demonstrates that the Share 35 policy ultimately resulted in decreased inpatient utilization, primarily through increased organ availability. This effect was noted as a mean effect across the entire transplant population, with predicted reductions in admissions and admitted days when all else is equal, yet more specifically as an effect that is moderated by a patient's allocation MELD score such that with increasing allocation MELD scores, patients saw increasing benefit from the Share 35 policy, with corresponding reductions in both admissions and admitted days. The magnitude of these effects indicates that Share 35 has a much greater effect on admitted days than individual admissions, suggesting that overall Share 35 reduced inpatient length of stay, while having less of an effect on readmissions.

When the predicted effects are extrapolated across the number of transplants completed within the U.S. each year the true impact on utilization and the corresponding economic impact of the policy can be assessed. Amongst the highest acuity patients (allocation MELD scores ≥30), the policy resulted in a decrease in 2-4 admitted days and 0.1-0.3 admissions. Given that annually, approximately 6400 adults undergo liver transplantation and over 25% are transplanted at an allocation MELD of ≥35, and 15% with an allocation MELD score of 30-34, a conservative estimate[vii] of the admissions and admitted days saved per year amongst high acuity patients following the policy would be approximately 550 admissions and 8,050 admitted days. Although these are approximations, these estimates demonstrate that the policy was associated with substantial reductions in inpatient utilization nationally, which was likely associated with notable savings to the healthcare system.

As previously discussed, the Share 35 policy ultimately altered intra-regional organ allocation, and therefore was evaluated at the regional level. On subanalysis, significant reductions in inpatient utilization were seen within regions 1, 5 and 9, but not in region 3. Regions 1, 5 and 9 are similar, in that these regions were categorized as having a high likelihood of response to Share 35 (high median allocation MELD scores, and high intra-regional variability such that certain DSAs within the region had more high acuity patients than others). Alternatively, region 3 was predicted as being less likely to respond to Share 35. As such, the difference in the intra-regional findings are concordant with the expected effect of the policy. These differences are of significant importance, as to date, analyses of Share 35 have only been

[vii] Estimates of admissions and admitted days saved were made by multiplying the number of patients transplanted at an allocation MELD score of 30-34, 35-39 and 40 by the predicted change in admissions and admitted days for allocation MELD scores of 30, 35 and 40 respectively. Number of transplanted patients within each group is based upon the number of adult patients transplanted nationally from January – December 2015.

completed at the national level, which hinders the ability to accurately assess the success and/or failure of the policy. In considering the variability in regions across the U.S. and that this study suggests the greatest effect of Share 35 is most likely isolated within high acuity/high variability regions, it is likely that current national estimates of the effect of Share 35 underestimate the potential effect in some regions, and overestimate those seen in others. This is even more apparent when the magnitude of effects are considered, as the reductions in utilization seen within high acuity / high variability regions are equal to or greater than the national estimates, demonstrating that potential benefits of the policy were likely diluted within the pooled analyses.

Overall, the Share 35 policy lead to significant reductions in inpatient utilization. These results are seen both nationally, but even more significantly within regions with a high likelihood of response to Share 35. These findings suggest that after Share 35, patients spent less time hospitalized after their transplantation, and were less likely to be readmitted, overall suggesting that patients had better functional and medical outcomes than in the Pre-Share 35 period. When considered in conjunction with prior literature, Share 35 ultimately has allowed for the transplantation of more high acuity patients with no change in post-transplant mortality, and no consequential increase in utilization. As such, the findings of this study strengthen the view of Share 35 as a success amongst allocation policy changes, as it has both decreased geographic inequities and also improved post-transplant outcomes.

9.1.4 Impact of Share 35 on Post-Transplant Disability

Similar to the conceptual model for inpatient utilization, Share 35 was theorized to improve post-transplant disability through increased organ availability, such that by transplanting patients earlier they have a greater potential for full recovery. To assess these changes, this study evaluated both return to work and the change in post-transplant functional status. Although there

were no statistically significant differences in the predicted probability of returning to work identified in the national analyses, the results demonstrate the expected trend, with higher likelihood of returning to work following Share 35 and a greater increase in the probability of returning to work with increasing allocation MELD score. Prior to Share 35 the predicted probability of returning to work amongst men and women with high allocation MELD scores (≥30) not working prior to transplant was relatively low, 23-24% for men and 17-21% for women, and amongst men working prior to transplant was relatively high (73-75%). Across each of these groups the predicted increase in the probability of returning to work ranged from 1-4%, which by conservative estimates[viii] is likely to result in at least 50 additional transplant patients (who were transplanted at high allocation MELD scores) returning to work annually. This trend towards increased likelihood of return to work indicates that the policy has provided a greater opportunity for patients to fully recover from their transplant, allowing them the ability to return to the work force and regain functional independence.

Upon further regional analyses, there were statistically significant differences identified amongst men not working prior to transplant in regions with a high likelihood of response to Share 35, such that after Share 35 men had a five percentage point increase in the predicted probability of returning to work post-transplant. This trend was further identified across almost all subgroups (by sex and pre-transplant work status), yet it again did not reach statistical significance. These findings suggest that there was likely a small improvement in return to work,

[viii] Estimate is made based upon 6,400 patients transplanted annually, with approximately 2,600 patients transplanted with high allocation MELD scores (≥30). Given the change in the predicted probability of returning to work ranged from 1-4%, conservative estimates were made using a 2% increase in the predicted probability of returning to work.

which is strongest amongst the subset of patients most likely to benefit from the Share 35 policy, those with high allocation MELD scores in regions likely to respond to the policy.

With regards to functional status, this study did identify small improvements by one year of post-transplant follow-up, but the incremental improvement was very small (1.5%). Post-hoc analysis of the change in functional status between the pre- and post-Share 35 cohorts demonstrated that there is no obvious difference between these two groups (Appendix 7A). The lack of association between the Share 35 policy and the change in functional status may ultimately be related to the way in which functional status is abstracted (often based on chart review and not based upon real-time assessment of the patient), or due to the fact that the scale is not granular enough to discern changes in functional status (scale ranges from 0-100% but is measured only at deciles).

Overall, the assessment of post-transplant disability is encouraging. The findings suggest that Share 35 was associated with very mild improvements in both return to work as well as improved functional status, collectively indicating a reduction in post-transplant disability. These findings are concordant with the reductions seen in inpatient utilization, as collectively these results suggest that Post-Share 35 patients were less likely to be hospitalized and more likely to return to work, overall suggesting more functional independence.

9.2 Limitations

9.2.1 Data Limitations

There are several limitation to the current analysis which should be considered during interpretation of the results. These limitations can be classified as either threats to internal or external validity.

Internal Validity

The current study aimed to evaluate the impact of Share 35 through a pre- post- study design in which different factors (utilization, disability) were assessed between groups based on the date of transplantation. Inherent in this study design is the lack of a control group, as the policy was implemented across the entire UNOS system, affecting all liver transplant recipients, centers and regions at the same time. To mitigate this threat the study included multiple sub analyses which strengthened the design. Specifically, the comparison of differences across allocation MELD scores and by region allowed for many of the hypotheses to be assessed using a methodology akin to a difference-in-differences study design, identifying changes within specific patient cohorts. One of the concerns associated with the lack of a control group is that the study is limited in its ability to discern if the changes identified are directly related to the implementation of the Share 35 policy or are simply secular trends. To assess if secular trends were present, in-patient utilization and post-transplant work-status were plotted over time (Appendix 7B). This visual assessment does not suggest that either utilization or disability were changing in the Pre-Share 35 period, prior to policy implementation. Such assessment does not eliminate this threat to validity, as only use of a control group, randomization or other specific study design alteration would make this possible

The second threat to internal validity relates to the measurement of various predictors and the method of data collection. Secondary data analysis, particularly of administrative data, is often hindered by concerns related to data accuracy. [129,130] Such accuracy is improved when clinical databases are linked to verify reporting between administrative and clinical datasets. Within this study, the evaluations of utilization were done with linked data where medical comorbidities, insurance status, state of residence and other covariates were cross-validated

between databases. Variables contained only within one dataset, such as functional status and return to work, were unable to be validated and therefore validity of these measures relies solely on a single database. These variables are derived from the SRTR registry which obtains data from standardized UNOS reports which are completed by transplant centers for each patient at the time of listing, transplantation and follow-up. A recent study comparing chart review done for a clinical trial and the UNOS registry forms indicated over 90% concordance between the two data sources, but did note greater discrepancy within the functional status (10.6% with discrepant functional status scores) and education (7.8% with discrepant status, 19.2% with missing status).[131] Unfortunately, the direction of discrepancy (reporting higher or lower functional status for example) was not reported within this study, and therefore inferences about potential impact of these missing or discrepant data cannot be made. Additionally, one must consider that there is potential for bias in reporting of functional status at the time of transplantation and follow-up, as each of these reported values are used for risk adjustment in reporting center-level patient outcomes. If present, this bias could result in reporting of lower functional status at listing and higher functional status at follow-up. Overall, such bias is likely to be stable over time as there were not interval changes in how functional status was considered in risk adjustment over the course of the study period.

A third threat to internal validity arises from the grouping and classification of regions with respect to their likelihood of response to Share 35. Within this dissertation the likelihood of effect of Share 35 is defined both by the overall regional acuity as well as the intra-regional variability. To my knowledge there are no previous studies which have attempted to make such classifications, and therefore in developing this scale the cut points are rather ambiguous. One could argue that there are other factors that contribute to the likelihood of response to Share 35,

or other factors that define regional acuity, decreasing the overall validity of the definitions presented within this study. With this in mind, the national results are heavily emphasized over the regional comparisons when discussing the main results of the study.

A fourth consideration is that this analysis focuses solely on the impact of Share 35 on those patients who underwent transplantation. This dissertation does not consider the impact on patients who were not transplanted as a result of this policy and therefore does not consider the potential opportunity costs associated with delayed or missed opportunities for transplantation on patients of lower allocation MELD scores that were not offered organs due to the new intra-regional sharing. It is unknown what the direct impact is on these patients, whether this resulted in longer wait list times, longer pre-transplant hospitalization, increased pre-transplant complications, loss of work, or even death prior to transplantation. It is important to note that prior studies have demonstrated that amongst patients with physiologic MELD scores <35 that there was no change in waitlist mortality following implementation of Share 35.[11] While mortality is only one consideration, as emphasized by this dissertation, it is reassuring that regional sharing for the highest acuity patients has not resulted in greater mortality amongst those patients at risk for poorer outcomes secondary to the policy.

A fifth threat to internal validity is the limitation that utilization within this study is constricted to the geographic boundaries of each state included within the study. Inherent in the types of administrative databases selected for this study, patient utilization that occurs outside of the state providing the data, is excluded. In order to minimize this threat, patients who were not state residents of the same state they underwent transplantation were excluded, yet this does not fully mitigate possible out-of-state utilization. This is particularly true for patients that live close

to state borders. Given this limitation, utilization may be underestimated, and therefore the findings should be considered conservative estimates of inpatient utilization.

Finally, as with any administrative database, there is the possibility that unmeasured variables contribute bias to the results. In the assessments of utilization, unmeasured factors which may bias the results include the lack of adequate measures of patient preferences (demand for medical services) as well as accurate measures of social support (post-discharge environment). In the assessment of disability, the analysis was limited to only variables within the SRTR dataset and therefore information that was previously attained using patient zip code (supply of inpatient and outpatient services, zip code median income, rural/urban continuum, and distance to the transplant center) were all excluded. Inclusion of these variables within the disability model would have likely decreased the amount of unmeasured error and allowed for more precise measurement of the effect of Share 35.

External Validity

Threats to external validity are those which may decrease the generalizability of the results of this study. Within this study, generalizability relies on how accurately the study cohorts represent the transplant population, both within each region and nationally. While the study cohort for the disability outcomes was inclusive of all patients who underwent transplantation, and met study criteria, the utilization analysis was limited to a six-state cohort. Comparisons between the six-state cohort and the remaining patients transplanted in the U.S. during that same time period indicated only small differences between the two groups. Amongst those differences (included in Appendix 2A), the most important are related to patient acuity. The six-state cohort included a higher rate of patients at allocation MELD scores ≥35, and is inclusive of a greater proportion of patients from high acuity regions than the remaining national sample. While these

differences may bias the results, making the national estimates more representative of high acuity regions, the sample did include a large proportion of patients from lower acuity regions (regions 3 and 8) which ultimately contribute variability to the sample, and additionally on regional sub analyses provided estimates for lower acuity regions. Overall, while there are some limitations of the sample, it is very similar to that of the national cohort of transplanted patients and therefore the results can be considered generalizable to the national population.

A secondary concern is that data limitations did not allow for complete data collection for all states within each region, with the exception of region 9. Comparisons between cases included and excluded from the utilization cohort within each region indicated that overall the utilization cohorts were very similar to the remaining patients within their region, yet there were notable differences in regions 5 and 8. The utilization cohort for region 5 accounted for over 70% of transplanted patients from this region. Patients included in the utilization cohort were at much higher acuity as compared to the remaining region. Although it is difficult to predict exactly how this difference may affect the generalizability of the estimates, one should consider that when considering Share 35 for this region, without adjustments for medical acuity or the moderating effect of allocation MELD score, that the estimates be larger than would be expected if the entire region were included. When medical acuity and allocation MELD score are accounted for, the models may alternatively underestimate the effect due to the lack of patient variability within the utilization cohort. With these two considerations in mind, given that the utilization cohort for region 5 accounts for such a large percent of the overall population of transplanted patients within the region, our estimates are likely reflective of the average patients within this region. Alternatively, the region 8 utilization cohort was lower acuity as compared to the remaining region, driven heavily by the high rate of transplantation for malignancy. Regional

analysis for region 8 alone was precluded due to sample size, but it is important to note this difference.

9.3 Implications of Findings

This dissertation evaluates inpatient utilization and post-transplant disability in response to UNOS's Share 35 policy. The results of this study have implications specific to the Share 35 policy as well as for future allocation policy changes.

9.3.1 Impact of Share 35, Beyond Patient Survival

Since the approval of 'The Final Rule' in 1998, liver transplant organ allocation policy has been aimed at distributing organs in terms of medical urgency and with the goal of geographic equity. Prior policy changes including the transition to MELD based allocation in 2002, Share 15 in 2005 and regional sharing for status 1A candidates in 2010 were all targeted at these two goals. Share 35 is the most recent of these policies, specifically aimed at diminishing intra-regional inequities and increasing access to patients with the highest allocation MELD scores. Initial reports of this policy indicated that there was a higher rate of allocation to patients with MELD scores ≥35, with no associated change in post-transplant mortality. Yet the majority of these results were limited both through the method of analysis and also in scope.

Previous studies of Share 35 focused primarily on national analyses of the policy. As highlighted in previous sections, analysis at this level does not account for the fact that Share 35 was ultimately a regional policy and that each individual region had a different potential response based on their patient population and the intra-regional variation. Specifically this study demonstrates that regions had an increase in allocation to very high MELD patients (≥35) between 0 and 13.5%, and that while many saw an increase in their mean allocation MELD score, only 5 saw an increase in the physiologic MELD score. By analyzing the policy at a level

higher than the level of implementation, there is a risk of diminishing potential improvements of the policy, but also hiding possible consequences of the policy.

In regard to scope, previous Share 35 policy evaluations have relied, almost, solely on the assessment of waitlist and post-transplant mortality. While it is clear that these two outcomes are of the utmost importance, they do not fully address the potential impact of this policy. In particular, to date, there have been no prior studies evaluating the impact on health resource utilization or patient-centered outcomes such as post-transplant disability. This study demonstrates that while the policy has led to an increase in the transplantation of high acuity patients, that through increased organ availability it has resulted in decreased inpatient utilization. While this may seem counter-intuitive, by increasing access to donor organs for patients at the highest MELD scores, these patients were likely less sick due to decreased wait times, resulting in patients who were less debilitated at the time of transplantation. This theory is supported by the fact that the decreases in utilization were most profound amongst patients with high allocation MELD scores and were greatest within regions most likely to benefit from the Share 35 policy. Additionally, this dissertation assessed the impact of the Share 35 policy on disability, in terms of both return to work after transplantation and change in functional status. Patient disability had not previously been evaluated in the context of allocation policy changes. Results of this study indicated that amongst men not working prior to transplant that within high acuity regions there was an increase in the predicted probability of returning to work. Similar trends were identified within other subgroups, but they did not reach statistical significance. Such results suggest that the Share 35 policy may have improved disability amongst patients most likely to benefit from the policy. Unfortunately, this study did not demonstrate clinically significant improvement within functional status. Although the differences identified in this

study are relatively small and subscribed to only a subset of patients, it does suggest that allocation policies which improve access to organs for the sickest patients may in fact lead to improvements in post-transplant disability. Both utilization and disability are important outcomes to consider when assessing allocation policies as they go beyond the binary outcome of survival and provide insight into how well patients do following transplantation. A policy that results in increases in utilization and disability, but does not change survival, is one that results in a more debilitated and less functional population of transplant recipients, an outcome that many would not view as successful. Alternatively, this study demonstrates that while there have yet to be substantial improvements in survival following Share 35, the policy has resulted in reduced inpatient utilization and mildly reduced disability, overall suggesting improvement in post-transplant outcomes.

9.3.2 Implications for Future Allocation Policy Changes in Liver Transplantation

A variety of ethical and economic theories can be employed when designing systems to allocate scarce resources. Four of the most common theories include: treating people equally, favoring the worst-off, maximizing total benefits and rewarding social usefulness. Over time, although policies have changed, UNOS has relied heavily on the principle of worst-off prioritarianism in allocating livers for transplantation; this theory of allocation is most commonly referred to as either the 'rule of rescue' or 'sickest first allocation.' Share 35, the topic of this dissertation, is in many ways an example of this theory, yet the effect of the policy is also derived from treating people equally with respect to geography (a key component to 'The Final Rule').

Share 35 employed principles of sickest first allocation by prioritizing patients with allocation MELD scores of 35 or higher over patients with lower allocation scores. This

component of the policy aligns with worst-off prioritarianism. In isolation, policies which rely solely on this principle prioritize the desire to rescue those in greatest need over post-treatment prognosis. If this were the only principle guiding Share 35, we would have then expected to see increased utilization and greater disability following implementation, but on the contrary, Share 35 resulted in the opposite. This alternative arises because Share 35 additionally aims to treat patients, within the borders of each UNOS region, equally once they reach an allocation MELD score of 35, by providing them equal access to all organs within the specified region. This intra-regional sharing is the principle which results in increased organ availability, the pathway through which the effect of Share 35 was identified within this study.

Intra-regional sharing is a principle that is often debated in the field of organ transplantation. Proponents suggest that greater sharing will lead to greater equity, while opponents raise concerns about the feasibility of sharing over great distances and the concern that exporting organs does an injustice to the community from which they were donated. While it is important to acknowledge the limits of sharing across great distances as well as the ethical arguments against moving donated organs outside of their community, achieving equity in transplantation has been an aim since the approval of 'The Final Rule.' This dissertation supports that regional sharing is a step towards such equity as well as a step towards improved patient outcomes.

As future allocation policy changes are considered, the impact of regional sharing should be viewed as a potential avenue for improved patient outcomes. Potential expansions of the Share 35 policy could include lowering the threshold for intra-regional sharing (at present proposals exist to lower this threshold to an allocation MELD score of 30) or expanding sharing beyond regional borders – ultimately allowing shares between UNOS regions. Based upon the

results of this dissertation, it would be expected that such policies would result in reduced inpatient utilization, and at least minor improvements in patient disability.

9.3.3 Implications for Future Allocation Policy Changes in Other Fields of Transplantation

Beyond liver transplantation, UNOS regulates allocation policy for kidney, heart, lung, multi-visceral (small intestines), vascular allograft, and pancreas transplantation. Each organ has a separate allocation system with unique policies and distribution areas. For the purpose of this discussion we will consider potential implications of this dissertation's findings on the allocation systems for similarly high-volume organ allocation systems, kidney, heart and lung. All three of these organ allocation systems are designed with common components: a measure of medical urgency or recipient medical condition, geographic location, degree of compatibility between the donor organ and the recipient, and wait list time. Patients are primarily organized by medical urgency within geographic regions based on the degree of organ compatibility. Wait list time is used across systems as a way to break ties between patients with equivalent medical urgency. The measure of medical urgency and donor-recipient compatibility varies widely as each is customized to the organ for transplantation. Geography, which is most important for the discussion of the implications of this studies results, varies between organ allocation systems. Kidney allocation is most similar to liver allocation, such that organs are allocated first within the donor organ's local area (DSA), then within the region and then nationally. Alternatively, both heart and lung allocation utilize concentric circle allocation systems. Under heart allocation the order of allocation is first within the donor organ's local area (DSA), and then within a 500 nautical mile concentric area from the donor's hospital, then to concentric areas with increasing radii (1000 miles, 1500 miles, 2500 miles and >2500 miles). Lung allocation is similar to that of heart allocation, except that they have eliminated local area (DSA) allocation and replaced it with a smaller, 250 nautical mile, concentric circle as the area for primary organ allocation.

This dissertation demonstrates that broader donor organ sharing, across wider geographic areas, improves patient outcomes in terms of both inpatient utilization and disability. The current policies within both kidney and heart allocation rely primarily on DSA based allocation, and therefore one could expect that if allocation policies were modified to extend sharing beyond the boundaries of the DSAs that similar improvements would be seen as were documented here in liver transplantation. DSA based allocation systems restrict allocation by geography, and do so within geographic areas that vary drastically by geographic size and population density. Eliminating these constricting boundaries would be an appropriate first step in improving geographic equity in allocation, and would likely be associated with improved patient outcomes. The lung allocation system has already taken this step, creating an allocation system that is primarily directed by concentric allocation, beginning with a 250 nautical mile radius. As a proof of concept, an evaluation of the change in utilization and disability could be completed for the policy change in lung transplantation, as DSA allocation was replaced with concentric circle allocation in November 2017.

Overall, this dissertation provides support for continued expansion of organ sharing across broader geographic areas. While this research focused on liver transplant allocation, the findings have implications for other allocation systems which continue to utilize DSA and regional based allocation (heart and kidney allocation). Reducing geographic boundaries across allocation systems is likely to decrease utilization and improve post-transplant disability.

9.4 Additional Avenues for Research

This dissertation and its evaluation of alternative metrics for evaluating organ allocation policies sheds light on one of many important issues within the field of liver transplantation, yet it also illuminates many other potential avenues for research.

9.4.1 Utilization Outside of the Index Transplant Center

One of the key limitations to prior studies of utilization was their inability to assess transplantation beyond the index hospital (transplant center). The current study was able to capture utilization at both the index hospital as well as all other hospitals within the same state, providing a more holistic view of post-transplant inpatient utilization. Yet, the degree to which utilization occurred outside of the index hospital has not yet been explored. Understanding patterns of utilization as well as the proportion of care sought outside of the index hospital is important for many reasons. Primarily, liver transplantation is a complex operation and is associated with a variety of potential post-operative complications related not only to the surgical procedure, but also to post-transplant care, such as the use of immunosuppressive medications and the associated risk of infection. It is possible that seeking care at a facility that has limited experience with these specific complications could result in poorer quality of care and potentially increased utilization.

9.4.2 Changes in Listing Behavior Amongst Transplant Centers

As presented within this study, different regions responded differently to the Share 35 policy, with some experiencing dramatic increases in patient acuity, while other saw very little to no difference after policy implementation. While much of this can be accounted for based on the expected effect of the policy, variations seen within and between regions also suggest that there may have been changes to patient selection. In particular, transplant centers may have been more likely to list patients at higher allocation MELDs (either due to higher physiologic MELD score or due to the use of MELD exception points). Understanding how transplant centers responded to the Share 35 policy would further explain the differences identified between regions and DSAs.

9.5 Summary

Since its origination, the field of liver transplantation has been faced with the challenge of allocating the scarce resource of donor organs. In a stepwise manner allocation policies have evolved with the continuous aim of reaching the principles of 'The Final Rule', providing equal access to patients, irrespective of geography, based on medical need. These various policy changes have been noted to have substantial improvements in patient survival both while awaiting and after transplantation, yet there has been little focus on the economic or patient centered outcomes related to these policy changes. The most recent policy, Share 35, has been noted to have only modest improvements in the traditional markers evaluation, pre- and post-transplant mortality. Yet as demonstrated within this dissertation, the intra-regional sharing imposed by this policy has led to decreases in inpatient utilization and post-transplant disability. These findings support future policy changes which promote greater sharing across current geographic boundaries (DSAs and regions), suggesting that such changes result not only in substantial economic savings, but also improved patient outcomes. This work has also highlighted the need for more work assessing policies both at their level of implementation, given the varying responses seen both in markers of acuity but also in inpatient utilization on regional subanalysis. Finally this work suggests that there is room for improvement in the assessment of functional status and other quality of life markers collected by the national databases, as the assessment of these outcomes was likely hindered by the lack of granularity in the Karnofsky scale and lack of objective measures of function or quality of life post-transplant. Improvement in this area would provide a greater ability to assess the impact of allocation policy on patient-centered outcomes.

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Appendix

1. Background – Supplemental Information

1A. Milan Criteria for Hepatocellular Carcinoma

The Milan Criteria for liver transplantation in the setting of hepatocellular carcinoma requires that patients meet all the following criteria to be eligible for liver transplantation:

(1) 1 lesion less than 5cm in diameter OR up to 3 lesions each less than 3cm in diameter

(2) No extrahepatic manifestations or sites of malignancy

(3) No evidence of gross vascular invasion

1B. AASLD Liver Transplant Evaluation Criteria

The AASLD 2013 Practice Guidelines for the evaluation of liver transplantation in adults recommends a 14-point evaluation process which is detailed in the table below. This table was adapted from the guideline document[129].

Evaluation Component	Criteria / Purpose
Financial screening	Secure approval for evaluation
Hepatology evaluation	Assess disease severity and prognosis Confirm diagnosis Optimize pre-transplant management
Surgical evaluation	Confirm need for liver transplantation Identify technical challenges Discuss donor options (deceased, living, extended criteria)
Laboratory testing	Assess hepatic synthetic function, serum electrolytes, renal function, viral serologies, markers for other causes of liver disease, tumor markers, ABO-Rh blood typing, creatinine clearance, urinalaysis, urine drugs screening
Cardiac evaluation	Assess cardiac risk factors (hyperlipidemia, hypertension, diabetes, smoking history, age >60 years) Non-invasive echocardiography Non-invasive stress testing
Hepatic imaging	Ultrasound with Doppler to document portal vein patency Triple-phase CT or gadolinium enhanced MRI for tumor diagnosis and staging
General health assessment	Chest XRay Preventative screening measures: pap smear and mammography for females, colonoscopy if patient >50 years old or history of primary sclerosing cholangitis

Dental assessment	Identify dental caries, buried roots and dental abscesses Coordinate dental extractions if necessary
Anesthesia evaluation	Required for high intra-operative risks (i.e. portopulmonary hypertension, hypertrophic obstructive cardiomyopathy, previous anesthesia complications)
Psychiatric, psychology or mental health professional consultation	Determine previous history of substance abuse, psychiatric illness or potential adjustment difficulties (i.e. behavioral or adherence problems)
Social work evaluation	Address potential psychosocial issues, adequacy of support, and possible effect of transplantation on patient's personal and social system
Financial and insurance counseling	Itemize costs of transplantation and post-transplantation care Review insurance coverage Help develop financial management plans
Nutritional evaluation	Assess nutritional status and patient education
Infectious disease	Identify infectious processes that require intervention prior to transplant (i.e. latent tuberculosis)

2. Methods Section – Supplemental Information

2A. Comparison between Utilization Cohort and Remaining Transplanted Patients

A total of 18,161 patients underwent liver transplantation between January 1, 2010 and June 30, 2014 and met the inclusion criteria for research question 1 and 2 (underwent MELD based liver allocation, age ≥ 18, recipient of a liver or liver + kidney transplant, no prior history of organ transplantation, underwent transplantation within their home state of residence); 6,156 (33.9%) were included within the utilization cohort (UC) and 12,005 (66.1%) were not included (remaining national cohort (NC)). The UC differed from the remaining NC by age, race/ethnicity, insurance status, educational achievement, rate of renal failure, liver disease etiology, disease acuity at transplant, location at transplantation, and functional status at the time of both listing and transplantation (Table 2A – 1). The UC, by age was slightly younger (mean 56.39 years versus 55.40 years); by race/ethnicity had a higher rate of white-latinos (22.1% versus 11.3%) and Asians (8.1% versus 3.0%) and a lower rate of white non-latinos (60.8% versus 73.3%) and blacks (8.3% versus 11.0%); by insurance status had lower rates of privately insured patients (52.1% versus 54.4%) and higher rates of Medicaid patients (19.0% versus 14.5%); and by educational status had a greater proportion of patients with less than a high school education/GED (7.7% versus 4.5%) and fewer patients with a high school education (38.0% versus 43.4%) or a missing educational status (7.8% versus 9.0%). By liver disease etiology the UC had more patients with a primary diagnosis of malignancy (37.8% versus 34.4%) and subsequently had a greater number of a patients who had been approved for MELD exception points (34.2% versus 32.1%). In terms of patient acuity, the UC was at higher acuity than the remaining NC; they had a higher rate of patients with allocation MELD scores ≥ 30 and ≥ 35 (47.4% versus 32.2% and 27.1% versus 18.2%), which corresponded with both a greater mean physiologic MELD score and greater mean allocation MELD score in the UC. Patients in

the UC also had a higher rate of ventilator dependence (5.0% versus 3.5%), dialysis dependence (17.1% versus 13.0%) and use for life support measures (9.1% versus 5.5%) at the time of transplant. Patients in the UC were also more debilitated at the time of listing and transplant as compared to the remaining NC such that the mean functional status was 1.11% lower at listing and 1.19% lower at transplant in the UC. There were no differences between the two cohorts in terms of patient sex, mortality, physiologic or allocation MELD scores at listing.

Table 2A – 1. Comparison Between Utilization Cohort and Remaining Transplants in the United States within the Same Time Period (National Cohort)

	All Transplants 2010 - 6/30/2014				
	National Cohort n = 12,005		Utilization Cohort n = 6,156		
Categorical Variables					
Patient Demographics	n	%	n	%	p-value
Race / Ethnicity					
White, non-latino	8804	73.3%	3740	60.8%	<0.001 **
White, latino	1348	11.3%	1362	22.1%	
Black	1321	11.0%	511	8.3%	
Asian	355	3.0%	501	8.1%	
Other	167	1.4%	42	0.7%	
Sex					
Male	8061	67.2%	4142	67.3%	0.852
Female	3944	32.9%	2014	32.7%	
Ability to Pay for Care					
Insurance Status					
Private insurance	6545	54.5%	3205	52.1%	<0.001 **
Medicare	3337	27.8%	1689	27.4%	
Medicaid	1743	14.5%	1169	19.0%	
Other	380	3.2%	93	1.5%	
Education					
Less than High School/GED	543	4.5%	471	7.7%	<0.001 **
High School / GED	5207	43.4%	2340	38.0%	
Some college or technical school	2695	22.5%	1474	23.9%	
Associate or bachelors degree	1820	15.2%	988	16.0%	
Post-college graduate degree	656	5.5%	402	6.5%	
Unknown	1084	9.0%	481	7.8%	
Medical Condition / Disability at Transplant					
Medical Comorbidities					
Chronic obstructive pulmonary disease	267	2.8%	121	2.0%	0.233
Diabetes	3152	26.4%	1608	26.1%	0.789
Hypertension	2781	30.1%	1465	23.8%	0.677
Renal failure	1566	13.0%	1098	17.8%	<0.001 **
Vascular disease	198	2.1%	113	1.8%	0.395
Liver Disease Etiology					

Acute liver failure	137	1.1%	94	1.5%	<0.001 **
Autoimmune hepatitis	251	2.1%	138	2.2%	
Cholestatic liver disease	822	4.7%	369	6.0%	
Cryptogenic cirrhosis	566	4.7%	257	4.2%	
Genetic/metabolic	306	2.6%	97	1.6%	
Hepatitis C	2239	18.7%	1096	17.8%	
Malignancy	4126	34.4%	2325	37.8%	
Steatohepatitis (NASH/Alcoholic Hepatitis)	3224	26.9%	1569	25.5%	
Other	334	3.8%	211	3.4%	
MELD Point Trends					
Approved for MELD Exception Points	3851	32.1%	2103	34.2%	0.005 *
Allocation MELD Score ≥30	3869	32.2%	2919	47.4%	<0.001 **
Allocation MELD Score ≥35	2186	18.2%	1671	27.1%	<0.001 **
Disease Acuity at Transplant					
Ventilator Dependence	423	3.5%	305	5.0%	<0.001 **
Dialysis Dependence	1566	13.0%	1052	17.1%	<0.001 **
Life support measures	664	5.5%	559	9.1%	<0.001 **
Location at time of Transplant					
Intensive Care Unit	1159	9.7%	961	15.6%	<0.001 **
Hospitalized, ward bed	2378	19.8%	1281	20.8%	
Not Hospitalized	8468	70.5%	3914	63.6%	
Mortality After Transplant					
Death within transplant admission or 30d of discharge	519	4.3%	274	4.5%	0.69
Death within 90 days of transplant	581	4.8%	298	4.8%	0.997
Continuous Variables					
Patient Demographics					
Age (years)					
mean	55.401		56.387		<0.001 **
Mean difference, p-value		-0.986			
Disease Severity at Listing					
Physiologic MELD at Listing					
mean	18.369		18.518		0.301
Mean difference, p-value		-0.149			
Allocation MELD at Listing					
mean	20.078		19.998		0.5602
Mean difference, p-value		0.079			
Karnofsky Score at Listing					
mean	63.874		62.761		0.002 *
Mean difference, p-value		1.113			
Disease Severity at Transplant					
Physiologic MELD at Transplant					
mean	21.946		22.392		0.006 *
Mean difference, p-value		-0.446			
Allocation MELD at Transplant					
mean	27.198		28.927		<0.001 **
Mean difference, p-value		-1.730			
Karnofsky Score at Transplant					
mean	52.335		51.150		0.001 *
Mean difference, p-value		1.185			

Secondary analysis of those factors which differed between the UC and the remaining NC indicated that differences between the two cohorts were constant in both magnitude and direction in both the Pre- and Post-Share 35 periods for age, race/ethnicity, insurance status, education, rate of renal failure, liver disease etiology, rate of allocation MELD scores ≥30 and ≥35, ventilator dependence, dialysis dependence, use of life support measures, and location at the time of transplant (Table 2A – 2). When the UC and NC were compared within the Pre- and Post-Share 35 time periods, the use of MELD exception point scores was no different between the NC and UC in the Pre-Share 35 period, but rates were higher in the UC in the Post-Share 35 period (35.7% versus 31.9%). Additionally, while functional status was lower in the UC in the Pre-Share 35 period at listing (63.06% versus 64.52%) and at transplant (51.8% versus 53.0%), there was no difference between the UC and NC in the Post-Share 35 period. Similarly, while the physiologic MELD score at transplant was higher in the UC in the Pre-Share 35 period (22.14 versus 21.72), there was no difference in the Post-Share 35 period. Overall the difference between the UC and NC are relatively stable over time, with some shift in the Post-Share 35 period within the UC towards increased use of MELD exception points, and an equalization of the differences between UC and NC in disease acuity as measured by functional status and physiologic MELD score.

Table 2A – 2. Comparison between the Utilization Cohort and National Cohort within the Pre- and Post-Share 35 Periods

	All Transplants 2010 - 6/30/2014									
	Pre-Share 35					Post-Share 35				
	National Cohort n = 8,874		Utilization Cohort n = 4,681			National Cohort n = 3,131		Utilization Cohort n = 1,475		
Categorical Variables										
Patient Demographics	n	%	n	%	p-value	n	%	n	%	p-value
Race / Ethnicity										
White, non-latino	6546	73.8%	2831	60.5%		2258	72.1%	908	61.6%	
White, latino	964	10.8%	1034	22.1%	<0.001**	394	12.6%	329	22.3%	<0.001**
Black	973	11.0%	396	8.5%		348	11.1%	115	7.8%	

Asian	261	2.9%	387	8.3%		94	3.0%	114	7.7%	
Other	130	1.5%	33	0.7%		37	1.2%	9	0.6%	
Ability to Pay for Care										
Insurance Status										
Private insurance	4885	55.1%	2480	53.0%		1660	53.0%	721	48.9%	
Medicare	2418	27.3%	1227	26.2%	<0.001**	919	29.4%	458	31.1%	<0.001**
Medicaid	1278	14.4%	900	19.2%		465	14.9%	274	18.6%	
Other	293	3.3%	74	1.6%		87	2.8%	22	1.5%	
Education										
Less than High School/GED	388	4.4%	356	7.6%		155	5.0%	116	7.9%	
High School / GED	3870	43.6%	1752	37.4%		1337	42.7%	590	40.0%	
Some college or technical school	1997	22.5%	1099	23.5%		698	22.3%	379	25.7%	
Associate or bachelors degree	1299	14.6%	757	16.2%	<0.001**	521	16.6%	231	15.7%	<0.001**
Post-college graduate degree	472	5.3%	308	6.6%		184	5.9%	94	6.4%	
Unknown	848	9.6%	409	8.7%		236	7.5%	65	4.4%	
Medical Condition / Disability at Transplant										
Medical Comorbidities										
Renal failure	1096	12.4%	759	16.2%	<0.001**	470	15.0%	293	19.9%	<0.001**
Liver Disease Etiology										
Acute liver failure	96	1.1%	82	1.8%		41	1.3%	15	1.0%	
Autoimmune hepatitis	194	2.2%	96	2.1%		57	1.8%	43	2.9%	
Cholestatic liver disease	621	7.0%	292	6.2%		201	6.4%	77	5.2%	
Cryptogenic cirrhosis	429	4.8%	206	4.4%		137	4.4%	49	3.3%	
Genetic/metabolic	231	2.6%	72	1.5%	<0.001**	75	2.4%	25	1.7%	0.001*
Hepatitis C	1673	18.9%	837	17.9%		566	18.1%	256	17.4%	
Malignancy	3071	34.6%	1755	37.5%		1055	33.7%	575	39.9%	
Steatohepatitis (NASH/Alcoholic Hep)	2309	26.0%	1178	25.2%		915	29.2%	390	26.4%	
Other	250	2.8%	163	3.5%		84	68.0%	45	3.1%	
MELD Point Trends										
Approved for MELD Exception Points	2851	32.1%	1577	33.7%	0.065	1000	31.9%	526	35.7%	0.012*
Allocation MELD Score ≥30	2697	30.4%	2099	44.8%	<0.001**	1172	37.4%	820	55.6%	<0.001**
Allocation MELD Score ≥35	1422	16.0%	1158	24.7%	<0.001**	764	34.4%	513	34.8%	<0.001**
Disease Acuity at Transplant										
Ventilator Dependence	285	3.2%	214	4.6%	<0.001**	138	4.4%	91	6.2%	0.010*
Dialysis Dependence	1096	12.4%	759	16.2%	<0.001**	470	15.0%	293	19.9%	<0.001**
Life support measures	455	5.1%	392	8.4%	<0.001**	209	6.7%	167	11.3%	<0.001**
Location at time of Transplant										
Intensive Care Unit	795	9.0%	649	13.9%		364	11.6%	312	21.2%	
Hospitalized, ward bed	1745	19.7%	983	21.0%	<0.001**	633	20.2%	298	20.2%	<0.001**
Not Hospitalized	6334	1.4%	3049	65.1%		2134	68.2%	865	58.6%	
Continuous Variables										

Patient Demographics						
Age (years)						
mean	55.190	56.209	<0.001**	55.999	56.953	0.001*
Mean difference, p-value	-1.019			-0.954		
Disease Severity at Listing						
Karnofsky Score at Listing						
mean	64.520	63.056	<0.001**	62.052	61.837	0.7631
Mean difference, p-value	1.464			0.215		
Disease Severity at Transplant						
Physiologic MELD at Transplant						
mean	21.720	22.139	0.022*	22.589	23.198	0.075
Mean difference, p-value	-0.419			-0.609		
Allocation MELD at Transplant						
mean	26.862	28.452	<0.001**	28.148	30.437	<0.001**
Mean difference, p-value	-1.589			-2.289		
Karnofsky Score at Transplant						
mean	52.977	51.767	0.004*	50.521	49.193	0.077
Mean difference, p-value	1.210			1.329		

2B. Comparison between Regional Utilization Cohorts and Remaining Transplanted Patients

For Regions 1, 3, 5, and 8, the UC which was employed for the Share 35 evaluation does not cover all DSAs within each region. The following section discusses the differences between the UC and the remaining patients within each region. The DSAs (intra-regional areas) included and excluded from the UC analysis are included in Table 2B – 1.

Table 2B – 1. Utilization Cohort States and DSAs Included and Excluded from Analysis by UNOS Regions

	Included in UC		Excluded from UC	
	DSA	**States**	**DSA**	**States**
Region 1	1A	Massachusetts	1A	Connecticut
			1B	Connecticut
Region 3	3A	Florida	3B	Mississippi
	3C	Florida	3D	Alabama
	3F	Florida	3E	Louisiana
	3H	Georgia	3G	Arkansas
	3I	Florida	3J	Puerto Rico
Region 5	5B	California	5A	Utah
	5C	California	5D	Arizona
	5E	California		
Region 8	8D	Nebraska	8A	Colorado
			8B	Missouri
			8C	Missouri
				Kansas
			8E	Iowa
Region 9	9A	New York		
	9 B	New York		

Region 1

From January 1, 2010 to June 30, 2014 there were 684 transplants completed within Region 1 (Massachusetts, Connecticut) that met inclusion criteria, 517 (75.6%) were included in the UC (underwent transplantation in Massachusetts) and 167 (24.4%) were not included (underwent transplantation in Connecticut) (Table 2B – 2). The Region 1 UC differed from the remaining Region 1 cases by: race/ethnicity, educational achievement, rate of renal failure, liver disease etiology, dialysis dependence, physiologic MELD at transplant and functional status at transplant. In terms of patient demographics, the Region 1 UC contained a higher proportion of white-non-latinos (75.2% versus 67.1%) and fewer white latinos (12.0% versus 21.6%), and had a higher proportion of patients with less than a high school education/GED (8.9% versus 4.8%) and associates or bachelors degrees (17.8% versus 10.2%) but fewer patients with High School / GED as the highest level of education (29.7% versus 52.7%). By liver disease diagnosis, the UC

had more patients with steatohepatitis (34.6% versus 27.5%) and fewer with autoimmune hepatitis (1.5% versus 4.2%) and Hepatitis C (14.5% versus 24.6%). In terms of patient acuity, the UC had a lower rate of renal failure or dialysis dependence (10.4% versus 20.4%), a lower mean physiologic MELD score (20.2 versus 23.0) and lower mean functional status at transplant (52.4% versus 59.0%). The two groups did not differ by: age, sex, insurance status, comorbidities other than renal failure, rate of allocation MELD scores ≥ 30 and ≥ 35, use of MELD exception points, ventilator dependence or need for life support measures at the time of transplant, location at the time of transplant, mortality, disease severity at the time of listing, or allocation MELD score at transplant. Overall there were only very minor differences between the two groups, and therefore the Region 1 UC is likely representative of the entire region.

Table 2B – 2. Regional Comparisons Between Utilization Cohorts and Remaining Transplants Within Each Region – Regions 1 and 3

	Region 1 n = 684					**Region 3 n = 3335**				
	Region 1 n = 167		**Region 1 UC** n = 517			**Region 3** n = 1025		**Region 3 UC** n = 2310		
Categorical Variables										
Patient Demographics	n	%	n	%	p-value	n	%	n	%	p-value
Race / Ethnicity										
White, non-latino	112	67.1%	389	75.2%		757	73.9%	1682	72.8%	
White, latino	36	21.6%	62	12.0%		99	9.6%	329	14.2%	
Black	16	9.6%	41	7.9%	0.013*	150	15.6%	246	10.6%	<0.001**
Asian	2	1.2%	20	3.9%		15	1.5%	47	2.0%	
Other	1	0.6%	5	1.0%		4	0.4%	6	0.3%	
Sex										
Male	120	71.9%	364	70.4%	0.72	662	64.6%	1525	66.0%	0.422
Female	47	28.1%	153	29.6%		363	35.4%	785	34.0%	
Ability to Pay for Care										
Insurance Status										
Private insurance	70	41.9%	252	48.7%		581	56.7%	1221	52.9%	
Medicare	54	32.3%	151	29.2%	0.461	285	27.8%	676	29.3%	<0.001**
Medicaid	38	22.8%	98	19.0%		118	11.5%	378	16.4%	
Other	5	3.0%	6	1.2%		41	4.0%	35	1.5%	
Education										
Less than High School/GED	8	4.8%	46	8.9%		56	5.5%	76	3.3%	
High School / GED	88	52.7%	205	39.7%		457	44.6%	817	35.4%	
Some college or tech. school	30	18.0%	100	19.3%	0.022*	210	20.5%	579	25.1%	<0.001**
Associate or bachelors degree	17	10.2%	92	17.8%		133	13.0%	431	18.7%	

Post-college graduate degree	10	6.0%	38	7.4%		43	4.2%	153	6.6%	
Unknown	14	8.4%	36	7.0%		126	12.3%	254	11.0%	
Medical Condition / Disability at Transplant										
Medical Comorbidities										
Chronic obstructive pulmonary disease	10	6.8%	17	3.3%	0.125	8	1.1%	42	1.8%	0.175
Diabetes	49	29.3%	132	25.5%	0.332	335	32.9%	567	24.5%	<0.001**
Hypertension	40	27.0%	135	26.1%	0.529	249	35.1%	724	31.3%	0.154
Renal failure	34	20.4%	54	10.4%	0.001*	75	7.3%	213	9.2%	0.071
Vascular disease	2	1.4%	16	3.6%	0.193	10	1.4%	42	1.9%	0.436
Liver Disease Etiology										
Acute liver failure	1	0.6%	10	1.9%		17	1.7%	54	2.3%	
Autoimmune hepatitis	7	4.2%	8	1.5%		29	2.8%	80	3.5%	
Cholestatic liver disease	6	3.6%	19	3.7%		63	6.2%	154	6.7%	
Cryptogenic cirrhosis	5	3.0%	25	4.8%		58	5.7%	116	5.0%	
Genetic/metabolic	3	1.8%	6	1.2%	0.032*	24	2.3%	44	1.9%	0.036*
Hepatitis C	41	24.6%	75	14.5%		258	25.2%	460	19.9%	
Malignancy	56	33.5%	185	35.8%		249	24.3%	639	27.7%	
Steatohepatitis	46	27.5%	179	34.6%		294	28.7%	680	29.4%	
Other	2	1.2%	10	1.9%		33	3.2%	83	3.6%	
MELD Point Trends										
Approved for MELD Exception Points	132	36.2%	168	32.5%	0.257	444	23.3%	561	24.3%	0.430
Allocation MELD Score ≥30	182	49.9%	224	43.3%	0.055	388	20.3%	478	20.7%	0.762
Allocation MELD Score ≥35	93	25.5%	113	21.9%	0.21	229	12.0%	284	12.3%	0.763
Disease Acuity at Transplant										
Ventilator Dependence	4	2.4%	24	4.6%	0.203	23	2.2%	58	2.5%	0.644
Dialysis Dependence	34	20.4%	54	10.4%	0.001*	75	7.3%	213	9.2%	0.071
Life support measures	5	3.0%	29	5.6%	0.176	45	4.4%	76	3.3%	0.117
Location at time of Transplant										
Intensive Care Unit	13	7.8%	63	12.2%		89	8.7%	196	8.5%	
Hospitalized, ward bed	41	24.6%	123	23.8%	0.288	181	17.7%	421	18.2%	0.918
Not Hospitalized	113	67.7%	331	64.0%		755	73.7%	1693	73.3%	
Mortality After Transplant										
Death within transplant admission or 30d of discharge	13	7.8%	27	5.2%	0.22	49	4.8%	68	2.9%	0.008*
Death within 90 days of transplant	15	9.0%	32	6.2%	0.215	62	6.1%	83	3.6%	0.001*
Continuous Variables										
Patient Demographics										
Age (years)										
mean	55.024		56.366		0.09	55.003		56.012		0.005*
Mean difference, p-value	-1.342					-1.009				
Disease Severity at Listing										
Physiologic MELD at Listing										
mean	18.910		17.538		0.111	18.808		19.062		0.4073

Mean difference, p-value	1.372			-0.255		
Allocation MELD at Listing						
mean	20.521	19.859	0.4117	19.763	20.282	0.0171
Mean difference, p-value	0.662			-0.519		
Karnofsky Score at Listing						
mean	64.072	66.459	0.2689	61.693	62.344	0.4575
Mean difference, p-value	-2.387			-0.651		
Disease Severity at Transplant						
Physiologic MELD at Transplant						
mean	23.018	20.219	0.004*	21.395	21.226	0.609
Mean difference, p-value	2.799			0.170		
Allocation MELD at Transplant						
mean	28.539	27.611	0.095	24.411	24.974	0.024*
Mean difference, p-value	1.278			-0.563		
Karnofsky Score at Transplant						
mean	59.042	52.398	0.002*	51.374	57.328	<0.001**
Mean difference, p-value	6.643			-5.954		

Region 3

From January 1, 2010 to June 30, 2014 there were 3,335 transplants completed within Region 3 (Alabama, Arkansas, Florida, Georgia, Louisiana, Missouri, Puerto Rico) that met inclusion criteria, 2,310 (69.3%) were included in the Utilization Cohort (underwent transplantation in Florida or Georgia) and 1,025 (30.7%) were not included (underwent transplantation in outside of Florida or Georgia) (Table 2B – 2). The Region 3 UC differed from the remaining Region 3 cases by: age, race/ethnicity, insurance status, educational achievement, rate of diabetes, liver disease etiology, mortality, allocation MELD at transplant and functional status at transplant. In terms of patient demographics, the Region 3 UC was slightly older (mean age 56.0 versus 55.0), had a higher proportion of white-latinos (14.2% versus 9.6%) and fewer blacks (10.6% versus 15.6%), had a higher proportion of Medicaid patients (15.4% versus 11.5%) and a lower proportion of patients with private (52.9% versus 56.7%) other insurance (1.5% versus 4.0%), had more patients with some college or technical school (25.1% versus

20.5%), associates or bachelors degrees (18.7% versus 13.0%) and post-college graduate degrees (6.6% versus 4.2%). By liver disease diagnosis, the UC had more patients with malignancy (27.7% versus 24.3%) and fewer with Hepatitis C (19.9% versus 25.2%). In terms of patient comorbidities, the UC had a lower rate of diabetes (24.5% versus 32.9%). In terms of mortality, the rates of death were lower in the UC both within 30 days of transplant or during the transplant admission (2.9% versus 4.8%) and at 90 days post-transplant (3.6% versus 6.1%). In terms of patient acuity at transplant, the mean allocation MELD at transplant was on average 0.6 points higher in the UC (25.0 versus 24.4) and functional status was on average 6.0% higher (57.3% versus 51.4%). The two groups did not differ by: sex, medical comorbidities other than diabetes, rate of allocation MELD scores ≥ 30 and ≥ 35, use of MELD exception points, ventilator dependence, dialysis dependence, need for life support measures at the time of transplant, location at the time of transplant, disease severity at the time of listing, or physiologic MELD score at transplant. Overall the UC represents a more educated cohort with a slightly higher allocation MELD score and better functional status at the time of transplant. Given that these differences are very small, the UC for Region 3 is likely representative of the entire region.

Region 5

From January 1, 2010 to June 30, 2014 there were 2,936 transplants completed within Region 5 (Arizona, California, Utah) that met inclusion criteria; 2,273 (77.4%%) were included in the UC (underwent transplantation in California) and 663 (22.6%) were not included (underwent transplantation in outside of California) (Table 2B – 3). The Region 5 UC differed from the remaining Region 5 cases by: age, race/ethnicity, insurance status, educational achievement, rate of renal failure, liver disease etiology, use of MELD exception points, rate of allocation MELD scores ≥ 30 and ≥ 35, dialysis dependence, life support measures, location at

the time of transplant, functional status at both listing and transplantation, and allocation MELD at transplant. In terms of patient demographics, the Region 5 UC was slightly older (mean age 56.6 versus 54.9), had a higher proportion of white latinos (33.4% versus 25.9%), blacks (4.7% versus 2.1%) and Asians (13.9% versus 4.1%) and a lower proportion of white non-latinos (46.8% versus 64.1%), had a higher proportion of Medicaid patients (19.9% versus 16.4%), had fewer patients with associates or bachelors degrees (14.1% versus 18.6%) and a greater proportion of patients with less than a high school / GED (10.6% versus 8.3%). By liver disease diagnosis, the UC had more patients with malignancy (44.9% versus 35.0%) and fewer with steatohepatitis (22.5% versus 29.0%), which corresponds with the higher rate of MELD exception point use in the UC (41.1% versus 33.3%). In terms of patient comorbidities, the UC had a higher rate of renal failure (30.1% versus 24.7%). In terms of patient acuity at transplant, the UC had a higher rate of patients with an allocation MELD score of ≥ 30 (73.7% versus 53.6%) and ≥ 35 (45.4% versus 34.0%) which corresponds with the higher mean allocation MELD at transplant was on average 2.5 points higher in the UC (33.2 versus 30.6). The UC also had a lower mean functional status at the time of transplant (44.0% versus 50.2%) and had a higher proportion of patients in the ICU (27.1% versus 20.2%) at the time of transplant. The two groups did not differ by: sex, medical comorbidities other than renal failure, ventilator dependence, disease severity at the time of listing, or physiologic MELD score at transplant. Overall the UC represents a higher acuity cohort as compared to the remaining patients within Region 5, and as such these differences should be considered in the interpretation of regional results.

Table 2B – 3. Regional Comparisons between Utilization Cohorts and Remaining Transplants within Each Region – Regions 5 and 8

	Region 5 n = 663		Region 5 UC n = 2273		Region 5 n = 2936	Region 8 n = 990		Region 8 UC n = 126		Region 8 n = 1116
Categorical Variables										
Patient Demographics	n	%	n	%	p-value	n	%	n	%	p-value
Race / Ethnicity										
White, non-latino	425	64.1%	1064	46.8%		790	79.8%	111	88.1%	
White, latino	172	25.9%	759	33.4%		95	9.6%	7	5.6%	
Black	14	2.1%	106	4.7%	<0.001**	71	7.2%	5	4.0%	0.258
Asian	29	4.1%	317	13.9%		30	3.0%	3	2.4%	
Other	5	3.8%	27	1.2%		4	0.4%	0	0.0%	
Sex										
Male	431	65.0%	1538	67.7%	0.200	697	70.4%	86	68.3%	0.619
Female	232	35.0%	735	32.3%		293	29.6%	40	31.7%	
Ability to Pay for Care										
Insurance Status										
Private insurance	364	54.9%	1221	53.7%		561	56.7%	73	57.9%	
Medicare	172	25.9%	578	25.4%	0.002*	254	25.7%	24	19.0%	0.004*
Medicaid	109	16.4%	452	19.9%		165	16.7%	23	18.3%	
Other	18	2.7%	22	1.0%		10	1.0%	6	4.8%	
Education										
Less than High School/GED	55	8.3%	242	10.6%		43	4.3%	2	1.6%	
High School / GED	257	38.8%	842	37.0%		395	39.9%	72	57.1%	
Some college or tech. school	168	25.3%	592	26.0%	<0.001**	252	25.5%	23	18.3%	0.005*
Associate or bachelors degree	123	18.6%	321	14.1%		169	17.1%	17	13.5%	
Post-college graduate degree	44	6.6%	135	5.9%		52	5.3%	8	6.3%	
Unknown	16	2.4%	141	6.2%		79	8.0%	4	3.2%	
Medical Condition / Disability at Transplant										
Medical Comorbidities										
COPD	10	1.6%	27	1.2%	0.453	16	2.0%	5	4.0%	<0.001**
Diabetes	170	25.7%	597	26.3%	0.672	217	22.0%	30	23.8%	0.643
Hypertension	151	24.5%	277	12.2%	0.192	170	21.5%	22	17.5%	<0.001**
Renal failure	164	24.7%	685	30.1%	0.007*	112	11.3%	6	4.6%	0.024*
Vascular disease	9	1.5%	17	1.4%	0.837	5	0.6%	2	2.8%	0.050
Liver Disease Etiology										
Acute liver failure	8	1.2%	19	0.8%		11	1.1%	3	2.4%	
Autoimmune hepatitis	10	1.5%	34	1.5%		15	1.5%	5	4.0%	
Cholestatic liver disease	44	6.6%	116	5.1%		89	9.0%	8	6.3%	
Cryptogenic cirrhosis	25	3.8%	80	3.5%		49	5.0%	3	2.4%	
Genetic/metabolic	14	2.1%	27	1.2%	<0.001**	34	3.4%	5	4.0%	0.009*
Hepatitis C	123	18.6%	392	17.2%		179	18.1%	16	12.7%	
Malignancy	232	35.0%	1021	44.9%		356	36.0%	35	27.8%	
Steatohepatitis	192	29.0%	511	22.5%		234	23.6%	46	36.5%	
Other	15	2.3%	73	3.2%		23	2.3%	5	4.0%	
MELD Point Trends										
Approved for MELD Exception Points	317	33.3%	935	41.1%	<0.001**	488	31.7%	29	23.0%	0.044*

Allocation MELD Score ≥30	511	53.6%	1676	73.7%	<0.001**	433	28.1%	30	23.8%	0.301
Allocation MELD Score ≥35	324	34.0%	1032	45.4%	<0.001**	216	14.0%	15	11.9%	0.509
Disease Acuity at Transplant										
Ventilator Dependence	57	8.6%	206	9.1%	0.7112	5	0.5%	4	3.2%	0.002*
Dialysis Dependence	164	24.7%	685	30.1%	0.007*	112	11.3%	6	4.8%	0.024*
Life support measures	76	11.5%	423	18.6%	<0.001**	15	1.5%	8	6.3%	<0.001**
Location at time of Transplant										
Intensive Care Unit	134	20.2%	617	27.1%		49	5.0%	8	6.3%	
Hospitalized, ward bed	145	21.9%	480	21.1%	0.001*	200	20.2%	25	19.8%	0.798
Not Hospitalized	384	57.9%	1176	51.7%		741	74.9%	93	73.8%	
Mortality After Transplant										
Death within transplant admission or 30d of discharge	32	4.8%	110	4.8%	0.989	30	3.0%	6	4.8%	0.300
Death within 90 days of transplant	27	4.1%	112	4.9%	0.362	34	3.4%	6	4.8%	0.45
Continuous Variables										
Patient Demographics										
Age (years)										
mean	54.890		56.599		<0.001**	55.167		54.254		0.322
Mean difference, p-value	-1.709					0.913				
Disease Severity at Listing										
Physiologic MELD at Listing										
mean	19.725		18.837		0.0606	17.480		17.262		0.7894
Mean difference, p-value	0.889					0.218				
Allocation MELD at Listing										
mean	20.913		20.575		0.4628	19.423		17.357		0.007*
Mean difference, p-value	0.338					2.066				
Karnofsky Score at Listing										
mean	62.864		60.195		0.022*	64.767		58.175		0.002*
Mean difference, p-value	2.669					6.592				
Disease Severity at Transplant										
Physiologic MELD at Transplant										
mean	25.057		24.521		0.3154	21.264		21.865		0.516
Mean difference, p-value	0.564					-0.601				
Allocation MELD at Transplant										
mean	30.661		33.194		<0.001**	26.946		25.119		0.002*
Mean difference, p-value	-2.533					1.827				
Karnofsky Score at Transplant										
mean	50.151		44.036		<0.001**	53.691		45.238		<0.001**
Mean difference, p-value	6.115					8.453				

Region 8

From January 1, 2010 to June 30, 2014 there were 1,116 transplants completed within Region 8 (Colorado, Iowa, Kansas, Montana, Nebraska) that met inclusion criteria, 126 (11.3%) were included in the UC (underwent transplantation in Nebraska) and 990 (88.7%) were not

included (underwent transplantation outside of Nebraska) (Table 2B – 3). The Region 8 UC differed from the remaining Region 8 cases by: educational achievement, insurance status, rate of medical comorbidities, liver disease etiology, use of MELD exception points, dialysis dependence, ventilator dependence, life support measures at the time of transplant, allocation MELD at both listing and transplant and functional status at both listing and transplant. In terms of patient demographics, the Region 8 UC contained a higher proportion of Medicaid patients (18.3% versus 16.7%) and a lower proportion of Medicare patients (19.0% versus 25.7%), and had a higher proportion of patients with a high school education/GED (57.1% versus 39.9%) and fewer with associates or bachelors degrees (18.3% versus 25.5%). In terms of patient comorbidities the UC had a higher rate of COPD (4.0% versus 2.0%), hypertension (17.5% versus 21.5%) and renal failure (4.6% versus 11.3%). By liver disease diagnosis, the UC had more patients with steatohepatitis (36.5% versus 23.6%) and fewer with malignancy (27.8% versus 36.0%), which corresponds to the lower rate of MELD exception points (23.0% versus 31.7%), and a lower mean allocation MELD score at listing (17.4 versus 19.4) and at transplant (25.1 versus 26.9). In terms of patient acuity, the UC had a higher rate of ventilator dependence (3.2% versus 0.5%) and life support measures at transplant (6.3% versus 1.5%), as well as lower mean functional status at listing (58.2% versus 64.8%) and transplant (45.2% versus 53.7%). The two groups did not differ by: age, sex, race/ethnicity, rates of diabetes or vascular disease, rate of allocation MELD scores ≥ 30 and ≥ 35, location at the time of transplant, mortality, and physiologic disease severity at the time of listing or transplant. Overall there were minor differences between the two groups, much of which is attributable to the higher rate of transplantation for malignancy outside of the UC (use of MELD exception points, higher

allocation MELD scores, less physiologic illness). This difference should be accounted for when interpreting the results for Region 8.

Region 9

No additional subanalysis was completed for Region 9 given that New York makes up the entire region and therefore no additional states or transplant centers contributed cases within this region.

2C. Database Linkage

Case Identification

Transplant cases were identified in the SRTR database by selecting all patients who underwent liver transplantation between January 1, 2010 and December 31, 2014. Transplants were then isolated by the transplant center state and individual files for California, Florida, Georgia, Massachusetts, Nebraska and New York were created. Given that these files are constructed such that each transplant represents a unique case, individual patient identifiers were utilized to identify patients who had multiple transplants either within a single admission or within multiple admissions. In the event that multiple transplants occurred within a single admission, the primary transplant case was utilized for matching and the additional transplant dates were appended. The subsequent transplants were dropped from the merge analysis (this was done in order to assure that a single transplant admission was being merged to a single admission within the utilization databases). For patients with more than 1 transplant, that occurred in separate admissions, the cases were tagged to indicate multiple transplantations. Each case, which represented a distinct hospital admissions, remained within the dataset during database linkage. After manipulating these cases, each case within the transplant file represented a single hospital admission.

Transplants were identified in the OSHPD and HCUP datasets by selecting cases which included an ICD-9 procedure code indicating liver transplantation (ICD9 code 5051 or 5059) in any of the possible procedure code variables. Each case within OSHPD or HCUP identifies a single hospital admission.

Linkage Stages

The database linkage, between utilization and transplant datasets, was carried out with the use of indirect patient identifiers. A table of linkage variables is included below. Linkages variables differ somewhat between the AHRQ-HCUP-SIDs and the OSHPD database as shown in Table 2C – 1 below.

Table 2C – 1. Linkage Variables by Dataset

	SRTR	HCUP: GA, MA, NE, NY	HCUP: FL	OSHPD: CA
Age	Age at transplant	Age at admission	Age at admission	Age at admission
Gender	Candidate gender	Sex	Sex	Sex
Admit Date: m/d/y	Recipient admission date			Admission date
Admit Date: month	Recipient admission date	Admission month		--
Admit Date: year	Recipient admission date	Admission year		--
Discharge Date: month	Recipient discharge date	Discharge month		Discharge date
Discharge Date: quarter	Recipient discharge date	--	Discharge quarter	--
Discharge Date: year	Recipient discharge date	Discharge year	Discharge year	--
Transplant Center/Hospital	Transplant center ID number	HCUP hospital ID	Data source hospital identifier	Hospital ID number
Payer	Recipient primary insurance	Primary insurance provider	Primary insurance provider	Payer for greater part of patient's bill
Procedure Date: m/d/y	Recipient transplant date			Procedure date
Procedure Date: month	Recipient transplant date	Procedure month		--
Procedure Date: year	Recipient transplant date	Procedure year	Procedure year	--
Procedure Date: days between admit and procedure	Calculated: (procedure date - admission date)	Days from admission to procedure	Days from admission to procedure	Days between admission and principal procedure
Length of stay	Calculated: (discharge date - admission date)	Admission length of stay	Admission length of stay	Length of stay
State	Recipient permanent state address	Patient's state of residence	Patient's state of residence	
Total linkage variables		13	10	9
-- : Variable with higher specificity available				

Linkages were carried out utilizing a deterministic matching algorithm with explicit heuristic categories. Given that the visit and patient identifiers are unique only within state inpatient databases, each state was independently matched to the transplant datasets, and then all states were merged after case identification. The first stage utilized a gold standard match of the OSHPD dataset to SRTR as it had the greatest degree of detail/specificity in matching variables.

The sensitivity and specificity of potential matching algorithms was then tested using the match criteria available for HCUP matches (Florida and then all other HCUP states). The matching algorithm that optimized both specificity and sensitivity and also resulted in a minimal degree of case loss was selected. This algorithm was then applied to each individual match between the utilization and transplant database.

Gold Standard Match Criteria (OSHPD)

Within the OSHPD dataset complete dates (month, day, year) of admission, discharge and transplantation (transplants were identified by ICD-9 procedure code 5059) were available which could be matched to complete dates within the SRTR dataset. In addition to these date variables, age, sex, payer, length of stay, pre-transplant length of stay and patient's home state (dichotomous variable in the OSHPD dataset, California or other) were used for matching. The first block identifies exact/criterion matches, and the second block utilized weighted heuristic scoring. After these two blocks, remaining unmatched cases were matched through clerical matching where closely matched cases which did not meet match criterion in the heuristic match were identified. Finally, in the fourth block the remaining unmatched SRTR cases were then matched using similar criteria from the first and second blocks (criterion and heuristic scoring) to OSHPD PDD files for 2010-2015 inclusive of all admissions to the transplant centers. Criteria for true matches within this secondary match are described below.

Block 1

The initial criterion match was completed utilizing the maximal number of linkage variables between OSHPD transplant cases and the SRTR database. Within this first block, cases which matched exactly on all available variables were considered criterion matches. Pairs in which duplicate SRTR or OSHPD IDs were matched were then evaluated by secondary criteria

in order to break discern the appropriate pair. Secondary criteria included comparison of death during admission, and diagnosis codes (hepatitis C, hepatitis B, hepatocellular carcinoma and alpha-1-anti-trypsin). Amongst duplicate cases the case which did not match on these 5 criteria was dropped, and the non-duplicate component of the pair was added back for matching in Block 2. The duplicate case which matched on these criteria was preserved as an exact match. In the event that duplicate pairs both matched on all criteria, pairs were inspected to discern if the duplicated component was due to a clerical duplication or if they represented two separate cases. If clerical duplicates were identified the more complete case was selected. If two separate cases which were equally matched were identified both cases were excluded due to inability to determine the better match. All preserved cases were then isolated and stored as Block 1 Exact Matches.

Block 2

The remaining unmatched cases from both OSHPD and SRTR were then assessed for potential candidate matches across each potential linkage variable. These remaining cases were matched in a pairwise fashion to all potential candidate matches based on transplant center/hospital. This pairwise match resulted in a series of potential candidate matches for all cases. An unweighted heuristic score was then calculated for each potential matching variable within each pairwise candidate match (Table 2C – 2). The scores ranged on a scale from 0 – 1.0 by degree of matching, where 0 is a non-match and 1 is an exact match (i.e. female to female, or exact age to exact age). Logical close matches were scored as 0.75, 0.50 or 0.25 based upon heuristic matching. A scores of 0.75 was assigned to logical errors or discrepancies across the two datasets by 1 unit (i.e. length of stay +/- 1 day, admission month +/- 1 month, age +/- 1 year). A score of 0.5 was assigned to logical errors or discrepancies across the two datasets by 2

units (i.e. length of stay +/- 2 days, age +/- 2 years) which were assigned a score of 0.50. A score of 0.25 was assigned for logical errors or discrepancies across the two datasets by 3 or 4 units (i.e. length of stay +/- 3 days or length of stay +/- 4 days). For categorical variables, such as primary insurance provider, exact insurance types were assigned a score of 1.0, heuristic matches which could be attributed to a patient having multiple insurance providers (i.e. Medicare to Private Insurance, or Medicare to Medicaid) were assigned a score of 0.25, and a score of 0 was assigned to matches that did not have a logical or heuristic match (i.e. Private Insurance to Self-Pay). Unweighted heuristic scores were then weighted based on the reliability and specificity of the variables. The weights range from 0 – 9, where higher scores are given to more granular and specific variables and lower scores are given to those variables which have a higher probability of error or are less specific. For each candidate pair, the weighted heuristic scores for all linkage variables were then summed to attain the overall candidate match score. This score was then divided by the criterion match score (weighted sum of perfect matches across all variables). The results of the summed candidate score divided by the criterion match score resulted in the final heuristic match score.

Table 2C – 2. Scores Assigned to Individual Variables for Heuristic Matching in Block 2. Heuristic match scores indicate the number of points assigned to each possible match between the utilization database and transplant database pair. Exact matches were given a score of 1.0; near matches were given lower scores based on the likelihood that the match was correct. The weight indicates the weight assigned to each pair heuristic match score for weighted scoring. Weights were assigned based on the reliability and specificity of each variable.

	Linkage Variable	Heuristic Match Score					Weight
		1.0	0.75	0.50	0.25	0	
Age	age	age = age	age = age +/- 1	age = age +/- 2		age > or < age +/-2	7.0
Gender	female	female = female male = male				female = male	9.0
Payer	payer	payer = payer			Medicare = Medicaid Medicare = Private Insurance		4.0
Admit Date: month	amonth	amonth = amonth	amonth = amonth +/- 1			amonth > or < amonth +/- 1	5.0
Admit Date: year	ayear	ayear = ayear	ayear = ayear +/- 1			ayear > or < ayear +/- 1	8.0
Discharge Date: month	dmonth	dmonth = dmonth	dmonth = dmonth +/- 1			dmonth > or < dmonth +/- 1	5.0
Discharge Date: quarter	dqtr	dqtr = dqtr		dqtr = dqtr +/- 1		dqtr > or < dqtr +/- 1	7.5
Discharge Date: year	dyear	dyear = dyear			dyear = dyear +/- 1		8.0
Procedure Date: month	olt_month	olt_month = olt_month	olt_month = olt_month +/- 1			olt_month > or < olt_month +/- 1	5.0
Procedure Date: year	olt_year	olt_year = olt_year			olt_year = olt_year +/- 1		8.0
Procedure Date: days between admit and procedure	los_pretx	los_pretx = los_pretx	los_pretx = los_pretx +/- 1	los_pretx = los_pretx +/- 2	los_pretx = los_pretx +/- 3 los_pretx = los_pretx +/- 4	los_pretx > or < los_pretx +/- 4	3.0
Length of stay	los	los = los	los = los +/- 1	los = los +/- 2	los = los +/- 3 los = los +/- 4	los > or < los +/- 4	6.0
State	state	state = state				state ≠ state	5.0

The greedy algorithm was then utilized to select the highest scoring, or best matched cases. Cases were then ranked by heuristic match score within transplant dataset unique IDs. The highest scoring match within each ID was selected, and the remaining cases were dropped. Amongst the highest scoring matches, unique by transplant dataset ID, cases were then ranked by heuristic match score within OSHPD dataset ID. Cases with the highest heuristic score by OSHPD dataset IDs were selected and lower scoring cases were then dropped. The remaining dataset therefore consisted of matched pairs unique within both the SRTR and OSHPD databases. These cases were considered the available best matches.

Cases which remained unmatched after the greedy algorithm were then re-run through Block 2 to discern any residual pairs.

Matched pairs from both rounds of Block 2 Heuristic matching were then saved, and residual unmatched cases were set aside for clerical assessment.

Evaluation of Matched Pairs

Matched pairs from Block 1 and Block 2 were merged and matches were assessed for appropriateness by assessing concordance of reporting of deaths during the transplant admission and diagnosis. Deaths were reported by OSHPD as patient disposition at discharge, and by SRTR through a series of variables indicating the date of death (death during admission was then derived by determining if this death date fell within the dates of the primary transplant admission). Diagnoses were compared using the ICD9 diagnostic codes in OSHPD (up to 24 were coded per admission) and the candidate and recipient diagnosis variables in SRTR (2 diagnoses coded at listing for transplant and 2 at the time of transplantation). Additionally the diagnosis of hepatocellular carcinoma was coded from the SRTR database by the indicator variable for use of exception points for hepatocellular carcinoma.

Overall the matched pairs scored well on concordance across the death and diagnosis variables. Therefore this collection of matched pairs was used as the gold standard comparison for determining the heuristic algorithm for HCUP database linkage to SRTR.

Evaluating Match Criteria Utilized for HCUP Matches Against OSHPD/Gold Standard

Case matching within the HCUP datasets requires two different matching algorithms due to data availability, these will be referred to as the Florida criteria and the HCUP criteria (used for all other HCUP states: GA, MA, NE, NY). The Florida criteria utilizes the following matching variables: age, sex, discharge quarter, discharge year, transplant year, pre-transplant length of stay, total length of stay, primary payer/insurance provider, patient's home state, and hospital. The HCUP criteria includes: age, sex, admission month, admission year, discharge month, discharge year, transplant month, transplant year, pre-transplant length of stay, total length of stay, primary payer/insurance provider, patient's home state and hospital. Given that

both of these matching criteria are less specific than the variables available in the OSHPD data set, in order to attain high sensitivity and specificity of matches additional criterion were tested to assure accurate matching. The 6 criteria tested included: inclusion of all matched cases regardless of heuristic score, inclusion of only cases with a heuristic score of 50% or higher, inclusion of only cases with a heuristic score of 70% or higher, or each of these three criteria with 2 rounds of heuristic matching. In order to test these different criteria, the OSHPD data was matched using the specified criteria and then matched cases based on the Florida or HCUP criteria were compared to the gold standard match attained with the OSHPD criteria. The sensitivity, specificity, positive predictive value, accuracy and overall match rate (defined as the number of cases matched divided by the total number of available cases) were calculated for each criteria for both the Florida and HCUP matching variables. The results of these matching algorithms are included in Table 2C - 3. Based upon these results the algorithm using a 70% threshold and 2 rounds of heuristic matching were selected for both Florida and HCUP matching.

Table 2C – 3. Comparison of Florida and HCUP Criteria Matches to California (OSHPD) Gold Standard Match. California (OSHPD) cases were sequentially matched utilizing the Florida or HCUP Criteria, with and without rematching. Results of matching based on these criteria were then compared to the California Criteria matches. The true positive, false negative, false positive, true negative, sensitivity, specificity, positive predictive value and accuracy were calculated for each comparison. Matched cases indicates the total number of matched cases between the SRTR and OSHPD dataset for each criteria. This algorithm was completed 3 times utilizing a different threshold for the heuristic score derived from the Florida or HCUP Criteria matches (any match ("all cases"), 50% threshold, 70% threshold).

	California Criteria Match		Florida Criteria Match		Florida Criteria (no rematch)		HCUP Criteria Match		HCUP Criteria Match (no rematch)	
	SRTR	OSHPD	SRTR	OSHPD	SRTR	OSHPD	SRTR	OSHPD	SRTR	OSHPD
Transplant Admissions	3164	3122	3164	3122	3164	3122	3164	3122	3164	3122
Versus California Criteria (CA:Other) – All cases										
True Positive			3067		3069		3104		3092	
False Negative			45		43		4		16	
False Positive			4		2		10		5	
True Negatives			48		50		46		51	
Sensitivity			**98.6%**		**98.6%**		**99.9%**		**99.5%**	
Specificity			**92.3%**		**96.2%**		**82.1%**		**91.1%**	
Positive Predictive Value			**99.9%**		**99.9%**		**99.7%**		**99.8%**	
Accuracy			**98.5%**		**98.6%**		**99.6%**		**99.3%**	
Matched Cases			**3071**		**3071**		**3114**		**3097**	
Match Rate			**97.1%**		**97.1%**		**98.4%**		**97.9%**	
Versus California Criteria (CA:Other) – 50% Threshold										
True Positive			3097		3069		3092		3108	
False Negative			15		43		16		4	
False Positive			6		2		5		6	
True Negatives			46		50		51		52	
Specificity			**99.5%**		**98.6%**		**99.5%**		**99.9%**	
Specificity			**88.5%**		**96.2%**		**91.1%**		**89.7%**	
Positive Predictive Value			**99.8%**		**99.9%**		**99.8%**		**99.8%**	
Accuracy			**99.3%**		**98.6%**		**99.3%**		**99.7%**	
Matched Cases			**3103**		**3071**		**3097**		**3114**	
Match Rate			**98.1%**		**97.1%**		**97.9%**		**98.4%**	
Versus California Criteria (CA:Other) – 70% Threshold										
True Positive			3049		3030		3099		3084	
False Negative			63		82		13		24	
False Positive			3		2		2		4	
True Negatives			49		54		50		52	
Specificity			**98.0%**		**97.4%**		**99.6%**		**99.2%**	
Specificity			**94.2%**		**96.4%**		**96.2%**		**92.9%**	
Positive Predictive Value			**99.9%**		**99.9%**		**99.9%**		**99.9%**	
Accuracy			**97.9%**		**97.3%**		**99.5%**		**99.1%**	
Matched Cases			**3052**		**3032**		**3101**		**3088**	
Match Rate			**96.5%**		**95.8%**		**98.0%**		**97.6%**	

Clerical Assessment

After completing Block 1 & Block 2 matches, remaining unmatched cases from SRTR and the utilization databases were assessed for potential matches. Matching was done by examination of all matching variables and determination of likely pairs between the two data sets. Pairs met criteria for matching if:

- Matched on all available criteria (exactly), but had missing discharge information in SRTR
- Matched on all available criteria (exactly), but had missing discharge information in SRTR and patient's home state is mismatched
- Matched on all available criteria (exactly), but had missing admission month and year, procedure month and year in HCUP
- Matched on all available criteria (exactly), but length of stay and length of stay pre-transplant differ between databases by a logical number (i.e. the pre-transplant length of stay in 1 of the databases)
- Matched on all available criteria (exactly), except payer is mismatched and length of stay variables differ by +/- 1

Clerical matches which met the above criteria were tagged and then added to the matched cases. Remaining unmatched cases were then utilized for repeat matching against the entire SID or OSHPD dataset (inclusive of all admissions at transplant centers within those states for 2010-2014).

Matching Against Full Utilization Databases

Across all states, the SRTR dataset had a greater number of cases as compared to the utilization databases. In order to try and attain these potential matches, the unmatched SRTR cases were matched against the utilization database for each state (inclusive of all admissions to

the transplant centers, identified by hospital identifiers). This match was carried out in a similar fashion to that described above. Block 1 matching was completed using all potential matching variables. All exact matches were then assessed to determine if the matched visits contained diagnostic codes consistent with liver disease and/or procedure codes indicative of a liver transplantation. Procedure codes were classified as either specific or nonspecific. Specific procedure codes included ICD9 5051, defined as "auxillary liver transplant", and 504, defined as "total hepatectomy". Nonspecific procedure codes included ICD 0093, defined as "transplant from cadaver" and 0091 defined as "transplant from liver related donor". Diagnosis codes are listed in Table 2C – 4 below.

Cases which were not duplicates of previously matched cases, contained both liver diagnosis codes and either specific or nonspecific procedure codes, and reached at least a 70% heuristic match were considered viable matches and were added to matched database.

Table 2C – 4. Diagnosis Codes Indicating End Stage Liver Disease

ICD9 Code	Definition
570	Acute necrosis of the liver
1150	Hepatic malignancy
5712	Cirrhosis, secondary to alcohol abuse
5715	Cirrhosis, NOS
5718	Chronic liver disease
5722	Hepatic encephalopathy
5723	Portal hypertension
5724	Hepatorenal syndrome
5728	Sequale of liver disease
78959	Ascites
57142	Autoimmune hepatitis
07032	Hepatitis B, chronic
07044	Hepatitis B, with hepatic coma
07054	Hepatitis C, chronic
07041	Hepatitis C, with hepatic coma
V4983	Awaiting organ transplant
99682	Complication of liver transplantation

Results of Matching by State

The results of each match are included in Table 2C – 5. Overall, 98.4% of cases were matched utilizing the algorithm (9247/9398). Matches within California, Georgia, Massachusetts and Florida all approached 99.0% or greater.

Table 2C – 5. Match Results by State. Stepwise results for each state are included below. Total number of matched cases as compared to the source databases are indicated in the last rows.

	California State Match		NY State Match		GA State Match		NE State Match		MA State Match		FL State Match	
	SRTR	**OSHPD**	**SRTR**	**HCUP**	**SRTR**	**HCUP**	**SRTR**	**HCUP**	**SRTR**	**HCUP**	**SRTR**	**HCUP**
Transplant Admissions	3164	3122	1550	1516	1016	1009	390	352	951	926	2327	2305
Exact Match, preliminary Duplicates	1967 0 duplicates		1002 2 duplicates, unable to break		648 0 duplicates		201 6 duplicates, SRTR:2HCUP, all 3 pairs appeared to be clerical duplicates		586 0 duplicates		1294 10 duplicates, SRTR:2HCUP, 4 pairs broken, 1 pair unable to break	
Exact Match, final count	1967		1000		648		198		586		1288	
Remaining unmatched cases	1219	1155	549	514	368	361	192	151	365	340	1056	1015
Pairwise Potential Matches by Hospital ID	214,112		214,112		75,818		28,992		31,326		223,937	
Heuristic Match Results	1141		455		350		146		334		954	
Heuristic Match Round 2	3		18		6		1		3		18	
Clerical Matches	1		24		0		2		2		24	
Subtotal	3112		1497		1004		347		925		2284	
Remaining Unmatched	52	10	53	19	12	5	43	5	26	1	43	21
Comparison to full state database	10		12		2		17		21		17	
Total Cases Matched	*3122*		*1509*		*1006*		*364*		*945*		*2301*	
Total Possible Cases by dataset	*3164*	*3132*	*1550*	*1526*	*1016*	*1011*	*390*	*369*	*951*	*947*	*2327*	*2322*
% Matched	*98.7%*	*99.7%*	*97.4%*	*98.9%*	*99.0%*	*99.5%*	*93.3%*	*98.6%*	*99.4%*	*99.8%*	*98.9%*	*99.1%*

3. Descriptive Comparisons – Supplemental Information

3A. National Comparison of Pre- and Post-Share 35 Cohorts

	All Transplants 2010 - 11/1/2016 n = 36,601				
	Pre-Share 35 n = 17,059		Post-Share 35 n = 19,542		
Categorical Variables					
Patient Demographics	n	%	N	%	p-value
Race / Ethnicity					
White, non-latino	12078	70.8%	13842	70.8%	
White, latino	2329	13.7%	2775	14.2%	
Black	1671	9.8%	1849	9.5%	0.400
Asian	744	4.4%	811	4.2%	
Other	237	1.4%	265	1.4%	
Sex					
Male	11659	68.3%	13194	67.5%	0.090
Female	5400	31.7%	6348	32.5%	
Ability to Pay for Care					
Insurance Status					
Private insurance	9461	55.5%	10183	52.1%	
Medicare	4441	26.0%	5769	29.5%	<0.001 **
Medicaid	2365	13.9%	2709	13.9%	
Other	792	4.6%	881	4.5%	
Education					
Less than High School/GED	847	5.0%	1026	5.2%	
High School / GED	6914	40.5%	8025	41.1%	
Some college or technical school	3874	22.7%	4736	24.2%	<0.001 **
Associate or bachelors degree	2671	15.7%	3331	17.0%	
Post-college graduate degree	1100	6.4%	1373	7.0%	
Unknown	1653	9.7%	1051	5.4%	
Medical Condition / Disability at Transplant					
Medical Comorbidities					
Chronic obstructive pulmonary disease	363	2.1%	291	1.5%	0.843
Diabetes	4458	26.1%	5614	28.7%	<0.001 **
Hypertension	3845	22.5%	3348	17.1%	<0.001 **
Renal failure	2383	14.0%	3282	16.8%	<0.001 **
Vascular disease	285	1.7%	249	1.3%	0.167
Liver Disease Etiology					
Acute liver failure	208	1.2%	233	1.2%	
Autoimmune hepatitis	371	2.2%	443	2.3%	
Cholestatic liver disease	1228	7.2%	1348	6.9%	
Cryptogenic cirrhosis	816	4.8%	767	3.9%	
Genetic/metabolic	415	2.4%	424	2.2%	<0.001 **
Hepatitis C	3148	18.5%	2750	14.1%	
Malignancy	6018	35.3%	6656	34.0%	
Steatohepatitis (NASH/Alcoholic hepatitis)	4314	25.3%	6332	32.4%	
Other	541	3.2%	589	3.0%	
MELD Point Trends					

Approved for MELD Exception Points	5480	32.1%	6127	31.4%	0.114
Allocation MELD Score ≥30	5789	33.9%	8256	42.3%	<0.001 **
Allocation MELD Score ≥35	3116	18.3%	4977	25.5%	<0.001 **
Disease Acuity at Transplant					
Life support measures					
Ventilator Dependence	592	3.5%	784	4.0%	0.007 *
Dialysis Dependence	2216	13.0%	3162	16.2%	<0.001 **
Life support measures	996	5.8%	1548	7.9%	<0.001 **
Location at time of Transplant					
Intensive Care Unit	1703	10.0%	2669	13.7%	
Hospitalized, ward bed	3429	20.1%	3872	19.8%	<0.001 **
Not Hospitalized	11927	69.9%	13001	66.5%	
Mortality After Transplant					
Death within transplant admission or 30 days of discharge	728	4.3%	770	3.9%	0.115
Death within 90 days of transplant	820	4.8%	816	4.2%	0.004 *
Continuous Variables					
Patient Demographics					
Age (years)					
mean	55.583		56.403		
Mean difference, p-value		-0.821			<0.001 **
Disease Severity at Listing					
Physiologic MELD at Listing					
mean	18.319		18.949		
Mean difference, p-value		-0.730			<0.001 **
Allocation MELD at Listing					
mean	19.913		20.391		
Mean difference, p-value		-0.479			<0.001 **
Karnofsky Score at Listing					
mean	64.228		60.622		
Mean difference, p-value		3.607			<0.001 **
Disease Severity at Transplant					
Physiologic MELD at Transplant					
mean	21.786		22.302		
Mean difference, p-value		-0.516			<0.001 **
Allocation MELD at Transplant					
mean	27.210		28.554		
Mean difference, p-value		-1.344			<0.001 **
Karnofsky Score at Transplant					
mean	52.910		50.363		<0.001 **
Mean difference, p-value		2.546			

P-values indicate statistical significance of differences between the Pre- and Post-Share 35 periods by chi-squared for binary comparisons and by t-test for continuous variables. * p<0.05, ** p<0.001. Abbreviations: MELD – Model for End Stage Liver Disease score, NASH – non-alcoholic steatohepatitis, GED –general equivalency diploma.

3B. National Comparison of Pre- and Post-Share 35 Cohorts by Region

	Region 1 n = 1429					Region 2 n = 4213					Region 3 n = 6828				
	Pre-Share 35 n = 666		Post-Share 35 n = 763			Pre-Share 35 n = 1919		Post-Share 35 n = 2294			Pre-Share 35 n = 3130		Post-Share 35 n = 3698		
Categorical Variables															
Patient Demographics	n	%	n	%	p-value	n	%	n	%	p-value	n	%	n	%	p-value
Race / Ethnicity															
White, non-latino	516	77.5%	606	79.4%	0.24	1358	70.8%	1625	70.8%	0.55	2277	72.7%	2711	73.3%	0.459
White, latino	78	11.7%	68	8.9%		43	2.2%	151	6.6%		427	13.6%	484	13.1%	
Black	45	6.8%	46	6.0%		331	17.2%	425	18.5%		350	11.2%	396	10.7%	
Asian	18	2.7%	25	3.3%		76	4.0%	84	3.7%		61	1.9%	93	2.5%	
Other	9	1.4%	18	2.4%		11	0.6%	9	0.4%		15	0.5%	14	0.4%	
Sex															
Male	489	73.4%	538	70.5%	0.222	1387	72.3%	1638	71.4%	0.53	2065	66.0%	2420	65.4%	
Female	177	26.6%	225	29.5%		532	27.7%	656	28.6%		1065	34.0%	1278	34.6%	0.644
Ability to Pay for Care															
Insurance Status															
Private insurance	352	52.9%	311	40.8%	<0.001**	1054	54.9%	1213	52.9%	<0.001**	1743	55.7%	2072	56.0%	<0.001**
Medicare	183	27.5%	286	37.5%		443	23.1%	573	25.0%		861	27.5%	1141	30.9%	
Medicaid	13	2.0%	152	19.9%		229	11.9%	346	15.1%		407	13.0%	354	9.6%	
Other	18	2.7%	14	1.8%		193	10.1%	62	2.7%		119	3.8%	131	3.5%	
Education															
Less than High School/GED	55	8.3%	31	4.1%	<0.001**	55	2.9%	79	3.4%	<0.001**	133	4.2%	144	3.9%	<0.001**
High School / GED	277	41.6%	395	51.8%		871	45.4%	1036	45.2%		1139	36.4%	1480	40.0%	
Some college or technical school	123	18.5%	144	18.9%		350	18.2%	461	20.1%		734	23.5%	909	24.6%	
Associate or bachelors degree	116	17.4%	125	16.4%		241	12.6%	334	14.6%		534	17.1%	670	18.1%	
Post-college graduate degree	48	7.2%	45	5.9%		123	6.4%	166	7.2%		208	6.6%	308	8.3%	
Unknown	47	7.1%	23	3.0%		279	14.5%	218	9.5%		382	12.2%	187	5.1%	
Medical Condition / Disability at Transplant															
Medical Comorbidities															
COPD	24	3.6%	18	2.4%	0.873	57	3.0%	43	1.9%	0.498	47	1.5%	55	1.5%	0.029*
Diabetes	191	28.7%	202	26.5%	0.352	463	24.1%	613	26.7%	0.068	865	27.6%	1115	30.2%	0.021*
Hypertension	177	26.6%	139	18.2%	0.954	479	25.0%	504	22.0%	0.004*	883	28.2%	684	18.5%	0.772
Renal failure	111	16.7%	83	10.9%	0.66	202	10.5%	345	15.0%	<0.001**	291	9.3%	512	13.8%	<0.001**
Vascular disease	17	2.6%	9	1.2%	0.329	33	1.7%	47	2.0%	0.007*	56	1.8%	39	1.1%	0.677
Liver Disease Etiology															
Acute liver failure	12	1.8%	8	1.0%		8	0.4%	19	0.8%		60	1.9%	63	1.7%	
Autoimmune hepatitis	13	2.0%	8	1.0%		41	2.1%	40	1.7%		95	3.0%	117	3.2%	
Cholestatic liver disease	27	4.1%	39	5.1%		116	6.0%	128	5.6%		223	7.1%	255	6.9%	
Cryptogenic cirrhosis	34	5.1%	17	2.2%		62	3.2%	68	3.0%		185	5.9%	168	4.5%	
Genetic/metabolic	12	1.8%	9	1.2%	0.058	38	2.0%	37	1.6%	<0.001**	63	2.0%	90	2.4%	<0.001**
Hepatitis C	113	17.0%	124	16.3%		402	20.9%	376	16.4%		686	21.9%	549	14.8%	
Malignancy	241	36.2%	295	38.7%		775	40.4%	811	35.4%		819	26.2%	1055	28.5%	
Steatohepatitis	202	30.3%	245	32.1%		418	21.8%	742	32.3%		886	28.3%	1276	34.5%	
Other	12	1.8%	18	2.4%		59	3.1%	73	3.2%		113	3.6%	125	3.4%	
MELD Point Trends															
Approved for MELD Exception Points	221	33.2%	278	36.4%	0.198	724	37.7%	742	32.4%	<0.001**	707	22.6%	960	26.0%	0.001*
Allocation MELD Score ≥30	285	42.8%	406	53.2%	<0.001**	690	36.0%	1086	47.3%	<0.001**	581	18.6%	967	26.2%	<0.001**
Allocation MELD Score ≥35	159	23.9%	170	22.3%	0.475	339	17.7%	637	27.8%	<0.001**	327	10.5%	624	16.9%	<0.001**
Disease Acuity at Transplant															
Life support measures															
Ventilator Dependence	28	4.2%	16	2.1%	0.021*	51	2.7%	101	4.4%	0.002*	62	2.0%	119	3.2%	0.002*
Dialysis Dependence	103	15.5%	81	10.6%	0.006*	184	9.6%	326	14.1%	<0.001**	260	8.3%	477	12.9%	<0.001**
Life support measures	36	5.4%	28	3.7%	0.114	61	3.2%	134	5.8%	<0.001**	96	3.1%	199	5.4%	<0.001**
Location at time of Transplant															
Intensive Care Unit	86	12.5%	69	9.0%		153	8.0%	255	11.1%		236	7.5%	419	11.3%	
Hospitalized, ward bed	158	23.7%	177	23.2%	0.050*	465	24.2%	625	27.2%	<0.001**	558	17.8%	651	17.6%	<0.001**
Not Hospitalized	422	63.4%	517	67.8%		1301	67.8%	1414	61.6%		2336	74.6%	2628	71.1%	
Mortality After Transplant															
Death within transplant admission or 30 days of discharge	40	6.0%	37	4.8%	0.334	63	3.3%	95	4.1%	0.144	114	3.6%	134	3.6%	0.967
Death within 90 days of transplant	44	6.6%	36	4.7%	0.121	76	4.0%	96	4.2%	0.714	141	4.5%	144	3.9%	0.209
Continuous Variables															
Patient Demographics															
Age (years)															
mean	56.146		56.442		0.5449	55.721		56.137		0.1673	55.573		56.442		<0.001**
Mean difference, p-value	-0.296					-0.416					-0.869				
Disease Severity at Listing															
Physiologic MELD at Listing															
mean	18.377		16.582		<0.001**	17.821		19.299		<0.001**	19.002		19.207		0.3122
Mean difference, p-value	1.795					-1.479					-0.205				
Allocation MELD at Listing															
mean	20.673		19.649		0.029*	20.247		21.112		0.002*	20.158		20.441		0.1439
Mean difference, p-value	1.024					-0.865					-0.283				
Karnofsky Score at Listing															
mean	65.038		65.118		0.9477	68.439		60.923		<0.001**	60.944		60.116		0.1249
Mean difference, p-value	-0.080					7.516					0.827				
Disease Severity at Transplant															
Physiologic MELD at Transplant															
mean	21.584		19.720		0.001*	21.635		22.885		<0.001**	21.159		21.521		0.1016
Mean difference, p-value	1.865					-1.250					-0.362				
Allocation MELD at Transplant															
mean	27.851		28.596		0.0893	27.640		29.518		<0.001**	24.421		26.103		<0.001**
Mean difference, p-value	-0.745					-1.877					-1.682				
Karnofsky Score at Transplant															
mean	53.850		54.363		0.6802	55.408		47.976		<0.001**	53.898		54.710		0.1296
Mean difference, p-value	-0.514					7.433					-0.812				

P-values indicate statistically signficant differences between the Pre- and Post-Share 35 periods by chi-squared and t-tests for binary and continuous outcomes respectively. *p<0.05, **p<0.005.
Abbreviations: COPD - chronic obstructive pulmonary disease, GED - general equivalency diploma, MELD - Model for End Stage Liver Disease

	Region 4 n = 3423					Region 5 n = 5175					Region 6 n = 1091				
	Pre-Share 35 n = 1557		Post-Share 35 n = 1866			Pre-Share 35 n = 2410		Post-Share 35 n = 2765			Pre-Share 35 n = 471		Post-Share 35 n = 620		
Categorical Variables															
Patient Demographics	n	%	n	%	p-value	n	%	n	%	p-value	n	%	n	%	p-value
Race / Ethnicity															
White, non-latino	972	62.4%	1084	58.1%	0.021 *	1293	53.7%	1431	51.8%	0.133	373	79.2%	458	73.9%	0.287
White, latino	376	24.1%	539	28.9%		718	29.8%	903	32.7%		28	5.9%	54	8.7%	
Black	128	8.2%	154	8.3%		88	3.7%	9	0.3%		11	2.3%	17	2.7%	
Asian	58	3.7%	56	3.0%		267	11.1%	268	9.7%		36	7.6%	52	8.4%	
Other	23	1.5%	33	1.8%		44	1.8%	54	2.0%		23	4.9%	39	6.3%	
Sex		0.0%		0.0%											
Male	1033	66.3%	1243	66.6%	0.869	1647	68.3%	1821	65.9%	0.058	335	71.1%	434	70.0%	0.686
Female	524	33.7%	623	33.4%		763	31.7%	944	34.1%		136	28.9%	186	30.0%	
Ability to Pay for Care															
Insurance Status															
Private insurance	881	56.6%	1059	56.8%	0.494	1380	57.3%	1415	51.2%	<0.001 **	262	55.6%	304	49.0%	0.150
Medicare	475	30.5%	592	31.7%		557	23.1%	779	28.2%		99	21.0%	146	23.5%	
Medicaid	120	7.7%	120	6.4%		432	17.9%	517	18.7%		53	11.3%	90	14.5%	
Other	81	5.2%	95	5.1%		41	1.7%	54	2.0%		57	12.1%	80	12.9%	
Education															
Less than High School/GED	103	6.6%	113	6.1%	<0.001 **	218	9.0%	305	11.0%	<0.001 **	15	3.2%	26	4.2%	0.020 *
High School / GED	540	34.7%	807	43.2%		902	37.4%	1054	38.1%		144	30.6%	215	34.7%	
Some college or technical school	384	24.7%	465	24.9%		620	25.7%	730	26.4%		136	28.9%	181	29.2%	
Associate or bachelors degree	45	2.9%	282	15.1%		370	15.4%	423	15.3%		92	19.5%	110	17.7%	
Post-college graduate degree	89	5.7%	104	5.6%		151	6.3%	183	6.6%		23	4.9%	3	0.5%	
Unknown	196	12.6%	95	5.1%		149	6.2%	70	2.5%		61	13.0%	45	7.3%	
Medical Condition / Disability at Transplant															
Medical Comorbidities															
COPD	16	1.0%	22	1.2%	0.067	28	1.2%	22	0.8%	0.595	7	1.5%	6	1.0%	0.879
Diabetes	419	26.9%	544	29.2%	0.179	608	25.2%	747	27.0%	0.178	93	19.7%	149	24.0%	0.084
Hypertension	388	24.9%	332	17.8%	0.358	350	14.5%	379	13.7%	0.008 *	59	12.5%	76	12.3%	0.002 *
Renal failure	237	15.2%	375	20.1%	<0.001 **	675	28.0%	900	32.5%	<0.001 **	42	8.9%	88	14.2%	<0.001 **
Vascular disease	23	1.5%	17	0.9%	0.951	26	1.1%	15	0.5%	0.145	3	0.6%	1	0.2%	0.438
Liver Disease Etiology															
Acute liver failure	16	1.0%	18	1.0%		22	0.9%	22	0.8%		8	1.7%	6	1.0%	
Autoimmune hepatitis	31	2.0%	39	2.1%		31	1.3%	65	2.4%		5	1.1%	13	2.1%	
Cholestatic liver disease	89	5.7%	77	4.1%		132	5.5%	168	6.1%		44	9.3%	39	6.3%	
Cryptogenic cirrhosis	89	5.7%	90	4.8%		90	3.7%	108	3.9%		13	2.8%	31	5.0%	
Genetic/metabolic	45	2.9%	49	2.6%	<0.001 **	32	1.3%	34	1.2%	<0.001 **	12	2.5%	7	1.1%	0.003 *
Hepatitis C	277	17.8%	305	16.3%		31	1.3%	65	2.4%		94	20.0%	83	13.4%	
Malignancy	686	44.1%	696	37.3%		432	17.9%	372	13.5%		179	38.0%	259	41.8%	
Steatohepatitis	279	17.9%	536	28.7%		1038	43.1%	1136	41.1%		101	21.4%	163	26.3%	
Other	45	2.9%	56	3.0%		69	2.9%	91	3.3%		15	3.2%	19	3.1%	
MELD Point Trends															
Approved for MELD Exception Points	651	41.8%	658	35.3%	<0.001 **	952	39.5%	1016	36.8%	0.042 *	167	35.5%	252	40.7%	0.081
Allocation MELD Score ≥30	560	36.0%	935	50.1%	<0.001 **	4603	66.5%	1987	71.9%	<0.001 **	117	24.8%	251	40.5%	<0.001 **
Allocation MELD Score ≥35	268	17.2%	572	30.7%	<0.001 **	943	39.1%	1391	50.3%	<0.001 **	64	13.6%	140	22.6%	<0.001 **
Disease Acuity at Transplant															
Life support measures															
Ventilator Dependence	67	4.3%	132	7.1%	0.001 *	193	8.0%	237	8.6%	0.464	4	0.8%	7	1.1%	0.647
Dialysis Dependence	222	14.3%	361	19.3%	<0.001 **	645	26.8%	886	32.0%	<0.001 **	40	8.5%	87	14.0%	0.005 *
Life support measures	156	10.0%	271	14.5%	<0.001 **	370	15.4%	547	19.8%	<0.001 **	4	0.8%	7	1.1%	0.647
Location at time of Transplant															
Intensive Care Unit	188	12.1%	379	20.3%		542	22.5%	810	29.3%		14	3.0%	40	6.5%	
Hospitalized, ward bed	344	22.1%	388	20.8%	<0.001 **	545	22.6%	534	19.3%	<0.001 **	88	18.7%	153	24.7%	0.001 *
Not Hospitalized	1025	65.8%	1099	58.9%		1323	54.9%	1421	51.4%		369	78.3%	427	68.9%	
Mortality After Transplant															
Death within transplant admission or 30d of discharge	65	4.2%	66	3.5%	0.333	115	4.8%	104	3.8%	0.072	6	1.3%	15	2.4%	0.173
Death within 90 days of transplant	73	4.7%	73	3.9%	0.263	118	4.9%	107	3.9%	0.071	10	2.1%	14	2.3%	0.88
Continuous Variables															
Patient Demographics															
Age (years)															
mean	55.542		56.203		0.042 *	55.955		56.850		<0.001 **	54.900		56.265		0.015 *
Mean difference, p-value	-0.661					-0.895					-1.364				
Disease Severity at Listing															
Physiologic MELD at Listing															
mean	17.663		19.529		<0.001 **	18.644		20.119		<0.001 **	17.817		18.706		0.1224
Mean difference, p-value	-1.866					-1.475					-0.889				
Allocation MELD at Listing															
mean	19.348		20.725		<0.001 **	20.361		21.518		<0.001 **	19.034		19.934		0.1104
Mean difference, p-value	-1.376					-1.158					-0.900				
Karnofsky Score at Listing															
mean	61.432		57.670		<0.001 **	61.423		59.920		0.040 *	72.574		71.705		0.5367
Mean difference, p-value	3.762					1.503					0.869				
Disease Severity at Transplant															
Physiologic MELD at Transplant															
mean	21.986		23.521		<0.001 **	24.360		25.050		0.040 *	21.093		21.656		0.37868
Mean difference, p-value	-1.536					-0.691					-0.560				
Allocation MELD at Transplant															
mean	28.597		30.012		<0.001 **	32.263		33.087		<0.001 **	26.866		29.296		<0.001 **
Mean difference, p-value	-1.415					-0.824					-2.410				
Karnofsky Score at Transplant															
mean	47.706		44.753		<0.001 **	46.939		45.615		0.076	65.914		67.944		0.1594
Mean difference, p-value	2.953					1.324					-2.029				

P-values indicate statistically signficant differences between the Pre- and Post-Share 35 periods by chi-squared and t-tests for binary and continuous outcomes respectively. *p<0.05, **p<0.005.
Abbreviations: COPD - chronic obstructive pulmonary disease, GED - general equivalency diploma, MELD - Model for End Stage Liver Disease

	Region 7 n = 2933					Region 8 n = 2529					Region 9 n = 1740				
	Pre-Share 35 n = 1387		Post-Share 35 n = 1546			Pre-Share 35 n = 1254		Post-Share 35 n = 1275			Pre-Share 35 n = 847		Post-Share 35 n = 893		
Categorical Variables															
Patient Demographics	n	%	n	%	p-value	n	%	n	%	p-value	n	%	n	%	p-value
Race / Ethnicity															
White, non-latino	1022	73.7%	1189	76.9%	0.177	1030	82.1%	1045	82.0%	0.196	451	53.2%	482	54.0%	0.778
White, latino	151	10.9%	142	9.2%		104	8.3%	114	8.9%		186	22.0%	209	23.4%	
Black	124	8.9%	120	7.8%		71	5.7%	70	5.5%		106	12.5%	106	11.9%	
Asian	53	3.8%	65	4.2%		36	2.9%	23	1.8%		102	12.0%	93	10.4%	
Other	37	2.7%	30	1.9%		13	1.0%	23	1.8%		2	0.2%	3	0.3%	
Sex															
Male	928	66.9%	1030	66.6%	0.871	870	69.4%	870	68.2%	0.535	592	69.9%	609	68.2%	0.444
Female	459	33.1%	516	33.4%		384	30.6%	405	31.8%		255	30.1%	284	31.8%	
Ability to Pay for Care															
Insurance Status															
Private insurance	721	52.0%	753	48.7%	0.033 *	716	57.1%	709	55.6%	0.518	429	50.6%	347	38.9%	<0.001 **
Medicare	386	27.8%	445	28.8%		330	26.3%	367	28.8%		219	25.9%	302	33.8%	
Medicaid	238	17.2%	271	17.5%		185	14.8%	180	14.1%		186	22.0%	228	25.5%	
Other	42	3.0%	77	5.0%		23	1.8%	19	1.5%		13	1.5%	16	1.8%	
Education															
Less than High School/GED	55	4.0%	71	4.6%	<0.001 **	38	3.0%	48	3.8%	<0.001 **	84	9.9%	89	10.0%	0.416
High School / GED	554	39.9%	682	44.1%		579	46.2%	467	36.6%		353	41.7%	355	39.8%	
Some college or technical school	311	22.4%	379	24.5%		281	22.4%	328	25.7%		173	20.4%	194	21.7%	
Associate or bachelors degree	198	14.3%	276	17.9%		205	16.3%	239	18.7%		121	14.3%	137	15.3%	
Post-college graduate degree	82	5.9%	94	6.1%		69	5.5%	80	6.3%		76	9.0%	91	10.2%	
Unknown	187	13.5%	44	2.8%		82	6.5%	113	8.9%		40	4.7%	27	3.0%	
Medical Condition / Disability at Transplant															
Medical Comorbidities															
COPD	32	2.3%	23	1.5%	0.322	25	2.0%	16	1.3%	0.957	27	3.2%	17	1.9%	0.315
Diabetes	382	27.5%	449	29.0%	0.404	292	23.3%	334	26.2%	0.084	251	29.6%	267	29.9%	0.942
Hypertension	190	13.7%	174	11.3%	0.707	223	17.8%	141	11.1%	0.839	268	31.6%	243	27.2%	0.106
Renal failure	299	21.6%	328	21.2%	0.020 *	145	11.6%	137	10.7%	0.001 *	87	10.3%	95	10.6%	0.081
Vascular disease	15	1.1%	19	1.2%	0.388	7	0.6%	5	0.4%	0.792	31	3.7%	24	2.7%	0.757
Liver Disease Etiology															
Acute liver failure	16	1.2%	18	1.2%		17	1.4%	13	1.0%		9	1.1%	12	1.3%	
Autoimmune hepatitis	22	1.6%	32	2.1%		29	2.3%	40	3.1%		12	1.4%	15	1.7%	
Cholestatic liver disease	102	7.4%	110	7.1%		114	9.1%	124	9.7%		76	9.0%	69	7.7%	
Cryptogenic cirrhosis	62	4.5%	44	2.8%		61	4.9%	50	3.9%		37	4.4%	14	1.6%	
Genetic/metabolic	52	3.7%	30	1.9%	0.001 *	46	3.7%	40	3.1%	<0.001 **	12	1.4%	18	2.0%	0.004 *
Hepatitis C	157	11.3%	36	2.3%		215	17.1%	150	11.8%		134	15.8%	108	12.1%	
Malignancy	476	34.3%	571	36.9%		425	33.9%	96	7.5%		387	45.7%	446	49.9%	
Steatohepatitis	454	32.7%	570	36.9%		313	25.0%	434	34.0%		141	16.6%	176	19.7%	
Other	46	3.3%	35	2.3%		34	2.7%	28	2.2%		39	4.6%	35	3.9%	
MELD Point Trends															
Approved for MELD Exception Points	411	29.6%	518	33.5%	0.024 *	393	31.3%	363	28.5%	0.115	355	41.9%	414	46.4%	0.062
Allocation MELD Score ≥30	674	48.6%	807	52.2%	0.051	344	27.4%	403	31.6%	0.021 *	421	49.7%	555	62.2%	<0.001 **
Allocation MELD Score ≥35	377	27.2%	474	30.7%	0.038 *	153	12.2%	243	19.1%	<0.001 **	192	22.7%	226	25.3%	0.198
Disease Acuity at Transplant															
Life support measures															
Ventilator Dependence	90	6.5%	75	4.9%	0.055	17	1.4%	11	0.9%	0.236	13	1.5%	7	0.8%	0.142
Dialysis Dependence	283	20.4%	320	20.7%	0.844	128	10.2%	131	10.3%	0.956	84	9.9%	93	10.4%	0.732
Life support measures	112	8.1%	173	11.2%	0.004 *	42	3.3%	23	1.8%	0.014 *	21	2.5%	11	1.2%	0.053 *
Location at time of Transplant															
Intensive Care Unit	195	14.1%	246	15.9%		65	5.2%	70	5.5%		57	6.7%	78	8.7%	
Hospitalized, ward bed	317	22.9%	328	21.2%	0.277	277	22.1%	271	21.3%	0.844	209	24.7%	200	22.4%	0.2
Not Hospitalized	875	63.1%	972	62.9%		912	72.7%	934	73.3%		581	68.6%	615	68.9%	
Mortality After Transplant															
Death within transplant admission or 30d of discharge	63	4.5%	82	5.3%	0.342	54	4.3%	39	3.1%	0.096	64	7.6%	42	4.7%	0.013 *
Death within 90 days of transplant	67	4.8%	80	5.2%	0.67	60	4.8%	41	3.2%	0.044 *	70	8.3%	40	4.5%	0.001 *
Continuous Variables															
Patient Demographics															
Age (years)															
mean	55.632		56.412		0.031 *	55.239		55.820		0.1337	56.758		57.695		0.048 *
Mean difference, p-value	-0.780					-0.581					-0.937				
Disease Severity at Listing															
Physiologic MELD at Listing															
mean	19.672		19.664		0.982	17.447		17.944		0.1433	16.983		16.578		0.3697
Mean difference, p-value	0.008					-0.497					0.406				
Allocation MELD at Listing															
mean	21.613		21.281		0.3353	19.173		19.087		0.7916	18.330		17.804		0.2378
Mean difference, p-value	0.331					0.086					0.526				
Karnofsky Score at Listing															
mean	59.853		57.676		0.008 *	63.512		62.123		0.1132	69.713		65.567		<0.001 **
Mean difference, p-value	2.177					1.389					4.146				
Disease Severity at Transplant															
Physiologic MELD at Transplant															
mean	24.133		23.599		0.1924	21.458		21.603		0.706	21.131		20.124		0.055
Mean difference, p-value	0.534					-0.145					1.007				
Allocation MELD at Transplant															
mean	29.667		30.380		0.007 *	26.746		27.081		0.2026	29.072		30.380		<0.001 **
Mean difference, p-value	-0.713					-0.335					-1.308				
Karnofsky Score at Transplant															
mean	48.218		48.464		0.7762	51.653		48.562		<0.001 **	53.731		56.305		0.022 *
Mean difference, p-value	-0.246					3.091					-2.574				

P-values indicate statistically signficant differences between the Pre- and Post-Share 35 periods by chi-squared and t-tests for binary and continuous outcomes respectively. *p<0.05, **p<0.005.
Abbreviations: COPD - chronic obstructive pulmonary disease, GED - general equivalency diploma, MELD - Model for End Stage Liver Disease

	Region 10 n = 3215					Region 11 n = 4025				
	Pre-Share 35 n = 1497		Post-Share 35 n = 1718			Pre-Share 35 n = 1921		Post-Share 35 n = 2104		
Categorical Variables										
Patient Demographics	n	%	n	%	p-value	n	%	n	%	p-value
Race / Ethnicity										
White, non-latino	1269	84.8%	1498	87.2%	0.260	1517	79.0%	1713	81.4%	0.012 *
White, latino	46	3.1%	52	3.0%		72	3.7%	59	2.8%	
Black	147	9.8%	135	7.9%		270	14.1%	271	12.9%	
Asian	26	1.7%	27	1.6%		11	0.6%	25	1.2%	
Other	9	0.6%	6	0.3%		51	2.7%	36	1.7%	
Sex										
Male	1020	68.1%	1168	68.0%	0.927	1293	67.3%	1423	67.6%	0.826
Female	477	31.9%	550	32.0%		628	32.7%	681	32.4%	
Ability to Pay for Care										
Insurance Status										
Private insurance	883	59.0%	922	53.7%	0.002 *	1040	54.1%	1078	51.2%	0.180
Medicare	391	26.1%	533	31.0%		497	25.9%	605	28.8%	
Medicaid	206	13.8%	229	13.3%		196	10.2%	222	10.6%	
Other	17	1.1%	34	2.0%		188	9.8%	199	9.5%	
Education										
Less than High School/GED	26	1.7%	47	2.7%	<0.001 **	65	3.4%	73	3.5%	0.126
High School / GED	756	50.5%	739	43.0%		799	41.6%	795	37.8%	
Some college or technical school	315	21.0%	455	26.5%		447	23.3%	490	23.3%	
Associate or bachelors degree	223	14.9%	324	18.9%		326	17.0%	411	19.5%	
Post-college graduate degree	115	7.7%	131	7.6%		116	6.0%	128	6.1%	
Unknown	62	4.1%	22	1.3%		168	8.7%	207	9.8%	
Medical Condition / Disability at Transplant										
Medical Comorbidities										
COPD	53	3.5%	32	1.9%	0.554	47	2.4%	37	1.8%	0.75
Diabetes	335	22.4%	519	30.2%	<0.001 **	559	29.1%	675	32.1%	0.115
Hypertension	383	25.6%	339	19.7%	<0.001 **	445	23.2%	337	16.0%	0.517
Renal failure	166	11.1%	232	13.5%	<0.001 **	128	6.7%	187	8.9%	<0.001 **
Vascular disease	47	3.1%	33	1.9%	0.931	27	1.4%	40	1.9%	0.004 *
Liver Disease Etiology										
Acute liver failure	21	1.4%	18	1.0%		19	1.0%	36	1.7%	
Autoimmune hepatitis	38	2.5%	34	2.0%		54	2.8%	40	1.9%	
Cholestatic liver disease	166	11.1%	175	10.2%		139	7.2%	164	7.8%	
Cryptogenic cirrhosis	77	5.1%	81	4.7%		106	5.5%	96	4.6%	
Genetic/metabolic	40	2.7%	57	3.3%	<0.001 **	63	3.3%	53	2.5%	<0.001 **
Hepatitis C	242	16.2%	218	12.7%		396	20.6%	329	15.6%	
Malignancy	437	29.2%	405	23.6%		555	28.9%	586	27.9%	
Steatohepatitis	437	29.2%	683	39.8%		519	27.0%	738	35.1%	
Other	39	2.6%	47	2.7%		70	3.6%	62	2.9%	
MELD Point Trends										
Approved for MELD Exception Points	404	27.0%	374	21.8%	0.001 *	495	25.8%	552	26.2%	0.735
Allocation MELD Score ≥30	245	16.4%	366	21.3%	<0.001 **	269	14.0%	493	23.4%	<0.001 **
Allocation MELD Score ≥35	153	10.2%	217	12.6%	0.033	141	7.4%	283	12.5%	<0.001 **
Disease Acuity at Transplant										
Life support measures										
Ventilator Dependence	46	3.1%	47	2.7%	0.569	21	1.1%	32	1.5%	0.234
Dialysis Dependence	148	9.9%	222	12.9%	0.007 *	119	6.2%	178	8.5%	0.006 *
Life support measures	53	3.5%	65	3.8%	0.715	45	2.3%	90	4.3%	0.001 *
Location at time of Transplant										
Intensive Care Unit	90	6.0%	128	7.5%		77	4.0%	175	8.3%	
Hospitalized, ward bed	203	13.6%	224	13.0%	0.261	265	13.8%	321	15.3%	<0.001 **
Not Hospitalized	1204	80.4%	1366	79.5%		1579	82.2%	1608	76.4%	
Mortality After Transplant										
Death within transplant admission or 30d of discharge	67	4.5%	82	4.8%	0.689	77	4.0%	74	3.5%	0.671
Death within 90 days of transplant	70	4.5%	96	5.6%	0.244	91	4.7%	89	4.2%	0.437
Continuous Variables										
Patient Demographics										
Age (years)										
mean	55.148		56.215		0.002 *	55.005		56.197		<0.001 **
Mean difference, p-value	-1.066					-1.192				
Disease Severity at Listing										
Physiologic MELD at Listing										
mean	17.511		18.038		0.0676	17.858		18.827		<0.001 **
Mean difference, p-value	-0.527					-0.970				
Allocation MELD at Listing										
mean	18.894		19.095		0.4751	19.774		20.437		0.005 *
Mean difference, p-value	-0.201					-0.663				
Karnofsky Score at Listing										
mean	66.334		60.419		<0.001 **	67.965		58.996		<0.001 **
Mean difference, p-value	5.914					8.970				
Disease Severity at Transplant										
Physiologic MELD at Transplant										
mean	19.997		20.725		0.021 *	20.010		21.158		<0.001 **
Mean difference, p-value	-0.728					-1.148				
Allocation MELD at Transplant										
mean	24.032		25.015		<0.001 **	23.906		26.002		<0.001 **
Mean difference, p-value	-0.982					-2.096				
Karnofsky Score at Transplant										
mean	56.278		48.179		<0.001 **	58.455		51.824		<0.001 **
Mean difference, p-value	8.099					6.631				

P-values indicate statistically signficant differences between the Pre- and Post-Share 35 periods by chi-squared and t-tests for binary and continuous outcomes respectively. *p<0.05, **p<0.005. Abbreviations: COPD - chronic obstructive pulmonary disease, GED - general equivalency diploma, MELD - Model for End Stage Liver Disease

3C. Regional Comparisons for Regions within the Utilization Cohort

	Region 1 n = 882					Region 3 n = 4220					Region 5 n = 3226				
	Region1 n = 365		Region 1 UC n = 517			Region3 n = 1910		Region 3 UC n = 2310			Region 5 n = 953		Region 5 UC n = 2273		
Categorical Variables															
Patient Demographics	n	%	n	%	p-value	n	%	n	%	p-value	n	%	n	%	p-value
Race / Ethnicity															
White, non-latino	290	79.5%	389	75.2%		1402	73.4%	1682	72.8%		627	65.8%	1064	46.8%	
White, latino	43	11.8%	62	12.0%		239	12.5%	329	14.2%		237	24.9%	759	33.4%	
Black	19	5.2%	41	7.9%	0.097	223	11.7%	246	10.6%	0.249	23	2.4%	106	4.7%	<0.001**
Asian	6	1.6%	20	3.9%		36	1.9%	47	2.0%		37	3.9%	317	13.9%	
Other	7	1.9%	5	1.0%		10	0.5%	6	0.3%		29	3.0%	27	1.2%	
Sex															
Male	267	73.2%	364	70.4%	0.374	1265	65.9%	1525	66.0%	0.884	647	67.9%	1538	67.7%	0.9
Female	98	26.8%	153	29.6%		645	33.6%	785	34.0%		306	32.1%	735	32.3%	
Ability to Pay for Care															
Insurance Status															
Private insurance	194	53.2%	252	48.7%		1141	59.7%	1221	52.9%		566	59.4%	1221	53.7%	
Medicare	108	29.6%	151	29.2%	0.35	516	27.0%	676	29.3%	<0.001**	227	23.8%	578	25.4%	<0.001**
Medicaid	54	14.8%	98	19.0%		143	7.5%	378	16.4%		124	13.0%	452	19.9%	
Other	9	2.5%	6	1.2%		110	5.8%	35	1.5%		36	3.8%	22	1.0%	
Education															
Less than High School/GED	20	5.5%	46	8.9%		95	5.0%	76	3.3%		75	7.9%	242	10.6%	
High School / GED	183	50.1%	205	39.7%		753	39.4%	817	35.4%		378	39.7%	842	37.0%	
Some college or technical school	56	15.3%	100	19.3%	0.036*	423	22.1%	579	25.1%	0.001*	238	25.0%	592	26.0%	<0.001**
Associate or bachelors degree	64	17.5%	92	17.8%		308	16.1%	431	18.7%		165	17.3%	321	14.1%	
Post-college graduate degree	21	5.8%	38	7.4%		129	6.8%	153	6.6%		66	6.9%	135	5.9%	
Unknown	21	5.8%	36	7.0%		202	10.6%	254	11.0%		31	3.3%	141	6.2%	
Medical Condition / Disability at Transplant															
Medical Comorbidities															
Chronic obstructive pulmonary disease	16	4.4%	17	3.3%	0.309	22	1.2%	42	1.8%	0.484	13	1.4%	27	1.2%	0.325
Diabetes	116	31.8%	132	25.5%	0.042*	617	32.3%	567	24.5%	<0.001**	233	24.4%	597	26.3%	0.247
Hypertension	95	26.0%	135	26.1%	0.614	478	25.0%	724	31.3%	0.257	216	22.7%	277	12.2%	0.051*
Renal failure	73	20.0%	57	11.0%	<0.001**	166	8.7%	232	10.0%	0.549	230	24.1%	705	31.0%	0.001*
Vascular disease	5	1.4%	16	3.1%	0.136	29	1.5%	42	1.8%	0.646	14	1.5%	17	0.7%	0.568
Liver Disease Etiology															
Acute liver failure	4	1.1%	10	1.9%		25	1.3%	54	2.3%		9	0.9%	19	0.8%	
Autoimmune hepatitis	8	2.2%	8	1.5%		53	2.8%	80	3.5%		15	1.6%	34	1.5%	
Cholestatic liver disease	18	4.9%	19	3.7%		140	7.3%	154	6.7%		60	6.3%	116	5.1%	
Cryptogenic cirrhosis	13	3.6%	25	4.8%		131	6.9%	116	5.0%		40	4.2%	80	3.5%	
Genetic/metabolic	11	3.0%	6	1.2%	0.037*	44	2.3%	44	1.9%	0.006*	17	1.8%	27	1.2%	0.003*
Hepatitis C	73	20.0%	75	14.5%		433	22.7%	460	19.9%		180	18.9%	392	17.2%	
Malignancy	138	37.8%	185	35.8%		497	26.0%	639	27.7%		346	36.3%	1021	44.9%	
Steatohepatitis (NASH/Alcoholic Hep)	95	26.0%	179	34.6%		527	27.6%	680	29.4%		258	27.1%	511	22.5%	
Other	5	1.4%	10	1.9%		60	3.1%	83	3.6%		28	2.9%	73	3.2%	
MELD Point Trends															
Approved for MELD Exception Points	132	36.2%	168	32.5%	0.257	444	23.3%	561	24.3%	0.43	317	33.3%	935	41.1%	<0.001**
Allocation MELD Score ≥30	182	49.9%	224	43.3%	0.055	388	20.3%	478	20.7%	0.762	511	53.6%	1676	73.7%	<0.001**
Allocation MELD Score ≥35	93	25.5%	113	21.9%	0.21	229	12.0%	284	12.3%	0.763	324	34.0%	1032	45.4%	<0.001**
Disease Acuity at Transplant															
Ventilator Dependence	10	2.7%	24	4.6%	0.148	51	2.7%	58	2.5%	0.754	66	6.9%	206	9.1%	0.046*
Dialysis Dependence	73	20.0%	54	10.4%	<0.001**	166	8.7%	213	9.2%	0.549	230	24.1%	685	30.1%	0.001*
Life support measures	16	4.4%	29	5.6%	0.415	90	4.7%	76	3.3%	0.018*	99	10.4%	423	18.6%	<0.001**
Location at time of Transplant															
Intensive Care Unit	38	10.4%	63	12.2%		165	8.6%	196	8.5%		181	19.0%	617	27.1%	
Hospitalized, ward bed	84	23.0%	123	23.8%	0.651	336	17.6%	421	18.2%	0.863	218	22.9%	480	21.1%	<0.001**
Not Hospitalized	243	66.6%	331	64.0%		1409	73.8%	1693	73.3%		554	58.1%	1176	51.7%	
Mortality After Transplant															
Death within transplant admission or 30d of discharge	27	7.4%	27	5.2%	0.185	83	4.3%	68	2.9%	0.015*	41	4.3%	110	4.8%	0.51
Death within 90 days of transplant	26	7.1%	32	6.2%	0.582	100	5.2%	83	3.6%	0.009*	39	4.1%	112	4.9%	0.306
Continuous Variables															
Patient Demographics															
Age (years)															
mean, p-value for difference	56.052		56.366		0.603	55.464		56.012		0.0641	55.160		56.599		<0.001**
Disease Severity at Listing															
Physiologic MELD at Listing mean, p-value for difference	18.153		17.538		0.35	18.993		19.062		0.7828	19.435		18.837		0.1462
Allocation MELD at Listing mean, p-value for difference	20.841		19.859		0.1076	20.162		20.282		0.6093	20.828		20.575		0.5262
Karnofsky Score at Listing mean, p-value for difference	64.027		66.459		0.1443	59.286		62.344		<0.001**	62.707		60.195		0.013*
Disease Severity at Transplant															
Physiologic MELD at Transplant mean, p-value for difference	22.279		20.219		0.006*	21.463		21.226		0.384	24.987		24.521		0.3143
Allocation MELD at Transplant mean, p-value for difference	29.186		27.611		<0.001**	24.754		24.974		0.2833	30.895		33.194		<0.001**
Karnofsky Score at Transplant mean, p-value for difference	56.814		52.398		0.007*	51.821		57.328		<0.001**	50.032		44.036		<0.001**

	Region 8 n = 1667					Region 9 n = 1129				
	Region 8 n = 1541		Region 8 UC n = 126			Region 9 n = 199		Region 9 UC n = 930		
Categorical Variables										
Patient Demographics	n	%	n	%	p-value	n	%	n	%	p-value
Race / Ethnicity										
White, non-latino	1257	81.6%	111	88.1%		130	65.3%	493	53.0%	
White, latino	140	9.1%	7	5.6%		34	17.1%	206	22.2%	
Black	86	5.6%	5	4.0%	<0.001**	18	9.0%	113	12.2%	0.031 *
Asian	41	2.7%	3	2.4%		17	8.5%	114	12.3%	
Other	17	1.1%	0	0.0%		0	0.0%	4	0.4%	
Sex										
Male	1067	69.2%	86	68.3%	0.818	151	75.9%	629	67.6%	0.022
Female	474	30.8%	40	31.7%		48	24.1%	301	32.4%	
Ability to Pay for Care										
Insurance Status										
Private insurance	879	57.0%	73	57.9%		123	61.8%	434	46.7%	
Medicare	415	26.9%	24	19.0%	0.008 *	56	28.1%	256	27.5%	<0.001 **
Medicaid	225	14.6%	23	18.3%		20	10.1%	223	24.0%	
Other	22	1.4%	6	4.8%		0	0.0%	17	1.8%	
Education										
Less than High School/GED	58	3.8%	2	1.6%		8	4.0%	106	11.4%	
High School / GED	660	42.8%	72	57.1%		59	29.6%	406	43.7%	
Some college or technical school	359	23.3%	23	18.3%	0.036 *	53	26.6%	184	19.8%	<0.001 **
Associate or bachelors degree	266	17.3%	17	13.5%		39	19.6%	127	13.7%	
Post-college graduate degree	89	5.8%	84	66.7%		32	16.1%	68	7.3%	
Unknown	109	7.1%	4	3.2%		8	4.0%	39	4.2%	
Medical Condition / Disability at Transplant										
Medical Comorbidities										
Chronic obstructive pulmonary disease	29	1.9%	5	4.0%	<0.001 **	4	2.0%	30	3.2%	0.322
Diabetes	357	23.2%	30	23.8%	0.882	62	31.2%	282	30.3%	0.798
Hypertension	258	16.7%	22	17.5%	<0.001 **	56	28.1%	307	33.0%	0.16
Renal failure	165	10.7%	9	7.1%	0.034	17	8.5%	95	10.2%	0.501
Vascular disease	7	0.5%	2	1.6%	0.028 *	7	3.5%	36	3.9%	0.748
Liver Disease Etiology										
Acute liver failure	19	1.2%	3	2.4%		1	0.5%	11	1.2%	
Autoimmune hepatitis	34	2.2%	5	4.0%		5	2.5%	12	1.3%	
Cholestatic liver disease	144	9.3%	8	6.3%		24	12.1%	72	7.7%	
Cryptogenic cirrhosis	77	5.0%	3	2.4%		10	5.0%	31	3.3%	
Genetic/metabolic	55	3.6%	5	4.0%	0.061	5	2.5%	15	1.6%	0.206
Hepatitis C	257	16.7%	16	12.7%		30	15.1%	150	16.1%	
Malignancy	528	34.3%	35	27.8%		80	40.2%	450	48.4%	
Steatohepatitis (NASH/Alcoholic Hep)	391	25.4%	46	36.5%		34	17.1%	152	16.3%	
Other	36	2.3%	5	4.0%		10	5.0%	37	4.0%	
MELD Point Trends										
Approved for MELD Exception Points	488	31.7%	29	23.0%	0.044 *	72	36.2%	410	44.1%	0.041 *
Allocation MELD Score ≥30	433	28.1%	30	23.8%	0.301	86	43.2%	511	55.0%	0.003
Allocation MELD Score ≥35	216	14.0%	15	11.9%	0.509	44	22.1%	227	24.4%	0.491
Disease Acuity at Transplant										
Ventilator Dependence	16	1.0%	4	3.2%	0.034 *	1	0.5%	13	1.4%	0.3
Dialysis Dependence	165	10.7%	6	4.8%	0.034 *	17	8.5%	94	10.1%	0.501
Life support measures	38	2.5%	8	6.3%	0.011 *	2	1.0%	23	2.5%	0.201
Location at time of Transplant										
Intensive Care Unit	80	5.2%	8	6.3%		8	4.0%	77	8.3%	
Hospitalized, ward bed	339	22.0%	25	19.8%	0.756	42	21.1%	232	24.9%	0.038 *
Not Hospitalized	1122	72.8%	93	73.8%		149	74.9%	621	66.8%	
Mortality After Transplant										
Death within transplant admission or 30d of discharge	57	3.7%	6	4.8%	0.547	14	7.0%	63	6.8%	0.895
Death within 90 days of transplant	63	4.1%	6	4.8%	0.715	18	9.0%	65	7.0%	0.313
Continuous Variables										
Patient Demographics										
Age (years)										
mean, p-value for difference	55.444		54.254		0.1752	56.859		57.104		0.741
Disease Severity at Listing										
Physiologic MELD at Listing										
mean, p-value for difference	17.611		17.262		0.6591	16.273		17.103		0.251
Allocation MELD at Listing										
mean, p-value for difference	19.295		17.357		0.009 *	17.662		18.323		0.349
Karnofsky Score at Listing										
mean, p-value for difference	63.683		58.175		0.008 *	70.000		68.535		0.404
Disease Severity at Transplant										
Physiologic MELD at Transplant										
mean, p-value for difference	21.581		21.865		0.752	20.030		21.369		0.115
Allocation MELD at Transplant										
mean, p-value for difference	26.854		25.119		0.004 *	27.754		29.761		<0.001 **
Karnofsky Score at Transplant										
mean, p-value for difference	51.378		45.238		0.004 *	56.984		53.301		0.041 *

3D. Changes in Patient Acuity in Region 1 During Utilization Study Period (2010 – 2014)

Within Region 1, 866 patients underwent liver transplantation during the study period, 666 and 200 patients in the Pre- and Post-Share 35 periods respectively. There are 2 DSAs within this Region 1, yet DSA 1A performs the majority of transplants (DSA 1A performed 93.0% of the transplants over the entire study period, 600 Pre-Share 35 and 186 Post-Share 35).

The mean physiologic MELD at transplant decreased by 2.1 points across the region from 21.58 to 19.48 ($p=0.018$), and a parallel decrease was seen in DSA 1A. There was no change in mean allocation MELD score across the region or within DSAs. The rate of high MELD allocation (defined as an allocation MELD score ≥ 30) increased by 10.4% for the region and 13.7% for DSA 1A ($p=0.001$), but there was no change in the rate of very high MELD allocation (defined as an allocation MELD score ≥ 35) for the region or DSAs. In terms of acuity there was no change in the rate of patients hospitalized or within the ICU at the time of transplant, use of life support measures, ventilator dependence, or hemodialysis dependence at the time of transplant. There was also no difference in mortality within 30 days (or prior to hospital discharge) or 90 days of transplant.

Table 3D – 1. Changes in Acuity within Region 1 by DSA and Share 35 Period.

	Pre-Share 35 (n=666)		Post-Share 35 (n=200)		Delta	
	n	%	n	%	(Post - Pre)	p-value
Rate of Allocation MELD ≥ 30						
Region 1	285	42.8%	112	53.2%	10.4%	0.001 *
DSA 1A	281	45.4%	110	59.1%	13.7%	0.001 *
DSA 1B	4	8.5%	2	14.3%	5.8%	0.524
Rate of Allocation MELD ≥ 35						
Region 1	159	23.9%	45	22.3%	-1.6%	0.688
DSA 1A	159	25.7%	44	23.7%	-2.0%	0.576
DSA 1B	0	0.0%	1	7.1%	7.1%	0.065
Hospitalized immediately prior to transplant						
Region 1	244	36.6%	64	29.6%	7.0%	0.060
DSA 1A	238	38.5%	62	31.2%	7.3%	0.063
DSA 1B	6	12.8%	2	11.8%	1.0%	0.915
Hospitalized within the ICU immediately prior to transplant						
Region 1	86	12.9%	15	6.9%	6.0%	0.017 *
DSA 1A	86	13.9%	15	7.5%	6.4%	0.018 *
DSA 1B	0	0.0%	0	0.0%	0.0%	--
Hemodialysis Dependent at transplant						
Region 1	103	42.8%	21	53.2%	10.4%	0.079
DSA 1A	100	16.2%	20	10.8%	-5.4%	0.070
DSA 1B	3	6.4%	1	7.1%	0.8%	0.920
Ventilator Dependent at Transplant						
Region 1	28	23.9%	6	22.3%	-1.6%	0.442
DSA 1A	28	4.5%	6	3.2%	-1.3%	0.440
DSA 1B	0	0.0%	0	0.0%	0.0%	--
Requiring life support at transplant						
Region 1	36	23.9%	7	22.3%	-1.6%	0.277
DSA 1A	36	5.8%	7	3.8%	-2.1%	0.275
DSA 1B	0	0.0%	0	0.0%	0.0%	--
Death within transplant admission or 30 days of discharge						
Region 1	40	6.0%	14	6.5%	0.5%	0.800
DSA 1A	35	5.7%	14	7.0%	1.3%	0.475
DSA 1B	5	10.6%	0	0.0%	-10.6%	0.161
Death within 90 days of transplant						
Region 1	44	6.6%	14	6.5%	0.1%	0.949
DSA 1A	38	6.1%	14	7.0%	1.1%	0.652
DSA 1B	6	12.8%	0	0.0%	-12.8%	0.122
	mean		mean		Mean Difference (Post - Pre)	p-value
Physiologic MELD at transplant						
Region 1	21.584		19.480		-2.10	0.018 *
DSA 1A	21.703		19.683		-2.020	0.032 *
DSA 1B	20.021		16.786		-3.236	0.160
Allocation MELD at transplant						
Region 1	27.85		28.71		0.86	0.2079
DSA 1A	28.270		28.995		0.72	0.3108
DSA 1B	22.340		24.929		2.59	0.0726

Statistical significance by chi-squared for binary outcomes and by t-tests for continuous outcomes. DSA numbers are randomly assigned. * p<0.05, ** p<0.001. Abbreviations: DSA - Donor Service Area, MELD - Model for End Stage Liver Disease, ICU - intensive care unit.

3E. Changes in Patient Acuity in Region 3 During Utilization Study Period (2010 – 2014)

Within Region 3, 4,147 patients underwent liver transplantation during the study period, 3,130 Pre-Share 35 and 1,017 Post-Share 35. There are 10 DSAs within Region 3, there are 3 larger DSAs (3E, 3H, and 3I), each conducting approximately 20% of the transplants, 3 medium DSAs (3A, 3C, and 3D) which each conduct approximately 10% of the transplants, and 4 smaller DSAs (3B, 3F, 3G, and 3J) which each conduct <10% of the transplants.

There was a mean increase in both the mean physiologic and allocation MELD scores for the Region, such that the physiologic score increased by 0.66 points ($p = 0.04$) and the allocation score increased by 1.74 points ($p<0.001$). Increases in the physiologic score were seen in DSAs 3C and 3H, by 1.86 and 0.62 points respectively, and increases in allocation score were see in DSAs 3A, 3C, 3G, 3H, 3I, by 2.75, 3.84, 3.39, 2.70, and 3.05 respectively. The rate of high MELD allocation increased in the region by 7.4% ($p<0.001$) from 18.6% to 26.0%, attributed to increases in DSAs 3C (11.4%, $p=0.002$), 3G (21.5%, $p=0.002$), 3H (15.6%, $p<0.001$), and 3I (10.7%, $p=0.003$). There was also a significant increase in very high MELD allocation by 12.0% ($p<0.001$) from 10.4% to 16.8%, which is attributed to significant increases in DSAs 3A (10.9%, $p=0.011$), 3C (12.4%, $p<0.001$), 3G (13.0%, $p=0.012$), and 3H (9.7%, $p<0.001$). In terms of acuity, there was a significant increase in the rate of patients hospitalized within the ICU or hospitalized not in the ICU (and a subsequent decrease in patients not hospitalized) within the region. DSAs 3C, 3F and 3H also demonstrated significant increases such that the increase in patients hospitalized within the ICU prior to transplant increased by 9.3% ($p=0.001$), 14.6% ($p=0.04$), and 7.1% ($p=0.001$) respectively. Increases were also seen in the use of life support measures at the time of transplantation across the region, with a regional increase of 6.4% ($p<0.001$), and DSA increases of 5.4% in 3C ($p<0.001$), 3.4% in 3D ($p=0.020$), 6.3% in 3G ($p=0.028$) and 5.6% in 3H ($p=0.001$). Similar increases in ventilator dependence were seen

across the region with a regional increase of 2.3% (p<0.001), and DSA increases of 5.4% in 3C (p<0.001), 6.3% in 3G (p=0.028) and 4.1% in 3H. As well a minor increase was seen in the rate of hemodialysis dependence by 2.7% for the region (p=0.009), and within DSA 3H by 9.3% (p<0.001). There was also no difference in mortality either within 30 days (or prior to hospital discharge) or 90 days of transplant between the Pre- and Post-Share 35 periods.

Table 3E – 1. Changes in Acuity within Region 3 by DSA and Share 35 Period.

	Pre-Share 35 n = 3,130		Post-Share 35 n = 1,017		Delta	
	n	%	n	%	(Post - Pre)	p-value
Rate of Allocation MELD ≥ 30						
Region 3	581	18.6%	264	26.0%	7.4%	<0.001 **
DSA 3A	47	14.2%	14	23.0%	8.7%	0.085
DSA 3B	1	20.0%	3	12.0%	-8.0%	0.631
DSA 3C	43	11.4%	27	22.9%	11.4%	0.002 *
DSA 3D	70	20.5%	19	20.4%	-0.1%	0.983
DSA 3E	123	22.2%	46	21.9%	-0.3%	0.930
DSA 3F	60	24.9%	13	31.0%	6.1%	0.408
DSA 3G	5	6.6%	9	28.1%	21.5%	0.002 *
DSA 3H	115	19.4%	78	35.0%	15.6%	<0.001 **
DSA 3I	116	19.8%	53	30.5%	10.7%	0.003 *
DSA 3J	1	3.8%	2	5.1%	1.3%	0.809
Rate of Allocation MELD ≥ 35						
Region 3	327	10.4%	171	16.8%	6.4%	<0.001 **
DSA 3A	29	8.8%	12	19.7%	10.9%	0.011 *
DSA 3B	1	20.0%	3	12.0%	-8.0%	0.631
DSA 3C	17	4.5%	20	16.9%	12.4%	<0.001 **
DSA 3D	39	11.4%	14	15.1%	3.6%	0.345
DSA 3E	68	12.3%	31	14.8%	2.5%	0.361
DSA 3F	38	15.8%	10	23.8%	8.0%	0.200
DSA 3G	2	2.6%	5	15.6%	13.0%	0.012 *
DSA 3H	62	10.4%	45	20.2%	9.7%	<0.001 **
DSA 3I	71	12.1%	30	17.2%	5.1%	0.079
DSA 3J	0	0.0%	1	2.6%	2.6%	0.411
Hospitalized immediately prior to transplant						
Region 1	794	25.4%	324	29.7%	4.4%	0.005 *
DSA 3A	59	17.9%	19	29.2%	11.4%	0.036 *
DSA 3B	2	40.0%	4	16.0%	-24.0%	0.221
DSA 3C	75	20.0%	38	30.4%	10.5%	0.015 *
DSA 3D	94	27.6%	27	27.3%	-0.3%	0.954
DSA 3E	179	32.3%	60	27.3%	-5.0%	0.171
DSA 3F	87	36.1%	23	47.9%	11.8%	0.124
DSA 3G	4	5.3%	5	14.3%	9.0%	0.106
DSA 3H	169	28.5%	96	40.0%	11.6%	0.001 *
DSA 3I	120	20.4%	47	24.7%	4.3%	0.210
DSA 3J	5	19.2%	5	11.6%	-7.6%	0.385
Hospitalized within the ICU immediately prior to transplant						
Region 3	236	7.5%	125	11.5%	3.9%	<0.001 **
DSA 3A	25	7.6%	12	18.5%	10.9%	0.006 *

DSA 3B	1	20.0%	0	0.0%	-20.0%	0.023 *
DSA 3C	13	3.5%	17	13.6%	10.1%	<0.001 **
DSA 3D	22	6.5%	10	10.1%	3.7%	0.218
DSA 3E	64	11.6%	22	10.0%	-1.6%	0.535
DSA 3F	28	11.6%	14	29.2%	17.6%	0.002 *
DSA 3G	0	0.0%	2	5.7%	5.7%	0.035 *
DSA 3H	35	5.9%	31	12.9%	7.0%	0.001 *
DSA 3I	47	8.0%	16	8.4%	0.4%	0.856
DSA 3J	1	3.9%	1	2.3%	-1.5%	0.715
Hemodialysis Dependent at transplant						
Region 3	260	8.3%	112	11.0%	2.7%	0.009 *
DSA 3A	26	7.9%	7	11.5%	3.6%	0.353
DSA 3B	1	20.0%	3	12.0%	-8.0%	0.631
DSA 3C	19	5.1%	6	5.1%	0.0%	0.989
DSA 3D	16	4.7%	3	3.2%	-1.5%	0.540
DSA 3E	56	10.1%	28	13.3%	3.2%	0.203
DSA 3F	23	9.5%	4	9.5%	0.0%	0.997
DSA 3G	0	0.0%	1	3.1%	3.1%	0.122
DSA 3H	54	9.1%	41	18.4%	9.3%	<0.001 **
DSA 3I	65	11.1%	19	10.9%	-0.2%	0.955
DSA 3J	0	0.0%	0	0.0%	0.0%	--
Ventilator Dependent at Transplant						
Region 3	62	2.0%	44	4.3%	2.3%	<0.001 **
DSA 3A	4	1.2%	1	1.6%	0.4%	0.785
DSA 3B	0	0.0%	0	0.0%	0.0%	--
DSA 3C	2	0.5%	7	5.9%	5.4%	<0.001 **
DSA 3D	3	0.9%	2	2.2%	1.3%	0.309
DSA 3E	17	3.1%	10	4.8%	1.7%	0.258
DSA 3F	10	4.1%	4	9.5%	5.4%	0.138
DSA 3G	0	0.0%	2	6.3%	6.3%	0.028 *
DSA 3H	10	1.7%	13	5.8%	4.1%	0.001 *
DSA 3I	16	2.7%	5	2.9%	0.1%	0.917
DSA 3J	0	0.0%	0	0.0%	0.0%	--
Requiring life support at transplant						
Region 1	96	0.0%	65	6.4%	6.4%	<0.001 **
DSA 3A	4	1.2%	1	1.6%	0.4%	0.785
DSA 3B	0	0.0%	0	0.0%	0.0%	--
DSA 3C	2	0.5%	7	5.9%	5.4%	<0.001 **
DSA 3D	3	0.9%	4	4.3%	3.4%	0.020 *
DSA 3E	41	7.4%	18	8.6%	1.2%	0.588
DSA 3F	10	4.1%	4	9.5%	5.4%	0.138
DSA 3G	0	0.0%	2	6.3%	6.3%	0.028 *
DSA 3H	20	3.4%	20	9.0%	5.6%	0.001 *
DSA 3I	16	2.7%	9	5.2%	2.4%	0.112
DSA 3J	0	0.0%	0	0.0%	0.0%	--
Death within transplant admission or 30 days of discharge						
Region 3	114	3.6%	35	3.4%	-0.2%	0.765
DSA 3A	10	3.0%	2	3.3%	0.2%	0.918
DSA 3B	0	0.0%	0	0.0%	0.0%	--
DSA 3C	13	3.5%	5	4.2%	0.8%	0.693
DSA 3D	19	5.6%	4	4.3%	-1.3%	0.628
DSA 3E	22	4.0%	11	5.2%	1.3%	0.442
DSA 3F	8	3.3%	2	4.8%	1.4%	0.640
DSA 3G	1	1.3%	2	6.3%	4.9%	0.154
DSA 3H	21	3.5%	6	2.7%	-0.8%	0.547
DSA 3I	19	3.2%	3	1.7%	-1.5%	0.296

DSA 3J	1	3.8%	0	0.0%	-3.8%	0.217
Death within 90 days of transplant						
Region 3	141	4.5%	39	3.8%	-0.7%	0.362
DSA 3A	12	3.6%	3	4.9%	1.3%	0.632
DSA 3B	0	0.0%	0	0.0%	0.0%	--
DSA 3C	15	4.0%	4	3.4%	-0.6%	0.768
DSA 3D	26	7.6%	6	6.5%	-1.2%	0.701
DSA 3E	28	5.1%	12	5.7%	0.7%	0.715
DSA 3F	10	4.1%	3	7.1%	3.0%	0.392
DSA 3G	1	1.3%	2	6.3%	4.9%	0.154
DSA 3H	23	3.9%	6	2.7%	-1.2%	0.416
DSA 3I	25	4.3%	3	1.7%	-2.5%	0.119
DSA 3J	1	3.8%	0	0.0%	-3.8%	0.217
	mean		**mean**		**Mean Difference (Post - Pre)**	**p-value**
Physiologic MELD at transplant						
Region 3	21.159		21.820		0.661	0.038 *
DSA 3A	19.873		19.459		-0.414	0.724
DSA 3B	21.400		17.920		-3.480	0.486
DSA 3C	19.202		21.059		1.857	0.041 *
DSA 3D	22.305		22.441		0.136	0.896
DSA 3E	21.986		21.543		-0.443	0.549
DSA 3F	22.867		24.738		1.871	0.207
DSA 3G	19.711		22.406		2.696	0.077
DSA 3H	21.751		22.371		0.620	<0.001 **
DSA 3I	20.779		21.316		0.537	0.500
DSA 3J	16.538		16.359		-0.179	0.908
Allocation MELD at transplant						
Region 3	24.421		26.164		1.743	<0.001 **
DSA 3A	23.312		26.066		2.754	0.002 *
DSA 3B	22.400		23.440		1.040	0.762
DSA 3C	22.330		26.165		3.835	<0.001 **
DSA 3D	25.161		25.237		0.075	0.919
DSA 3E	24.865		24.805		-0.060	0.913
DSA 3F	25.606		27.357		1.751	0.130
DSA 3G	22.053		25.438		3.385	0.004 *
DSA 3H	25.157		27.852		2.695	<0.001 **
DSA 3I	24.874		27.925		3.051	<0.001 **
DSA 3J	18.808		19.385		0.577	0.645

Statistical significance by chi-squared for binary outcomes and by t-tests for continuous outcomes. DSA numbers are randomly assigned. * p<0.05, ** p<0.001. Abbreviations: DSA - Donor Service Area, MELD - Model for End Stage Liver Disease, ICU - intensive care unit.

3F. Changes in Patient Acuity in Region 5 During Utilization Study Period (2010 – 2014)

There were 3,170 patients who underwent liver transplantation in Region 5 during the study period, 2,410 prior to Share 35, and 760 following implementation of Share 35. Within Region 5 there are 5 DSAs, two large DSAs (5B and 5C) which each complete more than 30% of

the region's transplants, one moderate sized DSA (5D) which makes up 16% and then two smaller DSAs which each complete less than 10% of the region's transplants (DSAs 5A and 5E).

Following Share 35 there was an increase in the mean physiologic and allocation MELD for Region 5, such that the physiologic MELD increased by 1.14 points to 25.5 and the allocation MELD increased by 0.95 points to 33.2 ($p=0.022$ and $p<0.001$, respectively). There was only one DSA that had an associated increase in physiologic MELD (5E, increased by 5.7 points to 27.8), while three DSAs saw an increase in mean allocation MELD (5B by 1.2 points, 5C by 1.1 points and 5E by 3.4 points, all $p<0.05$) and one saw a decrease (5D by 2.0 points, $p=0.006$). There were increases in both the rates of high MELD allocation (4.9%, $p=0.011$) and very high MELD allocation (11.5%, $p<0.001$) at the regional level. Only two DSAs had a significant increase in high MELD allocation (5A by 16.9%, $p=0.036$; 5E by 28.5%, $p<0.001$), while 3 DSAs had a significant increase in very high MELD allocation (5B by 15.3%, $p<0.001$; 5C by 10.0%, $p=0.003$; 5E by 24.9%, $p<0.001$). In terms of acuity, there was a significant increase in the rate of patients in the ICU prior to transplant, such that 31.8% of patients in region 5 were in the ICU in the Post-Share 35 period, up from 22.5% in the Pre-Share 35 period ($p<0.001$). At the DSA level, increases in the rate of ICU location prior to transplant was seen in DSAs 5B, 5C, and 5E by 14.6%, 8.6% and 18.4% respectively (all $p<0.05$). In terms of life support measures at transplant, there was a 3.1% increase in Region 5 ($p=0.045$) with increases only seen within 1 DSA (5E, increase of 7.5%, $p=0.008$). There was no significant change in the rate of ventilator dependence at the regional level, but there was an increase within 2 DSAs, 5B increased by 2.6% to a rate of 3.9% ($p=0.013$), and 5E increased by 6.2% to a rate of 9.2% ($p=0.023$). There was a 6.4% increase in the rate of hemodialysis dependence across the region, again with two DSAs experiencing increases, DSA 5C by 10.7% to a rate of 48.4% ($p=0.001$) and 5E by 20.2% to a

rate of 38.2% (p<0.001). There was also no difference in mortality either within 30 days (or prior to hospital discharge) or 90 days of transplant between the Pre- and Post-Share 35 periods.

Table 3F – 1. Changes in Acuity within Region 5 by DSA and Share 35 Period.

	Pre-Share 35		Post-Share 35		Delta	
	n	%	n	%	(Post - Pre)	p-value
Rate of Allocation MELD ≥ 30						
Region 5	1,603	66.5%	543	71.4%	4.9%	0.011 *
DSA 5A	78	49.1%	33	66.0%	16.9%	0.036 *
DSA 5B	540	72.3%	173	75.9%	3.6%	0.285
DSA 5C	695	78.7%	233	82.3%	3.6%	0.188
DSA 5D	175	45.2%	45	36.6%	-8.6%	0.092
DSA 5E	115	49.1%	59	77.6%	28.5%	<0.001 **
Rate of Allocation MELD ≥ 35						
Region 5	943	39.1%	385	50.7%	11.5%	<0.001 **
DSA 5A	52	32.7%	22	44.0%	11.3%	0.145
DSA 5B	253	33.9%	112	49.1%	15.3%	<0.001 **
DSA 5C	470	53.2%	179	63.3%	10.0%	0.003 *
DSA 5D	100	25.8%	31	25.2%	-0.6%	0.888
DSA 5E	68	29.1%	41	53.9%	24.9%	<0.001 **
Hospitalized immediately prior to transplant						
Region 5	1087	45.1%	409	50.1%	5.0%	0.013 *
DSA 5A	67	42.1%	24	44.4%	2.3%	0.767
DSA 5B	284	38.0%	114	45.6%	7.6%	0.034 *
DSA 5C	513	58.1%	191	63.5%	5.4%	0.102
DSA 5D	144	37.2%	41	30.6%	-6.6%	0.168
DSA 5E	79	33.8%	39	50.7%	16.9%	0.008 *
Hospitalized within the ICU immediately prior to transplant						
Region 5	542	22.5%	256	31.4%	8.9%	<0.001 **
DSA 5A	32	20.1%	15	27.8%	7.7%	0.241
DSA 5B	114	15.3%	71	28.4%	13.1%	<0.001 **
DSA 5C	311	35.2%	132	43.9%	8.6%	0.008 *
DSA 5D	48	12.4%	12	9.0%	-3.4%	0.281
DSA 5E	37	15.8%	26	33.8%	18.0%	0.001 *
Hemodialysis Dependent at transplant						
Region 5	645	26.8%	252	33.2%	6.4%	0.001 *
DSA 5A	37	23.3%	12	24.0%	0.7%	0.915
DSA 5B	157	21.0%	54	23.7%	2.7%	0.392
DSA 5C	333	37.7%	137	48.4%	10.7%	0.001 *
DSA 5D	76	19.6%	20	16.3%	-3.4%	0.404
DSA 5E	42	17.9%	29	38.2%	20.2%	<0.001 **
Ventilator Dependent at Transplant						
Region 5	193	8.0%	75	9.9%	1.9%	0.108
DSA 5A	12	7.5%	5	10.0%	2.5%	0.580
DSA 5B	10	1.3%	9	3.9%	2.6%	0.013 *
DSA 5C	143	16.2%	51	18.0%	1.8%	0.473
DSA 5D	21	5.4%	3	2.4%	-3.0%	0.173
DSA 5E	7	3.0%	7	9.2%	6.2%	0.023 *
Requiring life support at transplant						
Region 5	370	15.4%	140	18.4%	3.1%	0.045 *
DSA 5A	12	7.5%	5	10.0%	2.5%	0.580
DSA 5B	40	5.4%	18	7.9%	2.5%	0.156
DSA 5C	289	32.7%	106	37.5%	4.7%	0.144

DSA 5D	22	5.7%	3	2.4%	-3.2%	0.146
DSA 5E	7	3.0%	8	10.5%	7.5%	0.008 *
Death within transplant admission or 30 days of discharge						
Region 5	115	4.8%	35	4.6%	-0.2%	0.850
DSA 5A	6	3.8%	2	4.0%	0.2%	0.942
DSA 5B	20	2.7%	4	1.8%	-0.9%	0.431
DSA 5C	66	7.5%	19	6.7%	-0.8%	0.668
DSA 5D	16	4.1%	5	4.1%	-0.1%	0.973
DSA 5E	7	3.0%	5	6.6%	3.6%	0.159
Death within 90 days of transplant						
Region 5	118	4.9%	30	3.9%	-0.9%	0.280
DSA 5A	5	3.1%	2	4.0%	0.9%	0.769
DSA 5B	24	3.2%	6	2.6%	-0.6%	0.656
DSA 5C	63	7.1%	14	4.9%	-2.2%	0.197
DSA 5D	18	4.7%	4	3.3%	-1.4%	0.506
DSA 5E	8	3.4%	4	5.3%	1.8%	0.469
	mean		**mean**		**Mean Diff. (Post - Pre)**	**p-value**
Physiologic MELD at transplant						
Region 5	24.360		25.501		1.142	0.022 *
DSA 5A	24.868		26.320		1.452	0.377
DSA 5B	22.533		23.930		1.397	0.124
DSA 5C	26.374		27.329		0.955	0.265
DSA 5D	24.432		22.431		-2.001	0.083
DSA 5E	22.128		27.842		5.714	<0.001 **
Allocation MELD at transplant						
Region 5	32.263		33.217		0.954	<0.001 **
DSA 5A	29.906		32.260		2.354	0.0556
DSA 5B	32.174		33.377		1.203	0.012 *
DSA 5C	34.300		35.424		1.124	0.003 *
DSA 5D	30.163		28.171		-1.992	0.006 *
DSA 5E	29.932		33.316		3.384	<0.001 **

Statistical significance by chi-squared for binary outcomes and by t-tests for continuous outcomes. DSA numbers are randomly assigned. * p<0.05, ** p<0.001. Abbreviations: DSA - Donor Service Area, MELD - Model for End Stage Liver Disease, ICU - intensive care unit, Mean Diff. – Mean difference.

3G. Changes in Patient Acuity in Region 8 During Utilization Study Period (2010 – 2014)

Within Region 8, 1,635 patients underwent transplantation during the study period, 1,254 Pre-Share 35 and 381 Post-Share 35. There are 5 DSAs within Region 8, 4 larger DSAs which each account for 17-29% of the region's transplants, and 1 smaller DSA which accounts for 8.5% of the region's transplants.

There were no regional level differences in either mean physiologic or allocation MELD score at transplant, yet DSA 5D did have a significant decrease in allocation MELD score by 3.4 points to a mean of 23.0 (p<0.001). There was no regional increase in the rate of high MELD

allocation, by DSA 8A was a 13.7% increase (p=0.026) and DSA 8D saw a decrease by 19.0% (p=0.003). Alternatively, there was a significant increase in the rate of very high MELD allocation by 6.4% to a rate of 18.6% for Region 8 (p=0.001), increases were also seen in 3 of the 5 DSAs, 8A increased by 17.8% to 30.9% (p<0.001), 8C increased by 7.7% to a rate of 17.1% (p=0.039) and 8E increased by 13.3% to a rate of 22.6% (p=0.046). There was a regional decrease in the rate of life support measures at the time of transplant, by 2.3% (p=0.017), which is attributable to decrease in DSA 8C by 3.9% (p=0.040). There were no significant changes in the rate of location prior to transplantation (ICU, hospitalized or not hospitalized), ventilator or hemodialysis dependence at transplant. There was a decrease in morality within in 90 days of transplant of 2.4% at the regional level (p=0.039), but not decrease at 30 days or within the hospital admission.

Table 3G – 1. Changes in Acuity within Region 8 by DSA and Share 35 Period.

	Pre-Share 35		Post-Share 35		Delta	
	n	%	n	%	(Post - Pre)	p-value
Rate of Allocation MELD ≥ 30						
Region 8	344	27.4%	109	28.6%	1.2%	0.653
DSA 8A	98	35.6%	40	49.4%	13.7%	0.026 *
DSA 8B	105	28.2%	28	26.7%	-1.6%	0.753
DSA 8C	48	17.0%	27	25.7%	8.7%	0.054
DSA 8D	67	30.9%	7	11.9%	-19.0%	0.003 *
DSA 8E	26	24.1%	7	22.6%	-1.5%	0.863
Rate of Allocation MELD ≥ 35						
Region 8	153	12.2%	71	18.6%	6.4%	0.001 *
DSA 8A	36	13.1%	25	30.9%	17.8%	<0.001 **
DSA 8B	48	12.9%	16	15.2%	2.3%	0.535
DSA 8C	27	9.6%	18	17.1%	7.6%	0.039 *
DSA 8D	32	14.7%	5	8.5%	-6.3%	0.210
DSA 8E	10	9.3%	7	22.6%	13.3%	0.046 *
Hospitalized immediately prior to transplant						
Region 8	342	27.3%	110	26.6%	-0.6%	0.800
DSA 8A	78	28.4%	35	40.2%	11.9%	0.037 *
DSA 8B	110	29.6%	28	24.4%	-5.2%	0.277
DSA 8C	64	22.7%	25	22.1%	-0.6%	0.902
DSA 8D	70	32.3%	14	21.9%	-10.4%	0.111
DSA 8E	20	18.5%	8	23.5%	5.0%	0.522
Hospitalized within the ICU immediately prior to transplant						
Region 8	65	5.2%	23	5.6%	0.4%	0.761
DSA 8A	10	3.6%	4	4.6%	1.0%	0.685
DSA 8B	17	4.6%	6	5.2%	0.7%	0.775
DSA 8C	16	5.7%	7	6.2%	0.5%	0.842
DSA 8D	15	6.9%	2	3.1%	-3.8%	0.264
DSA 8E	7	6.5%	4	11.8%	5.3%	0.315
Hemodialysis Dependent at transplant						
Region 8	128	10.2%	40	10.5%	0.3%	0.870
DSA 8A	30	10.9%	9	11.1%	0.2%	0.959
DSA 8B	41	11.0%	10	9.5%	-1.5%	0.661
DSA 8C	34	12.1%	15	14.3%	2.2%	0.558
DSA 8D	15	6.9%	2	3.4%	-3.5%	0.318
DSA 8E	8	7.4%	4	12.9%	5.5%	0.337
Ventilator Dependent at Transplant						
Region 8	17	1.4%	3	0.8%	-0.6%	0.377
DSA 8A	0	0.0%	0	0.0%	0.0%	--
DSA 8B	6	1.6%	1	1.0%	-0.7%	0.619
DSA 8C	0	0.0%	0	0.0%	0.0%	--
DSA 8D	10	4.6%	1	1.7%	-2.9%	0.310
DSA 8E	1	0.9%	1	3.2%	2.3%	0.343
Requiring life support at transplant						
Region 8	42	3.3%	4	1.0%	-2.3%	0.017 *
DSA 8A	0	0.0%	0	0.0%	0.0%	--
DSA 8B	8	2.2%	1	1.0%	-1.2%	0.426
DSA 8C	11	3.9%	0	0.0%	-3.9%	0.040 *
DSA 8D	22	10.1%	2	3.4%	-6.7%	0.103
DSA 8E	1	0.9%	1	3.2%	2.3%	0.343
Death within transplant admission or 30 days of discharge						
Region 8	54	4.3%	9	2.4%	-1.9%	0.084
DSA 8A	10	3.6%	2	2.5%	-1.2%	0.609

DSA 8B	17	4.6%	3	2.9%	-1.7%	0.439
DSA 8C	7	2.5%	2	1.9%	-0.6%	0.737
DSA 8D	17	7.8%	2	3.4%	-4.4%	0.232
DSA 8E	3	2.8%	0	0.0%	-2.8%	0.348
Death within 90 days of transplant						
Region 8	60	4.8%	9	2.4%	-2.4%	0.039 *
DSA 8A	13	4.7%	2	2.5%	-2.3%	0.374
DSA 8B	15	4.0%	2	1.9%	-2.1%	0.299
DSA 8C	10	3.5%	3	2.9%	-0.7%	0.738
DSA 8D	17	7.8%	2	3.4%	-4.4%	0.232
DSA 8E	5	4.6%	0	0.0%	-4.6%	0.222
	mean		**mean**		**Mean Diff. (Post - Pre)**	**p-value**
Physiologic MELD at transplant						
Region 8	21.458		21.845		0.387	0.494
DSA 8A	21.215		24.593		3.378	0.009 *
DSA 8B	21.626		21.105		-0.522	0.637
DSA 8C	20.418		22.019		1.601	0.130
DSA 8D	23.101		18.932		-4.169	0.002 *
DSA 8E	20.907		22.129		1.222	0.505
Allocation MELD at transplant						
Region 8	26.746		26.596		-0.150	0.6918
DSA 8A	29.011		29.901		0.890	0.2119
DSA 8B	27.376		27.400		0.024	0.9713
DSA 8C	24.904		25.886		0.981	0.1891
DSA 8D	26.295		23.017		-3.278	<0.001 **
DSA 8E	24.519		24.452		-0.067	0.9629

Statistical significance by chi-squared for binary outcomes and by t-tests for continuous outcomes. DSA numbers are randomly assigned. * p<0.05, ** p<0.001. Abbreviations: DSA - Donor Service Area, MELD - Model for End Stage Liver Disease, ICU - intensive care unit, Mean Diff. – mean difference.

3H. Changes in Patient Acuity in Region 9 During Utilization Study Period (2010 – 2014)

A total of 1,107 patients underwent liver transplantation in Region 9 during the study period, 847 prior to Share 35 and 260 after Share 35 implementation. There are 2 DSAs within Region 9, DSA 9A contains the majority of transplants (88.1%), while DSA 9B only completes a minority (12.0%).

There were no significant changes in the physiologic MELD score at transplant at the regional or DSA level, but there was a significant increase in the mean allocation MELD score, increasing by 1.4 points to 30.4 (p=0.008). This difference is attributable to the increase in allocation MELD score by 1.7 points in DSA 9A (p=0.002). There was an increase in the rate of high MELD allocation across the region (increased by 11.8% to 61.5%, p=0.001) and within

DSA 9A (increased by 13.7% to 59.1%, $p<0.001$). There was no regional increase in the rate of very high MELD allocation at the regional level, but an increase of 6.4% to 25.7% was seen in region 9A ($p=0.037$). There was no difference in patient location at the time of transplant, life support measures prior to transplantation, ventilator or hemodialysis dependence at transplant between the Pre- and Post-Share 35 periods at the regional or DSA level. There was also no difference in mortality either within 30 days (or prior to hospital discharge) or 90 days of transplant between the Pre- and Post-Share 35 periods.

Table 3H – 1. Changes in Acuity within Region 9 by DSA and Share 35 Period.

	Pre-Share 35		Post-Share 35		Delta	
	n	%	n	%	(Post - Pre)	p-value
Rate of Allocation MELD ≥ 30						
Region 9	421	49.7%	160	61.5%	11.8%	0.001 *
DSA 9A	335	45.4%	140	59.1%	13.7%	<0.001 **
DSA 9B	86	78.2%	20	87.0%	8.8%	0.341
Rate of Allocation MELD ≥ 35						
Region 9	192	22.7%	72	27.7%	5.0%	0.096
DSA 9A	143	19.4%	61	25.7%	6.4%	0.037 *
DSA 9B	49	44.5%	11	47.8%	3.3%	0.774
Hospitalized immediately prior to transplant						
Region 9	267	31.5%	92	32.7%	1.3%	0.696
DSA 9A	208	28.2%	80	31.1%	3.0%	0.370
DSA 9B	59	53.6%	12	50.0%	-3.6%	0.746
Hospitalized within the ICU immediately prior to transplant						
Region 9	57	6.7%	28	10.0%	3.2%	0.074
DSA 9A	42	5.7%	23	9.0%	3.3%	0.069
DSA 9B	15	13.6%	5	20.8%	7.2%	0.370
Hemodialysis Dependent at transplant						
Region 9	84	9.9%	24	9.2%	-0.7%	0.744
DSA 9A	69	9.3%	20	8.4%	-0.9%	0.668
DSA 9B	15	13.6%	4	17.4%	3.8%	0.640
Ventilator Dependent at Transplant						
Region 9	13	1.5%	1	0.4%	-1.2%	0.147
DSA 9A	12	1.6%	1	0.4%	-1.2%	0.159
DSA 9B	1	0.9%	0	0.0%	-0.9%	0.646
Requiring life support at transplant						
Region 9	24	2.8%	1	0.4%	-2.4%	0.372
DSA 9A	20	2.7%	4	1.7%	-1.0%	0.375
DSA 9B	1	0.9%	0	0.0%	-0.9%	0.646
Death within transplant admission or 30 days of discharge						
Region 9	64	7.6%	260	12	-2.9%	0.101
DSA 9A	50	6.8%	237	12	-1.7%	0.345
DSA 9B	14	12.7%	23	0	-12.7%	0.070
Death within 90 days of transplant						
Region 9	70	8.3%	13	5.0%	-3.3%	0.080
DSA 9A	55	7.5%	13	5.5%	-2.0%	0.299
DSA 9B	15	13.6%	0	0.0%	-13.6%	0.060
	mean		mean		Mean Diff. (Post - Pre)	p-value
Physiologic MELD at transplant						
Region 9	21.131		20.885		-0.246	0.749
DSA 9A	20.237		20.494		0.256	0.746
DSA 9B	27.118		24.913		-2.205	0.381
Allocation MELD at transplant						
Region 9	29.072		30.431		1.359	0.008 *
DSA 9A	28.465		30.148		1.682	0.002 *
DSA 9B	33.136		33.348		0.211	0.8652

Statistical significance by chi-squared for binary outcomes and by t-tests for continuous outcomes. DSA numbers are randomly assigned. * p<0.05, ** p<0.001. Abbreviations: DSA - Donor Service Area, MELD - Model for End Stage Liver Disease, ICU - intensive care unit, Mean Diff. – mean difference.

4. Question 1 – Additional Tables & Figures

4A. Sensitivity Analysis – Single versus Multiple Imputation

	Admissions Model						Admitted Days Model					
	Imputed			Multiply Imputed			Imputed			Multiply Imputed		
Med. Condition/Disability	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Liver Disease Severity (H1a)												
MELD, physiologic	0.009	0.002	<0.001**	0.007	0.001	<0.001**	0.018	0.002	<0.001**	0.018	0.002	<0.001**
Liver Disease Etiology (H1b)												
Acute liver failure	-0.127	0.072	0.078	-0.087	0.049	0.075	-0.257	0.072	<0.001**	-0.247	0.072	0.001
Autoimmune hepatitis	0.056	0.110	0.614	0.054	0.074	0.467	0.047	0.096	0.622	0.049	0.095	0.610
Cholestatic liver disease	0.094	0.070	0.177	0.074	0.047	0.114	0.074	0.071	0.298	0.075	0.071	0.291
Cryptogenic cirrhosis	0.119	0.076	0.115	0.079	0.055	0.146	0.104	0.085	0.221	0.099	0.085	0.241
Genetic/metabolic	0.030	0.144	0.838	0.023	0.091	0.801	0.185	0.128	0.151	0.173	0.127	0.172
Hepatitis C	0.127	0.044	0.004*	0.094	0.030	0.002*	0.031	0.049	0.528	0.033	0.049	0.501
Malignancy	0.118	0.047	0.011*	0.088	0.031	0.005*	0.032	0.052	0.544	0.037	0.052	0.467
Steatohepatitis	ref.			ref.			ref.			ref.		
Other	-0.072	0.087	0.406	-0.032	0.053	0.544	-0.109	0.083	0.189	-0.095	0.082	0.249
Ability to Pay for Care(H1c)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Insurance Status												
Private insurance	ref.			ref.			ref.			ref.		
Medicare	0.027	0.036	0.456	0.016	0.025	0.519	0.020	0.039	0.605	0.022	0.039	0.571
Medicaid	0.081	0.041	0.047*	0.053	0.028	0.059	0.065	0.046	0.162	0.067	0.046	0.143
Veterans Affairs	-0.090	0.262	0.732	-0.035	0.168	0.834	-0.029	0.227	0.899	-0.009	0.231	0.968
Self-Pay	-0.720	0.296	0.015*	-0.353	0.126	0.005*	-0.172	0.299	0.564	-0.175	0.297	0.556
Other	-0.002	0.162	0.988	-0.007	0.115	0.953	-0.026	0.151	0.861	-0.027	0.149	0.857
Education												
Less than High School/GED	ref.			ref.			ref.			ref.		
High School/GED	0.004	0.059	0.951	0.009	0.040	0.822	-0.071	0.085	0.399	-0.042	0.083	0.617
Some college or tech. school	0.043	0.061	0.482	0.021	0.042	0.610	-0.065	0.090	0.471	-0.029	0.090	0.750
Associate or bachelors degree	-0.020	0.067	0.761	-0.014	0.046	0.764	-0.094	0.094	0.317	-0.048	0.094	0.607
Post-college graduate degree	0.024	0.081	0.763	0.027	0.055	0.628	-0.116	0.100	0.246	-0.053	0.103	0.606
Donor Organ Quality (H1d)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Donor Risk Index	0.123	0.041	0.003*	0.084	0.028	0.002*	0.182	0.045	<0.001**	0.180	0.044	<0.001**

Admissions model by Poisson regression and admitted days model by negative-binomial regression. Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. * p<0.05, **p<0.001.
Abbreviations: Coeff - coefficient, SE - standard error, ref. – reference category, MELD - Model for End Stage Liver Disease, GED - general equivalency diploma.

4B. Transplant Center Volume by Year

	Year				
Center	**2010**	**2011**	**2012**	**2013 (Jan - May)**	**Total**
California					
1	40	41	69	22	172
4	58	58	64	25	205
5	40	37	31	17	125
12	38	48	46	19	151
13	41	39	45	18	143
14	104	120	105	48	377
19	26	31	19	11	87
21	132	155	118	48	453
26	32	20	28	21	101
Florida					
3	80	80	78	30	268
9	21	26	25	7	79
15	83	112	88	33	316
20	77	64	68	30	239
24	28	22	13	12	75
25	79	74	86	31	270
Georgia					
6	71	73	76	36	256
11	83	80	91	41	295
Massachusetts					
2	54	55	43	19	171
16	20	25	16	8	69
17	30	31	26	11	98
28	25	27	16	6	74
Nebraska					
8	27	28	27	14	96
New York					
7	11	19	24	8	62
10	56	69	68	12	205
18	31	30	18	8	87
22	38	41	25	13	117
23	26	12	20	8	66
27	48	63	55	20	186
29	2	6	8	1	17

In order maintain center anonymity, center IDs were randomly generated and do not correspond to assigned identification numbers from UNOS or SRTR. Center volume indicates the number of transplantation done annually is calculated based on the date of transplantation. 2013 includes only those transplants done prior to the implementation of Share 35 (June 1, 2013).

4C. Full Regression Model for Total Number of Admissions

Covariate	Coefficient	SE	p-value	Margins	SE	p-value
MELD, physiologic	0.009	0.002	<0.001 **	0.017	0.004	<0.001 **
Functional status	-0.004	0.001	<0.001 **	-0.007	0.002	0.001 *
Liver Disease Etiology						
Acute Liver Failure	-0.127	0.072	0.078	-0.205	0.112	0.141
Autoimmune Hepatitis	0.056	0.110	0.614	0.098	0.199	0.606
Cholestatic Liver Disease	0.094	0.070	0.177	0.169	0.129	0.074
Cryptogenic Cirrhosis	0.119	0.076	0.115	0.218	0.144	0.164
Genetic/Metabolic	0.030	0.144	0.838	0.052	0.255	0.842
Hepatitis C	0.127	0.044	0.004 *	0.232	0.080	<0.001 **
Malignancy	0.118	0.047	0.011 *	0.216	0.085	0.013 *
Steatohepatitis	reference					
Other	-0.072	0.087	0.406	-0.119	0.140	0.423
Medical Comorbidities						
Hypertension	-0.015	0.034	0.656	-0.027	0.061	0.609
COPD	0.091	0.034	0.007 *	0.170	0.065	<0.001 **
Diabetes	0.075	0.034	0.027 *	0.140	0.064	0.034
Renal failure	0.136	0.036	<0.001 **	0.255	0.069	<0.001 **
Vascular disease	0.077	0.045	0.088	0.145	0.088	0.189
Insurance						
Private	reference					
Medicare	0.027	0.036	0.456	0.049	0.067	0.526
Medicaid	0.081	0.041	0.047 *	0.152	0.078	0.032 *
Veterans Affairs	-0.090	0.262	0.732	-0.154	0.430	0.724
Self-Pay	-0.720	0.296	0.015 *	-0.920	0.261	0.002 *
Other	-0.002	0.162	0.988	-0.004	0.289	0.988
Education						
Less than HS/GED	reference					
High School/GED	0.004	0.059	0.951	0.007	0.106	0.952
Some college or technical school	0.043	0.061	0.482	0.080	0.113	0.527
Associate or bachelors degree	-0.020	0.067	0.761	-0.036	0.120	0.790
Post-college graduate degree	0.024	0.081	0.763	0.045	0.149	0.688
Donor Risk Index	0.123	0.041	0.003 *	0.225	0.075	0.003 *
Race / Ethnicity						
White, non-latino	reference					
White, latino	-0.052	0.042	0.221	-0.096	0.077	0.275
Black	-0.058	0.053	0.272	-0.107	0.096	0.261
Asian	-0.177	0.067	0.009 *	-0.306	0.109	0.002 *
Native American	0.264	0.197	0.181	0.570	0.483	0.166
Other	-0.192	0.173	0.265	-0.330	0.270	0.126

Age (years)	0.004	0.002	0.016 *	0.008	0.003	0.013 *
Sex						
Male	reference					
Female	0.009	0.032	0.791	0.016	0.059	0.809
Hospital density	0.006	0.016	0.728	0.010	0.030	0.743
Primary care density	0.989	0.955	0.300	1.815	1.752	0.268
Specialty care density	0.431	0.669	0.520	0.790	1.228	0.551
Zip code median income						
1st Quartile	reference					
2nd Quartile	-0.065	0.047	0.163	-0.120	0.087	0.069
3rd Quartile	-0.041	0.044	0.352	-0.077	0.083	0.277
4th Quartile	-0.045	0.049	0.358	-0.084	0.092	0.265
Rural / Urban Continuum						
Metropolitan >= 1mill. pop.	reference					
Metropolitan 250,000 - 1 mill. pop.	-0.014	0.047	0.770	-0.025	0.086	0.68
Metropolitan <250,000 pop.	-0.015	0.079	0.849	-0.027	0.143	0.86
Urban >20,000 pop.	0.080	0.117	0.494	0.154	0.233	0.438
Urban 2,500-20,000 pop.	-0.134	0.134	0.319	-0.231	0.218	0.219
Completely rural or <2,500 urban pop.	-0.390	0.308	0.206	-0.595	0.387	0.134
Distance to Transplant Center (minutes)	0.001	0.000	0.111	0.001	0.001	0.080
Transplant Center						
1	reference					
2	-0.102	0.106	0.334	-0.260	0.268	0.059
3	-0.308	0.096	0.001 *	-0.711	0.225	<0.001 **
4	-0.368	0.097	<0.001 **	-0.827	0.222	<0.001 **
5	-0.265	0.112	0.018 *	-0.624	0.260	<0.001 **
6	-0.693	0.108	<0.001 **	-1.341	0.220	<0.001 **
7	-0.122	0.127	0.337	-0.309	0.315	0.020 *
8	-0.871	0.173	<0.001 **	-1.560	0.261	<0.001 **
9	-0.386	0.138	0.005 *	-0.860	0.287	<0.001 **
10	-0.444	0.104	<0.001 **	-0.962	0.231	<0.001 **
11	-0.558	0.107	<0.001 **	-1.147	0.228	<0.001 **
12	-0.445	0.107	<0.001 **	-0.964	0.231	<0.001 **
13	-0.288	0.095	0.002 *	-0.671	0.224	<0.001 **
14	-0.557	0.095	<0.001 **	-1.147	0.210	<0.001 **
15	-0.433	0.103	<0.001 **	-0.942	0.232	<0.001 **
16	0.206	0.109	0.058	0.614	0.330	<0.001 **
17	-0.608	0.152	<0.001 **	-1.222	0.273	<0.001 **
18	-0.505	0.148	0.001 *	-1.065	0.282	<0.001 **
19	-0.282	0.116	0.016 *	-0.659	0.263	<0.001 **
20	-0.022	0.093	0.814	-0.058	0.248	0.618
21	-0.454	0.077	<0.001 **	-0.980	0.189	<0.001 **

22	-0.266	0.110	0.016 *	-0.627	0.257	<0.001 **
23	-0.534	0.152	<0.001 **	-1.110	0.284	<0.001 **
24	-0.782	0.159	<0.001 **	-1.456	0.258	<0.001 **
25	-0.642	0.103	<0.001 **	-1.271	0.218	<0.001 **
26	-0.279	0.132	0.035 *	-0.653	0.296	<0.001 **
27	-0.475	0.114	<0.001 **	-1.014	0.242	<0.001 **
28	-0.101	0.140	0.471	-0.257	0.349	0.049 *
29	-0.335	0.323	0.300	-0.764	0.636	<0.001 **
Constant	-1.441	0.180	<0.001 **			
Model Significance & Fit Statistics						
Wald Chi-squared, p-value	610.25	p<0.001**				
Log pseudolikelihood	-7214.55					

Zero-truncated negative binomial regression with robust standard errors. Functional status is Karnofsky score as a percent of total function. Steatohepatitis is inclusive of non-alcoholic steatohepatitis (NASH) and alcoholic hepatitis. Primary insurance coverage indicates the patient's primary payer at the time of transplantation. Zip code median income is the median income of the patient's home zip code as it corresponds to the national quartiles for income during the calendar year the patient underwent transplantation. Rural / Urban Continuum is based on the patient's county classification by the 2013 Rural-Urban Continuum codes. Transplant center codes were randomly assigned. **Abbreviations:** MELD - model for end stage liver disease score, GED - general equivalency diploma, COPD - chronic obstructive pulmonary disease, pop. – population, SE – standard error.

4D. Full Regression Model for Total Number of Admitted Days

Covariate	Coefficient	SE	p-value	Margin	SE	p-value
MELD (physiologic)	0.018	0.002	<0.001 **	0.573	0.077	<0.001 **
Functional status	-0.008	0.001	<0.001 **	-0.261	0.034	<0.001 **
Liver Disease Etiology						
Acute Liver Failure	-0.257	0.072	<0.001 **	-6.982	1.841	<0.001 **
Autoimmune Hepatitis	0.047	0.096	0.622	1.485	3.069	0.629
Cholestatic Liver Disease	0.074	0.071	0.298	2.369	2.319	0.307
Cryptogenic Cirrhosis	0.104	0.085	0.221	3.380	2.861	0.237
Genetic/Metabolic	0.185	0.128	0.151	6.243	4.712	0.185
Hepatitis C	0.031	0.049	0.528	0.975	1.544	0.528
Malignancy	0.032	0.052	0.544	0.991	1.633	0.544
Steatohepatitis	reference					
Other	-0.109	0.083	0.189	-3.178	2.348	0.176
Medical Comorbidities						
Hypertension	-0.027	0.037	0.462	-0.846	1.147	0.461
COPD	0.162	0.044	<0.001 **	5.280	1.512	<0.001 **
Diabetes	0.034	0.042	0.419	1.057	1.319	0.423
Renal failure	0.110	0.042	0.008 *	3.496	1.363	0.010 *
Vascular disease	0.399	0.051	<0.001 **	14.509	2.140	<0.001 **
Insurance						

Private	reference					
Medicare	0.020	0.039	0.605	0.629	1.220	0.606
Medicaid	0.065	0.046	0.162	2.051	1.493	0.170
Veterans Affairs	-0.029	0.227	0.899	-0.871	6.754	0.897
Self-Pay	-0.172	0.299	0.564	-4.852	7.724	0.530
Other	-0.026	0.151	0.861	-0.801	4.505	0.859
Education						
Less than HS/GED	reference					
High School/GED	-0.071	0.085	0.399	-2.301	2.819	0.414
Some college or technical school	-0.065	0.090	0.471	-2.102	2.988	0.482
Associate or bachelors degree	-0.094	0.094	0.317	-3.010	3.099	0.331
Post-college graduate degree	-0.116	0.100	0.246	-3.669	3.241	0.258
Donor Risk Index	0.182	0.045	<0.001 **	5.684	1.394	<0.001 **
Race / Ethnicity						
White, non-latino	reference					
White, latino	-0.052	0.042	0.218	-1.608	1.293	0.214
Black	-0.024	0.053	0.648	-0.761	1.650	0.645
Asian	-0.071	0.079	0.372	-2.177	2.367	0.358
Native American	0.190	0.241	0.430	6.671	9.274	0.472
Other	-0.484	0.167	0.004 *	-12.209	3.323	<0.001 **
Age (years)	0.009	0.002	<0.001 **	0.267	0.056	<0.001 **
Sex						
Male	reference					
Female	0.007	0.035	0.832	0.231	1.091	0.832
Hospital density	0.016	0.017	0.348	0.484	0.515	0.348
Primary care density	0.957	1.413	0.498	29.841	44.224	0.500
Specialty care density	-0.323	0.728	0.657	-10.082	22.719	0.657
Zip code median income						
1st Quartile	reference					
2nd Quartile	-0.040	0.050	0.420	-1.266	1.576	0.422
3rd Quartle	-0.028	0.048	0.565	-0.886	1.547	0.567
4th Quartile	-0.066	0.051	0.199	-2.061	1.616	0.202
Rural / Urban Continuum						
Metropolitan >= 1million pop.	reference					
Metropolitan 250,000 - 1 million pop.	0.056	0.050	0.258	1.800	1.615	0.265
Metropolitan <250,000 pop.	-0.029	0.079	0.713	-0.882	2.375	0.710
Urban >20,000 pop.	0.028	0.106	0.792	0.882	3.380	0.794
Urban 2,500-20,000 pop.	-0.124	0.112	0.270	-3.599	3.098	0.245
Completely rural or <2,500 urban pop.	-0.308	0.175	0.079	-8.199	4.030	0.042 *

Distance to Transplant Center (minutes)	0.000	0.000	0.502	-0.007	0.010	0.502
Transplant Center						
1	reference					
2	-0.078	0.128	0.541	-2.715	4.409	0.538
3	-0.112	0.128	0.381	-3.840	4.346	0.377
4	-0.654	0.098	<0.001 **	-17.349	2.915	<0.001 **
5	-0.387	0.104	<0.001 **	-11.592	3.221	<0.001 **
6	-0.266	0.127	0.036 *	-8.455	4.006	0.035 *
7	0.137	0.144	0.343	5.304	5.761	0.357
8	-0.390	0.141	0.006 *	-11.672	4.067	0.004 *
9	-0.546	0.134	<0.001 **	-15.212	3.548	<0.001 **
10	-0.022	0.157	0.887	-0.800	5.585	0.886
11	-0.375	0.112	0.001 *	-11.297	3.502	0.001 *
12	-0.278	0.099	0.005 *	-8.787	3.216	0.006 *
13	0.187	0.125	0.137	7.423	5.202	0.154
14	-0.482	0.104	<0.001 **	-13.829	3.164	<0.001 **
15	-0.284	0.106	0.008 *	-8.932	3.458	0.010 *
16	0.141	0.139	0.308	5.492	5.495	0.318
17	-0.270	0.150	0.073	-8.550	4.568	0.061
18	-0.256	0.153	0.096	-8.154	4.657	0.080
19	-0.202	0.127	0.112	-6.612	4.034	0.101
20	-0.099	0.103	0.338	-3.411	3.582	0.341
21	0.148	0.074	0.046 *	5.765	2.782	0.038
22	0.300	0.135	0.026 *	12.658	5.961	0.034
23	0.012	0.177	0.944	0.453	6.468	0.944
24	-0.182	0.146	0.213	-6.025	4.674	0.197
25	-0.449	0.110	<0.001 **	-13.076	3.355	<0.001 **
26	-0.537	0.130	<0.001 **	-15.022	3.513	<0.001 **
27	0.050	0.132	0.707	1.844	4.945	0.709
28	-0.074	0.161	0.646	-2.575	5.504	0.640
29	-0.050	0.275	0.856	-1.761	9.490	0.853
Constant	0.950	0.190	<0.001 **			
ln(follow-up time)	1	(exposure)				

Model Significance & Fit Statistics		
Wald Chi-squared, p-value	1783.75	p<0.001**
Log pseudolikelihood	-20549.30	

Zero-truncated Poisson regression with robust standard errors. Functional status is Karnofsky score as a percent of total function. Steatohepatitis is inclusive of non-alcoholic steatohepatitis (NASH) and alcoholic hepatitis. Primary insurance coverage indicates the patient's primary payer at the time of transplantation. Zip code median income is the median income of the patient's home zip code as it corresponds to the national quartiles for income during the calendar year the patient underwent transplantation. Rural / Urban Continuum is based on the patient's county classification by the 2013 Rural-Urban Continuum codes. Transplant center codes were randomly assigned. **Abbreviations:** MELD - model for end stage liver disease score, GED - general equivalency diploma, COPD - chronic obstructive pulmonary disease, pop. – population, SE – standard error.

4E. Sensitivity Analysis – Definition of Malignancy

Covariate	Outcome: Admissions					
	Diagnosis v1		Diagnosis v2		Diagnosis v3	
	Margin	p-value	Margin	p-value	Margin	p-value
Liver Disease Etiology (9 groups)						
Steatohepatitis	reference		reference		reference	
Malignancy	0.246	0.012*	0.216	0.022*	0.210	0.021*
Acute Liver Failure	-0.189	0.123	-0.236	0.055	-0.229	0.065
Hepatitis C	0.301	<0.001**	0.276	0.001*	0.268	0.002*
Cholestatic Liver Disease	0.149	0.273	0.146	0.293	0.145	0.297
Cryptogenic Cirrhosis	0.265	0.059	0.188	0.184	0.207	0.149
Genetic/Metabolic	0.095	0.720	0.083	0.761	0.083	0.762
Autoimmune Hepatitis	0.132	0.522	0.131	0.543	0.144	0.515
Other	-0.235	0.087	-0.208	0.161	-0.205	0.169
Liver Disease Etiology (3 groups)						
Chronic liver disease						
Malignancy						
Acute liver failure						
Model Significance & Fit Statistics						
Wald Chi-squared, p-value	536.786		528.840		527.912	
Log pseudolikelihood	-6436.732		-6441.231		-6442.097	
Akaike Information Criterion	13019.465		13028.462		13030.194	
Baysian Information Criterion	13484.785		13493.782		13495.514	

Coefficient estimates from zero-truncated Poisson regression with the outcome of total admitted days within 6 months post -transplant. Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. Analysis included only patients with complete data, and was done prior to multiple imputation (n = 4,334). Diagnosis versions include differences in the classification of malignancy such that: (v1) malignancy only if included in the diagnosis variables indicated malignancy was the primary or secondary diagnosis, (v2) malignancy if diagnosis codes included malignancy as the primary or secondary diagnosis and if the physiologic score was less than the allocation score (physiologic score + any additional exception points), or (v3) malignancy if diagnosis codes included malignancy or if the patient was ever approved for exception points due to malignancy.

Outcome: Admitted Days						
Covariate	**Diagnosis v1**		**Diagnosis v2**		**Diagnosis v3**	
	Margin	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Liver Disease Etiology (9 groups)						
Steatohepatitis	reference		reference		reference	
Malignancy	1.286	0.457	1.318	0.458	0.997	0.564
Acute Liver Failure	-7.057	<0.001**	-7.205	<0.001**	-7.175	<0.001**
Hepatitis C	2.267	0.157	1.972	0.239	1.846	0.276
Cholestatic Liver Disease	1.928	0.419	1.957	0.425	1.901	0.440
Cryptogenic Cirrhosis	3.822	0.205	2.865	0.350	3.179	0.309
Genetic/Metabolic	4.783	0.326	5.377	0.289	5.284	0.298
Autoimmune Hepatitis	0.844	0.789	0.396	0.902	0.436	0.893
Other	-1.203	0.676	-2.146	0.441	-2.736	0.324
Liver Disease Etiology (3 groups)						
Chronic liver disease						
Malignancy						
Acute liver failure						
Model Significance & Fit Statistics						
Wald Chi-squared, p-value	1608.866		1618.007		1618.078	
Log pseudolikelihood	-18365.954		-18367.225		-18367.237	
Akaike Information Criterion	36879.908		36882.449		36882.475	
Baysian Information Criterion	37351.602		37354.143		37354.169	

Coefficient estimates from zero-truncated negative binomial regression with the outcome of total admitted days within 6 months post -transplant. Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. Analysis included only patients with complete data, and was done prior to multiple imputation (n = 4,334). Diagnosis versions include differences in the classification of malignancy such that: (v1) malignancy only if included in the diagnosis variables indicated malignancy was the primary or secondary diagnosis, (v2) malignancy if diagnosis codes included malignancy as the primary or secondary diagnosis and if the physiologic score was less than the allocation score (physiologic score + any additional exception points), or (v3) malignancy if diagnosis codes included malignancy or if the patient was ever approved for exception points due to malignancy.

4F. Sensitivity Analysis – Number of Diagnostic Groups

Outcome: Admissions				
Covariate	**Margin**	**p-value**	**Margin**	**p-value**
Liver Disease Etiology (9 groups)				
Steatohepatitis	reference			
Malignancy	0.210	0.021*		
Acute Liver Failure	-0.229	0.065		
Hepatitis C	0.268	0.002*		
Cholestatic Liver Disease	0.145	0.297		
Cryptogenic Cirrhosis	0.207	0.149		
Genetic/Metabolic	0.083	0.762		
Autoimmune Hepatitis	0.144	0.515		
Other	-0.205	0.169		
Liver Disease Etiology (3 groups)				
Chronic liver disease			reference	
Malignancy			0.104	0.201
Acute liver failure			-0.230	0.068
Model Significance & Fit Statistics				
Wald Chi-squared, p-value	527.912		501.104	
Log pseudolikelihood	-6442.097		-6454.761	
Akaike Information Criterion	13030.194		13043.521	
Baysian Information Criterion	13495.514		13470.595	

Coefficient estimates from zero-truncated Poisson regression for outcome of total admitted days within 6 months post -transplant. Only covariates of interest displayed; covariates not displayed: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. Analysis included only patients with complete data, and was done prior to multiple imputation (n = 4,334). Diagnosis 3 groups is the 9 diagnostic groups collapsed into 3 groups where chronic liver disease includes all diagnoses other than malignancy and acute liver failure.

Outcome: Admitted Days				
Covariate	**Margin**	**p-value**	**Margin**	**p-value**
Liver Disease Etiology (9 groups)				
Steatohepatitis	reference			
Malignancy	0.997	0.564		
Acute Liver Failure	-7.175	<0.001**		
Hepatitis C	1.846	0.276		
Cholestatic Liver Disease	1.901	0.440		
Cryptogenic Cirrhosis	3.179	0.309		
Genetic/Metabolic	5.284	0.298		
Autoimmune Hepatitis	0.436	0.893		
Other	-2.736	0.324		
Liver Disease Etiology (3 groups)				
Chronic liver disease			reference	
Malignancy			-0.020	0.989
Acute liver failure			-8.429	<0.001**
Model Significance & Fit Statistics				
Wald Chi-squared, p-value	1618.078		1589.397	
Log pseudolikelihood	-18367.237		-18369.872	
Akaike Information Criterion	36882.475		36875.744	
Baysian Information Criterion	37354.169		37309.193	

Coefficient estimates from zero-truncated negative binomial regression for outcome of total admitted days within 6 months post -transplant. Only covariates of interest displayed; covariates not displayed: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. Analysis included only patients with complete data, and was done prior to multiple imputation (n = 4,334). Diagnosis 3 groups is the 9 diagnostic groups collapsed into 3 groups where chronic liver disease includes all diagnoses other than malignancy and acute liver failure.

4G. Sensitivity Analysis – Admissions Model Comparisons

	OLS			Poisson			Zero-Truncated Poisson			Mixed Effects Poisson			Poisson with Transplant Center FE		
Medical Condition/ Disability	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Liver Disease Severity (H1a)															
MELD, physiologic	0.014	0.003	<0.001**	0.015	0.003	<0.001**	0.017	0.004	<0.001**	0.015	0.003	<0.001**	0.007	0.001	<0.001**
Liver Disease Etiology (H1b)															
Acute liver failure	-0.231	0.117	0.048*	-0.176	0.095	0.065	-0.205	0.112	0.066	-0.176	0.095	0.065	-0.087	0.052	0.094
Autoimmune hepatitis	0.037	0.161	0.820	0.114	0.162	0.481	0.098	0.199	0.622	0.114	0.162	0.481	0.053	0.072	0.466
Cholestatic liver disease	0.110	0.103	0.285	0.173	0.105	0.099	0.169	0.129	0.191	0.173	0.105	0.099	0.079	0.046	0.086
Cryptogenic cirrhosis	0.199	0.115	0.084	0.174	0.123	0.156	0.218	0.144	0.131	0.174	0.123	0.156	0.080	0.049	0.107
Genetic/metabolic	0.020	0.170	0.907	0.045	0.196	0.817	0.052	0.255	0.840	0.045	0.196	0.817	0.021	0.078	0.784
Hepatitis C	0.188	0.070	0.007*	0.207	0.068	0.002*	0.232	0.080	0.004*	0.207	0.068	0.002*	0.094	0.030	0.002*
Malignancy	0.163	0.071	0.022*	0.195	0.069	0.005*	0.216	0.085	0.011*	0.195	0.069	0.005*	0.089	0.032	0.005*
Steatohepatitis	ref.			ref.			ref.			ref.			ref.		
Other	-0.154	0.128	0.229	-0.067	0.109	0.537	-0.119	0.140	0.393	-0.067	0.109	0.537	-0.033	0.060	0.586
Ability to Pay for Care (H1c)	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Insurance Status															
Private insurance	ref.			ref.			ref.			ref.			ref.		
Medicare	0.039	0.055	0.485	0.034	0.054	0.526	0.049	0.067	0.457	0.341	0.054	0.526	0.016	0.025	0.529
Medicaid	0.103	0.062	0.098	0.118	0.064	0.066	0.152	0.078	0.051	0.118	0.064	0.066	0.053	0.027	0.056
Veterans Affairs	-0.168	0.340	0.622	-0.085	0.354	0.810	-0.154	0.430	0.720	-0.085	0.354	0.810	-0.040	0.156	0.799
Self-Pay	-0.675	0.440	0.125	-0.656	0.195	0.001*	-0.920	0.261	<0.001**	-0.656	0.195	0.001*	-0.358	0.239	0.134
Other	-0.099	0.234	0.673	-0.026	0.247	0.917	-0.004	0.289	0.988	-0.026	0.247	0.917	-0.012	0.102	0.907
Education															
Less than High School/GED	ref.			ref.			ref.			ref.			ref.		
High School/GED	0.007	0.088	0.933	-0.002	0.088	0.980	0.007	0.106	0.951	-0.002	0.088	0.980	-0.001	0.039	0.980
Some college or tech. school	0.072	0.095	0.445	0.053	0.093	0.573	0.080	0.113	0.477	0.053	0.093	0.573	0.024	0.042	0.572
Associates or bachelor's degree	0.005	0.101	0.962	-0.043	0.098	0.660	-0.036	0.120	0.762	-0.043	0.098	0.660	-0.020	0.045	0.659
Post-college graduate degree	0.052	0.120	0.667	0.023	0.120	0.847	0.045	0.149	0.763	0.023	0.120	0.847	0.010	0.054	0.846
Donor Organ Quality (H1d)	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Donor Risk Index	0.149	0.060	0.013*	0.188	0.061	0.002*	0.225	0.075	0.003*	0.188	0.061	0.002*	0.085	0.027	0.001*

Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center (except for Poisson with Transplant Center Fixed Effects). * p<0.05, **p<0.001. Abbreviations: OLS - ordinary least squares, SE - standard error, MELD - Model for End Stage Liver Disease, GED - general equivalency diploma.

4H. Sensitivity Analysis – Admitted Days Model Comparisons

	OLS			Negative Binomial			Zero-Truncated Negative Binomial			Mixed Effects Negative Binomial			Negative Binomial with Transplant Center FE		
Medical Condition/Disability	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Liver Disease Severity (H1a)															
MELD, physiologic	0.511	0.057	<0.001**	0.501	0.045	<0.001**	0.573	0.077	<0.001**	0.577	0.077	<0.001**	0.015	0.001	<0.001**
Liver Disease Etiology (H1b)															
Acute liver failure	-8.460	1.997	<0.001**	-6.170	1.294	<0.001**	-6.982	1.841	<0.001**	-6.844	1.863	<0.001**	-0.146	0.049	0.003*
Autoimmune hepatitis	-0.822	2.755	0.765	-0.466	2.141	0.828	1.485	3.069	0.629	1.591	3.082	0.606	0.068	0.067	0.309
Cholestatic liver disease	-1.699	1.760	0.335	-0.418	1.385	0.763	2.369	2.319	0.307	2.502	2.335	0.284	0.013	0.044	0.770
Cryptogenic cirrhosis	1.007	1.965	0.608	1.695	1.628	0.298	3.380	2.861	0.237	3.237	2.865	0.256	0.039	0.047	0.409
Genetic/metabolic	3.730	2.909	0.200	4.633	2.651	0.081	6.243	4.712	0.185	6.054	4.691	0.197	0.014	0.072	0.850
Hepatitis C	-0.529	1.196	0.658	-0.087	0.941	0.927	0.975	1.544	0.528	1.024	1.550	0.509	0.037	0.029	0.196
Malignancy	-0.697	1.221	0.568	-0.077	0.976	0.937	0.991	1.633	0.544	1.179	1.639	0.472	0.011	0.030	0.716
Steatohepatitis	ref.			ref.			ref.			ref.			ref.		
Other	-5.185	2.185	0.018*	-3.769	1.548	0.015*	-3.178	2.348	0.176	-2.854	2.379	0.230	-0.056	0.056	0.316
Ability to Pay for Care (H1c)	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Insurance Status															
Private insurance	ref.			ref.			ref.			ref.			ref.		
Medicare	0.825	0.945	0.383	1.354	0.747	0.070	0.629	1.220	0.606	0.615	1.225	0.616	0.039	0.024	0.098
Medicaid	1.097	1.068	0.304	1.157	0.841	0.169	2.051	1.493	0.170	1.988	1.496	0.184	0.040	0.027	0.128
Veterans Affairs	-4.895	5.820	0.400	-5.405	3.629	0.136	-0.871	6.754	0.897	-0.427	7.122	0.952	-0.037	0.152	0.807
Self-Pay	-4.541	7.529	0.546	-5.629	4.605	0.222	-4.852	7.724	0.530	-4.930	7.829	0.529	-0.195	0.201	0.333
Other	-3.187	4.008	0.427	-1.691	2.920	0.563	-0.801	4.505	0.859	1.063	4.475	0.812	-0.073	0.103	0.477
Education															
Less than High School/GED	ref.			ref.			ref.			ref.			ref.		
High School/GED	1.061	1.511	0.483	0.306	1.167	0.793	-2.301	2.819	0.414	-2.401	2.820	0.395	0.015	0.038	0.693
Some college or tech.school	0.961	1.618	0.553	0.948	1.260	0.452	-2.102	2.988	0.482	-2.178	2.988	0.466	0.012	0.040	0.760
Associate or bachelors degree	0.188	1.722	0.913	0.218	1.330	0.870	-3.010	3.099	0.331	-3.157	3.097	0.308	-0.013	0.043	0.759
Post-college graduate degree	1.525	2.051	0.457	0.198	1.593	0.901	-3.669	3.241	0.258	-3.736	3.244	0.250	-0.006	0.052	0.905
Donor Organ Quality (H1d)	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Donor Risk Index	3.374	1.026	0.001*	4.160	0.814	<0.001**	5.684	1.394	<0.001**	5.682	1.401	<0.001**	0.103	0.025	<0.001**

Outcome, total admitted days, is inclusive of the days admitted following transplantation during the index admission. Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center (except for Poisson with Transplant Center Fixed Effects). * p<0.05, **p<0.001. Abbreviations: OLS - ordinary least squares, FE - fixed effects, SE - standard error, MELD - Model for End Stage Liver Disease, GED - general equivalency diploma.

4I. Sensitivity Analysis – Inclusion of Patients Who Died Within 6 Months of Transplant

	Admissions Model						Admitted Days Model					
	All n = 4860			Deaths excluded n = 4518			All n = 4860			Deaths excluded n = 4518		
Medical Condition/Disability	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Liver Disease Severity (H1a)												
MELD, physiologic	0.009	0.002	<0.001**	0.010	0.002	<0.001**	0.018	0.002	<0.001**	0.019	0.002	<0.001**
Liver Disease Etiology (H1b)												
Acute liver failure	-0.127	0.072	0.078	-0.131	0.073	0.075	-0.257	0.072	<0.001**	-0.212	0.068	0.002*
Autoimmune hepatitis	0.056	0.110	0.614	0.074	0.113	0.511	0.047	0.096	0.622	-0.027	0.078	0.731
Cholestatic liver disease	0.094	0.070	0.177	0.100	0.071	0.164	0.074	0.071	0.298	0.017	0.058	0.770
Cryptogenic cirrhosis	0.119	0.076	0.115	0.111	0.077	0.147	0.104	0.085	0.221	0.056	0.064	0.382
Genetic/metabolic	0.030	0.144	0.838	0.085	0.143	0.552	0.185	0.128	0.151	0.139	0.118	0.236
Hepatitis C	0.127	0.044	0.004*	0.127	0.045	0.005*	0.031	0.049	0.528	0.005	0.040	0.909
Malignancy	0.118	0.047	0.011*	0.117	0.048	0.015*	0.032	0.052	0.544	-0.004	0.042	0.920
Steatohepatitis	ref.			ref.			ref.			ref.		
Other	-0.072	0.087	0.406	-0.049	0.089	0.581	-0.109	0.083	0.189	-0.122	0.070	0.083
Ability to Pay for Care (H1c)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Insurance Status												
Private insurance	ref.			ref.			ref.			ref.		
Medicare	0.027	0.036	0.456	0.030	0.037	0.424	0.020	0.039	0.605	0.068	0.032	0.033*
Medicaid	0.081	0.041	0.047*	0.088	0.042	0.037*	0.065	0.046	0.162	0.045	0.037	0.222
Veterans Affairs	-0.090	0.262	0.732	-0.054	0.257	0.833	-0.029	0.227	0.899	-0.131	0.166	0.430
Self-Pay	-0.720	0.296	0.015*	-0.677	0.297	0.023*	-0.172	0.299	0.564	-0.177	0.275	0.519
Other	-0.002	0.162	0.988	-0.174	0.152	0.253	-0.026	0.151	0.861	-0.151	0.124	0.222
Education												
Less than High School/GED	ref.			ref.			ref.			ref.		
High School/GED	0.004	0.059	0.951	-0.009	0.060	0.887	-0.071	0.085	0.399	-0.026	0.052	0.617
Some college or technical school	0.043	0.061	0.482	0.031	0.063	0.629	-0.065	0.090	0.471	0.009	0.057	0.871
Associate or bachelors degree	-0.020	0.067	0.761	-0.044	0.069	0.521	-0.094	0.094	0.317	-0.050	0.060	0.407
Post-college graduate degree	0.024	0.081	0.763	0.016	0.083	0.849	-0.116	0.100	0.246	-0.012	0.074	0.872
Donor Organ Quality (H1d)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Donor Risk Index	0.123	0.041	0.003*	0.122	0.042	0.004*	0.182	0.045	<0.001**	0.146	0.036	<0.001**

Admissions model by zero-truncated Poisson regression and admitted days model by zero-truncated negative binomial regression. Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. * p<0.05, **p<0.001. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease, GED - general equivalency diploma.

4J. Sensitivity Analysis – Classification of In-State Residence

	Admissions Model						Admitted Days Model					
	All n = 4860			Possible Out of State Excluded n = 4762			All n = 4860			Possible Out of State Excluded n = 4762		
Medical Condition/Disability	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Liver Disease Severity (H1a)												
MELD, physiologic	0.009	0.002	<0.001**	0.010	0.002	<0.001**	0.018	0.002	<0.001**	0.018	0.003	<0.001**
Liver Disease Etiology (H1b)												
Acute liver failure	-0.127	0.072	0.078	-0.138	0.065	0.033*	-0.257	0.072	<0.001**	-0.266	0.073	<0.001**
Autoimmune hepatitis	0.056	0.110	0.614	0.022	0.092	0.815	0.047	0.096	0.622	0.056	0.097	0.564
Cholestatic liver disease	0.094	0.070	0.177	0.072	0.059	0.217	0.074	0.071	0.298	0.075	0.074	0.315
Cryptogenic cirrhosis	0.119	0.076	0.115	0.091	0.060	0.132	0.104	0.085	0.221	0.078	0.086	0.365
Genetic/metabolic	0.030	0.144	0.838	0.046	0.099	0.644	0.185	0.128	0.151	0.134	0.128	0.294
Hepatitis C	0.127	0.044	0.004*	0.124	0.037	0.001*	0.031	0.049	0.528	0.029	0.050	0.563
Malignancy	0.118	0.047	0.011*	0.109	0.040	0.006*	0.032	0.052	0.544	0.025	0.053	0.635
Steatohepatitis	ref.			ref.			ref.			ref.		
Other	-0.072	0.087	0.406	-0.091	0.078	0.244	-0.109	0.083	0.189	-0.135	0.084	0.106
Ability to Pay for Care (H1c)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Insurance Status												
Private insurance	ref.			ref.			ref.			ref.		
Medicare	0.027	0.036	0.456	0.027	0.031	0.372	0.020	0.039	0.605	0.024	0.040	0.553
Medicaid	0.081	0.041	0.047*	0.075	0.034	0.025*	0.065	0.046	0.162	0.064	0.047	0.170
Veterans Affairs	-0.090	0.262	0.732	-0.253	0.225	0.261	-0.029	0.227	0.899	-0.028	0.247	0.911
Self-Pay	-0.720	0.296	0.015*	-0.930	0.478	0.052	-0.172	0.299	0.564	-0.192	0.338	0.570
Other	-0.002	0.162	0.988	0.022	0.123	0.858	-0.026	0.151	0.861	-0.084	0.153	0.583
Education												
Less than High School/GED	ref.			ref.			ref.			ref.		
High School/GED	0.004	0.059	0.951	0.012	0.048	0.804	-0.071	0.085	0.399	-0.068	0.086	0.427
Some college or tech. school	0.043	0.061	0.482	0.051	0.052	0.324	-0.065	0.090	0.471	-0.060	0.091	0.512
Associate or bachelors degree	-0.020	0.067	0.761	-0.016	0.056	0.777	-0.094	0.094	0.317	-0.092	0.095	0.333
Post-college graduate degree	0.024	0.081	0.763	0.034	0.067	0.609	-0.116	0.100	0.246	-0.120	0.102	0.239
Donor Organ Quality (H1d)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Donor Risk Index	0.123	0.041	0.003*	0.131	0.033	<0.001**	0.182	0.045	<0.001**	0.176	0.045	<0.00 **

Admissions model by zero-truncated Poisson regression and admitted days model by zero-truncated negative binomial regression. Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. * p<0.05, **p<0.001. Abbreviations: Coeff – coefficient, SE - standard error, MELD - Model for End Stage Liver Disease, GED - general equivalency diploma.

4K. Sensitivity Analysis – Inclusion of Simultaneous Liver and Kidney Recipients

	Admissions Model								
	All n = 4860			Excluding Liver Kidney n = 4530			Liver Kidney Covariate n = 4860		
Medical Condition/Disability	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Liver Disease Severity (H1a)									
MELD, physiologic	0.009	0.002	<0.001**	0.010	0.002	<0.001**	0.010	0.002	<0.001**
Liver Disease Etiology (H1b)									
Acute liver failure	-0.127	0.072	0.078	-0.123	0.065	0.060	-0.130	0.064	0.042
Autoimmune hepatitis	0.056	0.110	0.614	0.073	0.093	0.430	0.056	0.089	0.533
Cholestatic liver disease	0.094	0.070	0.177	0.112	0.059	0.059	0.095	0.057	0.096
Cryptogenic cirrhosis	0.119	0.076	0.115	0.096	0.064	0.133	0.119	0.059	0.042*
Genetic/metabolic	0.030	0.144	0.838	0.049	0.100	0.628	0.029	0.098	0.770
Hepatitis C	0.127	0.044	0.004*	0.138	0.039	<0.001**	0.128	0.037	<0.001**
Malignancy	0.118	0.047	0.011*	0.127	0.041	0.002*	0.117	0.039	0.003*
Steatohepatitis	ref.			ref.					
Other	-0.072	0.087	0.406	-0.017	0.083	0.842	-0.066	0.077	0.388
Ability to Pay for Care (H1c)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Insurance Status									
Private insurance	ref.			ref.					
Medicare	0.027	0.036	0.456	0.037	0.032	0.251	0.030	0.030	0.329
Medicaid	0.081	0.041	0.047*	0.087	0.035	0.013*	0.081	0.033	0.015*
Veterans Affairs	-0.090	0.262	0.732	-0.036	0.197	0.856	-0.091	0.197	0.645
Self-Pay	-0.720	0.296	0.015*	-0.718	0.387	0.063	-0.725	0.386	0.060
Other	-0.002	0.162	0.988	0.028	0.130	0.830	0.003	0.123	0.982
Education									
Less than High School/GED	ref.			ref.					
High School/GED	0.004	0.059	0.951	0.021	0.050	0.682	0.002	0.048	0.970
Some college or tech. school	0.043	0.061	0.482	0.066	0.054	0.217	0.041	0.051	0.417
Associate or bachelors degree	-0.020	0.067	0.761	-0.010	0.058	0.859	-0.022	0.055	0.696
Post-college graduate degree	0.024	0.081	0.763	0.024	0.070	0.726	0.023	0.066	0.726
Donor Organ Quality (H1d)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Donor Risk Index	0.123	0.041	0.003*	0.110	0.034	0.001*	0.120	0.033	<0.001**
Donor Organ Quality (H1d)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Liver + Kidney Transplant							-0.065	0.048	0.177

Admissions model by zero-truncated Poisson regression. Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. * p<0.05, **p<0.001. Abbreviations: Coeff – coefficient, SE - standard error, MELD - Model for End Stage Liver Disease, GED - general equivalency diploma.

	Admitted Days Model								
	All n = 4860			Excluding Liver Kidney n = 4530			Liver Kidney Covariate n = 4860		
Medical Condition/Disability	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Liver Disease Severity (H1a)									
MELD, physiologic	0.018	0.002	<0.001**	0.018	0.003	<0.001**	0.018	0.002	<0.001**
Liver Disease Etiology (H1b)									
Acute liver failure	-0.257	0.072	<0.001**	-0.260	0.074	<0.001**	-0.257	0.073	<0.001**
Autoimmune hepatitis	0.047	0.096	0.622	0.045	0.097	0.642	0.047	0.095	0.623
Cholestatic liver disease	0.074	0.071	0.298	0.068	0.072	0.346	0.074	0.071	0.298
Cryptogenic cirrhosis	0.104	0.085	0.221	0.122	0.089	0.171	0.104	0.085	0.221
Genetic/metabolic	0.185	0.128	0.151	0.109	0.134	0.415	0.184	0.128	0.151
Hepatitis C	0.031	0.049	0.528	0.040	0.053	0.450	0.031	0.049	0.528
Malignancy	0.032	0.052	0.544	0.042	0.054	0.440	0.032	0.052	0.543
Steatohepatitis	ref.			ref.			ref.		
Other	-0.109	0.083	0.189	-0.091	0.089	0.310	-0.110	0.082	0.184
Ability to Pay for Care (H1c)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Insurance Status									
Private insurance	ref.			ref.			ref.		
Medicare	0.020	0.039	0.605	0.022	0.041	0.588	0.020	0.039	0.610
Medicaid	0.065	0.046	0.162	0.067	0.048	0.165	0.065	0.046	0.162
Veterans Affairs	-0.029	0.227	0.899	0.012	0.231	0.959	-0.029	0.227	0.900
Self-Pay	-0.172	0.299	0.564	-0.170	0.294	0.564	-0.172	0.299	0.566
Other	-0.026	0.151	0.861	0.005	0.160	0.973	-0.027	0.151	0.859
Education									
Less than High School/GED	ref.			ref.			ref.		
High School/GED	-0.071	0.085	0.399	-0.092	0.091	0.313	-0.071	0.085	0.403
Some college or tech. school	-0.065	0.090	0.471	-0.082	0.097	0.400	-0.065	0.091	0.476
Associate or bachelors degree	-0.094	0.094	0.317	-0.119	0.101	0.236	-0.094	0.094	0.318
Post-college graduate degree	-0.116	0.100	0.246	-0.140	0.107	0.192	-0.116	0.100	0.247
Donor Organ Quality (H1d)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Donor Risk Index	0.182	0.045	<0.001**	0.179	0.046	<0.001**	0.183	0.044	<0.001**
Donor Organ Quality (H1d)	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**	**Coeff**	**SE**	**p-value**
Liver + Kidney Transplant							0.011	0.068	0.867

Admitted days model by zero-truncated negative binomial regression. Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. * p<0.05, **p<0.001. Abbreviations: Coeff – coefficient, SE - standard error, MELD - Model for End Stage Liver Disease, GED - general equivalency diploma.

5. Question 2 – Sensitivity Analyses & Supplemental Information

5A. Sensitivity Analysis – Single versus Multiple Imputation

	Admissions						Admitted Days					
	Single Imputation			Multiple Imputation			Single Imputation			Multiple Imputation		
Covariate	**Coeff.**	**SE**	**p-value**	**Coeff.**	**SE**	**p-value**	**Coeff.**	**SE**	**p-value**	**Coeff.**	**SE**	**p-value**
Share 35	-0.044	0.021	0.035*	-0.044	0.021	0.035*	-0.012	0.035	0.730	-0.012	0.035	0.740

Admissions model completed with Poisson regression. Admitted days model completed with negative binomial regression. Only covariate of interest displayed. Covariates not displayed: sex, age, insurance status, education, race/ethnicity, zip code median income, distance from transplant center, hospital density, primary care density, specialty care density, distance to transplant center, zip code median income, rural urban continuum, transplant center. P-values: * p<0.05, ** p<0.001. Abbreviations: Coeff - Coefficient, SE - standard error.

5B. Model Comparison – Number of Admissions

	OLS			Poisson			Zero-Truncated Poisson			Poisson with FE		
H2a - not controlling for medical status	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35	-0.082	0.046	0.073	-0.095	0.045	0.034*	-0.113	0.056	0.044*	-0.038	0.026	0.068
H2b - controlling for medical status	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35	-0.106	0.045	0.018*	-0.122	0.044	0.006*	-0.139	0.055	0.012*	-0.057	0.043	0.182
H2c - controlling for medical status and moderating effect of allocation MELD score on Share 35	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD = 10	0.193	0.130	0.137	0.162	0.121	0.182	0.180	0.151	0.234	0.082	0.056	0.143
Share 35 at aMELD = 15	0.118	0.101	0.243	0.098	0.097	0.313	0.112	0.123	0.361	0.048	0.045	0.285
Share 35 at aMELD = 20	0.044	0.075	0.559	0.031	0.074	0.678	0.039	0.095	0.679	0.014	0.038	0.710
Share 35 at aMELD = 25	-0.031	0.054	0.566	-0.040	0.054	0.463	-0.039	0.071	0.585	-0.020	0.038	0.604
Share 35 at aMELD = 30	-0.105	0.045	0.019*	-0.114	0.044	0.010*	-0.122	0.056	0.030*	-0.053	0.044	0.227
Share 35 at aMELD = 35	-0.180	0.055	0.001*	-0.193	0.052	<0.001**	-0.212	0.063	0.001*	-0.087	0.055	0.113
Share 35 at aMELD = 40	-0.254	0.077	0.001*	-0.275	0.073	<0.001**	-0.308	0.087	<0.001**	-0.121	0.068	0.075

OLS, Poisson, Zero-Truncated Poisson models are run with transplant center as a covariate. Outcome, total admissions days, is inclusive of index (transplant) admission. For hypothesis 2a, covariates not displayed include: sex, age, race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center; and for hypothesis 2b covariates not displayed include: all covariates in 2a and liver disease etiology, physiologic MELD score at transplantation, functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease). In hypothesis 2c, all covariates from 2b are included and Share 35 is moderated by the allocation MELD score (physiologic MELD score + exception points). Margin indicates the difference in predicted number of admissions between the pre- and post-Share 35 periods for all patients (H2a, H2b) and for patients at a given allocation MELD score (H2c). * $p<0.05$, ** $p<0.001$. Abbreviations: OLS - ordinary least squares, FE - fixed effects, SE - standard error, MELD - Model for End Stage Liver Disease score, aMELD – allocation MELD score.

5C. Model Comparison – Number of Admitted Days

	OLS			Negative Binomial			Zero-Truncated Negative Binomial			Negative Binomial with FE		
H2a - not controlling for medical status	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margins**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35	0.985	0.848	0.245	-0.365	1.111	0.743	-0.325	1.104	0.769	0.007	0.021	0.741
H2b - controlling for medical status	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margins**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35, mean effect	-0.336	0.839	0.689	-2.021	0.973	0.038*	-1.974	0.971	0.042*	-0.175	0.020	0.377
H2c - controlling for medical status and moderating effect of aMELD score on Share 35	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD = 10	0.755	2.452	0.758	0.984	2.067	0.634	1.014	2.063	0.623	0.005	0.059	0.926
Share 35 at aMELD = 15	0.483	1.863	0.795	0.417	1.770	0.814	0.453	1.769	0.798	0.000	0.047	1.000
Share 35 at aMELD = 20	0.211	1.318	0.873	-0.259	1.443	0.858	-0.218	1.443	0.88	-0.005	0.035	0.876
Share 35 at aMELD = 25	-0.062	0.902	0.946	-1.060	1.126	0.347	-1.014	1.127	0.369	-0.011	0.025	0.666
Share 35 at aMELD = 30	-0.334	0.837	0.690	-2.002	0.962	0.037*	-1.952	0.960	0.042*	-0.016	0.020	0.412
Share 35 at aMELD = 35	-0.606	1.182	0.608	-3.105	1.173	0.008*	-3.051	1.165	0.009*	-0.022	0.022	0.331
Share 35 at aMELD = 40	-0.878	1.704	0.606	-4.391	1.752	0.012*	-4.334	1.741	0.013*	-0.027	0.031	0.378

OLS, Negative Binomial, Zero-Truncated Negative Binomial models are run with transplant center as a covariate. Outcome, total admitted days, is inclusive of the days admitted following transplantation during the index admission. For hypothesis 2a, covariates not displayed include: sex, age, race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, distance from transplant center, rural/urban continuum, and transplant center; and for hypothesis 2b covariates not displayed include: all covariates in 2a and liver disease etiology, physiologic MELD score at transplantation, functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease). In hypothesis 2c, Share 35 is moderated by the allocation MELD score (physiologic MELD score + exception points). Margin indicates the difference in predicted number of admitted days between the pre- and post-Share 35 periods for all patients (H2a, H2b) and for patients at a given allocation MELD score (H2c). * $p<0.05$, ** $p<0.001$. Abbreviations: SE - standard error, Neg. - negative, FE - fixed effects, MELD – Model for End Stage Liver Disease, aMELD – allocation MELD score.

5D. Full Models and Marginal Effects for Count of Admissions and Admitted Days within 6 Months Following Liver Transplantation for Hypothesis 2A – Effect of Share 35 Through Medical Condition/Disability at Transplant & Organ Availability

	Admissions			Admitted Days		
Covariate	**Marginal Effect**	**SE**	**p-value**	**Marginal Effect**	**SE**	**p-value**
Share 35	-0.113	0.056	0.044*	-0.325	1.104	0.769
Insurance						
Private	reference			reference		
Medicare	0.126	0.059	0.032*	2.656	1.153	0.021*
Medicaid	0.219	0.072	0.002*	4.489	1.496	0.003*
Other	-0.065	0.198	0.741	0.767	3.548	0.829
Education						
Less than HS/GED	reference			reference		
High School/GED	0.061	0.094	0.518	-0.765	2.522	0.762
Some college or technical school	0.050	0.101	0.621	-1.143	2.685	0.670
Associate or bachelors degree	-0.051	0.108	0.637	-2.507	2.785	0.368
Post-college graduate degree	0.024	0.131	0.858	-1.948	3.108	0.531
Zip Code Median Income						
1st Quartile	reference			reference		
2nd Quartile	-0.124	0.078	0.111	-1.687	1.528	0.269
3rd Quartile	-0.063	0.075	0.398	-0.690	1.509	0.648
4th Quartile	-0.116	0.083	0.165	-2.178	1.565	0.164
Race / Ethnicity						
White, non-latino	reference			reference		
White, latino	-0.065	0.070	0.355	-1.374	1.314	0.296
Black	-0.120	0.088	0.173	-2.050	1.706	0.230
Asian	-0.499	0.088	<0.001**	-9.452	1.698	<0.001**
Other	0.393	0.342	0.251	-3.681	4.494	0.413
Age (years)	0.006	0.003	0.030*	0.188	0.054	<0.001**
Sex						
Male	reference			reference		
Female	0.149	0.052	0.004*	4.306	1.063	<0.001**
Hospital density	0.033	0.026	0.202	0.403	0.552	0.465
Primary care density	0.623	1.553	0.689	3.863	41.757	0.926
Specialty care density	-0.291	1.104	0.792	-17.349	22.654	0.444
Distance to Transplant Center	0.081	0.030	0.006*	0.041	0.601	0.946
Rural / Urban Continuum						
Completely rural or <2500 urban pop.	-0.397	0.345	0.249	1.843	7.350	0.399
Urban 2500 - 20,000 pop.	-0.411	0.180	0.023*	-3.990	3.397	0.900
Urban >20,000 pop.	-0.040	0.184	0.827	-0.935	3.029	0.758
Metropolitan <250,000 pop.	-0.022	0.126	0.864	-0.322	2.561	0.240

Metropolitan 250,000 - 1 mill. pop.	0.034	0.077	0.660	1.312	1.557	0.802
Metropolitan >1 mill. pop.	reference			reference		
Transplant Center						
1	reference			reference		
2	-0.821	0.241	0.001*	-11.395	4.086	0.005*
3	-1.212	0.195	<0.001**	-11.895	4.059	0.003*
4	-1.196	0.209	<0.001**	-21.764	3.171	<0.001**
5	-1.053	0.234	<0.001**	-14.459	3.712	<0.001**
6	-1.768	0.199	<0.001**	-17.158	3.812	<0.001**
7	-0.834	0.270	0.002*	-5.943	5.084	0.242
8	-2.001	0.233	<0.001**	-20.350	3.948	<0.001**
9	-1.276	0.291	<0.001**	-23.869	3.563	<0.001**
10	-1.374	0.213	<0.001**	-5.930	4.714	0.208
11	-1.632	0.196	<0.001**	-22.086	3.281	<0.001**
12	-1.288	0.215	<0.001**	-14.288	3.518	<0.001**
13	-1.103	0.211	<0.001**	-3.821	4.099	0.351
14	-1.500	0.190	<0.001**	-21.209	3.035	<0.001**
15	-1.573	0.196	<0.001**	-22.348	3.072	<0.001**
16	-0.044	0.290	0.879	-5.378	5.013	0.283
17	-1.724	0.239	<0.001**	-19.373	4.007	<0.001**
18	-1.565	0.255	<0.001**	-16.427	4.636	<0.001**
19	-0.978	0.246	<0.001**	-5.910	4.564	0.195
20	-0.802	0.208	<0.001**	-13.719	3.360	<0.001**
21	-1.159	0.177	<0.001**	13.614	3.277	<0.001**
22	-0.891	0.248	<0.001**	10.907	5.745	0.058
23	-1.362	0.258	<0.001**	-11.509	5.250	0.028*
24	-1.697	0.239	<0.001**	-6.112	5.556	0.271
25	-1.772	0.193	<0.001**	-22.511	3.227	<0.001**
26	-1.059	0.264	<0.001**	-15.682	4.658	0.001*
27	-1.448	0.216	<0.001**	-8.286	4.344	0.056
28	-0.937	0.307	0.002*	-10.661	5.187	0.040*
29	-1.323	0.560	0.018*	-11.271	11.619	0.332
30	-1.199	0.562	0.033*	-5.353	13.243	0.686

Admissions model completed with zero-truncated Poisson regression. Admitted days model completed with zero-truncated negative binomial regression. Marginal effects indicate the change in predicted number of admissions for a one unit change in the covariate. Primary insurance coverage indicates the patient's primary payer at the time of transplantation. Acute care hospital density is the number of hospital beds per 1,000 census population for patient's home county; PCP density is the number of practicing primary care providers per 1,000 census population for patient's home county; Specialty care density is the number of practicing outpatient gastroenterologists per 1,000 census population for patient's home county. Rural urban continuum indicates population of patient's home county by 2013 census. Transplant center codes were randomly assigned. P-values: * p<0.05, ** p<0.001. Abbreviations: SE - standard error, GED - general equivalency diploma, mill. - million, pop. - population.

5E. Full Models and Marginal Effects for Count of Admissions and Admitted Days within 6 Months Following Liver Transplantation for Hypothesis 2B – Mean Effect of Share 35 Through Organ Availability

	Admissions			Admitted Days		
Covariate	**Marginal Effect**	**SE**	**p-value**	**Marginal Effect**	**Std. Err.**	**p-value**
Share 35	-0.139	0.055	0.012*	-1.974	0.971	0.042*
Allocation MELD	0.017	0.004	<0.001**	0.581	0.086	<0.001**
MELD Difference (Allocation - Physiologic)	-0.015	0.005	0.003*	-0.376	0.086	<0.001**
Functional status	-0.005	0.002	0.001*	-0.266	0.031	<0.001**
Liver Disease Etiology						
Steatohepatitis	reference			reference		
Malignancy	0.136	0.079	0.085	-2.018	1.489	0.175
Acute Liver Failure	-0.008	0.148	0.958	-4.968	2.608	0.057
Hepatitis C	0.249	0.070	<0.001**	0.773	1.352	0.568
Cholestatic Liver Disease	0.193	0.113	0.088	2.657	2.045	0.194
Cryptogenic Cirrhosis	0.314	0.128	0.014*	5.255	2.711	0.053
Genetic/Metabolic	-0.222	0.196	0.258	6.724	4.613	0.145
Autoimmune Hepatitis	0.140	0.165	0.397	0.467	2.490	0.851
Other	-0.048	0.125	0.702	-0.977	2.302	0.671
Medical Comorbidities						
Hypertension	0.004	0.054	0.942	-0.451	1.006	0.654
COPD	0.195	0.057	0.001*	5.656	1.279	<0.001**
Diabetes	0.206	0.057	<0.001**	2.029	1.131	0.073
Renal failure	0.255	0.059	<0.001**	3.198	1.175	0.006*
Vascular disease	0.152	0.078	0.052	14.149	1.887	<0.001**
Insurance						
Private	reference			reference		
Medicare	0.090	0.057	0.117	1.849	1.072	0.085
Medicaid	0.155	0.070	0.027*	2.389	1.309	0.068
Other	-0.068	0.200	0.733	-0.153	3.036	0.960
Education						
Less than HS/GED	reference			reference		
High School/GED	0.049	0.093	0.598	-1.530	2.276	0.501
Some college or technical school	0.056	0.100	0.575	-1.723	2.397	0.472
Associate or bachelors degree	-0.014	0.108	0.900	-1.725	2.519	0.493
Post-college graduate degree	0.041	0.130	0.756	-3.071	2.675	0.251
Zip Code Median Income						
1st Quartile	reference			reference		
2nd Quartile	-0.092	0.076	0.227	-0.838	1.420	0.555
3rd Quartile	-0.041	0.072	0.566	-0.990	1.383	0.474
4th Quartile	-0.080	0.081	0.319	-2.095	1.459	0.151
Race / Ethnicity						

White, non-latino	reference			reference		
White, latino	-0.093	0.067	0.167	-1.169	1.182	0.323
Black	-0.162	0.085	0.058	-1.934	1.480	0.191
Asian	-0.351	0.096	<0.001**	-3.254	1.968	0.098
Other	0.301	0.312	0.334	-2.785	4.408	0.528
Age (years)	0.008	0.003	0.014*	0.298	0.053	<0.001**
Sex						
Male	reference			reference		
Female	0.082	0.052	0.113	1.285	0.965	0.183
Hospital density	0.022	0.026	0.394	0.347	0.475	0.466
Primary care density	0.602	1.530	0.694	3.299	35.537	0.926
Specialty care density	0.192	1.086	0.859	-17.727	20.313	0.383
Distance from Transplant Center	0.065	0.029	0.023*	-0.189	0.536	0.724
Rural / Urban Continuum						
Completely rural or <2500 urban pop.	-0.402	0.323	0.212	-5.771	3.905	0.139
Urban 2500 - 20,000 pop.	-0.375	0.180	0.038*	-4.988	2.785	0.073
Urban >20,000 pop.	-0.002	0.185	0.993	-1.894	2.607	0.467
Metropolitan <250,000 population	-0.003	0.123	0.981	-0.745	2.086	0.721
Metropolitan 250,000 - 1 mill. pop.	-0.045	0.074	0.549	0.417	1.416	0.768
Metropolitan >1mill. pop.	reference			reference		
Transplant Center						
1	reference			reference		
2	-0.257	0.241	0.285	1.796	4.113	0.662
3	-0.681	0.197	0.001*	-0.303	3.672	0.934
4	-0.929	0.189	<0.001**	-15.532	2.473	<0.001**
5	-0.698	0.223	0.002*	-7.630	2.873	0.008*
6	-1.333	0.193	<0.001**	-6.618	3.350	0.048*
7	-0.451	0.264	0.087	4.806	4.747	0.311
8	-1.518	0.232	<0.001**	-8.590	3.685	0.020*
9	-0.782	0.295	0.008*	-12.924	3.270	<0.001**
10	-1.021	0.198	<0.001**	1.431	4.405	0.745
11	-1.121	0.193	<0.001**	-9.781	2.860	0.001*
12	-0.907	0.202	<0.001**	-6.404	2.718	0.018*
13	-0.814	0.192	<0.001**	5.752	4.340	0.185
14	-1.164	0.176	<0.001**	-12.542	2.641	<0.001**
15	-0.978	0.201	<0.001**	-7.404	2.908	0.011*
16	0.409	0.280	0.144	8.690	5.034	0.084
17	-1.291	0.230	<0.001**	-8.967	3.610	0.013*
18	-1.112	0.248	<0.001**	-7.130	4.013	0.076
19	-0.779	0.217	<0.001**	-6.355	3.403	0.062
20	-0.188	0.216	0.385	-0.986	3.179	0.756
21	-0.982	0.159	<0.001**	6.873	2.416	0.004*

22	-0.631	0.228	0.006*	15.205	5.222	0.004*
23	-0.868	0.258	0.001*	2.095	5.694	0.713
24	-1.304	0.224	<0.001**	-0.796	4.244	0.851
25	-1.295	0.188	<0.001**	-11.449	2.830	<0.001**
26	-0.673	0.248	0.007*	-10.912	3.206	0.001*
27	-0.948	0.214	<0.001**	6.232	4.321	0.149
28	-0.429	0.304	0.159	1.821	5.438	0.738
29	-0.785	0.619	0.205	1.495	9.919	0.880
30	-0.774	0.621	0.213	7.283	13.579	0.592

Admissions model completed with zero-truncated Poisson regression. Admitted days model completed with zero-truncated negative binomial regression. Marginal effects indicate the change in predicted number of admissions for a one unit change in the covariate. Primary insurance coverage indicates the patient's primary payer at the time of transplantation. Acute care hospital density is the number of hospital beds per 1,000 census population for patient's home county; PCP density is the number of practicing primary care providers per 1,000 census population for patient's home county; Specialty care density is the number of practicing outpatient gastroenterologists per 1,000 census population for patient's home county. Zip code median income indicates the median income for the patient's home zip code as compared to the national distributions of incomes by quartile for the year the patient was transplanted. Distance from transplant center indicates the travel time, in hours, between the patient's home zip code (or 3-digit zip code for the state of Massachusetts) to the transplant center. Rural urban continuum indicates the population of the patient's county by 2013 US census. Transplant center codes were randomly assigned. P-values: * p<0.05, ** p<0.001. Abbreviations: SE - standard error, GED - general equivalency diploma, mill. – million, pop. – population.

5F. Full Models and Marginal Effects for Count of Admissions and Admitted Days within 6 Months Following Liver Transplantation for Hypothesis 2C – Mean Effect of Share 35 Through Organ Availability, Accounting for Moderating Effect of Allocation MELD Score

	Admissions			Admitted Days		
Covariate	**Margin**	**SE**	**p-value**	**Margin**	**Std. Err.**	**p-value**
Share 35	-0.117	0.057	0.041*	-2.153	0.959	0.025*
Allocation MELD, demeaned	0.017	0.004	<0.001**	0.587	0.085	<0.001**
MELD Difference (A-P)	-0.015	0.005	0.002*	-0.380	0.086	<0.001**
Functional status	-0.005	0.002	0.001*	-0.266	0.030	<0.001**
Liver Disease Etiology						
Steatohepatitis	reference			reference		
Malignancy	0.138	0.079	0.081	-1.942	1.487	0.191
Acute Liver Failure	-0.013	0.147	0.928	-4.978	2.609	0.056
Hepatitis C	0.253	0.070	<0.001**	0.788	1.349	0.559
Cholestatic Liver Disease	0.202	0.114	0.075	2.748	2.047	0.179
Cryptogenic Cirrhosis	0.313	0.128	0.015*	5.271	2.709	0.052
Genetic/Metabolic	-0.217	0.196	0.268	6.827	4.636	0.141
Autoimmune Hepatitis	0.151	0.166	0.364	0.551	2.488	0.825
Other	-0.038	0.125	0.760	-0.810	2.318	0.727
Medical Comorbidities						
Hypertension	0.002	0.054	0.967	-0.480	1.004	0.633
COPD	0.193	0.057	0.001*	5.631	1.277	<0.001**
Diabetes	0.207	0.057	<0.001**	2.054	1.130	0.069
Renal failure	0.251	0.059	<0.001**	3.176	1.176	0.007*
Vascular disease	0.153	0.078	0.051	14.240	1.893	<0.001**
Insurance						
Private	reference			reference		
Medicare	0.092	0.057	0.108	1.876	1.073	0.080
Medicaid	0.157	0.070	0.025	2.437	1.308	0.062
Other	-0.067	0.200	0.739	-0.154	3.033	0.959
Education						
Less than HS/GED	reference			reference		
High School/GED	0.045	0.093	0.632	-1.607	2.276	0.480
Some college or technical school	0.053	0.100	0.599	-1.757	2.400	0.464
Associate or bachelors degree	-0.019	0.108	0.862	-1.788	2.522	0.478
Post-college graduate degree	0.034	0.131	0.792	-3.130	2.674	0.242
Race / Ethnicity						
White, non-latino	reference			reference		
White, latino	-0.090	0.067	0.183	-1.129	1.182	0.340
Black	-0.157	0.086	0.067	-1.870	1.482	0.207
Asian	-0.348	0.096	<0.001**	-3.229	1.970	0.101
Other	0.306	0.313	0.328	-2.775	4.390	0.527

Zip Code Median Income						
1st Quartile	reference			reference		
2nd Quartile	-0.090	0.076	0.233	-0.822	1.418	0.562
3rd Quartile	-0.037	0.072	0.612	-0.934	1.383	0.499
4th Quartile	-0.076	0.081	0.345	-2.064	1.457	0.157
Age (years)	0.008	0.003	0.013*	0.299	0.053	<0.001**
Sex						
Male	reference			reference		
Female	0.084	0.052	0.108	1.311	0.966	0.175
Hospital density	0.020	0.026	0.429	0.316	0.471	0.503
Primary care density	0.596	1.530	0.697	3.488	35.589	0.922
Specialty care density	0.211	1.086	0.846	-16.808	20.268	0.407
Distance to transplant center	0.066	0.029	0.023*	-0.185	0.536	0.731
Rural / Urban Continuum						
Completely rural or <2500 urban pop.	-0.411	0.320	0.199	-5.729	3.993	0.151
Urban 2500 - 20,000 pop.	-0.376	0.181	0.038*	-4.966	2.789	0.075
Urban >20,000 pop.	0.002	0.185	0.991	-1.794	2.622	0.494
Metropolitan <250,000 pop.	0.002	0.123	0.985	-0.691	2.084	0.740
Metropolitan 250,000 - 1 mill. pop.	-0.043	0.074	0.560	0.429	1.417	0.762
Metropolitan >1mill. pop.	reference			reference		
Transplant Center						
1	reference			reference		
2	-0.263	0.241	0.276	1.864	4.123	0.651
3	-0.680	0.198	0.001*	-0.183	3.682	0.960
4	-0.946	0.189	<0.001**	-15.640	2.477	<0.001**
5	-0.708	0.223	0.001*	-7.700	2.864	0.007*
6	-1.335	0.194	<0.001**	-6.575	3.356	0.050
7	-0.466	0.264	0.078	4.758	4.759	0.317
8	-1.534	0.232	<0.001**	-8.693	3.677	0.018*
9	-0.780	0.295	0.008*	-12.874	3.277	<0.001**
10	-1.027	0.198	<0.001**	1.412	4.412	0.749
11	-1.135	0.193	<0.001**	-9.841	2.866	0.001*
12	-0.921	0.203	<0.001**	-6.489	2.724	0.017*
13	-0.827	0.193	<0.001**	5.604	4.329	0.195
14	-1.172	0.177	<0.001**	-12.576	2.644	<0.001**
15	-0.972	0.202	<0.001**	-7.295	2.915	0.012*
16	0.375	0.280	0.181	8.483	5.051	0.093
17	-1.302	0.230	<0.001**	-9.132	3.594	0.011*
18	-1.119	0.249	<0.001**	-7.128	4.029	0.077
19	-0.790	0.217	<0.001**	-6.390	3.419	0.062
20	-0.186	0.217	0.390	-0.936	3.187	0.769
21	-0.995	0.160	<0.001**	6.758	2.417	0.005*

22	-0.642	0.228	0.005*	15.103	5.223	0.004*
23	-0.867	0.259	0.001*	2.189	5.712	0.701
24	-1.305	0.226	<0.001**	-0.676	4.266	0.874
25	-1.301	0.189	<0.001**	-11.446	2.838	<0.001**
26	-0.671	0.250	0.007*	-10.838	3.226	0.001*
27	-0.965	0.214	<0.001**	6.083	4.320	0.159
28	-0.443	0.304	0.145	1.518	5.341	0.776
29	-0.787	0.623	0.206	1.540	9.971	0.877
30	-0.838	0.588	0.154	6.360	13.243	0.631

Admissions model completed with zero-truncated Poisson regression. Admitted days model completed with zero-truncated negative binomial regression. Marginal effects indicate the change in predicted number of admissions for a one unit change in the covariate. Primary insurance coverage indicates the patient's primary payer at the time of transplantation. Acute care hospital density is the number of hospital beds per 1,000 census population for patient's home county; PCP density is the number of practicing primary care providers per 1,000 census population for patient's home county; Specialty care density is the number of practicing outpatient gastroenterologists per 1,000 census population for patient's home county. Zip code median income indicates the quartile of the median income for the patient's come zip code as compared to the national distribution for the year the patient underwent transplantation. Distance from transplant center indicates the travel time, in hours, between the patient's home zip code (for 3-digit zip for the state of Massachusetts) and their transplant center. Rural urban continuum is the 2013 census population of the patient's home county based on patient zip code. Transplant center codes were randomly assigned. P-values: * $p<0.05$, ** $p<0.001$. Abbreviations: SE - standard error, GED - general equivalency diploma, (A-P) – allocation – physiologic MELD scores, mill. – million, pop. - population.

5G. Threshold for Statistically Significant Differences in Admissions and Admitted Days Between the Pre- and Post-Share 35 Period for H2c

	Admissions							
	Region 1 n = 517		Region 3 n = 2310		Region 5 n = 2273		Region 9 n = 930	
	Margin	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Share 35 at aMELD = 25	-0.622	<0.001**	0.103	0.214	-0.143	0.287	0.073	0.618
Share 35 at aMELD = 26	-0.624	<0.001**	0.080	0.324	-0.149	0.233	0.044	0.751
Share 35 at aMELD = 27	-0.626	<0.001**	0.056	0.484	-0.156	0.181	0.014	0.914
Share 35 at aMELD = 28	-0.628	<0.001**	0.032	0.693	-0.162	0.133	-0.016	0.898
Share 35 at aMELD = 29	-0.629	<0.001**	0.007	0.930	-0.168	0.093	-0.046	0.702
Share 35 at aMELD = 30	-0.631	<0.001**	-0.018	0.838	-0.175	0.060	-0.076	0.519
Share 35 at aMELD = 31	-0.633	0.001*	-0.043	0.637	-0.181	0.037*	-0.106	0.369
Share 35 at aMELD = 32	-0.635	0.001*	-0.069	0.480	-0.188	0.022*	-0.136	0.258
Share 35 at aMELD = 33	-0.637	0.002*	-0.095	0.362	-0.194	0.013*	-0.166	0.182
Share 35 at aMELD = 34	-0.639	0.004*	-0.122	0.278	-0.201	0.008*	-0.197	0.133
Share 35 at aMELD = 35	-0.641	0.006*	-0.149	0.218	-0.207	0.007*	-0.228	0.102
Share 35 at aMELD = 36	-0.643	0.011*	-0.177	0.175	-0.214	0.006*	-0.259	0.081
Share 35 at aMELD = 37	-0.645	0.016*	-0.205	0.143	-0.221	0.007*	-0.290	0.068
Share 35 at aMELD = 38	-0.646	0.024*	-0.234	0.120	-0.227	0.009*	-0.321	0.059
Share 35 at aMELD = 39	-0.648	0.034*	-0.263	0.103	-0.234	0.012*	-0.353	0.052
Share 35 at aMELD = 40	-0.650	0.046*	-0.292	0.089	-0.241	0.017*	-0.384	0.048*

Admissions model completed with zero-truncated Poisson regression. Only Share 35 marginal effects displayed. Covariates not displayed include: sex, age, race/ethnicity, liver disease etiology, demeaned allocation MELD score, difference between physiologic and allocation MELD score at transplantation, functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), hospital density, primary care density, specialist care density, zip code median income by quartile, distance from transplant center, rural/urban continuum and transplant center. Outcome, admissions, is inclusive of the index admission. Margin indicates the difference in predicted number of admissions between the pre- and post-Share 35 periods for patients at a given allocation MELD score. * p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease score, aMELD – allocation MELD score.

	Admitted Days							
	Region 1 n = 517		Region 3 n = 2310		Region 5 n = 2273		Region 9 n = 930	
	Margin	p-value	Margin	p-value	Margin	p-value	Margin	p-value
Share 35 at aMELD = 25	-0.732	0.797	-0.747	0.508	-0.827	0.669	-5.394	0.049*
Share 35 at aMELD = 26	-1.599	0.560	-0.797	0.480	-0.984	0.590	-5.235	0.047*
Share 35 at aMELD = 27	-2.465	0.357	-0.849	0.460	-1.145	0.505	-5.066	0.048*
Share 35 at aMELD = 28	-3.331	0.208	-0.902	0.449	-1.312	0.417	-4.886	0.051
Share 35 at aMELD = 29	-4.198	0.113	-0.958	0.446	-1.484	0.330	-4.696	0.058
Share 35 at aMELD = 30	-5.064	0.060	-1.015	0.451	-1.661	0.249	-4.496	0.072
Share 35 at aMELD = 31	-5.931	0.031*	-1.075	0.460	-1.843	0.180	-4.284	0.095
Share 35 at aMELD = 32	-6.798	0.017*	-1.137	0.473	-2.030	0.126	-4.061	0.129
Share 35 at aMELD = 33	-7.666	0.010*	-1.201	0.488	-2.224	0.088	-3.825	0.178
Share 35 at aMELD = 34	-8.535	0.006*	-1.267	0.504	-2.423	0.065	-3.578	0.241
Share 35 at aMELD = 35	-9.405	0.004*	-1.335	0.520	-2.627	0.051	-3.317	0.316
Share 35 at aMELD = 36	-10.276	0.003*	-1.406	0.535	-2.838	0.045*	-3.043	0.398
Share 35 at aMELD = 37	-11.149	0.002*	-1.479	0.550	-3.055	0.043*	-2.755	0.485
Share 35 at aMELD = 38	-12.024	0.002*	-1.555	0.564	-3.278	0.045*	-2.453	0.570
Share 35 at aMELD = 39	-12.900	0.001*	-1.634	0.577	-3.508	0.049*	-2.136	0.651
Share 35 at aMELD = 40	-13.778	0.001*	-1.715	0.589	-3.744	0.055	-1.803	0.727

Admitted days model by zero-truncated negative binomial regression. Only Share 35 marginal effects displayed. Covariates not displayed include: sex, age, race/ethnicity, liver disease etiology, demeaned allocation MELD score, difference between physiologic and allocation MELD score at transplantation, functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), hospital density, primary care density, specialist care density, zip code median income by quartile, distance from transplant center, rural/urban continuum and transplant center. Outcomes, total admitted days, is inclusive of the days admitted following transplantation during the index admission. Margin indicates the difference in predicted number of admitted days between the pre- and post-Share 35 periods for patients at a given allocation MELD score. * $p<0.05$, ** $p<0.001$. Abbreviations: MELD - Model for End Stage Liver Disease score, aMELD – allocation MELD score.

5H. Sensitivity Analysis – Exclusion of Patients who Died within 6 months of Transplantation

	Admissions						Admitted Days					
	Including Deaths n = 6156			Excluding Deaths n = 5740			Including Deaths n = 6156			Excluding Deaths n = 5740		
H2a – Full effect of Share 35, through medical condition & organ availability	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margins**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35	-0.113	0.056	0.044*	-0.117	0.059	0.046*	-0.325	1.104	0.769	0.622	0.858	0.469
H2b – Partial effect of Share 35 through organ availability; no interaction	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margins**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35	-0.139	0.055	0.012*	-0.142	0.058	0.014*	-1.974	0.971	0.042*	-0.781	0.736	0.289
H2c – Partial effect of Share 35 through organ availability, accounting for the moderating effect of aMELD score	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD = 10	0.180	0.151	0.234	0.172	0.158	0.275	1.014	2.063	0.623	1.701	1.587	0.284
Share 35 at aMELD = 15	0.112	0.123	0.361	0.106	0.129	0.412	0.453	1.769	0.798	1.251	1.357	0.357
Share 35 at aMELD = 20	0.039	0.095	0.679	0.034	0.100	0.735	-0.218	1.443	0.88	0.697	1.100	0.526
Share 35 at aMELD = 25	-0.039	0.071	0.585	-0.043	0.074	0.560	-1.014	1.127	0.369	0.023	0.850	0.979
Share 35 at aMELD = 30	-0.122	0.056	0.030*	-0.126	0.059	0.033*	-1.952	0.960	0.042*	-0.790	0.727	0.277
Share 35 at aMELD = 35	-0.212	0.063	0.001*	-0.214	0.065	0.001*	-3.051	1.165	0.009*	-1.763	0.917	0.055
Share 35 at aMELD = 40	-0.308	0.087	<0.001**	-0.309	0.091	0.001*	-4.334	1.741	0.013*	-2.919	1.403	0.037*

Admissions model completed with zero-truncated Poisson regression and admitted days model by zero-truncated negative binomial regression. Only Share 35 marginal effects displayed. Covariates not displayed include: sex, age, race/ethnicity, liver disease etiology, physiologic MELD score at transplantation, functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. Outcomes, admissions and total admitted days, are inclusive of the index admission and days admitted following transplantation during the index admission, respectively. Margin indicates the difference in predicted number of admissions or admitted days between the pre- and post-Share 35 periods for patients at a given allocation MELD score. * $p<0.05$, ** $p<0.001$. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease score, aMELD – allocation MELD.

5I. Sensitivity Analysis – State Residence

	Admissions						Admitted Days					
	Including Possible Out of State			Excluding Possible Out of State			Including Possible Out of State			Excluding Possible Out of State		
	n = 6156			n = 5972			n = 6156			n = 5972		
H2a – Full effect of Share 35, through medical condition & organ availability	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margins**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35	-0.113	0.056	0.044*	-0.111	0.058	0.055	-0.325	1.104	0.769	-0.062	1.148	0.957
H2b – Partial effect of Share 35 through organ availability; no interaction	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margins**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35	-0.139	0.055	0.012*	-0.084	0.060	0.161	-1.974	0.971	0.042*	-1.832	1.010	0.070
H2c – Partial effect of Share 35 through organ availability, accounting for the moderating effect of aMELD score	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD = 10	0.180	0.151	0.234	0.241	0.161	0.133	1.014	2.063	0.623	1.031	2.143	0.630
Share 35 at aMELD = 15	0.112	0.123	0.361	0.167	0.130	0.201	0.453	1.769	0.798	0.504	1.846	0.785
Share 35 at aMELD = 20	0.039	0.095	0.679	0.087	0.101	0.387	-0.218	1.443	0.88	-0.129	1.513	0.932
Share 35 at aMELD = 25	-0.039	0.071	0.585	0.002	0.075	0.979	-1.014	1.127	0.369	-0.886	1.185	0.455
Share 35 at aMELD = 30	-0.122	0.056	0.030*	-0.089	0.059	0.130	-1.952	0.960	0.042*	-1.781	1.001	0.075
Share 35 at aMELD = 35	-0.212	0.063	0.001*	-0.187	0.064	0.004*	-3.051	1.165	0.009*	-2.837	1.198	0.018*
Share 35 at aMELD = 40	-0.308	0.087	<0.001**	-0.291	0.089	0.001*	-4.334	1.741	0.013*	-4.074	1.790	0.023*

Admissions model completed with zero-truncated Poisson regression and admitted days model by zero-truncated negative binomial regression. Patients classified as "possible out of state" if either the utilization (OSHPD or HCUP) or transplant registry indicate the patient lived in a state other than that of the transplant center while the other registry indicated the patient was a state resident. Only Share 35 marginal effects displayed. Covariates not displayed include: sex, age, race/ethnicity, liver disease etiology, physiologic MELD score at transplantation, functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. Outcomes, admissions and total admitted days, are inclusive of the index admission and days admitted following transplantation during the index admission, respectively. Margin indicates the difference in predicted number of admissions or admitted days between the pre- and post-Share 35 periods for patients at a given allocation MELD score. * $p<0.05$, ** $p<0.001$. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease score, aMELD - allocation MELD.

5J. Sensitivity Analysis – Inclusion of Patients who Underwent Simultaneous Liver + Kidney Transplantation

	Admissions Model								
	All n = 6156			Excluding Liver Kidney n = 5702			Liver-Kidney Covariate n = 6156		
H2a – Full effect of Share 35, through medical condition & organ availability	**Margin**	**SE**	**p-value**	**Margins**	**SE**	**p-value**	**Margins**	**SE**	**p-value**
Share 35	-0.113	0.056	0.044*	-0.180	0.057	0.002*	-0.114	0.056	0.042*
Liver-kidney covariate	--	--	--	--	--	--	0.360	0.092	<0.001**
H2b – Partial effect of Share 35 through organ availability; no interaction	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35	-0.139	0.055	0.012*	-0.151	0.059	0.010*	-0.139	0.055	0.012*
Liver-kidney covariate	--	--	--	--	--	--	-0.027	0.086	0.751
H2c – Partial effect of Share 35 through organ availability, accounting for the moderating effect of allocation MELD score	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD = 10	0.180	0.151	0.234	0.248	0.156	0.113	0.180	0.151	0.235
Share 35 at aMELD = 15	0.112	0.123	0.361	0.154	0.126	0.220	0.112	0.123	0.363
Share 35 at aMELD = 20	0.039	0.095	0.679	0.054	0.096	0.573	0.039	0.095	0.681
Share 35 at aMELD = 25	-0.039	0.071	0.585	-0.052	0.071	0.468	-0.039	0.071	0.583
Share 35 at aMELD = 30	-0.122	0.056	0.030*	-0.165	0.058	0.004*	-0.123	0.056	0.030*
Share 35 at aMELD = 35	-0.212	0.063	0.001*	-0.285	0.065	<0.001**	-0.212	0.063	0.001*
Share 35 at aMELD = 40	-0.308	0.087	<0.001**	-0.413	0.090	<0.001**	-0.308	0.087	<0.001**
Liver-kidney covariate	--	--	--	--	--	--	-0.026	0.086	0.766

Admissions model by zero-truncated Poisson regression. Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. * p<0.05, **p<0.001. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease, aMELD – allocation MELD score, GED - general equivalency diploma.

	Admitted Days Model								
	All n = 6156			Excluding Liver Kidney n = 5702			Liver-Kidney Covariate n = 6156		
H2a – Full effect of Share 35, through medical condition & organ availability	**Margins**	**SE**	**p-value**	**Margins**	**SE**	**p-value**	**Margins**	**SE**	**p-value**
Share 35	-0.325	1.104	0.769	-0.922	1.126	0.413	-0.532	1.097	0.628
Liver-kidney covariate	--	--	--	--	--	--	10.938	2.098	<0.001**
H2b – Partial effect of Share 35 through organ availability; no interaction	**Margins**	**SE**	**p-value**	**Margins**	**SE**	**p-value**	**Margins**	**SE**	**p-value**
Share 35	-1.974	0.971	0.042*	-2.426	0.983	0.014*	-2.002	0.969	0.039*
Liver-kidney covariate	--	--	--	--	--	--	1.979	1.891	0.295
H2c – Partial effect of Share 35 through organ availability, accounting for the moderating effect of allocation MELD score	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD = 10	1.014	2.063	0.623	0.604	2.065	0.770	1.003	2.058	0.626
Share 35 at aMELD = 15	0.453	1.769	0.798	0.018	1.765	0.992	0.438	1.764	0.804
Share 35 at aMELD = 20	-0.218	1.443	0.88	-0.675	1.435	0.638	-0.238	1.439	0.869
Share 35 at aMELD = 25	-1.014	1.127	0.369	-1.489	1.123	0.185	-1.038	1.124	0.356
Share 35 at aMELD = 30	-1.952	0.960	0.042*	-2.441	0.972	0.012*	-1.980	0.958	0.039*
Share 35 at aMELD = 35	-3.051	1.165	0.009*	-3.548	1.196	0.003*	-3.084	1.163	0.008*
Share 35 at aMELD = 40	-4.334	1.741	0.013*	-4.830	1.778	0.007*	-4.371	1.736	0.012*
Liver-kidney covariate	--	--	--	--	--	--	1.990	1.891	0.293

Admitted days model by zero-truncated Poisson regression. Only covariates of interest displayed; covariates not displayed include: sex, age, functional status, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), race/ethnicity, hospital density, primary care density, specialist care density, zip code median income by quartile, rural urban continuum and transplant center. * p<0.05, **p<0.001. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease, aMELD – allocation MELD score, GED - general equivalency diploma.

5K. Sensitivity Analysis – Categorical Interaction Term for Allocation MELD Score and Share 35

	Admissions			Admitted Days		
Continuous aMELD	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD = 10	0.180	0.151	0.234	1.014	2.063	0.623
Share 35 at aMELD = 15	0.112	0.123	0.361	0.453	1.769	0.798
Share 35 at aMELD = 20	0.039	0.095	0.679	-0.218	1.443	0.88
Share 35 at aMELD = 25	-0.039	0.071	0.585	-1.014	1.127	0.369
Share 35 at aMELD = 30	-0.122	0.056	0.030*	-1.952	0.960	0.042*
Share 35 at aMELD = 35	-0.212	0.063	0.001*	-3.051	1.165	0.009*
Share 35 at aMELD = 40	-0.308	0.087	<0.001**	-4.334	1.741	0.013*
Binary aMELD	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Pre-Share 35, aMELD < 35	0.058	0.084	0.495	-1.473	1.547	0.341
Pre-Share 35, aMELD ≥35	ref	--	--	ref	--	--
Post-Share 35, aMELD < 35	-0.033	0.104	0.748	-3.094	1.875	0.099
Post-Share 35, aMELD ≥35	-0.194	0.086	0.024*	-2.463	1.554	0.113
3 Group aMELD	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Pre-Share 35, aMELD <20	-0.275	0.116	0.018*	-5.267	2.240	0.019
Pre-Share 35, aMELD 20-29	-0.059	0.076	0.433	-1.267	1.301	0.330
Pre-Share 35, aMELD ≥30	ref	--	--	ref	--	--
Post-Share 35, aMELD <20	-0.070	0.201	0.727	-0.142	3.579	0.968
Post-Share 35, aMELD 20-29	-0.155	0.112	0.165	-4.443	1.824	0.015*
Post-Share 35, aMELD ≥30	-0.215	0.072	0.003*	-2.258	1.239	0.069

Admissions model completed with zero-truncated Poisson regression and admitted days model by zero-truncated negative binomial regression. Only Share 35 marginal effects displayed. Covariates not displayed include: sex, age, race/ethnicity, liver disease etiology, physiologic MELD score (defined as allocation MELD score and MELD difference in continuous model), functional status at transplant, comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, renal disease, vascular disease), hospital density, primary care density, specialist care density, zip code median income by quartile, distance to the transplant center, rural/urban continuum and transplant center. Outcomes, admissions and total admitted days, are inclusive of the index admission and days admitted following transplantation during the index admission, respectively. Margin indicates the difference in predicted number of admissions or admitted days between the pre- and post-Share 35 periods for patients at a given allocation MELD score for the continuous allocation MELD model and the difference between the stated category and the reference value for the binary and 3 group allocation MELD score analyses. * p<0.05, **p<0.001. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease score, aMELD – allocation MELD score.

Question 3 – Sensitivity Analyses & Supplemental Information

6A. Predicted Probabilities of Returning to Work Pre- and Post-Share 35 by Allocation MELD Score, Sex and Pre-Transplant Work Status

	Not Working Pre-Transplant, Males				Not Working Pre-Transplant, Females			
	Pre-Share 35		Post-Share 35		Pre-Share 35		Post-Share 35	
	Pred. Prob.	**SE**	**Pred. Prob.**	**SE**	**Pred. Prob.**	**SE**	**Pred. Prob.**	**SE**
Share 35 at aMELD = 10	0.233	0.022	0.196	0.030	0.118	0.022	0.100	0.027
Share 35 at aMELD = 15	0.234	0.017	0.209	0.024	0.130	0.018	0.116	0.023
Share 35 at aMELD = 20	0.236	0.012	0.222	0.018	0.143	0.013	0.135	0.019
Share 35 at aMELD = 25	0.237	0.007	0.235	0.013	0.158	0.008	0.155	0.013
Share 35 at aMELD = 30	0.239	0.005	0.249	0.010	0.173	0.006	0.178	0.009
Share 35 at aMELD = 35	0.240	0.008	0.264	0.013	0.190	0.011	0.203	0.013
Share 35 at aMELD = 40	0.242	0.013	0.278	0.020	0.207	0.019	0.231	0.023

Logistic regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, difference between physiologic and allocation MELD score, functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), count of follow-up visits and transplant center. Predicted Probability indicates the likelihood of returning to work post-transplant for a given sex, pre-transplant work status and allocation MELD score. *p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, aMELD = allocation MELD score, Prob. - predicted probability, SE - standard error.

	Working Pre-Transplant, Males			
	Pre-Share 35		Post-Share 35	
	Pred. Prob.	**SE**	**Pred. Prob.**	**SE**
Share 35 at aMELD = 10	0.695	0.043	0.630	0.050
Share 35 at aMELD = 15	0.705	0.030	0.655	0.035
Share 35 at aMELD = 20	0.715	0.018	0.680	0.023
Share 35 at aMELD = 25	0.725	0.010	0.704	0.018
Share 35 at aMELD = 30	0.735	0.014	0.727	0.024
Share 35 at aMELD = 35	0.744	0.023	0.749	0.033
Share 35 at aMELD = 40	0.753	0.033	0.770	0.042

Logistic regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, difference between physiologic and allocation MELD score, functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), count of follow-up visits and transplant center. Predicted Probability indicates the likelihood of returning to work post-transplant for a given sex, pre-transplant work status and allocation MELD score. *p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, aMELD = allocation MELD score, Prob. - predicted probability, SE - standard error.

6B. Comparison of Patients with a Complete and Missing Work Status

Categorical Predictors	Complete Pre-Transplant Work Status n = 13,811		Missing Pre-Transplant Work Status n = 303		p-value
Patient Preferences					
Sex					
Male	6924	67.3%	214	70.6%	0.222
Female	3366	32.7%	89	29.4%	
Ability to Pay for Care					
Insurance Status					
Private insurance	5985	58.2%	181	59.7%	<0.001**
Medicare	1787	17.4%	49	16.2%	
Medicaid	2131	20.7%	36	11.9%	
Veterans Affairs	135	1.3%	30	9.9%	
Self-Pay	41	0.4%	0	0.0%	
Other	211	2.1%	7	2.3%	
Education					
Less than High School/GED	503	4.9%	13	4.3%	<0.001**
High School / GED	4530	44.0%	109	36.0%	
Some college or technical school	2385	23.2%	48	15.8%	
Associate or bachelors degree	1588	15.4%	45	14.9%	
Post-college graduate degree	520	5.1%	14	4.6%	
Unknown	764	7.4%	74	24.4%	
Medical Condition / Disability at Transplant					
Medical Comorbidities					
COPD	182	2.3%	3	1.6%	0.549
Diabetes	2063	20.2%	69	23.2%	0.203
Hypertension	1832	23.3%	61	32.1%	0.005*
Renal failure	1719	20.0%	20	9.4%	<0.001**
Vascular disease	130	1.6%	4	2.1%	0.638
Liver Disease Etiology					
Acute liver failure	175	1.7%	5	1.7%	<0.001**
Autoimmune hepatitis	321	3.1%	8	2.6%	
Cholestatic liver disease	929	9.0%	43	14.2%	
Cryptogenic cirrhosis	404	3.9%	8	2.6%	
Genetic/metabolic	324	3.2%	5	1.7%	
Hepatitis C	1992	19.4%	52	17.2%	
Malignancy	2334	22.7%	103	34.0%	
Steatohepatitis	3364	32.7%	65	21.5%	
Other	446	4.3%	14	4.6%	
Type of Transplant					
Liver only	9572	93.0%	284	93.7%	0.634
Liver + Kidney	718	7.0%	19	6.3%	

Steatohepatitis is inclusive of non-alcoholic steatohepatitis (NASH) and alcoholic steatohepatitis. Primary insurance coverage indicates the patient's primary payer at the time of transplantation. P-value indicates comparison between patients with a complete or missing work status by chi-squared. * indicates $p < 0.05$, ** $p < 0.001$. Abbreviations: GED - General equivalency diploma, COPD - chronic obstructive pulmonary disease.

Continuous Predictors	Complete Pre-Transplant Work Status	Missing Pre-Transplant Work Status
Patient Preferences		
Age (years), n	10290	303
mean	47.797	48.568
range	25 - 55	25 - 55
Mean difference, p-value	-0.770	0.06
Medical Condition / Disability at Transplant		
Liver Disease Severity		
Physiologic MELD at Transplant, n	10290	303
mean	24.158	18.531
range	6 - 40	6 - 40
Mean difference, p-value	5.626	<0.001**
Functional Status		
Karnofsky Score at Transplant, n	10225	287
mean	49.147	63.484
range	10 - 100	10 - 100
Mean difference, p-value	-14.327	<0.001**

P-value indicates comparison between patients with a completed or missing work status by independent samples t-tests. * indicates $p < 0.05$, ** $p < 0.001$. Abbreviations: MELD - model for end stage liver disease.

6C. Sensitivity Analysis – Inclusion of Simultaneous Liver + Kidney Transplants – Work Status

Hypothesis 3a – Mean effect of Share 35, no interaction term

	Not Working Pre-Transplant, Males				Not Working Pre-Transplant, Females			
	All n = 5371		Excluding L+K n = 4964		All n = 2754		Excluding L+K n = 2542	
	Margin	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Share 35	0.010	0.524	0.010	0.514	0.006	0.687	0.008	0.611
	Pred. Prob.	**SE**	**Pred. Prob.**	**SE**	**Pred. Prob.**	**SE**	**Pred. Prob.**	**SE**
Pre-Share 35	0.239	0.005	0.243	0.005	0.173	0.006	0.178	0.006
Post-Share 35	0.249	0.010	0.253	0.010	0.179	0.009	0.186	0.009

Logistic regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, physiologic MELD score, functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), follow-up time and transplant center. Margin indicates the change in the predicted probability of returning to work post-transplant. Predicted probabilities indicates the probability of returning to work in the Pre- or Post-Share 35 periods. *p<0.05, **p<0.001. Abbreviations: Pred. Prob. - predicted probability, SE - standard error, L+K – simultaneous liver and kidney transplant.

Hypothesis 3b – Effect of Share 35 accounting for the moderating effect of allocation MELD score

	Not Working Pre-Transplant, Males				Not Working Pre-Transplant, Females			
	All n = 7149		Excluding L+K n = 6,541		All n = 3,810		Excluding L+K n = 3,477	
	Margin	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Share 35 at aMELD = 10	0.075	0.009*	0.069	0.015*	0.052	0.098	0.054	0.088
Share 35 at aMELD = 15	0.082	0.001*	0.079	0.001*	0.058	0.034*	0.061	0.029*
Share 35 at aMELD = 20	0.090	<0.001**	0.087	<0.001**	0.064	0.005*	0.067	0.004*
Share 35 at aMELD = 25	0.098	<0.001**	0.097	<0.001**	0.069	<0.001**	0.074	<0.001**
Share 35 at aMELD = 30	0.105	<0.001**	0.107	<0.001**	0.076	<0.001**	0.081	<0.001**
Share 35 at aMELD = 35	0.113	<0.001**	0.117	<0.001**	0.082	<0.001**	0.088	<0.001**
Share 35 at aMELD = 40	0.121	<0.001**	0.127	<0.001**	0.088	<0.001**	0.095	<0.001**

Logistic regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, difference between physiologic and allocation MELD score, functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), follow-up time and transplant center. Margin indicates the change in the predicted probability of returning to work post-transplant for a given allocation MELD score. *p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, aMELD - allocation MELD score, L+K - simultaneous liver and kidney transplant.

	Working Pre-Transplant, Males			
	All n = 1408		Excluding L+K n = 1342	
	Margin	**p-value**	**Margin**	**p-value**
Share 35	-0.020	0.497	-0.022	0.429
	Pred. Prob.	**SE**	**Pred. Prob.**	**SE**
Pre-Share 35	0.726	0.010	0.728	0.010
Post-Share 35	0.707	0.019	0.706	0.018

Logistic regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, physiologic MELD score, functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), follow-up time and transplant center. Margin indicates the change in the predicted probability of returning to work post-transplant. Predicted probabilities indicates the probability of returning to work in the Pre- or Post-Share 35 periods. *p<0.05, **p<0.001. Abbreviations: Pred. Prob. - predicted probability, SE - standard error, L+K - simultaneous liver and kidney transplant.

6D. Sensitivity Analysis – Inclusion of Simultaneous Liver + Kidney Transplants – Functional Status

Hypothesis 3a – Mean effect of Share 35, no interaction term

	All n = 33,619			**Excluding L+K n = 30,887**		
6 months Post-Transplant	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35, no interaction	0.272	0.703	0.698	0.217	0.691	0.754
12 months Post-Transplant	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35, no interaction	1.534	0.694	0.027*	1.561	0.679	0.023*

Ordinary least squares regression with fixed effects for transplant center. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, difference between physiologic and allocation MELD, functional status at transplant, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), and follow-up time. Margin indicates the difference between the Pre- and Post-Share 35 periods in the change in functional status score (Karnofsky Score, %) between transplant and 6 or 12 month follow-up. *p<0.05, **p<0.001. Abbreviations: SE - standard error, MELD - Model for End Stage Liver Disease, L+K - simultaneous liver and kidney transplant.

Hypothesis 3b – Effect of Share 35 accounting for the moderating effect of allocation MELD score

	All n = 33,619			Excluding L+K n = 30,887		
6 months Post-Transplant	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD = 10	1.601	1.190	0.179	1.391	1.180	0.241
Share 35 at aMELD = 15	1.226	0.957	0.201	1.055	0.942	0.265
Share 35 at aMELD = 20	0.850	0.776	0.273	0.719	0.757	0.344
Share 35 at aMELD = 25	0.475	0.687	0.489	0.383	0.673	0.570
Share 35 at aMELD = 30	0.100	0.726	0.891	0.048	0.725	0.948
Share 35 at aMELD = 35	-0.276	0.877	0.753	-0.288	0.889	0.746
Share 35 at aMELD = 40	-0.651	1.093	0.552	-0.624	1.117	0.578
12 months Post-Transplant	**Margin**	**SE**	**p-value**	**Margin**	**SE**	**p-value**
Share 35 at aMELD = 10	1.117	1.163	0.337	0.847	1.152	0.464
Share 35 at aMELD = 15	1.235	0.959	0.198	1.051	0.943	0.267
Share 35 at aMELD = 20	1.353	0.796	0.089	1.255	0.778	0.109
Share 35 at aMELD = 25	1.471	0.705	0.037*	1.460	0.689	0.036*
Share 35 at aMELD = 30	1.589	0.713	0.026*	1.664	0.705	0.020*
Share 35 at aMELD = 35	1.706	0.817	0.037*	1.868	0.820	0.025*
Share 35 at aMELD = 40	1.824	0.987	0.065	2.072	1.001	0.041*

Ordinary least squares regression with fixed effects for transplant center. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, MELD difference (allocation MELD - physiologic MELD), functional status at baseline, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), and follow-up time. Margin indicates the difference between the Pre- and Post-Share 35 periods in the change in functional status score (Karnofsky Score, %) between transplant and 6 or 12 month follow-up at the stated allocation MELD score. *p<0.05, **p<0.001. Abbreviations: SE - Standard Error, MELD - Model for End Stage Liver Disease, aMELD - allocation MELD, L+K - simultaneous liver and kidney transplant.

6E. Sensitivity Analysis – Categorical Allocation MELD Score – Work Status

	Not Working Pre-Transplant				Working Pre-Transplant			
	Males n = 5371		Females n = 2,754		Males n = 1,408		Females n = 424	
Continuous aMELD	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Share 35 at aMELD = 10	-0.036	0.243	-0.018	0.529	-0.065	0.293	-0.187	0.081
Share 35 at aMELD = 15	-0.026	0.329	-0.014	0.580	-0.049	0.285	-0.086	0.281
Share 35 at aMELD = 20	-0.014	0.508	-0.009	0.675	-0.035	0.312	0.015	0.809
Share 35 at aMELD = 25	-0.002	0.903	-0.003	0.879	-0.021	0.473	0.114	0.047*
Share 35 at aMELD = 30	0.010	0.499	0.005	0.734	-0.007	0.816	0.210	0.003*
Share 35 at aMELD = 35	0.023	0.169	0.014	0.440	0.005	0.897	0.302	0.001*
Share 35 at aMELD = 40	0.036	0.091	0.024	0.368	0.017	0.735	0.389	0.001*
Binary aMELD	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Pre-Share 35, aMELD < 35	-0.004	0.778	-0.007	0.773	-0.018	0.789	0.239	0.075
Pre-Share 35, aMELD ≥35	ref	--	ref	--	ref	--	ref	--
Post-Share 35, aMELD < 35	-0.003	0.896	-0.007	0.788	-0.043	0.531	0.324	0.026*
Post-Share 35, aMELD ≥35	0.023	0.284	0.019	0.436	0.016	0.850	0.434	0.004*
3 Group aMELD	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**	**Margin**	**p-value**
Pre-Share 35, aMELD <20	0.007	0.786	-0.032	0.310	0.062	0.198	0.239	0.087
Pre-Share 35, aMELD 20-29	0.008	0.642	-0.047	0.051	-0.017	0.685	0.147	0.144
Pre-Share 35, aMELD ≥30	ref	--	ref	--	ref	--	ref	--
Post-Share 35, aMELD <20	-0.026	0.508	-0.137	0.022*	-0.212	0.736	0.012	0.928
Post-Share 35, aMELD 20-29	0.014	0.549	-0.028	0.279	-0.037	0.432	0.284	0.040*
Post-Share 35, aMELD ≥30	0.021	0.253	0.010	0.600	0.020	0.708	0.395	<0.001**

Logistic regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, difference between physiologic and allocation MELD score, functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), count of follow-up visits and transplant center. Margin indicates the change in the predicted probability of returning to work post-transplant for a given allocation MELD score for continuous allocation MELD model. Margin indicates difference in predicted probability of returning to work as compared to the reference value for binary and 3 group allocation MELD analyses. *p<0.05, **p<0.001.
Abbreviations: MELD - Model for End Stage Liver Disease, aMELD – allocation MELD.

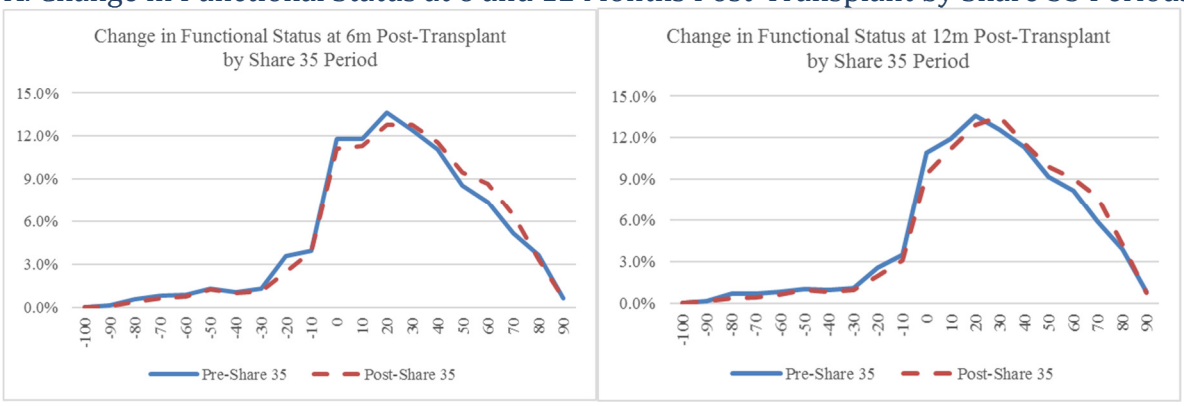
6F. Sensitivity Analysis – Categorical Allocation MELD Score – Functional Status

	6 Months Post-Transplant		12 Months Post-Transplant	
	n = 33,619		n = 33,619	
Continuous Allocation MELD	**Margin**	**p-value**	**Margin**	**p-value**
Share 35 at aMELD = 10	1.601	0.179	1.117	0.337
Share 35 at aMELD = 15	1.226	0.201	1.235	0.198
Share 35 at aMELD = 20	0.850	0.273	1.353	0.089
Share 35 at aMELD = 25	0.475	0.489	1.471	0.037*
Share 35 at aMELD = 30	0.100	0.891	1.589	0.026*
Share 35 at aMELD = 35	-0.276	0.753	1.706	0.037*
Share 35 at aMELD = 40	-0.651	0.552	1.824	0.065
Binary Allocation MELD	**Margin**	**p-value**	**Margin**	**p-value**
Pre-Share 35, aMELD < 35	-9.877	<0.001**	-9.309	<0.001**
Pre-Share 35, aMELD ≥35	ref	--	ref	--
Post-Share 35, aMELD < 35	-8.268	<0.001**	-6.740	<0.001**
Post-Share 35, aMELD ≥35	-1.079	0.403	1.324	0.243
3 Group Allocation MELD	**Margin**	**p-value**	**Margin**	**p-value**
Pre-Share 35, aMELD <20	-7.937	<0.001**	-7.341	<0.001**
Pre-Share 35, aMELD 20-29	-7.141	<0.001**	-6.660	<0.001**
Pre-Share 35, aMELD ≥30	ref	--	ref	--
Post-Share 35, aMELD <20	-6.099	<0.001**	-5.294	0.001*
Post-Share 35, aMELD 20-29	-4.949	<0.001**	-3.531	0.007*
Post-Share 35, aMELD ≥30	-0.592	0.636	1.443	0.205

Ordinary least squares regression. Only covariates of interest displayed. Covariates not displayed include: insurance, education, demeaned allocation MELD score, difference between physiologic and allocation MELD score, functional status at transplantation, liver disease etiology, medical comorbidities (diabetes, hypertension, COPD, renal failure, vascular disease), follow-up time and transplant center. Margin indicates the difference between the Pre- and Post-Share 35 periods in the change in functional status score (Karnofsky Score, %) between transplant and 6 or 12 month follow-up at the stated allocation MELD score. Margin indicates difference in change in functional status (Karnofsky Score, %) as compared to the reference value for binary and 3 group allocation MELD analyses. *p<0.05, **p<0.001. Abbreviations: MELD - Model for End Stage Liver Disease, aMELD – allocation MELD score.

6. Discussion – Supplemental Information

7A. Change in Functional Status at 6 and 12 Months Post-Transplant by Share 35 Periods

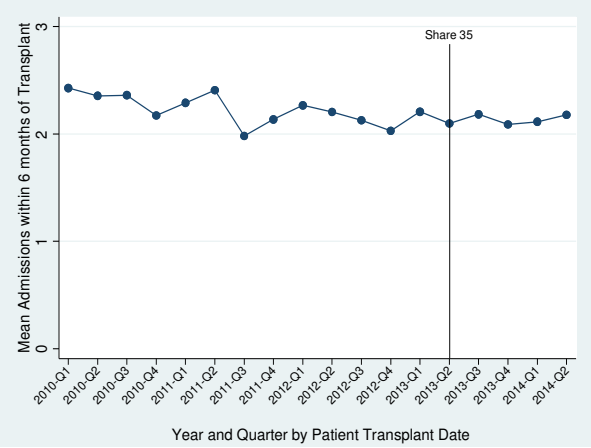


7B. Outcomes – Secular Trends

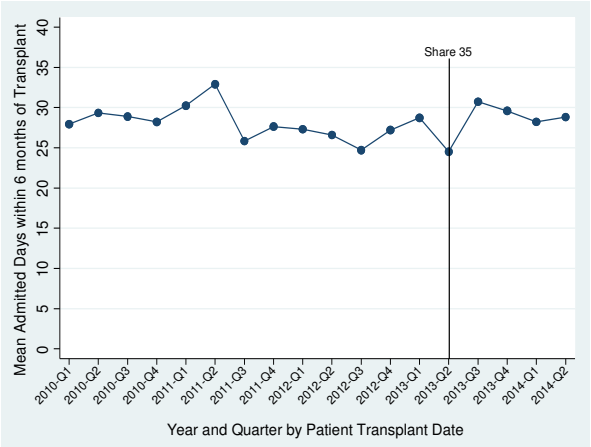
In-Patient Utilization

The secular trends of both admissions (A) and admitted days (B) were plotted by year and quarter. Patients were grouped by transplant dates into year and quarter and then mean number of admissions and admitted days were plotted over time. Share 35 was implemented in June 2013, corresponding to 2013 Quarter 2. There is no visual indication that there is a secular trend occurring prior to the implementation of Share 35.

A.



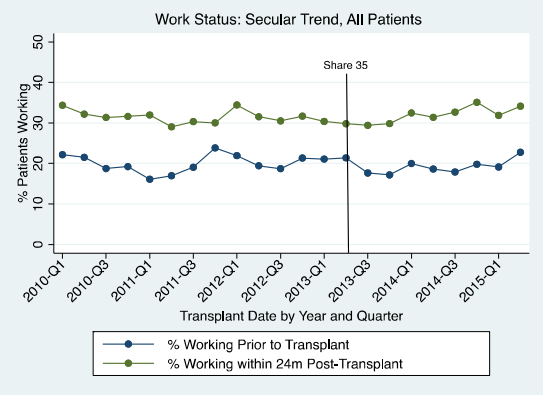
B.



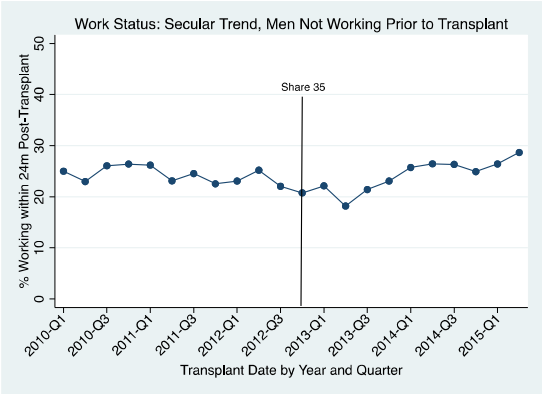
Work Status

The rate of patients working by quarter and year is plotted below. Share 35 was implemented in June 2013, corresponding to 2013 quarter 2, which is indicated on the graphs below. (A) Rates of pre- and post-transplant work status for all patients over time. (B) Rate of working post-transplant amongst men not working prior to transplant. (C) Rate of working post-transplant amongst females not working prior to transplant over time. (D) Rate of working post-transplant amongst men working prior to transplant over time.

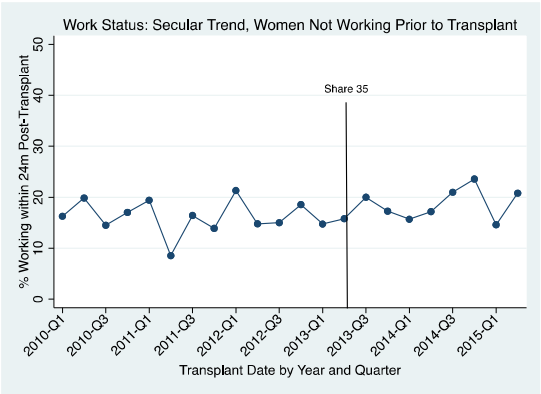
A.



B.



C.



D.