

September 11, 2018

American College of Surgeons
633 N Saint Clair Street
Chicago, IL 60611

Dear Members of the American College of Surgeons Scholarship Committee,

Thank you for your consideration of my proposed research project, *The Impact of Domestic and International Travel for Transplantation on Disparities in United States Solid Organ Transplantation*, for the 2019-2021 American College of Surgeons Resident Research Scholarship. I am applying for this opportunity to provide financial support for a two-year research plan that will serve as a foundation for a career in academic transplant surgery.

Upon completion of my residency in general surgery, I plan to pursue a fellowship in abdominal transplant surgery. I am passionate about transplantation because it is an exciting multidisciplinary field with elements of surgery, medicine, research, ethics, and policy. Since my first year of medical school at the University of California, San Francisco (UCSF), I have been mentored by Dr. Nancy Ascher, who has been instrumental in my development as a clinician and surgeon. As a direct result, my goal is to become a transplant surgeon scientist who is not only technically and clinically skilled, but also engaged with professional societies and active in leadership roles at the institutional, national, and international levels.

In order to achieve these goals, I must first establish a solid foundation in clinical decision making, technical skills, and research capabilities, and it will be the goal of my two dedicated research years to focus on the latter. In particular, I aim to bolster my skills in biostatistics, data analysis and management, and study design during these two years by completing the requirements for a Master's in Clinical Research, as offered through UCSF's Training in Clinical Research program.

The proposed research protocol provides a roadmap to achieving my career goals. The overall proposal, and each of the aims specifically, require database management and biostatistical analysis in order to generate results. The core of the proposed research, therefore, will dovetail appropriately with my proposed coursework and academic training. Equally important is my ability to continue working with Dr. Ascher and my co-mentor, Dr. Peter Stock. As the former Chair of the Department of Surgery at UCSF, Past President of The Transplantation Society, and member of the World Health Organization Task Force on Donation and Transplantation of Human Organs and Tissues, Dr. Ascher is uniquely able to advocate for my professional advancement within the field of transplantation. Dr. Stock is the Surgical Director of the Kidney and Pancreas Transplant Program at UCSF as well as the Chair of the Department of Surgery Research Committee. In these roles, he will help cultivate my development as leader in academic surgery.

In summary, by supporting my training in outcomes research and facilitating relationships with impactful mentors, the ACS Resident Research Scholarship will provide an unparalleled opportunity for professional development. Thank you in advance for your consideration.

Sincerely,



Hillary J. Braun, MD

Brief Research Plan

Title of Research Plan

The Impact of Domestic and International Travel for Transplantation on Disparities in United States Solid Organ Transplantation

Summary

The purpose of my research project is to characterize the impact of domestic and international travel for transplantation on the organ transplant system in the United States (US). Each year in the US, more than 30,000 solid organ transplants are performed¹, but the demand for organs continues to outpace the supply, and as a result, nearly 7000 people die each year awaiting transplant². Organs are allocated according primarily to disease severity (liver) and waiting time (kidney) and are distributed within arbitrary geographic regions in the US. Patients awaiting transplant, therefore, face different waiting times according to the area of the country in which they reside. Patients who have the means to travel- either within the US or from foreign countries to the US- are technically permitted to do so, but it is hypothesized that their presence may cause increased competition within regions and detrimentally impact the waitlisted patients who do not have the luxury of mobility. In the US, as many as 10% of individuals listed for kidney or liver transplantation travel to regions outside of their home region where it is perceived they may have a better chance at a more timely transplant^{3,4}. International travelers, referred to as non-citizen, non-residents (NCNR), make up approximately 2% of the transplant population each year, but the amount of transplants performed in these patients is highly variable according to region⁵.

The objective of this scholarship will be to provide funding for academic coursework and salary support during my dedicated two years of research. Our proposed study will utilize data available from the United Network for Organ Sharing (UNOS) and the Scientific Registry of Transplant Recipients (SRTR). These organizations provide comprehensive demographic and outcomes data on organ donors, transplant candidates, and transplant recipients. We will address three primary aims in both liver and kidney transplant populations: 1) compare demographics of domestic travelers, international travelers, and non-traveler patients; 2) compare outcomes of domestic travelers, international travelers, and non-traveler patients; 3) determine the impact of domestic and NCNR travelers on waitlisted transplant candidates in the destination regions. Our overall goal is to generate data to inform national policy around domestic and international travel for transplantation.

Goals for Scholarship Period

1. Strengthen my foundation in study design, biostatistics, and data management.

To date, my experience in study design, biostatistics, and data management has come largely from experience, independent study, and consultation with statisticians. In order to lay a concrete foundation in clinical research, it is essential that I supplement my existing knowledge with formal training in each of these three domains. The Master's in Clinical Research through the University of California, San Francisco (UCSF) Training in Clinical Research (TICR) program will provide me with the coursework and structure necessary to firmly establish these tools in my research armamentarium.

2. Develop my skills in scientific writing and communication.

A critical part of academic surgery is the ability to translate research findings into clinical practice, and this relies on one's ability to communicate effectively. In order to further hone my skills in scientific writing, audiovisual presentations, and grant writing, I will take the Scientific Writing Course offered by the UCSF Department of Surgery and the Grant Writing Workshop through TIGR.

3. Accrue experience presenting research at academic meetings.

While refining my ability to communicate, I will simultaneously submit abstracts to institutional, national, and international meetings to gain experience and exposure presenting in these forums. We plan to present the findings of this research, which aims to describe the impact of travel for transplantation on disparities in kidney and liver transplantation, at a number of major academic surgical conferences, including the Academic Surgical Congress, the Scientific Forum of the American College of Surgeons, the American Transplant Congress, and The Transplantation Society.

4. Seek professional development and academic career cultivation.

I am fortunate to have two mentors who have held a variety of institutional, national, and international leadership positions. Dr. Ascher is the former Chair of the Department of Surgery at UCSF, Past President of The Transplantation Society, and member of the World Health Organization Task Force on Donation and Transplantation of Human Organs and Tissues. As a result, Dr. Ascher is in the unique position to understand the dynamics of international transplantation and will serve as a critical liaison between our work and the international transplant community. I will meet with Dr. Ascher weekly to review our progress on this project and discuss any issues that arise. Dr. Stock is a senior advisor to the SRTR, an at large UNOS board member, and principal investigator in The Transplantation Lab at UCSF; as a result, I will be integrated into his weekly lab meetings and monthly educational seminars. I will also work closely with Dr. Ryutaro Hirose, a Professor of Surgery and abdominal transplant surgeon at UCSF, whose research has focused on organ allocation policy in the US for the past 20 years.

As a surgery research fellow at UCSF, I will also participate in weekly clinical and research conferences within the Department of Surgery and Division of Transplantation. I will have the opportunity to present my works in progress at lab meetings within UCSF and to the entire Department of Surgery on at least two occasions during each research year. An additional component of my work at UCSF will involve clinical coverage for the inpatient kidney transplant and liver transplant services, as well as deceased donor organ recovery.

5. Gain leadership experience.

An understanding of leadership techniques and acquisition of skills and experience in leadership roles is essential for success in academic surgery. My mentors have begun integrating me into leadership roles within various societies related to transplantation. For example, with Dr. Ascher's oversight, I am serving as the US liaison to the Overseas Transplant Registry, a collaborative international effort aimed at collecting data on international travel for transplantation. I am in the process of becoming a board member

for The Transplantation Society's Young Member Committee and am working with the chairs of Women in Transplantation to establish a trainee group. I will continue to develop these opportunities and seek out additional opportunities for leadership throughout the period of this scholarship.

Activities Planned Under This Award

Year 1: July 2019-July 2020

Research: The majority of my efforts during my first year of the scholarship will be focused on data acquisition, database management, and initial statistical analyses. These efforts will be supplemented by my didactic training in these domains.

Didactic Learning: The first year of coursework in the TICR program will consist of the following courses: Designing Clinical Research, Epidemiological Methods, Biostatistical Methods for Clinical Research, Database Management Systems for Clinical Research, Statistical Computing in Clinical Research.

Presentations: Internally, I will present preliminary data at the UCSF Grand Rounds series in December 2019 and at our Resident Research Symposium in June 2020. I will submit preliminary data to the 2020 American Transplant Congress and 2020 Meeting of the Transplantation Society. I will also attend the 2019 American College of Surgeons Clinical Congress.

Career Development: I will interact with the Transplant Surgery division through the Transplant Seminar Series, will attend lab meetings of The Transplantation Lab, and will participate in the Department of Surgery educational program which includes weekly service and teaching conferences. I will meet weekly with Dr. Ascher and twice monthly with Dr. Stock.

Manuscript Preparation: In preparation for ensuing manuscripts, I will take the aforementioned Scientific Writing Course offered by the UCSF Department of Surgery and the Grant Writing Workshop through TICR.

Year 2: July 2020-July 2021

Research: After the dataset is established and cleaned during year one, the second year of this scholarship will focus on statistical analyses, which we will refine and mature as necessary according to the feedback we receive during presentations of our initial data. I aim to have the final analyses completed by December 2020 to allow time to prepare the data for manuscript submission.

Didactic Learning: The majority of formal didactic training will be completed in Year 1. However, anticipated coursework in Year 2 includes Introduction to the Science of "Big Data", Medical Informatics, and advanced courses in the biostatistical methods series.

Presentations: I will attend the Clinical Congress of the American College of Surgeons to present our findings at the Scientific Forum. I will also submit our findings to the 2021 American Transplant Congress.

Career Development: I will continue to meet regularly with my mentors and participate in the education conferences offered by the Department of Surgery and the Division of Transplantation.

Manuscript Preparation: I will focus on manuscript preparation and revision. I anticipate our study will result in 2-3 manuscripts, and my goal will be to have these submitted by March 2021 to allow time for revision and acceptance prior to my return to clinical duties in July 2021.

Addenda

1. Global Observatory of Donation and Transplantation. *Global Observer of Donation and Transplantation* 2018; <http://www.transplant-observatory.org>. Accessed 7/18/2018, 2018.
2. OPTN Waiting List Data. 2018; <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#>, 2019.
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EXPANDED RESEARCH PROJECT DESCRIPTION

A. Hypothesis and Specific Aims

Allocation of organs for transplantation in the United States (US) is governed by “The Final Rule”, a federal law implemented in 1998 that outlines the function of the Organ Procurement and Transplantation Network (OPTN) and establishes a framework for organ allocation³. In theory, organ allocation is based on the principles of equity, utility, and efficiency, and in accordance with The Final Rule, should not penalize patients awaiting transplantation based on socioeconomic status or geographic location³. Unfortunately, a plethora of geographic, socioeconomic, and racial disparities in access to transplantation have been identified.

Currently, two specific phenomena exacerbate these disparities and challenge the ethical pillars of organ allocation: 1) multiple listings for transplantation and 2) international travel for transplantation. With multiple listings, US transplant candidates are permitted to be listed at more than one transplant center in order to decrease their time on the waiting list. With travel for transplantation, non-citizen non-resident (NCNR) transplant candidates may receive a transplant in the US, using organs from US donors, despite their status as visitors. **The overall goal** of our research is to characterize the impact of both multiple listings for transplantation and travel for transplantation on the organ transplant system in the US. **The specific objective** of this proposal is to examine the impact of multiple listings and travel for transplant on liver and kidney transplant recipients and on the waitlist population that is displaced by these travelers. **The central hypothesis** is that travel for transplantation (domestic and international) provides an advantage to patients with the means to travel and undermines the organ allocation system in the travel destinations, which adversely impacts patients awaiting transplant in those areas. **The ultimate goal of this proposal** is to generate data to inform national policy decisions around domestic and international travel for transplantation. We have three specific hypotheses which will be tested with the following aims:

Hypothesis 1: Patients who travel domestically for transplantation are more affluent, more highly educated, and more often Caucasian than those who are listed at the home or destination center but do not travel.

Aim 1. Describe the demographics of patients who travel both domestically and internationally (NCNR) for transplantation and compare these with the demographics of waitlisted patients at both the home and destination centers. *Using data from the United Network for Organ Sharing (UNOS), compare demographics between traveler and non-traveler candidates awaiting a) liver transplantation, and b) kidney transplantation.*

Hypothesis 2: Patients who travel for transplantation (both domestic and NCNR) have better outcomes than patients with comparable disease severity listed at the home and destination centers.

Aim 2. Compare the pre- and post-transplant outcomes of traveling patients with those of patients listed for transplant who do not travel. *On a national level, using data from UNOS and the Scientific Registry of Transplant Recipients (SRTR), compare outcomes among multiply-listed, NCNR, and singly-listed patients awaiting a) liver transplantation, and b) kidney transplantation.*

Hypothesis 3: The presence of domestic and NCNR travelers in a given donor service area (DSA) adversely impacts non-travelers awaiting transplant in that DSA.

Aim 3. Determine the impact of domestic and NCNR travelers on waitlisted transplant candidates in the destination DSAs. *At the level of DSAs, examine the trends in multiply-listed transplant candidates and NCNR imports and analyze the effect of these traveling patients on non-travelers awaiting a) liver transplantation, and b) kidney transplantation.*

B. Significance

Each year, more than 30,000 solid organ transplants are performed in the US⁵. Nevertheless, the number of patients awaiting solid organ transplantation continues to outpace the donor organ supply by 400%⁶. Consequently, patients are forced to endure long periods on the transplant waitlists, and nearly 7000 people die each year waiting for transplant in the US⁶.

The demand for solid organs has always exceeded the donor supply, and it is this incongruity that drives the evolution of allocation policy. The distribution of this limited resource relies on a system that prioritizes and balances equity, utility, and efficiency. However, the success of solid organ transplantation is wholly dependent on the altruism of donors and donor families. As such, the field of transplantation must constantly earn and maintain the public trust. While technically permissible, the phenomena of multiple listing and travel for transplantation disrupt the intended system of equitable organ allocation. As a result, they pose a significant threat to the public's perception of equitable organ allocation, as prior work has shown that multiply-listed patients are more often white, male, privately insured, and more highly educated than singly-listed patients^{1,7}. Protecting the equitable distribution of deceased donor organs is paramount to ensuring the longevity of transplant in this country, and this mandates an examination of domestic and international travel for transplantation and the impact this has on our system and the patients awaiting transplantation. The proposed study will provide comprehensive data about the impact of travel for transplantation on kidney and liver transplant waitlist candidates and recipients; the goal is to use this data to develop national policies to ensure that travelers do not detract from our organ allocation system.

C. Background

The National Organ Transplant Act (NOTA) was enacted in 1984 and mandated that deceased donor organs should be regarded as a national resource to be used for the public good⁸. This principle has formed the basis of allocation policy within the U.S. and served as an example for the implementation of other national organ donation systems throughout the world. The current UNOS allocation scheme distributes organs locally (DSAs), regionally, and nationally; there are 11 regions which encompass 58 DSAs across the country. It is important to note that the regions and DSAs are based on arbitrary geographic boundaries.

United States Liver Allocation: Liver allocation proceeds according to the Model for End Stage Liver Disease (MELD) score, which was implemented in 2002 and is a direct reflection of disease severity. The MELD score is calculated based on bilirubin, INR, and creatinine, and ranges from 6 to 40; liver transplantation is indicated for patients with a MELD score >14. There are several exceptions to this laboratory-based allocation scheme, including additional points granted to patients with hepatocellular carcinoma (HCC), potential for additional points based on individual petitions, and Status 1 listing, which is reserved for patients with acute liver failure.

United States Kidney Allocation: In contrast to liver allocation, kidney allocation is multifactorial and driven largely by a transplant candidate's time on the waiting list. Other factors that influence kidney allocation include sensitization, histocompatibility, and Estimated Post-Transplant Survival (EPTS) score, which accounts for a diagnosis of diabetes, prior transplant, age, and time on dialysis.

Domestic Travel for Transplantation: The implementation of the MELD score in 2002 illuminated differences in national and regional disease severity, and highlighted a large disparity among DSAs and regions. These findings suggested that the sickest patients might be disadvantaged according to their location, which is a direct violation of The Final Rule. Differences in waiting time for both liver (**Figure 1, next page**)² and kidney transplants fueled the practice of multiple listings, whereby patients obtain

listing at more than one transplant center in order to gain quicker access to transplantation. This practice was initially approved in 1987 out of respect for patients' autonomy and has subsequently been the topic of considerable debate. The current policy states, "Candidates may be registered for an organ at multiple transplant programs within the same Donation Service Area (DSA) or different DSAs. A transplant program may choose whether or not to accept a candidate seeking multiple registrations for an organ." ⁹ Additionally, transplant centers are obligated to inform patients of waiting times at their institution, provide information regarding waiting times in other parts of the country, and inform them that the rule permits multiple listing.

Previous work has shown that 3-10% of patients travel domestically for transplantation ^{7,10}. In comparison to their peers who do not travel, patients who travel for transplantation have a lower waitlist mortality and shorter time to transplant ¹¹. Among the 11 UNOS regions, regions 1, 5, and 9 perform liver transplants at the highest MELD; as to be expected, the majority of patients who pursue multiple listing come from these regions.

International Travel for Transplantation:

Since the early 2000s, the World Health Organization (WHO) has emphasized the importance of national self-sufficiency. The concept of self-sufficiency is that countries can meet the transplant needs of their citizens and residents through donors from their own population, and through regional collaboration. The importance of self-sufficiency is that it provides all the transplant needs from within a given country and eliminates the need to rely on the population or practices of another country as an organ source ¹².

In accordance with NOTA, citizenship cannot be used as a criteria for transplantation, and as a result, NCNR patients may undergo transplantation in the US. Transplant centers are allowed to perform transplants in NCNR patients; historically, these cases were limited to 5% of the transplant center's volume and recipients were termed "non-resident aliens". Beginning in 2012, UNOS/OPTN required centers to report the residency and citizenship status of all transplant recipients, and for the purposes of simplification, required classification of citizen versus non-citizen and resident versus non-resident. In 2014, this policy changed; the 5% restriction was removed but centers were required to report whether recipients had traveled to the US specifically for the purpose of undergoing transplantation. While the US has successfully established a sustainable deceased donor transplant system, it continues to fall short of meeting the needs of its population in the sense that the demand for organs outweighs the supply. NCNR transplantation, therefore, raises interesting ethical questions regarding the detrimental impact on the U.S.'s ability to achieve self-sufficiency and whether NOTA and the WHO emphasis on self-sufficiency are in conflict.

D. Preliminary Observations

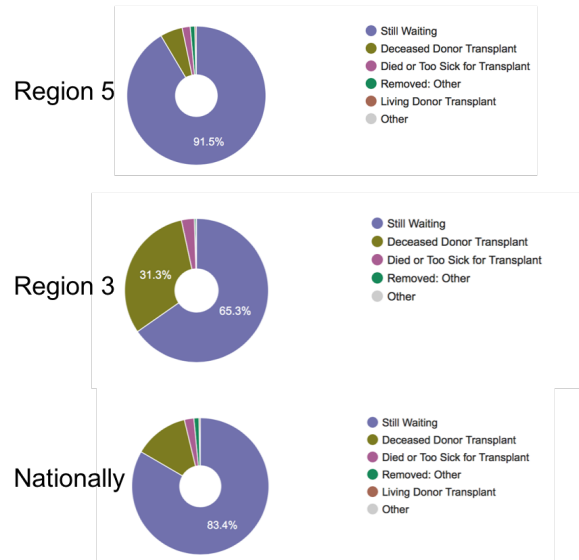


Figure 1. Differences in 30-day outcomes for patients with MELD 25-29 awaiting liver transplant in a high acuity region (5), low acuity region (3), and nationally².

U.S. geographic disparities in access to liver transplantation: The Division of Transplant at UCSF has considerable experience in outcomes research in transplantation, particularly with regard to organ allocation and disparities. Hirose and colleagues have published numerous papers examining geographic disparities and the impact of various policy changes on these disparities¹³⁻¹⁷. Most directly related, Roberts and colleagues conducted the only comprehensive study examining multiple listings in liver transplant recipients since the MELD score was implemented in 2002. Multiply-listed patients accounted for 2.3% of the liver transplant waitlist population, traveled a median of 588 miles to get listed at a second center, and more often were transplanted at the secondary listing DSA and at a lower MELD score¹. This study highlighted the persistent geographic disparities in access to liver transplantation and identified regions to and from which patients most often travel (**Figure 2**).

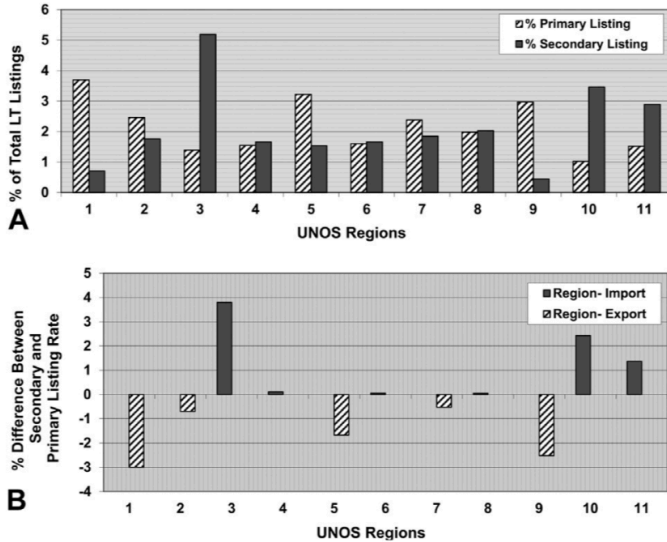


Figure 2. Regional distribution of primary and secondary listings in multiply listed patients¹.

Existing data on international travel for transplantation is sparse; however, our group has begun examining this phenomenon: In 2018, Ascher and colleagues investigated the phenomenon of transplants performed in the United States in NCNR recipients between 2013-2016⁴; 1176 transplants were performed in this cohort, constituting approximately 2% of the total transplant volume in the US during that time period. Approximately 50% of the NCNR patients who underwent transplantation during the study period had traveled to the US with the explicit purpose of undergoing transplantation (**Figure 3**).

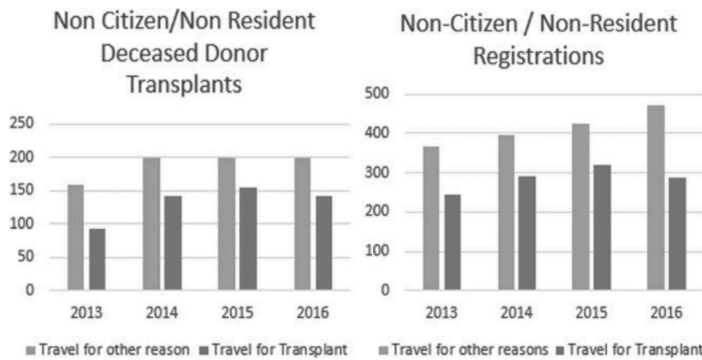


Figure 3. Non-resident, non-citizen patients who underwent transplantation in the US between 2013-2016⁴.

These preliminary findings demonstrate that the US continues to serve as a destination for international travelers seeking transplantation. The authors concluded that a more comprehensive look at transplantation in NCNR patients is essential for ensuring the transparency of organ allocation.

E. Research Plan

Data Sources and Definitions

The study period will be from 2002-2018. This time period was chosen to study organ allocation since the paradigm shifting implementation of the MELD score in 2002. The analyses for all three aims will be performed using data from the United Network for Organ Sharing (UNOS) and the Scientific Registry of Transplant Recipients (SRTR). Income statistics will be determined using the publicly available Census Bureau income statistics by zip code.

The exact data points available from the UNOS dataset on transplant donors, waitlist candidates, and recipients can be reviewed at the following link: <https://transplantpro.org/technology/data-collection-forms/>. All data points referenced below are confirmed to exist in this dataset.

A multiply-listed liver transplant candidate will be defined as follows: any patient >18 years of age who is non-status 1 and listed for liver transplant at more than one center. Using the criteria employed by Roberts et al, patients will be excluded if they were multiply-listed within the same DSA, traveled <50 miles between centers, or lacked time overlap between listings¹.

A multiply-listed kidney transplant candidate will be defined as follows: any patient > 18 years of age who is listed for kidney transplant at more than one center. For the sake of consistency, we will exclude patients in the same fashion as that delineated above for liver transplant candidates.

A domestic traveler is a patient who is multiply-listed for either liver or kidney transplant.

An NCNR transplant candidate will be defined as follows: from 2002 to 2012, any patient listed for liver or kidney transplant recorded as “non-resident alien”; from 2012-2018, any patient listed for liver or kidney transplant recorded as NCNR.

An international traveler is a NCNR.

Study Design and Data Analysis

Aim 1. Describe the demographics of patients who travel both domestically and internationally (NCNR) for transplantation and compare these with the demographics of waitlisted patients at both the home and destination centers. Using data from the United Network for Organ Sharing (UNOS), compare demographics between traveler and non-traveler candidates awaiting **a) liver transplantation, and **b)** kidney transplantation.**

Liver and kidney populations will be analyzed separately. Within each population, we will examine four subgroups: 1) patients awaiting transplant at the home center; 2) patients awaiting transplant at the destination center; 3) domestic travelers; 4) NCNR. Demographic data will include the following: gender, age at listing, ethnicity, blood type, etiology of disease, insurance status, median income according to originating zip code, time on the waiting list (since first listing in the case of domestic travelers), match MELD (liver recipients only), distance from original center, time between first and second listing, distance between first and second listing centers. Demographics will be compared among our four groups using Chi-square and Wilcoxon rank sum tests as appropriate. Multivariate regression models will be used to predict odds of multiple listing.

Aim 2. Compare the pre- and post-transplant outcomes of traveling patients with those of patients listed for transplant who do not travel. On a national level, using data from UNOS and the Scientific

Registry of Transplant Recipients (SRTR), compare outcomes among multiply-listed, NCNR, and singly-listed patients awaiting a) liver transplantation, and b) kidney transplantation.

Liver and kidney populations will be analyzed separately. Within each population, we will examine four subgroups: 1) patients awaiting transplant at the home center; 2) patients awaiting transplant at the destination center; 3) domestic travelers; 4) NCNR. Pre-transplant outcomes will include the following: time on the waiting list, dropout from the waiting list (defined as removal for being too sick, medically unsuitable, or death on the waiting list). Post-transplant outcomes will include graft survival, patient survival, and organ quality. Donor characteristics to be assessed include Donor Risk Index (DRI), which is a composite score indicating risk of deceased donor livers; Kidney Donor Profile Index (KDPI), which is a predictive index of kidney graft failure; age, gender, blood type, ethnicity, share type, graft type, cold ischemia time, cause of death, and CDC high risk. The Kaplan-Meier method will be used to estimate graft and patient survival. The log-rank test will be used to compare graft survival and patient survival between singly-listed patients and multiply-listed patients. Cox proportional hazards regression will be used to determine whether there is an independent effect of multiple listing on post-transplant outcomes. Competing risks regression will be used to evaluate pre-transplant outcomes.

Aim 3. Determine the impact of domestic and NCNR travelers on waitlisted transplant candidates in the destination DSAs. *At the level of DSAs, examine the trends in multiply-listed transplant candidates and NCNR imports over time and analyze the effect of these traveling patients on non-travelers awaiting a) liver transplantation, and b) kidney transplantation.*

Liver and kidney populations will be analyzed separately. We will identify DSAs with a “low” versus a “high” amount of NCNR, multiply listed patients, or both. The exact cutoffs will be determined after we examine the data to see how these travelers are distributed. Our outcomes of interest will be time on the waiting list, dropout from the waiting list (defined as removal for being too sick, medically unsuitable, or death on the waiting list), graft survival, and patient survival. To evaluate these outcomes, we will compare DSAs with a high number of travelers and DSAs with a low number of travelers and use the traveler volume as our predictor variable. To analyze outcomes for waitlisted patients, we will conduct a competing risk regression with transplant as our competing risk¹⁸. To analyze post-transplant outcomes (graft survival, patient survival), we will use Cox proportional hazards regression

Potential Pitfalls

This project proposes the use of data from national registries. We anticipate that the data will be complete, but limited in granularity, as this is often a limitation of data that is systematically collected. We have designed our research plan with this limitation in mind, and have selected only variables that we know to be accessible from the UNOS/SRTR files and the Census Bureau Income Statistics. Our research team at UCSF includes investigators and statistical analysts employed through the UCSF Liver Center who have extensive experience with UNOS data analysis, so we anticipate minimal pitfalls with regard to the methodology. Our IRB approval is pending and we have submitted our request to UNOS for access to this data, so we do not anticipate any significant delays from a regulatory perspective.

Feasibility

Despite the minor potential pitfalls discussed above, we believe this project is highly feasible. The successful completion of this project will involve the acquisition, linkage, and analysis of multiple large datasets. The senior investigators who will mentor this project include Dr. Nancy Ascher, Dr. Peter Stock, and Dr. Ryutaro Hirose. All three investigators are senior transplant surgeon scientists who have extensive experience with outcomes research in transplantation, and have utilized this research to impact public policy both nationally and internationally. During her two years of dedicated research time, Dr. Braun will pursue a Master’s Degree in Clinical Research, which includes rigorous training in

biostatistics, study design, and data analysis. Throughout the period of the grant, the data analysis will be supervised by Jennifer Dodge, MPH, who is a full-time statistician employed through UCSF's Liver Center. Ms. Dodge has collaborated with all of the investigators included in this study and has extensive experience with large dataset management through her work with the following databases: UNOS/OPTN, SRTR, Adult to Adult Living Donor Liver Transplant Study (A2ALL), HCV Partner's, and Women's Interagency HIV Study. As mentioned previously, all of the data points included in this analysis exist in the UNOS dataset (<https://transplantpro.org/technology/data-collection-forms/>). This guaranteed availability ensures we will be able to pursue the aims highlighted in this proposal. Given the availability of the data, the expertise of the research team, and the resources available at UCSF, we are extremely confident in the feasibility of this project.

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