MODELING, SIMULATION, AND ANALYSIS
OF THE US ORGAN TRANSPLANT SYSTEM

by

Christine E. Harvey
A Dissertation
Submitted to the
Graduate Faculty
of
George Mason University
in Partial Fulfillment of
The Requirements for the Degree
of
Doctor of Philosophy
Computational Science and Informatics

Committee:

_____	Dr. Andrew Crooks, Committee Chair
_____	Dr. Robert Weigel, Committee Co-Chair
_____	Dr. James Gentle, Committee Member
_____	Dr. Hamdi Kavak, Committee Member
_____	Dr. Jason Kinser, Department Chairperson
_____	Dr. Donna M. Fox, Associate Dean, Office of Student Affairs & Special Programs, College of Science
_____	Dr. Ali Andalibi, Interim Dean, College of Science
Date: _____	Fall Semester 2019 George Mason University Fairfax, VA

Modeling, Simulation, and Analysis of the US Organ Transplant System

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at George Mason University

By

Christine E. Harvey
Master of Science
Stockton University, 2013
Bachelor of Science
Stockton University, 2011

Director: , Professor
Department of Physics and Astronomy

Fall Semester 2019
George Mason University
Fairfax, VA

Copyright © 2019 by Christine E. Harvey
All Rights Reserved

Dedication

To all those who contributed data to this research.

Acknowledgments

I would like to express my deepest appreciation to my committee and especially my advisor for their support, lessons, and guidance through this entire process. I greatly value everything I've learned during this experience.

I'm extremely grateful to my employer, The MITRE Corporation and my leadership including James Souza, David Goldberg, Dr. Ernie Page, and Jim Dear for encouraging my continuing education and providing valuable lessons along the way that inspired and contributed to this work.

The Computational Science program at Stockton University was instrumental in encouraging me in my academic ambitions. I am extremely grateful to Dr. Russell Manson, Dr. Monir Sharobeam, Dr. Chia-Lin Wu, and Dr. Robert Olsen for taking the time to teach me and so many others through my undergraduate and graduate programs.

I would like to thank the Organ Procurement and Transplantation Network and the United Network for Organ Sharing for providing the data used in this research.

I'm deeply indebted to the Open Science Data Cloud Partnerships for International Research and Education program, especially Dr. Robert Grossman and Dr. Heidi Morgan for giving me the opportunity to learn about and develop a passion for open science while traveling the world. I would also like to acknowledge Dr. Rosa Filgueira Vicente, Dr. Paul Martin, Dr. Malcolm Atkinson, and Dr. Paola Grosso for hosting and mentoring me during my time in the program.

Thanks should also go to my family, both immediate and extended, for their support throughout school and always being there when I needed them.

Finally, I would like to thank the wonderful people in my life that listened to me struggle, reminded me I was capable, brought me coffee, offered a place to stay, and helped in countless other ways. I wouldn't have enjoyed this process without you there.

Table of Contents

List of Tables

List of Figures

Acronyms

ABM Agent-Based Model.

BMI Body Mass Index.

CDC Center for Disease Control.

CIG Caregiver Informant Group.

CKD Chronic Kidney Disease.

CMS Centers for Medicare and Medicaid Services.

CPRA Calculated Panel Reactive Antibody.

CSV Comma Separated Value.

DBD Donor after Brain Death.

DCD Donor after Circulatory Death.

DMV Department of Motor Vehicles.

DSA Donor Service Area.

ECD Expanded Criteria Donor.

EMT Emergency Medical Technician.

EPTS Estimated Post Transplant Survival.

ESRD End Stage Renal Disease.

GFR Glomerular Filtration Rate.

GUI Graphical User Interface.

H.R. House of Representatives.

HCV Hepatitis C Virus.

HHS Department of Health and Human Services.

HLA Human Leukocyte Antigen.

HRSA Health Resources and Services Administration.

ICU Intensive Care Unit.

IRS Internal Revenue Service.

JSON JavaScript Object Notation.

KDPI Kidney Donor Profile Index.

KDRI Kidney Donor Risk Index.

KTPM Kidney Transplant Process Model.

MASON Multi-Agent Simulator Of Neighborhoods.

MELD Model for End-Stage Liver Disease.

NA Not Available.

NOTA National Organ Transplant Act.

ODD Overview, Design Concepts, and Details.

OPO Organ Procurement Organization.

OPTN Organ Procurement and Transplantation Network.

SCD Standard Criteria Donor.

SQL Standardized Query Language.

SRTR Scientific Registry of Transplant Recipients.

STAR Standard Transplant Analysis and Research.

TSV Tab-Separated Values.

UAGA Uniform Anatomical Gift Act.

UNOS United Network for Organ Sharing.

Abstract

MODELING, SIMULATION, AND ANALYSIS OF THE US ORGAN TRANSPLANT SYSTEM

Christine E. Harvey, PhD

George Mason University, 2019

Dissertation Director:

Analysis, modeling, and simulation of organ transplantation and donation can enhance the understanding of this complex system and guide strategic policy improvements. Four major research questions are addressed in this work: (1) how can we further enable data-driven research of the transplant system for future scientists?; (2) what demographic factors influence donations and access to transplantation?; (3) how do laws and policies affect organ donations?; and (4) how do certain patient advantages impact the overall system as well as those lacking advantages?

A data pipeline and associated software were developed and published that address how to further data-driven research of the transplant system for future scientists. This software simplifies access to and analysis of data from proprietary Organ Procurement and Transplantation Network (OPTN) Standard Transplant Analysis and Research (STAR) files to an open-source database format. These files contain data on every organ donor, waitlist registrant, and transplant recipient since 1987 in the US. This data pipeline directly facilitated the next phase of research which involved performing an analysis of the transplant system using this dataset. The exploratory data analysis scales transplant data to the relative populations to gain a better understanding of the differences between demographic

groups and reveals important differences across education levels, gender, race, and ethnicity.

Demographic factors influencing organ donation and access to transplants are analyzed in this work through exploratory visualizations and predictive modeling. A visual exploratory analysis is presented which examines demographic features of organ donors and highlights differences in intersectional data across the population of donors compared to the relative population described by the US Census. Additionally, a random forest model is used to determine the features of patients on the waitlist for a kidney transplant to determine if certain attributes may inadvertently drive the allocation system. This model predicts patient outcomes based on features represented in the model with an accuracy above the zero-rule baseline. The analysis found that patient age, year of listing, body weight, and zip code are important factors in determining a patient's outcome - other demographic factors such as race and gender were not important prediction features.

State and local laws, policies, and their impact on organ donation are evaluated through a statistical analysis that compares donations after the implementation of a policy to areas without the policy implementation. A database of state and local laws and policies and the years of implementation was developed to compare donations across the country. The results demonstrated that some policies can be correlated with a change in donation, but only for certain demographic subgroups in a population.

Finally, discrete event simulation models of a representative patient population were built to determine the impact of changes to the transplant system that can not be easily demonstrated in the real world. A transplant process model was developed to determine how increasing living and deceased donation overall and within racial sub-groups would impact the number of donors each year. Additionally, an agent-based queuing model was used to understand the impact of allowing patients to register within more than one area. This model provides a valuable tool for examining policy changes that shows the global and local impacts of multiple listing. The analysis found that multiply listed patients have improved access to transplants and are less likely to die while waiting for a transplant. Altogether, this work enhances our understanding of the US organ transplant system through computational methods.

Chapter 1: Introduction

1.1 Overview of Dissertation

This dissertation presents a data-driven approach to analysis, modeling, and simulation of the organ transplant system. There are over 112,000 people on the waitlist in need of an organ transplant in the US [1]. It is important to research this system to better understand the dynamics of organ allocation to improve the system. There are various aspects of the system that provide room for improvement such as increasing donation rates, decreasing patient waiting time, and increasing the successful outcomes from transplantation. Besides the general mechanics of the transplant system, many social aspects that may contribute to the likelihood of receiving a donated organ, such as providing incentives for donation, the ethical issues of donation, and disparities in the system in regards to care and access.

Analysis, modeling, and simulation of organ transplantation and donation can enhance the understanding of this complex system and guide strategic improvements. Four major research questions are addressed in this work:

1. How can we further enable data-driven research of the transplant system for future scientists?
2. What demographic factors influence donations and access to transplantation?
3. How do laws and policies affect organ donations?
4. How do certain patient advantages impact the overall system as well as those lacking advantages?

The organ donation system is complex, with many components contributing to the number of successful transplants. In Chapter 1, a literature review of the organ transplant

system is provided and used to inform and guide the research, which intends to provide background and context to the organ transplant system. This is a subset of a complete literature review performed on the topic of organ transplantation in the US as well as in other countries around the world.

Chapter 2 discusses the data transformation process and the tool built to handle data obtained from the Organ Procurement and Transplantation Network (OPTN) [1]. This fundamental work developed a system for transforming Standard Transplant Analysis and Research (STAR) data [2] from tab-separated value files into a database for querying and the exploratory analysis, `transplant2mongo`. The codebase is available on GitHub and the overall work has been published in the Journal of Open Science Research [3].

With the STAR file collection data fully available in MongoDB, research was expanded to perform an exploratory analysis of the transplant system on deceased and living donors, as discussed in Chapter 3. This exploratory analysis considers demographic groups such as race, ethnicity, and gender as well as other patient attributes highlighted in the literature review such as a person's level of education.

Analysis of the OPTN data was performed in Chapter 4 to examine the impact of laws and policies on the transplant system including patient treatment outcomes and the efficacy of these laws and policies on increasing donation across the entire population and specific demographic groups. This work uses a comparative analysis and random forest models to perform additional data analysis on the data processed and transformed with the `transplant2mongo` tool described in Chapter 2 with a specific focus on the impact of state policies and patient attributes.

Chapter 5 presents two models developed to explore hypothetical scenarios in controversial areas of organ transplantation. A model was developed to explore possible increases in deceased and living organ donation and the impact this could potentially have on the growing waitlist. Additional research analyzes the effect of multiple registrations on the waitlist at a global and local Organ Procurement Organization (OPO) level.

An overall summary of this work and the major findings is provided in Chapter 6. This

chapter also discusses the limitations of this research, plans for future work, and proposed further contributions.

1.2 Organ Transplantation in the US

The OPTN is responsible for reporting data on the transplant system including donations, transplants, and the waitlist [1]. There were 14,256 organ donors in 2014, 8,596 of these were deceased donors. All of these donors corresponded to the removal of 28,259 patients receiving a transplant. The reports and research presented in this section tend to look at limited subsets of the population, with the resources developed in this dissertation, it is easy to build interactive exploratory tools. This research is motivated by the a desire to understand the data and state of the practice and to use this information to study the transplant system.

This chapter presents a literature review that discusses an overview of the organ transplant system as well as previous research in areas of interest such as racial disparities in the transplant system. An overview of the transplant system includes information on system management, the kidney transplant system, deceased and living donation, and the patient waitlist for a transplant. Additional sections on prior research focus on promoting donation, the economics of donation, incentives for donation, and disparities in the transplant system.

All aspects of the organ transplantation system in the US is managed under the department of Department of Health and Human Services (HHS). HHS is the overarching organization of the Health Resources and Services Administration (HRSA), which is the parent organization for all programs specific to transplantation. HRSA administers the contracts for the OPTN and the Scientific Registry of Transplant Recipients (SRTR). The OPTN was established by the National Organ Transplant Act (NOTA) in 1984 [4] and is responsible for linking all professionals involved in the US donation and transplantation system [1]. A brief overview of this system can be seen in Figure 1.1. The goals of the OPTN are listed on the organization's website and include increasing the number of transplants

performed, providing equal access to transplants, improving outcomes for all participants in the system, promoting living donation, and promoting the efficient management of the organization [1]. OPTN's contract has been managed by the United Network for Organ Sharing (UNOS) since 1984 [5].

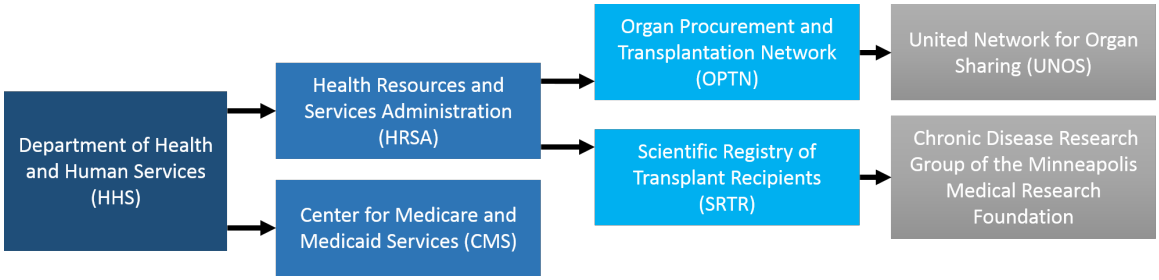

Figure 1.1: Organizations involved in the transplant system in the US from the overarching parent organization, HHS, to the contracted management organizations.

The purpose of the SRTR is to maintain a database of information on solid organ transplants in the US. There is some overlap between the roles of the SRTR and the OPTN. The SRTR uses the provided data to develop reports and analyses for HRSA, the OPTN committees that create policies for organ allocation, and the Centers for Medicare and Medicaid Services (CMS) to monitor the system [6]. Currently, the SRTR is managed by the Chronic Disease Research Group of the Hennepin Healthcare Research Institute [6]. An annual data report is generated by the OPTN and the SRTR which includes detailed information and analysis on transplants and waitlists for the kidney, liver, pancreas, intestine, heart, and lung along with information on deceased donation [7]. Appendix A provides a summary of laws and policies governing organ donation and transplantation in the US.

1.3 Donation

To become an organ donor, the individual must have blood and oxygen flowing through their organs until recovery. This is not a concern with living donors but creates specific

standards for cadaver donors [8]. A donation can come from living or deceased donors depending on the organ transplanted. Deceased donors can provide a heart, lungs, liver, pancreas, intestine, and two kidneys. Several of these organs, such as intestine, liver, and lungs can be split into multiple sections for distribution to multiple patients depending on the patient's needs. Living donation can be performed for kidney, liver, intestine, and certain parts of the lungs.

Every year, the Donate Life America organization compiles the National Donor Designation Report Card [9]. This report includes data from donor registries in the US and Puerto Rico. Donate Life America is responsible for reporting the number of donor designations, which is a documented and legally authorized commitment by a person to make an anatomical gift. For many people, this is the registration completed when obtaining a driver's license. In the US, 48% of the adult population is registered as an organ donor. One important statistic, the donor registration rate is the rate at which people join (or choose remain) in the state donor registry, Donate Life America's goal for registrations is 50% of the population. Although these rates are not as high as desired, the national donor designation rate has risen to 44.0% in 2013 from 36.3% in 2008.

Chapter 3 provides an in-depth exploratory analysis of living and deceased donor data from the OPTN STAR files. This data and analysis is further leveraged in Chapter 5 to model the kidney transplant system for both donor types with the Kidney Transplant Process Model.

1.3.1 Deceased Donors

The process to become a deceased organ donor begins when an individual suffers an injury or life-threatening medical episode that requires treatment and care. This process is depicted in Figure 1.2. In this process, efforts at every step are to save the patient's life, and organ donation is only considered once the patient has been declared deceased. Appendix C gives a complete overview of the deceased donation process.

OPOs are responsible for reporting all eligible deaths to the OPTN. An eligible death

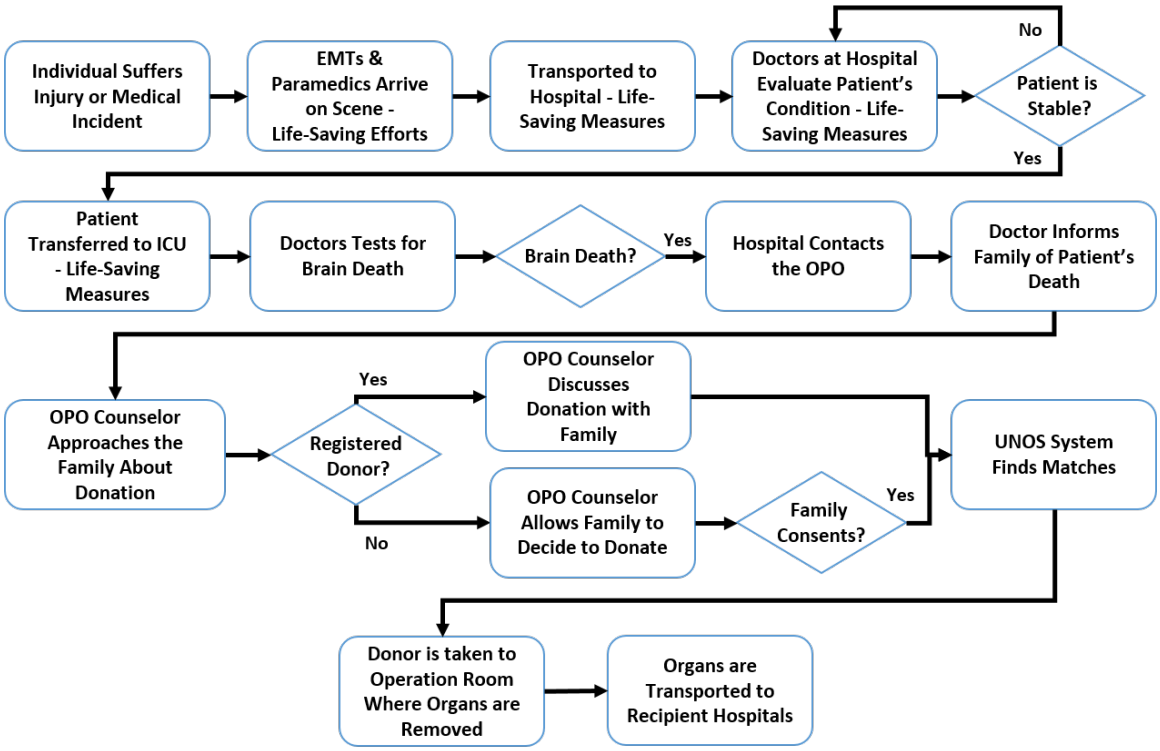

Figure 1.2: Overview of the process defined by UNOS for Deceased Donation [10]. At decision points where there is not an option for "no" pictured, this marks the end of the process for the patient and they do not become an organ donor.

is defined as the death of a person 70 years of age or younger that is legally declared to be brain dead [11]. In 2012, there were fewer reported eligible deaths than in 2011 and 2010. OPOs also measure the donation/conversion rate, which is how often an eligible death becomes a deceased donor. This rate was reported as 72.5 in 2012, which had also declined from 2011, but increased since 2009 and 2010. These rates varied across specific organs and Donor Service Area (DSA)s. The trend of deceased donation can be seen in Figure 1.3 [12].

The Deceased Donor Potential Study was completed by UNOS [13]. The research from the OPO and Caregiver Informant Group (CIG) subcommittees performed separate analyses and found that as many as 35,000 to 40,00 deceased organ donors may be available each year. This is significantly more than the approximately 10,000 deceased donors in 2018 and

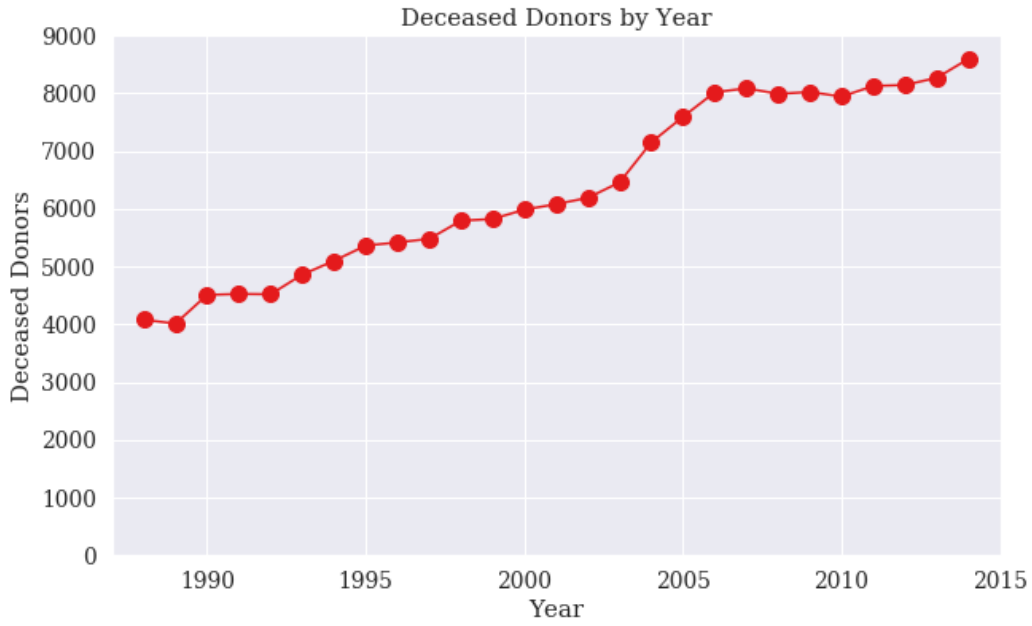

Figure 1.3: The total number of deceased donors in the US from 1988 to 2013 [12].

2017. The gap may not be as large as suggested by the analysis. OPOs pursue more cases than the actual 8,000 donors each year, many of these potential donors are not completely viable. For example, in 2010 there were about 18,300 potential cases identified by the OPO, many of which were not eligible and only resulting in 8,000 actual donors. Additional information about the estimated number of donors, such as the lab values, serologies, and whether brain death was declared was not available. Many of these items could preclude donation, which would reduce the estimate. The difference between potential and actual donors was greatest among older individuals (aged 50-75), who accounted for two-thirds of the gap. Only about half of potential donors 18-34 become actual donors.

In analyzing the recovery of organs from deceased donors, the 2012 Annual Report found that in 2012, 16,288 kidneys were procured and transplanted [11]. Poor organ function was listed as the most common reason for not procuring a donor kidney followed by donor medical history. Biopsy findings and failure to locate a recipient were the most common reason for not transplanting a kidney. An increase in transplants could be caused by increasing

risks OPOs are taking to obtain organs from donors that are not ideal for transplant [11]. The discard rate for kidneys is 19%, largely due to of biopsy results [11]. This is likely biased because the biopsy results are obtained when the donor kidney is already suspected of being suboptimal [11].

Even though the waitlist has grown, the 2013 Annual Report shows that deceased donation rates have not increased [14]. With the current kidney allocation system, a reported 10% of standard criteria donor kidneys were not transplanted, this could be cleared up by the newer Kidney Donor Profile Index (KDPI) scoring system which indicated that many of these discarded organs are of a higher KDPI score. The number of patients with a cause of death listed as head trauma increased from 2012 to 2013.

1.3.2 Living Donors

Donation for specific organs, such as the kidney, liver, and intestines, can come from living donors. These donors are measured for compatibility by the specific standards determined by UNOS [15]. The majority of living donors are biological family members of the recipient. Although it is often easier to match a donor with a biological relative, donors can also be spouses or partners, friends, acquaintances, or strangers. There has been a recent decline in living donor donation which is most prevalent in non-white, low-income, and older transplant candidates [16]. There is an increase in living donors that are unrelated, non-spousal donors from the extended social network. The amount of living donors as a proportion of total transplants varies widely across transplant programs and regions, suggesting variable practices and processes. One of the suggestions made by the report is to implement an independent national clearinghouse for the general public and potential donors. The total number of living donors from 1988 to 2013 can be seen in Figure 1.4.

Living donation rates for kidneys have not increased in recent years [11]. This decrease in living donation rates is seen in both genders and all races. Related living donation has decreased by roughly 40% since 2002 while paired and other unrelated donations have

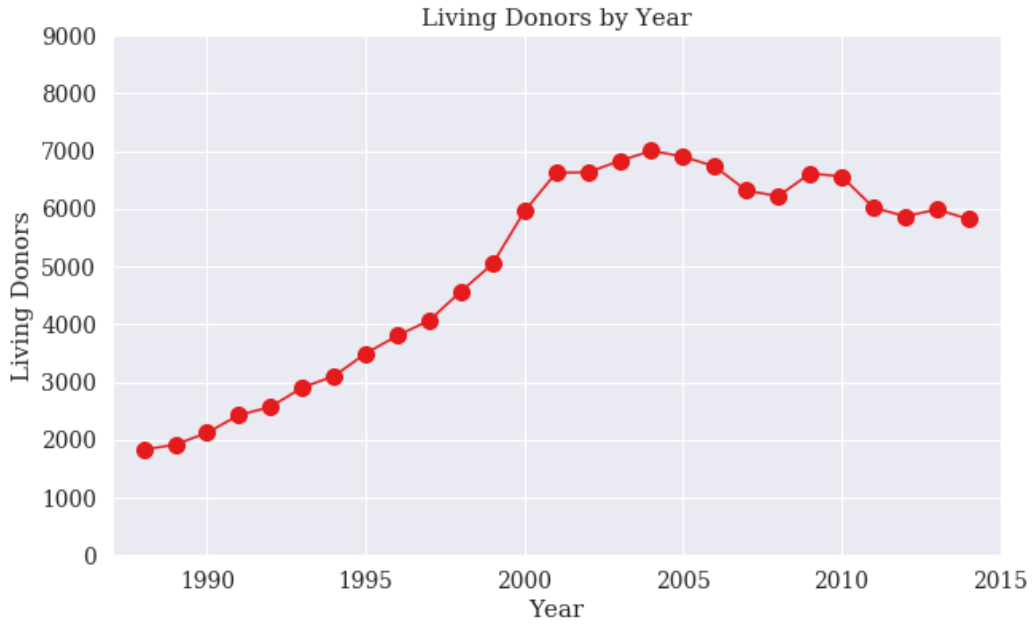

Figure 1.4: Data from the OPTN shows the total number of living donors in the US from 1988 to 2013 [12]

increased in more recent years. Of those who become living donors, the female gender, white race, and age range 35 to 49 are most prevalent.

1.4 Kidney Donation and Transplantation

Kidney donation and transplantation is an area of definite concern in the medical system as kidneys have the largest transplant waitlist in the US [1]. Over 94,000 candidates are waiting for a kidney transplant from a living or deceased donor [1]. Of patients currently waiting for a kidney, the most common diagnoses are Hypertensive Nephrosclerosis and Type II diabetes [17]. In 2018 a total of 38,792 candidates were added to the waitlist but only 36,436 people were removed [12]. Of these removed candidates, 14,714 received deceased donor transplants, 6,430 received living donor transplants, and 8,304 were removed because they died or became too sick to remain on the waitlist [12].

At the end of 2014, the kidney allocation system policies were modified to reduce existing

disparities in the system, improve the matches between donor kidney longevity, and increase the post-transplant survival of the recipient [18]. Allocation of kidneys is determined by an Estimated Post Transplant Survival (EPTS) score, the waitlist time, and the classification of the deceased donor kidney using the KDPI score. Full details on the new allocation policies are provided in Appendix B.

The overall distribution of kidneys for deceased donors with KDPI scores is done according to the candidate rating category and then by the geographic units [19]. Generally, candidates with high Calculated Panel Reactive Antibody (CPRA) have the highest priority, with a 0-ABDR mismatch, following this are candidates with an EPTS score in the top 20% and candidates under 18. Within these categories, kidneys are first offered within the OPO's DSA, then the OPO's region, and finally across the nation. Exploration of the kidney transplant system is completed through modeling and simulation in Chapters 4 and 5.

1.5 Patient Waitlist

The waitlist consists of patients in need of a solid organ transplant including heart, lung, liver, kidney, pancreas, and intestine. Patients that need an organ are listed after they have been deemed medically suitable for a transplant, the requirements for each type of transplant vary across organs. These patients remain on the waitlist until an organ becomes available and they are the highest-ranked person on the list. Organs allocated to patients on the waitlist come from cadaver donors. Every waitlist has a different structure and regulations for ranking the candidates waiting for a transplant.

Certain organs, such as kidneys and livers, may be donated to someone on the waitlist from a living person. Despite the possibility of living donation, there are still over 94,000 candidates waiting for a kidney. Candidates are often listed for a kidney transplant due to End Stage Renal Disease (ESRD) - the final stage of Chronic Kidney Disease (CKD), which happens when a person's kidneys stop working well enough to survive without dialysis or a transplant [17]. The waitlist for kidneys is a specific concern; in 2018 only 36,436 people

were removed from the waitlist. Of these removed candidates, 14,714 received deceased donor transplants, 6,430 received living donor transplants, and 8,309 were removed because they died or became too sick to receive a transplant [1].

Patients in need of a transplant must go through a process to join the national waitlist for a transplant, this process is described in Figure 1.5. The waitlist is a database with information on every person awaiting a transplant in the US [20]. First, patients must obtain a referral from their physician. Then the patient needs to contact a transplant hospital and schedule an appointment for an evaluation. This evaluation by the transplant center determines if the individual is a suitable candidate for transplantation. If the hospital's transplant team determines that the patient is a good transplant candidate, they will add the patient to the national waitlist. The transplant center will notify the patient of their application status within ten days of listing.

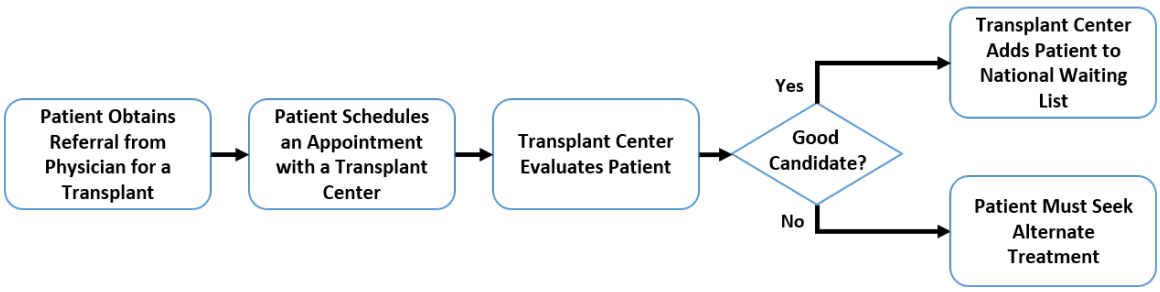

Figure 1.5: Overview of the process for patients to join the waitlist.

The waitlist for an organ transplant is not a set list of people, numbered first to last in line for an organ; it is a pool of candidates with certain attributes. When an organ becomes available, a list is dynamically created in DonorNet that lists the candidates who are the best match for the available organ. The waitlist takes age, weight, diagnosis, time on the waitlist, and medical suitability of the match between the candidate and the donor into consideration. UNOS collects information about these candidates and the donors that would be most appropriate from and age, height, and weight perspective. Medical and

social history is also occasionally used to make these matches [21].

According to the 2013 Annual Report, the number of candidates on the waitlist has almost doubled from 2002 to 2012 [14]. This report also found the number of candidates 50 years and older has increased along with the number of diabetic candidates since 2003. Of the candidates on the waitlist, roughly 30% have been receiving dialysis treatments for six or more years. In 2013, over 7,000 candidates were removed from the waitlist because they passed away or became too sick to undergo a transplant.

The Ethics Committee of UNOS is careful in considering and implementing limits on who should be eligible for a transplant [22]. Many transplant programs have implemented a type of non-medical evaluation of patients for transplantation, including psychosocial evaluations. The ethics committee addresses the criteria of life expectancy, organ failure caused by behavior, compliance, and adherence to care, repeat transplantation, and alternative therapies in this report. This organization recognizes that donated organs are very scarce and should be given to the best potential recipients. The committee does not recommend age or co-morbidity limits for transplantation, but the candidate's reasonable life expectancy should be considered. Another recommendation is that past behaviors, such as drug abuse, smoking, alcoholism, and eating disorders should not be considered as the sole basis for excluding candidates, and transplantation should be cautiously considered for potential candidates that have shown serious, consistent, documented non-compliance in their previous treatments. The waitlist is modeled in Chapter 5, specifically analyzing the practice of multiple listings in the transplant system and the global and local ramifications of this policy.

1.6 Promoting Donation and Transplantation

Etzioni argues for changing the moral culture and attitude towards donation so that members of society recognize that organ donation is the moral thing to do [23]. Realizing this type of culture would require more effort than simply sharing information and advertising the benefits of donation. For this to be put into place, a moral dialog is needed to engage the

public. This research suggests that a public statement, endorsed by leaders and community members that organ donation is the right thing to do would be a positive measure.

The federal government and states have implemented laws and policies to help promote organ donation and transplantation across the population. These laws and policies are briefly reviewed in the following subsections and in further detail in Appendix A. In Chapter 4, I use analysis and modeling techniques to evaluate the impact of these policies.

1.6.1 Education

Some studies have argued that deaths that occur while waiting for a kidney are more of a political failure than a medical issue, as the current average waiting time for a kidney is seven years [24]. Research by Strumwasser et al. suggests that implementing better education and enforcement of the legally-binding commitments of donors would increase organ donation. This falls on the education of hospital staffers and their families to dispel myths about the transplant system.

Research by Kutnet et al. has shown that many patients do not have enough early exposure to information on kidney transplantation as a choice of treatment [25]. Kidney disease education has been designated as a service covered by Medicare Part B for Stage 4 CKD patients. This research used survey respondes from patients who participated in a US Renal Data System special study to explore outcomes that may come with the new kidney disease education benefit. The study found that only half of the patients could recall having transplantation discussed with them before they began dialysis. Black and white patients were equally likely to recall having the discussion and there was no difference in the educational level of patients that reported transplantation was discussed. Patients that reported transplantation had been discussed with them were younger, and rater their physical health status higher. This group of patients were also more likely to have private insurance. These are all also attributes that enhance the probability of transplant success.

Siminoff et al. also studied factors that influence families in consenting for solid organ donation from a deceased relative [26]. This work uncovered that there are numerous factors

associated with the decision to donate. The sociademographics and prior knowledge of the patient's wishes were associated with the willingness to donate. Families that discussed more topics and had more conversations about donation were more likely to consent to donation. Socioeconomic and communication variables also contributed to the likelihood of donation. The authors recommend that public education is needed to correct mistaken attitudes before the opportunity for donation arises.

Emerging data on the long-term medical and psychosocial outcomes of living donors have implications for how healthcare providers educate candidates on how to find potential donorss [16]. The living donor education of patients with advanced stages of chronic kidney disease should occur repeatedly throughout disease progression and process. Medical caregivers need to ensure patients have earlier access to education about transplants. Research also suggests that a financial toolkit be created reviewing living donor financial risks, estimation of costs, and available resources.

One of the biggest high priority items from the consensus conference on best practices includes creating culturally-tailored living donor education to racial minority patients with historically lower living donation rates and their support systems [16]. The system needs to provide patients and their caregivers with training on how to identify and approach living donors.

1.7 The Economics of Donation

The economics of kidney transplants are discussed in the 2013 Annual Data Report as being one of the most cost-effective procedures in medicine [27]. From the initial transplant through the first year following, the average reimbursement for recipients of a kidney with Medicare as their primary coverage was a total of $83,000 [27]. Variance is primarily due to re-hospitalization which is highly likely in the first year following transplant [27]. The second year following the transplant is roughly $24,000, less than one-third of the initial cost [27]. According to the report, in 2012, Medicare costs for kidney transplant recipients

were $2.8 billion, including Part A and Part B. The Medicare per person per year costs are highest for recipients over 65, female patients, black patients, and patients with a primary diagnosis of diabetes.

Axelrod et al. examined the economics of kidney transplantation using discrete-event simulation over 10 years [28]. Outcomes were evaluated using quality-adjusted life-years and the associated costs. Kidney transplantation is cost-effective for all types of donors – living and deceased – although lower-compatibility donations are costly. The economics of donation are an important motivator for increasing donation and removing patients from dialysis, in addition to the quality of life benefits for patients.

The supply and demand aspect of organ donation has made this area an enticing research field for economists [29]. As organs become available for deceased donor transplants, additional transplant candidates are added to the list, indicating that the supply is driving the demand [30].

1.8 Incentives for Donation

For living donation, there have been recent initiatives including non-directed donation, paired exchanges, and desensitization protocols. Although these efforts have been successful and resulted in a 15% increase in living donors from 2004 to 2012, they raise ethical issues and increase the workload on the transplant center [11]. This report questions if now is the appropriate time to energize a major public policy initiative to increase organ donation. The Consensus Conference on Best Practices for organ donation in 2014 suggested including credits for living donation and remove barriers to donation by non-residents [16].

One solution to the shortage of organ donors is to increase the number of donated kidneys [31]. The realistic solution proposed in [31] is a system of compensation. This proposed framework would be virtually identical to the system currently used to evaluate altruistic living donor organs. The idea is to use a predefined algorithm for matching and a waitlist. There is an added element of a fixed payment to donors by the government. Compensation could take many forms including a fixed payment, long term health insurance,

college tuition, tax deductions, or some combination of these alternatives.

Chapter 5 describes the construction of a model that explores the impact of increasing living and deceased donors and finds that the most feasible way to address the donor shortage is through increasing the number of living donors. Some incentives for donation, such as tax benefits and leave of absences, implemented through state policies, are reviewed using an epoch analysis in Chapter 4.

1.8.1 Financial Neutrality

The medical costs of becoming a living donor are covered by the transplant recipient's insurance, which includes the evaluation, surgery, and a limited number of follow-up tests and doctor's visits. If medical issues arise from the donation process, the recipient's insurance may not cover these problems. The recipients' insurance is not likely to cover the costs of transportation, lodging, communications, child care, or lost wages of the living donors [32]. A 2006 survey on public attitudes towards incentives for organ donation determined that 91% of survey participants were in favor of covering medical expenses for living organ donors [33]. Many professional organizations such as the International Transplant Nurses Society have expressed full support for the removal of financial disincentives for living donation as an ethically acceptable best practice for increasing donations [16, 34, 35]

In the past ten years, the number of kidney transplants made possible by living donors has declined by approximately a thousand; an open letter to the Secretary of HHS reviewed ethically increasing organ donations [34]. The authors of this letter believe that one major reason is the cost incurred by living donors in the US, which is estimated to be $6,000 of out-of-pocket costs. To increase donations, it is necessary to remove these financial disincentives if we want to increase donation. Pilot programs could be developed to test out means of removing the financial and other obstacles to donation. The objective should be to ensure that becoming a donor is a financially neutral act.

Klarenback, Garg, and Vlaicu discuss the need for a national reimbursement policy for living donors [36]; a living kidney donation is estimated to result in a net increase of

2 to 3.5 quality-adjusted life-years as well as a net healthcare savings of $100,000. This research found that direct costs incurred by the donor include traveling for tests, appointments, hospital admission, accommodations, and incidental costs for medication following the transplant. Many donors experience financial hardship or burdens when donating a kidney and some donors report lost income [36].

1.8.2 Non-Monetary Incentives

Research by Delmonico et al. discusses ethical incentives for organ donation provides several suggestions for ways to ethically incentivize organ donation including a donor medal of honor, reimbursement for funeral expenses, medical leave for organ donation, priority on the waitlist for living donors, and donor insurance [37]. This article also explains why we should focus on incentives instead of payment, "the fundamental truths of our society, of life and liberty, are values that should not have a monetary price." The 2006 survey on public attitudes towards incentivizing organ donation found that 84% of respondents were in favor of paid leave from work and 59% supported priority for the donor on the waitlist if needed in the future [33].

Tax Deductions and Credits

During the 111th Congress, Representative Joe Wilson of South Carolina introduced House of Representatives (H.R.) Bill 218 to amend the Internal Revenue Service (IRS) code of 1986 to provide a personal credit to individuals that become living organ donors [38]. This act is meant to be referred to as the "Living Organ Donor Tax Credit Act of 2009." The purpose of this tax credit would be to provide a tax credit to living organ donors to cover costs of transplantation paid by the donor that were not reimbursed and any lost wages stemming from the transplant procedure. In the proposal, the credit would be limited to $5,000 and include donations of kidney, liver, lung, pancreas, intestine, bone marrow, or any parts of these organs. This bill was introduced to the house on January 6, 2009 and was referred to the Subcommittee on Health on January 14, 2009. No further actions were taken following

this referral. It is not entirely clear whether this law would violate the stipulations in the NOTA that prohibits transferring human organs for "any valuable consideration" [4].

Although there is no clear federal policy at this time for tax benefits of organ donation, several states have policies in effect. Seventeen states have policies in place for tax benefits for living donors. Arkansas, Georgia, Iowa, Maryland, Minnesota, Mississippi, New Mexico, New York, North Dakota, Ohio, Oklahoma, South Carolina, Virginia, and Wisconsin all have a $10,000 tax deduction for organ donation. Residents of Louisiana and Utah can claim up to a $10,000 credit for becoming a living organ donor, while Idaho residents are eligible for up to a $5,000 credit [39, 40]. Even with these incentives, the number of living donors has not increased. Despite this lack of an increase in donation, many feel that the tax breaks should stay to help out those who choose to donate [41].

Leave of Absence

The 106th Congress of the US passed the Organ Donor Leave Act in 1999, which permits a federal employee to take leave to become an organ donor [42]. This act permits a federal employee to have, in any calendar year, seven days of paid leave to serve as a bone marrow donor or up to 30 days of paid leave to serve as an organ donor.

Many states have a public leave of absence programs, which provide leave for state employees. Arkansas, California, the District of Columbia, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Maryland, Massachusetts, Mississippi, Missouri, New York, North Dakota, Ohio, Oklahoma, South Carolina, Texas, Utah, Virginia, West Virginia, and Wisconsin all have paid leave programs for state employees [39]. The guaranteed amount of leave varies across these states, but generally, these states all allow for 30 days of paid leave to become an organ donor. Colorado allows two days of paid leave for state employees to become an organ donor and Delaware limits the program to teachers and school employees. Connecticut only offers unpaid leave for state employees to become an organ donor.

Fewer states have laws in place that require private companies (often of a certain size) to allow employees to take leave to become a living organ donor [39]. Unpaid leave is provided

in Arkansas, Connecticut, and Maine. Paid leave is provided in California, Illinois, and Minnesota.

1.9 Disparities in the Transplant System

Many disparities exist in the organ transplant system in the US. These differences depend on geographic, cultural, age, and racial/ethnic groups. These disparities are rarely intentional but can have serious and significant impacts on the outcomes of the transplant system. In Chapter 3, an exploratory analysis of disparities across organ donors is performed. Disparities are also examined in the epoch analysis in Chapter 4 where I determine which laws and policies impact different demographics groups and in the feature analysis in Chapter 4 in building the random forest model

Basiske, London, and Ellison studied the racial and socioeconomic factors that influence early placement on the waitlist for kidney transplants [43]. This study used patient registrations between April 1, 1994 and June 30, 1996 from the transplant waitlist. It was found that independent predictors of pre-dialysis listing included female gender, age under 55, prior transplant, an education level of attending college or having a degree, white race, full-time employment, private insurance and being listed at a high volume center.

Flattau et al. considered how frequently liver transplant programs encounter social barriers in patients undergoing an evaluation and whether programs with higher proportions of Medicaid patients, historically disadvantaged minority patients, and rural patients come across these social barriers more frequently [44]. The following social barriers were encountered frequently: inadequate or unstable health insurance, a chaotic social environment. Barriers encountered sometimes were inadequate housing, language barrier, no reliable contact, difficulty obtaining child care, and food insecurity. The frequencies of perceived social barriers did not differentiate between programs with higher/lower portions of the people of interest. Results suggest that program-level operational planning for addressing social barriers should be considered regardless of these specific populations.

1.9.1 Geographic

The US is split geographically into 58 DSAs; each DSA is managed by an OPO. OPOs are the only organizations legally allowed to perform organ recovery and transplantations [4]. At a higher level, the OPOs are organized into 11 geographic regions which each cover multiple states - OPOs are each fully contained with a specific region, regions are pictured in Figure 1.6 [45]. These OPOs are often compared to one another to measure progress and success across the organizations and the country. Research by Ojo et al. explains the need for the recent OPO evaluation methodology. One of the major improvements involves using "notifiable deaths" as the descriptor of the standardized maximum pool of potential donors. Another denominator used for ratios concerning donation rates is "eligible deaths" which only includes deaths that meet the criteria for organ donation [46].

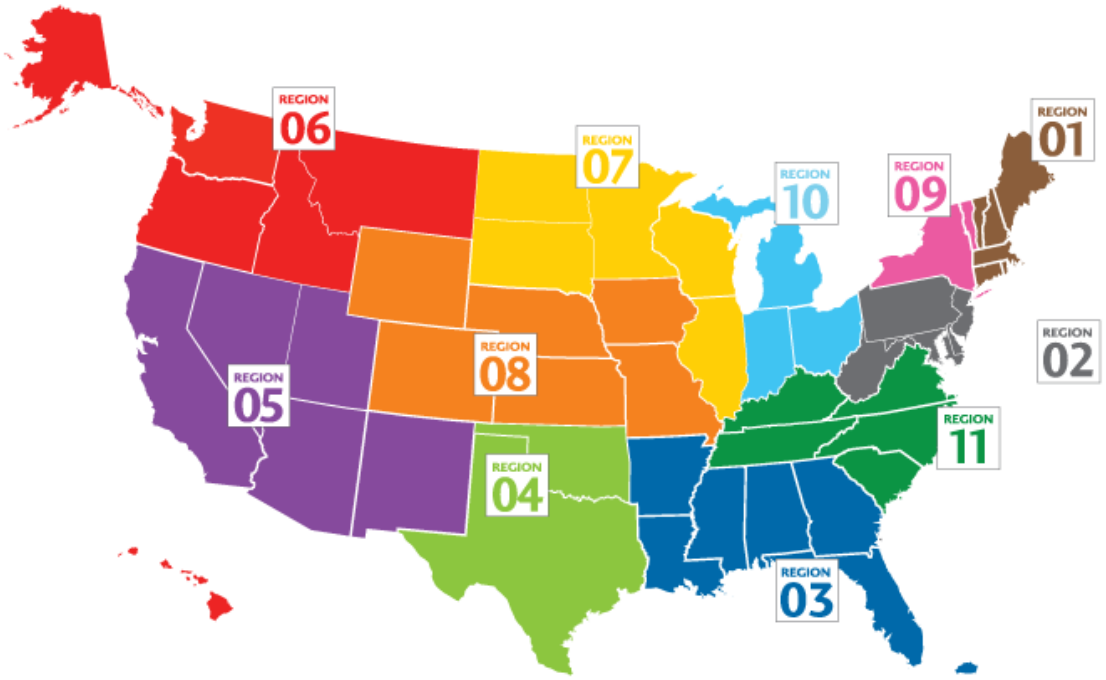

Figure 1.6: Geographic regions referenced by the OPTN [45].

Goldberg, Halpern, and Reese provided insight into the geographic differences in the

transplant system [47]. They found there is significant OPO variability in the proportion of consents obtained from prior donor documents. Consent rates across UNOS regions varied slightly with the lowest consent rates in regions 9, 6, 11 and the highest in regions 7 and 8. The regional variation is dependent on differences in patient demographics, religious beliefs, about the value of transplants, the practices of the OPO and hospital personnel when encountering donor families. Regional differences in consent corresponded to the racial and ethnic distribution of the UNOS regions, with regions 7 and 8 having the first and third higher proportion of white potential donors. The age distribution of UNOS regions were associated with differences in consent rates with region 9 having the highest proportion of potential donors aged over 55 years of age.

1.9.2 Religion

The organ donation website, OrganDonor.gov, gives information on various religious views on organ donation. Most religious communities support organ donation [48]. Detailed information provided by this resource shows that the Evangelical Covenant Church, Islam, Catholicism, the United Methodist Church, the Southern Baptist Church, the Church of Jesus Christ of the Latter-Day Saints, Judaism, and the Episcopal church all support organ donation.

Several studies and areas of research have revealed that people claim religion affects their decision to participate in organ donation (e.g. [49], [48], [50], [51]). In a recent study completed on the attitudes towards donation of Turkish medical students, results revealed that 42.7% of respondents to a survey reported that their religion restricts organ donation [49]. This is contrary to the outcomes of the Fourth Conference of the Islamic Fiqh Council which declared that organ donation is permissable as long as the "shar'i guidelines and controls that protect human dignity" are met [48]. It is acceptable to perform a transplant from a deceased person to a living person that needs the organ as long as permission has been granted by the deceased or their heirs following death [48]. This statement also explains that living donor transplants are also permissible "in order to keep

the beneficiary alive or to keep some essential or basic function of his body working" [48].

Publications on the religious aspects of organ donation detail the cultural dilemmas and the stances of organized religions. Although no religions formally forbid organ donation or transplantation, some cultures discourage deceased or living donation such as Native Americans, Roma Gypsies, Confucians, Sintoists, and some Orthodox Rabbis [50]. Oliver et al. suggests religious concerns may have a more significant role than clinicians and transplant teams believe as patients may not come forward with religious issues and health professionals may wish to avoid sensitive topics such as religion [51].

1.9.3 Racial and Ethnic

Differences in healthcare outcomes across racial and ethnic demographics exist in the diagnosis of ESRD, attitudes towards the system, access to the waitlist, outcomes from the waitlist, participation in organ donation programs, and transplant outcomes. Xue et al. investigated the racial differences in ESRD by patients' diabetes and hypertension status in a longitudinal manner with a focus on patients over 66 [52]. The study performed an adjustment for age and gender and showed that across patients with diabetes, black patients and other races/ethnicities were more likely than white patients to develop ESRD. For patients without diabetes or hypertension, black patients were still more likely to develop ESRD. Compared to their white counterparts, mortality was higher for black patients. Minority women are at a greater risk for ESRD than white women.

In the 1993 survey on organ donation, researchers found differences in beliefs about the deceased donation across white, black, and Hispanic people [53]. The study found that 42.9% of white, 31.2% of Hispanic, and 22.5% of black participants were willing to donate their organs after death. A significantly greater portion of white participants compared to the other races saw more information about donation in the past year, had discussed death arrangements with their families, and agreed that doctors exert all possible life-saving efforts before pursuing donation. Findings also showed that a significantly greater percentage of white and black participants compared to Hispanics knew that families did not incur extra

costs for organ donation. Hispanic and black respondents also reported significantly higher levels of concern about body disfigurement compared to whites. A strong correlation also existed between willingness to donate and concerns about body disfigurement [53].

Differences in attitude towards donation could be based on socio-geographic differences instead of race, as indicated by a study in Missouri on indicators for registering as an organ donor [54]. This work used spatial regression analysis to identify relationships between the location of Department of Motor Vehicles (DMV) offices and Census tract-level concentrated disadvantages such as educational attainment, poverty, and single-headed households. There is a significant negative relationship between these disadvantages and organ donor registration rates.

Schold et al. found that certain characteristics, such as age, race, gender, insurance coverage, and Body Mass Index (BMI) were associated with a likelihood for a patient being added to the waitlist with 'poor' prognosis, but not listing with 'good' prognosis [55]. Particularly, the research found that the rates of being listed were higher for younger and older white patients compared to black patients.

Clark et al. showed that black patients were less likely than white patients to have a physician recommend a transplant as treatment, but both races reported similar levels of instrumental dialysis center staff and patient support [56]. A high correlation was reported between higher levels of instrumental support networks and the likelihood of receiving a complete transplant evaluation. The study could not explain racial disparities in completing the pre-transplant evaluation through social support networks. A greater instrumental social support network was strongly associated with completing a post-transplant evaluation among women and white men.

Mathur et al. considered access to liver transplants for racial and ethnic minorities [57]. The goal of this research was to evaluate the association between candidate race/ethnicity, adjusted for the patient's geography and disease progression. This research found that Hispanics have a lower deceased donor rate compared to whites when averaging across Model for End-Stage Liver Disease (MELD) scores. Racial and ethnic disparities were

prominent across subgroups of Hispanic and Asian candidates.

Gil et al. considered the racial disparities in access to living donor transplants in the US which focused on patient factors and analyzed the associations between living kidney donation and donor median household income and race [25]. The incidence of living kidney donation was greater in higher incomes for both black and white populations. For this high-income group, the total cases of living kidney donation were higher for the black population than for white donors, but the ratios varied by income. The incidence of living kidney donation was lower for the black population than the white population in the lowest income groups [58].

Research from the Medical Clinics of North America covers health disparities in transplantation, with a focus on black candidates for transplantation [59]. Black people in the US are significantly more likely to develop ESRD than the white population and are less than half as likely as whites to receive a kidney transplant. Other studies referenced in this article noted that blacks are less likely than whites to participate in their own medical decision making and are less likely to trust their physicians.

A large collaboration of researchers completed a study on the access and outcomes for minority transplant patients from 1999 to 2008 in the US [60]. This paper reviewed trends in access to solid organ transplantation and post-transplant outcomes by organ type, race, and ethnicity. Additionally, an analysis of categories of factors that contribute to the racial/ethnic variation seen in kidney transplant outcomes. Disparities in minority access to transplantation among wait-listed candidates are improving but, persist for those awaiting kidney and simultaneous kidney-pancreas transplants. In general, graft and patient survival are highest for Asians and Hispanics, intermediate for whites, and lowest for the black population. Age and duration of pre-transplant dialysis exposure emerged as the most important determinants of survival. The analyses in this article were based on the OPTN database. The data source was supplemented with ESRD statistics from CMS and with status information from the Social Security Death Master File (SSDMF). Cox regression models were used to compute survival probabilities with adjustments for age, sex, and

primary diagnosis.

For kidneys, transplant percentages for black, Hispanic, and Asian patients lag behind their perspective portions on the waitlist [60]. Whites were transplanted at a greater rate than their representation on the waitlist. In contrast, blacks, Hispanics, and Asians were transplanted at rates lower than expected from their waiting-list prevalence. An interesting aspect of graft survival is the Asian recipient's survival time. Asians enjoy the highest adjusted and unadjusted graft survival followed by Hispanics, then whites. A similar pattern exists for living donor graft survival.

1.10 Summary

The literature review provided in this chapter is the foundation for work conducted in the following chapters. Research studies discussed in this chapter, particularly those on disparities in the transplant system and promoting organ donation, guided the exploratory analysis in Chapter 3. This exploratory analysis directed the analysis, modeling and simulation work presented in Chapters 4 and 5.

Chapter 2: Data Preparation[1]

The Organ Procurement and Transplantation Network (OPTN) keeps a record of all organ donations, transplants, and waiting list registrations since 1987 in the US [1]. This complex data set can be used to review, query, and analyze the US organ donation system over time and across various facets. The total size of this data is $\sim$ 9 GB and contains records on hundreds of thousands of donors and over a million patients [2]. OPTN provides Standard Transplant Analysis and Research (STAR) data as Tab-Separated Values (TSV) files, SPSS files, or SAS files. SPSS and SAS are proprietary software and the TSV files are not suitable for non-trivial queries.

A request for the STAR files must be submitted through the OPTN website [2]. The OPTN provides data to members as well as the general public on request. A member of the general public can obtain the data by completing the forms on the OPTN website [2]. STAR files are described as "limited datasets that contain patient-level information about transplant recipients, deceased and living donors, and waiting list candidates back to 10/1/1987" [2]. To obtain the files, the requester must also sign a Data Use Agreement which specifies appropriate use of the data and forbidden uses and handling of the data [62].

The STAR data files were obtained for exploratory analysis, modeling, and simulation and first needed to be cleaned and processed into a database to be easily queried. To perform data cleaning, the `transplant2mongo` Python scripts were developed as part of this research and published for public use on GitLab [61]. The development of this software has also been published in the Journal of Open Research Software [3].

TSV data is inserted into a MongoDB database with the `transplant2mongo` Python scripts. `transplant2mongo` was developed to allow researchers to use open-source software

[1]This chapter contains content drawn directly from the Journal of Open Research Software publication on the `transplant2mongo` tool [61].

to explore, manage, and analyze the data without the need for proprietary software. There is no similar open-source software available for transferring STAR data into a database that does not require proprietary software for use. Working with the TSV files in the raw format would require manually merging header files and data files and the hierarchical data structure would require constructing data mappings within the analysis scripts which is much more time consuming than directly querying a database.

Due to the sensitive nature of STAR data, the development of `transplant2mongo` was completed in a secure lab environment at The MITRE Corporation and the code repository does not include any STAR files. Special consideration was made to process the data and remove erroneous symbols and characters that are not compatible with MongoDB. The resulting MongoDB database has been used to perform an analysis of the OPTN dataset which is presented in the following chapters.

The `transplant2mongo` code base was developed to be easily accessible to other users without sharing the private STAR files. Users can test the code using sample synthetic TSV data. For users to run the code on actual United Network for Organ Sharing (UNOS) STAR data, they must update the Makefile to specify the file types they have and the data location using instructions detailed fully in the README file. Once users have updated the Makefile to their specifications, the `make all` command will populate the database with all referenced STAR files.

Although originally developed for OPTN STAR files, additional development has been conducted to expand the tool to work with the Scientific Registry of Transplant Recipients (SRTR) data files. This expanded code is under development at the request of the SRTR and is being published in the code repository as this work has caught the attention of the SRTR and they have requested additional development to transform the SRTR files to MongoDB.

2.1 Implementation and architecture

This software was developed on a machine running CentOS with Python 3.6 and MongoDB 3.6 and was tested using all available OPTN STAR TSV files obtained from the OPTN in June 2014 and then in March 2015. The general file configuration of OPTN STAR files and directories is shown in Figure 2.1. This tool was developed in a flexible manner because users of `transplant2mongo` may not have the complete set of OPTN STAR files, and may only have certain subsets of this information. In this case, the Makefile can be edited so that only a subset of the STAR files are processed.

As shown in Figure 2.1, the TSV files are all stored in subdirectories of the `Delimited Text Files` directory. This directory contains a sub-directory for each of the data types: `Deceased Donor`, `Intestine`, `Kidney_Pancreas_Kidney-Pancreas`, `Liver`, `Living Donor`, and `Thoracic`. The `Kidney_Pancreas_Kidney-Pancreas` sub-directory contains information on all patients and transplant recipients for kidney and pancreas, and combined kidney/pancreas transplants. Data on both heart and lung transplant patients is in the `Thoracic` sub-directory. The `Deceased Donor` and `Living Donor` sub-directories contain details on all organ donors, while the other subdirectories provide data on all patients registered to the waiting list and those who received a transplant. Each of these major groups is represented as collections in the generated MongoDB database with the patient or donor information as documents and the sub-folders as sub-documents.

MongoDB was chosen as the database due to its NoSQL format, allowing multiple patient fields to be combined into a single document with multiple sub-documents. Many of the STAR file fields have changed over the years, and many of the patient fields are missing information, making this data suitable for NoSQL storage. Alternatively, a Standardized Query Language (SQL) database system could be used. However, with such a structured database implementation, the number of columns would be very large and there would be many null fields in the database.

A Makefile is used to execute the scripts that build the database from the contents of the

`Delimited Text Files` folder. The Makefile has targets for cleaning, processing, and inserting the data into a MongoDB database. Users need to specify their database server and port in the Makefile before execution. The default server and port is `localhost:27017` and the default database name is `organ_data`. Users also need to define the components to process, which corresponds to the STAR files that the researcher has obtained from the OPTN (corresponding to the subdirectories of `Deceased Donor` shown in Figure 2.1). These values are selected from the following list: `deceased, living, intestine, kidpan, liver`, and `thoracic`. Data are first copied from the original location and file structures are flattened to establish a simple structure for parsing.

Once the flattened data files have been generated, another Python script is run to generate JSON and add the documents into the MongoDB database. For the base files, corresponding to the main donor and organ data files, the `add_patients.py` script is run to generate major documents in the appropriate tables. Additionally, for files that contain sub-document information such as follow-up visits or medications, the `supplemental_data.py` script adds this information as a sub-document to the main patient or donor document. This script uses a unique identifier, such as `DONOR_ID`, `TRR_ID_CODE`, or `WL_ID_CODE`, to match the supplemental data file entry with a unique record for the donor or organ type. Once a match is found, the supplemental data is added to the document in the database. The TSV files, having the extension `.DAT`, only contain data and do not include column names; columns are determined by the `.htm` files corresponding to each `.DAT` files.

Data are cleaned before insertion into the database. The cleaning process is handled in the Python scripts `add_patients.py` and `supplemental_data.py`, which use the `clean_string` function. These scripts remove extraneous values such as extra commas, quotations, and newlines and the scripts do not assume a particular data type for any column. The database contains many different columns and the typing is automatically determined by Python and MongoDB. All data are by default imported as strings. The Python scripts check if the data is a date or an integer, and if not, the data are kept as strings.

Following the execution of each of the import scripts, follow-up scripts are run to add age bins to all age fields of the data to allow fast and simple aggregation queries.

2.2 Quality Control

The scripts have been tested on two distinct UNOS STAR file data sets from 2014 and 2015. Each script prints out the number of lines in the file being processed and then the number of patient documents successfully imported into the database. With the two data sets, the line count results match the imported entry counts in all scenarios with the exception of a particular data file where a newline was hidden with quotation marks and the reported file length is one more than the imported record count. The data were manually confirmed in this situation and additional manual spot checks were performed.

The GitHub repository includes sample data that can be used for testing the installation. These data contain no real patient information and were generated by the developers of the software. The Makefile is set up by default to run on this sample data set with the `localhost` MongoDB database by following the directions provided in the `README`. A `test` target in the Makefile can be used to verify that the sample data was imported correctly and a query can be performed.

A MongoDB viewer, such as Robo 3T, is recommended for browsing and spot-checking the data after the sample data or STAR data has been inserted into the database. The code base contains a Python script is included, `query.py`, that performs database queries and prints the output to a Comma Separated Value (CSV) file. Additionally, a Jupyter Notebook, `query-examples.ipynb`, is also included that can be used as a starting point for analysis and demonstrates querying the database, performing statistical analysis, and graphics.

2.3 Dependencies

MongoDB 2.6+ (Tested with 2.6 and 3.4)

Python packages: `pymongo, pandas, tqdm, and seaborn`

Users need to obtain UNOS STAR files directly from the OPTN. This data contains private health data and can only be obtained directly from the OPTN.

2.4 Applications

The `transplant2mongo` tool is used to perform data queries for exploratory analysis of the data and to pull valuable information to build models and simulations of the organ transplant system. Complex queries are developed within MongoDB to merge data and to pull information to explore donors across various facts shown in Chapter 3 and Chapter 5.

Additionally, the tool is available for re-use by anyone working with UNOS STAR files seeking to do research on the organ transplant system. This tool generates a database that can be used with open-source software. The software has a high potential for extension. These database creation scripts are written in Python 3 and they could be modified to allow the insertion of the data into alternative databases such as SQL. A Graphical User Interface (GUI) could be developed that allows visualization and query of the contents of the database that is customized for the type of analysis done by organ transplant researchers.

2.5 Future Work

The `transplant2mongo` tool will be expanded to work with SRTR data files in addition to the OPTN STAR files and published as options for the command line inputs to build the database. Additional work could also be completed to expand the tools to port data to a SQL format.

Figure 2.1: Structure of the OPTN STAR files. The top-level directory is `Delimited Text Files` and the subdirectories are shown to the right.

Chapter 3: Exploratory Analysis

An exploratory analysis was performed using the data obtained from the Organ Procurement and Transplantation Network (OPTN) and transitioned into a MongoDB database using `transplant2mongo` [2,61] to understand differences in donor population demographics. Prior research has been done on the national scale, regional levels, or over small sections of the US as discussed in Chapter 1; in this chapter, I aim to answer large-scale questions involving and in-depth analysis that is not provided in previous research. Many previous research studies on donor demographics focus only on a few patient attributes or cover a single geographic area, this work explores multiple patient descriptors across the entire US for living and deceased donors [47,57–59,63–66]. The analysis performed in this chapter is used to guide and inform the analysis and modeling performed in Chapter 4 and Chapter 5.

3.1 Data Preparation

The `transplant2mongo` tool discussed in Chapter 2 was used to transform and format the data into a MongoDB database for simplified querying and analysis [61]. In addition to the OPTN data, information from the US Census on the current population was obtained to explore how the patient population compares to the larger US population [2,67].

Additional research was completed on best practices for data preparation when merging data from the Census to the OPTN database [67]. The Census database only considers six categories of races: White, Black, Asian, American Indian/Alaskan Native, Hawaiian Native/Other Pacific Islander, and Two or More Races. Hispanic origin is considered an ethnicity, not a race category. The United Network for Organ Sharing (UNOS) database has the same races as the Census, but with an additional category for Hispanic. Hispanic origin is also considered as another field.

Table 3.1: Mappings used for racial and ethnic groups between the UNOS data and Census data.

UNOS Classification	**Census Classification**
White & Non-Hispanic	White & Non-Hispanic
Black & Non-Hispanic	Black & Non-Hispanic
Asian & Non-Hispanic	Asian & Non-Hispanic
American Indian/Alaskan Native & Non-Hispanic	American Indian/Alaskan Native & Non-Hispanic
Hawaiian Native/Other Pacific Islander & Non-Hispanic	Hawaiian Native/Other Pacific Islander & Non-Hispanic
Hispanic & Hispanic	Hispanic & Hispanic
Multiracial & Non-Hispanic	Multiracial and Non-Hispanic
Multiracial & Hispanic	Black & Hispanic, Asian & Hispanic, American Indian/Alaskan Native & Hispanic, Hawaiian Native/Other Pacific Islander & Hispanic

For the UNOS data categories, the only cases where someone identifies as being of Hispanic origin is when they identify themselves of being of Hispanic race or multi-racial. With the Census categories, people of all races can consider themselves to be Hispanic. To have the Census populations map properly to the UNOS data, the system used to perform the mappings is show in Table 3.1.

3.2 Exploratory Analysis

This exploratory analysis was first conducted on the data for both deceased and living donors to gain a better understanding of the population demographics and differences in groups of donors. The OPTN Standard Transplant Analysis and Research (STAR) files contain up to 327 pieces of metadata for each deceased donor and up to 175 pieces of metadata for each living donor [1]. Due to the addition and removal of columns from the OPTN database, there are high instances of missing data for donors, for readability in this

section, cases of unknown or missing data are ignored unless otherwise specified.

3.2.1 Summary of Deceased Donor Data

An exploratory analysis was completed to gain an overall picture of the donor data and general trends for the deceased donors in the system. Information contained in this section is intended to provide a very high-level overview of donor demographics in the system. Deceased donor gender, race, ethnicity, blood type, age, citizenship, cause of death, history of substance abuse, consent for donation, Kidney Donor Profile Index (KDPI), Body Mass Index (BMI), and home state are all reviewed.

In 1987, the first year of recorded data for the OPTN, there were 970 deceased organ donors. This number increased to 4,080 in 1988, the first full year with deceased donor data. Since 1988, the number of deceased donors has increased by over 100% to a total of 8,598 deceased donors in 2014. As shown in Figure 3.1, the number of deceased donors experienced a sharp increase from 2004 to 2004 and has been on a steady increase since 2010.

Figure 3.1: Deceased donors from 1988 to 2014.

Deceased donors are more commonly male than female with the database showing that from 1987 to 2015, there were 104,566 male deceased donors and only 70,690 deceased female donors, with males making up nearly 60% of the donor population. Figure 3.2 shows the number of male and female deceased donors over time. Since 1988, the number of male donors has increased by 102.74% while the number of female donors has had a much larger increase of 123.87% from 1988 to 2014.

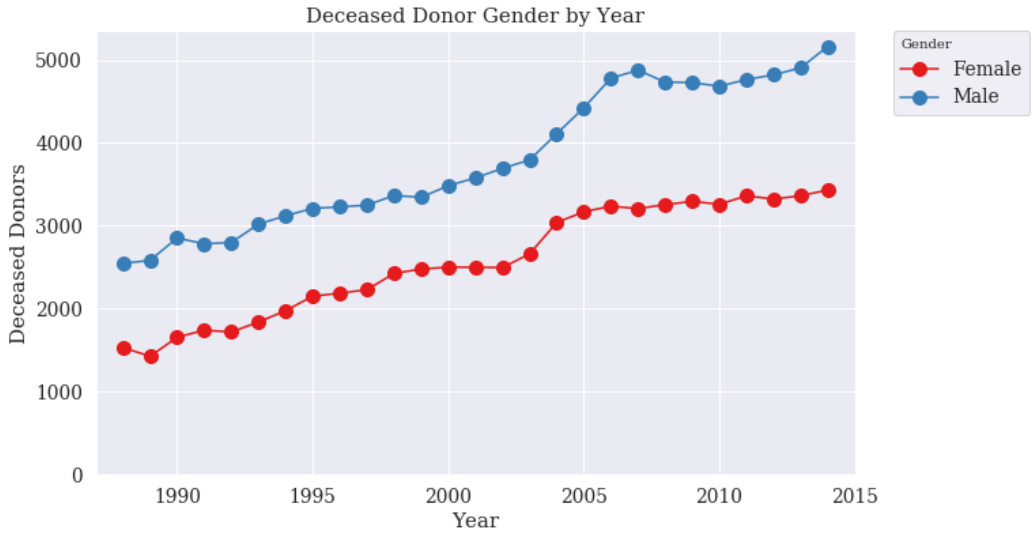

Figure 3.2: Male and female deceased donors over time.

The OPTN and UNOS recognize six races: White, Black, Asian, Hispanic, American Indian/Alaska Native, and Native Hawaiian/Pacific Islander. These organizations also account for a Multiracial category which refers to those who identify as being of more than one race. It can be seen below that the majority of donors are white, which is followed by Black and Hispanic donors at a relatively close level. Later, how this corresponds to the population levels according to the US Census will be shown. For graphs and images displayed in this section, the unknown demographic will largely be omitted from the results for simplicity. The unknown demographic was only used before the year 2001, since that time all donors have been racially identified.

There are clear differences in donation rates across different races for deceased donation as shown in Figure 3.3. White patients have the highest rates of deceased donation, Caucasians also make up the largest racial group in the US. Since each of these racial groups has a very different representation in the US population, this is compared compare to the population demographics in Figure 3.4. When compared to the 2010 Census population data, the rate of deceased donations from the white racial group is similar to that of Black/African American donors. The relative rate of Native Hawaiian/ Pacific Islander donors is the highest at approximately 800 donors per 1 million people in the population.

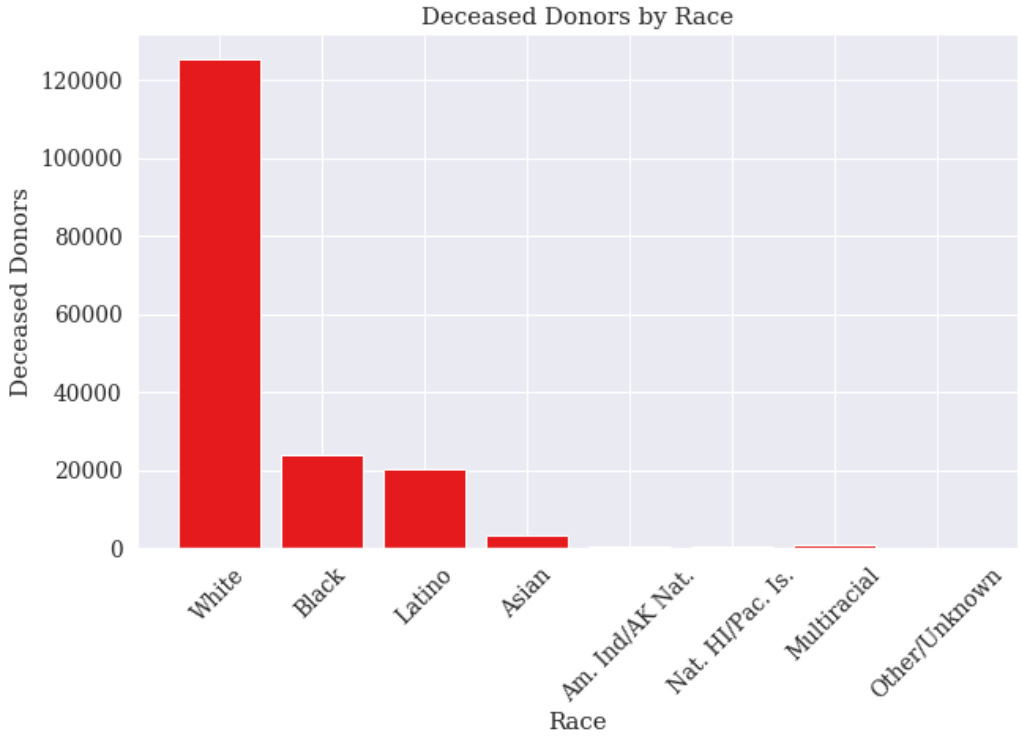

Figure 3.3: Number of deceased donors by racial groups.

The number of deceased donors per year by race is shown in the Figure 3.5. White donors make up the largest portion of deceased donors but have had the smallest increase in population since 1988. Large increases of over 200% have been recorded for all other

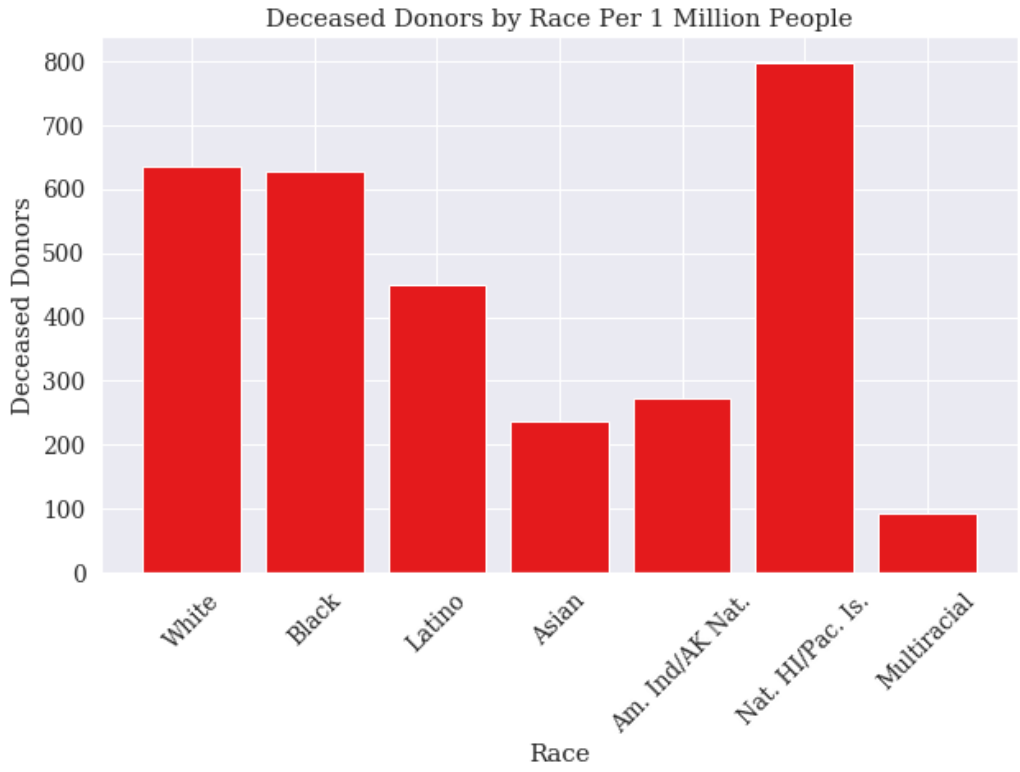

Figure 3.4: Race of deceased donors per one million people in population demographic.

racial groups. In recent years, the number of black and Native Hawaiian / Pacific Islander donors per capita have exceeded that of white donors. The number of Black and Latino donors steeply increased from 2000 to 2005 while the number of Asian donors has had a fairly linear increase. White and Latino donors stabilized in 2005 and have seen little increase since that time. American Indian/Alaska Native donors and Native Hawaiian / Pacific Islander donors have fairly low numbers and clear patterns are difficult to distinguish. The number of Multiracial donors had a very steep increase from 2009 to 2010. Donors with a designated racial group of Other/Unknown has decreased and fallen out of use since approximately the year 2000.

As seen in Figure 3.6, since 1988, the number of Latino deceased donors has increased by over 360% while non-Latino donors have increased by 95%. Beginning in 2004, the gap in donors per capita has decreased between Latino and non-Latino donors has decreased to

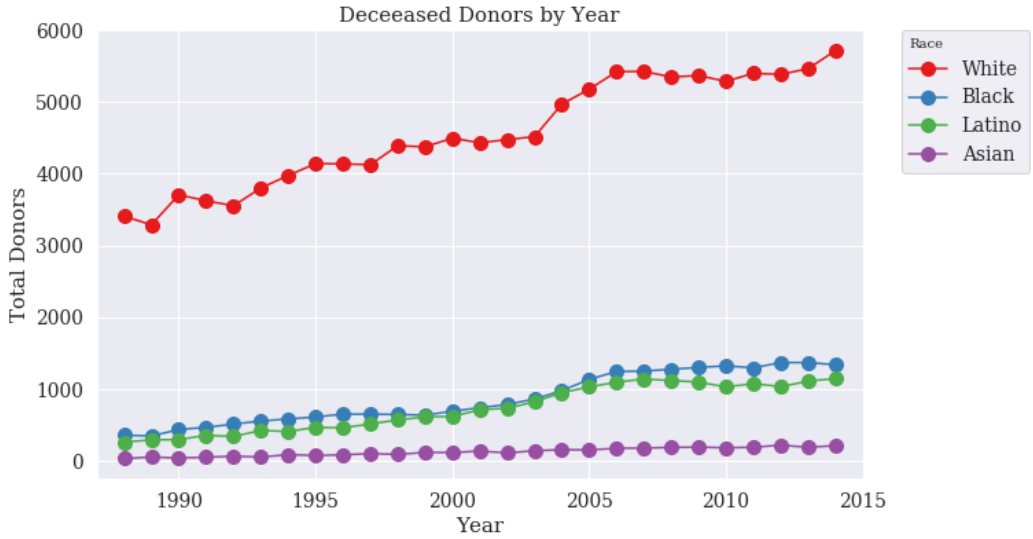

Figure 3.5: Race of deceased donors over time.

a difference of fewer than 5 donors per respective population.

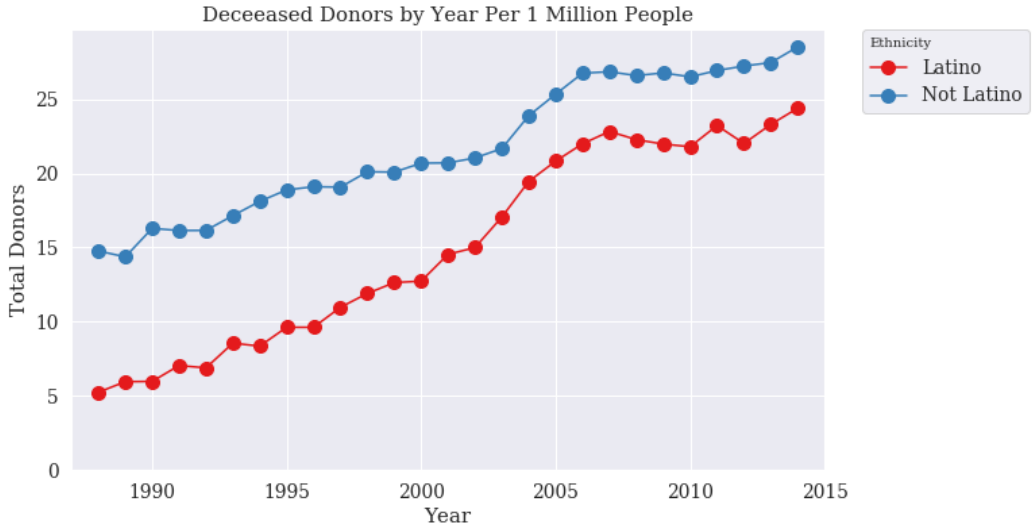

Figure 3.6: Ethnicity of deceased donors over time.

The ages of donors are sorted into bins for simplicity and easy presentation. Age bins for adults are 15 years in range and the age groups for children are in smaller increments.

For many of the graphs displayed in this chapter, donors under the age of 18 will be omitted as well as Not Available (NA) items.

Figure 3.7 shows the total number of donors per age group. Overall, the highest groups of donors are patients 18-34, 35-49, and 50-64 with the younger adult groups contributing the most to the number of deceased donors. The 50-64 age group has the highest rate of donors per 1 million people. Of all the adult categories, the adult group of deceased donors over age 65 is the lowest. When reviewed per 1 million population as of the 2010 census data in Figure 3.8, the adult aged organ donor all have similar organ donation rates except patients over 65. The age range 6-10 has the lowest rate of donors per population and has a much lower rate than all adult and child donation rates.

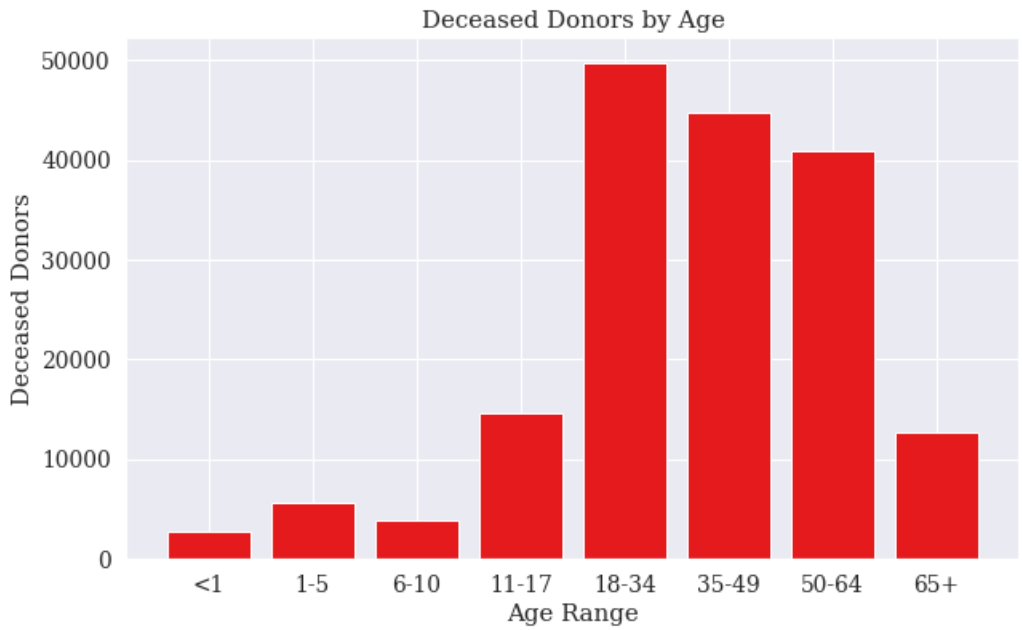

Figure 3.7: Deceased donors by age.

The number of deceased donors by age range over time is shown in Figure 3.9. This number for every age group has increased from 1988 to 2014 with the smallest increase in donors 18-34. Deceased donors in the 50-64 age range have increased by over 400%, since

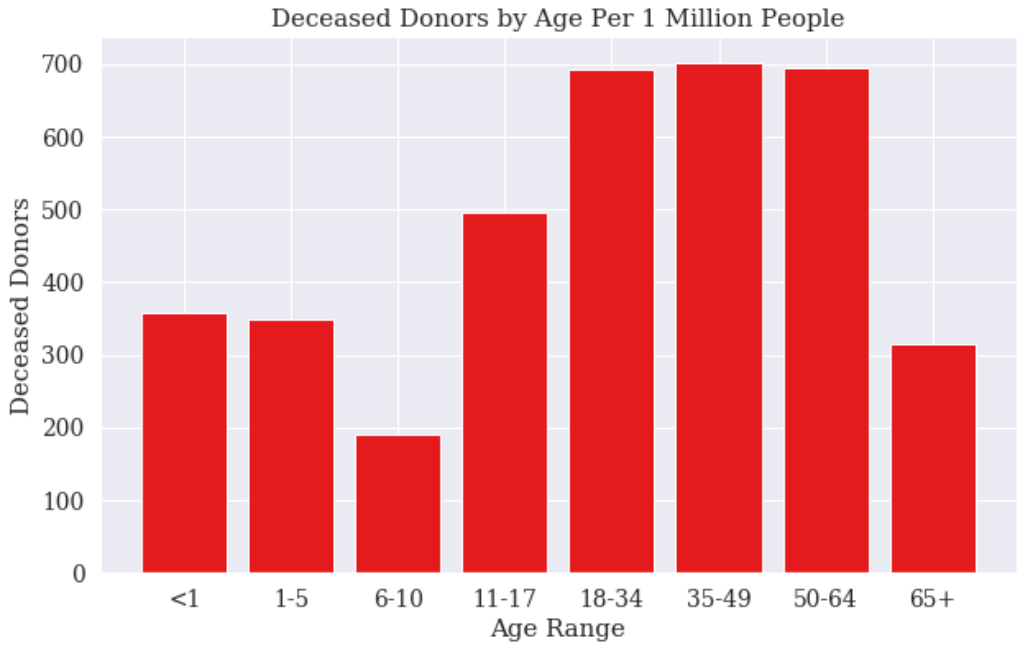

Figure 3.8: Deceased donors by age per one million people in population demographic.

data was first collected. The increasing number of older donors is likely due to advances in screening and organ donation protocols to include a wider range of patients.

Donor blood types are broken down into various levels: A, A1, A1B, A2B, AB, B, and O. It should be noted that although there is some amount of correlation between blood type and race, this is not significantly reported and all races include all blood types. The NA values will be ignored in most visualizations; since 2001 all blood types have been properly identified. More general categories for blood types are also used which will be demonstrated in plots in this analysis.

The citizenship of donors was also recorded and has the following groups: US Citizen, Resident Alien, Non-Resident Alien, Non-US CZ/US Res (Non-US Citizen and US Resident), Non-US Cz/Non-US Res - Not 4 Trans (Non-US Citizen and Non-US Resident, did not come to the country to perform the transplant), Non-US Cz/Non-US Res - 4 Trans (Non-US Citizen and Non-US Resident, did come to the country to perform the transplant), and unknown. A large majority of donors are US Citizens.

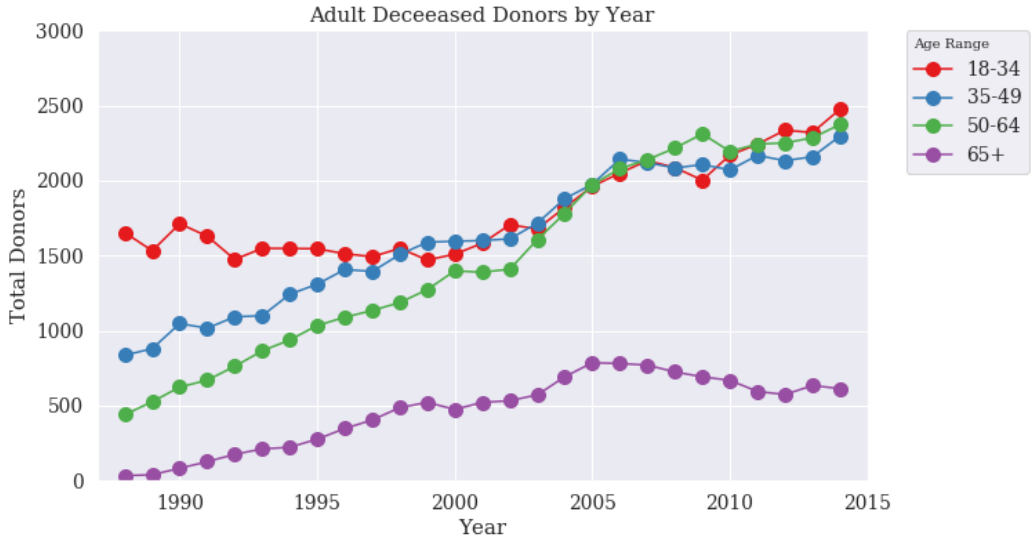

Figure 3.9: Adult deceased donors by age over time showing the adult aged organ donor all have similar organ donation rates with the exception of patients over 65.

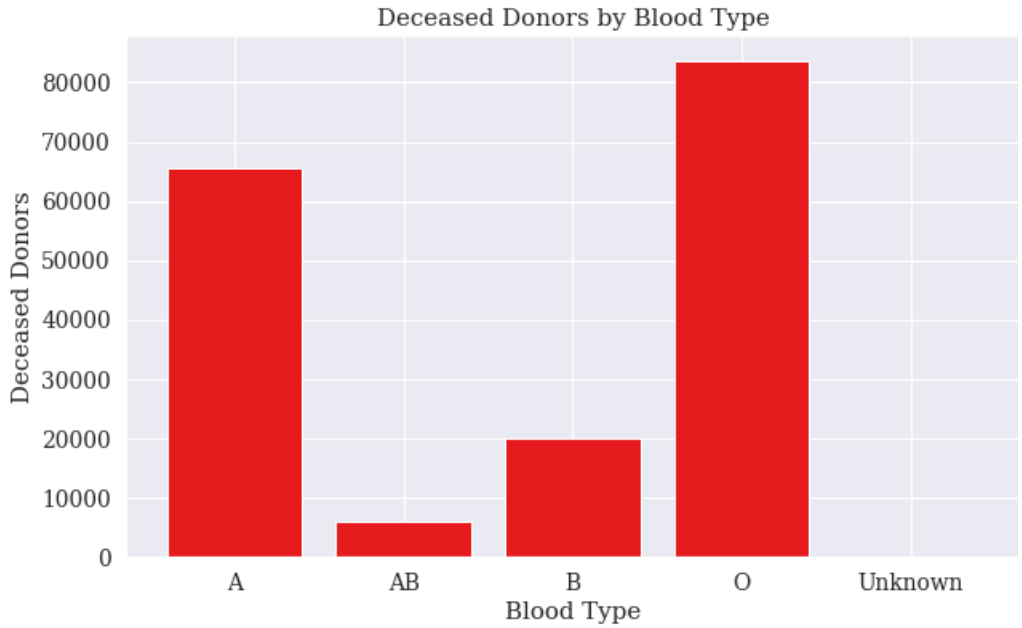

Figure 3.10: Deceased donors by major blood types.

The cause of death for donors falls into one of the following major categories or is

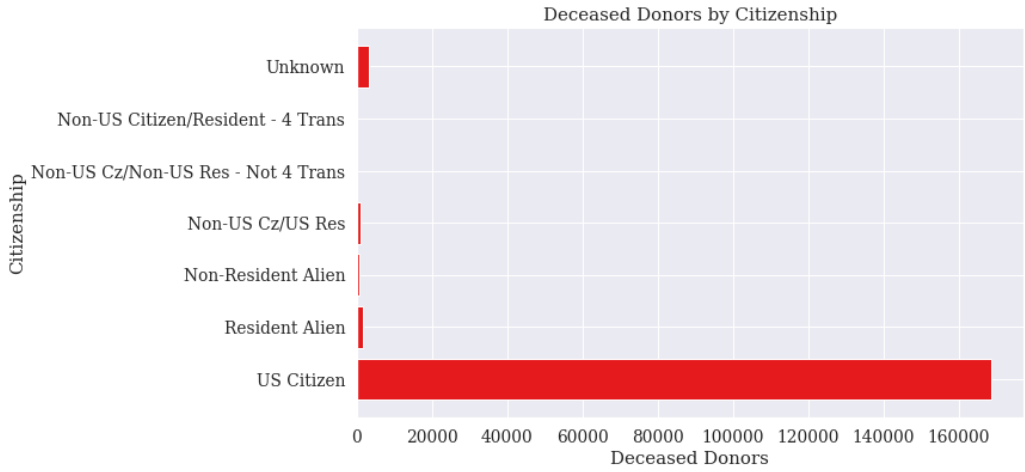

Figure 3.11: Deceased donors by citizenship status.

specified by other [13, 68–70]:

- Anoxia: Lack of oxygen to the brain
- CNS Tumor: Central Nervous System tumors
- Cerebrovascular/Stroke
- Head Trauma

3.2.2 Summary of Living Donor Data

A separate exploratory analysis was completed to gain an overall picture of the donor data and general trends for the living donors in the system. Information contained in this section is intended to provide a very high-level overview of donor demographics in the system. In this section, living donor gender, race, ethnicity, blood type, age, citizenship, level of education, relationship to the transplant recipient, BMI, and home state are all reviewed.

In 1987, the first year of recorded data for the OPTN, there were only 402 living organ donors. This number increased to 1829 in 1988, the first full year with living donor data. Since 1988, the number of living donors has increased by 218% to a total of 5822 living donors in 2014. As shown in Figure 3.12, the number of living donors experienced a sharp

increase from 2004 to 2004 and has been on a steady increase since 2010.

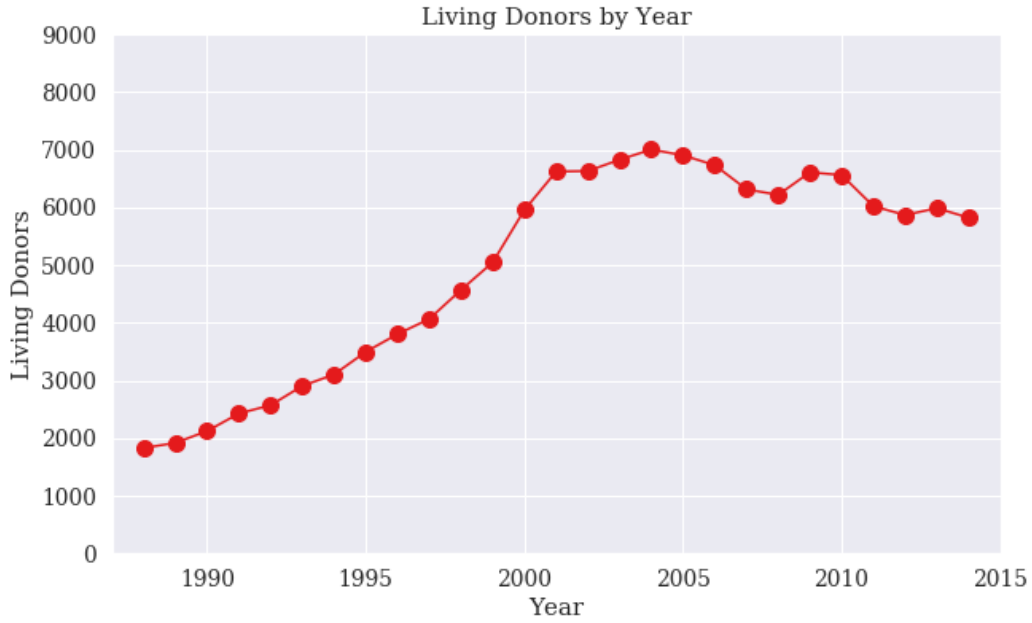

Figure 3.12: Living donors over time.

While there are typically more male than female deceased donors, females are more commonly living organ donors. Since 1987, when the UNOS first began tracking donations in the OPTN database there have been many more female than male living donors. There is one donor with an unknown gender, this patient is included from further records and visualizations for simplicity. Figure 3.13 shows the number of male and female living donors over time. Every year there are more female than male living organ donors. Both genders have followed similar trends in increasing steeply since the beginning until about 2004. Females experienced a steep drop in 2007 while males experienced a quick drop a year later in 2008. One data point exists for an unknown gender. Male organ donation has increased by 165% since 1988 while female donation has increased by more than 260%.

When looking at the race of living donors in Figure 3.14, the majority of donors are white, which is followed by Black and Hispanic donors at a relatively close level. For graphs

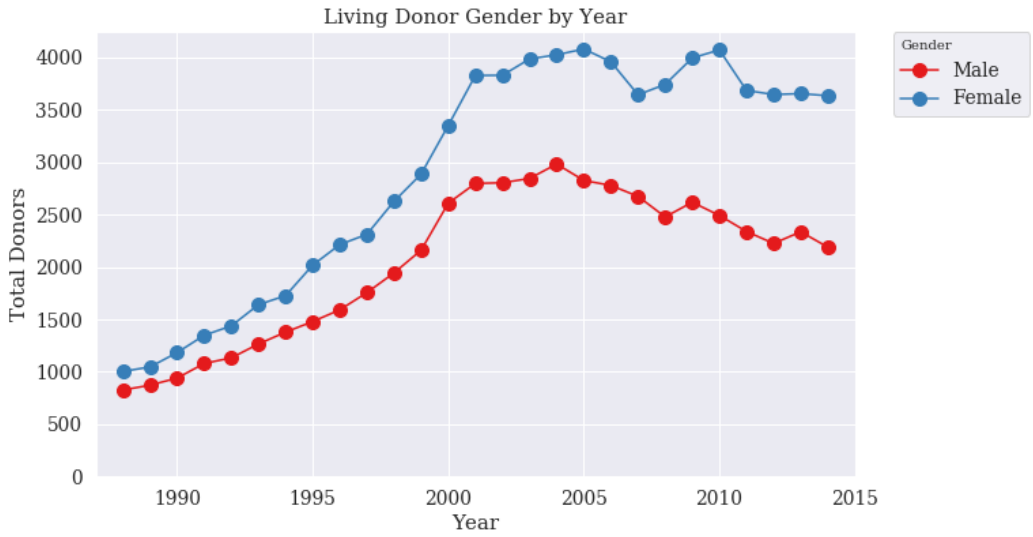

Figure 3.13: Male and female living donors over time, showing females are more commonly living organ donors.

and images displayed in this chapter, the unknown demographic will largely be omitted from the results for simplicity. Donors were only identified using the "unknown" category before the year 2001, since that time all donors have been racially identified. The living donor data category does not have separate categories for race and ethnicity.

There are clear differences in donation rates across different races for living donation as shown in Figure 3.14. White patients have the highest rates of living donation, Caucasians also make up the largest racial group in the US. When compared to the 2010 Census population data in Figure 3.15, the rate of living donations from the white racial group is only slightly higher than that of Black/African American donors. The relative rate of Native Hawaiian/ Pacific Islander donors is the highest at approximately 1350 donors per 1 million people in the population.

The overall breakdown of living donors over time by race shows very different trends across the races. Like the overall data for living donors, the number of White living donors peak in 2004. White living donors experience a slightly less severe drop in donors than the overall population. The overall drop in living donors for the Black population is much more

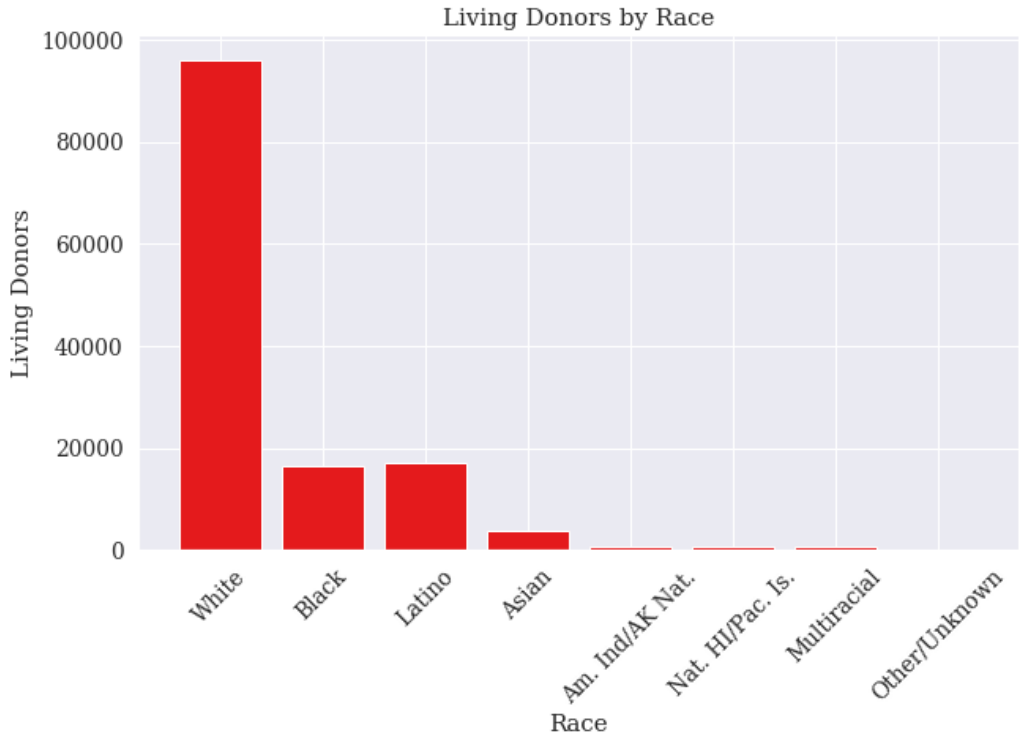

Figure 3.14: Living donors by race; the majority of donors are white, which is followed by Black and Hispanic donors at a relatively close level.

significant, the number of Black donors has dropped 30.9% between 2004 and 2013.

There is a deviation from the general pattern for the rest of the racial groups. Hispanic donors have increased very steadily over time. Hispanic donors also experienced a slight drop since 2004, but only by 5.2%. The peak year for Hispanic donors was slightly later, in 2009. Asian donors have increased steadily and have not dropped since 2004. Asian donors interestingly have their largest increase in donation from 1999 to 2000.

All other races have much fewer donors, none of these populations ever had more than 50 donors per year. Donation varies greatly from year to year for the American Indian/Alaskan Native population and peaks in 2001, followed by an overall decline. The number of Native Hawaiian/Pacific Islander population follows a very different pattern and peaked much earlier than any other group, in 1993 and has had an overall decline since that time. Multiracial donors have increased overall and have steadily increased since 2009.

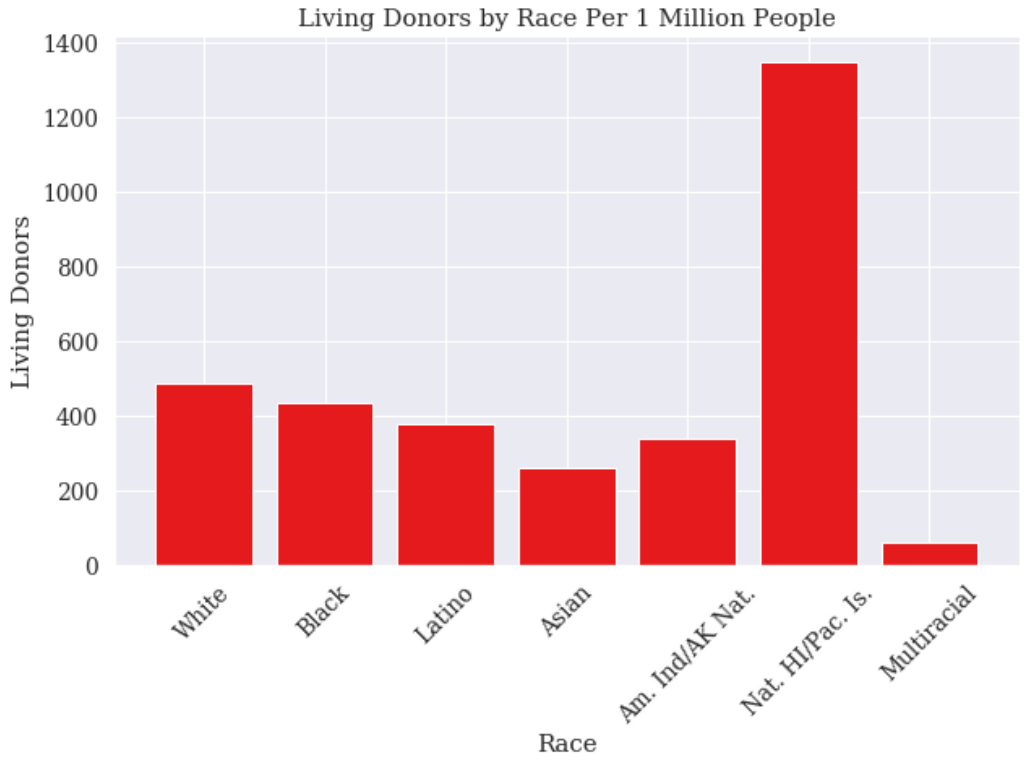

Figure 3.15: Race of living donors per one million people in population demographic; the rate of living donations from the white racial group is only slightly higher than that of Black/African American donors.

The breakdown of living donors by age shows the groups with the largest number of living organ donors in Figure 3.17. Since 1994, the 35-49 group has the most donors followed closely by adults 18-34 years old. These two groups follow a similar pattern over time, increasing and decreasing at similar points in time. The 50-64 age group has followed a different trend and has steadily increased since 1988 and is now approaching the donation dates of the 18-34 group. Figure 3.18 shows the demographics of the group per one million people in the age range based on the US Census data.

Although the most common age for deceased donors is from the 18-34 population, this is not the largest group of living donors. The largest proportion of living organ donations come from patients aged 35-49. There was a substantial increase in living donors from the year 2000-2005 for donors aged 35-49 followed by a decrease for this age range and donors

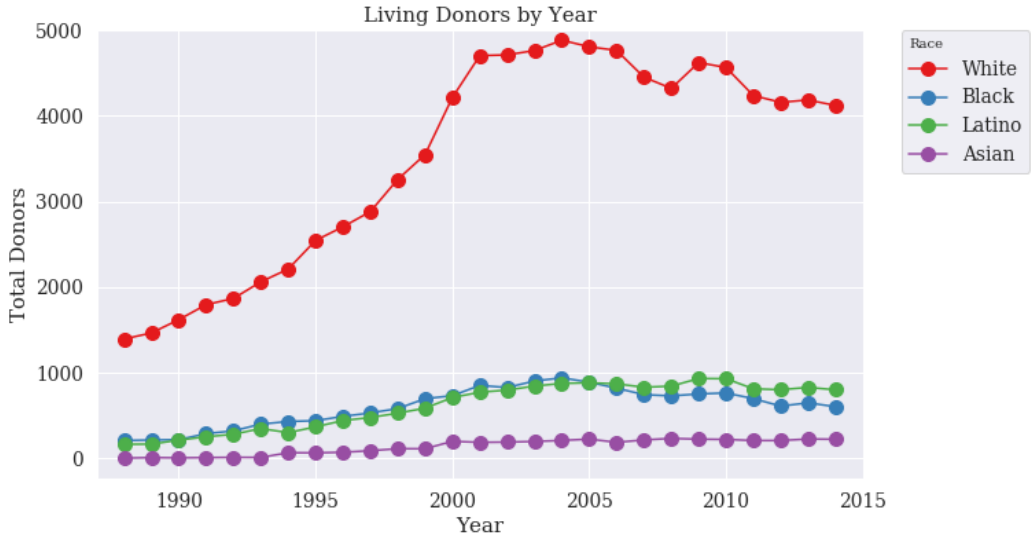

Figure 3.16: Race of living donors over time.

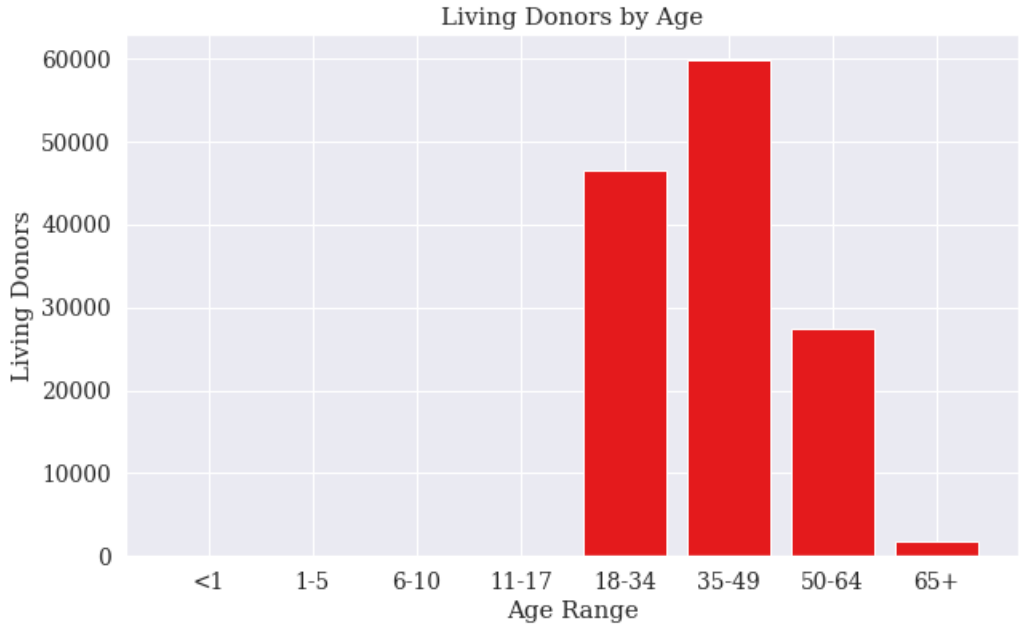

Figure 3.17: Living donors by age.

18-34 from 2005 to the present data in 2014.

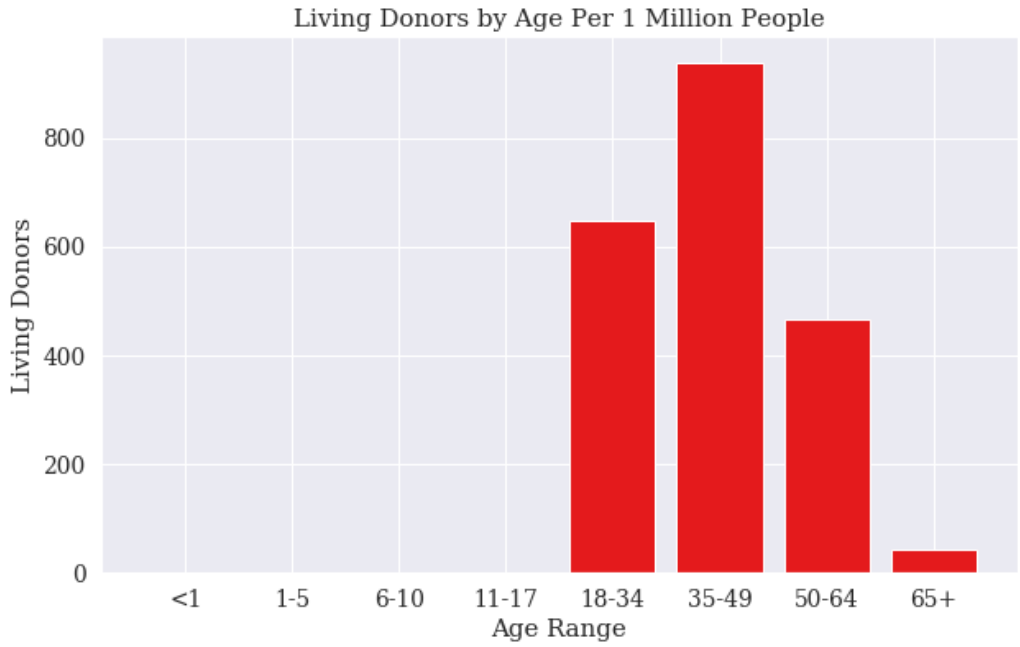

Figure 3.18: Living donors by age per one million people in population demographic.

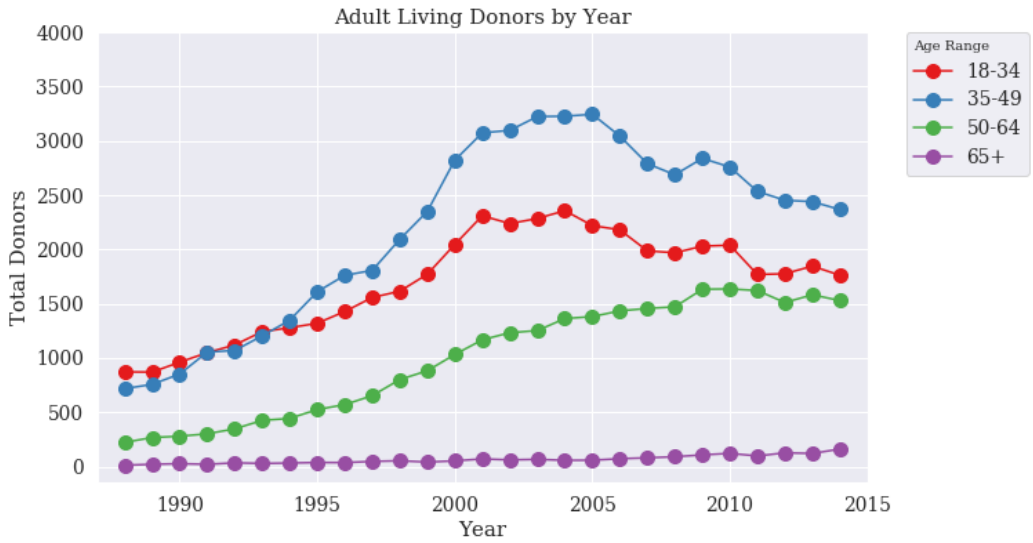

Figure 3.19: Adult living donors by age over time.

Donor blood types are broken down into various levels: A, A1, A1B, A2B, AB, B, and O. It should be noted that although there is some amount of correlation between blood type

and race, this is not significantly reported and all races include all blood types. The NA values will be ignored in most visualizations since 2001 all blood types have been properly identified. More general categories for blood types are also used which will be demonstrated in plots in this analysis. Figure 3.20 does not seem to reveal any special information on donation rates by blood type. Blood type O accounts for the majority of donors followed closely by type A, which corresponds to overall levels of the population.

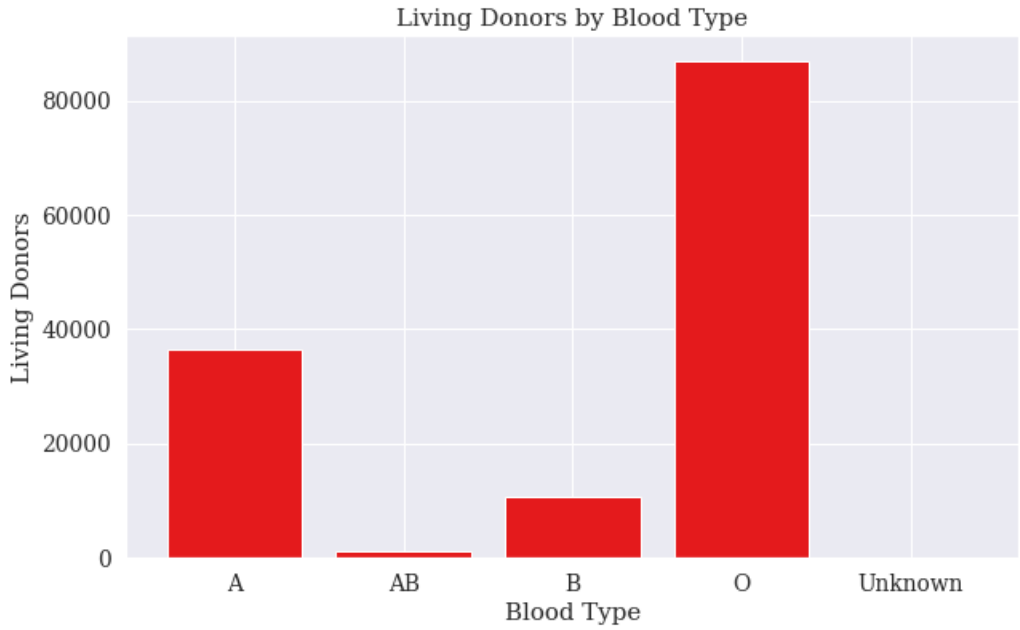

Figure 3.20: Living donors by major blood types.

The citizenship of donors was also recorded and has the following groups: US Citizen, Resident Alien, Non-Resident Alien, Non-US CZ/US Res (Non-US Citizen and US Resident), Non-US Cz/Non-US Res - Not 4 Trans (Non-US Citizen and Non-US Resident, did not come to the country to perform the transplant), Non-US Cz/Non-US Res - 4 Trans (Non-US Citizen and Non-US Resident, did come to the country to perform the transplant), and unknown. A large majority of donors are US Citizens.

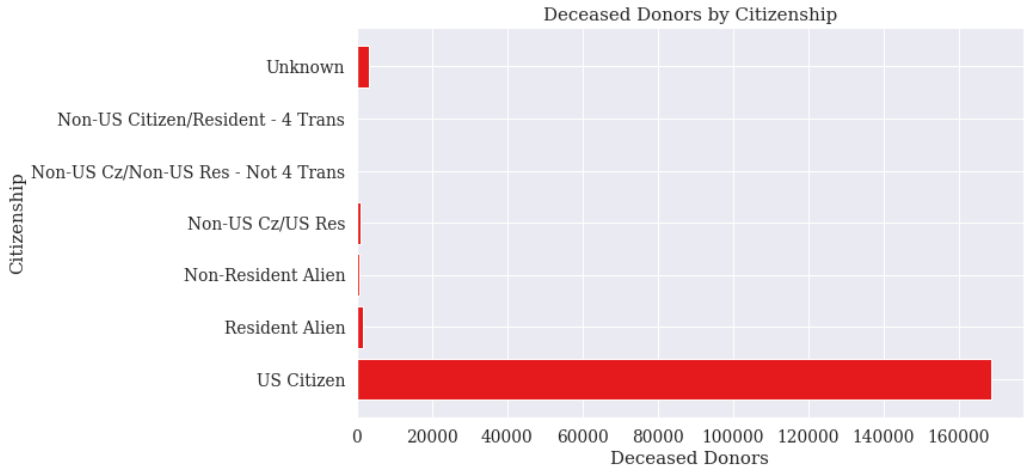

Figure 3.21: Living donors by citizenship status.

Education levels of donors are broken down into: None, NA/ <5 YO (Not reported for donors under 5), Grade School, High School, Some College/Tech School, AS/BS Degree (obtained an Associates or a Bachelors degree), Grad Degree (obtained a graduate degree) and an unknown group. Most donors are listed as unknown, before 2001, this answer was not often recorded.

Figure 3.22 shows the education level of living donors beginning in the year 2000. Education was not frequently tracked before 2000, so prior years have been left out as well as the unknown category. This graph also removed the "None" and "NA" groups to simplify the image and focus on data points containing valuable demographic information. People with grad degrees and college degrees have increased steadily over recent years. The majority of donors have at least finished high school, with the two highest categories are people with at least some college.

The level of education in the US could be an indicator of the likelihood of living donation. Educational demographics over time are shown in Figure 3.23, which shows the top three education groups in the US for living organ donation are High School, Some College/Technical School, and those with an Associates or Bachelors degree. These groups are followed by donors with a graduate degree. The top three groups vary greatly over the

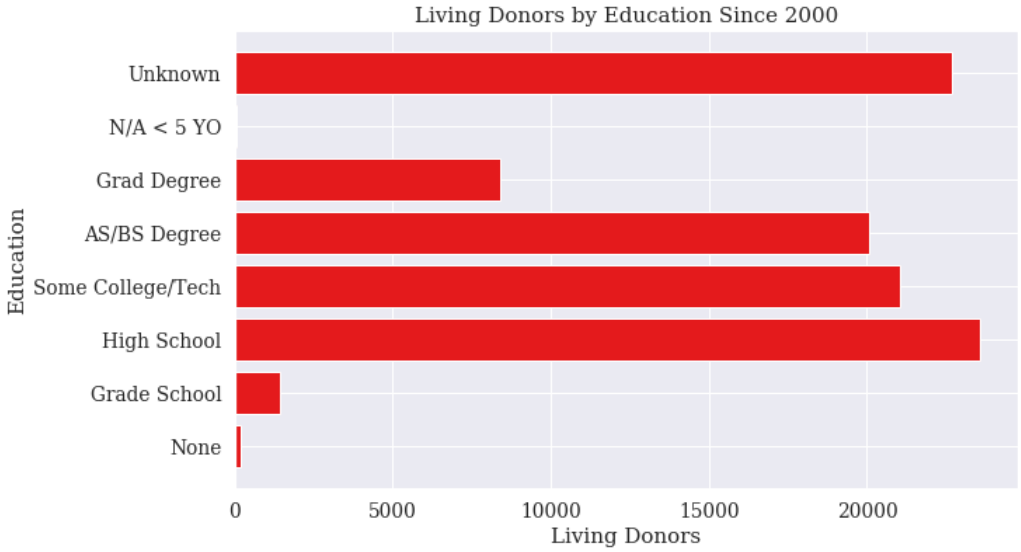

Figure 3.22: Living donor education levels since the year 2000.

years and there is little consistency for which has the highest number of donors cine 2009. Since 2000, the number of donors with a graduate degree has steadily increased.

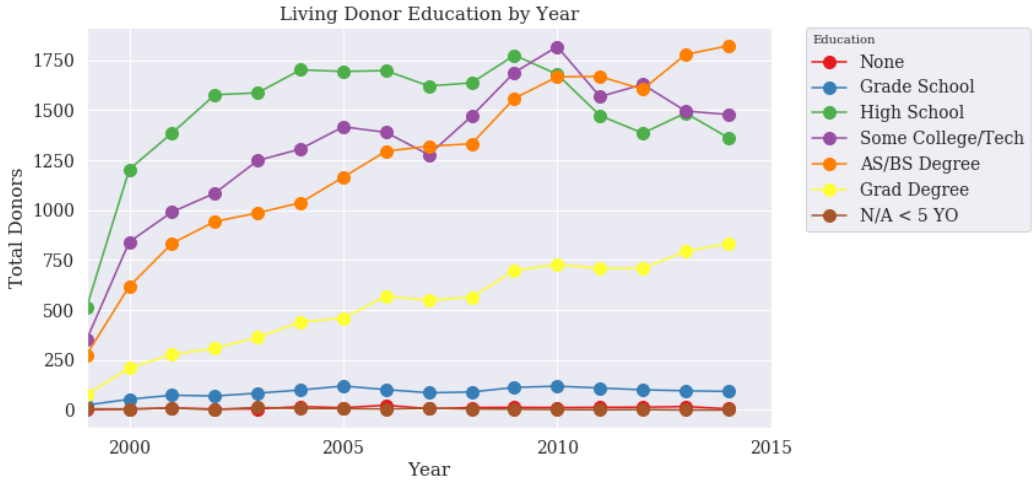

Figure 3.23: Living donor education levels over time.

Donor's educational attainment data can be compated to the data from the Census for

Table 3.2: Educational attainment from the Census for individuals over 18 [71]

None	Grade School	High School	Some College/Tech	AS/BS Degree	Grad Degree
824	26,349	71,368	56,516	65,167	7,689

Educational Attainment [71] as shown in Table 3.2. The numbers displayed in the table are in thousands. This table gives us enough information to calculate the proportions of donors withcertain educational attainment that become donors. Donors with a graduate degree have the highest donation rate per education level, with 3.2% of citizens (per thousand) becoming living organ donors. This is closely followed by donors with an Associates or Bachelors Degree at 3.08%. Adults with some college or trade school have a 2.66% donation rate per thousand while donors with a high school diploma are at 2.10%. One of the most telling areas is those with only a grade-school education. Although this group makes up 12.0% of the population, they only account for 1.69% of living organ donors.

The relationship levels of donors are broken down into Bio Parent (Biological Parent), Bio Child (Biological Child), Bio Twin (Biological Identical Twin), Bio Full Sib (Biological Full Sibling), Bio Half Sib (Biological Half Sibling), Bio Other (Other Biological Relative), Non-Bio Spouse (Non-Biological Spouse), Non-Bio Partner (Non-Biological Life Partner), Non-Bio, unrel: Anon (Anonymous Non-Biological Donor), Non-Bio L/D Donation, Non-Bio, unrel: Domino (Domino Donation from a Donor Chain), Non-Bio, unrel Paired (Non-Biological Unrelated Paired Donor), Non-Bio other unrel directed (Directed Donation from an Other Non-Biological Donor), and an unknown group. These are also split into broader categories of Biological, Non-Biological Known, Non-Biological Unknown, and Other. An overview of the living donors by relationship type is shown in Figure 3.24.

Living donors can be more generally grouped by the broad relationship type:

- Bio: Biological relative including parent, child, twin, full sibling, half-sibling, and other.
- Non-Bio Known: Non-Biological donor that is known to the recipient. This includes

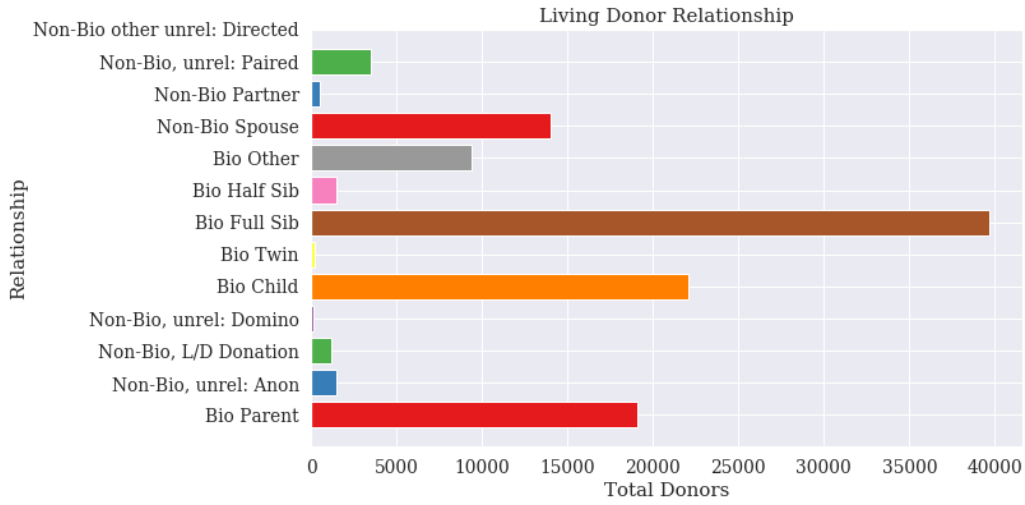

Figure 3.24: Living donors by relationship to transplant recipient.

a spouse, partner or other unrelated directed donation.

- Non-Bio Unknown: Non-Biological Unknown donor is unknown to the recipient. This includes an anonymous donor, a domino donation or a paired donation.

- Other: Donors in the unknown category and donors classified as non-biological L/D donors.

Figure 3.25 shows the relationship trends over time. The number of Biological donors has consistently been the highest category, although it has dropped a lot since 2001. Non-Biological, but known donors has increased over the years and has approached the numbers of the biological donors.

Specific familial relationships between biological donors are shown in Figure 3.26. Full siblings is the largest group, which has consistently been the largest group over the span of the data. This group has also experienced the largest group in donations since 2001. The number of children that donate to parents has increased over the years and in 2000 this number surpassed that of parents donating to children, which was the third-largest group. Other biological relatives rank slightly below parents in recent years.

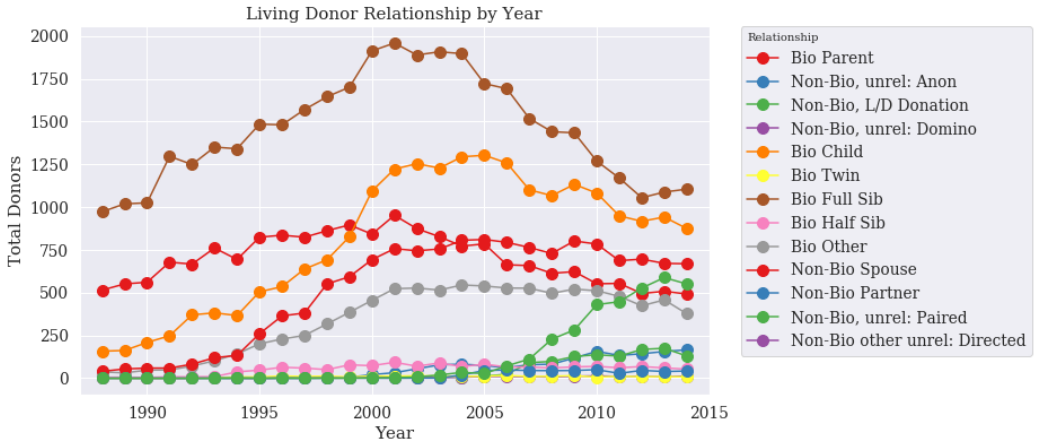

Figure 3.25: Living donors over time by relationship to transplant recipient.

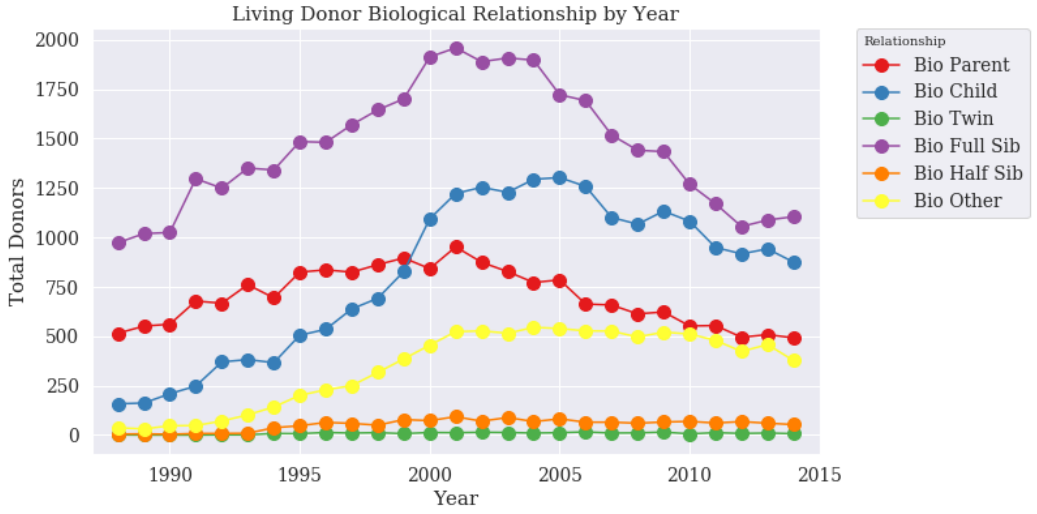

Figure 3.26: Biological living donors by relationship type over time.

The number of Non-Biological donors that know the recipient has experienced an overall increase over the years as shown in Figure 3.27. Donations from spouses and life partners have increased and remained nearly steady, since about 2000. The number of Non-Biological donors that know the recipient, but are not a spouse has increased very quickly since 1988 and in 2000, this number completely surpassed that of a spousal connection.

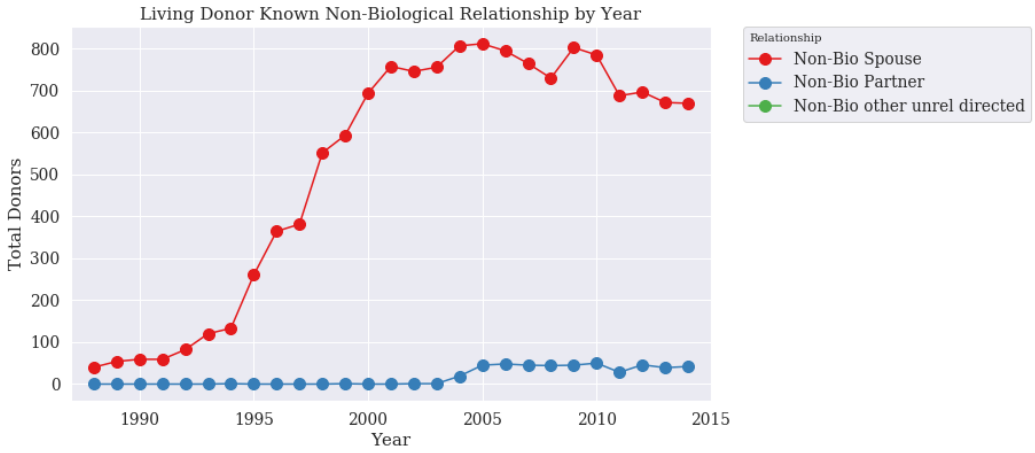

Figure 3.27: Non-Biological living donors known to the recipient by relationship type over time.

3.2.3 Cross-Sectional Analysis of Living and Deceased Donors

This section of the work explores the intersectionality of components of both living and deceased donors. Donations have steadily risen for deceased donors but have dropped since 2004 for living donors. In 2001, 2002, and 2003, there were slightly more living than deceased donors as shown in Figure 3.28.

Donors by Gender and Race

Additional insights can be gained by looking at cross-sections of the data at a deeper level. Reviewing the trends of deceased and living donors over time by race and gender shows interesting patterns across demographic groups. Figure 3.29 shows the patterns for deceased donors by gender and race over time. African-American and Caucasian donors seem to follow the same general pattern, with a big rise between 2002 and 2007 for the males, with male donor numbers being higher than females. Looking at trends over the years, the number of Caucasian donors has stayed fairly consistent since 2006 and the number of African-American donors has an interesting drop in 2008 for males.

Hispanic/Latino donors experienced a large increase between 2002 and 2007, nearly

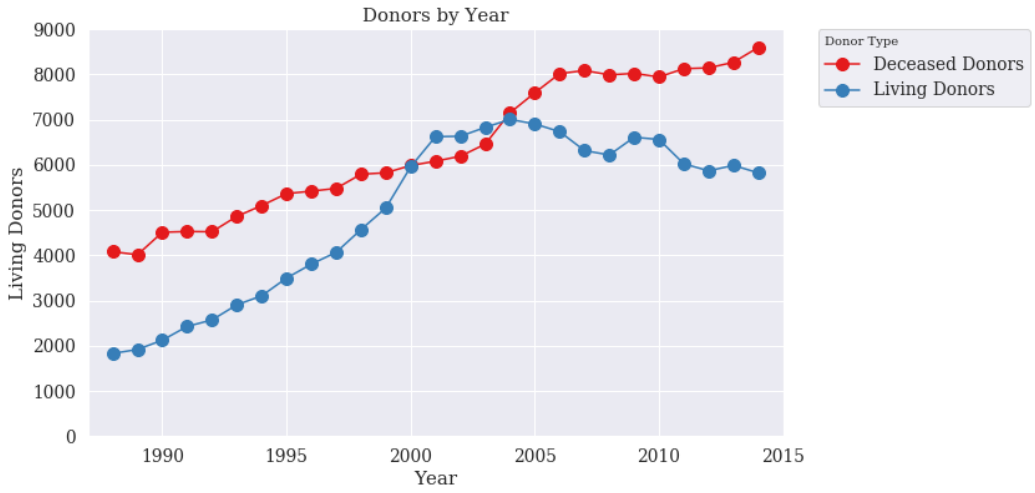

Figure 3.28: Living and deceased donors over time.

doubling the number of deceased donors in this period, similar to African-American and Caucasian donors. Males of Hispanic/Latino origin donate at a rate almost double that of Hispanic/Latino females, although Hispanic/Latino males have experienced a drop in donor numbers since 2007.

Asian males and females have highly variable deceased donor data with some females occasionally being donors more often than males. The Asian population of deceased donors is a very small group compared to the three largest donor demographic groups. American Indian/Alaskan Native donors have a high amount of variance, there are rarely more than 20 donors a year for males and females in the past 10 years with a recent uptick in Male Donors in 2013 and 2014. Native Hawiian / Pacific Islander also have high variance and low numbers for the donors.

Multiracial donors increased significantly from 2009 to 2014 The interesting peak of multi-racial donors in 2011 for both makes and females. The “Unknown” category is rarely used after 2003, indicating this data has been tracked more accurately in recent years.

Figure 3.30 reviews the patterns across races over the years for living donors. For all the major races of donors, there are more female donors than males every year. This gap between male and female living donors has increased over time. This is true for the White

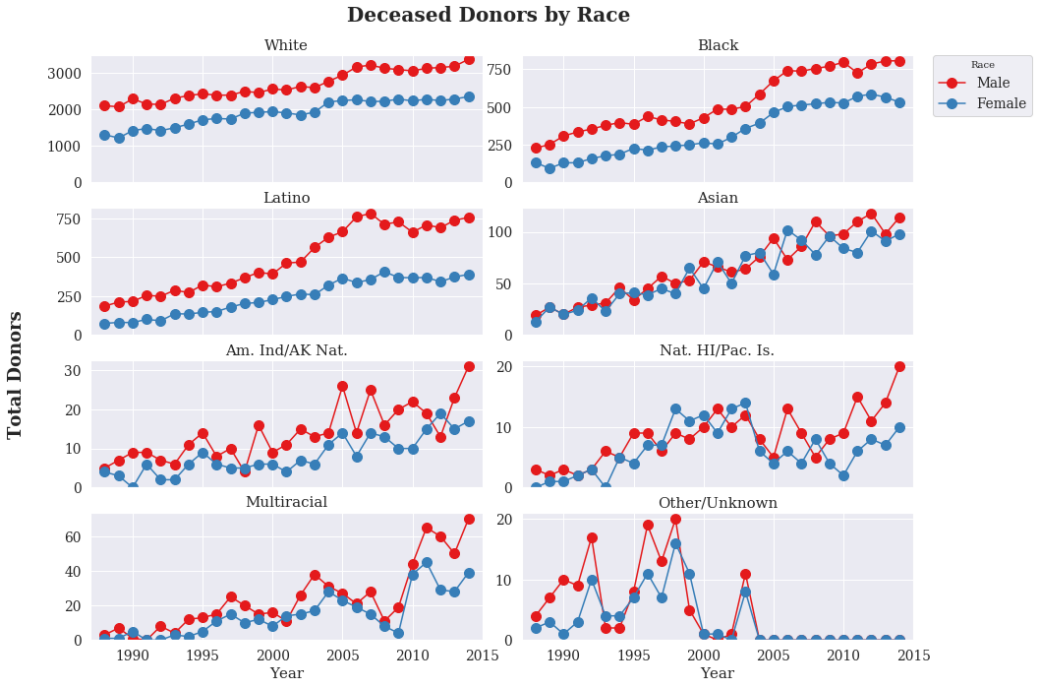

Figure 3.29: Deceased donors by gender and race over time.

donors and in 2013, there were 58.3% more female than male donors. Black donors also follow a similar pattern for both genders to the overall race over time. In 2013 there were 73.6% more female than male donors. For Hispanic donors, the gap between male and female donors has been increasing since 2006 and reached 64.6% in 2013.

Asian donors had an extremely small gap between men and women until 2008, where the gap went from 12.7% more females than males in 2007 to 51.6% in 2013. The gap between American Indian/Alaskan Native donors is highly variable over time, but the women always have a higher donation rate than men, with the exception of 1993. There is a high variation for the proportion of Native Hawaiian/Pacific Islander donors and there is no consistency in the ratio of male to female donors. The Multiracial donors are also variable, but since 2005 there have consistently been more men than women.

Figure 3.30: Living donors by gender and race over time.

Donors by Gender, Age, and Race

There are interesting differences across age, gender, and race for the populations of deceased donors, as shown in Figure 3.31. For all male racial groups besides Asians, younger age rates have higher rates of donation than the next oldest age group. For Asian men, the largest group of donors is that of males 50-64, followed by males 35-49 and then finally the youngest age group. The quantities of deceased donors across females does not follow the same strict pattern as males. For women, the largest age groups tend to be 35-39 and 50-64. The Asian female deceased donor population follows the same pattern as Asian males.

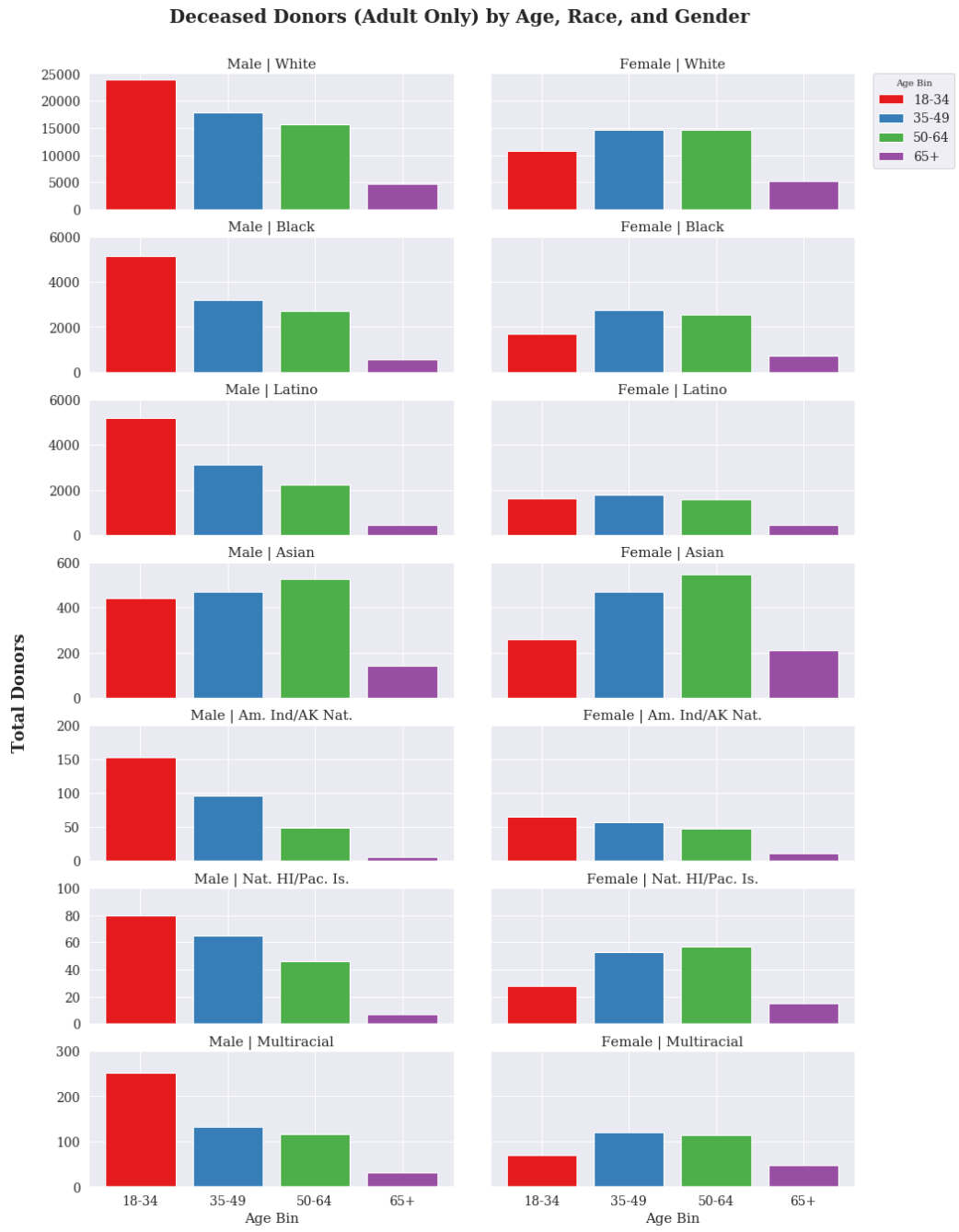

Figure 3.31: Deceased donors by gender, age, and race.

The breakdown of living donors across age, gender, and race are shown in Figure 3.32.

Trends between men and women are very similar to the 35-49 age group, even though the female donor rates are much higher. For female donors, the 35-49 age group is much higher than any other age bins, this gap becomes prominent in 2000. Since 2000, the 35-49 group continues to grow and the 18-34 group drops off and remains closer to the 50-64 group. For male donors, the 18-34 and the 35-49 groups are extremely close in donor numbers over the years with males 18-34 only slightly under the 35-49 age group since 1998.

The age breakdown for living donors shows a different demographic than that of deceased donors. Women in the 35-49 age range are the most frequent donors across all races. White men aged 35-49 are the most frequent donors of the white race while for all other racial groups, the most frequent donors are males 18-34.

Donors by Gender, Education, and Race

A breakdown of donors by gender and education is shown in Figure 3.33. Although there are many more female than male donors, with the educational breakdown by gender, there is little difference in the overall trends in the two facets. When this data is compared to the overall population data, interesting information is revealed. Females with a graduate degree have the highest donation rate at 3.70% (per thousand), followed closely by 3.57% for those with an Associates or Bachelors Degree. Males with similar education levels have donation rates of just 2.67% and 2.49%, respectively.

Figure 3.34 shows the total number of donors by gender, race, and education. Women are higher than male donors in all categories with the exception of Native Hawaiian/Pacific Islander donors. The Hispanic/Latino racial group has the highest proportion of donors with an education level lower than high school diplomas. Asian living donors have the highest proportion of graduate degree donors.

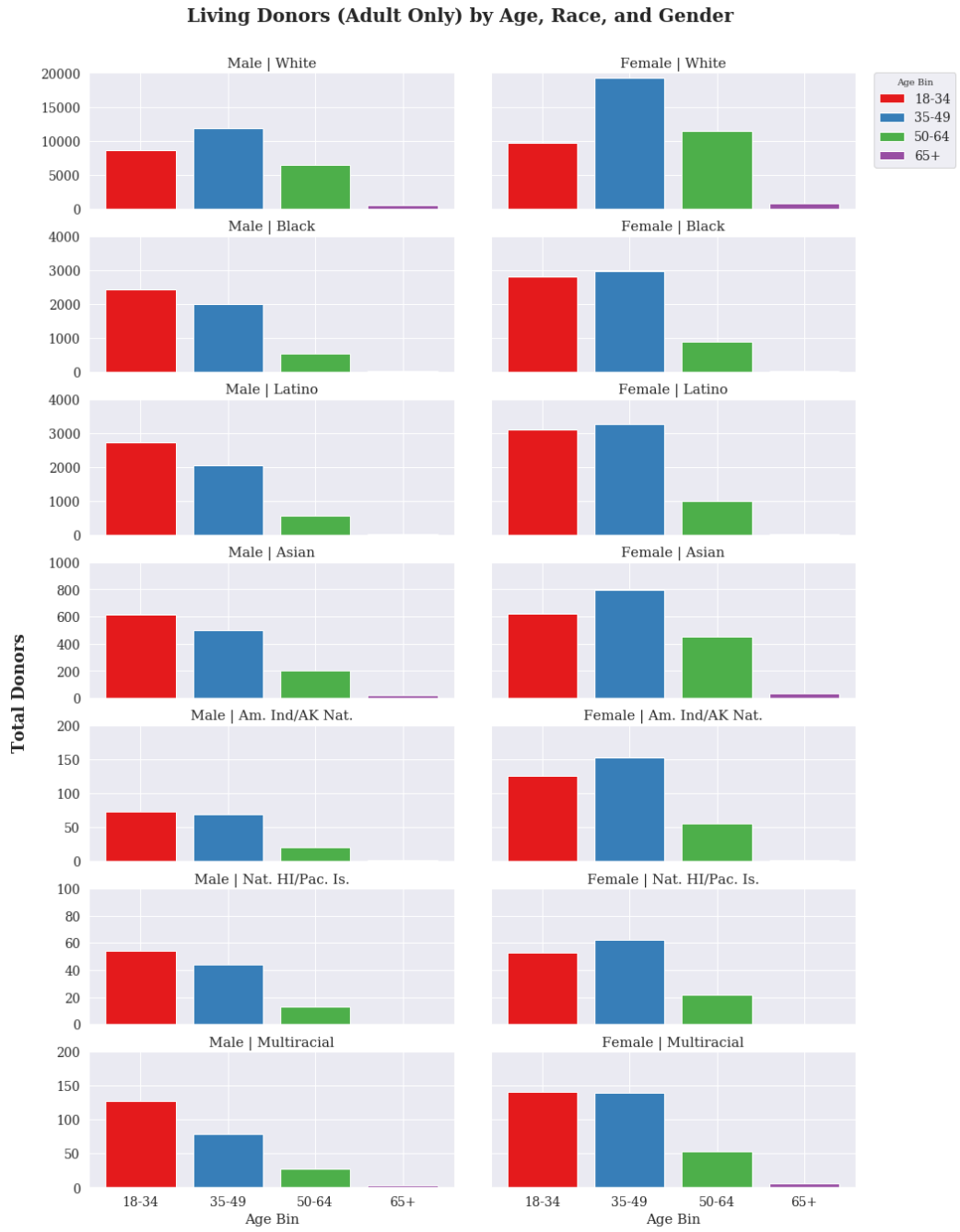

Figure 3.32: Living donors by gender, age, and race.

Donors by Relationship and Other Demographic Groups

The overall trends of male and female donors appear similar in Figure 3.35, but the proportion of donations varies across the genders. For female donors, 49.3% of donations were to

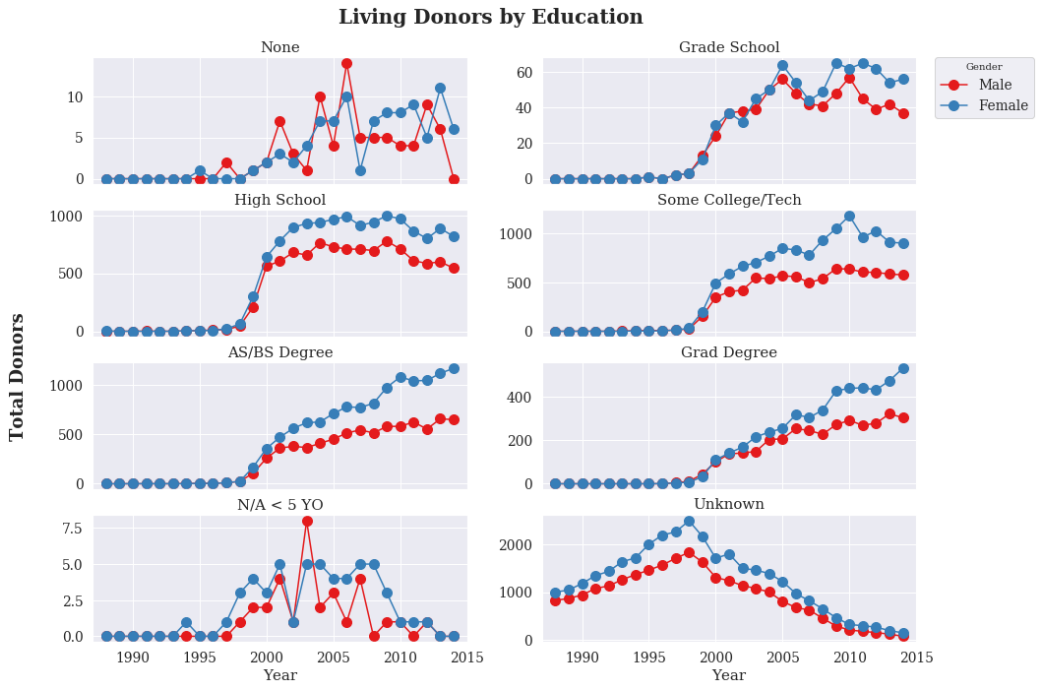

Figure 3.33: Living donors by gender and education over time. Although there are many more female than male donors, with the educational breakdown by gender, there is little difference in the overall trends in the two facets.

a Biological connection, compared to 54.0% of male donors. A higher percentage of female donors, 35.5%, donated to a non-biological but known recipient, compared to just 29.1% of males.

Figure 3.36 shows a subset of the relationship data and only reviews biological relationships. There are similarities in the trends between male and female biological donors. For both genders, full sibling is the largest group, but for males, this number has experienced a greater decrease than the female population.

Biological relationships over time by racial groups are shown in Figure 3.37. There has been a large decrease in the number of White biological related living donors and a large increase in the number of non-biological, known donors. The gap between these two groups is much closer than in other areas. White donors have the highest proportion of non-biological donors. Non-biological and known living donors for African-American donors

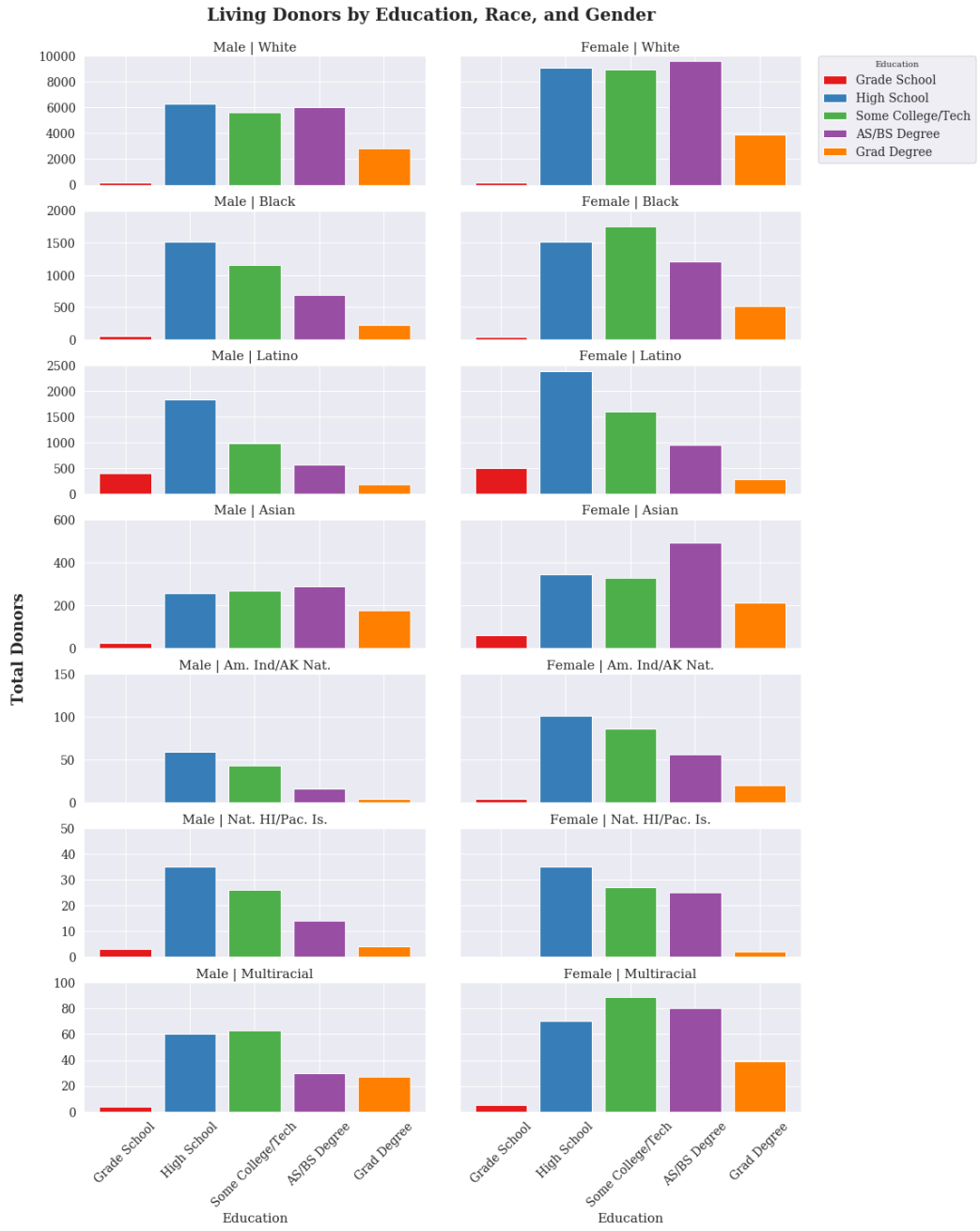

Figure 3.34: Living donors by gender, race, and education over time.

have decreased since 2005 and the number of biologically related living donors has decreased since 2004. Biological donors for Hispanic/Latinos have not suffered as large of a decrease as Blacks and Hispanics, the number of non-biological, known donors has stayed relatively

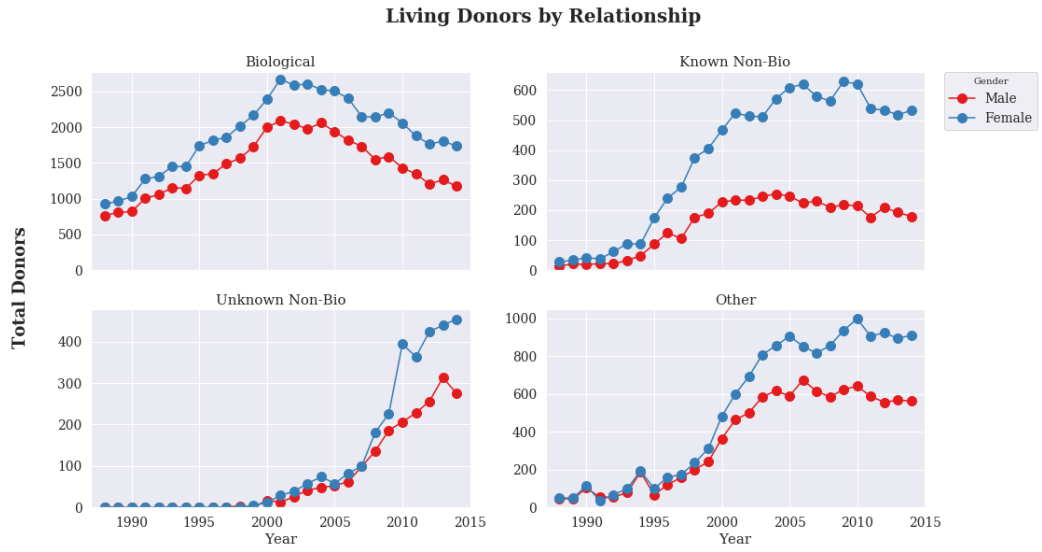

Figure 3.35: Living donors by gender and donor relationship to the recipient over time.

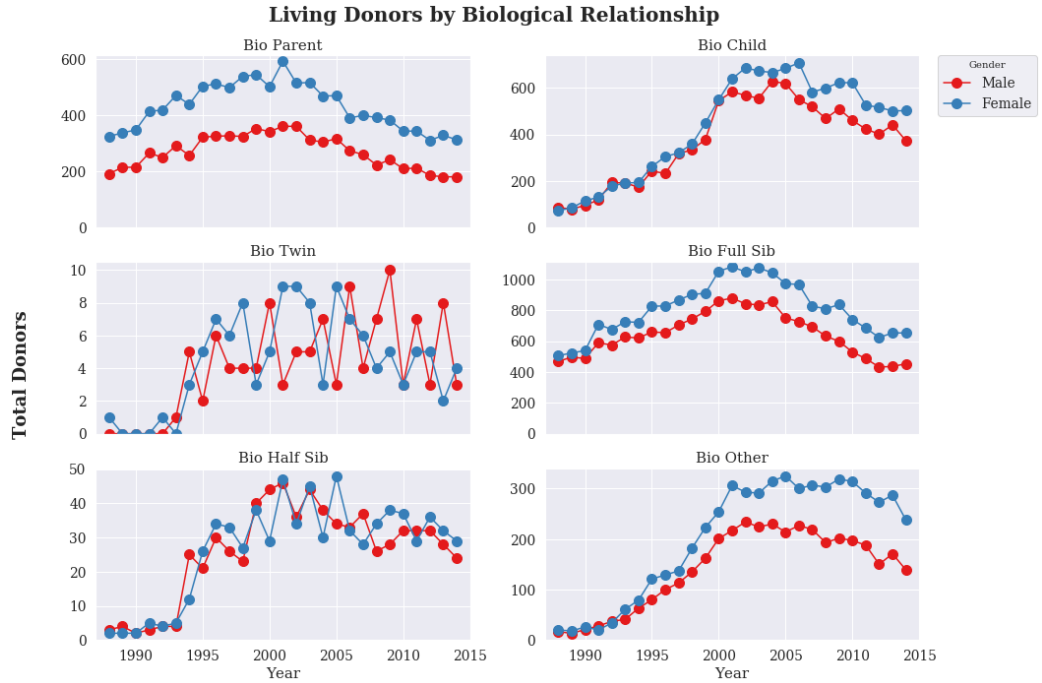

Figure 3.36: Living donors by gender and biological donor relationship to the recipient over time.

stable. There are fewer Asian living donors than the other major race categories and the number of Asian donors has decreased for Biological donors and has remained stable for non-biological known donors since 2004. American Indian / Alaska Native living donors that are of a biological relationship has decreased overall since 2001. The number of all other donor relationship types has remained low. Native Hawaiian / Pacific Islander donors have decreased overall and the number of biological donors has decreased overall since 1993. Donations rates among people from a multiracial background are highly variable.

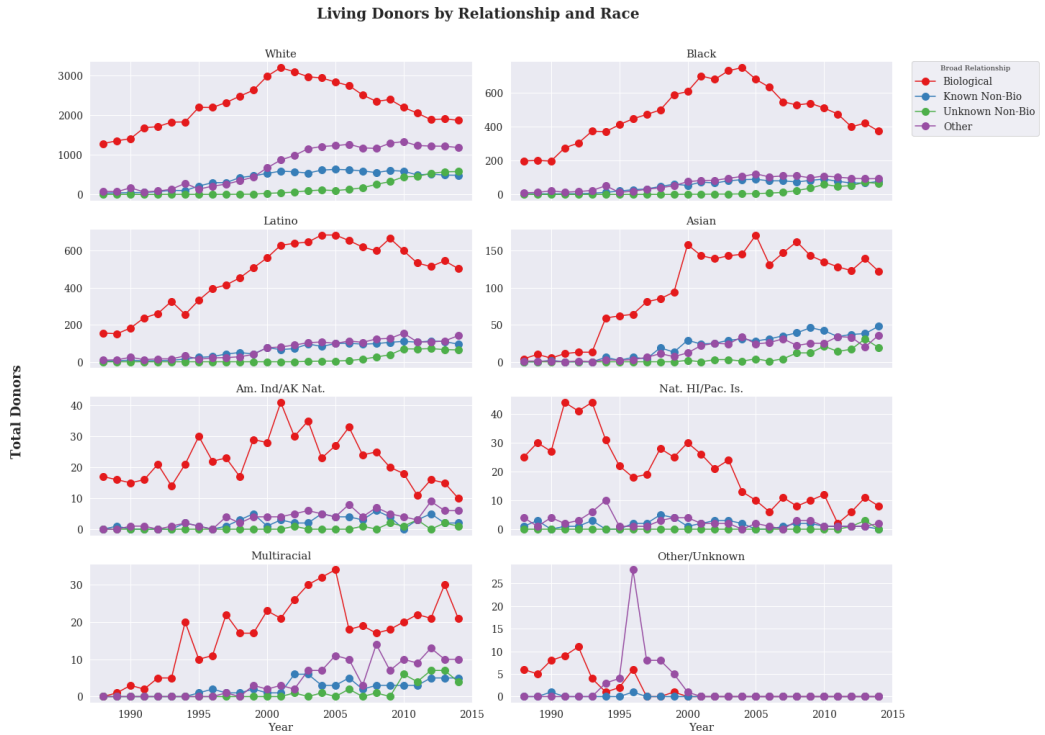

Figure 3.37: Living donors by race and relationship to transplant recipient over time.

3.3 Conclusions

Reviewing multiple aspects of the donor population at once shows patterns and trends that differ across demographic groups. Combining the OPTN data with Census data allows us

to examine the demographics on a scaled view. The demographic categories discussed and explored visually in this chapter are commonly referenced patient and donor descriptors used in research on differences in the transplant population, as reviewed in Chapter 1. There are differences in gender donor populations across different racial and age groups which could help describe the differences across populations. A greater understanding of these differences could help provide context a guide targeted donor outreach programs.

In Chapter 4, I continue to explore these demographics and others through the analysis of state laws and policies and waiting time for a transplant. Chapter 5 covers modeling and simulation efforts that further explore differences in populations.

3.4 Future Work

In this chapter, extensive visualizations have been presented on donors in the transplant system. Additional work will explore transplant recipients and those waiting for a transplant as well as donors. Similar demographic analysis along with metadata on which patients receive transplants could provide valuable insights to the system. Additional data features, such as more detailed geographic regions could provide further insights into the donor data. To explore multiple attributes at once, a dashboard could be developed to filter attributes and dynamically investigate features. Updating geographic visualizations to display data on a map of the area would also provide valuable visual insights, implementing the graphics with micromaps would enhance the quality information conveyed [72].

Chapter 4: Analysis of Policy Influence on Organ Donation and Waitlist Outcomes

Organ donation and transplantation rates are highly varied across the US. Prior research has shown that many of these differences are correlated with geographic disparities in the transplant system [9, 43, 44, 46, 47, 73–75] and is explicitly reviewed in Section 1.9. In this work, I use data from the Organ Procurement and Transplantation Network (OPTN) to explore a variety of factors on the success of the transplant system. First, I analyze the impact of state and local policies on donation rates by analyzing differences in areas with and without certain policies form the point of policy implementation. Second, a random forest model is developed to determine the most prominent factors in predicting if and when a patient will receive a deceased or living donor transplant. This research is all supported with data from the OPTN Standard Transplant Analysis and Research (STAR) files with the data accessed through the MongoDB database developed in Chapter 2 and motivated by the exploratory analysis in Chapter 3.

The growing gap between the need for and supply of transplantable organs in the US has led to several initiatives over the past decade (discussed in detail in Appendix A). United Network for Organ Sharing (UNOS) implemented policies intended to facilitate the use of expanded criteria donor kidneys with mixed success [76]. Several organ donation and transplantation collaboratives were sponsored by the US government, leading to significant increases in organ donation over several years [77]. The use of organs from donors dying from cardiac death has increased steadily over the past decade, with such donors now exceeding 10% of the total [11]. Revisions of state/local anatomic death acts allowed persons to declare their intention to donate by enrolling in state/local donor registries, facilitating the identification of willing donors by organ procurement organization [78]. Despite

these initiatives, the disparity between organ demand and supply has continued to grow, primarily as a result of a marked increase in the number of candidates awaiting kidney transplantation [23, 79]. The research presented in this chapter seeks to better understand the underlying policies and demographic factors that influence and drive organ donation and waitlist outcomes for patients.

4.1 State and Local Policies

To compare laws and policies, research was completed on the legal mandates regarding organ donation and education. Most of this data came from the different reports and online repositories of laws [75, 80–83] and each the dates for the laws was verified through a review of the legal documentation to determine when the law or policy was implemented. The information collected from the legal review was formatted in JavaScript Object Notation (JSON) to be easily imported into MongoDB. A full summary of state laws and the years of implementation are available in Appendix D. This legal summary only includes data on the fifty US states, the District of Columbia, and Puerto Rico. Other US territories are not included in the major transplantation references used for the literature review and are therefore excluded [75, 80–83].

4.2 Time-based Policy Analysis

An analysis similar to a superposed epoch analysis was conducted to determine if there is a significant increase in states where the policy was implemented [84]. This takes a deeper look at the work done by Chatterjee et al. and dives more into demographics differences for populations and includes all fifty states in the analysis [85]. In this analysis, states with a policy change are compared to states with no such policy change and analyzed the differences using statistical methods described in the following section. This analysis uses OPTN data, stored in a MongoDB database using the `transplant2mongo` tool and a curated database of state policies and the year of implementation. Results from the analysis show that some

policies have a significant impact on donation rates, while others have no clear effect. The analysis also examines demographic subgroups to provide a better understanding of where the policy has the largest impact.

Chatterjee et. al reviewed the policies states have implemented to increase organ donation and the impact these policies have had on donation and transplantation rates [85]. This research looked at the number of organ donors per state population and transplants performed per state population from 1988 through 2010 using data from UNOS and information on consent laws, donor registries, revenue streams for donor recruitment activities, population education programs, paid leave for donation, and tax incentives. Data on state laws and policies for this research was based on an evaluation done in 2013 and found that no state-level policies had any significant impact on the rate of donation (per capita) and transplantation in the US.

Similar analyses have been completed on carbon emissions in Canada [86], maternity leave in Switzerland [87], and junk food purchases in states that have legalized recreational marijuana [88]. Differences-in-differences detection was used to examine if the introduction of a carbon tax led to a significant reduction in aggregate carbon dioxide emissions in British Columbia, Canada [86]. Research on Swiss maternal leave following the birth of a child found that the implementation of a law requiring paid maternity leave increased the mother's future earnings, but only by a small amount [87]. The differences-in-differences study found that counties located within states where recreational marijuana is legal, sales of high-calorie food increased [88].

4.2.1 Methods and Materials

Using the state policy data collected through the review of legal documentation described in Section 4.1 and data collected from the OPTN, an epoch analysis was developed the examine the differences policies make over time. The epoch analysis was used to examine state policies including mandatory donor education in schools or driver's education classes, tax incentives for living donation, mandated leave of absence for employees in the private

sector, and mandated leave of absence for employees of the state. For donor education, the impact on deceased and living donors is examined, while for all other policies, only the impact on living donation is examined.

Each of these policies was examined in the region where they were implemented for the ten years before and the ten years following the law's passing. All US states, the District of Columbia, and Puerto Rico with the policies are compared to areas that do not have a version of the policy in place. Only areas with a full ten years of data before and after the policy change are considered in the analysis. Statistical testing is not performed on policies where there is data for fewer than five areas.

A data frame is formed for each policy by selecting data from all areas with the policy from a period of ten years before the policy change to ten years after the policy change. If an area has the policy and does not have the full time-span of data, it is completely dropped from the analysis. The epoch point is considered to be the year of the policy change. To conduct a comparison to areas without the policy change, areas are selected that have never implemented the policy and use the median year of policy implementation as the epoch point in time.

Data are normalized so all states are represented on the same scale using the total number of donors at the epoch point. The donor data are scaled by first subtracting the number of donors at the epoch and then dividing the data by the number of donors at epoch. This tracks the percent change before and after the policy change.

$$Donors = 100 \times \frac{Donors - Donors_{epoch}}{Donors_{epoch}}$$

A t-test was performed at each time point to examine differences in the data at individual time steps as well as on all data post-epoch to compare areas with the policy to areas without. Results at $p < 0.05$ are considered significant and are reported, this statistic is referred to as p_{point}. Additionally, overall testing was performed to determine if there is a difference in the mean donation rates after the epoch point between areas with and without

the policy. This is also performed using a t-test and is referred to as p_{epoch}. Additionally, demographic groups of the donor population are explored using the methodology described above for groups including age, ethnicity, race, gender, relationship to the recipient, physical capacity, marital status, and level of education.

4.2.2 Results

Results presented in this section are displayed in a visualization format developed specifically for this research. Similar analyses display data as normalized continuous superimposed lines comparing data with the policy change to data without the policy change [86–88]. This work contains encompassing visualizations that display the normalized number of donors across all areas with the policy, as well as all areas without the policy from ten years before the epoch to seven years after the epoch. The mean normalized number of donors is shown across all displayed years for areas with and without the policy. A yellow plus marker displayed on the graph shows whether there was a significant difference in the individual year. The p-value of the overall post-epoch t-test is shown in the figure's title.

Additional analysis on the demographic groups found that although differences were not always visible for overall donors, there were significant changes in subsets of the population. It should be noted that multiple tests were run, therefore increasing the likelihood of a Type I error. For brevity, only the demographic subgroups and policies with statistically significant findings and more than one area in the analysis are included in the results of this research.

Deceased Donors and Mandatory Education

Figure 4.1 shows the data on the number of deceased donors from nine areas compared to areas without the policy over ten years before and after the policy change in each of the nine areas. In total, 19 areas have a policy on donor education, but only nine have data spanning ten years before and after the policy change including Arizona, Illinois, Iowa,

Maine, Minnesota, Oklahoma, Texas, Virginia, and Wisconsin. Overall, there is no significant difference between the areas without the policy and areas with the policy implemented.

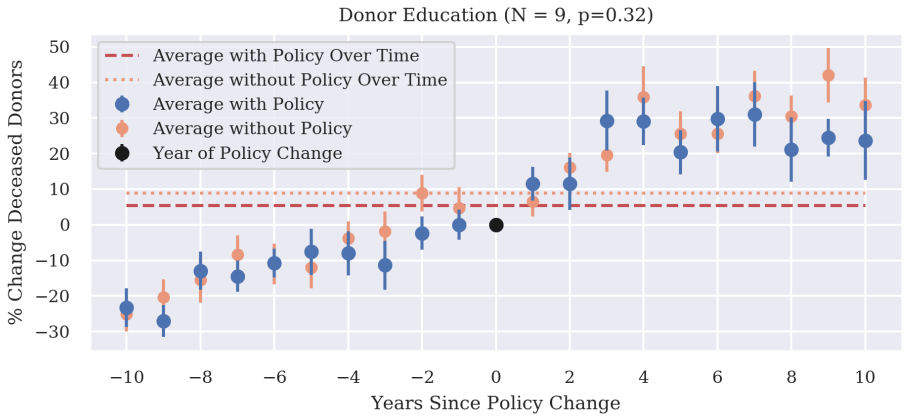

Figure 4.1: Visualization for the percent change in deceased donors ten years before and after the donor education policy implementation.

When examining the impact of mandatory donor education on racial groups, the analysis showed that only the African American / Black racial demographics had a statistically significant increase in deceased donors over areas without the policy, $p_{epoch} < 0.05$. Figure 4.2 shows a summary of the epoch analysis.

Living Donors and Mandatory Education

The education policy was also analyzed for living donors across the nine areas with the policy implemented and the areas with no policy change. A summary of the results is shown in Figure 4.3. Leading up to the policy change, donation increased for both areas with and without the eventual policy change. Post-policy change, the areas with a policy mandating education on organ donation in drivers' education or schools has a significantly larger increase in living donors, $p_{epoch} < 0.05$.

Figure 4.4 shows a summary of the analysis for female donors before and after mandatory donor education policies were implemented. Results show that donor education laws had a

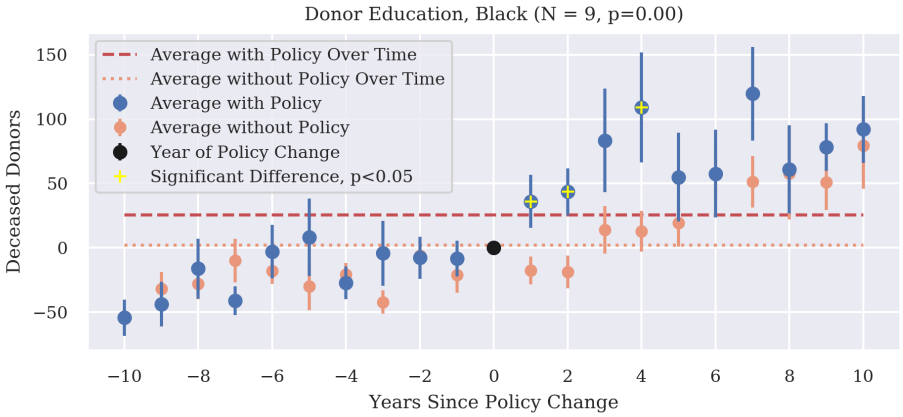

Figure 4.2: Visualization for the percent change in African American / Black deceased donors ten years before and after the tax benefit policy implementation.

statistically significant impact on increasing the prevalence of female living donors, $p_{epoch} < 0.05$.

Donor education policies have significantly increased Biological and Known Non-Biological living organ donors since policy implementation, as summarized in Figure 4.5 and Figure 4.6, $p_{epoch} < 0.05$.

Figure 4.7 shows a summary of the analysis for donors with an associate or bachelor's degree before and after mandatory donor education policies were implemented. Results show that donor education laws had a statistically significant impact on increasing the prevalence of living donors with a college degree, $p < 0.05$.

Living Donors and Private Leave of Absence

Only ten areas have implemented policies on mandatory leaves of absences for employees of privately-owned companies, as described in Appendix D. Three of these areas have implemented the policy and have data spanning ten years before and after the policy change including Connecticut, Maine, and Mississippi. Statistical testing for these areas was not performed due to the very low number of areas with the complete timeframe of data necessary.

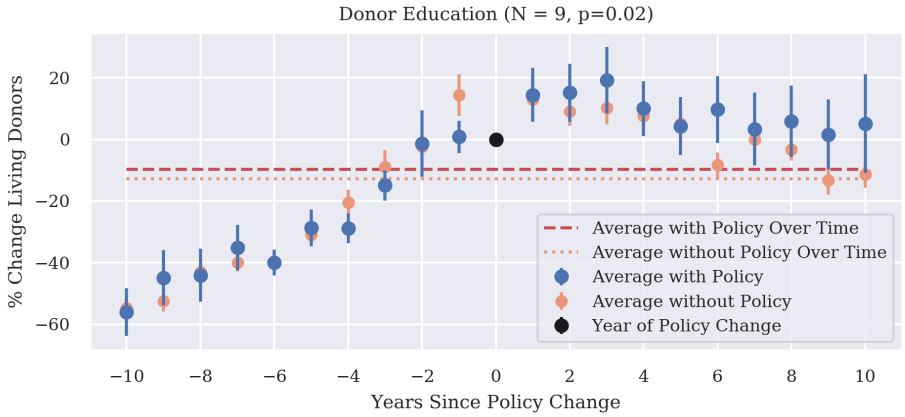

Figure 4.3: Visualization for the percent change in living donors ten years before and after the donor education policy implementation.

Living Donors and Public Leave of Absence

Figure 4.8 shows a summary of the analysis for living donors on the public leave of absence policy. Although 35 areas have a policy in place requiring employers to give public employees a leave of absence to become a living organ donor, as described in Appendix D, only 23 of the areas have enough data for an analysis ten years before and after the policy implementation. Areas included in the analysis are Arkansas, Colorado, Delaware, the District of Columbia, California, Georgia, Illinois, Indiana, Iowa, Kansas, Maine, Maryland, Mississippi, Montana, New York, Oklahoma, Ohio, South Carolina, Texas, Utah, Virginia, Washington, and Wisconsin. There is no statistically significant differences between areas with and without the policy for changes in living donations.

The implementation of public leave of absence laws led to a statistically significant increase for both African American / Black and Latino living donors since the policy implementation, $p < 0.05$. Figure 4.9 and Figure 4.10 show a summary of the analysis performed.

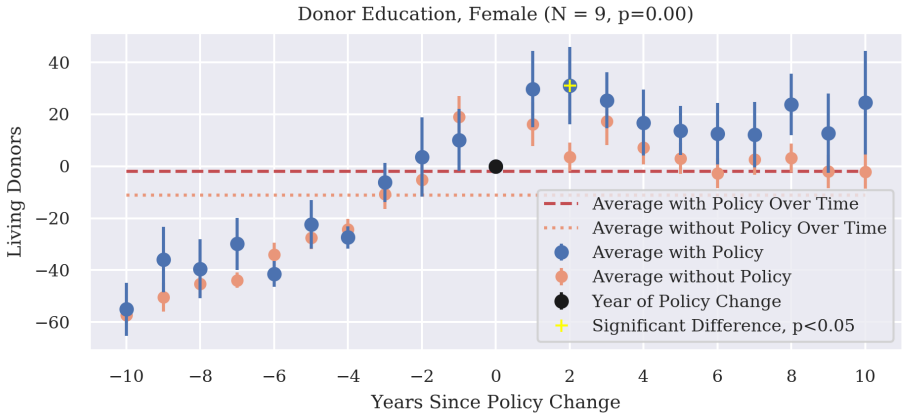

Figure 4.4: Visualization for the percent change in female living donors ten years before and after the donor education policy implementation.

Living Donors and Tax Benefits

Seventeen areas have a policy in place to provide living organ donors with a tax benefit the year of their donation to offset expenses. Due to the recent implementations in many areas, data for the analysis is only available for Georgia, Wisconsin, and Rhode Island (see Appendix D). Statistical testing for these areas is not performed due to the very low number of areas with the complete timeframe of data necessary.

4.2.3 Policy Impact Conclusions/Discussion

Policy impacts can be difficult to measure, especially accounting for the vast differences across the populations and cultures in different areas. Considering these difficulties, I approached the problem by analyzing demographic sub-groups of the population. It was found that policies made a significant, positive difference in some cases. Implementation of policies and laws requiring mandatory education in schools or driver's education programs significantly increased living donations. This is also significant within the female demographic, for donors with a biological or known but non-biological relationship to the recipient, and donors with an associates or bachelors degree. These educational policies also significantly increased the number of African American / Black deceased donors. Public leave of absence

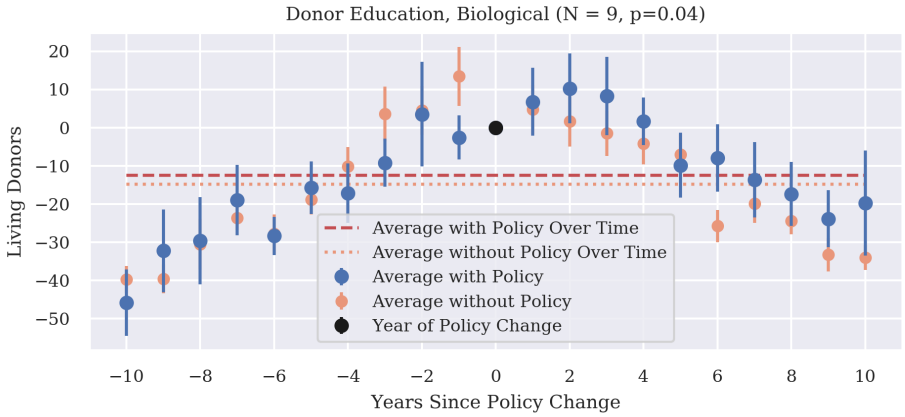

Figure 4.5: Visualization for the percent change in living donors of a biological relationship to the recipient for ten years before and after the donor education policy implementation.

laws corresponds to an increase in living donation rates for both African American / Black and Latino populations. Since these laws and policies are provent to be effective, national regulations should be implemented to ensure all states and people are impacted.

4.2.4 Policy Impact Future Work

This analysis is limited by available data and should be updated to include areas with more recent data than 2014, which would include four additional years of donation data across areas. An extensive expansion of the work could be completed on other policy changes or state initiatives, such as California allowing undocumented immigrants to obtain legal driver's licenses, which provided an opportunity to register as an organ donor [89] or direct programs implemented by Organ Procurement Organization (OPO)s to increase donation. Economists have theorized that the supply of donor organs can drive the demand, future work could examine the impact of increased deceased donor organ availability on the number of transplants and frequency of living donations [30].

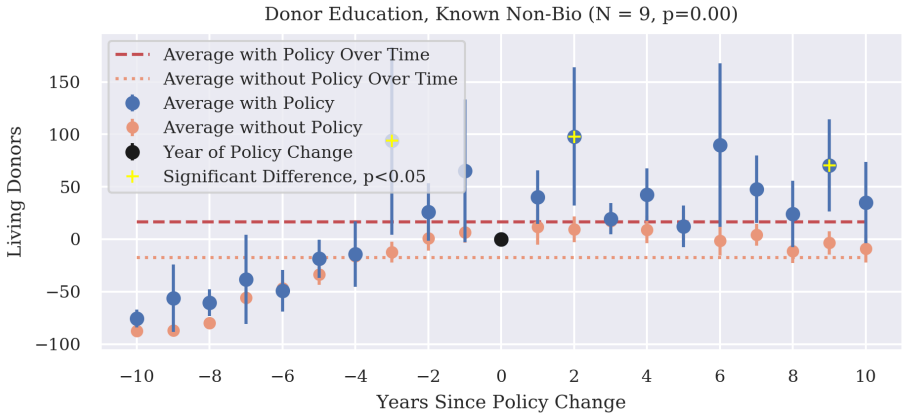

Figure 4.6: Visualization for the percent change in living donors of a known but non-biological relationship to the recipient ten years before and after the donor education policy implementation.

4.3 Random Forest Model

In addition to understanding the factors influencing organ donation, this research also applied data-driven analysis techniques to investigate outcomes for patients waiting for an available donor organ. To better understand the factors influencing whether a patient on the waiting list for a kidney transplant receives an organ, the type of donor (living or deceased) and how long patients must wait for a transplant, a random forest model was developed using the Python module Scikit-learn to understand logical decision points in determining patient outcomes and to demonstrate a data-driven modeling approach with the OPTN data [90].

The literature review of disparities in the transplant system, Section 1.9, highlighted studies that found differences across racial, ethnic, and geographic groups [60, 91]. Fan et al found that transplants for African American / Black, Latino, and Asian patients lag behind their perspective portions on the waiting list and white patients were transplanted at a greater rate than their representation on the waiting list [86]. The exploratory analysis found in Chapter 3 also found differences in donation for living and deceased donors across levels of educations, racial, and ethnic groups. In building the random forest model I found

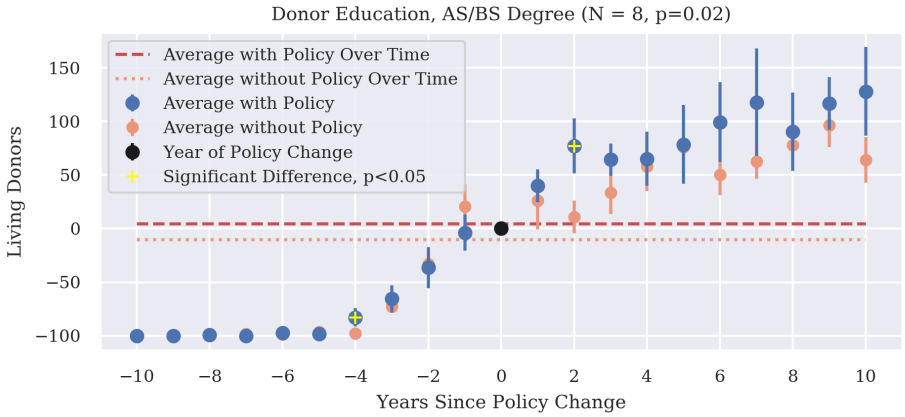

Figure 4.7: Visualization for the percent change in living donors with an associates or bachelor's degree ten years before and after the donor education policy implementation.

zip code, year of listing, age at listing, patient weight, and the median rent of two-bedroom housing unit can be important featured in predicting outcomes on the transplant system.

4.3.1 Methods and Materials

Random forests are supervised learning algorithms where a model is developed by an ensemble of multiple decision trees [90]. As with other machine learning techniques, random forest models have been used in medical research to explore a variety of patient outcomes. This modeling approach was selected based on success in similar research [92–94] in organ transplantation and the straightforward implementation process in Scikit-Learn. Research by Roysden and Wright used random forest classifiers to predict patient outcomes following a behavioral health encounter [92]. Additional research has been done to predict outcomes Intensive Care Unit (ICU) patients using random forest models [93]. Scientists have even begun to apply decisions trees and random forest models to research on kidney transplantation and incompatible antibodies [94].

All data for building the model came from the OPTN STAR data stored in the MongoDB database generated by the `transplant2mongo` tool [3]. Data for patients waiting for a kidney has 448 possible features for each individual. Only a select subset of these features

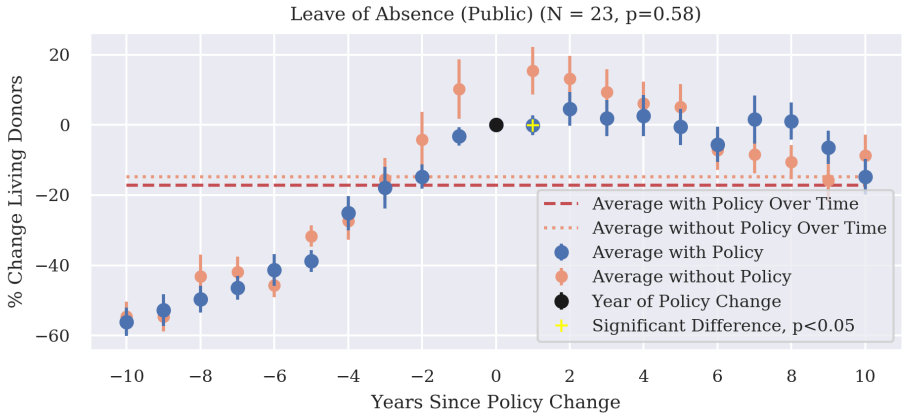

Figure 4.8: Visualization for the percent change in living donors ten years before and after the public leave of absence policy implementation.

were used to build the model as only information pertaining to the patient before they received the transplant were used. Any columns on the patient's eventual donor were omitted from the model inputs as this would have given the model too much information to make the prediction. Appendix E shows a full list and brief definition for each of the factors included in the model. This includes data such as the patient's blood type, level of education, age, Body Mass Index (BMI), Human Leukocyte Antigen (HLA) details, and dialysis type.

The data used for the model was further limited to patients with a valid number recorded for time waiting, patients waiting for a kidney transplant (excluding patients waiting for a simultaneous kidney-pancreas transplant), and patients that have been removed from the waiting list for a deceased donor transplant, a living donor transplant, or death/too sick to transplant. A data feature describing the patient's reason for removal from the waiting list, the `REM_CD` data feature, was used to distinguish the data points. This data was cleaned to use the correct data types and to correct minor typographical errors for human entered data.

Additional data sets were incorporated into the model to provide context and further details not explicitly listed in patient data. Data on local laws and policies from the database

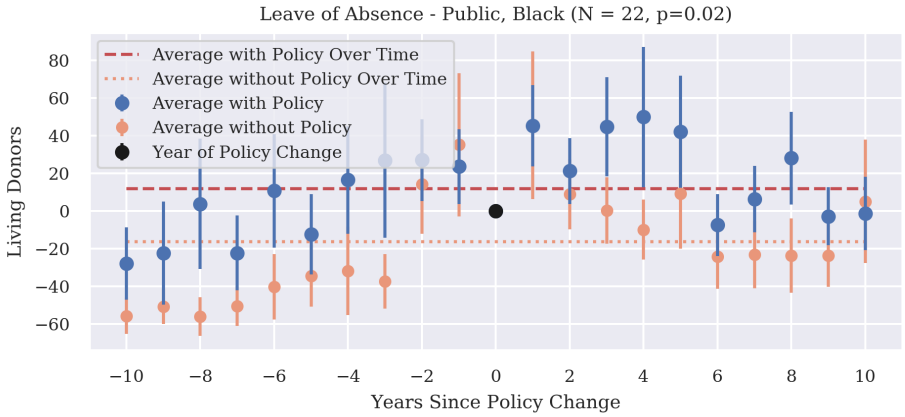

Figure 4.9: Visualization for the percent change in African American / Black living donors ten years before and after the public leave of absence policy implementation.

discussed earlier in this chapter, in Section 4.1, were included [75, 80–83]. A full summary of state laws and the years of implementation are available in Appendix D. Patient data entries were updated using their home state data to include fields on whether the state ever had the policy and whether the policy was in effect in the individual's home state when the initially joined the transplant waitlist. This information only applies to the fifty US states, the District of Columbia, and Puerto Rico.

To provide economic context, 2010 data from the US Department of Housing and Urban Development on Fair Market Rent areas [95] and the Center for Disease Control (CDC) Social Vulnerability Index were added to the model [96]. The median price of a two-bedroom housing unit for all Fair Market Rent areas are merged to patient data using the patient's home zipcode at time of listing [95]. Additionally, the CDC's Social Vulnerability Index uses US Census data to quantify the social vulnerability of census tracts using metrics such as poverty, lack of vehicle access, and crowded housing [96]. In particular, the total population, number of households, proportion of persons in poverty, proportion of unemployed persons, per capita income estimate, and proportions of persons with no high school diploma as well as flags marking portions of the population in the 90th percentile for social vulnerability risk factors are used. This data was merged with patient data using the patient's home zip

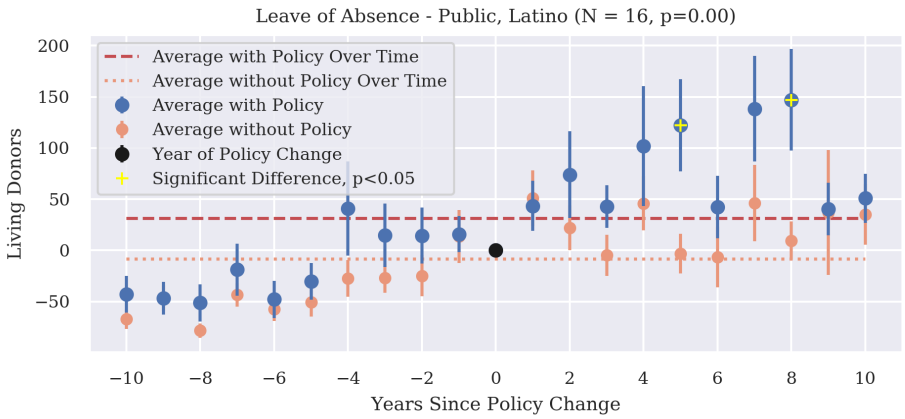

Figure 4.10: Visualization for the percent change in Latino living donors ten years before and after the implementation of public leave of absence policies.

code at the time of listing. Zip codes may be comprised of more than one census tract so the mean value per zip code is used in the analysis for each patient.

A random forest classification model makes predictions by grouping data into categories. For this research the following categories were used to represent patient outcomes:

- Received transplant from a living donor
- Received transplant from a deceased donor, <1 month waiting
- Received transplant from a deceased donor, <6 months waiting
- Received transplant from a deceased donor, <1 year waiting
- Received transplant from a deceased donor, <3 years waiting
- Received transplant from a deceased donor, <5 years waiting
- Received transplant from a deceased donor, >5 years waiting
- Patient died while waiting for a transplant

The data was manually classified using the `DAYSWAIT_CHRON_KI` and `REM_CD` data features. Missing data, represented as Not Available (NA) values in Python, were converted

to match the missing data values already used for the data feature. SciKit Learn's label encoder was used to transform text data into numerical categories as requires by the random forest classifier in Python.

To build and then validate the model, a test/training split was used to ensure the model was developed and then evaluated on different partitions of patient data. For this model, 80% of the data was used to train the model and the remaining 20% was used for testing to evaluate the model. In total, 125 features were used to develop the random forest classifier (detailed in Appendix E). Due to changes in the data collected and the overall transplant system over time, three different version of the model were developed: one for all data, one with recent years only (2000-2012), and one for data farther in the past (1987-1999) in order to understand the model better and examine differences in feature importance over time.

Scikit-learn's `RandomForestClassifier` model was used with 1,000 estimators to build the classifier, meaning the forest was generated from 1,000 individual decision trees. The classification model was run with bootstrapping enabled and with a set random state of 55 for reproducibility. Evaluation of the model was performed using the precision, recall, and F_1 metrics as well as an overall accuracy score. Definitions from these metrics come from the Scikit-learn documentation [97]. A stratified K-Fold cross-validation was also used to understand the stability of the model which preserves the representation of samples for each class.

Precision (P) is defined as the number of true positives (T_p) over the number of true positives plus the number of false positives (F_p).

$$P = \frac{T_p}{T_p + F_p}$$

Recall (R) is defined as the number of true positives (T_p) over the number of true positives plus the number of false negatives (F_n).

$$R = \frac{T_p}{T_p + F_n}$$

These quantities are also related to the (F_1) score, which is defined as the harmonic mean of precision and recall.

$$F_1 = 2\frac{PR}{P + R}$$

Accuracy is measured with the Jaccard similarity coefficient which measures the fraction of correctly classified samples. Additionally, feature importance is measured, Sci-kit learn calculates feature importance for each feature on a scale of zero to one where all values sum to one.

4.3.2 Results

All Years

First, the model was developed for all years using data from 593,345 patients on the waiting list. A baseline statistic for accuracy was computed using the Zero Rule method, which performs a classification of the data by always predicting the majority class. According to this measurement, the baseline accuracy is 29.97%. A summary of the patient data and outcomes is shown in Table 4.1.

The resulting precision, recall, and F_1 scores are reported in Table 4.2. This model is most accurate in classifying living and deceased donors and the greatest difficulty is in classifying patients that receive a transplant after waiting from 6 months to one year. Accuracy is above the baseline with an accuracy score of 62.47%. Cross-validation found the model was stable and accuracy ratings across the 10-fold cross-validation scores were within 1%.

Figure 4.11 shows the scaled confusion matrix for the model predictions. Each cell, $C_{i,j}$ is equal to the number of observations with a ground truth value of i and a predicted value

Table 4.1: Summary of all patient outcomes.

Wait Category	Total Patients	% of Outcomes
Deceased Donor, <1 Month	16,461	2.73
Deceased Donor, <6 Months	47,896	7.94
Deceased Donor, <1 Year	38,469	6.37
Deceased Donor, <3 Years	180,891	29.97
Deceased Donor, <5 Years	37,596	6.23
Deceased Donor, >5 Years	17,256	2.86
Living Donor	86,956	14.41
Patient Deceased	178,045	29.50

Table 4.2: Classification metrics for all patient outcomes.

Patient Outcome	Precision	Recall	F_1	Correct Classifications
Deceased Donor, <1 Month	0.15	0.61	0.24	830
Deceased Donor, <6 Months	0.42	0.44	0.43	9019
Deceased Donor, <1 Year	0.05	0.50	0.08	707
Deceased Donor, <3 Years	0.54	0.54	0.54	36409
Deceased Donor, <5 Years	0.39	0.62	0.48	4807
Deceased Donor, >5 Years	0.54	0.80	0.65	21886
Living Donor	0.74	0.58	0.65	21886
Patient Deceased	0.93	0.75	0.83	44731
Average / Total	0.70	0.62	0.65	120714

of j divided by the total number of observations with a truth value of i. This model has over 90% accuracy for determining patients that die while waiting for a transplant.

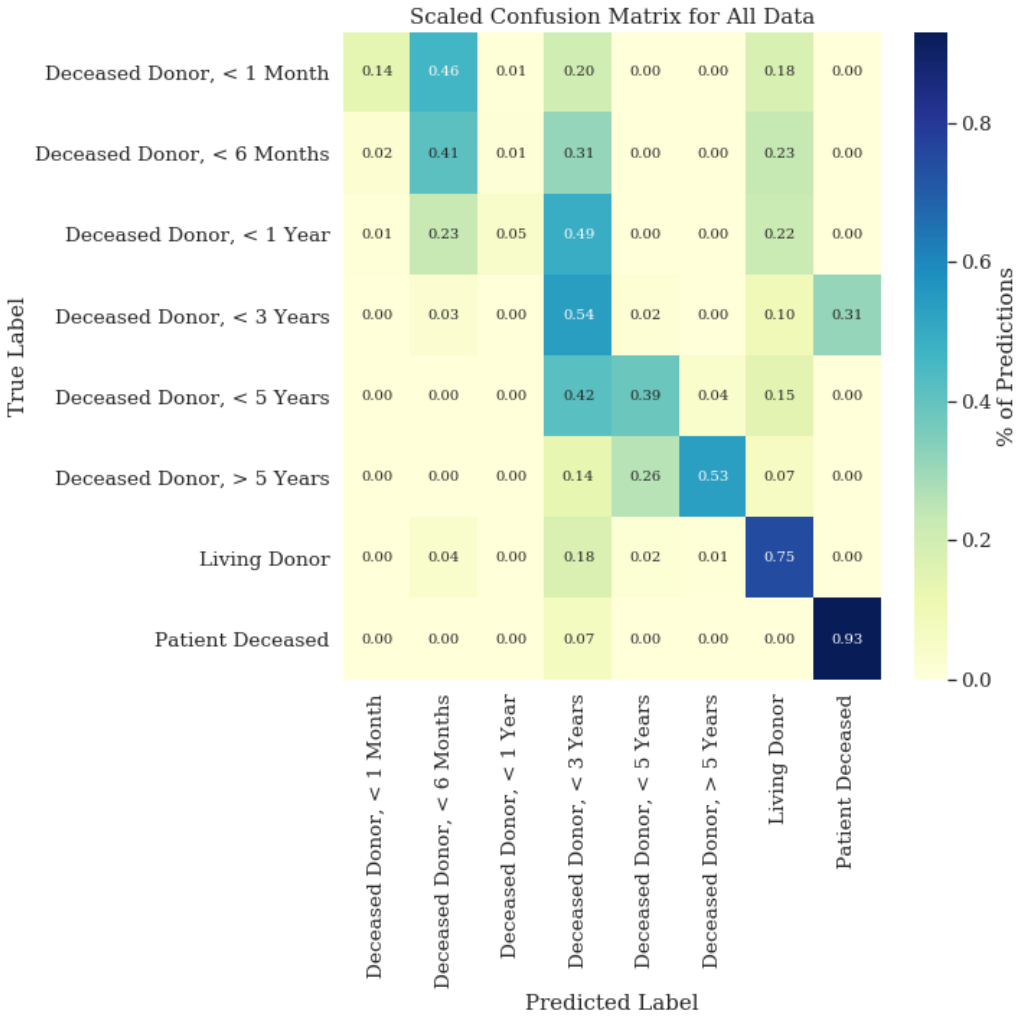

Figure 4.11: Scaled confusion matrix showing the accuracy for prediction of each label.

Feature importance was also examined using Scikit-learn and the top ten highest-ranked features are shown in Table 4.3. The intial year of listing, age at listing, zip code of home address, weight at listing, median cost of rent for a two-bedroom home in the patient's home zip code, B2 antigen score, per capita income estimate in the patient's home zip code, proportions of persons below poverty in the patient's home zip code, proportion of residents

Table 4.3: Top ten important features for classification model built on all years.

Rank	Feature	Importance	Standard Dev.
0	INIT_DATE_year	0.0302	0.0036
1	INIT_AGE	0.0290	0.0011
2	PERM_ZIP	0.0206	0.0006
3	INIT_WGT_KG	0.0190	0.0004
4	Median_Rent_2BR_INIT	0.0174	0.0004
5	B2	0.0173	0.0003
6	E_P_POV	0.0166	0.0009
7	E_PCI	0.0165	0.0008
8	E_P_NOHSDIP	0.0163	0.0008
9	INIT_DATE_month	0.0159	0.0004

in the patient's home zip code without a high school diploma, and month of listing were the most important features for building this model. Overall, the top features are largely comprised of temporal, geographic, and social vulnerability.

Early Years (1987-1999)

The baseline for predicting outcomes during the early years of the transplant system is established at 29.50%, which is the percent of patients on the waitlist that die while waiting for a transplant, the most likely outcome out of all possibilities. This model was developed using data from 211,115 patients on the waitlist. Earlier years had fewer recorded features in the database, so it would be expected for this model to have worse performance than the model across all years. The overall accuracy of this model was 60.30%, which out-performs the baseline; summary for model metrics are shown in Table 4.4. Cross-validation found the model was stable and accuracy ratings across the 10-fold cross-validation scores were within 1%.

Figure 4.12 shows the scaled confusion matrix for the model built using only data from 1987-1999. The model is highly accurate at predicting patients that die while waiting for a transplant, but frequently over-classified patients that waited less than a month as waiting more than three but less than five years.

Table 4.4: Classification metrics for all patient outcomes from 1987-1999 model.

Patient Outcome	Precision	Recall	F_1	Correct Classifications
Deceased Donor, <1 Month	0.03	0.68	0.06	72
Deceased Donor, <6 Months	0.60	0.44	0.50	7024
Deceased Donor, <1 Year	0.06	0.47	0.11	532
Deceased Donor, <3 Years	0.58	0.50	0.53	14138
Deceased Donor, <5 Years	0.43	0.62	0.51	1784
Deceased Donor, >5 Years	0.50	0.74	0.60	857
Living Donor	0.38	0.58	0.46	2251
Patient Deceased	0.98	0.77	0.86	16225
Average / Total	0.71	0.60	0.64	42883

Table 4.5: Top ten important features for classification model built on older years.

Rank	Feature	Importance	Standard Dev.
0	INIT_DATE_year	0.0292	0.0031
1	INIT_AGE	0.0282	0.0009
2	PEAK_PRA	0.0215	0.0009
3	B2	0.0205	0.0007
4	PERM_ZIP	0.0200	0.0009
5	INIT_DATE_month	0.0199	0.0009
6	INIT_WGT_KG	0.0188	0.0008
7	WGT_KG_CALC	0.0184	0.0238
8	A2	0.0183	0.0007
9	B1	0.0182	0.0007

Feature importance was also examined using Scikit-learn which showed that year of listing, age at time of listing, peak Calculated Panel Reactive Antibody (CPRA) score, B2 antigen score, zip code of their home address, the median rent for a two-bedroom home in the patient's zip code, proportion of people living in poverty in the patient's home zip code, number of households, and per capita income estimate in the patient's home zip code were the most important features for building this model. The top ten highest-ranked features are shown in Table 4.5.

Table 4.6: Classification metrics for all patient outcomes for 2000-2012 model.

Patient Outcome	Precision	Recall	F_1	Correct Classifications
Deceased Donor, <1 Month	0.24	0.57	0.34	580
Deceased Donor, <6 Months	0.18	0.46	0.26	1526
Deceased Donor, <1 Year	0.03	0.69	0.05	120
Deceased Donor, <3 Years	0.54	0.56	0.55	21321
Deceased Donor, <5 Years	0.39	0.61	0.48	3158
Deceased Donor, >5 Years	0.60	0.81	0.69	1600
Living Donor	0.82	0.59	0.69	17133
Patient Deceased	0.91	0.74	0.82	26878
Average / Total	0.73	0.64	0.67	72316

Recent Years (2000-2012)

Data from 355,084 patients that were added to the waiting list after the year 2000 were examined as well. The baseline for this model is established at 31.01%, the percent of patients with an outcome of receiving a deceased donor transplant after between one and three years of waiting as is the most likely outcome. Table 4.6 shows a summary of the metrics for the model. Overall, this model has an accuracy score of 64.25% which exceeds the baseline and is the highest of all models generated in this work. Cross-validation found the model was stable and accuracy ratings across the 10-fold cross-validation scores were within 1%.

Figure 4.13 shows the scaled confusion matrix for the model built using only data from 2000 to 2012. Outcomes are correctly classified at over 80% for patients that die while waiting for a transplant and patients that receive a living donor. This model frequently incorrectly classifies patients as living donors and as waiting less than three years but more than one for a deceased donor transplant.

Feature importance was also examined using Scikit-learn which showed that age at time of listing, year of listing, zip code, weight at listing, median cost of rent for a two-bedroom home in the patient's home zip code, number of households in the patient's home zip code, per capita income estimate in the patient's home zip code, proportion of the population without a high school diploma in the patient's home zip code, and proportions of persons

Table 4.7: Top ten important features for classification model built on recent years.

Rank	Feature	Importance	Standard Dev.
0	INIT_AGE	0.0309	0.0022
1	INIT_DATE_year	0.0247	0.0028
2	PERM_ZIP	0.0213	0.0007
3	INIT_WGT_KG	0.0191	0.0006
4	Median_Rent_2BR_INIT	0.0181	0.0006
5	WGT_KG_CALC	0.0181	0.0354
6	E_P_POV	0.0175	0.0009
7	E_PCI	0.0175	0.0008
8	E_P_NOHSDIP	0.0173	0.008
9	HH	0.0172	0.0005

below poverty in the patient's home zip code were the most important features for building this model. The top ten highest-ranked features are shown in Table 4.7.

4.3.3 Random Forest Conclusions/Discussion

Modeling patient outcomes with a random forest model is effective above the baseline zero rule method for predicting outcomes. The models are most effective for determining which patients will die while waiting for a transplant as well as patients that are removed from the list to receive a living donor transplant.

The model was built using only data from patients joining the waitlist after the year 2000 has the highest precision, recall, F_1 score, and accuracy. More recent patient entries often have more features due to better record-keeping and the OPTN adding new patient characteristics to their system. All models were largely unable to predict if a patient would wait between six months and one year for a transplant, this is a small time frame and there are no clear indicators to distinguish this from other waiting times. The models all had high precision (>50%) for predicting the outcome for patients waiting one to three years for a transplant and patients waiting for more than five years for a transplant.

A review of the commonly listed important features found that year of listing, age, home zip code, and weight are some of the most valuable features for predicting outcomes

for older and more recent years. The model with patients joining the waitlist after 2000 had more impactful geographic features (e.g. total population, mean rent of a two-bedroom home, per capita income) while the model with patients joining the waitlist before 2000 more commonly had antigen levels and medical attributes as the most important factors. These results are supported by findings by Shacham et al that there is a significant negative relationship in Missouri between organ donor registration rates and Census-tract level disadvantages such as educational attainment, poverty, and single-headed households [54].

Other research in this field has focused on demographic components such as race, gender, and ethnicity [25, 52–60]. None of these features were in the top 20 features influencing the random forest models. A closer examination of the model built with patients added to the waitlist after 2000 finds that patient education is the 48th most important feature and race is the 60th most important feature. Whether the patient was working for income at the time of listing, gender, ethnicity, citizenship, and current academic progress were all ranked in the bottom half of the important features.

This random forest model is a basic example of what can be performed with access to the OPTN STAR files in combination with geographical details on patients. There are ample opportunities for expanding this work including using alternate classification algorithms, improved data filtering for model inputs, access to more recent data, and altering the outcome categories.

4.3.4 Future Work

The random forest classification model provided valuable insights to the transplant system and expanding this work could lead to a greater understanding of the most important features determining which patients receive transplants or die while waiting to receive a transplant. Additional models such as singular value decomposition, regression models, neural networks, and deep learning algorithms could be applied to the data in a similar method to make predictions on patient outcomes. Feature pruning and analysis of impact

will also be completed to evaluate the extent of the feature's effect on the model. Additionally, the models presented in this paper represent all available data that contains a large number of unknown values. Filtering the data to minimize unknown values could provide a higher level of accuracy.

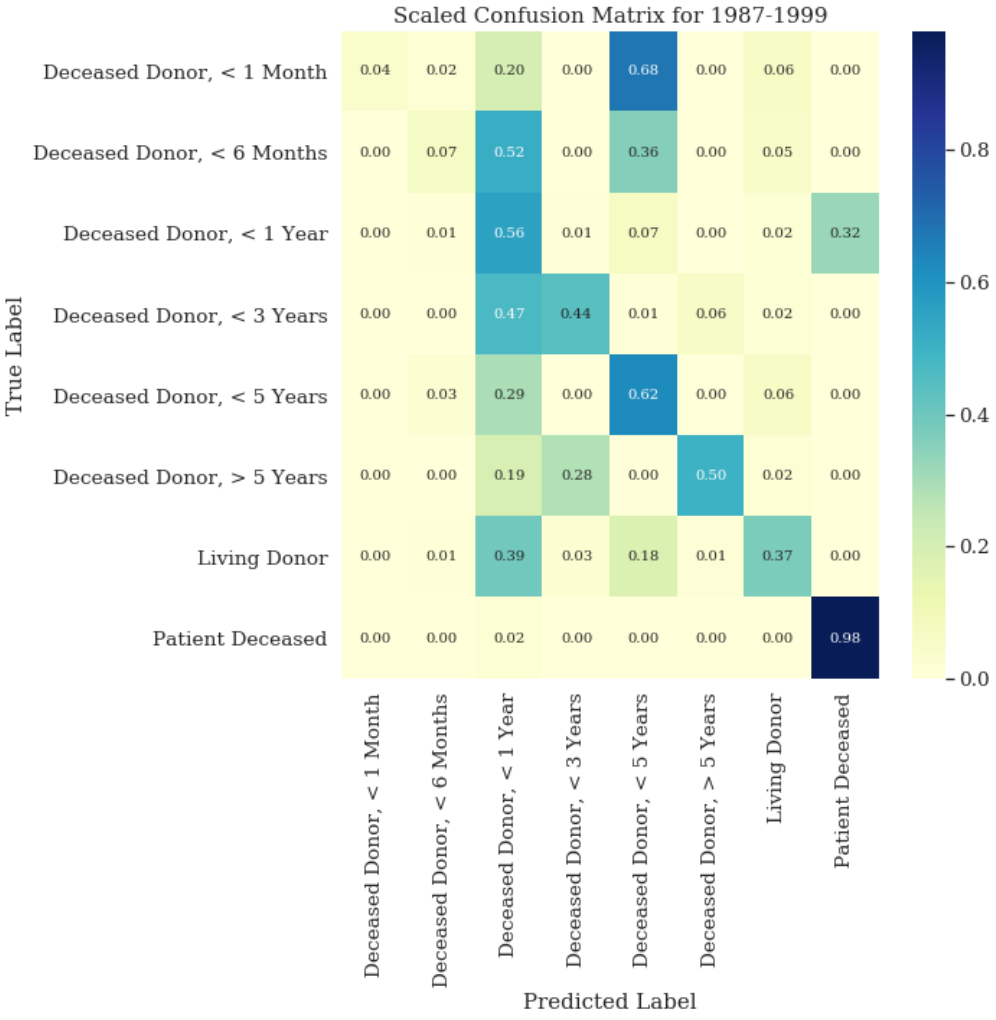

Figure 4.12: Scaled confusion matrix showing the accuracy for prediction of each label from the model built using 1987-1999 data.

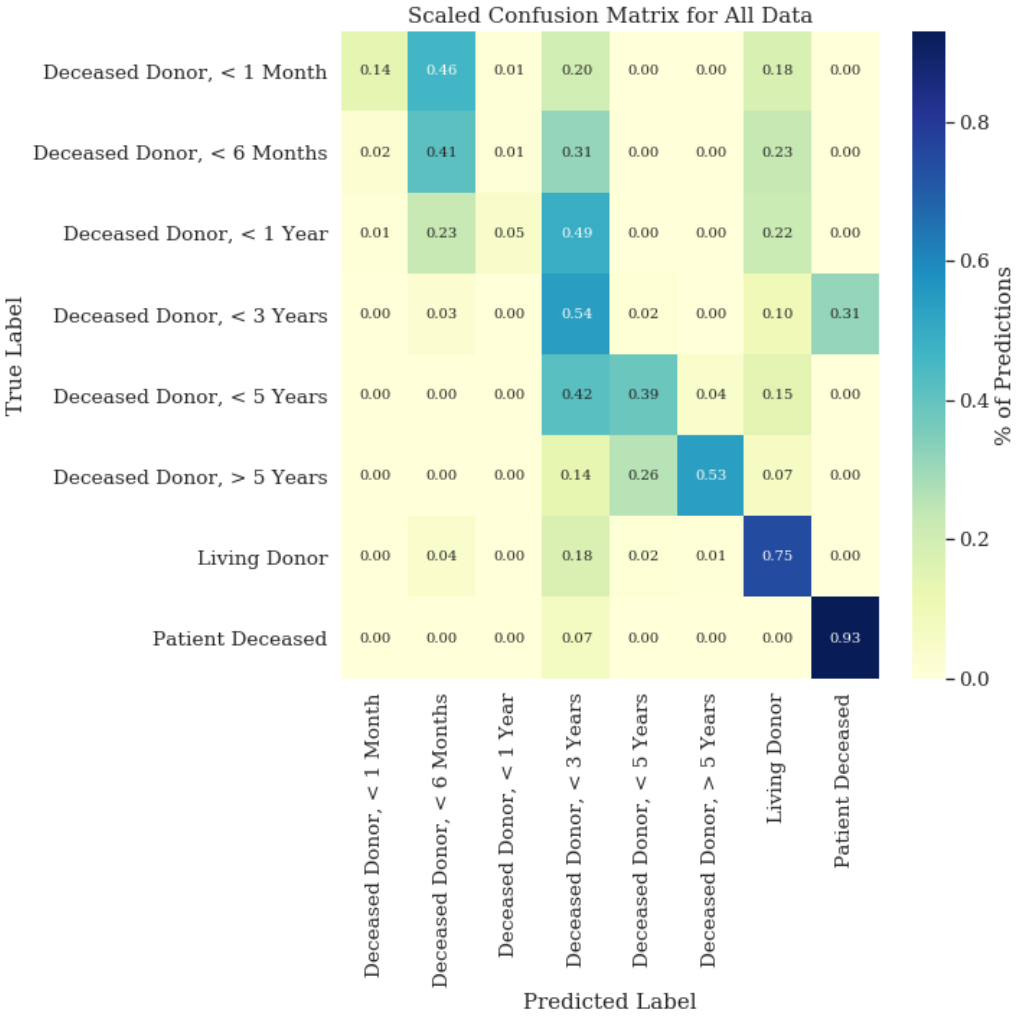

Figure 4.13: Scaled confusion matrix showing the accuracy for prediction of each label from the model built using 2000-2012 data.

Chapter 5: Modeling and Simulation[2]

Two models have been completed in working on this research to explore the impact of policies and assumptions about the transplant system that can not be clearly examined through existing data. The first work is on the Kidney Transplant Process Model which explores the transplant process and the outcomes using an Agent-Based Model (ABM). This model investigates increases in the number of living and deceased donors and the impacts across demographic groups on the number of transplants performed. This work was published in the 2016 Summer Simulation Conference Proceedings [98] and the code repository is available on GitHub [100]. The second developed is a queuing model exploring the effects of multiple registrations on the waiting list for donor organs. An early version of this model was published in the 2016 Winter Simulation Conference Proceedings [99] and an extended version of this work has been submitted as a paper with revisions to the American Journal of Transplantation. The code used to generate the multiple listings model is available on GitHub [101]. Models developed in this chapter were motivated by the exploratory analysis performed in Chapter 3.

A review of models and simulations of the transplant system was conducted prior to developing the models discussed in this chapter. The discrete event simulation model, KSIM, was developed to simulate kidney allocation policies with a focus on Donor Service Area (DSA) patient numbers, death rates, and patient blood type [102]. A family of models was developed by the Scientific Registry of Transplant Recipients (SRTR) to simulate the transplant system and allocation policies [103]. These discrete event simulation models use statistical data to evaluate potential policies. One of the SRTR models is the United

[2]This chapter contains content drawn directly from the work published in the 2016 Summer Simulation Conference Proceedings [98] and content drawn directly from the work published in the 2016 Winter Simulation Conference Proceedings [99].

Network for Organ Sharing (UNOS) Liver Allocation Model (ULAM) was developed to support policy evaluation and fits patient arrival processes and computes patient survival times in a discrete event simulation framework [104, 105]. Additional models have been developed on specific organ allocation policies or practices with slight variations on the SRTR models such as adding a biological focus to the model or modeling the European transplant system [106–109].

The SRTR also has the Kidney-Pancreas Simulated Allocation Model (KPSAM) which was designed to simulate the allocation of kidneys and pancreata to candidates on the waiting list as well as the outcomes for these patients [110]. This model takes in specifications including arrivals of candidates, an initial waiting list, and a history of waiting list status changes. The model has several limitations, including the reliance on historical data, the assumption of standard behavior across the Organ Procurement Organization (OPO)s, a lack of dependency on specific patient diagnosis, the use of listings instead of patients, and fixed organ discards. Another limitation of this model is the use of patient listings instead of the patients themselves. Many patients sign up to be listed at multiple transplant centers. In the model, this is represented as multiple patients, which ignores the fact that many of these people receive a transplant at another center and can then be removed from the waiting list. The models discussed in this chapter address areas not already considered by current models including increasing donation among specific patient demographics and modeling multiply listed patients.

5.1 Kidney Transplant Process Model

5.1.1 Introduction

There are currently over 100,000 people on the waiting list for a kidney transplant in America [1]. If the current transplant process remains as is, this number of waiting patients will only continue to grow. Even though the growth rate of active patients on the waiting list has slowed, it has been predicted that the waiting list will grow by over 4,000 people

per year [77].

Patients are often placed on the kidney transplant waiting list after being diagnosed with End Stage Renal Disease (ESRD). ESRD is an irreversible condition and occurs when the kidneys are no longer working well enough for a person to live without some form of treatment: dialysis or a transplant. ESRD can be caused by either Acute or Chronic Renal Failure [17]. The two most commonly listed diagnoses for patients added to the waiting list in 2012 were Type II diabetes and Hypertensive Nephrosclerosis [1]. Appendix B and Appendix C provide a comprehensive overview of the transplant and deceased donor systems.

A basic outline of the transplant process, which is managed by the Organ Procurement and Transplantation Network (OPTN) is shown in Figure 5.1. Once a patient is diagnosed with ESRD and begins dialysis, they are responsible for seeking out a referral to be added to the national waiting list for a new kidney. Once a patient receives a referral, they are added to the registry with their waiting time dating back to their first day of dialysis [111].

Due to the shortage of donor organs, patients often wait months to years for a suitable donor organ to become available. While waiting for a kidney transplant, patients undergo dialysis treatments that take over the kidney's former job of filtering the bloodstream. Dialysis is generally completed by patients at a facility three times a week for three to four hours at a time. While this treatment allows patients to continue to live a relatively normal daily life, the quality of life for patients on dialysis is generally lower than patients that receive transplants [112].

Patients on the waiting list only need to continue dialysis until they have been selected to receive a transplant. Having a transplant greatly increases the patient's quality of life and patients can often resume a normal lifestyle following recovery from surgery.

The motivation behind this research is to explore the effects of changes in the waiting list and use this information to help inform policy and decision making for the transplant waiting list. This includes policies for allocation of donor organs as well as education and awareness for patients on the waiting list.

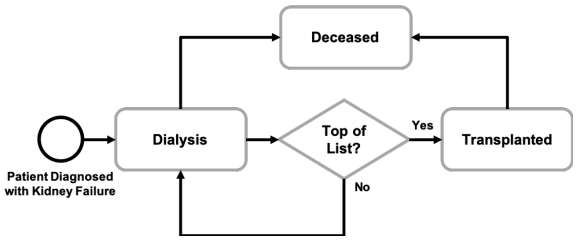

Figure 5.1: Simple outline of the transplant process. Patients can transition between the stages of the process according to the directions on the chart. The Kidney Transplant Process Model (KTPM) focuses on the transition between the dialysis and transplant stages as well as the post-transplant stage.

Table 5.1: Outcomes probabilities of patients on the waiting list for a kidney transplant. Data collected from the OPTN Database records from years 2010-2012 [1].

Race	**Deceased Donor**	**Living Donor**	**Other**
All	10.91%	5.21%	7.54%
White	12.90%	9.28%	9.01%
Black	10.41%	2.22%	6.98%
Latino	8.56%	4.03%	6.37%
Asian	9.72%	3.30%	5.79%
Other	8.80%	3.08%	7.33%

Table 5.2: Survival probabilities of patients receiving an organ transplant. Data collected from the 2009 OPTN annual report [113].

	Deceased Donor				**Living Donor**			
Race	3 Mo.	1 Yr.	5 Yr.	10 Yr.	3 Mo.	1 Yr.	5 Yr.	10 Yr.
All	95.4%	91.2%	69.1%	41.8%	98.1%	96.4%	81.4%	58.9%
White	95.7%	91.5%	70.9%	44.8%	98.1%	96.3%	82.2%	60.2%
Black	94.2%	89.3%	62.2%	32.2%	97.7%	95.4%	73.2%	45.3%
Latino	95.9%	92.9%	75.0%	49.7%	97.9%	96.9%	84.8%	65.7%
Asian	96.8%	94.0%	76.3%	54.2%	99.0%	97.7%	88.9%	68.9%
Other	97.1%	93.5%	75.3%	45.0%	99.3%	97.2%	81.2%	58.0%

5.1.2 Background

Previous research and studies have realized that there are currently racial and ethnic disparities in the access to transplants for minority patients, as discussed in detail in Section 1.9. Currently, the percentage of deceased donor transplants for African Americans, Asians, and Hispanic/Latinos in the US lag behind the respective proportions of whites. In an ideal and fair kidney transplant system, there would be no disproportions [60]. The disparity in access to deceased donor transplants has been narrowing significantly for African Americans patients in recent years, but not for Asian and Hispanic patients [60].

Kutner et al. determined that there is no existing racial difference in patients receiving a living donor organ [25]. Research by Clark and Hicks determined that the completion of pre-transplant evaluations on potential recipients may pose a greater barrier to transplants among women, the poor and minorities [56]. This work also stated that African American patients are less likely than whites to be placed on waiting lists and receive transplants.

There are also discrepancies in patient survival among different ethnicities; a comparison was conducted between the mortality of African American and other racial/ethnic groups for simultaneous pancreas and kidney transplantation. This study found that African American patients were twice as likely to lose the graft due to rejection compared to non-African Americans [91]. An analysis of transplant survival focusing on whites, African Americans, Asians and Hispanics noted that Asian kidney recipients have the highest graft survival rate of all observed ethnicities. The five-year survival rate for Hispanics and Asians demonstrates "superior patient survival", compared to African Americans and whites [60].

Table 5.1 shows the probabilities of patient removal from the waiting list. Patients can be removed for various reasons such as a transplant or death. This data was collected and then aggregated from the OPTN database, considering the years 2010 to 2012 [1]. The table shows the probability of patients receiving a deceased donor transplant, a living donor transplant, or to pass away or become too ill to receive a transplant. This shows that very large differences exist between whites and all other ethnicities particularly for receiving living donor transplants. The listed probabilities with the added influence of patient age were

used in the model to determine the probability of patient outcomes while on the waiting list.

Table 5.3: Probability of receiving an organ transplant by race and age. Data collected from the OPTN Database records from years 2010-2012 [1].

	Deceased Donor				**Living Donor**			
Race	18-34	35-49	50-64	65+	18-34	35-49	50-64	65+
White	12.57%	12.82%	13.05%	12.81%	18.64%	12.08%	8.49 %	5.40%
Black	10.81%	10.32%	10.69%	9.60%	4.17%	2.62%	1.83%	1.23%
Latino	9.79%	8.64%	8.30%	8.23%	9.07%	4.92%	2.80%	2.13%
Asian	10.28%	10.62%	9.30%	9.40%	8.72%	4.86%	2.33%	1.62%
Other	9.43%	8.33%	9.14%	8.40%	4.88%	4.28%	2.36%	1.89%

Table 5.2 contains data collected from the 2009 annual report of the OPTN [113]. This data shows the survival rate for patients at three months, one year, five years and ten years post-transplant. This supports the study by Fan et al. that Asians and Hispanic/Latinos have a superior survival rate compared to other ethnicities [60]. There have been many recent discussions and initiatives taken to counteract the realized discrepancies between ethnicities and to improve the overall transplant system.

In Table 5.3, data is provided from the OPTN database which describes the probability of receiving a transplant across four different age groups and all racial classifications in the database. These rates are broken down into both living and deceased donor transplant rates.

It has been estimated that 10 to 12 thousand medically suitable people for organ donation die every year but only six thousand donate [23]. This knowledge, in combination with the potential for increased living kidney donation, could significantly decrease the current waiting list. One of the goals of this research is to study how increases in deceased and living donor transplant availability could affect the waiting list.

5.1.3 Methods

The KTPM was built using data from the OPTN database. This system was developed by the United Network for Organ Sharing (UNOS) and contains all OPTN data related to every organ donation and transplant event in America since 1987 [1]. Statistics taken from this database as well as from OPTN reports were used to generate and then validate the model [113]. All code used to develop this model is available on GitHub [100].

Multi-Agent Simulator Of Neighborhoods (MASON), a Java library core designed for discrete-event multi-agent simulations [114] was used to develop the model. This paper follows a simplified version of the Overview, Design Concepts, and Details (ODD) Protocol as set by Grimm et al. to detail the model in a standardized format used for ABMs [115]. Verification of the model was performed by running simulations of the model under different conditions and stepping through outputs to ensuring the results were consistent with the implementation [116].

Overview

Purpose The purpose of the KTPM is to demonstrate the kidney transplant process, from the initial placement of patients on the waiting list to post-transplant survival. In particular, this model focuses on the effects of varied organ availability on the entire transplant process. Thousands of Americans die every year waiting for a transplant, this model is a tool that can provide analysis for the effects of increased organ availability. Increases in living and / or deceased donor transplants can be simulated and the resulting survival rates can then be analyzed. This model includes a specific focus on patient age and ethnicity.

Entities, state variables, and scales Agents experiencing the transplant process are the represented entities in the KTPM. These agents can be divided into three collectives: patients on the waiting list, post-transplant patients, and deceased or otherwise removed patients. All patients have attributes that help determine their specific journey through the transplant process. Every patient has age and ethnicity. Each agent also tracks how long

they spend on the waiting list and how long they survive post-transplant. When patients are removed from the simulation, the tool records how long the patient survived in addition to their cause of death (died waiting for a transplant or died post-transplant).

Simulaiton time steps are measured in one-year increments which corresponds to the granularity of the input data. Simulations are set to run for a 15-year period to allow several generations of patients to be simulated in the model. At the end of this time frame, all agents, living and deceased, are fully recorded for analysis.

Process Overview and Scheduling The KTPM has several setup procedures that initialize the model and import all required probability matrices from external files. These files contain the calculated probabilities obtained from the OPTN database. The initial setup first assigns all agents to be waiting for an organ transplant and assigns ethnicity and age to every agent according to the OPTN database probabilities. Every new patient in the model is created with no time recorded on the waiting list. This version of the model excludes patients under the age of 18; the available data for underage patients is considerably lower than all other age groups so the model was programmed to be able to run without this particular demographic. After the initial setup has completed, the model runs over time steps that correspond to one year. Each time step consists of the following four actions completed in the following order.

First, it is determined whether or not the agent will receive a transplant. If the agent is currently on the waiting list, the Assign Transplant submodel will determine their next stage. Agents can receive a living donor transplant, receive a deceased donor transplant, pass away while waiting for a transplant, be removed from the waiting list for another reason, or remain on the waiting list. Patients that are removed from the waiting list for other reasons or that pass away are removed from the processes. The agent's passage through this submodel is determined using OPTN data based on the patient's age and ethnicity.

Next, the agents enter the Get Older submodel. All living patients increase in age by one year. This submodel includes a process for post-transplant patients that determines

their odds of post-transplant survival. This survival data comes from probabilities based on the agent's type of transplant, the number of years post-transplant, and ethnicity. These probabilities are again based on the OPTN database. In this submodel patients either survive the year or become deceased. The post-transplant survival is only evaluated at certain years for which data exists.

Adding new patients to the waiting list is the third process in each time step. A specified number of agents are added to the model and are initialized in the same process as the original waiting list patients in the model setup. New agents added to the simulation each time step is determined using the statistics of wait-list additions from previous years. The assignment of ethnicity and age for these patients is determined using waitlist additions probabilities from the OPTN database over the past three years.

Finally, the last stage in each time step is the updating of global variables. All information about the current state of the model is updated, including the percentage of transplanted patients, deceased patients, as well as the number of patients on the waiting list.

Design Concepts

Basic Principals The KTPM is based on the current American organ waiting list and transplantation processes. This model can expand and extrapolate from the current state of the system using calculated probabilities for increased organ availability which is implemented in the Assign Transplant submodel. The model was verified by testing each of the submodels individually and confirming the model outomes are consistent with real-world behaviors.

This model provides insights into the transplant process by simulating the results stemming from improvements in organ availability. The KTPM uses theories and ideas on increased organ availability stemming from the previous research [60].

Emergence Individual patient records and aggregate statistics on changes to the waiting list are the two primary outputs of the model. Individual patient data is produced for every

patient in each simulation. This output can be aggregated to determine agent survival over time among different age and ethnic groups. These results emerge from which patients receive transplants and how well each individual survives the process. The second primary output is the overall statistics for each run. This includes the final waiting list size, the number of surviving patients for each demographic and transplant type. Data also emerges from the individual patient's journey through the process.

The second form of output is particularly useful to determine and compare the effects of increased organ availability. When multiple simulations have been completed with varying levels of increased organ availability for living and deceased transplants, these results can be analyzed and compared.

Adaption Agents themselves are not responsible for the decision of whether or not they receive a transplant. For this reason, agents do not have any adaptive traits. The probabilities of an agent receiving a transplant can vary depending on the number of available organs but this is not a decision made by the agent itself, this is an adaption of the environment.

Interaction Although the agents do not interact directly, the availability of resources affects the way the agents have access to organs. The probability of an agent receiving a deceased donor transplant varies with the size of the waiting list. Therefore if the waiting list decreases in size by more agents receiving transplants, the percentage of agents able to receive transplants will increase.

Stochasticity Due to the probabilistic nature of the KTPM, there are multiple instances of stochasticity implemented in the model. Stochastic processes are used in the initial determination of the agent's age and ethnicity when agents are added to the model. Stochasticity is also used in the Assign Transplant submodel to distinguish which patients receive transplants and which have alternative outcomes. The final use of stochasticity in the model is the determination of agent survival post-transplant. In all of these instances, a randomly generated number is used to establish which path the agent will follow. These randomly

generated numbers are in accordance with the probabilities from the OPTN database to determine the agent's path in the process.

Details

Initialization The model can be initialized with any number of agents, in the Graphical User Interface (GUI) version of the model, the number of patients can be adjusted using the NumPatients box. These agents are initialized in the model according to demographic probabilities from the OPTN database. This model has been designed to run according to probabilities so all other initializations and calculations, such as the additions to the waitlist are determined based on this initial number of patients. For the experiments conducted in this research, 30,000 patients are used as an initial input of the waiting list size.

In addition to initializing the number of patients in the model, the living and deceased factor can be adjusted. The values used for these parameters are listed in the experiments section of the paper for the individual experiments. Generally, the deceased factor should be between 0.0 and 1.0, this range represents no increase to a 100% increase in the number of available deceased donor kidneys. The deceased factor is generally limited by the realistic number of potential deceased donors in the country which heavily depends on the circumstances of a potential donor's death. Scientific estimates have limited the potential number of deceased donors to double the current number [117]. The living factor can range from 0.0 to 2.0; this range represents no increase to tripling the number of living kidney transplants. The upper bound for this parameter can be higher than 2.0 if desired.

Another initialization variable is the parameter to set up the model to equalize the probabilities of receiving a living donor transplant across ethnicities. Setting this Boolean value to true sets all probabilities for living donor transplants as if the patient was of the white ethnicity. By default, this parameter is set to false.

Input Data The KTPM processes a large amount of input data. Most of this data are statistics extracted from the OPTN database that determines agent demographics, probability of being taken off the waiting list, and the survival probabilities for patients.

This data is imported for each simulation from external files.

Two factors represent the increased availability of organs, the Living Factor and the Deceased Factor. The Living Factor determines the percent increase in living donor transplants, relative to the waiting list. For example, a Living Factor of 1.5 would correspond to a 150% increase in living donor transplants on the waiting list. The overall availability of deceased donor organs is determined by the Deceased Factor. A Deceased Factor of 2.0 would double the number of available deceased donor transplants overall. The number of deceased donor transplants that can be performed is not proportional to the size of the waiting list; therefore, the same number of organs from deceased donors will be available, regardless of the size of the waiting list.

Submodels The KTPM consists of two major submodels: Assign Transplant and Get Older. An agent's next phase is determined by the Assign Transplant submodel. This submodel takes into account the agent's age and ethnicity and then determines the probabilities for each possible outcome. The possible outcomes for a patient include living donor transplant, deceased donor transplant, death, removal from the waiting list for another reason, or remaining on the waiting list. Data for this submodel came from the waiting list removal report of candidates from 2010 to 2012 [1]. The number of living and deceased donor transplants can be affected if the model is run with a living or Deceased Factor. If one or both of these factors are used, the corresponding probability will be altered.

When a patient receives a living or deceased donor transplant their state is changed to make them a transplant recipient and the specific type of transplant is recorded. Patients that pass away while waiting for a transplant are removed from the waiting list and marked as deceased. These patients are also recorded in the complete patient log written for every simulation. This probability was composed of data gathered from the waiting list removal report with removal reasons listed as "Died" or "Too sick to transplant" [1]. It was assumed that if a patient was removed from the waiting list because they were too ill to transplant, they would not recover.

The final outcome of patients that result from this submodel are patients that were

removed from the list for other reasons. Reasons for removal from the transplant list include: "transplanted in another country," "unable to contact candidate," "refused transplant" as well as other various reasons. These patients were completely removed from the simulation and recorded in the report as having left for "other" reasons [1].

Living patients all experience the Get Older submodel. This submodel begins by aging all of the agents by one year. This submodel then splits into two paths, one for waitlisted patients and one for transplanted patients. The patients still on the waiting list simply have one more year added to their recorded number of years on the waitlist. Post-transplant patients experience a much more complex process.

Post-transplant patients need to be evaluated for survival at certain times. Data is only available for post-transplant survival at three months, one year, five years and ten years [113]. This post-transplant survival data is from the 2009 annual report of the OPTN [113]. Due to this specific data availability, patient's post-transplant survival is evaluated at the post-transplant years of zero, one, five and ten. In other years, no survival evaluation is completed.

If the agent is in one of the post-transplant evaluation years, their specific transplant survival probability, based on their ethnicity and number of years post-transplant, is used to determine their survival. Different survival probabilities exist for Living and deceased donor transplant patients. If a patient does not survive, they are marked as deceased and recorded in the complete patient log. Patients that do survive the evaluation have one year added to their post-transplant years and continue in the simulation. There is a special case for post-transplant patients since there is a lack of data for patient survival for more than ten years. Once a patient reaches eleven post-transplant years they are removed from the simulation and recorded as "Over 10 Year Survival" patients.

5.1.4 Experiments

Two sets of experiments were run for this model. The first set of experiments takes a close look at the effects of the Living Factor and Deceased Factor on the model. These trials

involved a run over a wide range of parameters which are detailed in Table 5.4. This set of experiments resulted in 231 trials with one replication for each trial. The results for this particular set of experiments can be visualized in Figure 5.2. The generation of the second set of experiments was facilitated with the MITRE Goal-Directed (MEG) simulation framework [118]. With this framework, a simple parameter sweep over the areas of interest was completed and the output data was aggregated into a MySQL database for easy review. Both sets of experiments were run with an initial waiting list size of 30,000.

These particular parameters were chosen because according to the current research, these are options within a reasonable scope. There is a finite upper limit on the availability of deceased donors due to the number of available suitable deceased donors [23]. A deceased factor of 2.0 corresponds to a doubling the availability of deceased donor kidneys. This could be achieved if every medically suitable person would become an organ donor [23]. There is not such a strict limit on the availability of living donors. Living donor kidneys can come from family members, friends, or even anonymous donors. Despite the absence of a strict limit on this portion, it is not necessarily reasonable to assume that so many living donor transplants are feasible. A living factor of 2.0 corresponds to a 300% increase in living donors.

The second experiment focused on equality in living donation. As noted earlier, there is a significant disparity between ethnicities in living donor transplants [60, 65]. Experiment II explores how the waiting list would be affected if all ethnicities had exactly equal opportunities to receive a living donor transplant. This is implemented by making all ethnicities have the same probabilities as the white ethnicity of receiving a living donor transplant. The probabilities are still different for each age group, but all probabilities are changed to match those of the white racial group.

Table 5.4: Experiment parameters for the large-scale experiment.

Parameter	Min	Max	Step Size
Living Factor	1.0	3.0	0.1
Deceased Factor	1.0	2.0	0.1

5.1.5 Results

Experiment Set I

Results from Experiment Set I show the effects of the Living Factor and Deceased Factor on the transplant process. The results and parameters for several select points of this experiment are all displayed in Table 5.5. Data from Trial I shows that if nothing is done to improve the effectiveness of the transplant process, the waiting list will continue to grow. This will lead to an increased number of patients that will die while waiting for a transplant.

Doubling the availability of deceased donor kidneys would have a very crucial impact on the waiting list for kidney transplants, an increase in this field could decrease the size of the waiting list by 33%. Trial III shows how the waitlist will be affected if there is a 100% increase in living donor transplants. While there is not a significant decrease in the size of the waiting list, it is important to note that this change could stop the size of the list from increasing. Doubling the number of living and deceased donors would have the largest impact and correspond to a 45% decrease in the size of the waiting list.

Table 5.5: Results from Experiment I.

Trial Number	Living Factor	Deceased Factor	Waiting List Effect
Trial I	1.0	1.0	18% Increase
Trial II	1.0	2.0	33% Decrease
Trial III	2.0	1.0	2% Decrease
Trial IV	2.0	2.0	45% Decrease

Findings from the expanded experiment provide a more detailed look into how the size of the waiting list could be affected if there were to increase in the number of living and

deceased donors. Results from this experiment are visualized in Figure 5.2. This representation shows the Living Factor and the Deceased Factor respectively on the x and y axes. The color of the point at each combination reflects the size of the waitlist after 15 years. The red points in the bottom left corner correspond to an increased waiting list and little increase in the living and deceased donor factors. Points in the upper right corner represent the highest living and deceased factors as well as the largest decrease in the waiting list size. A living factor of 3.0 along with a deceased factor of 2.0 could lead to a 52% decrease in the size of the waiting list.

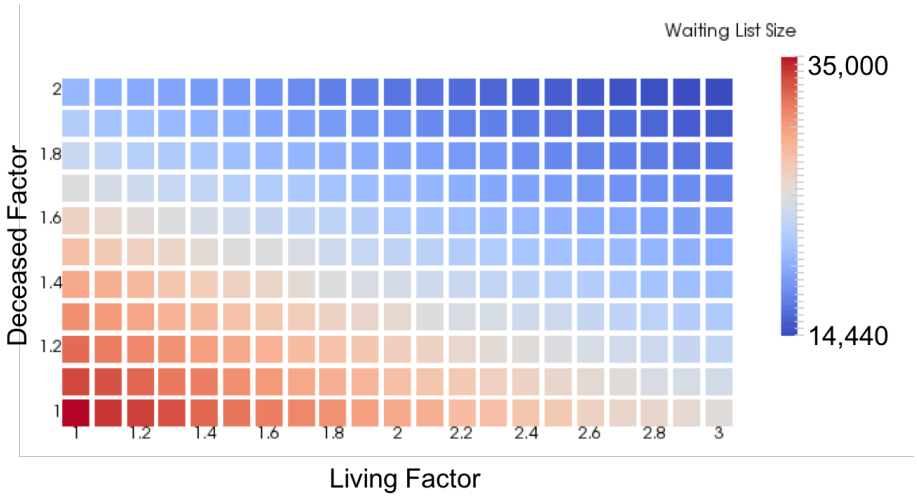

Figure 5.2: Visualization created in Paraview to show the size of the list after 15 years when various living and deceased factors are used in the experiments.

Experiment Set II

The goal of the second experiment set was to explore the effects of equalizing the living transplant probabilities across all ethnic groups. For this experiment, the probabilities to receive a living donor transplant were set based on the patient's age group and the white ethnic group. This is an attempt to improve the vast differences in probabilities observed in Table 5.3.

If the probability of receiving a living donor transplant for all ethnicities was increased to match that of the white ethnicity, the waitlist would decrease in size over the next 15 years. This change would account for a 3.5% decrease in the size of the waiting list. While this might seem like a small percentage, this would correspond to over 3,000 people. In this experiment, the total number of donors was higher to represent the increased number of donors for the racial group with a higher probability of receiving a living donor organ.

5.1.6 KTPM Conclusions

The simulation results gathered from the model showed that an increase in donors is necessary to keep the transplant waiting list from growing. These results are in agreement with the study by Leichtman et al., that the size of the waiting list will continue to increase unless there is a change [77].

Results from Experiment Set I showed that if there are significant increases in the number of deceased and living donors, the size of the waiting list will decrease. Although this model demonstrates that a decrease is feasible, the implementation of such dramatic changes to the current transplant system could be very difficult. In the simulation, a 100% increase in deceased donors and a 200% increase in living donors only led to a 52% reduction over 15 years. While this outcome would be a significant improvement, the result is still very far from eliminating the waitlist in just ten years.

Outcomes observed from Experiment Set II show that improvements to the equality in living donor transplants could help decrease the transplant waiting list. Even small measures taken to remove disparities between can help to stop the rapid growth of the transplant list and possibly reduce the size of the waiting list.

Many assumptions from previously conducted research in the field were used to create this model, as discussed in Section 1.9. The data used to create the model was based on recent years passed and does not account for improved medical technologies or improvements. Therefore, the model assumes that organs will continue to be distributed in the same manner. Additional information is available in the OPTN database which also impacts the

patient survival and likelihood of receiving an organ transplant including gender, blood type, health history, and various other factors. Future work could include incorporating many of these factors.

The model also assumes that patients will be added and removed from the waiting list in the same pattern observed between 2010 to 2012. This disregards general improvements in kidney health in the future. The KTPM also does not account for surviving failed transplant patients. Patients can survive failed transplant surgeries and be added back to the waiting list [1]. Many of these items that were not considered in this version of the model could be implemented in the future.

5.1.7 Future Work

The KTPM can be used to simulate the entire kidney transplant process. Results from experiments generated with this model can be used to investigate potential changes to the process. It could be useful to see how changes to living and deceased donors, as well as changes to donor ethnicity could affect the entire process. The model's setup by ethnicity and age also makes it a valuable tool to investigate the differences in these areas in the transplant process. There are many interesting disparities between ethnicities in the transplant process that can be examined with this model.

There are many appealing areas of the transplant process for every organ that can be explored with an expanded version of this model. A particular area of interest that this model is suitable for would be an analysis of the effects of increased donor availability on patient survival. In conclusion, it has been shown that a computational model can be used to explore the effects of various hypothetical changes to the transplant process. This model has also shown that alterations must be made to the transplant process before the size of the waiting list becomes unmanageable.

5.2 Multiple Listings Model

In the US, patients who qualify for an organ transplant may register at transplant centers within multiple Organ Procurement Organizations (OPOs) provided they can cover the costs of any additional testing, have the psychosocial support required for the procedure and recovery, and have approval from the transplant center. In this work, the impact of multiply listed patients waiting for a kidney transplant on patient mortality and waiting time using an agent-based queuing model. On a national scale, and for a fraction of multiply listed patients less than 0.40, an increase in multiply listed patients causes a decrease in the number of deaths and an increase in the wait time. Varied data for patient additions and donations across OPOs lead to a heterogeneous distribution of deaths and transplants per listed patient; increasing the proportion of multiply listed patients leads to a more homogeneous distribution of waitlist times and deaths across OPOs. Therefore, at a local level, not all OPOs see the benefit; OPOs with more transplants per patient population see an increase in patient mortality as the fraction of multiply listed patients increases. This model provides a tool for future policymakers; careful consideration needs to be made on how to ethically multiply list patients to maximize benefits for all patients.

5.2.1 Introduction

The US is divided into 58 different Donor Service Areas that are each managed by an OPO. Research has shown that geographic disparities exist across the patient population; the median waiting time for a deceased donor kidney transplant varies across OPOs from 0.61 to 4.57 years [119]. Additional information on geographical disparities in the transplant system is provided in Section 1.9.1.

There are currently no UNOS restrictions in place on registration at multiple OPOs [120]. Patients can choose to register within more than one OPO and at multiple transplant centers within a single OPO if they have physician approval and the means to cover medical as well as travel expenses and have the psychosocial support required to recover in the area [15]. However, the lack of restrictions on multiple registrations has led some to believe that an

unfair advantage exists for those with the financial means to travel large distances [121,122]. Prior research has shown that patients who are multiply listed may be more likely to receive a transplant and have better survival outcomes [123–132].

Merion et al. found that 5.8% of kidney patients and 3.3% of liver patients were multiply listed [127]. Additional studies have found that white race, higher income, higher, and higher education levels are associated with a higher prevalence of multiple listing [124–126,131,133].

ABM allow the exploration of system-level behavior and the study of interactions among individuals (agents) in model simulations [134, 135]. This computational approach uses agents that can be humans or entities (e.g., government organizations) that follow a distinct set of rules and allows researchers to model and predict how a system of agents following a set of rules will evolve in time [136, 137]. ABMs are especially useful when the data needed for making predictions based on statistical considerations are not available or sufficient. These types of models have been used in the past to inform and guide policy for a variety of complex systems [138–140].

In this work, simulations of an ABM with a queuing component are used to examine the impact of multiply listed kidney transplant patients on the waitlist on the median wait time and the deaths and whether this allows an unfair advantage. Historical OPO-level data on kidney transplants including waitlist additions, removals, and deaths are used as input parameters for simulations of OPO waitlists. Each simulation had a different percentage of multiply listed patients and how this percentage influenced waiting time and deaths were examined.

5.2.2 Materials and Methods

The ABM was constructed using a simplified model of the kidney transplant waitlist system and was simulated for 20 years using 2017 data on transplants and waiting times for OPOs [1]. The model was implemented in the Python programming language and the Mesa module was used to design and build the ABM and to coordinate the scheduling of the model [141, 142]. Code used to generate the multiple listings model is available on

GitHub [101].

Model Overview

Figure 5.3 depicts the waitlist structure and demonstrates the advantage a patient may have by being multiply listed. In this simplified example, there are only three OPOs, each of which has a different number of patients and a different number of transplants each month, t. The left column shows a system in which patients are only able to register with a single OPO, i.e., a Single Registration System. At time step (month) zero, $t = 0$, all of the patients are shown in their position on the waitlist. At time $t = 1$, one or more patients in each OPO are selected to receive a transplant and additional patients are added to the end of each list. The right column shows a system in which patients can be listed on a secondary list, referred to as a Multiple-Registration System. **Patient H** is registered in OPO 2 and OPO 3; in OPO 3, **Patient H** is second on the list, and therefore receives a transplant at $t = 1$. As a result, **Patient K** does not receive a transplant. **Patient H** benefits and there is a low likelihood that **Patient K** is impacted. At $t = 2$, patients who received transplants in $t = 1$have been removed from the lists, additional patients were added each list, and the patients at the top of each list are selected for a transplant.

The model waitlists do not account for specific rules in the transplant system that give preference to certain individuals such as children, healthier adults, or difficult-to-match individuals such as those with a high calculated panel-reactive antibody (CPRA) [18]. This model also does not account for matching quality. That is, the patient population is assumed to be homogeneous, all are deemed equally matched with the organs that become available in their OPO, and a patient can have a transplant at any transplant center in the OPO they are listed in. To account for the inherent heterogeneity between OPOs in the model using historical kidney transplant data, each list has its own arrival rate of new waitlist patients and a distinct value for the number of transplants performed at each time step.

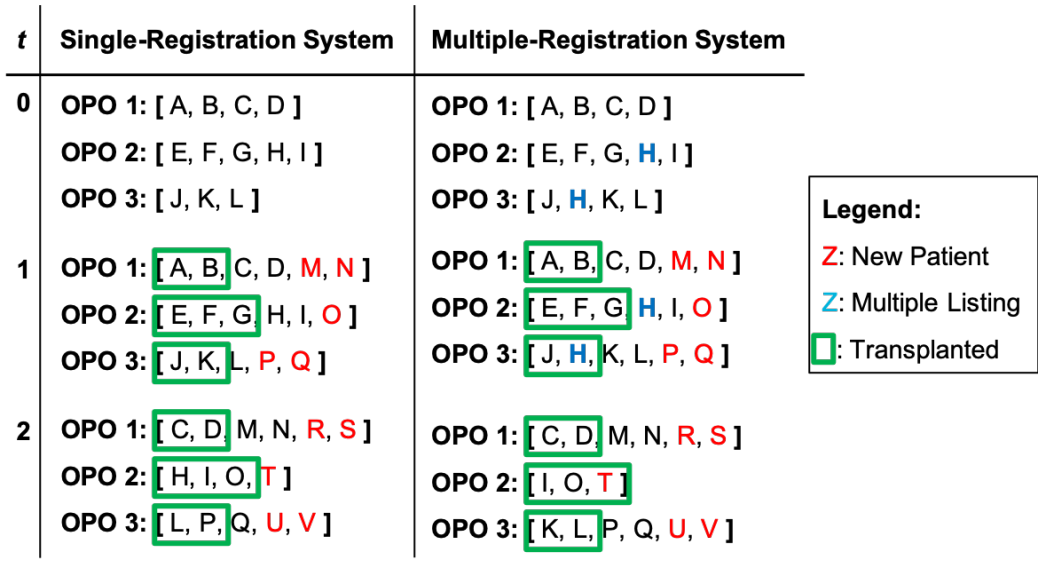

Figure 5.3: Three waitlists and the selection of transplant recipients in a Single Registration System and a Multiple Registration System.

Model Parameters

Input data for the model are from data obtained from the OPTN website [1] for the year 2017 and includes information on the kidney transplant waitlist sizes, removals, and additions at each of the 58 OPOs in the US Transplant rates are based on deceased donor transplants in each OPO. Waitlist additions are computed using yearly waitlist addition and removal values divided by 12 (to represent the time step of one month). The various reasons that patients are removed from the waitlist are not considered except for deceased donor transplantation; therefore, waitlist addition values were altered to account for ignoring these removal types. Waitlist additions represented in the model are the total additions minus the total patients of removal types that are ignored including: living donor transplants, patient transplanted in another country, OPO is unable to contact candidate, removals related to kidney/pancreas transplants, patient refused a transplant, patient's condition improved, patient transplanted at another center, and reasons listed as "other," leaving only waitlist removals that are represented in the model such as patient deaths, patients becoming too sick for a transplant, and deceased donor transplants.

The 2017 OPTN data was also used to generate the previously accrued time waiting for the patients already on the waitlist at the model initialization, $t = 0$. At the start of the simulation, many patients will have already been waiting for some time; the values displayed in Table 5.6 are the probabilities that are used to assign waiting times to these initial patients. This data comes from the advanced reporting tools on the OPTN website on 16 May 2018 [12] and reflects the distribution of time on the waitlist as of the date the data was extracted. The national distribution of previously accrued time was applied to all OPOs, as it is not available from the OPTN website at the OPO level [12].

Table 5.6: Number and percentage of patients, referred to as candidates, on the waitlist at the start of the simulation binned by the time already spent waiting for a transplant. The month bins are inclusive on the lower end and exclusive on the upper end of their ranges.

Months	[0,1)	[1,3)	[3,6)	[6,12)	[12,24)	[24, 36)	[36, 60)	[60, ¿60)
# Candidates	4,950	8,001	9,933	16,468	24,126	16,966	22,034	17,920
% Candidates	4.11%	6.65%	8.25%	13.68%	20.04%	14.09%	18.30%	14.88%

Model Design

In the model, each patient is in one of three states: Waiting, Transplanted, or Deceased. Waiting patients are registered on at least one OPO waitlist and have not yet been chosen for a transplant. Transplanted patients have received an organ and are removed from the list prior to the next time step. Deceased patients were in the Waiting state longer than their remaining time alive and thus died before entering the Transplanted state.

Each patient is randomly assigned to a primary waitlist based on the model input parameters for waitlist additions in each OPO. Independent of the primary waitlist assigned, each patient is also designated as either singly or multiply listed based on the model input for multiply listed population. Patients who are multiply listed are then added to one additional waitlist. Merion et al. [127]. showed that very few multiply listed patients were listed in more than one additional waitlist. Additional verification runs were performed to

explore the model when patients were limited to one additional waiting list, this is discussed in Section 5.2.2.

When multiply listed patients select the secondary OPO, they have the ability to intelligently select their additional waitlists. The probability that an OPO is selected is directly proportional to a computed transplant rate at that OPO. The computed transplant rate for each OPO at time step t is calculated as the ratio of the number of patients transplanted at that OPO in the previous time step to the OPO list size at the current time step. This implementation is based on the assumption that if a patient has the time and finances to multiply list, they will do so in a way that will give them the highest likelihood of receiving a transplant.

Each patient is assigned a lifetime parameter T_{life}, which represents the maximum amount of time the patient can be in the Waiting state, T_{wait}, before moving to the Deceased state. That is, if $T_{\text{wait}} > T_{\text{life}}$, the patient exits the Waiting state and enters the Deceased state. T_{life} for each patient is selected from a Gaussian distribution with an average of 91 months and a standard deviation of 5 years. The average lifetime of patients was determined using data from the US Renal Data System Annual Data Report [79] and the age demographics for life expectancy of the waitlist patients were taken from the OPTN dataset [1]. The mean life expectancy for a patient on dialysis was computed and weighted by the population representation on the waitlist. Although age is not explicitly represented in the model, it is indirectly represented through the average lifetime of patients. Figure 5.4 illustrates how this process is implemented in the model and how patients are initially waiting, transitioned to the Selected and then Transplanted state, or become deceased if they do not receive a transplant in T_{life} time steps of being added to a waitlist.

Figure 5.4 2 illustrates how this process is implemented in the model and how patients are initially waiting, transitioned to the Selected and then Transplanted state, or become deceased if they do not receive a transplant in T_{life}, time stamps of being added to a waiting list. This diagram maps the transition of patients from their initial addition to the waitlist, checking if they're at the top of the list and then continuing the loop until the patient is

either transplanted or deceased. A diamond shape represents a decision point, rectangles represent states, and the circle represents the initialization step.

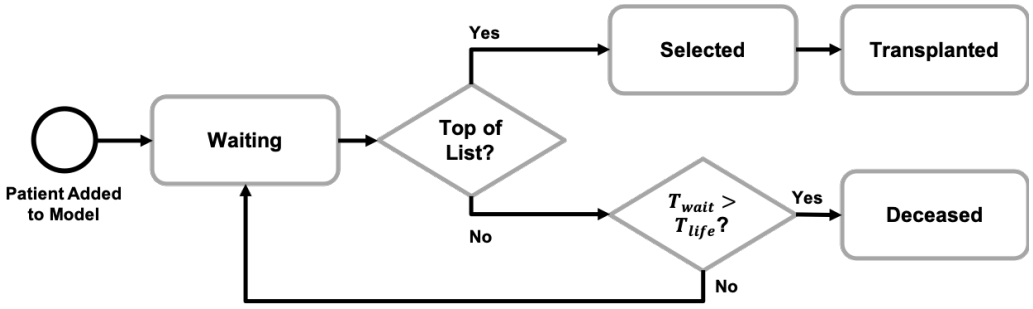

Figure 5.4: Process model diagram of the states of a patient in the model.

At $t = 0$ months, each waitlist is populated with patients established in the lists with a life expectancy and a previously accrued waiting time. If a generated patient has $T_{\text{wait}} > T_{\text{life}}$, this is considered to be a patient that died before the simulation start and this patient is not used and a new patient is generated. The probability of a patient being in an OPO is computed using waitlist data for each OPO and then patients are allocated to an OPO based on that probability.

During the following time step, at $t = 1$ month, the first N_i patients on each waitlist are selected to receive a transplant and are removed from that list. These are the patients that have been waiting for the longest for a transplant. N_i is determined by selecting a value from a Poisson distribution with a rate parameter, λ_i. The monthly rate parameter, λ_i, for each OPO was determined using the number of transplants at that OPO in 2017 divided by 12. The first Ni patients on each waitlist are selected to receive a transplant and are removed from that list. If a patient selected for a transplant is multiply listed, they are removed from the other lists before the kidneys in that OPO are allocated. To ensure that multiply listed patients are not chosen from the same OPOs more frequently, random ordering at each time step determines the procedure in which each of the waitlists are processed and patients receive transplants.

Next, another independent Poisson process is used to calculate the number of patients to add to the waitlists using the OPO distributions of new patients in the 2017 OPTN data. Multiply listed patients are then assigned to additional lists using the process described in the initialization phase of the model.

The process described at $t = 1$ month is repeated for a total of 240 simulated consecutive months (20 years). This model duration was chosen to allow multiple generations of patients to cycle through the system to generate sufficient patient outcome data for analysis. The entire simulation of 20 years is repeated using a different fraction of multiply listed patients between 0 and 1 in steps of 0.01. Due to the variability introduced by the random variables in the simulation, two simulations with the same fraction of multiply listed patients will not have the same output. To determine simulation results, 50 simulations are performed for each fraction of multiply listed patients and the average of these 50 is reported.

Model Scheduling and Process Overview

Time is modeled as discrete steps corresponding to approximately one month to provide a lower level of granularity than a year for patients to join and receive transplants in different OPOs. Each replication is run for 240 time steps, which equates to 20 years. The sequence of events executed at each time step is described in this section. For each DSA waiting list i, the number of organs available for transplant N_i is generated from a Poisson process calibrated to the i^{th} region. A Poisson distribution was chosen as it describes the probability of k events occurring within an observed time period, in this case, the k events are the number of available donor organs [143]. Next, the order of the waiting list is randomly shuffled to ensure each waiting list is equally likely to be selected first each time. Then, taking each waiting list in turn, the first N_i patients are marked as Selected and removed from the list. If any of those patients are multiply listed, they are subsequently removed from whatever position they held in the other waiting lists before the organs for that waiting list are allocated.

Once the lists are updated, the patients are updated to reflect the advancement of time.

Each of the patients that were not selected increment their waiting time T_{wait} by 1. If the patient is in the Selected stage, the patient transitions to the Transplanted stage. In the case that a patient is still in the Waiting stage and they have been waiting for longer than their predetermined lifetime, the patient will move to the Deceased stage.

Finally, new patients are added to the model according to an independent Poisson process calibrated to each region. A portion of these patients will be multiply listed and therefore listed in multiple regions. The model terminates when there are no longer any patients in the Waiting state or if the number of time steps has exceeded 120. Python's Mesa module provides the *DataCollector* to track patient states in the model over time [142]. Tracking these statistics allows for simple and quick visualizations of the process and model statistics. The user can specify which statistics are managed by the DataCollector at the start of each model run. The model also tracks the number of patients meeting the following criteria:

- Patients transplanted in their primary DSA
- Patients transplanted in a secondary DSA
- Patients with a primary DSA in the list that received a transplant elsewhere
- Patients with a primary DSA that died before receiving a transplant
- Patients with a primary DSA
- Patients listed in a secondary DSA

Calibration and Model Input

This model follows several basic concepts and theories related to the real-world allocation of organs in the US. Different DSAs are diffectly incorporated into the model and patient are allowed to join multiple listings in accordance with current policies and practices in the US. The model takes in multiple input parameters, most of which are optional. The multiply

listed probability specifies the percentage of patients that have are listed at multiple centers and the average lifetime can also be customized before each run.

Model Limitations

This theoretical model makes several assumptions that simplify the model and the underlying transplant system represented:

- All transplants are performed locally, available kidneys do not travel, only multiply listed patients cross OPO boundaries. Previous research has shown that population density and close geographic borders have an impact on multiple listings [127, 144].
- The previously accrued waiting time at model initialization and the predetermined patient lifetime was implemented using national numbers and was not specific to the OPOS.
- Kidneys are allocated based only on OPO and patient waiting time. No matching criteria are used, whenever a kidney is available it is assigned to the first person on the list.
- Patient mortality post-transplant and re-transplantation are not represented.
- Patients make their decision to list in a secondary OPO based solely on the number of patients receiving a transplant per total patients listed, the decision is not geographically motivated.
- Patient lifetime is modeled using a Gaussian distribution which is not a common practice in modeling patient survival.

These assumptions are made to reduce the model to basic elements of waitlists and to explore the theory and implications of a highly simplified waitlist with the allowance of multiple listings. This model was built to specifically address multiple listing in the kidney transplant system; the simulation implementation and results would be different for other solid organ transplant systems.

Model Verification and Sensitivity Testing

To verify the model and the computations and to test the model's sensitivity, simulation runs were performed using a variety of variations on the model [116]. These variations included modeling OPOs as having homogeneous transplant and patient addition rates, shorter mean patient lifetime, longer mean patient lifetime, multiply listed patients having a longer average lifetime, a maximum additional waitlist total of two and three, regional limitations on multiple listing, modeling patient lifespan with a Weibull distribution, and a subset of ten OPOs. Additional sensitivity testing was performed after running the model for one, two, five, and ten years, the time span of 20 years was chosen to allow the model to fully develop and examine patients over several generations. Generally, peaks of the results were consistent with the original findings and verified the results of the main model, alternate findings will be explored in future work.

Experiment verification runs with shorter and longer mean lifetimes results followed a similar pattern to the main experiment runs. During verification runs where patients have a longer average lifetime, patients waited longer on average and there were fewer patient deaths than in the main experiment runs across all rates of multiply listed patients. Verification runs with shorter average lifetimes resulted in higher patient death rates and shorter waiting list times than in the main experiment runs for all percentages of multiply listed patients.

The model was also run with the inputs altered so the waiting list sizes, additional patients, and transplant rates were homogeneous across the entire population, meaning that every OPO had the same input values, equal to the mean across all population. For these runs, the results were the same for all percentages of multiply listed patients and matched the results of the main model when the percentage of multiply listed patients is greater than 50%. A system with a large percentage (greater than $\sim 50\%$) of multiply listed patients has a similar behavior as a system when all OPOs are homogeneous, as expected.

Model runs performed with a Weibull distribution used to model patient lifetime by converting the Gaussian distribution parameters to represent the shape and scale of the

Weibull distribution[145]. Overall, the results are similar to that of the main model with a lower median wait time, more deceased patients, and fewer waiting patients across all fractions of the multiply listed population. For simulations where patients are limited to registration at one additional OPO, the results are similar to that of the main model with a slightly lower median waiting time and higher death rates for low (greater than $\sim 50\%$) percentage of the multiply listed patients. The final verification tested the stability of the model by selecting a subset of OPOs and performing the same experiment. These results for waiting time and death rates followed a similar pattern to the main experiment, showing the model's stability for a small population.

5.2.3 Results

At each time step, the simulation outputs (1) the total number of primary transplant listings and alternate transplant listings, which sum to the size of the national waiting list; (2) the number of primary listing transplants and the number of alternate listing transplants, which sum to the total number of transplants; (3) the OPO of transplants; (4) the number of multiply listed patients receiving a transplant for comparison with the total number of transplants; (5) the median waiting time on each OPO transplant list; and (6) the number of patients transitioning to the Deceased state. The mean of the fifty simulation replications are used in this section and presented as the results.

Figure 5.5 shows the number of primary listing transplants, alternate listing transplants, and total transplants performed versus the percentage of multiply listed patients in the population in the range of 0%–100%. When no patients are multiply listed, all transplants are to patients on their primary waitlist and when 100% of patients are multiply listed, approximately 50% of transplants occur at the primary listing OPO. The total number of transplants slightly increases when the multiply listed patient percentage increases from 0% to 10%.

Figure 5.6 shows the number of patients waiting for a transplant and deceased versus the percentage of the population that is multiply listed. The dashed vertical line displayed

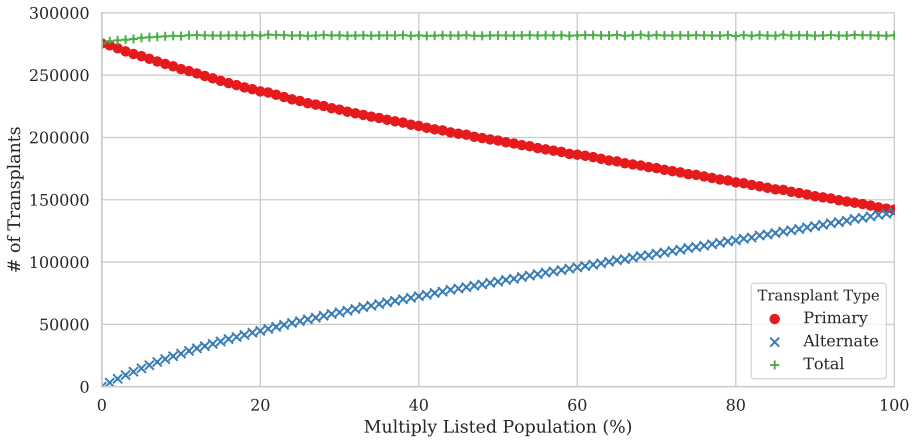

Figure 5.5: Total number of transplants and the number of transplants performed at either the primary or alternate waitlist.

shows the current proportion of multiply listed patients at 5.8% [127]. As the percentage of multiply listed patients increases, fewer patients leave the waitlist because they are deceased. Because the total number of organs available for transplant is independent of the percentage of multiply listed patients, lower patient mortality causes the waitlist size to increase. When no patients are multiply listed, there are approximately 141,600 patients on the waitlist at the end of the simulation, which increases to approximately 157,500 ($\sim$ 11%) when $\sim$ 15% or more of the population is multiply listed. The number of deaths, approximately 116,600, is the highest when no patients are multiply listed. When approximately 15% of the patients are multiply listed, this number decreases to about 94,000 (a 19% decrease).

As shown in Figure 5.7, in a system without multiply listed patients, the median wait time for a transplant is 74 months (6.2 years), this based on the patients that received a transplant during the simulation. When the percentage of multiply listed patients increases to approximately 25%, the median waiting time for all patients increases to 83 months (6.9 years), corresponding to a 12% increase; more patients having access to an additional waitlist increases the overall waiting time. This image also shows the comparison between singly and multiply listed patients, multiply listed patients have a lowed median wait time up until approximately 50% of the population is multiply listed.

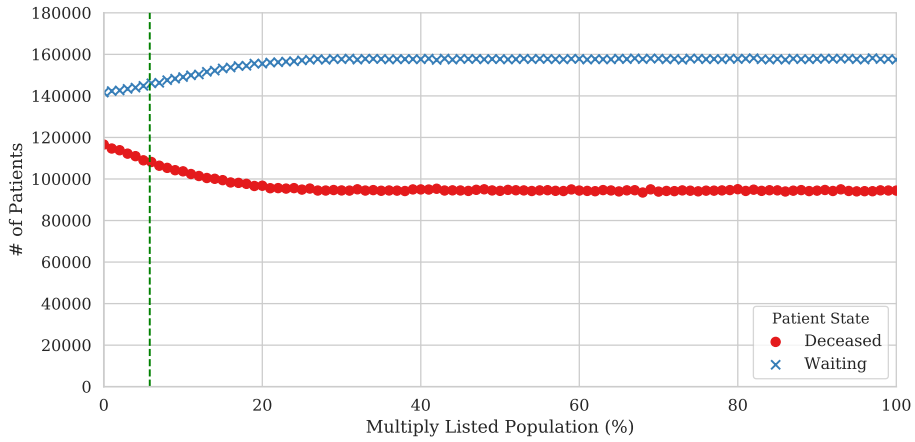

Figure 5.6: Total number of patients waiting and deceased across levels of the multiply listed population at the end of the 20 years.

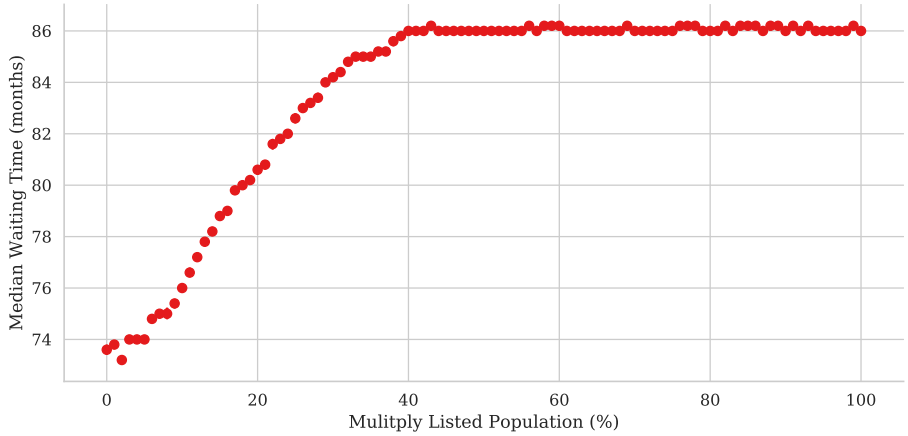

Figure 5.7: The median wait time as the multiply listed population increases for all patients, multiply listed patients and singly listed patients.

One method for assessing fairness is to test whether multiply listed patients are disproportionately represented among those receiving transplants and those avoiding death. That is, if multiply listed patients constitute 20% of the population, in a fair system they should receive at most 20% of the transplants and make up 20% of the total deaths. In a fair system, the difference between the multiply listed patient transplants per total patients

and the percentage of multiply listed patients in the population should be zero.

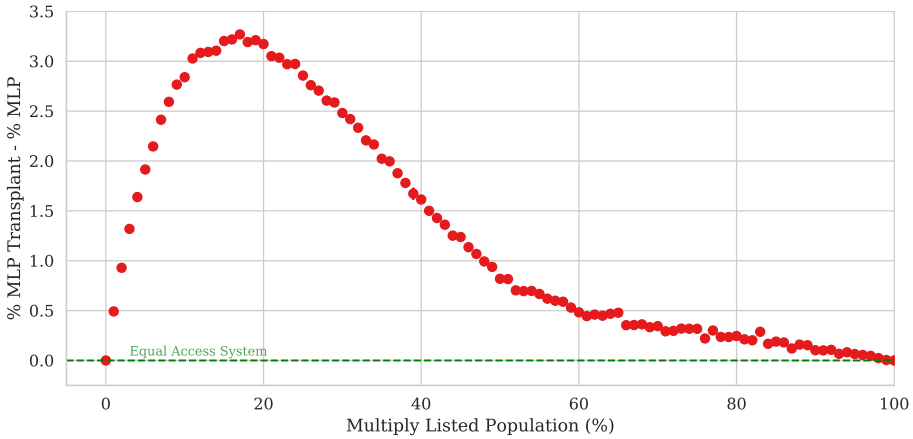

Figure 5.8: The impact of the multiply listed patients on transplants per waiting patient.

Figure 5.8 shows that multiply listed patients receive slightly more transplants than they would in a fair system. When multiply listed patients make up between 6% to 36% of the patient population, they receive over 2% more transplants, with 3.3% as the maximum when 17% of patients are multiply listed. Additionally, Figure 5.9 shows that multiply listed patients are less likely to die while waiting for a transplant – they are up to 8.3% less likely to die while waiting to receive a transplant, and the largest discrepancy occurs when 21% of the population is multiply listed.

Figures 5.10 and 5.11 show the impact of multiple listings on deaths and waiting time at the OPO-level. Due to the large number of OPOs (58), only a subset is shown. The subset was determined by first ordering the OPOs by the number of deaths per patient population at the end of the simulation with the no multiply listed patients and then selecting every sixth OPO from this sorted list. The OPOs shown in Figure 8 and Figure 9 include: LiveOnNY (New York; NYRT), LifeSource (Minnesota; MNOP), Lifesharing (California; CASD), LifeQuest (Florida; FLUF), LifeNet (Virginia; VATB), Legacy of Hope (Alabama; ALOB), Indiana Donor Network (INOP), Tennessee Donor Services (TNDS), and LifeShare

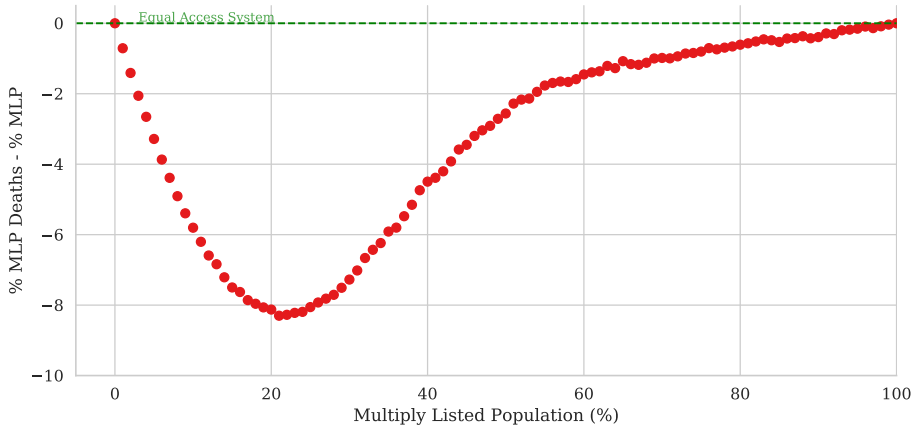

Figure 5.9: The impact of the multiply listed patients on deaths per waiting patient.

(Oklahoma; OKOP).

The percentage of patients that died waiting for a transplant at the end of a simulation as a function of the percentage of multiply listed patients in the population are shown in Figure 5.10.. As the percentage of multiply listed patients increases, OPOs with a higher percentage of deceased patients in the population see a decrease in their percentage of deceased patients, the opposite is true of OPOs with a lower percentage of deceased patients in the population.

Figure 5.11 shows that the median transplant waiting time for patients is also heterogeneous across OPOs when a small percentage of the population is multiply listed and becomes more homogeneous as the percentage of multiply listed patients in the population increases. OPOs with a longer (shorter) waiting time when there are no multiply listed patients in the population see a decrease (increase) in their waiting time as the percentage of multiply listed patients increases. As the percentage of multiply listed patients increases, OPOs with longer wait times see a decrease in wait time while the opposite is true for OPOs with shorter wait times.

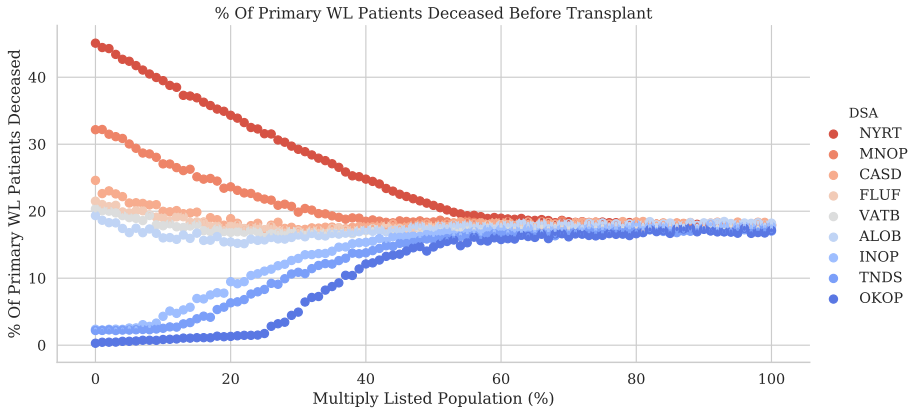

Figure 5.10: The percentage of deceased patients in an OPO versus the percentage of multiply listed patients in the population. Deceased patients are only accounted for in their primary OPO.

5.2.4 Discussion and Conclusions

Increased multiply listed patients lead to a longer national waitlist and a longer median waiting time are fewer deceased patients at the end of the simulation. Fewer patients dying while waiting for a transplant results in more patients surviving and therefore more patients waiting for a transplant. The model results indicate that the slight increase in waiting time is not enough to also increase the number of patients that die while waiting for a transplant. Because the number of deaths is lower, the number of surviving patients waiting for a transplant is higher, increasing the waiting time. These findings, especially those showing decreased deaths support the current OPTN policy for multiple listing [15].

Due to the simplified approach of this model, organs are not transplanted outside of the local OPO therefore, multiply listed patients help fill up the shorter waitlists. According to research published in Kidney International, 14.6% of kidneys are discarded due to the inability to locate a recipient [146], therefore this change in transplant numbers is not unreasonable.

Research on the OPTN transplant data has shown that multiply listed patients are more likely to receive a transplant and have lower mortality while waiting for a transplant [127].

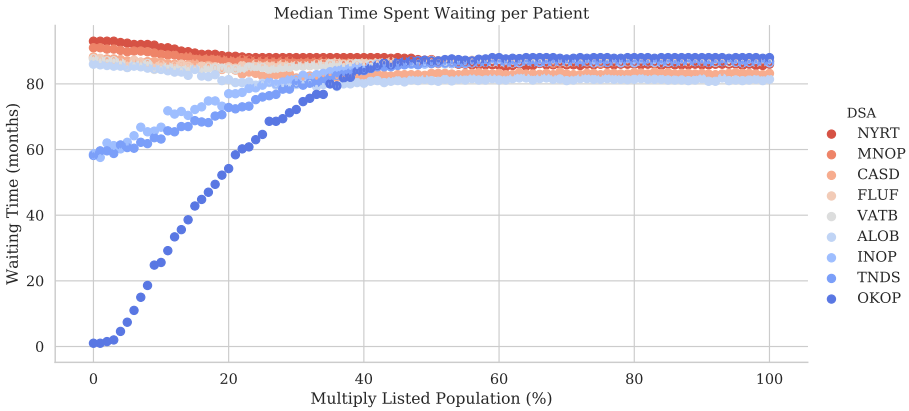

Figure 5.11: The median waiting time per patient in their primary OPO versus the percentage of multiply listed patients in the population.

Analysis by Merion et al. found that at a population of 5.8% multiply listed patients, multiply listed patients were 88% more likely to receive a transplant and were 28% less likely to die while waiting for a transplant [127]. In this model, when multiply listed patients make up 6% of the population, they are 20% more likely to receive a transplant and 14% less likely to die while waiting for a transplant. This simplified model does not include other factors that would increase the likelihood of a patient multiple listing which may explain the large difference in probability of receiving a transplant.

The motivation for using an agent-based queuing simulation approach is that it allows an analysis of both the system- and local-level impact of having multiply listed patients present in the model population. Additionally, ABMs allow for a richer representation of agent behaviors which could be added in future versions of the model. Although there is an overall improvement at the national level when patients are allowed to be listed at more than one OPO, not all OPOs see an improvement. When a large percentage (>40%) of the population is multiply listed, patients with a primary listing in OPOs with higher rates of donations per waiting patient will have a higher rate of deaths per patient. A model such as this can be used to investigate whether the allowance of multiple listings unfairly disadvantages communities with a high ratio of donors to waitlist patients that may become

target areas for a domestic form of transplant tourism [147–149].

This model and the simulation results show that patient deaths at the national level reach a minimum limiting value when approximately 25% of the population is multiply listed; the current proportion of patients with multiple listings is much lower, at approximately 5.8% [127]. The majority of the impact occurs when only a small percentage of the population is multiply listed.

An increase in the number of multiply listed patients could be accomplished through increased education on the ability to multiply list, travel grants or funding for transportation to patients with the highest potential for positive outcomes, or by adding a fee to the cost for multiple listings and using the proceeds to fund other patients who demonstrate a financial need to be multiply listed. Recent changes to the kidney allocation process should also help to demonstrate the same benefits as multiple listings [15]. The economic benefit of transplantation compared to dialysis has been demonstrated in previous research [11,27,28]. Improved allocation policies put in place for kidney transplants help to address the same issues through a greater level of sharing across OPOs [15,111].

5.2.5 Future Work

This model takes a highly simplified approach to modeling the transplant system and the process of multiple listings. The sensitivity analysis demonstrates many potential options for future work expanding this model including implementing regional limitations and modeling multiply listed patients as having a longer expected lifetime. Alternate methods for modeling the patient lifetime should be investigated, the Weibull distribution is commonly used to model patient lifetime and the model could be updated to include different distributions and to explore variations of these distributions [150, 151]. Improvements can be made to the model input data to include projections of transplant additions and removals into the future instead of using a single year to parameterize the model.

This research does not consider the impact of geography on the prevalence of multiple

listing. Previous research has shown that population density and close DSA geographic borders have an impact on multiple listings [127]. Stewart et al. assessed system performance by quantifying the degree of disparity in access to deceased donor kidney transplantation and showed that the DSA was the factor most associated with disparities in the new kidney allocation system [144]. An extension of this model could be used to determine the impact of geography and take into consideration the higher incidences of multiple listings in close geographic regions.

The model used in this work can be extended, and future research will consider (1) allowing the population of patients to be considerably more heterogeneous to determine if additional disparities exist between aggregate measures and more specific ones; (2) a more advanced decision-making algorithm to model the patient's behavior; and (3) experimenting with different levels of granularity for the time step to allow differing rates of transplantation across months or years. Although the model and simulations addressed the major components of the transplant system, it is expected that further simulation will be needed to determine the impact of policy changes concerning multiple listings.

Chapter 6: Summary and Conclusions

The focus of this research was to establish a data-driven approach to analysis, modeling, and simulation of the organ transplant system in the US. This work was motivated by the principle that leveraging these tools leads to a greater understanding of the complexities of the transplant system which will inform decision-makers and improve the process. Four major research questions are addressed in this dissertation:

1. How can we further enable data-driven research of the transplant system for future scientists?
2. What demographic factors influence donations and access to transplantation?
3. How do laws and policies affect organ donations?
4. How do certain patient advantages impact the overall system as well as those lacking advantages?

Each of the above questions are addressed throughout this dissertation in an encompassing body of work on the organ transplant system. This research created an open-source pipeline for the organ transplant data for accessible, open-source research and uses this resource to perform modeling and analysis of the transplant system. Additionally, methods for exploring multi-dimensional data, performing outcome and policy impact analysis, and modeling the transplant system were developed in this work with multiple opportunities for further research.

6.1 Enable Data-Driven Research of the Transplant System

To propel data-driven research in the field of organ transplantation, the `transplant2monog` tool was developed, as described in Chapter 2. This open-source tool transitions Organ

Procurement and Transplantation Network (OPTN) Standard Transplant Analysis and Research (STAR) files from proprietary formats and flat files into a database. The tool enables a dynamic environment for querying data with the capacity to accelerate research. This resource has been published in the Journal of Open Research Software and is publicly available to the transplant research community on Github [61]. The `transplant2mongo` tool will be extended to work with data files from the Scientific Registry of Transplant Recipients (SRTR) and I will be working with the organization to implement this data management system [3]. Continued updates will be published to the Github repository as they are developed.

6.2 Demographic Factors, Donation, and Transplantation

The demographic factors influencing organ donation and access to transplantation are discussed in the exploratory analysis presented in Chapter 3. This exploratory data analysis scales `transplant2mongo` data to the relative populations to gain a better understanding of differences between demographic groups, revealing important differences across education levels, gender, race, and ethnicity. Analysis conducted in Chapter 4 builds on the exploratory analysis and uses a random forest model to predict patient waitlist outcomes based on their `transplant2mongo` data. Random forest classification was able to predict patient outcomes with 64% accuracy. It was found that key socioeconomic factors, such as the percent of the geographic area without a high school diploma or living in poverty, influence patient outcomes and can be valuable indicators for the transplant process. Results from this research imply that increased focus should be placed on educating and improving access to transplantation for patients with a high social vulnerability, as defined by the Center for Disease Control (CDC) variables [96].

Data used in this work only includes patient information up until 2015 and the available data does not always include full patient details. Many data fields in the OPTN STAR files are null, which limited the exploratory analysis and the building of the random forest

model to omit potentially valuable patient information.

Publication of the work on visualizing the transplant system and the intersections of patient demographic subgroups is planned. There is also ample opportunity to extend the work to focus on transplant recipients as well as additional data features. Much of the OPTN data is geographically linked and expanded choropleth maps or micromaps would add value to the graphics presented in this work [72]. The random forest analysis work presented in Chapter 4 will also be submitted for publication in a scientific journal. This research can be extended to evaluate different models, further prune important features, and filter the data to reduce the frequency of unknown values.

6.3 Impact of Laws and Policies on Donation

The impact of laws and policies on organ donation as well as demographic factors influencing donation are explored in the statistical analysis on state and local regulations presented in Chapter 4. I developed a key methodology for evaluating and visualizing the impact of a policy on the population. This analysis of policy changes found that while some policies can be correlated with a change in donation, such as the impact of donor education laws on living donation, this may only be true for demographic subgroups a population. These educational policies also significantly increased the number of African American / Black deceased donors. Public leave of absence laws corresponds to an increase in living donation rates for both African American / Black and Latino populations.

Results from this analysis indicate that policies related to education on organ donation in driver's education classes and schools are effective in increasing donation. Laws on education should be implemented in all states or at a federal level to increase donation rates and confidence in the overall transplant system. Policies supporting a leave of absence for public employees successfully increase the number of living donors in African American / Black and Latino populations. Public leave of absence programs should also be expanded to all states to help increase donation among these communities.

Research on the impact of laws and policies was limited by the available data on the

transplant system as well as open-source tools and research methods published in this area. The data used in this work only includes patient information up until 2015, excluding more recently implemented laws and policies from the analysis. Much of the statistical analyses and modeling in this field are performed in proprietary software tools and authors do not commonly open-source their code or provide supplemental data. This also limits the ability to reproduce previous studies; the publication of analysis code is extremely rare in this field.

Analysis performed on the state policies will be submitted for publication in a scientific journal in the future. This analysis could be updated to include more recent years which would involve more states in the analysis and provide data to execute additional statistical tests as well as additional policies and initiatives.

6.4 Patient Advantages

The final part of this research, presented in Chapter 5, explores how certain patient advantages impact the overall system as well as those lacking advantages. This examination is conducted with an agent-based queuing model that analyzes the impact of multiply listed patients on the overall transplant system and how the prevalence of these patients impacts patient deaths and waiting times on a global as well as a local scale. Results from this modeling effort demonstrate that multiply listed patients are always more likely to receive a transplant and less likely to die than patients that are not multiply listed. Although there is an overall improvement at the national level when patients are allowed to be listed at more than one Organ Procurement Organization (OPO), not all OPOs see an improvement. When a large percentage (>40%) of the population is multiply listed, patients with a primary listing in OPOs with higher rates of donations per waiting patient will have a higher rate of deaths per patient.

Based on results from the multiple listings model, the OPTN should re-evaluate this policy and consider methods encouraging or allowing different demographics of patients to multiply list. The models developed in this work make many assumptions about how patients enter the system and receive transplants. Variations of these assumptions could be

explored in future work. As part of this research, multiple variations of the multiple listings model were generated to perform sensitivity testing and model verification. Each of these models could be further explored for additional research and more patient features could be added to the model to better mimic the real-world transplant system.

Appendix A: Laws and Policies for Organ Donation and Transplantation

The US has had formal laws regulating organ donation since 1968 when the Uniform Anatomical Gift Act (UAGA) was passed. This statue was adopted by every state and Washington, DC. The law provides a legal foundation for providing organ and tissue donations, referred to as "anatomical gifts". A person's right to consent to organ donation or the responsibility of their next of kin to provide consent is described in the law [78].

Public Law 92-603 in 1973 amended the Social Security Act to provide Medicare eligibility to persons with chronic kidney failure [152]. Eligibility is limited to individuals under 65 that are medically determined to have chronic renal disease and require dialysis or a transplant as treatment. The law also requires that the person is fully covered or insured, is already covered by Medicare, is the spouse or dependent child of someone who is currently or fully insured, or is the spouse or dependent child of a person that is entitled to Medicare or Medicaid This law stipulates that Medicare coverage is activated on the third month following the initial month of a course of renal dialysis. This eligibility ends one year following the month in which a person has a kidney transplant. This law considers eligible individuals to be regarded as disabled for the purpose of coverage.

In 1978, Public Law 95-292 further amended the Social Security Act to extend coverage for individuals about to receive a kidney transplant [153]. It also extends coverage of medical insurance for a patient receiving a transplant to three years following the transplant or one year following the termination of dialysis. Coverage is also extended to patients diagnosed with End Stage Renal Disease (ESRD) [153]. Public Law 95-292 also stipulates standards for experiments, pilot projects, and studies. The law states that the Secretary of Department of Health and Human Services (HHS) should carry out pilot projects for financial assistance in purchasing new or used medical equipment for at-home dialysis. Additionally, the law specifies that experiments should be conducted to evaluate methods for reducing costs of the ESRD program and experiments for evaluating methods for dietary control to reduce

the costs of the ESRD program. The law also requires that the Secretary of HHS conduct a full study of methods to increase public participation in kidney and other organ donation programs [153].

The Uniform Brain Death Act was created in 1978 by The Uniform Law Commissioners which intended to clearly define brain death as the "irreversible cessation of all functioning of the brain, including the brain stem", which is equivalent to death [154]. This law was replaced in 1980 by The Uniform Determination of Death Act. The new law provides a definition for the determination of death as an individual that has sustained either "irreversible cessation of circulatory and respiratory functions" or "reversible cessation of all functions of the entire brain, including the brain stem" and the determination has to be made under acceptable medical standards. The law clarifies that is applies to all situations, not just the UAGA and that it is specifically concerned with determining death of an individual [155].

In 1984, Public Law 98-507, the National Organ Transplant Act (NOTA) was passed [4]. This law established the Task Force on Organ Transplantation, created the Organ Procurement and Transplantation Network (OPTN), the Scientific Registry of Transplant Recipients (SRTR), and an administrative unit within the HHS be established to manages these organizations. The law also established the Organ Procurement Organization (OPO)s and guidelines for these organizations to follow. The OPTN is established as a nonprofit entity only engaged in organ procurement [4]. Finally, Title III of the NOTA prohibits the purchase of organs, "it shall be unlawful for any person to knowingly aquire, receive, or otherwise transfer any human organs for valuable consideration for use in human transplantation if the transfer affects any interstate commerce" [4].

The Omnibus Budget Reconciliation Act of 1985 states that there must be written standards for the provision of organ transplants [156]. If states do not have written plans and procedures for organ donation, the federal payments for organ transplants may be denied [156]. This law was followed by the Omnibus Budget Reconciliation Act of 1986 which established hospital protocols for organ procurement and provides standards for for organ procurement agencies. One important aspect of this law is it establishes that hospitals

must have written protocols for identifying potential organ donors that "assure that families of potential organ donors are made aware of the option of organ or tissue donation and their option to decline". This law also provides requirements for hospitals wanting to participate in the Medicare and Medicaid programs [157]. The deadline for requirements given in this law were extended by the Balanced Budget and Emergency Deficit Control and Reaffirmation Act of 1987 act [158].

The Omnibus Budget Reconciliation Act of 1987 was passed as Public Law 100-203 [159]. This law sets the rules for designating pediatric hospitals as heart transplant facilities. The pediatric heart transplant program must be operated jointly by the hospital and another facility that meets the criteria, the program shares the same transplant surgeons and quality assurance program, and the hospital demonstrates that is is able to completely meet the needs required by pediatric heart transplant patients [159].

The final federal legal action related to organ donation passed in 1987 was the 1987 Version of the Uniform Anatomical Gift Act [160]. This revision to the 1968 UAGA law was meant to be adopted in every jurisdiction in the US. This new version declares a person's legal consent to donate irrevocable. This addresses problems in organ donation such as the failure of individuals to sign directives to transplant, and the failure to locate these directives. This law simplifies the consent process by only requiring that an anatomical gift be made by a document of gift signed by the donor [160].

The Health Omnibus Programs Extension of 1988 includes Title IV, which is a section on Organ Transplant Amendments of 1988 [161]. This law has several aspects to change the donation system. The law authorizes the Secretary of HHS to provide grants to fund special projects to increase the number of organ donors. The law also requires the OPTN to carry out studies and demonstration projects in regards to procurement and organ allocation and clarifies what constitutes a "human organ". The Act also implements a immunosuppressive drug therapy block grant to provide patients with medications that will prevent the rejection of transplanted organs [161].

The Transplant Amendments of 1990 were passed as Public Law 101-616 [162]. These

amendments repealed the rules that prohibited the OPTN from engaging in activities unrelated to transplants. This law also modifies some of the requirements and provisions to the transplant system [162].

The Notice of Proposed Rulemaking was passed and issued in the Federal Register and proposed regulations governing the OPTN, these proposed regulations were finalized and published in the Federal Register as the Final Rule in 1998 [163] [164]. Effectiveness of the Final Rule was delayed by Public Law 106-170 in 1999 [164].

In 1999, the Organ Donor Leave Act was passed which allowed federal employees to take paid leave to become living organ donors [42]. The 106th Congress also passed the Children's Health act of 2000, which included Title XXI on the special needs of children regarding organ transplantation. This law recognizes that there are different issues in transplantation between children and adults. Studies must be done to attempt to improve the system for populations with special needs, which includes children and people of racial and ethnic minority groups. The law also recommends studies on the costs of immunosuppressive drugs provided to children and the coverage of these drugs, the extent of the denial of organs to be released for transplant by coroners and medical examiners, the growth and developmental issues that children have pre- and post-organ transplantation, and other issues specific to the special health and transplant needs of children [165].

The reach of the NOTA was expanded by the Organ Donation and Recovery Improvement Act of 2004 [166]. This law begins with stating the sense of Congress, which states that the government should carry out programs to educate the public on organ donation. Expanded reach provided organizations the authority to develop a grant program that reimburses travel and expenses for living organ donors [166].

The UAGA was revised again in 2006 and was meant to be adopted by all jurisdictions in the US, although not all have adopted the act [167] The updated act hoped to removed previous inconsistencies in the adoption of previous UAGA versions. This version of the act strengthens the legal bar preventing anyone from revoking the consent of a legally registered donor following their death. The revised version also simplifies the documentation of a gift

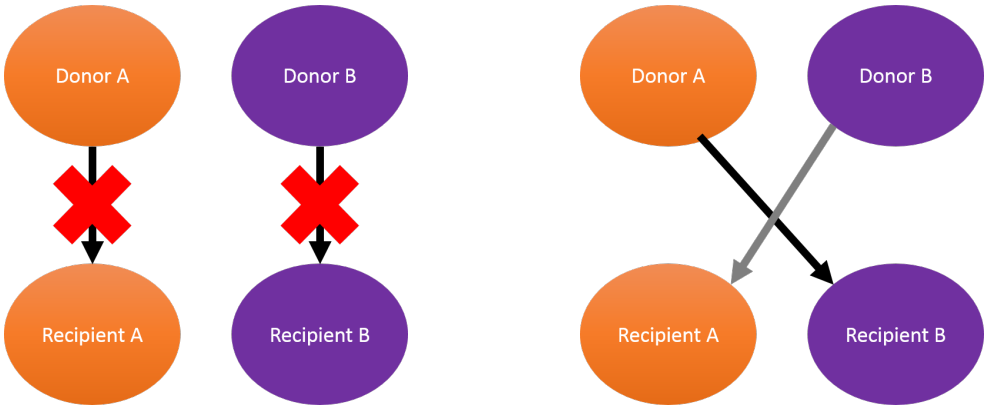

Figure A.1: Explanation of paired donation for kidney transplants. (a) Paired donation happens when a person in need of a transplant can find a donor, but that donor is not a compatible match. (b) To complete a paired kidney exchange, a match is made across donor / recipient pairs, which allows all involved to reach their desired outcome.

and accommodates the forms found on the back of driver's licenses. This law also covers how families should discuss their beliefs and wishes in regards to organ donation. A person can also sign a refusal that disallows others from making a gift of their parts following their death. This version of the UAGA has been adopted in every jurisdiction of the US except Florida, New York, Pennsylvania, and Puerto Rico [167].

In 2007, the 100th Congress passed Public Law 110-144, which amended the NOTA. This law defined the term "paired donation" [168]. Paired donation is described in Figure A.1 and takes place when there are two sets of patients and donors that are willing but biologically incompatible, demonstrated in Figure A.1a. The first donor is compatible with the second recipient and the first recipient is compatible with the second donor, and transplants are performed between the newly formed biologically compatible pairs [168], as seen in Figure A.1b. The law clarifies that this is not considered "valuable consideration" under Title III of the NOTA, and is a legal practice [4, 168].

The most recent law passed, Public Law 110-413, the Stephanie Tubbs Jones Gift of Life Medal Act of 2008 [169]. This law allows the entity operating the OPTN to award a

medal to individuals or family members of individuals that have made an organ donation. These medals are regulated to be designed to "commemorate the compassion and courage manifested by and the sacrifices made by organ donors and their families". The medals are declared to be "National Medals" and will be selected by the Secretary of the Treasury [169]. These medals are not to be treated as "valuable consideration", for the purposes of NOTA [4, 169].

When it comes to public policy considerations, there have been no new initiatives to increase donation since the mid-1990s. According to recent annual reports, there also has not been an increase in the rate of deceased donor transplants [11,66]. The report mentions it is clear that additional efforts are needed to expand the supply of donated organs and to use these organs more efficiently [11].

Every state also has independent laws regarding organ donation. These laws include policies on tax benefits, leave of absence, donor education, funding of donor programs, and state registries. These laws are further expanded on in Section 1.9.1, dealing with geographic disparities in organ donation.

Appendix B: The Kidney Allocation System

At the end of 2014 the kidney allocation system was updated to reduce existing disparities in the system, improve the matches between donor kidney longevity, and increase the expected post-transplant survival of the recipient [18]. Allocation of kidneys is determined by an Estimated Post Transplant Survival (EPTS) score, the waitlist time, and the classification of the deceased donor kidney, which is the Kidney Donor Profile Index (KDPI) score. Candidates waiting for a kidney are allocated points according to the Table B.1 and Table B.2. Candidates that are registered for a transplant receive 1/365 points for every day since the qualifying period for waiting time. Younger candidates with a 0-ABDR mismatch, also known as a zero-antigen mismatch, receive more points. A lower KDPI for patients ten or younger is also awarded higher points. Status as a prior living donor is worth four points in the system. Single and zero Human Leukocyte Antigen (HLA)-DR mismatches with the donor are awarded points and the scales for a sensitized Calculated Panel Reactive Antibody (CPRA) is also worth points, which are described in Table B.2 [19].

The waiting time in the new system is calculated according to different standards. For candidates that register as adults (18 years or older), the candidate's waiting time is based on the earliest of the following: registration date with a creatinine clearance or Glomerular Filtration Rate (GFR) less than or equal to 20mL/min, date following registration with a creatinine clearance or GFR less than or equal to 20mL/min, or the date the candidates began regularly administered dialysis as an End Stage Renal Disease (ESRD) patient. Restrictions are less strict for candidates that register before the age of 18. For these patients, waiting time begins the date the candidate is registered on the waiting list or the date that the candidate began regularly administered dialysis as an ESRD patient. If a candidate receives a kidney but must return to the waiting list, their waiting time is based only on the dates after the most recent transplant, unless the transplanted kidney is determined non-functioning [19].

Table B.1: Points allocated to patients on the waiting list for a kidney transplant. These points are used to rank candidates of equal standing in other areas across the waiting list. This information is from the Organ Procurement and Transplantation Network (OPTN) Policy [19].

Candidate Description	**Kidney Types**	**Points**
Registered for transplant and eligible to for waiting list	All	1/365 for every day since wait official waiting list start date
Present age is 0-10, and 0-ABDR mismatch with donor	KDPI <= 85%	4 points
Present age is 11-17, and 0-ABDR mismatch with donor	KDPI <= 85%	3 points
Present age is 0-10, and KDPI <35%	KDPI <35%	1 point
Prior living donor	KDPI <= 85%	4 points
Sensitized (CPRA 20%+)	KDPI <= 85%	Refer to Table B.2 Table
Single HLA-DR mismatch with donor	KDPI <= 85%	1 point
Zero HLA-DR mismatch with donor	KDPI <= 85%	2 points

Table B.2: Description of the points awarded to waiting list candidate based on the patient's CPRA. This information is from the OPTN Policy [19].

CPRA Score	**Points**	**CPRA Score**	**Points**	**CPRA Score**	**Points**
0-19	0.00	70-74	1.09	96	12.17
20-29	0.08	75-79	1.58	97	17.30
30-39	0.21	80-84	2.46	98	24.40
40-49	0.34	85-89	4.05	99	50.09
50-59	0.48	90-94	6.71	100	202.10
60-69	0.81	95	10.82		

Table B.3: Description of the variables used in Equation B.1 to compute the candidate's EPTS score. This information is derived from the OPTN Policy [19].

Variable	Value	Type	Description
α	MAX(Age-25, 0)	Integer	The maximum of the candidate's age less 25 years or 0
β	Diabetes	Binary	Binary indicator for diabetes, 1 = Diabetic, 0 = Not Diabetic
γ	Prior Transplant	Binary	Binary indicator for a prior transplant, 1 = Prior Transplant, 0 = No Prior Transplant
δ	Years on Dialysis + 1	Integer	Total number of years spend on dialysis + 1 year
Δ	0 Years on Dialysis	Binary	Binary indicator for <1 year on Dialysis, 1 = Less than 1 year on Dialysis, 0 = At least 1 year on dialysis

Adult candidates on the waiting list receive an EPTS score, this represents the percentage of kidney candidates in the United States with a longer expected post-transplant survival time. For this metric, a lower EPTS score is generally better for the candidate. Many of the allocation policies favor recipients with a lower EPTS score. This score is based on the candidate's time on dialysis, diagnosis of diabetes, prior transplant history, and age. These scores are calculated when the candidate registers on the waiting list and the OPTN updates the EPTS score once each day and when the transplant hospital reports changes to any of the necessary factors of a candidate [19].

The EPTS score is calculated using Equation B.1:

$$EPTS = 0.047\alpha + 0.398\gamma + 0.315\log(\delta) + 0.130\Delta$$
$$- \beta(0.015\alpha + 0.237\gamma + 0.099\log(\delta) + 0.0348\Delta - 1.262) \quad \text{(B.1)}$$

Table B.4: Description of the factors and variables used to compute a donor kidney's KDRI and KDPI scored. This information is derived from the OPTN Policy [19].

Factor	**Variable**	**Applies to:**	**Score Component**
Age	α	All donors	0.0128(age - 40)
		Donors under 18	-0.0194(age-18)
		Donors over 50	0.0107(age - 50)
Race	β	African-American	0.1790
Creatinine (mg/dL)	γ	All donors	0.2200(creatinine - 1)
		Donors with creatinine >1.5	-0.2090(creatinine - 1.5)
Hypertension	ε	Hypertensive donors	0.1260
Diabetes	ζ	Diabetic donors	0.1300
Cause of Death (COD)	η	Donors with cerebrovascular accident as COD	0.0881
Height (cm)	θ	All donors	-0.0464(height - 170)/10
Weight (kg)	ι	Donor weight <80 kg	-0.0199(weight - 80)/5
Donor Type	κ	Donor after Cardiac Death	0.1330
HCV Status	λ	HCV positive donors	0.2400

The variables for Equation B.1 are explained in Table B.3.

The kidneys obtained from deceased donors are classified according to the KDPI, which is derived from the Kidney Donor Risk Index (KDRI) score. The KDPI score is defined as the percentage of donors in the reference population with a KDRI less than or equal to the donor's KDRI. The KDRI score is based on the donor's age, ethnicity, creatinine, history of hypertension, history of diabetes, cause of death, height, weight, donor type, and Hepatitis C Virus (HCV) status. Table B.4 describes the KDRI score components [19].

The KDRI score is the sum of all of the factor score components, as seen in Equation B.2.

$$KDRI = e^{\alpha+\beta+\gamma+\varepsilon+\zeta+\eta+\theta+\iota+\kappa+\lambda} \tag{B.2}$$

Then the candidate's KDPI is calculated by dividing the KDRI of the median KDRI

Table B.5: Permissible and preferred blood type allocations from deceased donors to transplant recipients. This information is derived from the OPTN Policy [19].

Donor Blood Type	Recipient Blood Type
O	O
A	A or AB
B	B
AB	AB

value of the most recent donor reference population and then using the contractor's KDRI-to-KDPI mapping table. This reference population to determine the mapping is reviewed annually and updated by United Network for Organ Sharing (UNOS) [19].

Patients that are on the waiting list for a kidney must give a transplant program written consent if they're willing to accept a kidney with a KDPI score greater than 85%. Within each classification, candidates are first sorted by total points, then by the date and time of their registration, with older registrations ranking higher. Blood type of the donor and recipient also plays a role in the allocation process. Organs are allocated to the blood type matches seen in Table B.5. Other exceptions also apply, kidneys with blood type O and B may be transplanted to candidates with other blood types if the candidates are in zero mismatch categories. Patients with blood type A and AB (but not A1 or A1B) may be transplanted to candidates with blood type B that meet certain criteria [19].

The OPTN Allocation Policy does have a section which details the rules for exceptions [19]. This section of the policy allows for exceptions due to medical urgency, which allows a candidate's transplant physician to use medical judgment to transplant a candidate out of sequence if they determine the situation requires medical urgency. For this to occur, the candidate's physician must obtain agreement from the other kidney transplant programs in the Donor Service Area (DSA). There is also an exception for deceased donor kidneys with discrepant HLA typings. Allocations are based on the HLA typings identified by the donor histocompaibility laboratory. The recipient HLA laboratory may identify a different

HLA type for the deceased donor, in this case the kidney may be allocated according to the original typing or the recipient transplant hospital may try to reallocate the kidney locally.

Appendix C: The Deceased Donor Process

The process to become a deceased organ donor begins when an individual suffers and injury or life-threatening medical episode that requires treatment and care [10]. This process is depicted in Figure C.1. In this process, efforts at every step are to save the patient's life, organ donation is only considered once the patient has been declared deceased.

Life saving efforts begin at the scene of the incident and the team of specialized Emergency Medical Technician (EMT)s and paramedics begin transporting the patient to an emergency room to receive further care. Once the patient arrives at the facility, doctors and nurses evaluate the patient's condition and continue to provide life-saving measures. Once a patient has stabilized, they are transferred to the Intensive Care Unit (ICU), where a doctor performs tests to see the extent of damage to the patient's brain and organs. Even at this point in time, measures are still being taken to save the patient's life [10].

If the doctor determines that there has been an irreversible loss of blood flow to the entire brain, which caused the brain to die. This is classified as brain death. After the declaration of brain death, the donor's body is kept alive using artificial means. The hospital contacts the OPO to send out specially-trained medical practitioners to the hospital. These specialists determine if the patient is medically suitable to become an organ donor [10].

The doctor informs the family of the patient's death, followed by the OPO representative or a specially trained member of the hospital staff talking to the family about donation. If the patient is registered in the state registry, this information is given to the family and the counselor explains the donation process to the family and answers any questions. In the case that the patient was not a registered donor, the family can decide if they are willing to donate the patient's organs [10].

If consent is given for donation, either from the registry or the donor's next of kin, the donor's blood type, height, weight, hospital zip code, and other supplemental data are entered into UNOS's national computer system to begin the allocation and matching

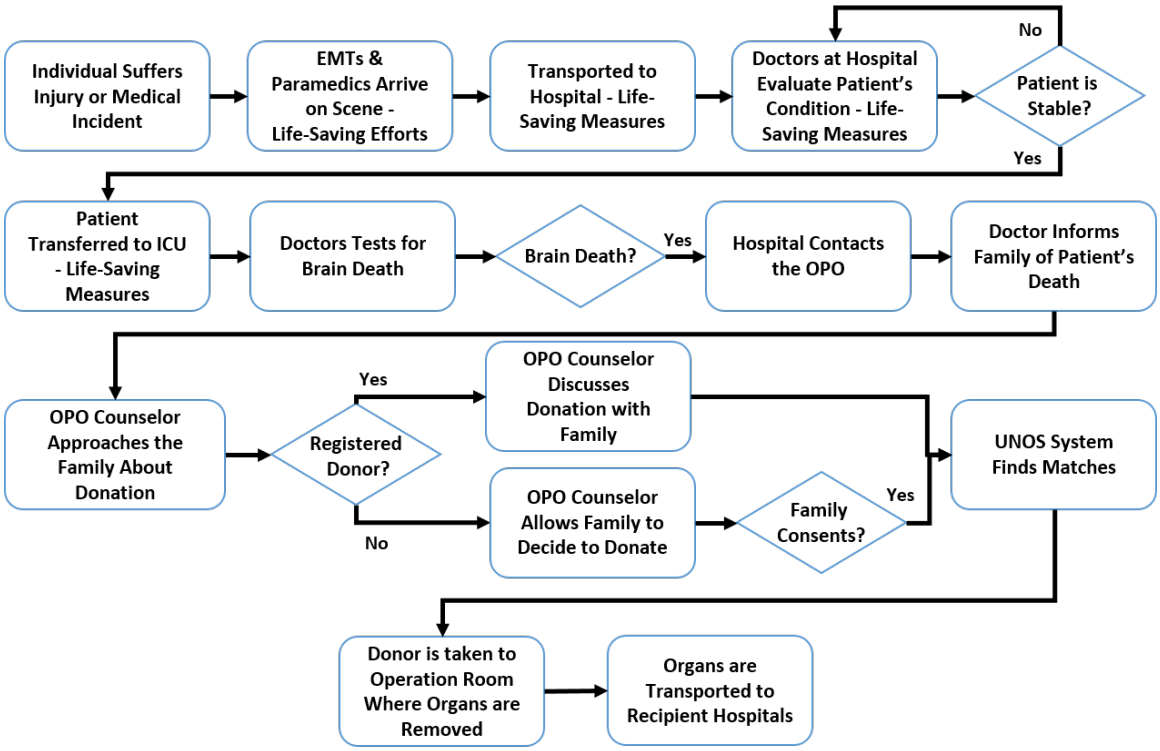

Figure C.1: Overview of the the process defined by United Network for Organ Sharing (UNOS) for Deceased Donation [10]. At decision points where there is not an option for "no" pictured, this marks the end of the process for the patient and they do not become an organ donor.

process. This system finds the optimal candidates that match the donor's organs based on matching algorithms. Then the donor is moved into an operating room where the organs are surgically removed. The organs are then sent to the transplant hospitals of the selected recipients for the transplant procedure. The donor is then taken to a funeral home and the OPO works with the home to facilitate the donor and their family's wishes [10].

Following the funeral, the OPO sends a letter to the donor's family, notifying them which organs were transplanted, while keeping the names of the recipient's confidential. Donor families and recipients may correspond with each other following the OPO and transplant program's guidelines [10].

The standards and qualifications vary for deceased donor kidneys used in organ transplants. The two basic types of donor are Standard Criteria Donor (SCD) and Expanded

Criteria Donor (ECD) [68, 170]. ECDs are donors that are either 60 years of age or older or over 50 with other health problems. ECD kidneys have a higher probability of failure compared to SCD kidneys. A second classification of donor organs is used to describe the method of death for the donor. Donor after Brain Death (DBD) describes a donor with brain death and had maintained cardiac and repository function. A DBD donor can be an ECD or SCD. Donation can also occur after cardiac death, Donor after Circulatory Death (DCD), which is when an individual does not meet the necessary criteria for brain death, but had cardiac standstill or lost cardiac function before donation.

The clinical outcomes vary for these different types of donor kidneys. SCD kidneys have a 65% 5-year graft survival compared to 49% for ECD kidneys [68]. The 5-year patient survival rate is 82% for SCD donors and 70% for ECD donor kidneys. The difference between DBD and DCD kidneys is much smaller, there's no difference at the 5-year graft survival and the 5-year patient survival rate is 82% for DBD donors and 81% for DCD donors.

From 1998 to 2008, the number of SCD, ECD, and DCD donors expanded; the greatest numerical increment has been with SCD donors [77]. The percentage of SCD kidneys allocated to candidates over the age of 50 has declined, these candidates continue to receive SCD kidneys at higher rates than their proportion on the waiting list [77]. Most of the growth in performed deceased donor transplants since 2002 is driven by an increase in conversion rates, which is the number of people meeting eligibility criteria per eligible deaths [77].

Appendix D: State Laws

In order to compare laws and policies, extensive research was completed on the legal mandates regarding organ donation and education. The majority of this data came from the different reports and online repositories of laws [75, 80–83]. Table D.1 shows the state laws and policies and the years of implementation used in our modeling. This only includes the 50 US states, the District of Columbia, and Puerto Rico as these are the main areas included in the available literature, other territories are managed by the US transplant system but the legal information is not readily available and these patients make up a small portion of the waiting list and donation populations [75, 80–83].

Table D.1: State laws and policy implementations.

State	Tax Benefit	Donor Education	Private Leave	Public Leave
AK				2008
AL		2017		2017
AR	2005	2003	2005	2003
AZ		2013		2010
CA			2011	2002
CO				1998
CT			2004	2006
DC			2007	2002
DE				2001
FL				
GA	2004			2002
HI				2005
IA	2005	2001		2003

Continued on next page

Table D.1 – continued from previous page

State	Tax Benefit	Donor Education	Private Leave	Public Leave
ID	2006			2006
IL		1998	2005	2002
IN		1993		2002
KS	2016			2001
KY				
LA	2005	2006	2007	2007
MA	2012	2012		2005
MD	2018			2000
ME		2003	2002	2002
MI		2010		
MN	2005	2002		2006
MO				2001
MS	2006	2014	2004	2004
MT				
NC				
ND	2005			2005
NE				
NH				
NJ		2008		
NM	2005	2006		2007
NV		2017		
NY	2006			2001
OH	2007	2017		2001
OK	2008	2000		2002
OR				

Continued on next page

Table D.1 – continued from previous page

State	Tax Benefit	Donor Education	Private Leave	Public Leave
PA			2006	2006
PR				
RI	2004			
SC		2016	2006	2002
SD				
TN		2007		
TX		2003		2003
UT	2005			2002
VA	2007	2002		2001
VT				
WA		2006		2002
WI	2004	2001		2000
WV				2005
WY				

The OrganDonor.gov website provides a detailed view of the various laws and policies in place to facilitate organ and tissue donation in the 50 states, Washington DC, and Puerto Rico. Of the reviewed areas, 36 fund their organ donation support and education programs with voluntary contributions. Only 11 states directly provide funds to their programs, including Arizona, Connecticut, Illinois, Indiana, Louisiana, Massachusetts, Mississippi, New York, North Carolina, Rhode Island, and Puerto Rico. Every state has a program for legal consent including donor designation registries and donor designation on a driver's license [75]. Every area except Connecticut, Illinois, Missouri,Oregon, Pennsylvania, Tennessee, Texas, and Puerto Rico has passed a law facilitating donation by individuals in the

custody of a medical examiner or coroner [75].

In regards to donor education, few states have formal programs in place to inform citizens about organ donation. Arizona, Arkansas, Illinois, Indiana, Louisiana, Mississippi, New Jersey, Ohio, Oklahoma, and Tennessee are the only states with a donor education in school specified in the law [75]. While New Jersey and Mississippi laws require that organ donation be taught in schools [171,172], the Arizona policy simply allows organ donation to be taught in schools [173]. The Ohio law stipulates that a program be compiled on organ donation and transplantation to be taught in schools [174]. Tennessee law encourages educational opportunities to teach students about organ and tissue donation and transplantation [175]. Oklahoma implemented the Cheryl Selman Organ Donor Education and awareness Act which requires an education and awareness curricula in schools [176].

Other areas have passed laws that refer to a donor education program in a driver education program. These states include Alabama, Arkansas, Indiana, Iowa, Louisiana, Maine, Massachusetts, Michigan, Minnesota, Mississippi, New Mexico, Ohio, Rhode Island, Virginia, Washington, and Wisconsin [75]. The Ohio law on dissemination information regarding anatomical gifts declares that the driver's education classroom shall include the sharing of information regarding anatomical gifts and anatomical gift procedures, or include a presentation and discussion of these areas. The law specifies that they will not approve any material that contains religious content for use in a driver education course run by a school district or educational service center. The law also gives very specific guidelines on the length and quality of the presentation [177]. The Alabama Code of 1975 stipulates that the Alabama Procurement Organization must provide a brochure explaining the methods of expressing intent to make an anatomical gift to every applicant or licensee when they apply for a new driver's license or identification card [178].

In Iowa, an approved driver's education course must provide instruction on becoming an organ donor under the Uniform Anatomical Gift Act (UAGA). In Maine and Washington, the law requires the Secretary of State to distribute information on organ and tissue donation in driver education programs [179]. The state of Michigan gives specific guidelines

for instruction of the right to become an organ donor. The instructional materials must be developed in cooperation with the state Organ Procurement Organization (OPO) and include information on how to register as a donor [180]. The Minnesota and Wisconsin laws on driver education content begins with the requirement that education programs provide a minimum of 30 minutes of instruction relating to organ and tissue donation [181, 182]. In Mississippi the donor education program is part of the school's curriculum [172]. Virginia law requires that organ and tissue donor awareness be taught as a part of the driver education programs [183]. The law in Rhode Island declares that all driver's education programs must include information on the Anatomical Gift Act and provide information on donor cards [184].

Most states have public leave of absence programs, which provide leave for state employees. Fewer states have laws in place that require private companies (often of a certain size) to allow employees to take leave to become a living organ donor. Unpaid leave is provided in Arkansas, Connecticut, and Maine. Paid leave is provided in California, Illinois, and Minnesota [39].

Appendix E: Random Forest Features

E.1 OPTN Variables

Organ Procurement and Transplantation Network (OPTN) features included in the Random Forest model [12], descriptions have been taken directly from the OPTN STAR file documentation:

- A1: Candidate A1 Antigen from Waiting List
- A2: Candidate A2 Antigen from Waiting List
- ABO: Recipient Blood Group @ Registration
- ACADEMIC_LEVEL_TCR: Academic Activity Level at Listing
- ACADEMIC_PRG_TCR: Academic Progress at Listing
- ACYCLOVIR: Biological or Anti-Viral Treatment - Acyclovir
- AGE_DIAB: Recipient Age of Diabetes Onset @ Registration-KI
- AMIS: A Locus Mismatch Level
- ANGINA: Recipient ANGINA/CAD @ Registration
- B1: Candidate B1 Antigen from Waiting List
- B2: Candidate B2 Antigen from Waiting List
- BMIS: B Locus Mismatch Level
- BMI_TCR: BMI at Listing
- CITIZENSHIP: Recipient Citizenship @ Registration
- CREAT_CLEAR: Candidate Measured Creatinine Clearance (ML/MIN)
- CURRENT_PRA: Candidate Most Recent "Current" PRA from Waiting List/Allocation
- CYTOGAM: Biological or Anti-Viral Treatment - Cytogamn

- DAYSWAIT_CHRON_KI: Total Days on Kidney Waiting List
- DGN_TCR: Primary Diagnosis at time of Listing
- DIAB: Recipient Diabetes @ Registration
- DONATION: WL Will Receive Donation Points due to a Previous Living Organ Donation
- DR1: Candidate DR1 Antigen from Waiting List
- DR2: Candidate DR2 Antigen from Waiting List
- DRMIS: DR Locus Mismatch Level
- DRUGTRT_COPD: Recipient Drug Treated COPD @ Registration
- ECMO: Recipient Life Support Type ECMO @ Registration
- EDUCATION: Recipient Highest Educational Level @ Registration
- END_CPRA: Candidate Most Recent Calculated PRA
- ETHCAT: Recipient Ethnicity Category
- ETHNICITY: Recipient Ethnicity
- EXH_PERIT_ACCESS: Recipient Exhausted Vascular Access @ Registration
- EXH_VASC_ACCESS: Recipient Exhausted Peritoneal Access @ Registration
- FLUVACCINE: Biological or Anti-Viral Treatment - Fluvaccine
- FUNC_STAT_TCR: Recipient Functional STATUS @ Registration
- GAMIMUNE: Biological or Anti-Viral Treatment - Gamimune
- GAMMAGARD: Biological or Anti-Viral Treatment - Gammagard
- GANCICLOVIR: Biological or Anti-Viral Treatment - Ganciclovir
- GENDER: Recipient Gender
- GFR: Candidate GFR Score
- HBIG: Biological or Anti-Viral Treatment - HBIG

- HBV_CORE: Recipient Hepatitis B-CORE Antibody
- HBV_SUR_Antigen: Recipient HEP B Surface Antigen
- HGT_CM_CALC: Calculated Recipient Height(cm)
- HGT_CM_TCR: Recipient Height @ Registration
- IABP: Recipient Life Support Type IABP @ Registration
- INFECT_PA: Recipient Graft Failure Contributory Cause: INFECTION-PA
- INIT_AGE: Candidate Age in Years at Time of Listing
- INIT_CPRA: Candidate Calculated PRA at Listing
- INIT_CURRENT_PRA: Candidate First Current PRA
- INIT_EPTS: Initial Calculated EPTS (since 5/27/2014)
- INIT_HGT_CM: Candidate Height in CM at Listing
- INIT_PEAK_PRA: Recipient PEAK PRA at Listing
- INIT_STAT: Initial Waiting List Status Code
- INIT_WGT_KG: Candidate Weight in KG at Listing
- INOTROPES: Recipient Life Support TYPE IV INOTORPES @ Registration
- LAMIVUDINE: Biological or Anti-Viral Treatment - Lamivudine
- MAX_KDPI_IMPORT_NON_ZERO_ABDR: WL Maximum Acceptable KDPI for Import non-0 ABDR Mismatch (since 5/27/2014)
- MAX_KDPI_IMPORT_ZERO_ABDR: WL Maximum Acceptable KDPI for Import 0 ABDR Mismatch (since 5/27/2014)
- MAX_KDPI_LOCAL_NON_ZERO_ABDR: WL Maximum Acceptable KDPI for Local non-0 ABDR Mismatch (since 5/27/2014)
- MAX_KDPI_LOCAL_ZERO_ABDR: WL Maximum Acceptable KDPI for Local 0 ABDR Mismatch (since 5/27/2014)

- MULTIORG: Multi-Organ Transplant
- NPKID: Number Previous TXs -KIDNEY
- ON_DIALYSIS: WL Candidate Has Had Regularly Administered Dialysis for ESRD (Y/N)
- ON_EXPAND_DONOR: Accept Local EXPANDED DONOR KIDNEY?
- ON_IEXPAND_DONOR: Accept Imported Expanded Donor Kidney?
- ORGAN: Organ Type Transplanted
- OTH_LIFE_SUP: Recipient Life Support Type OTHER @ Registration
- OTH_LIFE_SUP_OSTXT: Recipient Life Support Type OTHER SPECIFIED @ Registration
- PAYBACK: Transplant as a Result of a Payback?
- PEAK_PRA: Candidate Most Recent "PEAK" PRA from Waiting List/ALLOCATION
- PERIP_VASC: Recipient Peripheral Vascular Disease @ Registration
- PERM_STATE: Recipient State of Residency @ Registration
- PERM_ZIP: Recipient Zip Code of Residency @ Registration
- PGE: Recipient Life Support Type PGE @ Registration
- PK_DA1: Previous Kidney-Donor A1 Antigen
- PK_DA2: Previous Kidney-Donor A2 Antigen
- PK_DB1: Previous Kidney-Donor B1 Antigen
- PK_DB2: Previous Kidney-Donor B2 Antigen
- PK_DDR1: Previous Kidney-Donor DR1 Antigen
- PK_DDR2: Previous Kidney-Donor DR2 Antigen
- PREV_KI_TX: If KI or KP Transplant, is there a history of KI or KP Transplant
- PREV_PREG: Recipient number of previous pregnancies-KI @ Transplant

- PREV_TX: History of a Previous Transplant Involving Exace Same Organ as Current TX
- PRI_PAYMENT_CTRY_TCR_KI: Recipient-Foreign Government as Projected Payment Source-KI @ Registration
- PRI_PAYMENT_CTRY_TCR_PA: Recipient-Foreign Government as Projected Payment Source-PA @ Registration
- PRI_PAYMENT_TCR_KI: Recipient-Primary Projected Payment Source-KI @ Registration
- PRI_PAYMENT_TCR_PA: Recipient-Primary Projected Payment Source-PA @ Registration
- RA1: Recipient A1 Antigen
- RA2: Recipient A2 Antigen
- RB1: Recipient B1 Antigen
- RB2: Recipient B2 Antigen
- RDR1: Recipient DR1 Antigen
- RDR2: Recipient DR2 Antigen
- REM_CD: Reason for Removal from the Waiting List
- SECONDARY_PAY_TCR_KI: Recipient Secondary Projected Pay Source at Listing
- TOT_SERUM_ALBUM: Recipient Total Serum Albumin @ Registration
- VAD_TAH: Recipient Life Support Type VAD Brand @ Registration
- VALGANCYCLOVIR: Biological or Anti-Viral Treatment - Valganciclovir
- VENTILATOR: Recipient Life Support TYPE Ventilator @ Registration
- WGT_KG_CALC: Calculated Recipient Weight (kg)
- WGT_KG_TCR: Recipient Weight (kg) @ Registration
- WL_ORG: Organ Listed For

- WORK_INCOME_TCR: Work for Income at Registration?

The state policies features included in the Random Forest model are based on the literature and policy review performed:

- DonorEd: Binary variable indicating the presence of a donor education policy in the state during the year the patient was added to the WL
- DonorEducation_Year: Year the law was passed in the recipient's home state.
- LOA_Public: Binary variable indicating the presence of a public leave of absence policy in the state during the year the patient was added to the WL
- LOA_Public_Year: Year the law was passed in the recipient's home state.
- LOA_Private: Binary variable indicating the presence of a private leave of absence policy in the state during the year the patient was added to the WL
- LOA_Private_Year: Year the law was passed in the recipient's home state.
- TaxBreak: Binary variable indicating the presence of a public leave of absence policy in the state during the year the patient was added to the WL
- Tax_Year: Year the law was passed in the recipient's home state.

The fair market rent features included in the Random Forest model [95] and is based on FIPS region, this is mapped to the patient's zip code:

- ent50_2: 50th percentile of rent in a FIPS area for a two bedroom unit

Variables from the CDC's Social Vulnerability Index features included in the Random Forest model [96] by Census Tract, which was mapped to the patient's zip code:

- TOTPOP: Total population, 2010
- HH: Number of households, 2010
- E_P_POV: Proportion of persons below poverty estimate based on persons below poverty estimate, 2006-2010 ACS

- E_P_UNEMP: Proportion of civilian (age 16+) unemployed estimate based on civilian (age 16+) unemployed estimate, 2006-2010 ACS
- E_PCI: Per capita income estimate, 2006-2010 ACS
- E_P_NOHSDIP: Proportion of persons with no high school diploma (age 25+) estimate based on persons (age 25+) with no high school diploma estimate, 2006-2010 ACS

The data also includes flags marking portions of the population:

- F_PL_POV: Flag - for poverty, the proportion is in the 90th percentile (1=yes, 0=no)
- F_PL_UNEMP: Flag - for civilian unemployed, the proportion is in the 90th percentile (1=yes, 0=no)
- F_PL_PCI: Flag - for per capita income, the proportion is in the 90th percentile (1=yes, 0=no)
- F_PL_NOHSDIP: Flag - for no high school diploma, the proportion is in the 90th percentile (1=yes, 0=no)
- F_PL_AGE65: Flag - the proportion of persons aged 65 and older is in the 90th percentile (1=yes, 0=no)
- F_PL_AGE17: Flag - the proportion of persons aged 17 and younger is in the 90th percentile (1=yes, 0=no)
- F_PL_SNGPRNT: Flag - the proportion of single parent households is in the 90th percentile (1=yes, 0=no)
- F_PL_MINORITY: Flag - the proportion of minority is in the 90th percentile (1=yes, 0=no)
- F_PL_LIMENG: Flag - for limited English, the proportion is in the 90th percentile (1=yes, 0=no)
- F_PL_MUNIT: Flag - for multi-unit housing, the proportion is in the 90th percentile (1=yes, 0=no)

- F_PL_MOBILE: Flag - for mobile homes, the proportion is in the 90th percentile (1=yes, 0=no)
- F_PL_CROWD: Flag - for crowded housing, the proportion is in the 90th percentile (1=yes, 0=no)
- F_PL_NOVEH: Flag - for no vehicle access, the proportion is in the 90th percentile (1=yes, 0=no)
- F_PL_GROUPQ: Flag - the proportion of persons in institutionalized group quarters is in the 90th percentile (1 = yes, 0=no).

Appendix F: Data Acknowledgement Statements

F.1 OPTN Data

This work was supported in part by Health Resources and Services Administration contract 234- 2005-37011C. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

F.2 USRDS Data

The data reported here have been supplied by the United States Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the U.S. government.

Bibliography

Bibliography

[1] Organ Procurement and Transplantation Network, "OPTN Website," [Online]. Available: http://optn.transplant.hrsa.gov/, 2015. [Online]. Available: http://optn.transplant.hrsa.gov/

[2] ——, "Standard Transplant Analysis and Research (STAR) Dataset Files." [Online]. Available: https://optn.transplant.hrsa.gov/data/request-data/{#}

[3] C. E. Harvey and R. S. Weigel, "Transplant2Mongo: Python scripts that insert Organ Procurement and Transplantation Network (OPTN) data in MongoDB," *Journal of Open Research Software*, vol. 7, no. 1, p. 5, 2019. [Online]. Available: http://doi.org/10.5334/jors.229

[4] U.S. House. 98th Congress, "Public Law No. 98-507, National Organ Transplant Act," [Online]. Available: http://history.nih.gov/research/downloads/PL98-507.pdf, Oct. 1984. [Online]. Available: http://history.nih.gov/research/downloads/PL98-507.pdf

[5] United Network for Organ Sharing, "UNOS," [Online]. Available: https://www.unos.org/about/. [Online]. Available: https://www.unos.org/about/

[6] S. Leppke, T. Leighton, D. Zaun, S. C. Chen, M. Skeans, A. K. Israni, J. J. Snyder, and B. L. Kasiske, "Scientific Registry of Transplant Recipients: Collecting, analyzing, and reporting data on transplantation in the United States," *Transplantation Reviews*, vol. 27, no. 2, pp. 50–56, 2013. [Online]. Available: http://dx.doi.org/10.1016/j.trre.2013.01.002

[7] Chronic Disease Research Group of the Hennepin Healthcare Research Institute, "The SRTR/OPTN Annual Data Report," 2019. [Online]. Available: https://www.srtr.org/reports-tools/srtroptn-annual-data-report/

[8] Donate Life America, "Organ Donation," May 2015. [Online]. Available: http://donatelife.net/organ-donation/

[9] ——, "National Donor Designation Report Card," Richmond, VA, 2014. [Online]. Available: https://www.donatelife.net/wp-content/uploads/2016/06/Report-Card-2014-44222-Final.pdf

[10] The United Network for Organ Sharing, "Deceased Donation," 2015. [Online]. Available: https://www.unos.org/donation/basic-path-to-donation/

[11] U.S. Department of Health & Human Services, "OPTN/SRTR 2012 Annual Data Report." U.S. Department of Health and Human Services, Jun. 2014. [Online]. Available: http://srtr.transplant.hrsa.gov/ADR.aspx

[12] Organ Procurement and Transplantation Network, "OPTN Data Reports," Richmond, VA, 2014. [Online]. Available: https://optn.transplant.hrsa.gov/data/view-data-reports/

[13] United Network for Organ Sharing, "OPTN Deceased Donor Potential Study (DDPS)," 2013. [Online]. Available: http://optn.transplant.hrsa.gov/media/1161/ddps{_}03-2015.pdf

[14] A. J. Matas, J. M. Smith, M. A. Skeans, B. Thompson, S. K. Gustafson, D. E. Stewart, W. S. Cherikh, J. L. Wainright, G. Boyle, J. J. Snyder, K. Israni, and B. L. Kasiske, "OPTN/SRTR 2013 Annual Data Report: Kidney," 2015. [Online]. Available: http://onlinelibrary.wiley.com/doi/10.1111/ajt.v15.s2/issuetoc

[15] Organ Procurement and Transplantation Network, "OPTN Policies," 2018. [Online]. Available: https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf

[16] D. LaPointe Rudow, R. Hays, P. Baliga, D. J. Cohen, M. Cooper, G. M. Danovitch, M. A. Dew, E. J. Gordon, D. A. Mandelbrot, S. McGuire, J. Milton, D. R. Moore, M. Morgievich, J. D. Schold, D. L. Segev, D. Serur, R. W. Steiner, J. C. Tan, A. D. Waterman, E. Y. Zavala, and J. R. Rodrigue, "Consensus conference on best practices in live kidney donation: recommendations to optimize education, access, and care," *American Journal of Transplantation*, vol. 15, no. 4, pp. 914–922, 2015. [Online]. Available: http://doi.wiley.com/10.1111/ajt.13173

[17] American Kidney Fund, "End Stage Renal Disease (ESRD)," 2013. [Online]. Available: http://www.kidneyfund.org/kidney-health/kidney-failure/end-stage-renal-disease.html

[18] J. J. Friedewald, C. J. Samana, B. L. Kasiske, A. K. Israni, D. Stewart, W. Cherikh, and R. N. Formica, "The kidney allocation system," *Surgical Clinics of North America*, vol. 93, no. 6, pp. 1395–1406, 2013. [Online]. Available: https://doi.org/10.1016/j.suc.2013.08.007

[19] Organ Procurement and Transplantation Network, "OPTN Policies," Aug. 2015. [Online]. Available: http://optn.transplant.hrsa.gov/governance/policies/

[20] The United Network for Organ Sharing, "The National Waiting LIst," Dec. 2011. [Online]. Available: http://www.transplantliving.org/before-the-transplant/getting-on-the-list/the-national-waiting-list/

[21] UnosNews, "How the national organ transplant waiting list works," 2015. [Online]. Available: https://www.youtube.com/watch?v=tQtEbH40yYU{&}feature=youtu.be{&}a

[22] Organ Procurement and Transplantation Network, "General Considerations in Assessment for Transplant Candidacy." [Online]. Available: http://optn.transplant.hrsa.gov/resources/ethics/general-considerations-in-assessment-for-transplant-candidacy/

[23] A. Etzioni, "Organ donation: a communitarian approach." *Kennedy Institute of Ethics Journal*, vol. 13, no. 1, pp. 1–18, 2003. [Online]. Available: https://dl.acm.org/citation.cfm?id=3015587

[24] S. Strumwasser, "The tragedy of American organ donations: So many more people could be saved," Mar. 2014. [Online]. Available: https://www.salon.com/2014/03/23/the_tragedy_of_american_organ_donations_so_many_more_people_could_be_saved/

[25] N. G. Kutner, K. L. Johansen, R. Zhang, Y. Huang, and S. Amaral, "Perspectives on the new kidney disease education benefit: Early awareness, race and kidney transplant access in a USRDS study," *American Journal of Transplantation*, vol. 12, no. 4, pp. 1017–1023, 2012. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/22226386

[26] L. Siminoff, N. Gordon, J. Hewlett, and R. Arnold, "Factors influencing families' consent for donation of solid organs for transplantation." *Journal of the American Medical Association*, vol. 286, no. 1, pp. 71–77, 2001. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/11434829

[27] M. A. Schnitzler, M. A. Skeans, D. A. Axelrod, K. L. Lentine, J. J. Snyder, A. K. Israni, and B. L. Kasiske, "OPTN/SRTR 2013 Annual Data Report: Economics," 2013, pp. 1–24. [Online]. Available: http://onlinelibrary.wiley.com/doi/10.1111/ajt.13201/epdf

[28] D. A. Axelrod, M. A. Schnitzler, H. Xiao, W. Irish, E. Tuttle-Newhall, S.-H. Chang, B. L. Kasiske, T. Alhamad, and K. L. Lentine, "An economic assessment of contemporary kidney transplant practice," *American Journal of Transplantation*, vol. 18, no. 5, pp. 1168–1176, 2018. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1111/ajt.14702

[29] A. E. Roth, T. Soenmez, and M. U. Uenver, "Efficient kidney exchange: coincidence of wants in markets with compatibility-based preferences," *The American Economist Review*, vol. 97, no. 3, pp. 828–851, 2007. [Online]. Available: https://www.aeaweb.org/articles?id=10.1257/aer.97.3.828

[30] S. Dickert-Conlin, T. E. Elder, and K. Teltser, "Allocating scarce organs: How a change in supply affects transplant waiting lists," *American Economic Journal: Applied Economics*, vol. 11, no. 4, pp. 210–39, 2017. [Online]. Available: https://doi.org/10.2139/ssrn.3048882

[31] A. J. Matas, "A gift of life deserves compensation: How to increase living kidney donation with realistic incentives," *Policy Analysis*, no. 604, 2007. [Online]. Available: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=1030369

[32] The United Network for Organ Sharing, "Living Donation: Information you need to know," Richmond, VA, 2015. [Online]. Available: https://www.unos.org/wp-content/uploads/unos/Living_Donation.pdf

[33] L. E. Boulware, M. U. Troll, N. Y. Wang, and N. R. Powe, "Public attitudes toward incentives for organ donation: A national study of different racial/ethnic and income

groups," *American Journal of Transplantation*, vol. 6, no. 11, pp. 2774–2785, 2006. [Online]. Available: https://doi.org/10.1111/j.1600-6143.2006.01532.x

[34] F. L. Delmonico, "An open letter to HHS Secretary Burwell on ethically increasing organ donation," *Transplantation Direct*, vol. 1, no. 1, 2015. [Online]. Available: https://doi.org/10.1097/TXD.0000000000000509

[35] R. Arnold, S. Bartlett, J. Bernat, J. Colonna, D. Dafor, N. Dubler, S. Gruber, J. Kahn, R. Luskin, H. Nathan, S. Orloff, J. Prottas, R. Shapiro, C. Ricordi, S. Younger, and F. L. Delmonico, "Financial incentives for cadaver organ donation: an ethical reappraisal," *Transplantation*, vol. 73, no. 8, pp. 1361–1367, 2002. [Online]. Available: http://asts.org/docs/default-source/education/financial-incentives-for-deceased-organ-donation.pdf?sfvrsn=0

[36] S. Klarenbach, A. X. Garg, and S. Vlaicu, "Living organ donors face financial barriers: A national reimbursement policy is needed," *CMAJ*, vol. 174, no. 6, pp. 797–798, 2006. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1402383/

[37] F. L. Delmonico, R. Arnold, N. Scheper-Hughes, L. a. Siminoff, J. Kahn, and S. J. Youngner, "Ethical incentives - not payment - for organ donation," *The New England Journal of Medicine*, vol. 346, no. 25, pp. 2002–2005, 2002. [Online]. Available: https://www.nejm.org/doi/full/10.1056/NEJMsb013216

[38] US House. 111th Congress, "Bill H.R. 218, Living Organ Donor Tax Cerdit Act of 2009," pp. 1–4, Jan. 2009. [Online]. Available: https://www.congress.gov/bill/111th-congress/house-bill/218

[39] The National Kidney Foundation, "Donor Leave Laws and Tax Deductions / Credits for Living Donors," Jun. 2015. [Online]. Available: http://www.kidney.org/sites/default/files/LDTaxDed{_}Leave.pdf

[40] State Treasurer, "Idaho Individual Income Tax," no. 208, 2010. [Online]. Available: https://tax.idaho.gov/forms/EIN00046_10-12-2010.pdf

[41] American Transplant Foundation, "Tax Incentives and Organ Donation," Nov. 2012. [Online]. Available: http://www.americantransplantfoundation.org/2012/11/15/tax-incentives-and-organ-donation/

[42] U.S. Senate. 106th Congress, "Public Law No. 106-174, Organ Donor Leave Act," Jun. 1999. [Online]. Available: https://www.govinfo.gov/app/details/PLAW-106publ56

[43] B. L. Kasiske, W. London, and M. Ellison, "Race and socioeconomic on the kidney transplant factors waiting influencing list placement," *Journal of the American Society of Nephrology*, vol. 9, no. 11, pp. 2142–2147, 1998. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/9808103

[44] A. Flattau, M. Olaywi, P. J. Gaglio, P. Marcus, P. Meissner, E. B. L. Dorfman, and J. F. Reinus, "Social barriers to listing for adult liver transplantation: Their prevalence and association with program characteristics," *Liver Transplantation*, vol. 17, pp. 1167–1175, 2011. [Online]. Available: http://onlinelibrary.wiley.com/doi/10.1002/lt.22357/epdf

[45] The Organ Procurement and Transplantation Network, "Regions," 2019. [Online]. Available: https://optn.transplant.hrsa.gov/members/regions/

[46] A. O. Ojo, R. E. Pietroski, K. O'Connor, J. J. McGowan, and D. M. Dickinson, "Quantifying organ donation rates by donation service area." *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons*, vol. 5, no. 4 part 2, pp. 958–966, 2005. [Online]. Available: http://onlinelibrary.wiley.com/doi/10.1111/j.1600-6135.2005.00838.x/epdf

[47] D. S. Goldberg, S. D. Halpern, and P. P. Reese, "Deceased organ donation consent rates among racial and ethnic minorities and older potential donors," *Critical Care Medicine*, vol. 41, no. 2, pp. 496–505, 2013. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/23263585

[48] U.S. Department of Health & Human Services, "Religious Views on Donation." [Online]. Available: http://www.organdonor.gov/about/religiousviews.html

[49] O. Tontus, M. Karabey, and N. Gurdal, "Survey of medical students' attitudes, religious beliefs, and knowledge of organ donation," *Organs, Tissues and Cells*, no. 14, pp. 203–206, 2011. [Online]. Available: https://www.academia.edu/1169280/Survey_of_medical_students_attitudes_religious_beliefs_and_knowledge_of_organ_donation

[50] P. Bruzzone, "Religious aspects of organ transplantation," *Transplantation Proceedings*, vol. 40, no. 4, pp. 1064–1067, 2008. [Online]. Available: https://doi.org/10.1016/j.transproceed.2008.03.049

[51] M. Oliver, A. Woywodt, A. Ahmed, and I. Saif, "Organ donation, transplantation and religion," *Nephrology Dialysis Transplantation*, vol. 26, no. 2, pp. 437–444, 2010. [Online]. Available: https://doi.org/10.1093/ndt/gfq628

[52] J. L. Xue, P. W. Eggers, L. Y. Agodoa, R. N. Foley, and a. J. Collins, "Longitudinal study of racial and ethnic differences in eeveloping end-stage renal disease among aged medicare beneficiaries," *Journal of the American Society of Nephrology*, vol. 18, no. 4, pp. 1299–1306, 2007. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/17329578

[53] P. McNamara, E. Guadagnoli, M. J. Evanisko, C. Beasley, E. A. Santiago-Delpin, C. O. Callender, and E. Christiansen, "Correlates of support for organ donation among three ethnic groups," *Clinical Transplantation*, vol. 13, no. 1, pp. 45–50, Feb. 1999. [Online]. Available: http://dx.doi.org/10.1034/j.1399-0012.1999.t01-2-130107.x

[54] E. Shacham, T. Loux, E. K. Barnidge, D. Lew, and L. Pappaterra, "Determinants of organ donation registration," *American Journal of Transplantation*, vol. 18, no. 11, pp. 2798–2803, Nov. 2018. [Online]. Available: https://doi.org/10.1111/ajt.15025

[55] J. D. Schold, T. R. Srinivas, L. K. Kayler, and H. U. Meier-Kriesche, "The overlapping risk profile between dialysis patients listed and not listed for renal transplantation," *American Journal of Transplantation*, vol. 8, no. 1, pp. 58–68, 2008. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/17979999

[56] C. R. Clark, L. S. Hicks, J. H. Keogh, A. M. Epstein, and J. Z. Ayanian, "Promoting access to renal transplantation: The role of social support networks in completing pre-transplant evaluations," *Journal of General Internal Medicine*, vol. 23, no. 8, pp. 1187–1193, 2008. [Online]. Available: http://dx.doi.org/10.1007/s11606-008-0628-7

[57] A. Mathur, D. E. Schaubel, Q. Gong, M. K. Guidinger, and R. M. Merion, "Racial and ethnic disparities in access to liver transplantation," *Liver Transplantation*, vol. 16, pp. 1033–1040, 2010. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/20818740

[58] J. Gill, J. Dong, C. Rose, O. Johnston, and D. Landsberg, "The effect of race and income on living kidney donation in the United States," *Journal of the American Society of Nephrology*, vol. 24, pp. 1872–1879, 2013. [Online]. Available: http://www.jasn.org/cgi/doi/10.1681/ASN.2013010049

[59] C. J. Young and C. Kew, "Health disparities in transplantation: Focus on the complexity and challenge of renal transplantation in African Americans," *Medical Clinics of North America*, vol. 89, no. 5, pp. 1003–1031, 2005. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/16129109

[60] P. Y. Fan, V. B. Ashby, D. S. Fuller, L. E. Boulware, A. Kao, S. P. Norman, H. B. Randall, C. Young, J. D. Kalbfleisch, and A. B. Leichtman, "Access and outcomes among minority transplant patients, 1999-2008, with a focus on determinants of kidney graft survival," *American Journal of Transplantation*, vol. 10, no. 4 part 2, pp. 1090–1107, 2010. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/20420655

[61] C. Harvey, "transplant2mongo," 2015. [Online]. Available: https://github.com/ceharvs/transplant2mongo

[62] United Network for Organ Sharing, "Data Use Ageement," Richmond, VA, 2007.

[63] H. C. Bodenheimer, J. M. Okun, W. Tajik, J. Obadia, N. Icitovic, P. Friedmann, E. Marquez, and M. J. Goldstein, "The impact of race on organ donation authorization discussed in the context of liver transplantation," *Transactions of the American Clinical and Climatological Association*, vol. 123, pp. 64–78, 2012. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3540608/

[64] A. Salim, C. Berry, E. J. Ley, D. Schulman, C. Desai, S. Navarro, and D. Malinoski, "The impact of race on organ donation rates in southern California," *Journal of the American College of Surgeons*, vol. 211, no. 5, pp. 596–600, 2010. [Online]. Available: http://dx.doi.org/10.1016/j.jamcollsurg.2010.06.390

[65] C. Kierans and J. Cooper, "Organ donation, genetics, race and culture: The making of a medical problem," *Anthropology Today*, vol. 27, no. 6, pp. 11–14, Dec. 2011. [Online]. Available: http://dx.doi.org/10.1111/j.1467-8322.2011.00837.x

[66] A. K. Israni, D. A. Zaun, J. D. Rosendale, J. J. Snyder, and B. L. Kasiske, "OPTN/SRTR 2013 Annual Data Report: Deceased Organ Donation," in *American journal of transplantation : official journal of the American Society of Transplantation*

and the American Society of Transplant Surgeons, 2013, pp. 1–13. [Online]. Available: http://onlinelibrary.wiley.com/doi/10.1111/ajt.13202/epdf

[67] U.S. Census Bureau Population Division, "Annual State Resident Population Estimates for 6 Race Groups (5 Race Alone Groups and Two or More Races) by Age, Sex, and Hispanic Origin: April 1, 2010 to July 1, 2013," 2014. [Online]. Available: https://www.census.gov/data/tables/time-series/demo/popest/2010s-state-detail.html

[68] P. S. Rao and A. Ojo, "The alphabet soup of kidney transplantation: SCD, DCD, ECD - Fundamentals for the practicing nephrologist," *Clinical Journal of the American Society of Nephrology*, vol. 4, no. 11, pp. 1827–1831, 2009. [Online]. Available: https://cjasn.asnjournals.org/content/4/11/1827

[69] A. K. Singhal, X. Sheng, S. G. Drakos, and J. Stehlik, "Impact of donor cause of death on transplant outcomes: UNOS registry analysis," *Transplantation Proceedings*, vol. 41, no. 9, pp. 3539–3544, 2009. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S004113450901327X

[70] G. A. Westphal, V. D. Garcia, R. L. de Souza, C. A. Franke, K. D. Vieira, V. R. Z. Birckholz, M. C. Machado, E. R. B. de Almeida, F. O. Machado, L. A. d. C. Sardinha, R. Wanzuita, C. E. S. Silvado, G. Costa, V. Braatz, M. Caldeira Filho, R. Furtado, L. A. Tannous, A. G. N. de Albuquerque, E. Abdala, A. d. M. I. Brasileira, and A. B. d. T. de Órgãos, "Guidelines for the assessment and acceptance of potential brain-dead organ donors TT - Diretrizes para avaliação e validação do potencial doador de órgãos em morte encefálica," *Revista Brasileira de terapia intensiva*, vol. 28, no. 3, pp. 220–255, 2016. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/27737418https://www.ncbi.nlm.nih.gov/pmc/PMC5051181/

[71] Census, "Educational Attainment in the United States: 2018," 2018. [Online]. Available: https://www.census.gov/data/tables/2018/demo/education-attainment/cps-detailed-tables.html

[72] D. B. Carr and L. W. Pickle, *Visualizing Data Patterns with Micromaps*, 1st ed. Boca Raton, FL: Chapman and Hall, 2010. [Online]. Available: https://doi.org/10.1201/EBK1420075731

[73] J. Gill, J. Dong, and J. Gill, "Population income and longitudinal trends in living kidney donation in the United States," *Clinical Epidemiology*, vol. 26, no. 1, pp. 201–207, 2015. [Online]. Available: http://www.jasn.org/cgi/doi/10.1681/ASN.2014010113

[74] D. F. Maron, "More millennials are having strokes," *Scientific American*, 2017. [Online]. Available: https://www.scientificamerican.com/article/more-millennials-are-having-strokes/

[75] OrganDonor.gov, "State Organ Donation Legislation." [Online]. Available: http:{%}0A//www.organdonor.gov/legislation_micro/

[76] J. J. Wynn and C. E. Alexander, "Increasing organ donation and transplantation: The U.S. experience over the past decade," *Transplant International*, vol. 24, no. 4, pp. 324–332, 2011. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/21208297

[77] A. B. Leichtman, D. Cohen, D. Keith, K. O'Connor, M. Goldstein, V. McBride, C. J. Gould, L. L. Christensen, and V. B. Ashby, "Kidney and pancreas transplantation in the United States, 1997-2006: The HRSA breakthrough collaboratives and the 58 DSA challenge," pp. 946–957, 2008. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/18336698

[78] National Conference of Commissioners on Uniform State Laws, "Uniform Anatomical Gift Act," Philadelphia, PA, 1968. [Online]. Available: http://www.uniformlaws.org/shared/docs/anatomical_gift/uaga1968_scan.pdf

[79] National Institutes of Health National Institute of Diabetes and Digestive and Kidney Disease, "2018 USRDS annual data report: Epidemiology of kidney disease in the United States. s, Bethesda, MD, 2018." Bethesda, MD, 2018. [Online]. Available: https://www.usrds.org/2018/view/Default.aspx

[80] S. Satel, J. C. Morrison, and R. K. Jones, "State organ-donation incentives under the national organ transplant act," *Law and Contemporary Problems*, vol. 77, no. 217, pp. 217–252, 2014. [Online]. Available: https://scholarship.law.duke.edu/lcp/vol77/iss3/9

[81] Donate Life America, "Youth Educational Guide," Richmond, VA, 2017. [Online]. Available: https://www.donatelifetexas.org/wp-content/uploads/2015/02/Youth_Educational_Guide_DLA_111717.pdf

[82] J. Shimaiukuro and C. Foley, "State Family and Medical Leave Laws," 2008. [Online]. Available: http://congressionalresearch.com/RL33710/document.php?study=State+Family+and+Medical+Leave+Laws

[83] N. Bowman, "Opioids and organ donations: A tale of two crises," Atlanta, GA, 2018. [Online]. Available: https://www.scribd.com/document/378933868/Opioids-and-Organ-Donations-A-Tale-of-Two-Crises

[84] Y. P. Singh and Badruddin, "Statistical considerations in superposed epoch analysis and its applications in space research," *Journal of Atmospheric and Solar-Terrestrial Physics*, vol. 68, no. 7, pp. 803–813, Apr. 2006. [Online]. Available: https://doi.org/10.1016/j.jastp.2006.01.007

[85] P. Chatterjee, V. AS, A. Vijayan, W. JR, and M. EG, "The effect of state policies on organ donation and transplantation in the united states," *JAMA Internal Medicine*, Jun. 2015. [Online]. Available: http://dx.doi.org/10.1001/jamainternmed.2015.2194

[86] F. Pretis, "Does a carbon tax reduce CO2 emissions? Evidence from British Columbia," 2019. [Online]. Available: https://dx.doi.org/10.2139/ssrn.3329512

[87] E. M. Ginsberger, L. Hassani-Nezhad, K. Karunanethy, and R. Lalive, "Mothers at work in Switzerland: Impact of first paid maternity leave

on mothers' earnings and employment," 2019. [Online]. Available: http://conference.iza.org/conference_files/SUM_2019/karunanethy_k28091.pdf

[88] M. Baggio and A. Chong, "Recreational marijuana laws and junk food consumption: Evidence using border analysis and retail sales data," *SSRN Electronic Journal*, 2019. [Online]. Available: https://doi.org/10.2139/ssrn.3328613

[89] The California Transplant Donor Network, "Donor registrations jump by 30 percent," 2015. [Online]. Available: https://www.donornetworkwest.org/wp-content/uploads/3.9.15-Possibly-more-organ-donors.pdf

[90] S. Raschka and V. Mirjalili, *Python Machine Learning*, 2nd ed. Birmingham, UK: Packt Publishing, 2017.

[91] F. L. Luan, M. Kommareddi, D. M. Cibrik, M. Samaniego, and A. O. Ojo, "Influence of recipient race on the outcome of simultaneous pancreas and kidney transplantation," *American Journal of Transplantation*, vol. 10, no. 9, pp. 2074–2081, 2010. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/20645942

[92] N. Roysden and A. Wright, "Predicting health care utilization after behavioral health referral using natural language processing and machine learning," *AMIA Annual Symposium Proceedings*, vol. 2015, pp. 2063–2072, 2015. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4765610/

[93] J. Lee, "Patient-specific predictive modeling using random forests: An observational study for the critically ill," *JMIR medical informatics*, vol. 5, no. 1, p. e3, Jan. 2017. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/28096065

[94] T. Shaikhina, D. Lowe, S. Daga, D. Briggs, R. Higgins, and N. Khovanova, "Decision tree and random forest models for outcome prediction in antibody incompatible kidney transplantation," *Biomedical Signal Processing and Control*, vol. 52, pp. 456–462, 2019. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1746809417300204

[95] U.S. Department of Housing and Urban Development, "50th Percentile Rent Estimates," 2010. [Online]. Available: https://www.huduser.gov/portal/datasets/50per.html{#}2010

[96] B. E. Flanagan, E. W. Gregory, E. J. Hallisey, J. L. Heitgerd, and B. Lewis, "A Social Vulnerability Index for Disaster Management," *Journal of Homeland Security and Emergency Management*, vol. 8, no. 1, Jan. 2011. [Online]. Available: https://doi.org/10.2202/1547-7355.1792

[97] F. Pedregosa, G. Varoquaux, A. Gramfort, V. Michel, B. Thirion, O. Grisel, M. Blondel, P. Prettenhofer, R. Weiss, V. Dubourg, and Others, "Scikit-learn: Machine learning in Python," *Journal of Machine Learning Research*, vol. 12, pp. 2825–2830, 2011. [Online]. Available: https://arxiv.org/abs/1201.0490

[98] C. Harvey, "The Kidney Transplant Process Model (KTPM): Simulation tool for the transplant process," in *Proceedings of the Summer Computer*

Simulation Conference, ser. SCSC '16. San Diego, CA: Society for Computer Simulation International, 2016, pp. 13:1—-13:8. [Online]. Available: http://dl.acm.org/citation.cfm?id=3015574.3015587

[99] C. Harvey and J. R. Thompson, "Exploring advantages in the waiting list for organ donations," in *Proceedings of the 2016 Winter Simulation Conference*, ser. WSC '16. Piscataway, NJ, USA: IEEE Press, 2016, pp. 2006–2017. [Online]. Available: http://dl.acm.org/citation.cfm?id=3042094.3042345

[100] C. E. Harvey, "Kidney Transplant Process Model (KTPM)," 2019. [Online]. Available: http://dx.doi.org/10.5281/zenodo.3474245

[101] ——, "Multiple Listings on the Organ Transplant List," 2019. [Online]. Available: https://doi.org/10.5281/zenodo.3474255

[102] A. Davis, S. Mehrotra, J. Friedewald, and D. Ladner, "Characteristics of a simulation model of the national kidney transplantation system," in *Winter Simulation Conference Proceedings*, 2013, pp. 2320–2329. [Online]. Available: https://dl.acm.org/citation.cfm?id=2676272

[103] D. Thompson, L. Waisanen, R. Wolfe, R. M. Merion, K. McCullough, and A. Rodgers, "Simulating the allocation of organs for transplantation," *Health Care Management Science*, vol. 7, no. 4, pp. 331–338, Nov. 2004. [Online]. Available: https://doi.org/10.1007/s10729-004-7541-3

[104] A. A. B. Pritsker, D. L. Martin, J. S. Reust, M. A. Wagner, O. P. Daily, A. M. Harper, E. B. Edwards, L. E. Bennett, J. R. Wilson, M. E. Kuhl, J. P. Roberts, M. D. Allen, and J. F. Burdick, "Organ transplantation policy evaluation," in *Proceedings of the 27th Conference on Winter Simulation*, ser. WSC '95. Washington, DC, USA: IEEE Computer Society, 1995, pp. 1314–1323. [Online]. Available: http://dx.doi.org/10.1145/224401.224813

[105] A. M. Harper, S. E. Taranto, E. B. Edwards, and O. P. Daily, "An update on a successful simulation project: The UNOS Liver Allocation Model," in *2000 Winter Simulation Conference Proceedings*, vol. 2, Orlando, FL, 2000, pp. 1955–1962. [Online]. Available: https://ieeexplore.ieee.org/abstract/document/899192

[106] S. M. Shechter, C. L. Bryce, O. Alagoz, J. E. Kreke, J. E. Stahl, A. J. Schaefer, D. C. Angus, and M. S. Roberts, "A clinically based discrete-event simulation of end-stage liver disease and the organ allocation process," *Medical Decision Making*, vol. 25, no. 2, pp. 199–209, Mar. 2005. [Online]. Available: https://doi.org/10.1177/0272989X04268956

[107] W. B. van den Hout, J. M. A. Smits, M. C. Deng, M. Hummel, F. Schoendube, H. H. Scheld, G. G. Persijn, and G. Laufer, "The heart-allocation simulation model: a tool for comparison of transplantation allocation policies1," *Transplantation*, vol. 76, no. 10, pp. 1492–1497, 2003. [Online]. Available: http://dx.doi.org/10.1097/01.TP.0000092005.95047.E9

[108] J. Ratcliffe, T. Young, M. Buxton, T. Eldabi, R. Paul, A. Burroughs, G. Papatheodoridis, and K. Rolles, "A simulation modelling approach to evaluating alternative policies for the management of the waiting list for liver transplantation," *Health Care Management Science*, vol. 4, no. 2, pp. 117–124, 2001. [Online]. Available: https://doi.org/10.1023/A:1011405610919

[109] J. Kreke, A. J. Schaefer, D. C. Angus, C. L. Bryce, and M. S. Roberts, "Methods for special applications: Incorporating biology into discrete event simulation models of organ allocation," in *Proceedings of the 34th Conference on Winter Simulation: Exploring New Frontiers*, ser. WSC '02. Winter Simulation Conference, 2002, pp. 532–536. [Online]. Available: http://dl.acm.org/citation.cfm?id=1030453.1030527

[110] H. Chen, D. Dickinson, and R. M. Merion, "Kidney-Pancreas Simulated Allocation Model User's Guide," Minneapolis, MN, 2015. [Online]. Available: http://www.srtr.org/sam/content/KPSAM.pdf

[111] A. K. Israni, N. Salkowski, S. Gustafson, J. J. Snyder, J. J. Friedewald, R. N. Formica, X. Wang, E. Shteyn, W. Cherikh, D. Stewart, C. J. Samana, A. Chung, A. Hart, and B. L. Kasiske, "New national allocation policy for deceased donor kidneys in the United States and possible effect on patient outcomes." *Journal of the American Society of Nephrology*, vol. 25, no. 8, pp. 1842–1848, 2014. [Online]. Available: http://www.ncbi.nlm.nih.gov/pubmed/24833128

[112] R. W. Evans, D. L. Manninen, L. P. Garrison, L. G. Hart, C. R. Blagg, R. A. Gutman, A. R. Hull, and E. G. Lowrie, "The quality of life of patients with end-stage renal disease," *New England Journal of Medicine*, vol. 312, no. 9, pp. 553–559, Feb. 1985. [Online]. Available: http://dx.doi.org/10.1056/NEJM198502283120905

[113] U.S. Department of Health and Human Services Health Resources and Services Administration Healthcare Systems Bureau Division of Transplantation, "2009 Annual Report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients: Transplant Data 1999-2008," 2011. [Online]. Available: http://www.srtr.org/annual_reports/archives/2009/2009_Annual_Report/

[114] S. Luke, C. Cioffi-Revilla, L. Panait, K. Sullivan, and G. Balan, "MASON: A Multiagent Simulation Environment," *Simulation*, vol. 81, no. 7, pp. 517–527, 2005. [Online]. Available: http://dx.doi.org/10.1177/0037549705058073

[115] V. Grimm, U. Berger, D. L. DeAngelis, J. G. Polhill, J. Giske, and S. F. Railsback, "The ODD protocol: A review and first update," *Ecological Modelling*, vol. 221, no. 23, pp. 2760–2768, 2010. [Online]. Available: http://dx.doi.org/10.1016/j.ecolmodel.2010.08.019

[116] P. Ormerod and B. Rosewell, "Validation and verification of agent-based models in the social sciences," in *Epistemological Aspects of Computer Simulation in the Social Sciences*, F. Squazzoni, Ed. Berlin, Heidelberg: Springer Berlin Heidelberg, 2009, pp. 130–140.

[117] E. Guadagnoli, C. L. Christiansen, and C. L. Beasley, "Potential organ-donor supply and efficiency of organ procurement organizations," *Health care financing review*, vol. 24, no. 4, pp. 101–110, 2003. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/14628403

[118] E. Page, L. Litwin, M. McMahon, B. Wickham, M. Shadid, and E. Chang, "Goal-directed grid-enabled computing for legacy simulations," in *2012 12th IEEE/ACM International Symposium on Cluster, Cloud and Grid Computing (CCGrid)*, 2012, pp. 873–879. [Online]. Available: https://ieeexplore.ieee.org/document/6217526

[119] A. E. Davis, S. Mehrotra, L. M. McElroy, J. J. Friedewald, A. I. Skaro, B. Lapin, R. Kang, J. L. Holl, M. M. Abecassis, and D. P. Ladner, "The extent and predictors of waiting time geographic disparity in kidney transplantation in the United States," *Transplantation*, vol. 97, no. 10, pp. 1049–1057, May 2014. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/24374790

[120] The United Network for Organ Sharing, "Questions & Answers for Transplant Candidates about Multiple Listing and Waiting Time Transfer," 2015. [Online]. Available: https://www.unos.org/wp-content/uploads/unos/Multiple{_}Listing.pdf

[121] M. L. Volk, G. J. W. Warren, R. R. Anspach, M. P. Couper, R. M. Merion, and P. A. Ubel, "Foreigners traveling to the U.S. for transplantation may adversely affect organ donation: A national survey," *American Journal of Transplantation*, vol. 10, no. 6, pp. 1468–1472. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-6143.2010.03111.x

[122] P. P. Reese and A. L. Caplan, "Better off living: The ethics of the new UNOS proposal for allocating kidneys for transplantation," *Clinical Journal of the American Society of Nephrology*, vol. 6, no. 9, pp. 2310–2312, 2011. [Online]. Available: https://cjasn.asnjournals.org/content/6/9/2310

[123] American Heart Association, "Wealthiest – not sickest – patients may have edge in organ transplants," 2015. [Online]. Available: http://blog.heart.org/wealthiest-not-sickest-patients-may-have-edge-in-organ-transplants/

[124] S. Adam, S. Thomas, K. Leona, and F. Sander, "Geographic disparity: the dilemma of lower socioeconomic status, multiple listing, and death on the liver transplant waiting list," *Clinical Transplantation*, vol. 28, no. 10, pp. 1075–1079, 2014. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1111/ctr.12429

[125] P. A. Vagefi, S. Feng, J. L. Dodge, J. F. Markmann, and J. P. Roberts, "Multiple listings as a reflection of geographic disparity in liver transplantation," *Journal of the American College of Surgeons*, vol. 219, no. 3, pp. 496–504, 2014. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1072751514003603

[126] R. C. Givens, T. Dardas, K. J. Clerkin, S. Restaino, P. C. Schulze, and D. M. Mancini, "Outcomes of multiple listing for adult heart transplantation in the United States: Analysis of OPTN data from 2000 to 2013," *JACC. Heart failure*, vol. 3, no. 12, pp. 933–941, Dec. 2015. [Online]. Available: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4681637/

[127] R. M. Merion, M. K. Guidinger, J. M. Newmann, M. D. Ellison, F. K. Port, and R. A. Wolfe, "Prevalence and outcomes of multiple-listing for cadaveric kidney and liver transplantation," *American Journal of Transplantation*, vol. 4, no. 1, pp. 94–100. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1600-6135.2003.00282.x

[128] M. S. Ardekani and J. M. Orlowski, "Multiple listing in kidney transplantation," *American Journal of Kidney Diseases*, vol. 55, no. 4, pp. 717–725, 2010. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S0272638609016540

[129] V. Kumar, B. A. Julian, M. H. Deierhoi, and J. J. Curtis, "Secondary listing for deceased-donor kidney transplantation does not increase likelihood of engraftment at a large transplant center," *American Journal of Transplantation*, vol. 9, no. 7, pp. 1671–1673. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-6143.2009.02677.x

[130] A. J. White, R. J. Ozminkowski, A. Hassol, J. M. Dennis, and M. Murphy, "The effects of New York state's ban on multiple listing for cadaveric kidney transplantation." *Health Services Research*, vol. 33, no. 2 part 1, pp. 205–222, Jun. 1998. [Online]. Available: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1070261/

[131] R. J. Ozminkowski, A. Hassol, A. White, M. Murphy, J. M. Dennis, and C. F. Shield, "Socioeconomic factors and multiple listing for cadaveric kidney transplantation among medicare end-stage renal disease program beneficiaries," *Transplantation Reviews*, vol. 11, no. 2, pp. 70–75, 1997. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S0955470X9780002X

[132] J. J. Mooney, L. Yang, H. Hedlin, P. Mohabir, and G. S. Dhillon, "Multiple listing in lung transplant candidates: A cohort study," *American Journal of Transplantation*, vol. 19, no. 4, pp. 1098–1108, 2019. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1111/ajt.15124

[133] D. Zorzi, C. Rastellini, D. H. Freeman, G. Elias, A. Duchini, and L. Cicalese, "Increase in mortality rate of liver transplant candidates residing in specific geographic areas: Analysis of UNOS data," *American Journal of Transplantation*, vol. 12, no. 8, pp. 2188–2197. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-6143.2012.04083.x

[134] E. Bonabeau, "Agent-based modeling: methods and techniques for simulating human systems." *Proceedings of the National Academy of Sciences of the United States of America*, vol. 99, no. 3, pp. 7280–7287, May 2002. [Online]. Available: https://doi.org/10.1073/pnas.082080899

[135] M. Tracy, M. Cerdá, and K. M. Keyes, "Agent-based modeling in public health: Current applications and future directions," *Annual Review of Public Health*, vol. 39, no. 1, pp. 77–94, 2018. [Online]. Available: https://doi.org/10.1146/annurev-publhealth-040617-014317

[136] R. A. Kelly, A. J. Jakeman, O. Barreteau, M. E. Borsuk, S. ElSawah, S. H. Hamilton, H. J. Henriksen, S. Kuikka, H. R. Maier, A. E. Rizzoli, H. van Delden, and

A. A. Voinov, "Selecting among five common modelling approaches for integrated environmental assessment and management," *Environmental Modelling and Software*, vol. 47, pp. 159–181, 2013. [Online]. Available: https://doi.org/10.1016/j.envsoft.2013.05.005

[137] A. T. Crooks and A. B. Hailegiorgis, "An agent-based modeling approach applied to the spread of cholera," *Environ. Model. Softw.*, vol. 62, no. C, pp. 164–177, Dec. 2014. [Online]. Available: http://dx.doi.org/10.1016/j.envsoft.2014.08.027

[138] S. C. Bankes, "Tools and techniques for developing policies for complex and uncertain systems," *Proceedings of the National Academy of Sciences*, vol. 99, no. 3, pp. 7263–7266, 2002. [Online]. Available: https://www.pnas.org/content/99/suppl{_}3/7263

[139] A. C. Skeldon, F. Schiller, A. Yang, T. Balke-Visser, A. Penn, and N. Gilbert, "Agent-based modelling to predict policy outcomes: A food waste recycling example," *Environmental Science & Policy*, vol. 87, pp. 85–91, 2018. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1462901117301946

[140] J. Anderson, A. Chaturvedi, and M. Cibulskis, "Simulation tools for developing policies for complex systems: Modeling the health and safety of refugee communities," *Health Care Management Science*, vol. 10, no. 4, pp. 331–339, Dec. 2007. [Online]. Available: https://doi.org/10.1007/s10729-007-9030-y

[141] The Python Software Foundation, "Python 3," 2019. [Online]. Available: https://docs.python.org/3/reference/

[142] Project Mesa Team, "Mesa: Agent-based modeling in Python 3+," [Online]. Available: https://github.com/projectmesa/mesa/, 2015. [Online]. Available: https://github.com/projectmesa/mesa/

[143] T. E. Oliphant, *Guide to NumPy*, 2nd ed. USA: CreateSpace Independent Publishing Platform, 2015.

[144] D. E. Stewart, A. R. Wilk, A. E. Toll, A. M. Harper, R. R. Lehman, A. M. Robinson, S. A. Noreen, E. B. Edwards, and D. K. Klassen, "Measuring and monitoring equity in access to deceased donor kidney transplantation," *American Journal of Transplantation*, vol. 18, no. 8, pp. 1924–1935, 2018. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1111/ajt.14922

[145] H. V. Kulkarni and S. K. Powar, "A simple normal approximation for Weibull distribution with application to estimation of upper prediction limit," *Journal of Probability and Statistics*, vol. 2011, no. 863274, p. 10, 2011. [Online]. Available: http://dx.doi.org/10.1155/2011/863274

[146] S. Mohan, M. C. Chiles, R. E. Patzer, S. O. Pastan, S. A. Husain, D. J. Carpenter, G. K. Dube, R. J. Crew, L. E. Ratner, and D. J. Cohen, "Factors leading to the discard of deceased donor kidneys in the United States," *Kidney International*, vol. 94, no. 1, pp. 187–198, 2018. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S0085253818302060

[147] K. P. Croome, "Domestic transplant tourism: More than just model for end-stage liver disease score variation," *Liver Transplantation*, vol. 24, no. 12, pp. 1653–1654, Dec. 2018. [Online]. Available: https://doi.org/10.1002/lt.25366

[148] D. Goldberg and R. Lynch, "Analysis of the nature and frequency of domestic transplant tourism in the United States," *Liver Transplantation*, vol. 24, no. 12, pp. 1762–1764, Dec. 2018. [Online]. Available: https://doi.org/10.1002/lt.25347

[149] A. J. Kwong, A. Mannalithara, J. Heimbach, M. A. Prentice, and W. R. Kim, "Migration of patients for liver transplantation and waitlist outcomes," *Clinical Gastroenterology and Hepatology*, 2019. [Online]. Available: http://www.sciencedirect.com/science/article/pii/S1542356519304926

[150] R. Reindl-Schwaighofer, A. Kainz, M. Kammer, A. Dumfarth, and R. Oberbauer, "Survival analysis of conservative vs. dialysis treatment of elderly patients with CKD stage 5," *PloS one*, vol. 12, no. 7, p. e0181345, 2017. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/28742145

[151] J. D. Urrutia, W. S. Gayo, L. A. Bautista, and E. B. Baccay, "Survival analysis of patients with end stage renal disease," *Journal of Physics: Conference Series*, vol. 622, p. 12014, Jun. 2015. [Online]. Available: https://doi.org/10.1088/1742-6596/622/1/012014

[152] U.S. House. 92nd Congress, "Public Law No. 92-603, Social Security Amendments of 1972," Oct. 1972. [Online]. Available: http://www.gpo.gov/fdsys/pkg/STATUTE-86/pdf/STATUTE-86-Pg1329.pdf

[153] US House. 95th Congress, "Public Law No. 95-292, An Act to amend titles II and XVIII of the Social Security Act to make improvements in the end stage renal disease program presently authorized under section 226 of that Act, and for other purposes," Jun. 1978. [Online]. Available: https://www.govtrack.us/congress/bills/95/hr8423/text

[154] The Uniform Law Commission, "Uniform Brian Death Act," [Online]. Available: http://www.uniformlaws.org/ActSummary.aspx?title=Determination of Death Act, 1979. [Online]. Available: http://www.uniformlaws.org/ActSummary.aspx?title=DeterminationofDeathAct

[155] National Conference of Commissioners on Uniform State Laws, "Uniform Determination of Death Act," pp. 1–3, 1980. [Online]. Available: http://pntb.org/wordpress/wp-content/uploads/Uniform-Determination-of-Death-1980{_}5c.pdf

[156] US House. 99th Congress, "Public Law No. 99-272, Consolidated Omnibus Budget Reconciliation Act of 1985," Apr. 1986. [Online]. Available: https://www.ssa.gov/OP{_}Home/comp2/F099-272.html

[157] ——, "Public Law No. 99-509, Omnibus Budget Reconciliation Act of 1986," pp. 1874–2078, Oct. 1987. [Online]. Available: https://www.govtrack.us/congress/bills/99/hr5300

[158] US House. 100th Congress, "Public Law No.100-119, Balanced Budget and Emergency Deficit Control Reaffirmation Act of 1987," sep 1987. [Online]. Available: https://www.congress.gov/bill/100th-congress/house-joint-resolution/324

[159] ——, "Public Law No. 100-203, Omnibus Budget Reconciliation Act of 1987," Dec. 1987. [Online]. Available: https://www.ssa.gov/OP{_}Home/comp2/F100-203.html

[160] National Conference of Commissioners on Uniform State Laws, "Uniform Anatomical Gift Act (1987)," Philadelphia, PA, Feb. 1988. [Online]. Available: http://people.bu.edu/wwildman/WeirdWildWeb/courses/thth/projects/thth_projects_2003_lewis/uaga.pdf

[161] U.S. House. 100th Congress, "Public Law No. 100-607, Health Omnibus Programs Extension of 1988," Nov. 1988. [Online]. Available: https://history.nih.gov/research/downloads/PL100-607.pdf

[162] U.S. Senate. 101st Congress, "Public Law No. 101-616, Transplant Amendments Act of 1990," Nov. 1990. [Online]. Available: https://www.congress.gov/bill/101st-congress/senate-bill/2946

[163] U.S. Department of Health & Human Services, "Final Rule, Federal Register," Apr. 1998. [Online]. Available: http://www.gpo.gov/fdsys/pkg/FR-1998-04-02/pdf/98-8191.pdf

[164] US Senate. 106th Congress, "Public Law No. 106-113, Consolidated Appropriations Act," Nov. 1999. [Online]. Available: https://www.govinfo.gov/content/pkg/PLAW-106publ113/pdf/PLAW-106publ113.pdf

[165] U.S. House. 106th Congress, "Public Law No. 106-310, Children's Health Act of 2000," pp. 2205–2206, Oct. 2000. [Online]. Available: https://www.congress.gov/bill/106th-congress/house-bill/4365

[166] US House. 108th Congress, "Public Law No. 108-216, Public Law Organ Donation and Recovery Improvement Act," pp. 1–8, Apr. 2004. [Online]. Available: https://www.congress.gov/108/plaws/publ216/PLAW-108publ216.pdf

[167] National Conference of Commissioners on Uniform State Laws, "Uniform Anatomical Gift Act (2006)," Aug. 2009. [Online]. Available: http://www.uniformlaws.org/shared/docs/anatomical_gift/uaga_final_aug09.pdf

[168] U.S. House. 100th Congress, "Public Law No. 110-144, Charlie W. Norwood Living Organ Donation Act," pp. 881–922, Dec. 2008. [Online]. Available: https://www.congress.gov/bill/110th-congress/house-bill/710

[169] U.S. House. 110th Congress, "Public Law No. 110-413, Stephanie Tubbs Jones Gift of Life Medal Act of 2008," pp. 6579–6582, Oct. 2008. [Online]. Available: https://www.congress.gov/110/plaws/publ413/PLAW-110publ413.pdf

[170] R. A. Metzger, F. L. Delmonico, S. Feng, F. K. Port, J. J. Wynn, and R. M. Merion, "Expanded criteria donors for kidney transplantation," *American Journal of Transplantation*, vol. 3, no. s4, pp. 114–125, 2003. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1034/j.1600-6143.3.s4.11.x

[171] New Jersey Legislature, "Code 18A:7F-4.3, Information relative to organ donation given to students in grades 9 through 12," 2008. [Online]. Available: http://law.justia.com/codes/new-jersey/2013/title-18a/section-18a-7f-4.3

[172] Mississippi Legislature, "Code 37-25, Driver Education and Training," Jul. 2002. [Online]. Available: http://www.organdonor.gov/legislation_micro/statutes/ms_school.html

[173] Arizona State Legislature, "Code 15-707, High schools; education about organ donation," 2014. [Online]. Available: http://www.azleg.gov/FormatDocument.asp?inDoc=/ars/15/00707.htm{&}Title=15{&}DocType=ARS

[174] The State of Ohio, "Code: 3301.07, State board of education - powers and duties," Apr. 2009. [Online]. Available: http://codes.ohio.gov/orc/3301.07

[175] Tennessee Legislature, "Code 49-6-1012, Promotion of organ and tissue donation and transplantation," 1997. [Online]. Available: http://law.justia.com/codes/tennessee/2010/title-49/chapter-6/part-10/49-6-1012

[176] Oklahoma Bar Association, "Organ and Tissue Donation Under Oklahoma Law," Oklahoma City, OK, 2003, vol. 2. [Online]. Available: http://www.okbar.org/Portals/14/PDF/Brochures/organ-donation.pdf

[177] Ohio Legislatre, "Code 4508.021, Dissemination of information regarding anatomical gifts and anatomical gift procedures," Oct. 2002. [Online]. Available: http://codes.ohio.gov/orc/4508.021

[178] The Alabama Legislature, "Code 22-19-71, Distribution of informational brochure; promotion of organ and tissue donation by Director of Public Safety," 1996. [Online]. Available: http://alisondb.legislature.state.al.us/alison/codeofalabama/1975/coatoc.htm

[179] Iowa Department of Transportation, "Code 321.178, Driver education," Jan. 2015. [Online]. Available: http://www.organdonor.gov/legislation_micro/statutes/ia_driver-education.html

[180] Michigan Legislature, "Act 384 of 2006, Driver Education Provider and Instructor Act," Oct. 2006. [Online]. Available: http://www.organdonor.gov/legislation_micro/statutes/mi-driver-education.pdf

[181] Minnesota Legislature, "Code 171.0701, Driver Education Content," p. 2008, 2008. [Online]. Available: https://www.revisor.leg.state.mn.us/data/revisor/statute/2008/171/2008-171.0701.pdf

[182] Wisconsin State Legislature, "Code 38.04, Technical College System." [Online]. Available: http://docs.legis.wisconsin.gov/statutes/statutes/38/04

[183] Virginia Legislation, "Code 22.1-205, Driver education programs," 2013. [Online]. Available: http://law.lis.virginia.gov/vacode/22.1-205/

[184] Rhode Island General Assembly, "Title 31-10-20, Operators' and Chaffeurs' Licenses," 2004. [Online]. Available: http://webserver.rilin.state.ri.us/Statutes/TITLE31/31-10/31-10-20.HTM

Curriculum Vitae

Christine Harvey is a High Performance and Analytic Computing Engineer at The MITRE Corporation in Washington, D.C. She specializes in data analysis and high performance computing in simulations. Her research interests include HPC in simulation, Agent Based Modeling, and Big Data Analysis particularity in the field of Healthcare. Christine received her Bachelor of Science degree from Stockton University in 2011 and then went on to earn a Master of Science degree in Computational Science from Stockton University in 2013. She is a member of the SC Conference committee and serves as the treasurer and membership coordinator for the Special Interest Group on High Performance Computing.