Modeling Kidney Transplantation Decisions: Regulatory Oversight, Information Sharing, and Post-Transplant Drug Choice

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MODELING KIDNEY TRANSPLANTATION DECISIONS:
REGULATORY OVERSIGHT, INFORMATION SHARING, AND POST-TRANSPLANT
DRUG CHOICE

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MODELING KIDNEY TRANSPLANTATION DECISIONS:
REGULATORY OVERSIGHT, INFORMATION SHARING, AND POST-TRANSPLANT
DRUG CHOICE

A Dissertation Presented to the Graduate Faculty of the
Lyle School of Engineering
Southern Methodist University
in
Partial Fulfillment of the Requirements
for the degree of
Doctor of Philosophy
with a
Major in Operation Research
by
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The leadership style one chooses can make that person unforgettable to others. Forever I am deeply indebted to my Ph.D. advisor, Dr. Michael Hahsler, who has led me in my eventful Ph.D. journey, dedicated a priceless amount of his time to my research and assisted me the most. If I want to name three most prominent things about him in my eyes, I will point to his intelligence, friendly personality, and athletic spirit. Within a few minutes of discussion with him on anything, whether it is his expertise or not, one can see the way he conceptually thinks of the subject. His insight when discussing research problems is always inspiring. The constructive suggestions and comments he made helped me to survive when I was stuck in my research. I especially thank him for being so caring to me. I always think people have to be brave enough to care about others since careening brings responsibility and responsibility requires actions. Besides technical talents, he is an athlete who owns many medals and soon he needs another medal holder for hanging new ones!

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distinctly remember how much we bothered Dr. Olinick with requesting assignment extension and exam rescheduling, and he always kindly and patiently accepted all of our requests.

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My lovely Ideen, I love you more than anything in this world. Thanks for being such a good and kind boy to me. I will defiantly miss my weekly meetings with my advisor, but more than that I will miss your cute voice of How did your meeting go mommy? Did you make Michael happy? As I am hopefully finishing the last stage of my study, you are also about to finish the first year of your school. More than wishing you a success at studying, I want to wish you a life full of health and happiness.

My beloved dad and beautiful mom, I wish I could take away the pain that I forced you to take, by being away from you. Thank you for letting me to find my own way, trusting my decisions and accepting me as I am with all flaws and defects. Your support and love mean the world to me.

Finally, I would love to thanks my special friends Dr. Sarah Ostadabbas for all the peaceful feelings that I had after each phone call with her when I was stuck in my research. Without the support and love of Azita, Misha, and Sahar the life would be tough. They treated my family as if it is their own families. Thank you so much for everything you have done for me, and I hope I can return your favors one day.
The United States and many other nations are encountering a disturbing obstacle: A shortage of available organs for patients who are in need of kidney transplantation. This dissertation strives to analyze this trend and present potential solution by focusing on three different aspects, namely regulatory oversight, information sharing, and post-transplant immunosuppressant drug choice. In my first essay, I propose a stochastic model that identifies a socially-optimal kidney transplant choice given the inherent trade-off between the expected wait time (driven by supply and demand) and the quality of received donor kidney. I modify the model to account for changes made by the introduction of performance assessment in 2007 and the new kidney allocation system in 2014. Empirical analysis indicates that the current risk-adjusted post-transplant performance assessment policy might be more effective if regulators also adjust the model based on the differences in organ availability by regions and candidate’s blood type.

Motivated by the high kidney discard rate in the US, in my second essay I develop a simulation model that considers the effect of several important factors that affect kidney utilization. Unlike most proposed models, the presented simulation reflects details of the offering process, the deterioration of patient health and kidney quality over time, the correlation between patient’s health and acceptance decision, and the probability of kidney acceptance. I apply the model to perform two different analyses. The former considers an...
individual-level strategy one may choose to contribute to the improvement of kidney discard rate, opting for simultaneously enlisting in multiple regions. The latter focuses on a macro-level aspect of transplantation, namely the contribution of information sharing on the social welfare and discard rates.

Long-term successful post-transplant outcome necessitates the use of immunosuppressant drug therapy to prevent immunologic rejection and maintain transplanted kidney function. Since kidney transplantation is primarily financed through public funds in the U.S. (Medicare), in my third essay I define, from the payer’s perspective, the incremental cost-effectiveness among four different treatment regimens, i.e., no-induction, IL2-RA, r-ATG, and alemtuzumab. The analysis indicates that antibody-based induction appears to offer substantial advantages regarding both cost and outcome compared to no-induction. Overall, depletional induction (preferably r-ATG) provides the highest benefit.

Organ transplantation is a complicated process which is continuously changing. This thesis cannot cover all aspects but provides valuable insights into several important issues.
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To my family
1.1. Motivation

The United States and many other nations are encountering a disturbing obstacle: A shortage of available organs for patients who are in need of kidney transplantation. In the US, currently more than 100,000 patients are waiting to receive kidney transplantation. In 2015, a total of 17,879 kidney transplantations were performed. Over 3,000 new patients are added to the kidney waiting list each month, and the average wait time for a suitable organ has increased to almost five years. On average, more than 4,000 patients die each year while waiting for a life-saving kidney transplant, and more than 3,000 patients become too sick to undergo transplantation surgery and thus are removed from the waitlist [50, 87, 92]. Despite an acute shortage of kidney donations, each year more than two thousand kidneys recovered from deceased donors are discarded without being transplanted. Dr. Dorry Segev, a transplant surgeon at Johns Hopkins University School of Medicine, said, “There is no doubt that organs that can help somebody and have a survival benefit are being discarded every day [68].” This has led to several recent changes made by several organizations involved in kidney transplantation.

In March 2007, the Centers for Medicaid and Medicare Services (CMS) issued Conditions of Participation (CoP) for kidney transplant centers. As a result, transplant centers must meet CMS expectations of risk adjusted post-transplant outcomes, especially one-year patient and kidney survival, to receive Medicare funding and public support. In particular, transplant centers that fail to meet CMS evaluation metrics are subject to quality review and most likely will require to enter a Systems Improvement Agreement (SIA). Transplant centers that lose CMS support will likely run out of business since private insurance companies
typically will not renew their contracts with such centers as well.

On the other hand, the Organ Procurement and Transplant Network (OPTN) applies a different set of evaluation metrics to assess transplant centers’ outcomes. Failure to satisfy OPTN performance metrics will result in transplant centers losing their status of “a member in good-standing,” which is a requirement to receive organs for transplantation. Risk-adjusted post-transplant outcomes of each transplant center are available to the general public through the Scientific Registry of Transplant Recipient (SRTR) website under the name of Program-Specific Reports (PSR).

The fact that CMS and OPTN have established their quality assurance policies in such a way that penalizes transplant centers for unexpected post-transplant outcomes was the main motivation for my research to study and analyze behavioral response of transplant centers to quality oversight. Since both CMS and OPTN do not take any action about the mortality rate of waitlisted patients, transplant centers might not worry about their pre-transplant outcomes as much as they are concerned with their post-transplant outcomes. A New York Times article [68] mentioned, “In interviews, dozens of transplant specialists said the threat of government penalties had made doctors far more selective about the organs and patients they accepted, leading to more discards.” This reflects a strategy that can save transplant centers from being identified as underperforming by only accepting higher quality donor kidneys as well as enlisting only relatively healthy patients. Dr. Michael Rees, a transplant surgeon at the University of Toledo Medical Center, stated in a New York Times article that his kidney program was cited by CMS in 2008 after several unlikely failures. To save the program from decertification, he cut back to about 60 transplants a year from 100, becoming far more selective about the organs and recipients he accepted. The one-year transplant survival rate rose from 88 percent to 96 percent, but Dr. Rees still is bothered by the trade-off [68]: “Which serves America better?” he asked. “A program doing 100 kidneys and 88 of them are working, or a program that does 60 kidneys and 59 of them are working? It’s rationing health care under the guise of quality, and it’s a tragedy that we are throwing away perfectly good organs.”
1.2. Research question and methods

In this dissertation, I investigate these trends and address the research question of how strategies like regulatory oversight, information sharing, and post-transplant immunosuppressant drug choice can improve medical outcomes and social welfare. I will use methods including stochastic modeling, simulation, optimization, and data analytics.

1.3. Structure of the dissertation

The focus of Chapter 2 is on the impact of performance measurement on kidney transplantation. It aims to assist the regulators in designing an optimal incentive structure using a performance assessment policy. The main questions I want to answer are how severe the action of the regulator should be when dealing with underperforming centers and how much evidence is needed to impose such an action. To address these questions, I first develop a stochastic model that considers the impact of the candidates health, organ quality, and expected wait time (affected by supply and demand) on a candidate’s and a center’s utilities. I define a simple threshold strategy on the acceptable range of kidney qualities and find the optimal thresholds for both candidates and centers. I also define the social optimal outcome using an overall utilitarian welfare function from the social planner’s perspective.

I show that rational centers have an incentive to make transplantation decisions that do not lead to an optimal social outcome and thus there is a need for performance assessment and penalties. Based on the proposed model, I derive the optimal incentive structure to minimize social loss. I show that penalties have to be adjusted not only for the risk due to a candidate’s health but also for supply and demand since they affect the candidate’s wait time and optimal kidney quality threshold. The direct effect of supply on the optimal incentive structure makes it necessary to investigate the way kidney are allocated to candidates. Recently, changes made to the Kidney Allocation System (KAS) resulted in shifting the kidney supply in favor of specific groups of healthier candidates. I show that changing the allocation system without adjusting the performance assessment leads to sub-optimal results, and I derive how the incentive structure needs to be modified.
An empirical analysis using the model suggests that the elements that affect a candidate’s wait time, including candidates blood type and region supply, need to be taken into consideration in making the best kidney transplant choice. By analyzing the transplant data from the Scientific Registry of Transplant Recipient (SRTR) I found that outcome assessment has been effective for transplant centers to achieve a transplant decision close to the social optimum for 42% of recipients. I also found that the current risk-adjusted post-transplant performance assessment policy might be more effective if regulators also adjust the model based on the organ availability in each of the 11 geographical transplantation regions and the candidate’s blood types.

In Chapter 3, I develop a flexible simulation model to analyze the effect of changes to the kidney allocation system and the offering process. The primary challenge of modeling the organ acceptance/rejection problem is incorporating real-world conditions and situations associated with making a crucial life-saving decision. For this reason, my primary intention as the main novelty of this work is to recognize, aggregate, and implement most essential elements that contribute to kidney selection criteria. The simulation model takes into account the candidate’s health and health deterioration, the deterioration of donor kidney quality during the allocation process, and supply and demand. Furthermore, the model considers the chance that a matching kidney cannot be accepted because of other reasons (e.g., short-term sickness of the patient, insufficient surgical resources, etc.), as well as the impact of information sharing on the efficiency of the offering process.

Using parameters estimated from data provided by UNOS and SRTR, I apply the simulation model to investigate two important trends in kidney transplantation: (1) multiple listing, which allows the patient to be enlisted simultaneously in several regions, and (2) information technology, to speed up the process of organ allocation. For the first application, I formulate the listing decision as a utility maximization problem under a set budget constrain with additional constraints on distance and facility specific parameters. The proposed model allows for diversity in candidate health and kidney quality as well as the correlation between a candidate’s health and the demanded kidney quality. Moreover, I include the quality
deterioration of kidneys caused by accumulating Cold Ischemia Time (CIT) as the offering process progresses down the waiting list to find a recipient. In addition to all aforementioned elements, I also model the impact of the candidate’s short term health and availability together with human and facility resources restriction. The model informs candidates about a multiple-enlisting policy by offering a set of regions to enlist in given distance, cost and transplant volume constraints.

The second application of the simulation model proposed in Chapter 2 draws attention to the social welfare aspect of kidney transplantation rather than focusing on finding an optimal solution as considered in the first model. I compare the social welfare results (i.e., donor kidney utilization and post transplant utility) in the presence and absence of perfect information submitted by the decision makers to the organ allocator. Such information includes the candidate’s willingness and transplant hospital’s readiness for performing a transplantation surgery. The simulation quantifies how collecting and sharing such precise data in a timely manner can be helpful to allocate retrieved organs more efficiently.

Chapter 4 deals with an important aspect that affects post-transplant outcomes. After a candidate receives a kidney transplant, his/her body recognizes the new organ as foreign and will attack the new kidney and try to destroy it. It is recommended that the patient takes immunosuppressive drugs which prevents the body from damaging the transplanted organ. The anti-rejection medicines which lower the body’s ability to reject a transplanted organ are expensive and under some certain specific conditions can be covered by Medicare up to three years following the transplant. However, the majority of patients need to take them for the rest of their life. Effective immunosuppressive drugs have a major impact on post-transplant outcomes. To cover this aspect, I use data analytics to conducted a cost-effectiveness analysis from the payer’s perspective to find the most cost-effective treatment option among four different induction groups. I link the United States Renal Data System dataset to Medicare claims to estimate cumulative costs, graft survival, and incremental cost-effectiveness ratio (ICER) within three years of transplantation in 19,450 (Deceased Donor Kidney Transplantation) DDKT recipients with Medicare as primary payer from 2000 to
2008. I divide the study cohort into high-risk (age > 60 years, panel reactive antibody > 20%, African American race, Kidney Donor Profile Index > 50%, cold ischemia time > 24 hours) and low-risk (not having any risk factors, comprising approximately 15% of the cohort). Following the elimination of dominated options, I estimate expected ICER among induction categories: no-induction, alemtuzumab, rabbit anti-thymocyte globulin (r-ATG), and interleukin-2 receptor-antagonist. The analysis confirms that induction therapy always offers substantial benefits in both cost and survival compared to no-induction. Overall, r-ATG induction provides the most significant benefits.

1.4. Contributions

The presented optimization and simulation models in conjunction with the empirical data analyses using the clinical dataset introduce several contributions to the current literature. In my work I aggregate the complex multi-stage processes of kidney transplant decision together from the perspective of different decision makers (patient, transplant center and social planner) by considering realistic factors that can affect their decisions. Detailed contributions include:

1. Model transplant decisions include enlisting the patients to the waitlist and accepting donor kidney offer.

2. Examine the impact of regulatory oversight and different kidney allocation systems on above decisions.


4. Investigate the role of technology and value of information sharing in kidney transplant area and its outcomes such as post transplant expected utility, kidney utilization and waitlist mortality rates.

5. Identify a cost-effective immunosuppression medication choice for kidney transplant recipient under different willingness-to-pay threshold.
Healthcare quality assessment was designed more than a decade ago to establish a basic level of quality through evaluating and reporting the performance outcomes of healthcare providers. Depending on the focus area of performance assessment which can be healthcare service delivery, patients outcomes, or both, the reported results of the performance evaluation may differ significantly. Furthermore, the legitimacy and fairness of performance outcomes are determined by the accuracy of data collection, the use of appropriate risk-adjustment of assessment metrics, and the organization that discloses the outcomes.

Private organizations and government regulators can use performance reports to assess the outcomes of healthcare providers, recognize underperforming care providers, and take appropriate actions to assure that patients will receive a high level of care. Patients and insurance companies can use the performance report to select providers who have appropriate or even outstanding outcomes. Outcome-based provider selection is an important mechanism which might lead to quality improvement since a rational response of providers is to increase their performance to stay competitive. Also, providers may be concerned with their reputation among peers as well as the patient population. Therefore, performance assessment outcomes are seen as a tool to motivate the healthcare providers to provide a high level of care.

In spite of constructive effects of performance reporting in the healthcare organization, there are some concerns expressed about public performance reporting. At the same time that performance outcomes can change the organizational behavior in beneficial ways, they can also alter it in problematic ways. The relevant concerns can be divided into three major groups.
The first group questions the validity of performance assessment itself, and whether or not it is appropriate to apply it to the healthcare system. This is based on the belief that the field of quality assessment in healthcare is still imperfect and metrics that have been approved for one purpose may not be applicable for other purposes. The performance metric derived from an administrative dataset may not be valid for supervising and comparing the performance outcomes across different healthcare organizations such as hospitals. Furthermore, comparing outcomes across institutions are constrained by the difficulties of carrying out appropriate statistical analysis that incorporates appropriate adjustments for differences in risk (e.g., differences in patient populations). Another concern brought up to the attention by the first group is that instead of focusing on the outcome measurement, the emphasis should be on process measurement. They believe that the performance of healthcare organizations should be evaluated based on what is performed to improve the quality rather than measuring patients outcomes such as mortality and morbidity rates [17,20,22,93,97].

The second group is concerned about the potential unintended consequences of performance assessment and whether the assessment metrics used for evaluation are accurate and appropriate [17,20,22,93,97]. Their concern is the potential dilemma arises with outcome-based performance assessment in a market with substantial excess demand. In such a case, underperforming organization may not improve their performance with assessment if gaming the system is less costly than actually improving the performance. Furthermore, an organization may enhance its measured performance through restricting access to the care for patients that are believed to carry risk to negatively impact the used outcome metrics. For these reasons, the design of regulations and the assessment factors are the essential elements that should be considered in designing successful performance assessment metrics.

The concern of the third group is regarding the interpretation of performance measurement and its application by different sectors and patients. Misinterpreting the performance outcomes by payers and regulators may develop the risk of shutting down the healthcare facility or the provider. On the other hand, misinterpretation of performance outcomes by patients may provide a significant risk in seeking the appropriate care given the limited
number of clinical areas for which the outcome assessment have originally been implemented. The reason stated is that strong performance in one area does not predict such performance in other clinical areas.

In this chapter we focus on the impact of performance measurement on kidney transplantation. Kidney transplantation is especially interesting since kidney transplant centers have more flexibility to game the system than other organ transplant centers. Candidates waitlisted for kidney transplantation can live on dialysis, and thus the center can delay transplanting riskier patients to improve their performance measures. To receive federal funding from the Medicare, transplant centers must perform at least three kidney transplants per year. Since most kidney transplant centers can easily meet this criterion, they can improve their outcomes by cherry picking donor kidneys and refusing those kidneys that are believed to pose a threat to their performance evaluation, even if the transplantation might be beneficial to the candidate. Furthermore, regulators have established a policy that penalizes transplant centers for their unexpected post-transplant outcomes by subjecting them to a review process. However, regulators do not take any action about the mortality rate of waitlisted patients. For this reason, transplant centers might not worry about their pre-transplant outcomes as much as they are concerned with their post-transplant outcomes. A New York Times article [68] mentioned, “In interviews, dozens of transplant specialists said the threat of government penalties had made doctors far more selective about the organs and patients they accepted, leading to more discards.” This clearly shows that worries about unindented consequences of performance evaluation need to be considered.

The goal of this chapter is to assist the regulators in designing an optimal incentive structure based on performance assessment policy. Actions by the regulator can include subjecting underperforming centers to a quality review and improvement process, excluding centers from having access to transplant organs, as well as direct financial incentives in the form of reduction of reimbursement rates, fines, or paying bonuses for exceptional performance. The main questions are how severe these actions should be (e.g, scope of the performance review or amount of the fine) and how much evidence is needed to impose the
action (e.g., the chance that an adverse event triggers an action).

To address these questions, we first develop a stochastic model that considers the impact of the candidates health, organ quality, and the expected wait time (affected by supply and demand) on candidate’s and center’s utility. We define a simple threshold strategy on the acceptable kidney quality and find the optimal thresholds for both candidates and centers. We also define the social optimal outcome using an overall utilitarian welfare function from the social planner’s perspective. We show that rational centers have an incentive to make transplantation decisions that do not lead to an optimal social outcome and thus there would be a need for performance assessment and penalties.

Based on the stochastic model, we derive the optimal incentive structure to minimize the social loss. We show that penalties have to be adjusted not only for the risk due to candidate’s health but also for supply and demand since they affect candidate’s wait time and optimal kidney quality threshold. The direct effect of supply on the optimal incentive structure makes it necessary to investigate the kidney allocation system (KAS). Recently, changes made to the kidney allocation system resulted in shifting the kidney supply in favor of specific groups of healthier candidates. We show that leaving the old incentive structure in place leads to sub-optimal results and how the incentive structure needs to be adjusted.

The rest of this chapter is organized as follows: Section 2.1 discusses the background on kidney transplantation and performance assessment. In Section 2.2 we perform medical and analytical literature reviews. The proposed model is described in Section 2.3. Section 2.4 derives the optimal organ acceptance decisions for both candidates and providers. In Section 2.5 we discuss the optimal regulatory oversight and the factors that affect it. Section 2.6 derives the optimal policy for the provider to accept a candidate to their waitlist. Section 2.7 analyzes the new allocation system and its impact on optimal transplant decision. The empirical analysis is performed in Chapter 2.8. Finally in Section 2.9 we talk about concluding remarks and future work.
2.1. Background on kidney transplantation

The United States and many other nations are encountering a shortage of available organs for patients who are in need of kidney transplantation. In the US, currently more than 100,000 patients are waiting to receive kidney transplantation. In 2015, a total of 17,879 kidney transplantations were performed. Over 3,000 new patients are added to the kidney waiting list each month and on average, more than 4,000 patients die each year while waiting for a life-saving kidney transplant and more than 3,000 patients become too sick to receive a kidney transplant and thus are removed from the waitlist [50, 87, 92].

Despite an acute shortage of kidney donations, each year more than two thousand kidneys recovered from deceased donors were discarded without being transplanted [43]. Dr. Dorry Segev, a transplant surgeon at Johns Hopkins University School of Medicine, said, “There is no doubt that organs that can help somebody and have a survival benefit are being discarded every day [68].” In another article, Dr. Michael Rees, a transplant surgeon at the University of Toledo Medical Center, stated in a New York Times article that his kidney program was cited by CMS in 2008 after several unlikely failures. To save the program from decertification, he cut back to about 60 transplants a year from 100, becoming far more selective about the organs and recipients he accepted. The one-year transplant survival rate rose to 96 percent from 88 percent, but Dr. Rees still is bothered by the trade-off [68]: “Which serves America better?” he asked. “A program doing 100 kidneys and 88 percent of them are working, or a program that does 60 kidneys and 59 of them are working? It’s rationing health care under the guise of quality, and it’s a tragedy that we are throwing away perfectly good organs.”

When making decisions about organ transplantations, several parties are involved. The main parties are depicted in Figure 2.1. Patients are concerned with the optimal health outcome for them. Transplantation centers care about the health of their patients, the center’s economic situation, and reputation. Finally, a social planner is interested in optimizing the effectiveness and efficiency of the overall system. The two most important regulatory agencies for transplant centers are the Center for Medicaid and Medicare Services (CMS) and the United Network for Organ Sharing (UNOS). Currently, CMS is the largest payer
Figure 2.1. Parties involved in kidney transplantation decisions and their relationships.

for transplantations and transplantation related expenses in the United States, and UNOS holds the organ procurement and transplant network contract. These two agencies apply two different evaluation metrics to assess transplant center outcomes. The Scientific Registry of Transplant Recipients (SRTR) collects and analyses transplant center data to produce several program-specific reports. After finalizing the assessment, SRTR publishes the risk-adjusted outcome for every transplant program, and the results are available to the general public. To assess the performance of transplantation programs, CMS currently employs a risk-adjusted frequentist statistical method. This method calculates an expected event count and compares it to the number of observed events. The hypothesis of “the program’s performance is as expected” can be ruled out only if the observed event count is unusually high or low when compared to the expected count. For more details on this method, readers are referred to [2]. On the other hand, OPTN currently uses Bayesian inference [69], a statistical approach which helps the observer to update a prior belief about the transplant program’s performance after observing a set of new data.
Naturally, in an environment with multiple parties, issues with misaligned incentives may occur. For kidney allocations, the social planner has recently implemented some new policies to improve system efficiency and outcomes. One change is the implementation of healthcare quality report cards. Such report cards are designed to promote the quality of medical care offered by the healthcare system. Report cards can assist healthcare providers to recognize possible quality deficiencies and take steps to address present shortcomings and ameliorate their effects. Different report cards consider different factors for measuring quality including patient health outcomes, patient experience and the process of delivering care. Regulators implement citation policies, where transplant programs that fail to satisfy regulatory agencies performance metric will be cited and are subject to review. In March 2007, the Centers for Medicaid and Medicare Services (CMS) issued Conditions of Participation (CoP) for kidney transplant centers. As a result, transplant centers must meet CMS expectations of risk adjusted post-transplant outcomes, especially one-year patient and kidney survival, to receive Medicare funding and public support. In particular, transplant centers that fail to meet CMS evaluation metrics are subject to quality review and most likely will require entering a Systems Improvement Agreement (SIA). Transplant centers that lose CMS support will likely run out of business since private insurance companies typically will not renew their contracts with such centers as well. On the other hand, the Organ Procurement and Transplant Network (OPTN) applies different evaluation metrics to assess transplant centers’ outcomes. Failure to satisfy OPTN performance metrics will cause transplant centers to lose their status of “a member in good-standing,” which is a requirement to participate in organ transplantation. Risk-adjusted post-transplant outcomes of each transplant center are available to the general public through the Scientific Registry of Transplant Recipient (SRTR) website under the name of Program-Specific Reports (PSR).

Quality assurance programs and the regulatory oversight provide incentives for quality monitoring to protect patients from harm. In fact, performance oversight has led to numerous quality reviews of transplant centers that identified deficiencies and led to improvement efforts [30, 31, 75]. However, even though report cards offer substantial potential
benefits, public reporting and quality oversight may cause unintended consequences, such as motivating providers to restrict access to care for patients that may bring a risk to negatively affect the used performance metrics [38]. This type of patient selection has been also been illustrated in other healthcare contexts associated with the implementation of report cards [35,97].

Another aspect of concern for report cards is that due to public reporting of performance, transplant centers may unintentionally become more selective of donor organs, which may result in a higher rate of organ discard and longer cold ischemia times, the time between the kidney is procured and it is transplanted to the recipient. A prolonged cold ischemia time reduces the quality of the organ and thus the potential benefit to the recipient. Additionally, the centers may not be enthusiastic to share their outcomes with patients, so they may apply adjustments that prevent full capture of risk levels regarding a given transplant [4,75]. Finally, according to some studies [37], even though report cards are designed to provide quality information to potential patients, their direct effect on patients selecting transplant centers has been shown to be minimal.

Designing a report card that reliably assesses clinical quality is challenging. The ideal evaluation of an outcome-oriented report card is based on reliable evidence such as available clinical data and appropriate statistical techniques. To have a credible outcome evaluation produced by statistical methods, the need for sufficient and accurate data is necessary. However, there are many areas in healthcare where it is evident that data collection is difficult. It is very challenging and complicated to assess the accuracy of report cards due to the ambiguity of what the gold standard should be when the measurement technique has potential shortcomings. The use of different evaluation methodologies and data sources produces different results, so the creditability of report cards necessitates constant investigation and improvements.

Wait time to transplant and quality of the received kidney are key factors. Across the US, the wait time for a kidney transplant currently ranges from a few months to up to 10 years. The US is divided into 11 geographic regions, each served by an organ procurement
organization (OPO) to facilitate organ allocation and transplantation. Multiple factors influence the wait time for the kidney transplant, but the two critical ones are candidate’s kidney supply and the kidney acceptance strategy. A candidate’s kidney supply is mainly determined by candidate’s blood type and the region of candidate’s transplant center. Figures 2.2 and 2.3 show the expected wait time and quality of transplanted kidneys across 4 different blood types and 11 regions using SRTR dataset. As it is shown, the wait time till first-time deceased kidney transplant varies significantly from one region and for different blood types. In the ideal situation, the decision maker should consider candidate’s kidney supply in making transplant decision. However, the data reveals that, the average quality of accepted kidneys is almost the same among candidates of four different blood types.

Kidney allocation affects supply. In 2013, the OPTN approved a new donor Kidney Allocation System (KAS) which came into effect in late 2014. The new KAS is designed based on two new features: (1) a Kidney Donor Profile Index (KDPI) which is a numerical measure that incorporates ten donor factors into a single number representing the quality of deceased donor kidney compared to other procured kidneys; (2) an Estimated Post Transplant Survival (EPTS) score for transplantation candidates, an indicator of expected life span after transplant. Both KDPI and EPTS scores range from 0% (the best) to 100% (the worst). The primary goal of KAS is to increase the efficiency by allocating top 20 percent of kidneys (KDPI ≤ 20%) to the top 20 percent of candidates (EPTS ≤ 20%). This follows the idea that allocating the best kidneys to the best candidates results in higher overall utility for the system.

2.2. Literature review

This section reviews research on regulatory oversight discussed in the medical and the analytical literatures. Modeling kidney transplantation processes and the effect of regularity oversight is an important topic discussed in the medical and the analytical literatures. Here we give a very short overview of current literature.
2.2.1. Medical literature

Pelletier et al. [61] focus on the PSRs managed by OPTN and CMS. For instance, PSRs intentionally aim to identify low-performing centers with the goal that their performance is eventually improved, which in turn results in improving post-transplant patient and graft survival. However, there is no significant correlation between public availability of report cards and how patients select their transplantation center. Moreover, current PSRs try to achieve high sensitivity to not miss low-performing centers. This has resulted in a high false-positive rate with significant impact on the centers mistakenly cited.

Many authors analyze unintended consequences of report cards including increased wait times, increased discard rates, and decreased transplantation volume. Schold et al. [75] have found a significant association between low-performing centers and reduced kidney transplant volume in the presence of CMS’s Conditions of Participation (COPs). Their analysis reveals an average decline of 22.4 cases among low-performing centers in contrast to an increase of 7.8 cases among other centers in regard to the transplant volume.

White et al. [100] have considered the effect of COPs by CMS on the volume and donor, recipient and candidate selection of kidney transplant programs. Although the trends in 1-
year kidney graft loss do not show a systematic reduction or shift in the number of marginal candidates and in the utilization of higher-risk donor kidneys, the total volume and donor organ utilization decreased overall among programs with ongoing noncompliance.

Schnier et al. [71] have studied the impact of CMS’s regulatory oversight on waiting time for transplantation finding a longer time on the waitlist for candidates registered in low-performing centers compared to those listed in other centers.

Schnier et al. [74] study the impact of performance oversight on candidate removals from the kidney transplant waitlist. Their analysis shows that low-performance centers have higher (risk adjusted) rates of waitlist removal compared to other centers. They show that although the performance oversight on low-performance centers improves their post-transplant outcomes, it also significantly decreases transplant rate while increasing waitlist removal.

Woodside et al. [104] point to the current performance evaluation program of organ transplantation by CMS, how the process is performed and factors that are present or missing in risk adjustment of outcomes. Although COPs by CMS have improved transplant survival outcomes, statistics show that this outcome is achieved at the cost of tremendous increase in risk-averse behavior by transplant centers, resource utilization, and innovation discour-
agement. OPTN and CMS has started to address these concerns in their recent regulatory changes.

Risk adjustment is another important topic. Schold et al. [72] compare frequentist (i.e., fixed-effects) methods with Bayesian inference for center performance evaluation. While the former methods assess outcomes using traditional statistical tests on count data, the latter ones update prior beliefs with new evidence in the form of observations. Due to lack of sufficient data for small centers, the frequentist approach may favor large centers as statistically more significant and base the results for smaller centers on a very small number of observations. In contrast, the use of prior beliefs in the Bayesian approach pushes small centers toward the prior beliefs. Several challenges exist with Bayesian approach such as choosing a valid prior belief distribution, the appearance of a shift in large centers versus small centers, and being prone to misinterpreting their outcomes by patients, centers and payers.

Discard rates of donor organs are a significant issue. Reese et al. [64] take the high discard rate of donor kidneys into account. Despite the long time (> 5 years) many candidates of kidney transplant have to spend on the national waitlist and the high waitlist morality, a considerable portion of kidneys recovered from deceased donors (> 17% in 2013) are discarded. This study examines the risks of accepting donor kidneys, including discarded ones, versus remaining on dialysis and offers some proposals to reduce the discard rate, such as rewarding with higher reimbursement and offering additional priority on next available kidneys when a high-KDPS kidney is transplanted by a center, encouraging centers to transplant two lower-quality kidneys into one recipient, excluding patients with highest-KDPS transplanted kidneys from report card evaluation, adopting a metric for a center’s organ acceptance rate that is not paired with a center’s transplant rate, fast tracking of high-KDPS kidneys to centers with a good history of accepting such kidneys, and changing the informed consent process to facilitate offering of high-KDPS kidneys.

Snyder et al. [79] challenge the belief that accepting high-risk kidneys (KDPS ≥ 0.85) worsen center’s PSRs. Their study shows that eliminating such high-risk kidneys from the
evaluation would not safe underperforming centers from being cited as underperforming. Also, their hypothetical examination indicates that transplanting additional kidneys with KDPIs similar to those of currently discarded kidneys would also not increase the risk for low-performance evaluations.

2.2.2. Analytical literature

Analytical literature mainly focuses on the response to the information revealed by report cards as well as optimal choices made by patients, providers and regulators.

Miller [47] has investigated the theoretical justification to model the provider’s response to quality reporting. The analysis is based on the assumption that the more information is given to patients, the more incentive they have to look for higher quality providers. The effect of report card is modeled by a noise random variable which illustrates the difference between consumer’s perception of provider’s quality and the actual quality of the provider. More available information by report cards is equate to a decrease in noise, or equivalently, an increase in the accuracy of information about a provider’s quality. The level of noise depends on the provider’s quality of care and thus, providers respond differently to quality oversight.

Dranove et al. [19] model transplantation as driven by market forces and propose a structural model to evaluate the efficacy of new information provided by report cards. The study finds that the report cards considerably raise the market share of hospitals only when the scores differ from prior beliefs. However, this effect is not symmetric, meaning that report cards cause a significant decrease in demand when the quality score is lower than the prior belief but do not bring much benefit when better-than-expected scores are related to high-ranking hospitals.

Modeling and improving the system design is another important stream of research. Su et al. [81] study the effect of patient choice on the high rate of organ discard. They employ a queuing model in which patients are served with a variable reward reflecting the quality of transplant organs. Moreover, patients are homogeneous, have complete information about
the size of the waitlist, and can reject an organ offer with the hope of receiving a better offer in the future. A dynamic programming approach is used to maximize the social welfare under first-come-first-serve (FCFS) and last-come-first-serve (LCFS) strategies. While FCFS intensifies the refusal rates of organs having marginal quality, LCFS results in optimal organ utilization. Their analysis shows that organ supply can be 25% improved by restructuring the queuing mechanism.

Ahn et al. [7] design a decision model in which patients’ preferences for kidney transplantation are involved in the allocation process, as opposed to the current allocation system which provides the patients little opportunity to choose their desired donor kidneys. The expected 1-year graft survival rate is used as the criterion to judge the acceptability of a donor kidney, which is estimated based on a model. Different health states are defined for patients and health development is modeled using a Markov chain. The results are compared with the UNOS system.

Fong et al. [23] investigates an optimal regulation in the form of a scoring rule to evaluate service providers who can take unobservable (private) actions to improve their outcomes at the expense of others. Her analysis is based on continuous-time techniques which consider a dynamic mixed model with instantaneous payment in examining the dynamic setting of healthcare provision.

To investigate the issue from the perspective of the transplantation center, Howard et al. [36] uses a dynamic programming model to investigate why surgeons turn down organs despite their shortage. His analysis shows consistency of surgeons behavior with an optimal stopping rule in which they turn down low-quality organs for healthy patients in the hope to see better organ offers in the future. With the growth of the waiting list, surgeons have now more incentives to use low-quality organs.

Zhang et al. [107] looks at the problem from the patient perspective. He investigates observational learning and information sharing among patients on the kidney waiting list. It means that patients get negatively biased by earlier refusals and accordingly refuse offered kidneys more easily. This negative effect is distributed sequentially on the waitlist and leads
to poor kidney utilization despite the prevailing shortage in kidney supply. A dynamic choice model is developed where patients make an optimal compromise between accepting the current kidney and waiting for future kidneys.

Finally, Levy et al. [44] takes into account the three main parties involved in a transplantation including the recipient, the donor, and the surgeon (or hospital). The well-being of the living donor and the recipient is modeled by the quality-adjusted life-years and the surgeon is assumed to be concerned by the well-being of the donor and recipient, and interested in acquisition of experience and knowledge from performing the transplant.

2.3. Model description and problem formulation

The last stage of chronic kidney disease is kidney failure, also called end-stage renal disease (ESRD). ESRD patients require frequent dialysis treatments to stay alive until they receive a donor kidney. To start this process, ESRD patients need to become transplantation candidates by being accepted by a transplant center and put on a centrally managed waitlist. Once a candidate advances to the front of the waitlist, he or she starts to receive offers of kidneys of varying quality and every time needs to make with his or her health care provider an acceptance decision. In case a kidney is accepted, the transplantation is performed and the candidate leaves the waitlist. Figure 2.4 shows the transplantation process.

We discuss the kidney acceptance decision of a candidate on the waitlist in the following several sections. The initial decision to accept a candidate to the center will be discussed later (in Section 2.7.2) since it is based on expected outcomes that depend on the kidney acceptance decision.

Modeling kidney acceptance decisions has to incorporate many very complicated relationships. In the following we will first introduce the general form of the model. The model can be used to derive optimal kidney acceptance decisions. Using some simplifying assumptions (e.g., assuming linear relationships, constant risk for survival, etc.), we obtain a closed form solution. Even with these simplifications, the resulting closed form solutions are still useful since they allow us to reason about the basic mechanics of the system and show that
the model is able to capture many important aspects observed in the real world. It is easy to replace the simplifications with more realistic functional forms or empirically obtained relationships and then resort to numerical methods or simulation to find optimal decisions.

### 2.3.1. Modeling framework of kidney acceptance decision

We model the waiting list as a set of queues. Each queue (see Figure 2.5) serves kidneys that match a certain type of candidates based on medical kidney matching criteria (e.g., blood type), and candidates can only join the queue they match. In the following, we will concentrate on only modeling a single queue, since the functioning of each of these queues is identical. Instead of serving candidates using the standard FIFO method, we adopt a more complicated process reflecting the fact that candidates can decide if they want to accept an offered kidney.

**Assumption 1** We assume that only the top $N$ candidates in front of the waiting list actively receive offers, and we call them the candidates in the active set. Since we do not model all details about the kidney assignment process, we simplify the process so that every time a kidney arrives to the queue, one of the top $N$ candidates in the active set is randomly chosen and offered the kidney. The candidate receiving the offer can then decide to accept the kidney, get served and leave the queue or reject the offer, deny the service and stay in place.

We use this method to reflect that the first candidate will not always be able to consider the offer. For example, the candidate may be currently traveling, too sick to perform the
transplantation, or for some other reasons not available.

**Assumption 2** Patients arrive with rate $\lambda$. *We do not make any assumptions about the arrival process, only that the arrival rate is greater than the transplantation rate, $\mu_a$.*

Although, the arrival rate is greater than the transplantation rate, the queue will only grow to finite length since candidates also leave the queue with the rate of $\theta$ without service due to death on the waitlist or other delisting for other reasons. We measure candidate health as the expected remaining life time on dialysis. We will use $h > 0$ to denote the expected remaining life time on dialysis of a candidate when he or she joins the active set.

**Assumption 3** We model the arrival process of donor kidneys (matching the respective queue) as a Poisson process with arrival rate $\mu$. Each kidney arrives with a quality $q$ in the range $[0,1]$ modeled as the realization of a sequence of i.i.d. random variables $Q$. Since the active set is of size $N$ and we assign the kidney randomly to a candidate, an individual’s offer rate in this setting is $\mu_o = \frac{\mu}{N}$.

We model the post-transplant candidate utility, $U^c$ for a candidate with health $h$ who receives a kidney of quality $q$ as

$$U^c(h, q, w_t) = B(h, q) \left[ 1 - C(h, w_t) \right], \quad (2.1)$$

where $B(\cdot)$ is the benefit the candidate receives from the transplant which increases with candidate health $h$ and the kidney quality, i.e., $\frac{\partial B(h)}{\partial h} > 0$ and $\frac{\partial B(q)}{\partial q} > 0$. $C(\cdot) \in [0,1]$ represents the candidate’s health deterioration factor after a wait time of $w_t$ starting when he or she joins the active set. The health deterioration strictly increases with the wait time and $C(\cdot)$ becomes 1 when $w_t = h$, and the candidate dies. Although any increasing function serves the purpose of the idea that the benefit from transplant increases as the kidney quality increases, we use for simplicity here a linear form

$$B(h, q) = m_h q, \quad (2.2)$$
where $m_h$ indicates the best outcome of a candidate with health level $h$, which occurs when the highest possible quality kidney is transplanted to her immediately after joining the active set.

**Assumption 4** We assume that the decision maker uses a simple threshold policy by accepting all kidneys with quality $q \geq k$, where $k$ is the chosen threshold.

**Proposition 1** If the decision maker faces kidneys being offered following a Poisson process with rate $\mu_o$ and the kidney quality is drawn from random variable $Q$, then the arrival of acceptable kidneys ($q \geq k$) also follows a Poisson process with rate $\mu_a = \mu_o \cdot P(Q \geq k)$.

**Proof:** Proof See [66].

The wait time is a random variable $W(k)$ following an exponential distribution with parameter $\mu_a$, i.e., $W(k) \sim \exp(\mu_a)$. The probability that the candidate has to wait longer than a given wait time $w_t$ is given by $P(W(k) \leq w_t) = F_{W(k)}(w_t)$. We can find the $w_t$ which will not be exceeded with probability $\alpha_c$.

$$w_t = F_{W(k)}^{-1}(\alpha_c) = \frac{\ln\frac{1}{1-\alpha_c}}{\mu_o P(Q \geq k)}$$ \hspace{1cm} (2.3)

$\alpha_c$ captures the decision maker’s risk preference and increases as the decision maker becomes more conservative and risk averse in terms of wait time. For candidates this reflects the risk of deteriorating health and for centers it means risk of loosing a patient on the
waitlist. In the following, we derive all results based on risk neutrality (i.e., \( \alpha_c = 1 - \frac{1}{e} \)), meaning that \( w_t \) is the expected time until a kidney of minimum quality \( k \) is accepted given by

\[
w_t = \mathbb{E}[W(k)] = \frac{1}{\mu_o P(Q \geq k)}.
\]

The results can be easily extended based on different levels of risk preference among decision makers.

To calculate the expected utility with respect to the expected wait time, we need to estimate the cost of deterioration \( C(h, w_t) \), which is a function of the candidate’s health and the time the candidate has to wait for the transplant. For simplicity, we also use linear deterioration with no deterioration if the wait time is zero and maximal deterioration when the wait time approaches \( h \), the expected remaining life time on dialysis.

\[
C(h, w_t) = \frac{1}{h} w_t \tag{2.4}
\]

The expected utility for selecting a kidney of quality \( q \geq k \) is then

\[
\mathbb{E}[U^c] = \frac{\int_{k}^{1} U^c(h, q, k) f(q) dq}{\int_{k}^{1} f(q) dq} \tag{2.5}
\]

where \( f(\cdot) \) is the kidney quality distribution function. For simplification, let’s assume that kidney quality scores are scaled such that the distribution of \( Q \) is uniform resulting in \( P(Q \geq k) = 1 - k \). This is a common assumption in the literature, since the KDPI score, which reflects kidney quality, is by construction close to uniformly distributed.

Substituting (3.1)-(2.4) into (2.5) the expected utility is given by

\[
\mathbb{E}[U^c] = \frac{m_h}{2} \left( 1 - \frac{1}{h} w_t \right) (k + 1). \tag{2.6}
\]
2.4. Acceptance decisions

Several parties are involved in the kidney transplantation process. In this section we
derive optimal organ acceptance decisions for the two parties involved in making acceptance
decision, namely the candidate and the provider and compare them to the outcome desired
by the social planner, who is interested in the utility created by the whole transplantation
system.

The actual decision is made by the candidate and the provider together and the decision
requires that both agree. However, it is reasonable to assume that many candidates will
trust the recommendation of their provider.

2.4.1. Candidate’s optimal decision

Each candidate tries to use a decision strategy to optimize her utility. For a threshold
strategy this can be formulated as the optimization problem

\[
\max_k \mathbb{E}[U^c] \\
\text{s.t.}
\]
\[
0 \leq k \leq 1 \\
0 \leq w(t) \leq h,
\]

where \( \mathbb{E}[U^c] \) is the candidate’s total expected utility to accept a kidney of minimum quality
\( k \).

**Proposition 2** The optimal kidney acceptance decision under different risk preferences ex-
pressed by \( \alpha_c \) is

\[
k^* = k_c^* = 1 - \sqrt{\frac{2\ln \frac{1}{1-\alpha_c}}{\mu_oh}}.
\]

**Proof:** Proof See Appendix B.1. \( \square \)

The optimal threshold in (2.13) is influenced by both donor kidney supply and the can-
didate’s health. A healthier candidate (higher $h$ value) demands a higher quality kidney. Moreover, in case of increase in kidney supply, which results in a higher offer rate, the candidate would become more selective regarding the kidney quality. A risk-averse candidate (with $\alpha_c < 1 - \frac{1}{e}$) has a tendency to set a lower $k^*_c$ threshold reducing the risk of long waiting time, while a risk-seeking candidate (with $\alpha_c > 1 - \frac{1}{e}$) is willing to wait longer for a better kidney.

2.4.2. Provider’s optimal decision

Although the provider is interested in the best transplant decision for candidates, the decision of accepting donor kidneys might be influenced by other factors as well. The other benefits associated with transplantation such as innovation, financial motivation and learning by experience contain enough incentives to create misalignment between social planner objectives and provider’s incentives. We first derive the optimal decision rule, expressed as a threshold on $q$, for a completely self-interested provider and then introduce the case when a provider’s tendency of benevolence increases.

2.4.2.0.1 Completely self-interested provider. We assume that every provider receives a fixed benefit $B$ for each transplant. A self-interested provider has an incentive to perform a transplant and thus receive this benefit before a candidate departs the system due to death on the waitlist or being delisted for other reasons. Therefore, the provider’s expected utility for using a threshold $k$ for a candidate with health $h$ is

$$E[U^p] = B \, P(W(k) \leq h), \quad (2.9)$$

where the random variable $W(k)$ represents the expected wait time on dialysis since the candidate joined the queue till she receives an offer of a kidney with quality $q \geq k$. A shown above, the wait time $W(k_p)$ has an exponential distribution with parameter $\mu_o \, P(Q \geq k)$ which depends this time on the provider’s threshold $k$. Hence, using a threshold of $k$ for a
candidate with health $h$ generates the expected provider utility of

$$
E[U^P] = B \int_0^h \mu_o(1 - k) \exp(\mu_o (1 - k) t) \, dt
$$

(2.10)

**Proposition 3** A self-interested provider maximizes his total expected utility by setting the kidney quality threshold to the lowest possible kidney quality, i.e., by accepting any kidney.

**Proof:** Since (2.10) is strictly decreasing with respect to $k$, the optimal choice for the provider is to always accept the first donor kidney offered by OPTN, regardless of the kidney’s quality. In other words, if OPTN offers kidneys with a minimum quality of $k$, the provider sets his kidney quality threshold to

$$
k^* = k^*_p = k. 
$$

(2.11)

\[ 2 \]

2.4.2.0.2 Self-interested vs. altruistic providers. Clearly, providers are not completely self-interested and care about their patients. A completely altruistic provider would choose the quality threshold that optimizes the patient utility, while a purely self-interested provider always accepts any kidney. To model the fact that the actual decision threshold $k_t$ applied by the provider can be affected by its expected utility and the candidate’s utility by

$$
k_t = \delta k^*_c + (1 - \delta) k^*_p,
$$

(2.12)

where $\delta$ represents the provider’s degree of benevolence in the range $0 \leq \delta \leq 1$. Here, the provider can choose depending on his incentive to obtain maximum benefit from transplant (i.e., completely self-interested with $\delta = 0$) as opposed to contribute to the best social outcome (i.e., completely altruistic with $\delta = 1$). The expected utility given up by an altruistic
provider is
\[ E[U_p(h, k)] - E[U_p(h, k_t)] \]
while the candidate gains an expected utility of
\[ E[U_c(h, k)] - E[U_c(h, k_t)]. \]

2.4.3. Social planner’s objective

The social planner is interested in maximizing social welfare which means optimizing the whole system in terms of realized utility. The system contains the candidates, the providers and the payers. Since the provider’s financial benefits come from payers, they cancel each other out and we can concentrate on the candidates’ utility.

**Proposition 4** In a setting without direct competition between candidates, the total post-transplant expected utility over the entire population, i.e., the social welfare utility function, is maximized if and only if each candidate optimizes her individual utility under risk neutrality.

**Proof:** Since our model does not consider effects of competition between candidates,

\[ S = \sum_{i=1}^{N} E[U_i^e], \]

it is easy to see that the sum is maximized when each individual candidate maximizes her own post-transplant expected utility.

\[ \square \]

**Lemma 2.1** The optimal threshold for kidney quality that maximizes the expected utility of a candidate with health \( h \) under risk-neutrality is

\[ k^*_x = 1 - \sqrt{\frac{2}{\mu_0 h}}, \quad (2.13) \]
Proof: Proof See Appendix B.2.

If the candidate is risk neutral and the provider completely altruistic then all involved parties have the same optimal decision threshold \( k_s^* = k_c^* = k_t \) and the system would be optimal without intervention. However, if not completely altruistic providers with \( k_t < k_s^* \) convince the candidate to accept a lower quality kidney, then the candidate looses utility and social welfare is not maximized resulting in social loss. This happens because incentives are not aligned between the provider and the candidate or social planner. In this case regulatory oversight is needed to align incentives and reduce social loss.

2.5. Optimal regulatory oversight

In this section, we identify factors that affect regulatory oversight, investigate the relationship among factors to introduce an optimal citation policy (CP) for low-performing providers. We demonstrate how a CP influences accepting offered kidneys by the provider, i.e., how it changes \( k_p \). An optimal citation program must be strong enough to encourage the provider to prioritize candidates’ outcomes from transplantation over all other potential incentives, however it should not cause any risk-averse behavior which might lead to limited access to care for ESRD candidates. Since CPs are usually based on post-transplant survival of the candidate or the kidney, we first introduce a post-transplant survival model.

2.5.1. Post-transplant survival

We define the continuous random variable \( T \) to represent the time until the occurrence of an event of interest to the regulator, such as kidney failure or candidate loss after transplantation. We define \( g(t) \) and \( G(t) \) to be the probability density function and the cumulative distribution function of \( T \), respectively. The standard survival function is defined as

\[
S(t) = P(T > t) = 1 - G(t) = \int_t^\infty g(x)dx,
\]

(2.14)

where \( S(t) \) is the probability of the candidate being alive up to time \( t \). The hazard function
or instantaneous rate of occurrence of the event is

\[
\lambda(t) = \lim_{dt \to 0} \frac{P(T \leq t + dt | T \geq t)}{dt}.
\] (2.15)

And \(S(t)\) written in terms of \(\lambda(t)\) is

\[
S(t) = \exp(-\lambda(t)).
\] (2.16)

The numerator in (2.15) is the conditional probability that the event of interest occurs in the time interval \([t, t + dt]\) given that it has not happened before, and the denominator is the width of the interval. Using a constant risk over the first one-year post-transplant period for kidney of quality \(q \geq k\), we define the hazard function as

\[
\lambda(q, h, t) = \lambda(q, h) \quad \text{for all } t \leq 1
\]

. The reason that \(t\) is dropped form the hazard function is that we assume constant risk over the relatively short period of one year. We model \(\lambda(q, h)\) by the functional form \(\lambda'_h q\). Since the exact quality \(q\) of the accepted kidney is unknown, we use the expectation over \(q \geq k\),

\[
\lambda(q, h) = \lambda'_h (1 - E[Q | Q \geq k]) = \lambda_h (1 - k).
\] (2.17)

The hazard function is decreasing in \(k\), which reflects the fact that as the quality of the accepted kidney increases, the risk of post-transplant kidney failure decreases. The resulting survival function for one-year post transplant survival is

\[
S(k, h, t) = \exp(-\lambda_h (1 - k)) \quad \text{for all } t \leq 1,
\] (2.18)

and the failure function (i.e., the probability of failure) is defined as

\[
F(k_p, h, t) = 1 - S(k, h, t) \quad \text{for all } t \leq 1.
\] (2.19)
Detailed derivations are given in Appendix B.3. Note that different formulations of the hazard function with non-constant risk and different functional forms can be easily used.

2.5.2. Provider’s decision policy under regulatory oversight

We model the impact of a citation strategy imposed by a regulator on behavior of providers toward accepting kidney offers for their candidates. The total expected net utility of performing a transplant under a given citation policy $CP$ is

$$E[U^p] = [B - C_p P(\text{citation})] P(W(k) \leq h),$$  
(2.20)

where $B$ is a fixed benefit for the transplantation, $C_p$ is the cost of being cited as low-performing by the regulator, and $P(\text{citation})$ is the estimated probability of the event of being cited as a result of performing the transplanting. $P(W(k) \leq h)$ is the probability that the candidate receives a transplantation in time when setting a threshold of $k$.

Next, we need to find the probability of being cited. The regulator will only cite a provider if an adverse event, here called a failure, occurs. However not all failures will lead to being cited (e.g., the loss of a very sick patient should). The probability of being cited can be expressed by Bayes’ theorem

$$P(\text{citation}) = \frac{P(\text{citation} | \text{failure}) P(\text{failure})}{P(\text{failure} | \text{citation})}. \quad (2.21)$$

Since the provider is only cited for the candidate if a failure occurs, the following always holds $P(\text{failure} | \text{citation}) = 1$. The failure probability can be estimated by the provider using historic data, expert knowledge or the survival function defined above. A failure is considered if the post-transplant survival is less than a year, leading to $P(\text{failure}) = F(k, h, t)$. We will use $f_p = P(\text{citation} | \text{failure})$ for the probability of being cited given a failure.

Using $f_p$ and the survival function in (2.18) for $P(\text{citation})$ in (2.20), the net expected
utility can be written as

$$E[U_p] = (B - C_p f_p(1 - \exp(-\lambda_h (1 - k_p)))) P(W(k) \leq h). \quad (2.22)$$

**Assumption 5** The provider will not set a kidney quality threshold $k_p$ that makes the expected net benefit of the transplantation negative, i.e., the transplantation would reduce the provider’s expected overall profit.

**Proposition 5** Under Assumption 5, the provider’s optimal kidney quality threshold under regulatory oversight, which leads to a positive expected utility, is

$$k^*_p|_{CP} = 1 + \frac{1}{\lambda_h} \ln \left(1 - \frac{B}{C_p f_p}\right). \quad (2.23)$$

**Proof:** Proof See Appendix (B.4).

The regulator has control over $C_p$ and $f_p$ and thus can influence the optimal threshold $k^*_p|_{CP}$ chosen by the provider. Next, we will define the optimal citation policy and discuss the role of $C_p$ and $f_p$.

### 2.5.3. Optimal citation mechanism

The optimal citation mechanism needs to be designed to incentivize the provider to choose for each candidate the socially optimal kidney quality threshold. That is

$$k^*_p|_{CP} = k^*_s. \quad (2.24)$$

**Proposition 6** The optimal value of $C_p f_p$ denoted as $[C_p f_p]^*$ to achieve (2.24) for a single candidate is

$$[C_p f_p]^* = \frac{B}{1 - \exp \left(-\lambda_h \sqrt{\frac{2}{\mu_o h}} \right)} \quad (2.25)$$

**Proof:** Proof See Appendix (B.5).
\( C_p \) are the costs the regulator imposes on a provider that gets cited. These costs can include the cost for the personal and needed time to go through a quality review or a systems improvement agreement. The cost can also include the lost future revenue in case a provider is excluded from future organ transplantations. Alternatively, \( C_p \) could also be implemented as a direct fine or repayment of received transplantation fees. The severity and amount imposed by \( C_p \) is under the regulators control. The probability of getting cited in case of an adverse event \( f_p \) represents how strict the citation policy is. In the most extreme case of \( f_p = 1 \), every adverse event will lead to a citation and \( C_p \) will be imposed. The optimal value \([C_p f_p]^*\) represents all possible combinations of \( C_p \) and \( f_p \) for which \( C_p f_p = [C_p f_p]^* \), i.e., the same impact can be achieved with every combination of \( C_p \) and \( f_p \) that keeps the product constant. This presents the regulator with a set of equivalent citation policies ranging from citing more frequently imposing as lower cost to citing less frequently imposing higher cost per citation.

Equation (2.25) also shows that as the provider’s benefit \( B \) per transplant increases, the regulator needs to adjust their strategy accordingly to avoid deviation of provider’s optimal decision form the social optimum. Furthermore, according to (2.25), increasing \( h \) requires a higher value for \([C_p f_p]^*\). This corresponds to the need of risk-adjustment, i.e., the optimal citation policy needs to penalizing providers for loss of healthier candidates more than the loss of sicker ones. This is because by nature, the mortality rate among the high-risk population is higher than that of the low-risk population. Similarly, in (2.25), increasing \( \mu_o \) increases \([C_p f_p]^*\). As kidney supply increases, the regulator can expect to see better outcome since more choices are now available to the candidate and the transplantation center to select desired kidneys from.

After defining the optimal CP, we need to consider the cases of insufficiently intense and over-intense CPs.

**Corollary 1** If a given citation policy is insufficiently intense, i.e., \( C_p f_p < [C_p f_p]^* \), altruistic providers will keep their kidney quality threshold at \( k_s^* \), and non-completely altruistic providers will set their optimal kidney quality thresholds in the range of \([k_i, k_s^*]\). If a given
citation policy is over-intense, i.e., \( C_p f_p > [C_p f_p]^* \), all providers will set their kidney quality threshold in the range of \((k_s^*, 1]\).

**Proof:** Proof Follows directly from (2.23).

While insufficiently intense CPs affect only providers that are not completely altruistic, all providers are affected by over-intense CPs. This supports the argument that too strict report cards will have a negative effect on transplantations. If the citation policy does not take supply and demand in the region of the provider into account, then an over-intense citation policy is more likely to be observed among transplant centers that have a high demand-to-supply ratio (DSR). Lower deceased donor organ donation rate (supply) is one of the essential elements that influence DSR. The second element is the number of waitlisted candidates (demand). Transplant centers that are located in regions with might be at a higher risk of being unfairly cited, leading them to perform less transplantations with higher-quality kidneys to reduce their risk of being cited.

### 2.6. Optimal candidate admission policy

After modeling the kidney acceptance decision, we model the decision by the provider to accept a candidate to their wait list. Although this decision precedes the kidney acceptance decision, we present it here in this order, because expectations about the wait time and outcomes of the transplantation inform the candidate acceptance decision. To be eligible for a transplantation, the candidate need to be referred to a transplant center by a nephrologist. The transplant team evaluates candidate’s physical and mental health and if she is identified to be eligible for transplantation, she will be enlisted in both the transplant center’s and the national waitlist. In this section, we model the decision by a provider to accept candidates to their center and thus adding them to the waitlist. We are interested in how this decision is influenced by the citation program.

We assume that that the center will only accept a patient if the candidate is expected to survive till transplant. The transplant team finds the minimum candidate required health
threshold at the time of evaluation, i.e., $h'$ in Figure 2.4, and enlist the candidate if her health
score exceeds this threshold. The candidate’s health deterioration over time can be modeled
by a survival function. To estimate the candidate’s survival on the wait list until transplant
time, i.e., $S^w(h', t)$, we have to consider two time frames. The first time frame is represented
by $u'$, the estimated wait time until the candidate reaches the active set of the queue which
consists of $N$ active candidates who are receiving donor kidney offers. The second time
frame, the expected time till an acceptable offer is received by the active candidate, $w_t$, is
defined analogous to (2.3), but the provider uses this time his probability threshold $\alpha_p$ to
find the wait time for receiving a kidney of the provider’s minimum quality $k^*$ that is not
exceeded with probability $\alpha_p$. Since $w'$ does not depend on the individual candidate, but
rather on the rate with which the candidates leave the waitlist, these two wait times are
independent. The probabilities of candidate survival until transplant and death on dialysis
are respectively defined as

$$S^w(h', t) = \exp \left( - \int_0^{u' + w_t} \lambda^w(h', t) dt \right)$$

and

$$F^w(h', t) = 1 - S^w(h', t).$$

(2.26)

From the definition of health $h'$ as the remaining time the candidate can receive dialysis,
health deterioration after time $t$ is $h' - t$. That is, at time $t = 0$ the candidate has a life
expectancy on dialysis equal to $h'$, and as time approaches to $h'$ the candidate’s remaining
life expectancy approaches 0. We define the hazard function for the pre-transplant period,
i.e., the period from the time the candidate is accepted on the waitlist until she receives a
transplant, to be inversely proportional to the candidate’s health deterioration function

$$\lambda^w(h', t) = \frac{1}{h' - t}.$$  

(2.27)

To make the optimal candidate acceptance decision to the center’s waitlist, the provider
will accept a candidate if the expected benefit of accepting her, $B'S^w(h', t)$, becomes greater
then the expected cost of loosing her before transplantation, $C'F^w(h', t)$, i.e.,
\[ B'S^w(h', t) \geq C'F^w(h', t), \]  
(2.28)

where \( C' \) represents all cost associated with losing the patient including the cost of negative reputation caused by higher waitlist mortality rate.

**Proposition 7** The provider’s optimal health threshold to accept a candidate to the center’s waitlist given risk preference \( \alpha_p \) is

\[ h' \geq \left( 1 + \frac{C'}{B'w'} \right) (w' + w_t) = \left( 1 + \frac{C'}{B'w'} \right) \left( w' + \frac{ln \frac{1}{1-\alpha_p}}{\mu_o(1-k)} \right) \]  
(2.29)

**Proof:** Proof See Appendix (B.6).

The provider’s decision of accepting candidates to the waitlist is sensitive to the kidney supply \( \mu_o \). The increase in the availability of donor kidneys gives the provider a higher chance of performing more transplants. To increase the transplant volume, the provider would have to accept more candidates to the waitlist by lowering candidate’s health index threshold \( h'^* \).

According to (2.29), the more the provider is concerned about obtaining and maintaining high reputation among their peers and candidates for having a low mortality rate on the waitlist (represented by \( \alpha_p \)), the more cautious and selective they become to accept candidates. Increasing \( \alpha_p \) by the provider makes it harder for high-risk candidates to be enlisted since \( h'^* \) has a direct relation to \( \alpha_p \). The consequence of expecting higher-quality kidneys \( (k) \) leads providers to become more selective on enlisting a candidate to the waitlist. That being said, under the influence of quality oversight, the provider will require a higher \( k \) to improve expected post-transplant outcomes and this will set a higher health threshold for their candidate selection policy. This reflects the sentiment that to strict quality oversight may restrict access to transplantation services for patients with lower health.

2.7. Impact of changes to the kidney allocation system

In this section, we analyze the impact of the changes to the kidney allocation system
(we refer to it as the new or current KAS or simply KAS) introduced in 2007 on optimal transplant decisions in both stages of the kidney transplantation process, the candidate acceptance to a center and kidney acceptance decision. We also investigate changes the regulatory agency would need to make to adapt their optimal citation policy as a result of the new KAS.

2.7.1. Kidney transplant decision

We start again with discussing the kidney transplantation decision first. Under the old KAS, all candidates had equal access to all kidneys. The new KAS implements an access policy with preferential treatment of certain groups. It is implemented as a simple threshold strategy where the top 20 percent of kidneys with $\text{KDPI} \in [0, 0.2]$ are offered first to the top 20 percent most healthiest candidates with $\text{EPTS} \in [0, 0.2]$. The idea is that, from a social planner’s perspective, using the best kidneys for the best candidates will result in better total outcomes in terms of the total utility over the whole system.

To model this system, we classify candidate’s population into low- and high-risk classes by using the KAS threshold introduced by OPTN on the kidney quality $q$ of $\pi = 0.8$. In our model, the top-quality kidneys fall in the range of $[\pi, 1]$. As KDPI, the kidney quality $q$ has a close to uniform distribution and thus all the recovered kidneys with quality $q \geq \pi$ (i.e., top 20 percent of kidneys or low-risk kidneys) are assigned to the low-risk class, and harvested kidneys with quality $q < \pi$ are distributed among all (both low-and high risk class). Now we can modify our model to show the impact of exclusively assigning the top 20 percent of kidneys (low-risk kidneys) to the top 20 percent of candidates (low-risk candidates).

2.7.1.1. Low-risk candidate

The kidney arrival process is modeled as a Poisson process with an arrival rate of $\mu$. Top-quality (low-risk) kidneys arrive with a rate of $\mu_1 = \mu P(Q \geq \pi)$ and low-quality (high-risk) kidneys arrive with a rate of $\mu_2 = \mu P(Q < \pi)$. Under the new KAS, low-risk kidneys are exclusively offered to low-risk candidates and are shared among the $N_l = (1 - \pi)N$. 

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low-risk candidates in the active set. The low-quality kidneys get assigned to either one of the $N_l$ active low-risk candidates or one of the $N_h = \pi N$ active high-risk candidates. For simplification, we believe that low-risk kidneys have such high quality that any candidate and center will accept them for transplantation. Since they are only offered to low-risk candidates this can be represented by the constraint $k_l \leq \pi$ where $k_l$ is kidney quality threshold of low-risk candidate post KAS. Also, high-risk candidates will not demand a better kidney than low-risk candidates resulting in $k_h \leq k_l$ where $k_h$ is high-risk candidate kidney quality threshold post KAS. This second constraint is always met by our previous model and we will show that it is also automatically satisfied by the new KAS model.

The rate with which acceptable ($q \geq k_l$) kidneys are offered to low-risk candidate can be calculated as

$$\mu^l_a = \frac{\mu_1}{N_l} P(Q \geq \pi \geq k_l) + \frac{\mu_2}{N_l + N_h} P(Q < \pi \geq k_l). \quad (2.30)$$

Note that $P(Q \geq \pi \geq k_l)$ and $P(Q < \pi \geq k_l)$ represent the probability of $Q$ truncated above and below $\pi$ to be greater than $k_l$, respectively.

Substituting the probability values with a uniform distribution for $Q$, and $N = N_l + N_h$ gives

$$\mu^l_a = \frac{\mu}{N} (1 + \pi - k_l). \quad (2.31)$$

Since this constitutes a thinned Poisson process with rate $\mu^l_a$, $w_l(k_l)$, i.e., the expected wait time until an acceptable kidney offer under KAS implementation is

$$w_l(k_l) = \frac{1}{\mu^l_a}. \quad (2.32)$$

The total post-transplant expected utility for a low-risk candidate using the KAS kidney assignment is derived as follow:

$$E[U^l_c] = P(Q < \pi) \frac{\int_{k_l}^{\pi} U^l_c(h, q, k) f(q) dq}{\int_{k_l}^{\pi} f(q) dq} + P(Q \geq \pi) \frac{\int_{\pi}^{1} U^l_c(h, q, k) f(q) dq}{\int_{\pi}^{1} f(q) dq} \quad (2.33)$$
Proposition 8 The optimal kidney quality threshold of a low-risk candidate under KAS is

$$k^*_l = 1 + \pi - \sqrt{\frac{1 + 2\pi}{N h}}.$$  \hspace{1cm} (2.34)

Proof: Proof See Appendix (B.7).

Corollary 2 Under the new KAS implementation, the low-risk candidate increases the kidney quality threshold $k^*_l$ compare to the pre-KAS optimal kidney quality threshold $k^*_s$.

Proof: Proof See Appendix (B.8).

The justification of this behavioral change is given by the fact that the new KAS limits the competition for top-quality kidneys to only low-risk candidates while they still have access to both high- and low-quality kidneys. In this setting, the offer rate of an individual low-risk candidate increases, resulting in an effective supply increase for her. Thus, a candidate advantaged by the system will demand a higher kidney quality.

2.7.1.2 High-risk candidate

Under the new KAS, higher-risk candidates have access only to lower-quality donor kidneys. The arrival rate of this kidney type is $\mu_2 = \mu P(Q < \pi)$. Since all $N$ active candidates get offers for these kidneys the offer rate is $\frac{\mu_2}{N}$. The acceptance rate and the expected wait time are thus

$$\mu^h_a = \frac{\mu_2}{N} P(Q_{<\pi} \geq k_h) = \frac{\mu h}{N} (\pi - k_h).$$ \hspace{1cm} (2.35)

$$w_h(k_h) = \frac{1}{\mu^h_a}.$$ \hspace{1cm} (2.36)
The post transplant expected utility function is
\[
E(U_h^c) = \frac{\int_{k_h}^{\pi} U_h(h, q, k)f(q) dq}{\int_{k_h}^{\pi} f(q) dq}.
\] (2.37)

**Proposition 9** The optimal kidney quality threshold of a high-risk candidate under KAS is
\[
k_h^* = \pi - \sqrt{\frac{2}{\mu_h}}.
\] (2.38)

**Proof:** Proof See Appendix (B.9).

High-risk candidates respond to a threshold-based KAS by also accepting kidneys of lower quality as before because top-quality kidneys are no longer accessible to this group. The report published in [60] shows that after the introduction of a threshold-based KAS with \( \pi = 0.8 \), the kidney discard rate decreased. The model comes to the same conclusion, since higher-risk candidates reduce their kidney quality requirements and will now accept kidneys that would have been discarded before.

2.7.2. Candidate acceptance decision

As shown in Section 2.7.1, under KAS, the rates at which candidates receive kidney offers change, which changes their optimal decision thresholds \( k_l^* \) and \( k_h^* \), accordingly. The candidate selection strategy which is influenced by both kidney supply (i.e., kidney offer rate) \( \mu_o \) and kidney quality threshold is also subject to change as a result of executing KAS. We trust that the provider accepts all candidates who are identified as low-risk and only makes a decision on high-risk ones. Even though we only modeled above two classes of candidates, those within each class are heterogeneous and will have different health at the time of evaluation. According to (2.29), the candidate’s selection strategy post KAS, i.e. \( h_{kas}^* \), evolves in the following way.
Proposition 10 Under the assumptions that $w'$ and $\alpha_p$ remain the same under pre and post KAS, the provider increases their candidate's quality threshold, $h_{kas}'^*$, and so only accepts healthier candidates among high risk candidates.

$$h_{kas}'^* > h'^*$$ (2.39)

Proof: Proof See Appendix (B.10).

2.7.3. Citation policy

The regulatory agency needs to take into consideration that after implementing KAS the assessment criteria of evaluating transplant program’s performance needs to be adjusted. As shown in Sections 2.7.1 and 2.7.2, optimal transplant-related decisions have changed due to the effect of the introduction of KAS on kidney supply. These decisions have a major impact on post-transplant results. In our citation model, the optimally imposed cost and the citation probability depend on the kidney supply, individual offer rate, and social optimum. Since all these three factors have changed after implementing KAS, the optimal combination $[C_p f_p]^*$ also need to be appropriately adjusted to align providers’ incentives with candidates’ optimal outcomes under KAS.

Proposition 11 The new KAS optimal citation policy for low- and high-risk candidates are

$$[C_p f_p]^{l Kas} = \frac{B}{1 - \exp \left(-\lambda h\left(\sqrt{\frac{2\pi+1}{\mu_o h}} - \pi\right)\right)}$$

and

$$[C_p f_p]^{h Kas} = \frac{B}{1 - \exp \left(-\frac{\lambda h}{\pi} \sqrt{\frac{2}{\mu_o h}}\right)}$$

respectively.

Proof: Proof By substituting the new kidney arrival rates, individual (low- and high-risk)
offer rates (equations 2.31 and 2.35) and the corresponding wait time expectations (equations 2.32 and 2.36), one can derive the optimal citation policy $[C_p,f_p]^\text{kas}$.

As a result, the risk-adjustment outcome should be modified in a way that the provider is penalized by either lower cost or a lower chance for making an unsuccessful graft to a high-risk candidate.

### 2.8. Empirical analysis

This study uses data from the annual reports published by UNOS (national kidney waiting list) and the Scientific Registry of Transplant Recipient (SRTR) (clinical data). The SRTR data system contains detailed medical and demographic data for all donors, waitlisted candidates and transplant recipients in the United States, submitted by the members of OPTN between October 1987 and the end of 2016. The numerical illustration and data analysis conducted in this chapter is based on 395,950 patients who are first-time recipients of deceased donor kidney transplants.

#### 2.8.1. Parameter estimation

In the following we discuss how the parameters used in the model were estimated.

##### 2.8.1.1. Kidney Donor Profile Index

To estimate the quality of donor kidney, $q$, we use the Kidney Donor Profile Index (KDPI) for each kidney. KDPI incorporates ten clinical and demographical kidney donor factors and provides a predictive measure of donor kidney quality. Information on donor age, height, weight, ethnicity, history of hypertension and diabetes, serum Creatinine, Hepatitis C Virus (HCV) status, Donation after Circulatory Death (DCD) status, and cause of death are retrieved from our SRTR data set. We follow [56] to calculate KDPI. For example, a KDPI of 82% means the estimated risk of post-transplant kidney failure from this donor is higher than 82% of kidney donors recovered in that year. For our model, the kidney quality $q$ is estimated as $q = 1 - \text{KDPI}$. Since KDPI is close to uniformly distributed by construction,
kidney quality also follows a uniform distribution in the interval $[0, 1]$.

2.8.1.2. Estimated Post Transplant Survival.

The Estimated Post-Transplant Survival ($EPTS$) score is a numerical measure of a candidate’s post-transplant survival which incorporates four risk factors including age, diabetes status, prior solid organ transplant, and time on dialysis using a Cox proportional hazards model [55]. EPTS scores range from 0% to 100% and are an indicator of how long a candidate would need a functioning kidney transplant when compared with other candidates. Zero is the best EPTS score and candidates with higher EPTS scores are more likely to live fewer years with a functioning kidney compared to those with lower EPTS scores. For instance, a candidate with an EPTS score of 60 percent will likely need a kidney with a lifespan longer than the 40 percent candidates with a higher EPTS score.

We use the candidates EPTS score to estimate the hazard rate, $\lambda_h$. According to the literature [55], the average post-transplant kidney survival is between 8 to 12 years. To implement an average survival of 10 years and the fact that the mean time to failure for a constant hazard rate of $\lambda$ is $1/\lambda$, we use the following simplified functional relationship: $\lambda_h = \frac{1}{10(1-EPTS)}$. A candidate with the best EPTS score of 0 has a hazard rate of 0.1, and as a candidate’s EPTS score increases, the hazard rate also increases. The estimation is based on the best EPTS score, because patients with higher scores are also more likely to receive a transplantation before leaving the waitlist. Given post-transplant survival data, $\lambda_h$ can be estimated directly from the data using methods like the Cox proportional hazards regression.

2.8.1.3. Candidate life expectancy on dialysis.

Based on the USRDS report [84], we use two candidate risk factors, age and race, to estimate a candidates life expectancy on dialysis when she enlists with a center ($h'$). To calculate $h$, i.e., candidate’s life expectancy when she joins the top-$N$ list, we first estimate $w'$, which is the expected wait time from being accepted by a center until the candidate
joins the top-\(N\) list from the data. This wait time is not directly observable. For estimation, we subtract the model’s expected wait time in the top-\(N\) list until the candidate accepts a kidney with a quality threshold of \(k_t\) from the total observed wait time, i.e., \(h = h' - w'\). This relationship can also be seen in Figure 2.4 on page 22.

2.8.2. Effect of regulatory oversight on provider’s transplant decision

On March 30, 2007, CMS issued regulations and conditions of participation (CoP) for hospital-based kidney transplant programs that took effect on June 28, 2007. The new requirements move Medicare-covered transplant programs toward an outcome-focused system that reflects the clinical experience, resources, and commitment of each transplant program. Figure 2.6 displays candidate’s life expectancy on dialysis (health) and the expected wait time till receiving a kidney transplant. The average observed wait time till kidney transplant after 2007 over the entire population (11 regions) has increased by 194 days (from 587 to 780) which results in a reduction of waitlisted candidate’s health by six months on average. However, this does not necessarily mean that the introduction of CoP negatively affected transplantation programs. According to [1] between 2005 and 2014 the number of active candidates grew on average by 2% annually (before and after the introduction of CoP) an in total by 29% which led to increases in Demand to Supply Ratio (DSR). If the waitlist growth is independent of the introduction of CoP, then it could also explain the observed longer wait times, lower health, and lower utility. As a reaction to the lower supply, we would expect self-interested providers to drop their \(k^*\). However, we observed that the providers kept the \(k^*\) constant or even increased it slightly as a reaction to the introduction of the CoP. This moves the \(k^*\) closer to the new the social optimum and signals an improvement and a positive effect of the CoP. The model indicates that the drop in utility is actually due to external factors, and that without CoP, the utility would have dropped even more significantly.

Table 2.1 summarizes transplant outcomes (averages) before and after CoP implementation in 2007 for each region and compares the observed changes with the social optimal
Figure 2.6. Average waitlisted candidate health and wait time before and after CoP

Table 2.1. Transplant outcome and statistic before and after CoP (2007)

<table>
<thead>
<tr>
<th>Region</th>
<th>Outcomes before CoP</th>
<th>Outcomes after CoP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Observed</td>
<td>Social optimal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>k*</td>
</tr>
<tr>
<td>1</td>
<td>0.56</td>
<td>0.64</td>
</tr>
<tr>
<td>2</td>
<td>0.47</td>
<td>0.66</td>
</tr>
<tr>
<td>3</td>
<td>0.57</td>
<td>0.73</td>
</tr>
<tr>
<td>4</td>
<td>0.57</td>
<td>0.72</td>
</tr>
<tr>
<td>5</td>
<td>0.55</td>
<td>0.66</td>
</tr>
<tr>
<td>6</td>
<td>0.55</td>
<td>0.73</td>
</tr>
<tr>
<td>7</td>
<td>0.52</td>
<td>0.67</td>
</tr>
<tr>
<td>8</td>
<td>0.61</td>
<td>0.73</td>
</tr>
<tr>
<td>9</td>
<td>0.48</td>
<td>0.60</td>
</tr>
<tr>
<td>10</td>
<td>0.57</td>
<td>0.73</td>
</tr>
<tr>
<td>11</td>
<td>0.56</td>
<td>0.69</td>
</tr>
<tr>
<td>Average</td>
<td>0.55</td>
<td>0.69</td>
</tr>
</tbody>
</table>
outcomes when the optimal threshold policies $k^*$ are used. As a result of candidate’s health reduction due to longer wait time and lower DSR, the social optimum kidney quality threshold given by the model has decreased by 5%. Interestingly, not only the quality of observed accepted kidneys decreased (indicating that both, the providers and candidates are willing to accept lower quality kidneys), but the observed $k$ increases by 1% on average while the highest increase of 5% happens in region 2. One of the applications of our model is to provide a framework to evaluate the efficiency of CoP. Without taking into account the effect of donor kidney supply and demand on the transplant decisions, it might be difficult to capture the true effect of transplant center’s performance assessment in a dynamic environment where the waitlist may grow over time. If one only compares the average of accepted kidney quality in table 2.1 as an evaluation metric of CoP usefulness, we might find CoP to be detrimental since there is a reduction in the realized utility. However, considering the social optimum dependency upon the availability of donor organs and total demand can help explain the observed utility reduction. Next, we will illustrate how our model allows comparing these two systems (before and after CoP) and extracting an appropriate and practical conclusion even with changes in waitlist length which results in changes in wait length and patient health.

To assess the effect of performance assessment on provider’s response to kidney transplantation decisions and outcomes, we measure social loss, deficiency, and degree of benevolence for each candidate. Table 2.2 contains the average results of performance measurements for before and after COPs implementation. The social loss is defined as the difference between the social welfare utility function’s value given a social optimal kidney transplant decision($k_s^*$), and the provider’s decision observed from data ($k_t$).

$$\text{Social loss} = E(U^c|k_s^*) - E(U^c|k_t)$$

We define deficiency as the relative difference of the expected utility using the providers
Table 2.2. Provider’s performance comparison

<table>
<thead>
<tr>
<th>Provider’s risk preference</th>
<th>Social loss</th>
<th>Deficiency</th>
<th>Degree of benevolence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Averages before CoP introduction</td>
<td>0.73</td>
<td>1.15</td>
<td>0.09</td>
</tr>
<tr>
<td>Averages after CoP introduction</td>
<td>0.69</td>
<td>0.89</td>
<td>0.07</td>
</tr>
<tr>
<td>Changes</td>
<td>-5%</td>
<td>-22%</td>
<td>-14%</td>
</tr>
</tbody>
</table>

decision, $E(U^c|k_t)$, with respect to expected utility under the social optimal decision, $E(U^c|k_s^*)$.

\[
\text{Deficiency} = \frac{E(U^c|k_s^*) - E(U^c|k_t)}{E(U^c|k_s^*)} 
\]  

(2.41)

The degree of benevolence $\delta$ is calculated by solving the following equation.

\[
k_t = (1 - \delta)k_p^* + \delta k_s^* 
\]  

(2.42)

Note that by definition $k_p^*$ is equal to zero resulting in $\delta = k_t/k_s^*$. Our analysis on provider’s performance indicates that the introduction of the score card has on average decreased the social loss and deficiency by almost three months and 14%, respectively, and the degree of benevolence has increased by 9%. Also we observe 22% reduction in social loss and provider’s risk preference moved by 5% closer towards risk neutrality. This shows that the introduction of the CoP had a positive effect that was masked by the increase of the number of candidates waiting for transplant.

2.8.3. The optimal citation policy

In this section, we analyze the effect of suboptimal citation policy on the kidney acceptance decisions. We estimate the current citation policy $C_{pf_p}$ using provider’s data to assess whether the current evaluation system is close to the optimal policy, $C_{pf_p}^*$. In case the current performance assessment is not optimal, we measure how far it is from the optimal citation policy and how much it needs to change to reach the optimal goal.
Table 2.3. Optimal citation policy

<table>
<thead>
<tr>
<th>Region</th>
<th>Offer rate</th>
<th>h Wait time</th>
<th>k Utility</th>
<th>PF</th>
<th>Expected Cost</th>
<th>k Utility</th>
<th>PF</th>
<th>Expected Cost</th>
<th>Citation Policy</th>
<th>Delta</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.57</td>
<td>5.05</td>
<td>834</td>
<td>0.56</td>
<td>10.37</td>
<td>0.051</td>
<td></td>
<td>$259,302</td>
<td>$6,259</td>
<td>0.60</td>
</tr>
<tr>
<td>2</td>
<td>5.99</td>
<td>4.98</td>
<td>818</td>
<td>0.52</td>
<td>10.58</td>
<td>0.055</td>
<td></td>
<td>$228,077</td>
<td>$7,392</td>
<td>0.62</td>
</tr>
<tr>
<td>3</td>
<td>8.51</td>
<td>5.49</td>
<td>728</td>
<td>0.55</td>
<td>11.78</td>
<td>0.045</td>
<td></td>
<td>$274,472</td>
<td>$8,132</td>
<td>0.69</td>
</tr>
<tr>
<td>4</td>
<td>7.99</td>
<td>5.63</td>
<td>627</td>
<td>0.60</td>
<td>11.94</td>
<td>0.044</td>
<td></td>
<td>$283,909</td>
<td>$7,080</td>
<td>0.69</td>
</tr>
<tr>
<td>5</td>
<td>4.87</td>
<td>5.72</td>
<td>904</td>
<td>0.55</td>
<td>11.13</td>
<td>0.049</td>
<td></td>
<td>$267,067</td>
<td>$6,840</td>
<td>0.63</td>
</tr>
<tr>
<td>6</td>
<td>10.45</td>
<td>5.21</td>
<td>677</td>
<td>0.61</td>
<td>11.50</td>
<td>0.046</td>
<td></td>
<td>$272,461</td>
<td>$6,790</td>
<td>0.67</td>
</tr>
<tr>
<td>7</td>
<td>5.64</td>
<td>5.27</td>
<td>920</td>
<td>0.55</td>
<td>10.74</td>
<td>0.05</td>
<td></td>
<td>$256,210</td>
<td>$6,746</td>
<td>0.61</td>
</tr>
<tr>
<td>8</td>
<td>14.02</td>
<td>5.26</td>
<td>658</td>
<td>0.59</td>
<td>11.73</td>
<td>0.044</td>
<td></td>
<td>$284,139</td>
<td>$7,632</td>
<td>0.69</td>
</tr>
<tr>
<td>9</td>
<td>3.41</td>
<td>5.05</td>
<td>945</td>
<td>0.48</td>
<td>9.53</td>
<td>0.059</td>
<td></td>
<td>$218,991</td>
<td>$6,298</td>
<td>0.53</td>
</tr>
<tr>
<td>10</td>
<td>10.37</td>
<td>5.14</td>
<td>753</td>
<td>0.58</td>
<td>11.60</td>
<td>0.045</td>
<td></td>
<td>$268,734</td>
<td>$7,643</td>
<td>0.68</td>
</tr>
<tr>
<td>11</td>
<td>5.13</td>
<td>5.58</td>
<td>718</td>
<td>0.54</td>
<td>11.39</td>
<td>0.048</td>
<td></td>
<td>$263,215</td>
<td>$7,277</td>
<td>0.65</td>
</tr>
<tr>
<td>Average</td>
<td>7.45</td>
<td>5.31</td>
<td>780</td>
<td>0.56</td>
<td>11.12</td>
<td>0.05</td>
<td></td>
<td>$261,507</td>
<td>$7,099</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Table 2.4. Comparison of overintense and insufficiently intense citation policy

<table>
<thead>
<tr>
<th>Data</th>
<th>Social</th>
<th>Provider</th>
<th>Citation Policy</th>
<th>Provider’s Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offer rate</td>
<td>h</td>
<td>k Utility</td>
<td>k Utility</td>
<td>Optimal expected cost</td>
</tr>
<tr>
<td>Overintense</td>
<td>7.11</td>
<td>0.42</td>
<td>6.34</td>
<td>0.70</td>
</tr>
<tr>
<td>Insufficiently intense</td>
<td>7.61</td>
<td>0.70</td>
<td>13.25</td>
<td>0.40</td>
</tr>
</tbody>
</table>

For the example here, we suppose that the considered provider’s benefit (net of all other cost) from a performed transplant is $B = $5000. To calculate the optimal citation policy, we substitute the corresponding $\lambda_h$, $\mu_o$ and $h$ (estimated from the data), in equation 2.25 and calculate $C_p^*f_p^*$. Under the assumption that the provider reacts rationally to the citation policy, the provider will try to set the optimal $k_t = k_{p(CP)}^*$, given the policy. Therefore, the current citation policy $C_p f_p$ can be estimated from the data by substituting the probability of failure $F(k_t^*, h, t)$ with $F(k_t, h, t)$, the probability of failure given the used kidney quality threshold $k_t$ in 5.

We introduce $\Delta$ as the difference between provider’s expected cost and optimal-citation expected cost given his decision $k_t$.

$$\Delta = (C_p f_p - C_p^*f_p^*) F(k_t, h, t)$$  \hspace{1cm} (2.43)
If $\Delta$ is zero then the current $C_p f_p$ is the optimal citation policy. In other words, provider’s perception of citation policy leads to setting his threshold $k_t$ equal to the social optimum $k_s^*$. Table 2.3 presents the current and the optimal citation policy across 11 regions in the US. We compute $\Delta$ for every recipient across 11 regions after the implementation of CoP. Table 2.4 represents the average $\Delta$ of kidney transplant recipients over 11 regions. An over-intensive citation policy leads to positive values of $\Delta$, and an insufficiently-intensive citation policy is associated with negative values of $\Delta$. We assume the citation policy is sufficiently intense if $\Delta$ falls in the interval of $(-$1000, 1000). If a provider’s $\Delta >$ $1000$ then the provider’s response to the outcome oversight results in choosing $k_t > k_s^*$, which leads to a sub-optimal outcome. In this case, the social planner needs to reduce the expected cost of unsatisfactory outcome by $\Delta$ to avoid the negative effect of the provider’s risk-averse decision. On the other hand, when $\Delta < -$1000 provider’s decision is below the social optimum. To address provider’s improvement shortage, the social planner’s imposed expected cost has to be increased by $\Delta$ by adjusting $f_p^*$. In our model $f_p$ represents the risk adjustment aspect of the citation policy, while it does not depend only on donor and recipient risk factors. It can also be risk adjusted for the availability of organ in each region.

Overall, based on our analysis, on average the citation policy has caused 17% and 41% of recipients to receive suboptimal kidneys as a result of over-intensive and insufficiently-intensive effects, respectively. The remaining 41% of recipients receive optimal kidneys given their risk and health profiles. Figure 2.7 demonstrates the percentage of candidates that are affected by the citation policy at each region. The overall effect of CoP is shown in Figure 2.8. Despite increases in demand and wait time, the total saved life after 2007 reaches its highest value at region 5 where 54,224 candidates received their kidney transplants.

2.8.4. New kidney allocation

The new allocation rules became effective on December 4, 2014. The new KAS consists of several components. The major changes are designing new metrics to calculate and assign new scores for the quality of donor kidney (KDPI) and recipient (EPTS), giving priority to
Figure 2.7. CoP efficiency across 11 regions

Figure 2.8. Total saved life as a result of CoP implementation.
### Table 2.5. Average post-KAS outcomes for low- and high-risk recipients

<table>
<thead>
<tr>
<th>Provider</th>
<th>Wait Time</th>
<th>$k$</th>
<th>Utility</th>
<th>$C_f$</th>
<th>Expected Cost</th>
<th>Wait Time</th>
<th>$k$</th>
<th>Utility</th>
<th>$C_f$</th>
<th>Expected Cost</th>
<th>Delta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk recipients</td>
<td>31</td>
<td>0.70</td>
<td>0.70</td>
<td>15.95</td>
<td>$579,714$</td>
<td>34</td>
<td>0.80</td>
<td>0.80</td>
<td>16.71</td>
<td>$757,562$</td>
<td>-$2,682</td>
</tr>
<tr>
<td>High-risk recipient</td>
<td>267</td>
<td>0.54</td>
<td>0.54</td>
<td>9.62</td>
<td>$171,403$</td>
<td>62</td>
<td>0.391636</td>
<td>0.391636</td>
<td>9.83</td>
<td>$120,092$</td>
<td>871</td>
</tr>
</tbody>
</table>

Sensitized candidates, pediatric priority, new waiting time calculation rules, and eventually new kidney assignment. We focus on the new kidney assignment aspect of KAS. Based on the new KAS, the top 20% of recovered donor kidneys (i.e., $KDPI \leq 0.2$) are assigned to the top 20% of candidates (i.e., candidates with $EPTS \leq 0.2$). The remaining kidneys are allocated among everybody. To reflect this change, we divide the recipient population into two groups of low- and high-EPTS. We have updated the new kidney offer rate, optimal kidney threshold, wait time and post-transplant utility based on Equations 2.31 to 2.38.

The average for post-KAS results are summarized in Table 2.5 for low- and high-EPTS groups. As a result of new KAS allocation rules, the low-EPTS (i.e., low-risk) candidates now have higher access to donor kidneys, which increases their offer rates and consequently decreases their wait time. For the high-EPTS (high-risk) candidates, their offer rates decline since their access to high-quality kidneys is limited which results in a wait-time increase and at the same time their expected offered kidney quality also is reduced. If the pre-KAS citation policy is not adequately adjusted to these changes it will become suboptimal under the new conditions. This is shown as the $\Delta$ values in Table 2.5. The average of $\Delta$ values for low-EPTS candidates is negative, while for high-EPTS we see positive values. This indicates that the citation policy is now overintense for high-EPTS candidate, while it became insufficiently intense for low-EPTS candidates.

Also to study the effectiveness of the new KAS, we compare the impact of KAS on kidney transplant decision outcomes using social loss. We calculate the total social loss across all regions and candidates before and after the KAS implementation in 2014. Our analysis indicates that the social loss has decreased by 1,292 life years per year over the entire population and it supports the success of KAS.
2.8.5. The effect of risk preferences

The risk associated with organ transplant in the healthcare system can be defined in different ways depending on the area of concern. For instance, the concern can be regarding high waitlist mortality rates, long waiting times, unsatisfactory post-transplant outcomes, and high kidney discard rates. Also, different parties may have different risk preferences. In the medical literature, the standard assumption of a risk-neutral social planner is often used. However, the center and the patient, who make the actual acceptance decision, may have different risk preferences. For example, a patient may be more conservative to make sure to receive a kidney in time. Our model focuses on the effect of the risk of overly long wait times, and it is defined as the probability of patient dies on the waitlist due to demanding a high kidney quality. Figure 2.9 represents expected wait time and utility of the entire population (11 regions) across different risk preference levels represented by $\alpha_c$. Risk neutrality is represented by $\alpha_c = 0.66$ since this value yields the wait time in equation 2.3 to be equal to the expected wait time. As shown in Figure 2.9, decreasing the value of $\alpha_c$ represents and increasing willing to risk death on the waitlist in exchange for waiting for a higher kidney quality. On the other hand, a risk-averse decision maker ($\alpha_c > 0.66$) has to wait less to receive a kidney transplant, but at the expense of accepting also lower quality kidneys. Deviation from risk neutrality results in a reduction of expected utility. Our empirical analysis supports the assumption of having risk neutral social planner to receive the highest utility and find the social optimum.

2.9. Concluding remarks and future work

This study attempts to clarify the effect of performance assessment and different kidney allocation schemes on donor kidney and patient acceptance decisions. It is difficult to perform a direct empirical comparison for before and after the introduction of such a measure, because many factors change from year to year. The new modeling framework to accept deceased donor kidneys for candidates on the kidney transplant waiting list provides a tool to perform this comparison. It also sheds light on how changes affect the acceptance of patients by
The novelty of our work is aggregating multiple stages of difficult kidney transplant decision making from the perspective of different decision makers. We analytically inspect the effect of performance assessment that follows the citation policy to penalize underperforming providers on the social welfare. The efficiency and equity of the citation policy are highly correlated with designing well-established risk-adjusted models. To improve the effectiveness and fairness of this policy, we recognize fundamental components required to be reflected in the risk-adjusted model. As such, we show that as the kidney allocation rule changes, an update in the citation policy is needed to maintain its efficiency. We propose a unique closed-form solution to accept deceased organs. Our model considers several key factors: 1) heterogeneity for both kidney quality and candidate health, 2) organ supply, and 3) the role of decision maker’s risk preference in accepting offered organs.

The model balances the trade-off between the benefit and the cost of kidney transplantation. The benefit is a life-year gain from receiving kidney transplantation which depends on the quality of the accepted donor kidney. The cost includes candidate’s health deterioration as she waits for a better offer. A socially-optimal kidney transplantation decision depends on

Figure 2.9. Expected wait time and utility across different level of risk
candidate’s health and local donor kidney supply, which maximizes system’s welfare utility function. The optimal citation policy needs to be designed with the goal of minimizing the social loss resulting from the misalignment between transplant centers and social planner’s objectives and goals.

Our empirical study presents several important insights regarding effective and efficient kidney transplant decision and outcome oversight. First, we observe from our data that candidate’s blood type and region influence wait time significantly. However, the quality of accepted kidneys is almost the same among recipients with different blood types in different regions. This observation suggests that the role of the candidate’s offer rate which is the reflection of donor kidney supply is currently neglected in making the best transplant decision. The empirical results from our model indicates that the factors that influences candidate’s wait time such as blood type and region supply should be considered in making the optimal kidney transplant decision. Furthermore, our empirical study reveals that transplantation outcome assessment has been effective in providing for 42% of recipients socially optimal transplantation decisions. However, the current regulations for evaluation transplant center’s outcomes are risk-adjusted only based on recipient and donor risk factors.

Our model suggests that regulators might be more effective if they also take adjustment based on organ availability for eleven regions and four different blood types into account. This observation might reduce the tendency of risk-averse behavior among decision makers which currently leads suboptimal results. The other advantage of supply-based adjustment is that it can be performed under any kidney assignment rule by assessing the effects on individual candidate’s supply or offer rate. For instance, the post-KAS benefits the top 20% of patients by providing higher access to the kidneys whereas it has the opposite effect on the remaining candidates. However, the regulators still apply the same evaluation metric as before for transplant center’s outcome assessment. Not adjusting for the fact that the new kidney assignment causes changes in individuals offer rate might motivate transplant centers to limit access to the care for high-EPTS patients. The main reason is that high-EPTS patients do not have access to high-quality kidneys, so their post-transplant outcome
could be less desirable. If this concern is not reflected in the outcome assessment, it could encourage transplant centers to delay transplantation for these patients leading to potentially increased waitlist mortality, or the centers may even decide to remove enlisted high-EPTS candidates from the waitlist.

We also show that risk neutrality is the best risk preference for the decision maker to maximizes social welfare utility. Risk-seeking and -averse behaviors result in having suboptimal outcomes. Our empirical study demonstrates that after CoP, 4 regions out of 11 have adjusted their risk preference class to risk neutrality. The remaining 7 regions have become risk seeker for waiting more on the waitlist which could support the assumption of being selective for accepting offered donor kidney as a result of oversight policy. Even though our data analysis indicates that 58% of recipients are impacted by receiving sub-optimal kidneys, in general, the social loss and deficiency have decreased across all 11 regions. We also observe an increase in the degree of benevolence among 11 regions. Overall, based on our analysis, after 2007 as a result of CoP policy the total of 34,789 life years have been saved across all recipients who received donor kidney transplantation.

Although this research is carefully prepared, we are still aware of its shortcomings that place restrictions on our methodology and conclusions. First of all, in our model we assume that for each offer a new kidney quality is drawn from the kidney quality distribution. This allows us to derive a closed for solution, but it does not represent the fact that in reality rejected kidneys are re-offered several times, and that the kidney quality is reduced in this time consuming process. This limitation might influence the validation of all derivations and outcomes, if the goal of the researcher is to consider donor kidney discard rate which is beyond the purpose of our work.

Second, to allocate available donor kidneys to eligible candidates we use random kidney assignment in a fixed set of “active” candidates. We choose this strategy to simplify our analysis to model kidney transplant acceptance decisions rather than modeling kidney assignment. However, this assumption does not consider the correlation between a candidate position on the wait list and her individual donor kidney offer rate making this approach
appropriate to reason about the complete system, but not at the level of the individual candidate.

Third, we suppose that the decision makers are making kidney transplant decision in response to allocation and outcome monitoring systems implemented by the social planer, but are not affected by decisions made by competing centers or candidates. It would be interesting to investigate the role of competition among candidates, and the effects of information sharing and disclosure of kidney acceptance thresholds with the social planer and other decision makers.

Moreover, the impact of transplant center’s outcome and regulatory oversight can be investigated from patient and insurer perspectives. Beside meeting regulators oversight assessment policy which may incentives transplant center to choose high quality donor kidney and patient, they also need to compete for having a good market share. This competition among transplant centers might offset the unintended effect of regulatory oversight for cherry-picking patients and donor kidneys.
3.1. Introduction

The US currently faces a national kidney shortage. Over 100,000 patients are on the waiting list and on average over 3,000 new patients are enlisted each month. More than 4,000 patients pass away while waiting for a lifesaving kidney transplant and over 3,000 became too sick and are removed from the waiting list. Despite this shortage, approximately one in five kidneys recovered from deceased donors are discarded in the US [50].

To understand the reasons for such a high discard rate, it is necessary to understand the kidney allocation and offering process. The most important criteria for kidney allocation are (1) medical compatibility (e.g., blood and tissue type, medical needs of the patient, body size), (2) geographical factors (distance between donor and transplant hospitals), and (3) the position on the waitlist (e.g., waiting time, points). The offering process starts with local patients who are medical compatible and have the highest priority on the waitlist. If local allocation is not successful, then the organ is offered in the region (the US is divided into 11 transplantation regions) and finally nationwide. The reason for prioritizing local patients in the kidney assignment process is to reduce the time between harvesting the organ and the implantation. This time is called Cold Ischemia Time (CIT) and plays an essential role in kidney functioning after transplantation. Figure 3.1 represents the average CIT and wait time in US.

When CIT reaches 24 hours, it is typically hard to find a patient to accept the offer. Normally, after 48 hours passed by, all kidneys that failed to be accepted will be discarded [99]. As indicated in [41], the regional variations in kidney outcomes have been observed
and those regions with longer CIT are more likely to also have lower post-transplant kidney survival rates. This results in the suggestion that reducing kidney CIT through managerial improvements could be a cost-effective way to improve the current transplantation system.

Transplant surgeons and regulators have expressed their concerns regarding high observed kidney discard rates in the US. The most common reason for donor kidney refusal is the heterogeneity of donor kidneys concerning their quality. Data shows that transplant surgeons would rather reject low-quality kidneys for a relatively healthy patient in the hope of receiving a better offer in the future [36]. Marginal kidneys are believed to be still beneficial and transplantable for certain patients. However, allocation and transplantation has to be done in a timely manner so the kidney does not deteriorate and become unusable. Efficiently allocating marginal kidneys may help in reducing kidney discard rates.

In addition to the kidney quality, kidney acceptance and discard may also be affected by the allocation process itself [42]. There are several evidence that kidneys rejected early on in the allocation process are less likely to be accepted later on. Even almost identical kidneys from the same donor may receive different attention. For instance, it has happened that
one kidney of a pair is accepted early on in the allocation process, whereas the other one accumulates a very long CIT or even gets discarded. It seems like early rejection of donor kidneys by surgeons may effectively influence subsequent decisions by other surgeons [107].

Another concern is increasing risk aversion of transplantation centers due to Program-Specific Reports that evaluate post-transplant outcomes. These may provide incentives for the centers to demand higher-quality kidneys. Consequently, they might turn down kidneys that pose a risk of negatively impacting the evaluation of their post-transplant outcomes [12, 29, 42, 74–76, 88].

Patients may react to long wait times in their home region by either changing their acceptance strategy or by trying to improve their chances to receive a transplantation earlier by moving to a region with shorter wait times or by enlisting in multiple transplant centers [18]. Multiple listing involves registering more than one transplant centers. With the goal of receiving faster kidney transplants, patients would consider multiple enlisting at different regions rather than the same region due to kidney allocation distance priority rules. More than 4% of the patient waiting for kidney transplant are multiple listed which is the highest rate among all organs [9].

As with any transplant enlisting, the patient must complete evaluation tests and be committed to transplant center’s regulation, such as ability to arrive to the transplant center within a certain time limit to be admitted by the center. This process can be quiet costly, since most insurance companies may not reimburse the cost of additional evaluations [88, 89]. It is also important for a patient to learn if post-transplant care can be transferred to a center closer to her residence.

The Organ Procurement and Transplantation Network (OPTN) is in charge of of kidney assignment in the US. To address the high kidney discard rate (about 20%) in the US, OPTN has recently made major changes to modify the kidney assignment rules, by introducing a new Kidney Allocation System (KAS) [53]. OPTN has also modified the assessment metrics of transplant centers by using a Bayesian approach as opposed to frequent metrics used before [39, 70].
In this chapter, we introduce a flexible simulation model that can be used to analyze the effect of changes to the kidney allocation system and the offering process. The simulation model takes into account patient’s health, donor-kidney quality deterioration during the allocation process, and also supply and demand. Furthermore, the model considers the chance that a matching kidney cannot be accepted because of other reasons (e.g., short-term sickness of the patient, insufficient surgical resources, etc.), as well as the impact of information sharing on the efficiency of the offering process.

Using parameters estimated from data provided by United Network of Organ Sharing (UNOS) and SRTR, we apply the simulation model to investigate two important trends in kidney transplantation.

(1) **Multiple-listing:** Transferring to a region with shorter wait time or waitlisting in multiple regions can help a patient by increasing her chance to receive a kidney transplant earlier. Consequently, the patient can improve post-transplant outcome due to less health deterioration of staying on dialysis. However, it is not easy to develop a strategy to guide the patient’s decision for transferring or multi-listing. We formulate the decision as a utility
maximization problem under a set of budget, distance and facility constraints at the regional level. Supply and demand vary widely across the 11 regions in the US and for different blood types which results in widely varying wait times which should also lead to different expected utilities and different optimal kidney acceptance strategies expressed in the optimal kidney quality thresholds. To derive patient’s utility for different regions, we use the simulation model to obtain utility under individualized optimal kidney transplant acceptance decisions based on patient’s health status, and supply and demand for patient’s blood type in different regions. We use the obtained information to solve the optimization problem and derive an optimal regions selection policy.

(2) Information technology: Rapid and precise communication between UNOS and transplant centers is necessary to make the process of organ allocation more efficient. This even becomes more important in the face of multi-listed patients. UNOS has the goal to increase the use of information technology in the process of organ allocation and transplantation. They have implemented a secure online-based system that collects data to enhance the capability of the transplant system and not reduces patient’s chance of receiving a life-saving organ. As technology has evolved, UNOS also encourages for developing and using newer technology such as mobile devices for faster and efficient consideration of donor kidney offers that may results in higher kidney utilization rate [90]. Mobile devices will make it easier to collect availability of patients for transplantation (e.g., via an app). Using this information, the OPTN would be able to allocate the kidney faster, reducing kidney deterioration and discard. In the ideal case of perfect information, OPTN could find the first patient on the waitlist who will accept the kidney instantly which would reduce discard to a minimum. The simulation will evaluate the effect of a realistic case of limited information sharing.

3.2. Literature Review

In this section, we review studies relevant to this chapter. Most literatures fall within one or both of two streams of research concerned with decision-making for accepting kidneys and designing the allocation process.
Focusing on decision-making, Ahn et al. [7] develop a theoretical model that considers patient health in making an acceptance/rejection decision concerning the quality of offered kidney. Their analysis reveals that a relatively-healthy patient can afford to be selective about the quality of donor kidneys and so expect to receive a better post-transplant outcome by accepting a high-quality kidney.

Howard et al. [36] apply the optimal stopping problem to model organ acceptance decisions by patients. He proposes a model in which a transplant surgeon is in charge of accepting or rejecting an offered liver to the patient. He concludes that the surgeon desires to reject low-quality livers for a relatively-healthy patient in the hope of receiving better offers in the future.

Alagoz et al. [8] consider the optimal time of accepting living-donor transplantation. They formulate their problem using a Markov Decision Process (MDP) to maximize patient’s total reward. Their computational experiment confirms that the optimal policy is usually of control-limit type.

To analyze the allocation process, Zenios et al. [106] proposes a dynamic resource allocation that maximizes patient’s life expectancy from receiving a kidney transplant while minimizing the inequity. They construct a simulation model that shows the currently-employed organ allocation policy, boosts patient quality-adjusted life expectancy, and reduces the expected waiting time.

Su et al. [81] introduce a queuing model that study the effect of patient choice on organ allocation system analyzing the kidney rejection rate. They also evaluate the performance of the waiting system under both FCFS and LCFS policies. Their finding of analyzing these two extremes conclude that LCFS is efficient in opposed to FCFS. In fact, in contrast to LCFS, the FCFS settings desensitize patients to refuse low-quality kidney, so they subsequently observe low kidney utilization. On the other hand, they show that the LCFS policy obtains optimal organ utilization.

Su et al. [82] investigate the role of patient choice in kidney allocation. By using a sequential stochastic assignment model, they address the conflict between the patient choice...
and the social welfare. Their analysis considers two schemes. The first scheme develops under the assumption that patients will accept all kidneys offered. The first-best solution is to find an allocation policy that maximizes the social welfare. By introducing patient choice, they modify the first-best policy to achieve a second-best policy. As a result, they introduce an incentive compatibility condition, which forces the allocation policy to be designed in such a way that it assures that patients will accept all kidney offers.

Su et al. [83] introduce a mechanism design model that takes patient choice into account in the organ allocation system. Patients state the types of kidney they desire to receive upon joining the kidney transplant waiting list (not at the time of donor kidney offer) and join the queue that serves the declared kidney type. That way, the model reduces the long searching process, by identifying appropriate patients who desire to accept retrieved donor kidneys more effectively.

Bertsimas et al. [14] study geographical disparities in access to deceased donor kidneys. They use a fluid approximation to formulate the optimal way a patient can be enlisted in the waiting lists of multiple transplant centers. Patient’s perspective is to maximize life expectancy while minimizing the congestion cost. By combining analytical, simulation and numerical results, they show that multiple listing greatly promotes geographical equity and increases the donor kidney supply. Having more donors lead to a higher transplant rate and lesses the patient mortality rate on the kidney transplant waiting list.

As Koizumi et al. [41] report, regional variations in kidney outcomes have been observed, but the main reason behind it is unknown. Their findings revels Significant CIT variations across regions for both donor kidney and liver. Specifically, they find regions that have longer CIT are more likely to have a lower post transplant kidney survival rate. They suggest managerial improvements can be a cost-effective choice to enhance the current transplant system performance and potentiality reduces kidney discard rates.

Similar to this work, Ruth et al. [67] propose a simulation model for the organ allocation process. Their model assess the effect of changes in diseased donor kidneys on the waiting list. They found that under the organ allocation conditions in 1985, the length of waiting list
would continue to grow. The simulation focuses on waitlist length, while the simulation in this paper gives a more complete picture by also considering the effect of the patient decision rule and incorporating expected post-transplant utility.

3.3. Model description

We model the waitlist as a queue with patients joining when they enroll in a transplantation center and leaving when they accept an offered kidney or when they get too sick for transplantation. In the following we discuss the components of the simulation model including patients, kidneys, the allocation process, and post-transplant utility as shown in Figure 3.3.

3.3.1. Patients

We assume that patients can be split into several groups of competitive patients who can receive the same type of donor organ depending on blood type, HLA match, and other criteria. We will model each group separately and if there is interaction between groups (e.g., some patients with blood type AB may receive organs from donors with any blood type), then we will consider it by adjusting supply to the individual groups.

Each competitive patient group is modeled by a queue. While any process can be used, we assume here a Poisson process with the arrival rate of $\lambda$. Patients are assumed to join with a health status $h_0$ representing the remaining time they can survive on dialysis when they join. We model the distribution of $h_0$ in the patient population using a Weibull distribution, often used in survival analysis to represent time-to-failure since it is able to express failure rates that are decreasing, constant, or increasing over time. The health for a random patient can be seen as a realization of a random variable $H \sim \text{Weibull}(a, b)$, where $a$ and $b$ are the scale and shape parameters, respectively.

Patients depart from the waitlist if (1) they receive a transplant or (2) they leave the queue due to insufficient health. Since $h_0$ is the time the patient can survive on dialysis when she joins the waitlist (i.e., waited so far zero years), the actual health after waiting $w$ years...
is $h_w = h_0 - w$ which means the patient will leave the waitlist at the latest when $w = h_0$.

3.3.2. Kidneys

The kidney arrival process can follow any process and we use a Poisson process with arrival rate $\mu$. OPTN defined the Kidney Donor Profile Index (KDPI) which represents a quality metric of the kidney that incorporates ten clinical donor factors to estimate how long a kidney is expected to function [57]. By construction, KDPI is close to uniformly distributed over all kidneys harvested in a given year. Following KDPI, we model the quality of an arriving donor kidney shown with $q_0$ as the realization of a random variable $Q \sim \text{Unif}(0, 1)$. Here we use 0 to represent the worst kidney quality and 1 as the best.

For the case of donor kidney shortage we have $\mu < \lambda$. The queue still will only grow to a finite size, since a larger waitlist results in longer wait times which in turn will increase the rate of patients leaving because they are not healthy enough to receive a transplant.

3.3.3. Kidney allocation and acceptance

In the basic allocation system, when a new donor kidney becomes available, its quality $q_0$ is assessed and the kidney is simultaneously offered to a group of $g$ patients with a given window to decide. OPTN currently uses a group size of five and a time window of one hour.
At the time of offer, the kidney has accumulated CIT $t$ and the quality is reduced to $q_t$. We model the decision by the patient and surgeon using a threshold strategy governed by rejecting the offer if $q_t < k$, where $k$ is the set threshold. In case that the kidney meets the quality threshold (i.e., $q_t \geq k$), the offer will only be accepted with probability $p(\text{trans})$. This probability represents the fact that the patient or the surgeon may decide against the kidney for reasons not explained by purely kidney quality. Examples are that the patient is currently not available or that resources needed for the surgery cannot be provided in time. If nobody in the group of $g$ patients is able to accept the kidney after the alloted time, then the kidney is offered to the next group of $g$ patients on the waitlist. Over time, the kidney deteriorates. We model this deterioration as $q_t = q_0 (1 - \delta)^t$, where $\delta$ is a deterioration factor and $t$ is the accumulated CIT in hours. For convenience, we measure time here as multiples of the time allowed for one round of offering. If the patients have one hour to decide, then $t$ represents accumulated CIT in hours. When $q_t$ becomes zero, then the kidney needs to be discarded.

Patients choose their decision threshold $k$. The threshold is influenced by the patient’s health $h_0$, since a patient who has more time left on dialysis will be able to wait for a better quality kidney. We model this relationship by choosing $k$ for each patient from a random variable $K \sim \text{Unif}(0,1)$ which is correlated to the patient’s $h_0$ with Spearman’s rank correlation coefficient $\rho_{H,K}$.

3.3.4. Patient’s post-transplant utility

A patient’s post-transplant utility depends on the quality of the transplanted kidney $q_t$, patient’s health when she joins the wait list $h_0$, and the remaining time she waits for the transplant since she receives the first offer $w$. We use

$$U(q_t, h_0, w) = B(h_0, q_t) \cdot D(h_0, w),$$

(3.1)

where $B(h_0, q_t)$ is the patients utility if she receives a kidney with quality $q_t$ right after she joins the waitlist without waiting. $D(\cdot)$ represents a cost in the form of degradation factor.
due to waiting $w$ for the kidney. $B(\cdot)$ can be defined in the form of a logistic regression for survival proposed by Cox [65], which models the conditional odds of dying at any time point given survival up to that point.

$$B(h_0, q_t) = \frac{m(h_0)}{1 + e^{\beta(q_t - \alpha)}},$$

(3.2)

where $m(h_0)$ indicates the transplant outcome for a patient with health level $h_0$ who received a perfect kidney ($q_t = 1$) right after her first offer ($w = 0$). Natural, $m(h_0)$ is increasing with $h_0$. The benefit function therefore increases with patient’s health $h_0$ and also kidney quality $q_0$, since $\frac{\partial B(h_0, q_t)}{\partial q_t} > 0$.

For patient’s health deterioration factor we use

$$D(h_0, w) = \left(1 - \frac{w}{h_0}\right)^\gamma.$$  

(3.3)

The deterioration factor in Equation 3.3 equals one when the wait time is zero ($w = 0$). On the other hand, if the patient decides to wait for a very high-quality kidney, she cannot survive longer than $w = h_0$. In that case, equation 3.3 becomes zero. In equation 3.3, $\gamma$ controls the rate of deterioration. For $\gamma = 1$ the deterioration is linear, $\gamma > 1$ results in initially faster deterioration and for $\gamma < 1$ the deterioration is initially slower and then speeds up.

### 3.4. Applications and numerical results

We present three applications of the simulation model in this section. The first two application considers decisions at the patient level. If we assume that the patient wants to maximize the expected patient’s post-transplant utility, then we can use simulation to find the optimal threshold, $k^*$ for a patient with a given current position on the waitlist, a current health, and who is listed in a given region.

The second application provides a strategic guideline to support a patients choice for changing regions or enlisting in multiple regions. According to the [54], the patient can move
to a different region or apply for being enlisted in more than one center while preserving her current position in the national waiting list provided that she meets certain OPTN conditions. For an individual patient, we present an optimal region selection policy based on patient’s constraints over 11 US regions. The model can also be easily extended to inform optimal selection policy at the level of local Organ Procurement Organization (OPOs) or even transplant centers.

The third application of our simulation model is practical for an organ allocation agency to efficiently identify patients to whom a donor kidney can be offered using up-to-date information shared via app technology. The goal is to improve social welfare through increasing patient’s post-transplant utility and kidney utilization rate. First we discuss how the simulation model parameters are estimated.

3.4.1. Parameter estimation

We use data from UNOS and SRTR to estimate model parameters. The UNOS dataset is publicly available through its website [91]. We extract UNOS data for the year 2015 to estimate the waitlist additions and donor kidney supply. For kidney quality (KDPI) and wait time calculation, we use values reported by SRTR. The SRTR data system contains detailed medical and demographic data for all donors, waitlisted patients and transplant recipients in the United States, between October 1987 and the end of 2016. The used dataset consists of 395,950 patients who are first-time recipients of deceased donor kidney transplants.

In this chapter we report results for blood type A, but results for other blood types can be obtained in a similar fashion. The annual reports data from UNOS provides waiting list addition and removal statistics based on different factors such as patients’ blood types and regions. We use this data to estimate patients’ arrival rate $\lambda$ to the waiting list in each period. To estimate kidney arrival rate $\mu$, we use the donor kidney report of UNOS and the clinical data of SRTR. Table 3.1 shows donors and patient arrivals relevant for blood type A. Since patients with blood type A can receive organs from donors with blood type O, these are also included in the table. Based on SRTR data, patients with blood type A receive 94%
<table>
<thead>
<tr>
<th>Region</th>
<th>Donors O</th>
<th>Donors A</th>
<th>$\mu$</th>
<th>$\lambda$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>143</td>
<td>118</td>
<td>228</td>
<td>537</td>
</tr>
<tr>
<td>2</td>
<td>473</td>
<td>387</td>
<td>746</td>
<td>1769</td>
</tr>
<tr>
<td>3</td>
<td>625</td>
<td>461</td>
<td>892</td>
<td>1680</td>
</tr>
<tr>
<td>4</td>
<td>421</td>
<td>303</td>
<td>587</td>
<td>1154</td>
</tr>
<tr>
<td>5</td>
<td>636</td>
<td>452</td>
<td>875</td>
<td>1910</td>
</tr>
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<td>6</td>
<td>165</td>
<td>132</td>
<td>265</td>
<td>377</td>
</tr>
<tr>
<td>7</td>
<td>300</td>
<td>239</td>
<td>461</td>
<td>1008</td>
</tr>
<tr>
<td>8</td>
<td>296</td>
<td>226</td>
<td>436</td>
<td>688</td>
</tr>
<tr>
<td>9</td>
<td>146</td>
<td>114</td>
<td>220</td>
<td>735</td>
</tr>
<tr>
<td>10</td>
<td>349</td>
<td>284</td>
<td>548</td>
<td>1040</td>
</tr>
<tr>
<td>11</td>
<td>423</td>
<td>304</td>
<td>588</td>
<td>1080</td>
</tr>
</tbody>
</table>

Table 3.1. Estimation of annual kidney supply $\mu$ and patient arrival rates $\lambda$ for patients with blood type A over the 11 US regions (2015).

of the organs from donors with blood type A and an additional 2% of the organs from donors of blood type O. This is reflected in the kidney supply $\mu$. We perform the simulation using the information in Table 3.1 for the estimation of kidney supply and patient arrivals across 11 regions. Note that the supplies presented in Table 3.1 ignore that kidneys can be shared between regions. This simplification can be justified by the fact that high-quality kidneys recovered in any region have a high chance to be accepted locally, while low-quality kidneys are offered regionally first and the are offered nationwide already with a relatively high CIT, reducing their impact on the overall system utility.

Following the current offering scheme, we use the patient group size $g = 5$. We set the kidney degradation rate $\delta$ to 5%. This reflects reports that organs are rarely used after a CIT of 48 hours [41]. At $\delta = 0.05$ the quality of the kidney has deteriorated to $(1 - 0.05)^{48} = 8.5\%$ of its initial quality.

In our work, we set the transplantation probability to $p(\text{trans}) = 0.8$ for the simulations. However, the probability may differ between regions and an estimate could be obtained from offer data.
For \( m(h_0) \), the health outcome of a patient with \( h_0 \) receiving a perfect kidney we use a simple linear function \( m(h_0) = \theta h_0 \). For the simulations we use \( \theta = 5 \).

The parameters \( \alpha, \beta \) and \( \gamma \) for the benefit function \( B(h_0, q_t) \) and the cost factor \( C(h_0, w) \) can be estimated if outcome data including realized post-transplant survival is available. However, since this data was not available in the obtained data, we use for the simulation \( \alpha = 0.4, \beta = 8 \) and \( \gamma = 0.5 \).

We add patients to the wait list with a health \( h_0 \) drawn from a random variable \( H \) with a Weibull distribution. We use a scale parameter \( a = 8 \) and a shape parameter \( b = 2 \) to get an average health of close to 7 years and around 90% of the population below 12 years. We use a Spearman’s rank correlation \( \rho(H, K) \) of 0.2 which is close to the correlation between accepted kidney quality and patient health observed in the data.

3.4.2. Regions selection and multiple-listing

To assist the patient to identify a region to transfer to or with identifying a set of regions for multiple-enlisting, we present a simple, yet informative optimization model that maximizes patient’s post-transplant expected utility given constraints on distance \( D \), budget \( C \), and performance \( P \). To formulate our multiple-listing problem, we define the binary variable \( r_i \) which is equal to one if region \( i \in I = \{1, 2, \ldots, 11\} \) is selected and 0 otherwise.
\[
\begin{align*}
\max \quad & \sum_{i \in I} U_i(k^*_i)r_i \\
\text{s.t.} \quad & \sum_{i \in I} c_ir_i \leq C \\
\quad & \sum_{i \in I} d_ir_i \leq D \\
\quad & \sum_{i \in I} p_ir_i \geq P \\
\quad & \sum_{i \in I} r_i = 1 \\
\quad & r_i = 0 \quad \text{or} \quad 1
\end{align*}
\] (3.4)

The first constraint makes sure that the solution satisfies the total budget \(C\) of individual patient on the evaluation, traveling and loading expenses. The second constraint considers the maximum distance \(D\) the patient desires to travel. The third constraints consider patient’s expectation from region’s performance \(P\) and finally the last constraint restricts the model to select only one region. We execute the optimization iteratively. At each run, the model finds the region that maximizes patient’s expected post-transplant utility under the given constraints represented as the only 1 entry in the decision vector \(r\). After each optimization run, we remove the selected region and update the remaining budget as \(C = C - \sum_{i \in I} c_ir^*_i\) to find the next region. The model returns no region when it fails to find any region that satisfies the patient’s constraints. The generated optimal solution at each run forms a list that provides multiple-listing options to the patient in a descending order of post-transplant expected utility.

The objective function uses the maximum utility that a given patient can obtain by receiving transplant in different regions. These utilities can be obtained through the simulation model. The simulation model is run for each region to find the the optimal kidney quality threshold that maximizes the patient’s post-transplant utility. Without loss of generality we
perform the simulation for a target patient with blood type A with a remaining one life-year on dialysis $h_0 = 1$. We fill the waitlist with randomly generated patients and place the target patient at position $j = 100$ in the wait list. We perform the same simulation 100 times each for the decision threshold values $k \in \{0, 0.1, 0.2, \cdots, 0.9\}$ and average the results of the 100 runs.

In Table 3.2 we report the results for the best $k$ resulting in the largest average utility for each region. Note that the reported wait time (in years) is very short, since it only includes the time from when the patient already reached position $j = 100$ in the wait list. For instance, if the target patient is enrolled in region 6 a threshold of $k = 0.65$ is optimal which leads to a utility of 9.6 years, whereas if she is enlisted in region 2 the optimal decision can be as high as 0.85 with a utility of 13.22 years.

### 3.4.3. Information sharing to improve allocation efficiency

Information sharing, where the transplantation center and the patient share up-to-date information with OPTN, has the potential to speed up the kidney allocation process and thus reduce cold ischemia time (CIT). The following information can be shared:

1. Patient’s acceptance threshold $k$: Each patient reports their kidney quality acceptance threshold $k$ decided by herself and her physician.

2. Patient’s additional decision criteria: Patient’s and surgeon’s decision can be affected by information not included in the kidney quality assessment (KDPI). Having more standardized quality parameters, where the patient can prespecify what she accepts, would improve kidney allocation. Under complete information, OPTN would able to instantly identify the patients who would accept the kidney.

3. Patient’s current availability: An up-to-date indication if the patient can currently receive a transplantation. Factors include current health and traveling.

4. Transplant center’s availability: Considers the availability of transplant center’s facility such as preppeared operation rooms, free surgeons, nurses and staffs for performing the surgery in time.
Table 3.2. Optimal post-transplant utility $U$ under the optimal decision threshold in different regions for a patient in waitlist position 100.

<table>
<thead>
<tr>
<th>Region</th>
<th>$\mu$</th>
<th>$k^*$</th>
<th>$q_t$</th>
<th>w</th>
<th>U</th>
<th>$n_{reject}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>228</td>
<td>0.60</td>
<td>0.76</td>
<td>0.53</td>
<td>9.11</td>
<td>17</td>
</tr>
<tr>
<td>2</td>
<td>746</td>
<td>0.85</td>
<td>0.95</td>
<td>0.20</td>
<td>13.22</td>
<td>27</td>
</tr>
<tr>
<td>3</td>
<td>892</td>
<td>0.85</td>
<td>0.93</td>
<td>0.16</td>
<td>13.55</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>588</td>
<td>0.80</td>
<td>0.90</td>
<td>0.25</td>
<td>12.81</td>
<td>24</td>
</tr>
<tr>
<td>5</td>
<td>875</td>
<td>0.85</td>
<td>0.92</td>
<td>0.16</td>
<td>13.50</td>
<td>24</td>
</tr>
<tr>
<td>6</td>
<td>255</td>
<td>0.65</td>
<td>0.76</td>
<td>0.49</td>
<td>9.65</td>
<td>19</td>
</tr>
<tr>
<td>7</td>
<td>461</td>
<td>0.75</td>
<td>0.80</td>
<td>0.31</td>
<td>12.00</td>
<td>21</td>
</tr>
<tr>
<td>8</td>
<td>436</td>
<td>0.75</td>
<td>0.84</td>
<td>0.34</td>
<td>11.90</td>
<td>21</td>
</tr>
<tr>
<td>9</td>
<td>220</td>
<td>0.60</td>
<td>0.67</td>
<td>0.57</td>
<td>8.87</td>
<td>17</td>
</tr>
<tr>
<td>10</td>
<td>548</td>
<td>0.80</td>
<td>0.92</td>
<td>0.26</td>
<td>12.70</td>
<td>25</td>
</tr>
<tr>
<td>11</td>
<td>588</td>
<td>0.80</td>
<td>0.92</td>
<td>0.24</td>
<td>12.84</td>
<td>24</td>
</tr>
</tbody>
</table>

The first information is used in the acceptance decision where the patient requires $q_t \geq k$ before considering the organ. Perfect information, where OPTN knows all patients threshold, can speed up donor kidney assignment, by only offering the kidney to patients with $k \leq q_t$. The lack of complete information for 2–4 is reflected in the simulation model by the transplantation probability

$$p(\text{trans}) = p(\text{accept}) p(\text{patient}) p(\text{center}),$$

where the three probabilities represent three independent events which have to occur for the transplantation to be performed. Under perfect information, OPTN knows at any time for all patients acceptance thresholds $k$, any additional requirement for the organ and if the patient and center are available. Therefore, OPTN can directly identify the first patient on the waitlist who will receive the transplant. This will effectively reduce CIT $t$ to the minimum needed to extract the organ and perform the transplantation. This can be equivalently expressed by setting group size $g$ to infinity indicating that we can go through the
whole waitlist instantly. In a more realistic setting with some potentially imperfect information sharing, patients can be identified faster using the shared information expressed by an increased groups size that can be processed per hour.

We report in the following the results for patients of blood type A in region 6. We initialize the waiting list with 1000 patients and run it till the waitlist length stabilizes at around 1800 patients (200 month). We report results after this warm-up period averaged over 300 month. We vary the group size to $g$ to represent varying levels of information sharing. The baseline is the currently used group size of $g = 5$.

Table 3.3 shows the impact of information sharing expressed in the form of group size, which reflects how many patients on the waitlist can effectively be considered per hour. At the baseline group size of five, the average quality of accepted kidney is 0.66 which leads to receiving the average utility of 10.76 years per transplanted patient. The kidney can travel as far as 45 patients on the waitlist and is accepted on average by the 6th patient who waited 3.84 years. Table 3.4 presents kidney utilization and waitlist mortality rate in addition to the transplant rate. The kidney utilization rate increases significantly as the group size of patients expands. As Figure 3.4 demonstrates, the minimum improvement in the kidney transplant rate is 17% which can be obtained by slightly expanding patient’s search group size, and it reaches to 47% when the use of information is perfect. On the other hand, the waitlist mortality rate decreases by 7% when the group size is 10, and the reduction can be as high as 21%.

3.5. Concluding remarks

The first contribution of this research is a simulation model developed to provide an optimal deceased donor kidney acceptance guidance for the decision makers. The major challenge of modeling organ acceptance/rejection problem is incorporating real-world conditions and situations associated with making an important life-saving decision. For this reason, our primary intension as the main novelty of this work is to recognize, aggregate, and implement all essential elements that contribute to kidney selection criteria. The proposed model allows
<table>
<thead>
<tr>
<th>Group size $g$</th>
<th>Waitlist position (mean)</th>
<th>Waitlist position (max)</th>
<th>Average $q$</th>
<th>Average patient utility (year)</th>
<th>Average wait time (year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>6.00</td>
<td>45</td>
<td>0.66</td>
<td>11.03</td>
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<td>8.00</td>
<td>80</td>
<td>0.62</td>
<td>10.99</td>
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<tr>
<td>20</td>
<td>10.00</td>
<td>119</td>
<td>0.60</td>
<td>10.9</td>
<td>3.39</td>
</tr>
<tr>
<td>100</td>
<td>22.00</td>
<td>344</td>
<td>0.57</td>
<td>10.82</td>
<td>3.07</td>
</tr>
<tr>
<td>$\infty$</td>
<td>58.00</td>
<td>1383</td>
<td>0.55</td>
<td>10.80</td>
<td>3.00</td>
</tr>
</tbody>
</table>

Table 3.3. The effect of information sharing on patient post transplant expected utility based on region 6 kidneys supply and demand

<table>
<thead>
<tr>
<th>Group size $g$</th>
<th>Kidney utilization rate</th>
<th>Kidney discard rate</th>
<th>Waitlist removal rate</th>
<th>Kidney transplant rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>85.0%</td>
<td>15.0%</td>
<td>8.9%</td>
<td>17%</td>
</tr>
<tr>
<td>10</td>
<td>90.9%</td>
<td>9.1%</td>
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<td>94.3%</td>
<td>5.7%</td>
<td>7.9%</td>
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<tr>
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<td>1.5%</td>
<td>7.3%</td>
<td>23.8%</td>
</tr>
<tr>
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<td>99.98%</td>
<td>0.02%</td>
<td>7.1%</td>
<td>25.2%</td>
</tr>
</tbody>
</table>

Table 3.4. Kidney utilization, waitlist, and mortality rates in region 6.
for diversity in patients’ health and kidney’s quality as well as their correlation. Moreover, we include the quality deterioration of kidneys caused by accumulating CIT as they navigate down the waiting list to find a recipient. In addition to all aforementioned elements, we also monitor patients’ health and availability together with human and facility resources to propose an optimal transplant solution. Our model also informs multiple-enlisting policy to patient. It offers a set of regions for patient for being enlisted given distance, cost and transplant volume constraints.

The second application of our simulation model proposed in this work draws attention to the social welfare aspect of kidney transplantation rather than focusing on finding an optimal solution as considered in the first model. We compare the social welfare results (i.e. donor kidney utilization and post transplant utility) in the presence and absence of perfect information submitted by the decision makers to the organ allocation policy maker. The perfect information is a reflection of patient’s willingness and transplant hospital’s readiness for performing a transplantation surgery. Collecting and sharing precise and timely data can provide a solid and valuable information to the policy makers. The valid and up to date data can be helpful to allocate retrieved organs more efficiently.

Beside the current regulations and rules for donor kidney assignment, the usage of tech-
technology in medicine would be a superior help. Designing an organ transplantation application for a smartphone device can provide a safe, easy and fast way to submit and update the required information in a timely fashion. The policymaker may wish to establish a ground rule that all patients and transplant centers need to follow to be considered for receiving offer. For instance, using a mandatory app technology and service, transplant centers can revise or verify their submitted data in a timely base (i.e. every day) after patient’s position on the wait list passes a certain threshold. The application may also provide a unique environment based on this data and other assignment policy to rank and find patients in less time. By using this technology, they might expand the group size of patients that simultaneously receive kidney offers to a large number. Subsequently, less time would be devoted to the transplant team for accepting or refusing an offer.

Deceased donor kidneys are an scarce organ resource and making a prompt decision can preserve their qualities for a long time. Accordingly, the kidneys can be offered to more patients which results in alleviating kidney utilization and declining kidney discard rate. Increasing the transplant rate improves social welfare utility and reduces the length of kidney transplant waiting list, time and mortality rate.
COST-EFFECTIVENESS OF ANTIBODY-BASED INDUCTION THERAPY IN
DECEASED DONOR KIDNEY TRANSPLANTATION IN THE UNITED STATES

This chapter is the result of collaborative research with Mehmet Ayvaci, Michael Hahsler, Tracy Giacoma, Robert S. Gaston, and Bekir Tanriover and was published in [26].

4.1. Introduction

For most patients in the United States with end stage renal disease (ESRD), transplantation is the preferred modality of treatment, as it not only improves survival and quality of life, but is also more cost-effective than dialysis [21, 25, 105]. In 2010, kidney transplant care, delivered to 30% of the overall ESRD population, accounted for only 10% (approximately $2.8 billion) of total Medicare ESRD expenditures [85, 94]. Long-term successful engraftment necessitates use of immunosuppressant drug therapy to prevent immunologic rejection and maintain allograft function. How best to initiate effective immunosuppression at the time of transplantation remains controversial, with some preferring perioperative administration of potent biologic agents to enhance immediate efficacy, and others targeting early attainment of therapeutic levels of maintenance agents (no-induction). Beyond these broader approaches, many choose antibody-based induction only in selected patients, perhaps when delayed allograft function is anticipated or in high immunologic risk recipients [28]. Contemporary options include both lymphocyte-depleting antibodies (polyclonal rabbit antithymocyte globulin [r-ATG] and monoclonal humanized anti-CD52 antibody [alemtuzumab]) and non-depleting monoclonal antibodies (interleukin 2 receptor antagonists [IL2-RA], such as basiliximab) [33, 86]. Based on perceptions of efficacy, lymphocyte-depletion is now the favored approach in the U.S. (57% of recipients in 2011), though the Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend IL2-RA as first line induction in
all types of donor-recipient profiles [28,46].

Beyond issues surrounding efficacy of individual agents across a wide range of risk factors, antibody-based induction therapy adds cost to the care of kidney transplant recipients, a consideration only rarely included in decision-making regarding its use. Since renal transplantation is largely financed through public funds in the U.S. (Medicare), I sought to define, from the payers perspective, the incremental cost effectiveness among different agents/approaches to early immunosuppressive treatment in risk-stratified DDRT recipients: no-induction, IL2-RA, r-ATG, and alemtuzumab.

4.2. Material & methods

4.2.1. Design and study cohort

The United States Renal Data System (USRDS) collaborates with the ESRD networks and the United Network for Organ Sharing (UNOS), and incorporates Centers for Medicare & Medicaid Services (CMS)s billing (including ICD-9-CM diagnosis and procedure coding, CMS revenue center codes, HCPCS procedure codes, all eligible claims and payments) records into the USRDS database. This combined database allows researchers to analyze characteristics and outcomes of ESRD and renal transplant recipients and related cost for the medical services provided to them. Medicare is the primary payer for more than 70% of the recipients and secondary payer for all others [85,101]. Medicare coverage lasts only three-years except for those patients older than 65 years or non-ESRD related disabilities [85].

This study is a retrospective cohort analysis of the USRDS database that initially included all adults who listed and underwent DDKT between January 1, 2000 and September 30, 2008 (N=66,204). Exclusion criteria consisted of patients: (1) undergoing multiorgan transplants; (2) undergoing repeat kidney transplantations; (3) receiving multiple induction agents and other research induction drugs; (4) for whom Medicare was not primary payer (or the Medicare payment for the initial transplant hospitalization less than $15,000). A total of 19,450 patients were included in the final analysis. The study population was initially
divided into two risk groups (low vs. high) based on donor and recipient risk factors for overall graft failure including death with function. The high-risk group is defined as having any of the following: panel reactive antibody (PRA) > 20%, African American [AA] race, cold ischemia time [CIT] > 24 hours (higher risk for delayed allograft function), recipients age > 60 (higher risk for death with functioning graft), kidney donor risk profile [KDPI] 50-100% (mainly representing the range for expanded criteria donor kidneys in old allocation system prior to December 4, 2014) [15, 16, 27, 33, 62, 101]. Each risk group was further stratified based on induction categories including no-induction, alemtuzumab, r-ATG, and IL2-RA.

These research activities are consistent with the Principles of the Declaration of Istanbul on Organ Trafficking, and were approved by the Institutional Review Board of the Columbia University College of Physicians and Surgeons.

4.2.2. Cost estimations

Programming experts in the Pharmaceutical Research Computing at School of Pharmacy, University of Maryland, constructed the cost files. A study index date (date of transplant) was identified for each individual. All Medicare payments on a per patient basis were summarized as monthly (person 30-day period files) reimbursements (the amount paid for physician/supplier and institutional claims) during the first 36-months following transplantation, with the index date as reference. The aggregate of average monthly reimbursements were then summed to obtain total cumulative cost for each of the induction categories (including reimbursement for transplant and subsequent hospitalizations, infection, rejection and return to dialysis). Reimbursement for induction treatment is bundled in the initial transplant hospitalization payment by Medicare. A three-percent inflation factor was used to adjust Medicare payments to 2013 U.S. dollar value. Additionally, Medicare reimburses organ acquisition cost to transplant centers (including the kidney recovery surgery and other related costs, such as tissue typing, candidacy evaluation services, registration fees, and preservation - perfusion costs). Since Medicare data does not include kidney acquisition cost, I added
estimated $30,000 per kidneys with KDPI < 50% and $35,000 per kidney with KDPI > 50% (relatively marginal organs) as a cost of organ recovery (charges of the Organ Procurement Organization to the transplant center) [101].

4.2.3. Effect estimations

Effect was defined as number of the months of functioning allograft within 36 months post-transplantation period. Censoring occurred on return to dialysis, re-transplant, death, or end of the study period.

4.2.4. Main outcomes

The primary outcomes were cumulative cost (C), effect (E), and incremental cost-effectiveness ratio (ICER) within three-years of transplantation among induction categories under two-risk groups. Based on my choice of health outcome, ICER value represents the incremental cost per additional year of graft survival over three years for the alternative immunosuppression treatment as compared to the base treatment or no treatment at all.

4.2.5. Statistical and cost-effectiveness analysis

Donor and recipient characteristics were described using frequencies or means standard deviation. Comparison between groups was made using the t test, Kruskal-Wallis test, or chi-squared test. Graft survival rates were estimated using the Kaplan-Meier product limit method. The log-rank test was used for comparison of the unadjusted survival curves. P values < 0.05 were considered statistically significant. Statistical analyses were performed with Stata 14 MP4 (StataCorp LP, College Station, TX).

I used non-parametric bootstrapping method to estimate the expected values of cost and effect parameters for both low and high-risk recipient groups. Non-parametric bootstrapping is the primary choice for conducting cost-effectiveness when the theoretical distribution to be used for statistical inference is unknown. It yields estimate of error and confidence intervals by random sampling with replacement from the original cohort [78]. I used absolute and
extended dominance for an initial assessment of cost-effectiveness of induction choices. The absolute dominance occurs when a strategy is less costly and more effective than at least one alternative. The extended dominance is the case when the dominated strategy is less effective and less costly than any point located on the line of linear combination of two other strategies. When a treatment is dominated, it is eliminated from risk group. I then use incremental cost-effectiveness ratio (ICER) to compare cost-effectiveness of among final two induction choices within each risk group. To assess the comparative cost-effectiveness of two induction groups, say A and B, I determine the ICER values using the following equation:

$$\text{ICER} = \frac{\text{Total cost with induction } A - \text{Total cost of induction } B}{\text{Effectiveness with induction } A - \text{Effectiveness with induction } B}$$

(4.1)

where total cost or effectiveness of an induction group refers to the mean total cost or mean effectiveness of the bootstrap sample, respectively. ICER value indicates the amount of cost I would like to spend for each extra unit of effectiveness to achieve a more effective treatment. I then performed 1,000 replications to obtain randomly distributed ICER values. I converted the effects from months to years and assumed the baseline of willingness-to-pay to be $50,000. Using the independent bootstrap samples, I plotted the cost-effectiveness acceptability curves (CEAC) for both low and high-risk groups. CEAC shows the probability that a decided option was cost-effective for a given willingness-to-pay threshold. The shape of the CEAC provides the joint uncertainty in costs and effects [34]. The World Health Organization recommends that ICER less than a country’s gross domestic product per capita (GDP per capita: $52,980 in the U.S. in 2013) is considered very cost-effective, those with an ICER between one to three times GDP can be considered cost-effective ($52,980 to $158,940 for the U.S. in 2013), and any ICER three times or higher should not be considered cost-effective (> $158,940 for the U.S. in 2013) [13]. Different willingness-to-pay thresholds ($100,000 and $150,000) were used to explore whether any selected induction category remains cost effective at the respective threshold.
4.3. Results

4.3.1. Patient characteristics and outcomes

Figure 4.1. Induction types between 2000 and 2008 in our cohort of DDKT recipients.

Frequencies of induction categories among DDRT recipients between 2000 and 2008 are shown in Figure 4.1. Use of lymphocyte-depleting induction agents (r-ATG and alemtuzumab) increased during this interval, while IL2-RA and no-induction approaches declined. Characteristics of the final cohort are summarized in the Supplemental Table 1. Approximately 80% of the recipients across all induction categories had at least one high-risk factor. Recipients undergoing lymphocyte depletion were also more frequent recipients of kidneys from ECD or DCD donors with correspondingly higher KDPI percentiles, as well as longer CIT and more DGF. Despite this increased risk, lymphocyte depletion was associated with lower rates of acute rejection in the first post-transplant year. At three years, overall allograft survival was better in antibody induction groups compared to no-induction category (78.7% in no-induction, 80.2% in alemtuzumab, 81.8% in r-ATG, and 81.5% in IL-2 RA, p=0.02). A multivariable Cox regression analysis was performed to evaluate risk factors for
overall graft failure, shown in Supplemental Table S2. R-ATG was associated with overall graft survival compared to no induction, and there was steady improvement in graft survival over the study period.

4.3.2. Cumulative cost, effect and ICER

In the undiscounted analysis, the cumulative (non-parametric bootstrap) means for C and E within three-years of transplantation based on the risk groups and induction categories in DDRT recipients with Medicare primary coverage is shown in Table 1. In both low and high-risk groups, treatment with no-induction was the least effective and the most expensive compared with other induction categories. Alemtuzumab in the low-risk group and IL2-RA in the high-risk group had the lowest mean C. In both risk groups, r-ATG was the most effective induction treatment category. Among the high-risk subcategories, in general, IL2-RA was the least expensive (except in AA patients), while r-ATG appeared to be the most effective therapy (except in AA race and CIT > 24-hour subcategory). After applying absolute and extended dominance, I calculated the median ICERs in the low-risk group and among high-risk sub-categories as shown in Table 2. Note that my choice of reporting means for expected costs and expected effects in Table 1 is consistent with the non-parametric bootstrap methods. For the ICER values in Table 2, however, I reported the medians because simultaneously changing costs (numerator of ICERs) and effects (denominator of ICERs) in the bootstrapped samples creates doubly skewed distribution of ICER values. The bootstrapped ICER for r-ATG compared to alemtuzumab was $32,511 per additional graft years of graft survival saved in the low-risk group. For the high-risk group and its subcategories the bootstrapped ICER was very sensitive to the graft survival; overall r-ATG was still cost-effective, but for higher willingness to pay threshold except AA race and CIT > 24 hours subcategories where alemtuzumab was more cost-effective induction of choice.
4.3.3. Sensitivity analysis

The ICERs for different willingness-to-pay threshold values ($100,000 and $150,000) were performed Figure 4.2. In the low-risk group, r-ATG was the most cost-effective induction therapy for both thresholds. For the subcategories of high-risk group, depletional antibodies (r-ATG and alemtuzumab) remained the most cost-effective treatment for all risk profiles and both thresholds, except in recipients with KDPI > 50% and older patients (age > 60) where IL2-RA was more cost-effective for $100K threshold. The acceptability curves for r-ATG in both risk groups are shown in Figures 4.3 and 4.4. r-ATG continued to be cost-effective in at least 80% of cases at 50,000(50K) willingness to pay threshold in both risk groups except in patients older than 60 years.

I also calculated the ICERs using 3% discount rate applied to both the health and cost outcomes, shown in Supplemental Table S3. These analyses produced no important changes in the results for the high-risk group. In the low risk group, I could not provide an ICER value because the incremental effect (difference in health outcomes/years of graft survival between r-ATG and alemtuzumab) became zero. Overall alemtuzumab appears to be cost-effective strategy (lower cost and same effect).

4.4. Discussion

Over eighty percent of DDRT recipients in the U.S. receive antibody-based induction therapy; my analysis indicates, on the whole, this is a cost-effective approach to immunosuppression. Specifically, based on my undiscounted analysis, 1) no-induction was the least effective and most costly approach in both low and high-risk recipients; 2) r-ATG was the most cost-effective strategy for all willingness-to-pay thresholds (with an ICER of $32,511 per additional year of graft survival compared to alemtuzumab, cost-effective at the $50K threshold in approximately 80% of the recipients) in the low-risk group; 3) for the high-risk group and its subcategories, the bootstrapped ICER was very sensitive to the graft survival; overall, depletional antibodies were more cost-effective, but mainly for higher willingness to pay threshold. Though r-ATG induction increased costs significantly, it was the most cost-
Figure 4.2. Summary of the strategies of choice based on willingness-to-pay in low or high-risk recipients and individual high-risk subcategories (The ICER for African American category is not included in the figure because alemtuzumab had the least expected cost and highest effect, as indicated in Table 4.1, the most cost-effective induction of choice) based on the undiscounted analysis.

effective induction at higher thresholds, except in AA race and recipients with CIT > 24 hours (alemtuzumab was the induction of choice at any thresholds for this subcategory).
The discounted analysis largely confirmed these findings except in the low-risk group where alemtuzumab appeared to be more cost-effective (lower cost and same effect compared to r-ATG category), a less robust conclusion reflective perhaps of a much smaller sample size and wider variation in effect size in the alemtuzumab-treated low risk group.

There is no question that induction therapy (using IL2-RA, r-ATG, or alemtuzumab) increases initial cost during renal transplant hospitalization; my data indicate this is more than offset by other benefits, such as decreasing short-term rejection rates and intermediate-term graft survival in both low and high-risk recipients. Specifically, r-ATG appears to achieve excellent CEAC (in higher than 80% of the recipients) in both risk groups (except patients older than 60 years) even at $50,000 willingness to pay threshold (considered acceptable as a value parameter in the U.S.). For patients older than 60 years, based on less steep r-ATG CEAC Figure 4.4 and the ICERs for $100,000 willingness to pay threshold (Table 2), IL2-RA
might be more cost effective compared to r-ATG. Similarly, for AA race and patients with CIT > 24 hours, alemtuzumab should be a preferable induction of choice.

The literature regarding the impact of cost on choice of appropriate induction agent is limited and conflicting [48, 52, 62, 63, 103]. Morton et al. [48], using a Markov model based on health outcomes from a published meta-analysis (mainly maintained on cyclosporine, mycophenolate mofetile, and prednisone immunosuppression) [95, 96] and actual resource costs from Australian Transplant Hospitals, reported that IL2-RA improved survival 1.4 quality adjusted life years (QALY) and saved AU$79,302 (Australian dollar) per patient over a twenty year period compared to no-induction. IL2-RA was also cost-effective compared
to polyclonal antibodies (using rabbit anti-thymocyte globulin and horse anti-lymphocyte globulin) with the ICER of AU$14,803 per QALY saved. In a multicenter randomized trial (N=135, with 60% of subjects undergoing DDRT), Polsky et al. compared basiliximab (IL2-RA) and anti-thymocyte globulin (ATG) in cost and quality-adjusted survival [62]. Cost saving with Basiliximab was $8,872, while quality-adjusted survival was same for both groups at one-year. As part of a broader meta-analysis of newer immunosuppressants, a British group found consistent reduction in acute rejection with improved one-year graft survival when IL2-RA was compared to no-induction [103]. The Scottish Medicines Consortium recommended against r-ATG as an induction therapy in renal transplantation in 2008 due to lack of graft survival benefit and increased adverse effects compared to IL2-RA [77]. In a single center retrospective study reported from the UK (N=45), Popat et al. studied cost and outcomes of IL2-RA vs. r-ATG induction in recipients of donation after cardiac death (DCD) renal transplantation [63]. Rabbit ATG was associated with less delayed graft function, rejection, and rehospitalization; though graft and patient survival were similar, r-ATG was associated with significant overall savings in cost.

In the current study, the large sample size and robust financial and health outcomes data allow meaningful evaluation of even small differences. It addresses contemporary immunosuppression and reflects current practices in the U.S., including the impact of various induction approaches in high-risk subgroups. Because my analysis utilizes national data sources (combined Medicare claims and the UNOS registry) and incorporates the perspective of Medicare (actual payments), primary payer for at least first three years of renal transplantation, it should be generalizable in this country. Within Medicare, bundled payment (Diagnosis-Related Group 302) for the initial kidney transplant hospitalization is not adjusted for patient-specific comorbidities or resource utilization of a transplant center (such as selection of induction agent, diagnostic testing, intensive care observation, length of stay etc.). Consequently, differences in cost among induction categories most likely reflect subsequent hospitalizations and complication-related resource utilization. Furthermore, Medicare perspective does not include societal costs (indirect costs, such as time and opportunity
costs, and community preferences) [24]. Approximately 30% of recipients with a functioning graft lose Medicare coverage three-years after renal transplantation, with no obvious source of subsequent payment for maintenance immunosuppression, a factor that may indirectly increase graft loss beyond three years (5). Though these issues may limit determination of the overall costs of transplantation to the Medicare program, economic analyses from a Medicare perspective have been widely accepted due to sample size, quality of data, predominance of payer role, and its effect on related governmental policy decisions (access to transplant centers, kidney allocation, and long term immunosuppressive coverage).

The study has several limitations. Though it is the first to include analysis of costs related to alemtuzumab, those data were accumulated at a time when, though off-label, the drug was approved for use only in chronic lymphocytic leukemia, at a significantly lower price than current FDA-approved marketing for multiple sclerosis, (see Supplement for the cost of induction agents) [3, 5, 32]. The time frame of the study may reduce its ability to detect long-term impact of induction, both adverse effects (such as malignancy) and potential beneficial effects on long-term survival, which could either increase or reduce costs [33]. Total exposure to r-ATG and alemtuzumab was not reported in the UNOS registry. Transplant centers have increasingly been utilizing lower doses of r-ATG for induction purposes that may change adverse event profile [6, 33, 102]. It should be emphasized that Medicare aggregate data do not permit for fine cost analysis, such as readmission, complications, follow-up visits, malignancy to better define incidence and mechanisms of short and long-term complications related to use of induction agents. I also acknowledge that my choice of outcome variable as graft survival leads to an ICER description (additional cost per year of graft survival) that may be difficult to interpret as compared with the conventional use of cost per life years or quality-adjusted life years. However, my choice is consistent with the primary objectives of immunosuppression after transplantation. Finally, my analysis primarily relies on estimates derived from 2000-2008 cohorts. Clinical use of induction agents in renal transplantation may be different in 2016, at least partly as a consequence of implementation of a new kidney allocation system in 2014, risk-averse behavior of transplant centers under new regulations.
(the CMS and the Scientific Registry of Transplant Recipients report card system), and economic disincentives for using marginal organs. However, as newer data mature, the techniques utilized in my analysis can be applied to characterize the impact of alterations in practice and related ICER trends.

4.5. Conclusions

After extensive analysis of Medicare data, with the limitations noted above, antibody-based induction appears to offer substantial advantages in both cost and outcome within three-years of transplantation compared to no induction. Overall, for most but not all recipients, depletional induction (preferably r-ATG) appears to offer the most beneficial balance between cost and effect.
<table>
<thead>
<tr>
<th>Induction Type</th>
<th>Observed Cost (USD*)</th>
<th>Cost (USD*), 95% Confidence Interval</th>
<th>Observed Effect (months)</th>
<th>Effect (months), 95% Confidence Interval</th>
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<td>IL2-RA</td>
<td>$165,366</td>
<td>157,126-174,053</td>
<td>30.97</td>
<td>30.26-31.70</td>
</tr>
<tr>
<td>r-ATG</td>
<td>$169,651</td>
<td>164,339-174,206</td>
<td>31.02</td>
<td>30.68-32.27</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>$173,531</td>
<td>164,339-174,206</td>
<td>30.88</td>
<td>30.27-31.47</td>
</tr>
<tr>
<td>No-induction</td>
<td>$185,551</td>
<td>177,135-194,969</td>
<td>29.56</td>
<td>29.21-29.92</td>
</tr>
<tr>
<td><strong>African American</strong></td>
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<tr>
<td>Alemtuzumab</td>
<td>$161,850</td>
<td>152,408-171,999</td>
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<td>30.52-32.29</td>
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<tr>
<td>IL2-RA</td>
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<td>29.91-31.00</td>
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<tr>
<td>r-ATG</td>
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<td>165,347-173,123</td>
<td>31.22</td>
<td>30.82-31.60</td>
</tr>
<tr>
<td>No-induction</td>
<td>$198,683</td>
<td>192,062-205,993</td>
<td>29.37</td>
<td>28.81-29.90</td>
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<tr>
<td>IL2-RA</td>
<td>$177,122</td>
<td>172,105-182,262</td>
<td>29.87</td>
<td>29.40-30.33</td>
</tr>
<tr>
<td>r-ATG</td>
<td>$181,119</td>
<td>176,286-185,313</td>
<td>30.18</td>
<td>29.82-30.53</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>$183,900</td>
<td>174,605-192,251</td>
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<td>29.10-30.72</td>
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<td>No-induction</td>
<td>$206,932</td>
<td>200,836-213,083</td>
<td>28.69</td>
<td>28.21-29.18</td>
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<tr>
<td><strong>CIT&gt; 24 hours</strong></td>
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</tr>
<tr>
<td>IL2-RA</td>
<td>$164,512</td>
<td>158,283-171,369</td>
<td>30.91</td>
<td>30.32-31.42</td>
</tr>
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<td>Alemtuzumab</td>
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<td>159,332-181,889</td>
<td>31.37</td>
<td>30.44-32.28</td>
</tr>
<tr>
<td>r-ATG</td>
<td>$173,794</td>
<td>168,812-179,883</td>
<td>31.06</td>
<td>30.57-31.57</td>
</tr>
<tr>
<td>No-induction</td>
<td>$211,958</td>
<td>203,043-221,638</td>
<td>28.93</td>
<td>28.26-29.53</td>
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<tr>
<td><strong>Age&gt; 60 years old</strong></td>
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</tr>
<tr>
<td>IL2-RA</td>
<td>$172,433</td>
<td>167,803-177,096</td>
<td>30.32</td>
<td>29.89-30.77</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>$179,481</td>
<td>174,732-184,241</td>
<td>30.43</td>
<td>30.02-30.84</td>
</tr>
<tr>
<td>r-ATG</td>
<td>$185,350</td>
<td>174,202-196,315</td>
<td>29.55</td>
<td>28.47-30.50</td>
</tr>
<tr>
<td>No-induction</td>
<td>$204,865</td>
<td>198,057-211,631</td>
<td>28.74</td>
<td>28.18-29.34</td>
</tr>
</tbody>
</table>

Table 4.1. Cumulative mean cost and effect within three-years of transplantation based on the induction category in DDKT recipients with Medicare primary coverage.
<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost (C), USD*</th>
<th>Incremental Cost, USD*</th>
<th>Effect (E), years</th>
<th>Incremental Effect, years</th>
<th>C/E</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW-RISK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>138,414</td>
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<td>2.69</td>
<td></td>
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<td>51,455</td>
</tr>
<tr>
<td>r-ATG</td>
<td>141,340</td>
<td>2,926</td>
<td>2.78</td>
<td>0.09</td>
<td>50,841</td>
<td>32,511</td>
</tr>
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<tr>
<td>IL2-RA</td>
<td>164,750</td>
<td></td>
<td>2.55</td>
<td></td>
<td></td>
<td>64,607</td>
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<tr>
<td>r-ATG</td>
<td>167,357</td>
<td>2,607</td>
<td>2.57</td>
<td>0.02</td>
<td>65,119</td>
<td>130,350</td>
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<td>High-risk subcategories</td>
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<tr>
<td>PRA&gt;20%</td>
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</tr>
<tr>
<td>IL2-RA</td>
<td>167,270</td>
<td></td>
<td>2.56</td>
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<td>65,339</td>
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<td>r-ATG</td>
<td>171,485</td>
<td>4215</td>
<td>2.63</td>
<td>0.07</td>
<td>65,203</td>
<td>60,214</td>
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<td>KDPI&gt; 50%</td>
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</tr>
<tr>
<td>IL2-RA</td>
<td>176,284</td>
<td></td>
<td>2.47</td>
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<td>71,370</td>
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<tr>
<td>r-ATG</td>
<td>179,843</td>
<td>3,559</td>
<td>2.50</td>
<td>0.03</td>
<td>71,937</td>
<td>118,633</td>
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<td>CIT&gt;24 hours</td>
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<tr>
<td>IL2-RA</td>
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<tr>
<td>Alemtuzumab</td>
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<td>4,970</td>
<td>2.66</td>
<td>0.16</td>
<td>64,227</td>
<td>31,062</td>
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<td>Age&gt; 60 years-old</td>
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</tr>
<tr>
<td>IL2-RA</td>
<td>171,418</td>
<td></td>
<td>2.50</td>
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<td>68,567</td>
</tr>
<tr>
<td>r-ATG</td>
<td>179,452</td>
<td>8,034</td>
<td>2.56</td>
<td>0.06</td>
<td>70,098</td>
<td>133,900</td>
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<td></td>
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</tr>
<tr>
<td>Alemtuzumab</td>
<td>161,850</td>
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<td>2.62</td>
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<td>61,775</td>
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<tr>
<td>r-ATG</td>
<td>169,356</td>
<td>7,506</td>
<td>2.60</td>
<td>0.02</td>
<td>65,137</td>
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</tbody>
</table>

*The cost adjusted to 2013 U.S. dollar value.
**The ICER is not included because alemtuzumab is marginally dominant strategy for African American category in the high-risk group.

Table 4.2. Cost effectiveness analysis based on induction regimens for individual low and high-risk DDKT recipients.
Table 4.3. Inflation adjusted and outcomes discounted cost-effectiveness analysis based on induction regimens for low and high-risk recipients.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost 2013 USD value</th>
<th>Incremental Cost, 2013 USD value</th>
<th>Effect (E), years</th>
<th>Incremental Effect, years</th>
<th>C/E</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LOW-RISK</strong>*</td>
<td></td>
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<tr>
<td>Alemtuzumab</td>
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<td>r-ATG</td>
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<td>10,869</td>
<td>2.64</td>
<td>0.00</td>
<td>51,585</td>
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<tr>
<td><strong>HIGH-RISK</strong></td>
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<tr>
<td>IL2-RA</td>
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<td>2.43</td>
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<tr>
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<tr>
<td>IL2-RA</td>
<td>154,268</td>
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<td>2.43</td>
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<td>63,484</td>
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<tr>
<td>r-ATG</td>
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<td>3,299</td>
<td>2.49</td>
<td>0.06</td>
<td>63,279</td>
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<tr>
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</tr>
<tr>
<td>IL2-RA</td>
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<td>62,601</td>
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<tr>
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<td>65,141</td>
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<tr>
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<td>0.06</td>
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<tr>
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</tr>
<tr>
<td>Alemtuzumab</td>
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<td></td>
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</tr>
<tr>
<td>r-ATG</td>
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</table>

*The ICER is not included. The ICER is not defined for the low risk group because the incremental health effects among alemtuzumab and r-ATG is zero (division by zero). In the African American category, alemtuzumab is marginally dominant strategy.
5.1. Concluding remarks

This dissertation attempts to clarify the effect of kidney transplant center’s performance assessment and different kidney allocation schemes on donor kidney and patient acceptance decisions. Moreover I study the association between kidney transplant outcomes and changes in the kidney allocation scheme. I identify essential parameters that require to be considered in designing an optimal citation policy applied to underperforming transplant centers and whether they need to be adjusted upon kidney allocation modification. I propose a simulation model with two applications, one provides an optimal deceased donor kidney acceptance guidance for the decision makers, whereas the other one concentrates on the social welfare aspect of kidney transplantation. The work is completed with analyzing the cost-effectiveness of antibody-based induction therapy in deceased donor kidney transplantation in the United States.

In Chapter 2, I develop and analyze a theoretical model to examine the role of performance assessment and its subsequent citation policy for underperforming centers on kidney transplantation decisions. The first contribution is to propose a stochastic model that determines the socially optimum kidney transplant decision based on the inherent trade off between the waiting time and the kidney quality that optimizes the social welfare. I also model the optimal decision rule for a completely self-interested provider and then modify the model to the case that provider’s tendency of benevolence increases. I find the optimal citation policy that minimizes the social loss which is the difference between providers utility and welfares utility. Furthermore, I model the candidate’s acceptance decision to transplant center’s waitlist with the objective function of minimizing the waiting list mortality rate.
The model identifies candidates minimum health threshold at the time of evaluation as a guideline for enlisting the candidate, if her health score exceeds this threshold. I incorporate provider’s risk preference in the patient acceptance decision. I also show how the transplant decisions are influenced by changes made to the KAS and propose how the citation policy used by the regulator has to be modified accordingly. The model investigates how a citation policy can affect kidney transplant program’s decision making on accepting donor kidneys and candidates to program’s waitlist. In addition, the model allows for exercising different risk preferences (neutral, risk averse and risk seeking) adopted by the decision makers. For the numerical illustration and parameter estimation, I use combined clinical data from the national waiting list data included in the UNOS annual reports and the Scientific Registry of Transplant Recipient (SRTR).

The empirical study provides several important insights regarding an effective and efficient kidney transplant decision and an outcome oversight. First, observations from the data indicate that candidate blood type and region influence their wait time notably. However, I notice that the qualities of accepted kidneys are almost the same among recipients with different blood types in different regions. This could be an indication that the decision makers do not take the donor kidney supply into account. The importance of candidates’ individual offer rates needs to be of concern to the decision makers for making donor kidney acceptance/rejection decisions. The socially optimal kidney acceptance decision derived by using the developed model and real data varies notably from one region to another given its kidney supply. According to the analysis, Region 3 with $k_s^* = 0.69$ has the highest average utility of 12.87 years, whereas Region 9 shows the average utility of 10.4 as a result of $k_s^* = 0.53$

The empirical study also reveals that the current citation policy introduced as CoP in 2007 has been effective for 42% of the recipients in providing socially optimal transplantation decisions. The remaining 58% of the recipients are impacted by receiving sub-optimal kidneys; however, in general, the social loss and deficiency have decreased across all 11 regions. We also observe an increase in the degree of benevolence among the 11 regions. Overall,
based on the analysis, after the introduction of CoP in 2007 a total 34,789 life years have been saved across all recipients who received donor kidney transplantation.

The analysis indicates that the introduction of the new KAS in 2014 resulted in a reduction of the social loss by 1,292 life years per year over the entire population and this supports the still questioned notion that the introduction was a success. As a result of KAS, the access of high-EPTS patients to good quality kidneys is now reduced. This can change the post-transplant outcomes of this group of patients and subsequently the performance of transplant centers that perform their surgeries. To satisfy fairness and equity conditions and restrict the risk of discrimination of accessing to the care, it might be necessary for the regulators to modify or risk-adjust the citation policy accordingly.

In Chapter 3, the proposed simulation model considers the effect of several important factors for kidney allocation and transplantation. Factors such as the deterioration of patient health and kidney quality over time, the correlation between patient’s health and acceptance decision, and the probability of kidney acceptance are included in the model. As a result of the first application, the patient may benefit from selecting more than one region to be waitlisted and so reduces her wait time. The region-selection model relies on two facts: 1) The achievable optimal expected utility in any region, and 2) patient’s set of constraints on budget, distance and performance. The attention of the second application is on a macro-level aspect of transplantation, namely the contribution of information sharing on the social welfare and discard rates. I find that by providing up-to-date information to OPTN, we can accelerate the process of matching a patient to an available donor organ and potentially reduce the waitlist mortality rate. The information also assists in improving kidney utilization and transplant rates. For the numerical analysis I use data obtained from the Organ Procurement and Transplantation Network (OPTN) and the Scientific Registry of Transplant Recipients (SRTR). Modern technology using ubiquitous mobile devices could facilitate better procurement of up-to-date information by the OPTN and thus has the potential for significantly enhancing the efficiency of organ allocation. We show that by efficiently searching for matching patients the transplant and waitlist mortality rates can
improve up to 42% and 14%, respectively.

Transplantation is costly with wide discrepancy in utilization and a limited base of evidence, particularly in regard to cost-effectiveness. In Chapter 4 I link the United States Renal Data System dataset to the Medicare claims to estimate the cumulative costs, graft survival, and incremental cost-effectiveness ratio (ICER cost per additional year of graft survival) within 3 years of transplantation in 19,450 deceased donor kidney transplantation recipients with Medicare as the primary payer from 2000 to 2008. The study cohort is classified into high-risk and low-risk classes. By estimating the expected ICER among four induction categories: no-induction, alemtuzumab, rabbit anti-thymocyte globulin (rATG), and interleukin-2 receptor-antagonist our analysis indicates that no-induction is the least-effective and most-costly option in both risk groups. Depletional antibodies (r-ATG and alemtuzumab) are more cost-effective across all willingness-to-pay thresholds in the low-risk group. For the high-risk group and its subcategories, the ICER is very sensitive to the kidney survival. Depletional antibodies are more cost-effective, for higher willingness to pay thresholds (US $100,000 and US $150,000). Results show also that only r-ATG is associated with the kidney survival benefit. The extensive analysis of Medicare data suggests that antibody-based induction appears to offer substantial advantages in both cost and outcome three-years post-transplant compared to no induction.

5.2. Future study

Organ transplantation is a complex process with many participating parties and there is much room for further investigation. One major research thrust needs to address the effects of the interaction between actors. This includes sharing information between actors by observing other actor’s decisions and competition. For example, the fact that a waitlisted patient at any center has received an organ offer shows that all the previous patients turned that organ down. This information could bias the patient’s expectation of the quality of the organ. In a system where the decision makers can observe other agents’ decisions, gaming the system is not unlikely. Investigating the role of decision dependency among agents (pa-
tients and transplant centers) by disclosing individual information on organ acceptance and rejection criteria might provide useful insights to study the agents’ behaviors and responses which can potentially be used to improve the overall system. Competition between patients for organs and between centers for patients and organs also influences decisions, and the impact of these forces on welfare and the effectiveness of regulation needs to be thoroughly investigated.
Appendix A

Definition of variables and parameters

Table A.1. Definition of rates

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
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<tr>
<td>$\mu$</td>
<td>Kidney arrival rate</td>
</tr>
<tr>
<td>$\mu_o$</td>
<td>Kidney offer rate</td>
</tr>
<tr>
<td>$\mu_a$</td>
<td>Kidney acceptance rate</td>
</tr>
<tr>
<td>$\mu_a^l$</td>
<td>Kidney acceptance rate post KAS - low risk</td>
</tr>
<tr>
<td>$\mu_a^h$</td>
<td>Kidney acceptance rate post KAS - high risk</td>
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</tbody>
</table>

Table A.2. Definition of kidney quality

<table>
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<th>Description</th>
</tr>
</thead>
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<td>$q$</td>
<td>Kidney quality $\in [0, 1]$</td>
</tr>
<tr>
<td>$k_c^*$</td>
<td>Candidate’s optimal kidney quality threshold</td>
</tr>
<tr>
<td>$k_p^*$</td>
<td>Provider’s optimal kidney quality threshold</td>
</tr>
<tr>
<td>$k_s^*$</td>
<td>Social planer’s optimal kidney quality threshold</td>
</tr>
<tr>
<td>$k_l^*$</td>
<td>Low-risk candidate’s optimal kidney quality threshold post KAS</td>
</tr>
<tr>
<td>$k_h^*$</td>
<td>High-risk candidate’s optimal kidney quality threshold post KAS</td>
</tr>
</tbody>
</table>

Table A.3. Definition of utility and expected utility functions

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$U^c(h, q, k)$</td>
<td>Candidate’s post-transplant utility</td>
</tr>
<tr>
<td>$E(U^c)$</td>
<td>Candidate’s expected post-transplant utility, social welfare utility</td>
</tr>
<tr>
<td>$E(U^p)$</td>
<td>Provider’s expected post-transplant utility</td>
</tr>
<tr>
<td>$E(U_l^c)$</td>
<td>Low-risk candidates’s expected post-transplant utility post-KAS</td>
</tr>
<tr>
<td>$E(U_h^c)$</td>
<td>High-risk candidates’s expected post-transplant utility post-KAS</td>
</tr>
</tbody>
</table>
Table A.4. Definition of survival and hazard functions

<table>
<thead>
<tr>
<th>Expression</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S(k_p, h, t)$</td>
<td>One-year post-transplant survival</td>
</tr>
<tr>
<td>$F(k_P, h, t)$</td>
<td>One-year post-transplant failure</td>
</tr>
<tr>
<td>$S^{w}(h', t)$</td>
<td>Patient survival until transplant</td>
</tr>
<tr>
<td>$F^{w}(h', t)$</td>
<td>Patient failure before transplant</td>
</tr>
<tr>
<td>$\lambda(k_p, h)$</td>
<td>Hazard function post-transplant period</td>
</tr>
<tr>
<td>$\lambda_h$</td>
<td>Post-transplant hazard rate</td>
</tr>
<tr>
<td>$\lambda^{w}(h', t)$</td>
<td>Hazard function pre-transplant period</td>
</tr>
</tbody>
</table>

Table A.5. Other definitions

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha_c$</td>
<td>Candidate’s risk preference $\in [0, 1]$</td>
</tr>
<tr>
<td>$\alpha_p$</td>
<td>Provider’s risk preference $\in [0, 1]$</td>
</tr>
<tr>
<td>$\delta$</td>
<td>Provider’s degree of benevolence</td>
</tr>
<tr>
<td>$w_t$</td>
<td>Maximum wait time until receiving an acceptable offer</td>
</tr>
<tr>
<td>$B$</td>
<td>Provider’s benefit from tx</td>
</tr>
<tr>
<td>$B'$</td>
<td>Provider’s benefit from enlisting candidate</td>
</tr>
<tr>
<td>$C'$</td>
<td>Cost of losing candidates on the waitlist</td>
</tr>
<tr>
<td>$C_p$</td>
<td>Provider’s cost of being flagged</td>
</tr>
<tr>
<td>$f_p$</td>
<td>Provider’s probability of being flagged</td>
</tr>
<tr>
<td>$h$</td>
<td>Candidate’s life score when she joins the queue top part</td>
</tr>
<tr>
<td>$h'$</td>
<td>Candidate’s life score when she joins provider’s waitlist</td>
</tr>
<tr>
<td>$N$</td>
<td>Number of active candidates</td>
</tr>
<tr>
<td>$N_l, N_h$</td>
<td>Number of active low- and high-risk candidates</td>
</tr>
</tbody>
</table>
Appendix B
Proofs

B.1. Proof of Proposition (2)

Substituting (2.2)-(2.4) into (3.1) results in:

\[ U_c(h, q, k) = m_h q \left( 1 - \frac{\ln\left( \frac{1}{1-\alpha_c} \right)}{\mu_o h(1 - k)} \right) \]

By taking the expected value given \( Q \sim U(0, 1) \), we have:

\[ E(U_c) = \frac{m_h(1 + k)}{2} \left( 1 - \frac{\ln\left( \frac{1}{1-\alpha_c} \right)}{\mu_o h(1 - k)} \right) \]

Then, taking the first order derivative results in:

\[ \frac{\partial E(U_c)}{\partial k} = \frac{m_h}{2} \left( 1 - \frac{2\ln\left( \frac{1}{1-\alpha_c} \right)}{\mu_o h(1 - k)^2} \right) \]

Setting the above equation to zero results (2.13). The second derivative is obtained as:

\[ \frac{\partial^2 E(U_c)}{\partial k^2} = \frac{m_h}{2} \left( - \frac{\ln\left( \frac{1}{1-\alpha_c} \right)}{\mu_o h(1 - k)^2} \right) \]

which is always negative, so \( k^*_c \) in (2.8) is a maximum point.

B.2. Proof of Lemma 2.1

By substituting \( \alpha_c = 1 - \frac{1}{e} \) in B.1, \( k^*_s \) can be obtained.

B.3. Proof of (2.17)-(2.19)
The numerator of $\lambda(t)$ in (2.17) can be written as:

$$P(T \leq t + dt \mid T \geq t) = \frac{P(t \leq T \leq t + dt)}{P(T \geq t)} \approx \frac{g(t) dt}{S(t)}$$

Substituting in (2.15) results in:

$$\lambda(t) = \frac{g(t)}{S(t)}$$

which is the definition of hazard function. since $-g(t)$ is a derivative of $S(t)$, we can rewrite $\lambda(t)$ as:

$$\lambda(t) = -\frac{d}{dt} \ln(S(t))$$

Integrating from 0 to $t$ and applying the boundary condition $S(0) = 1$ (since the event cannot have occurred within a zero duration) results in:

$$S(t) = \exp\left(-\int_0^t \lambda(x)dx\right)$$

The above integral is called the cumulative hazard (or cumulative risk) which can be thought of as the sum of risk values from time 0 to $t$. Let’s suppose in our model, the survival distribution is obtained by assuming a constant risk over the first year post-transplant and the hazard function is defined as

$$\lambda(q, h) = \lambda'_h(1 - E[Q \mid Q \geq k_p])$$

with

$$E[Q \mid Q \geq k_p] = \frac{\int_{k_p}^1 qf(q)dq}{\int_{k_p}^1 f(q)dq} = \frac{1 + k_p}{2}.$$  

The hazard function for all $q \geq k_p$ and $t \leq 1$ is:
\[ \lambda(q, h) = \lambda'_h(1 - E[Q|Q \geq k_p]) = \frac{\lambda'_h}{2}(1 - k_p) = \lambda_h(1 - k_p) \]

A constant hazard is equivalent to exponentially distributed lifetime that has memoryless property and the corresponding survival and failure functions for aforementioned constant hazard function are respectively obtained as:

\[
S(k_p|t = 1) = \exp(-\lambda_h(1 - k_p)) \\
F(k_p|t = 1) = 1 - \exp(-\lambda_h(1 - k_p))
\]

B.4. Proof of Proposition (5)

From (2.22) we get \( \exp(-\lambda_h(1 - k_p)) \geq 1 - \frac{B}{C_p f_p} \). Taking the logarithm from both sides results in \( -\lambda_h(1 - k_p) \geq \ln(1 - \frac{B}{C_p f_p}) \) or \( k_p | CP \geq 1 + \frac{1}{\lambda_h} \ln(1 - \frac{B}{C_p f_p}) \). Thus, the optimal kidney quality threshold under the citation policy consideration given \( B < C_p f_p \) is obtained as (2.23).

B.5. Proof of Proposition (6)

Substituting (2.13) and (2.23) into (2.24) results in:

\[
1 - \sqrt{\frac{2}{\mu_o h}} = 1 + \frac{1}{\lambda_h} \ln(1 - \frac{B}{C_p f_p})
\]

By simple math calculation and rearrangement we get:

\[
-\lambda_h \sqrt{\frac{2}{\mu_o h}} = \ln(1 - \frac{B}{C_p f_p})
\]

\[
\exp(-\lambda_h \sqrt{\frac{2}{\mu_o h}}) = 1 - \frac{B}{C_p f_p}
\]

\[
C^*_{p,f_p} = \frac{B}{\exp(-\lambda_h \sqrt{\frac{2}{\mu_o h}})}
\]
B.6. Proof of Corollary (7)

By placing (2.26) and (2.27) in (2.28) we have:

\[
B' \left( h' - \left( w' + \frac{\ln \frac{1}{1-\alpha_p}}{\mu_o(1-k^*_h)} \right) \right) \geq C' \left( 1 - \frac{h' - \left( w' + \frac{\ln \frac{1}{1-\alpha_p}}{\mu_o(1-k^*_h)} \right)}{h'} \right)
\]

\[
B'h' \geq (B' + c') \left( w' + \frac{\ln \frac{1}{1-\alpha_p}}{\mu_o(1-k^*_h)} \right)
\]

which results in \( h'^* \) in (2.29).

B.7. Proof of Proposition (8)

Similar to proof of (2.13), by substituting (2.31) and (2.32) in (2.33) and take a derivative with respect to \( k \) equation (2.34) can be obtained.

B.8. Proof of Corollary (2)

By substituting \( \pi = 0.8 \) in the equation (2.34) and subtract equation (2.13) from it one can see \( 1.8 - \frac{1.61}{\mu_o h} - 1 + \frac{1.41}{\mu_o h} \) is always positive as long as \( \mu_o h > 0.06 \). This requirement is always met by low-risk candidate, meaning that the they increase their kidney quality threshold post-KAS.

B.9. Proof of Proposition (9)

similar to proof of (2.34) by using the expected wait time of \( w_h(k) = \frac{1}{\mu^*} \).

B.10. Proof of Proposition (10)

By substituting (2.38) and \( \mu_o = \frac{\mu \pi}{N} \), post KAS offer rate for high risk candidate, in (2.29) we have:

\[
\left( 1 + \frac{c'}{B'} \right) \left( w' + \frac{\ln \frac{1}{1-\alpha_p}}{\mu_o \frac{\mu \pi}{N}(1-k^*_h)} \right)
\]
The result of subtracting this equation from (2.29) is negative. Therefore $h'_{k\alpha s}$ is greater than $h'^*$. 


[60] Organ Procurement and Transplantation Network (OPTN). Analysis shows kidney allocation system achieving key goals. Online:


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