Abstract

Deceased-donor organs transplant has received significant research attention from the operations research community over the past few decades. This chapter organizes the research in this area from the perspective of various stakeholders. We first identify the stakeholders and provide relevant institutional details. Next, we discuss the research progress to date. Lastly, we identify and discuss several important future research directions for operations research scholars that can improve the deceased-donor organ transplant system further.

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1 Introduction

The first successful solid organ transplantation was done in 1954 between two identical twins (Merrill et al. 1956). With the discovery and rapid development of immunosuppressive drugs (Halloran 2004), organ transplantation became widely available. These outstanding achievements changed the course of treatment of many end stage diseases and brought hope to countless patients suffering from them.

Solid organ transplantation can be carried out using organs from either living or deceased donors. The former is preferred because the graft failure risk of the organ is lower in that case (Trotter et al. 2002). At the same time, a living donor needs to continue having a productive life after the organ donation. Kidney transplants are the primary example of living-donor transplants because the nephrological functions of human body can be handled by one kidney (Johnson et al. 1999). Living-donor partial liver transplants are another example (though they are much less common) because liver itself is regenerative (Hashikura et al. 2002).

Living organ donation occurs between a recipient and a consenting (living) donor. The donor and the recipient supposedly are usually biologically or emotionally related in this situation, and any type of monetary transactions are strictly prohibited by National Organ Transplantation Act (NOTA, 1984). A primary concern in living organ donation is to avoid a black market. For a comprehensive discussion of other ethical challenges in living-donor transplantation, see Gordon (2012).
Several researchers explored decision problems involving living-donor transplants. David and Yechiali (1985) and Alagoz et al. (2004) study the decision problem of a recipient-living donor pair for a kidney and liver transplant, respectively. They characterize the optimal timing of the surgical operation under the objective of maximizing the quality adjusted life years (QALY) of the recipient from the transplant. Living-donor kidney transplants are more challenging than living-donor liver transplants due to increased complexity of histocompatibility. Although a person is willing to donate her kidney to a specific patient, this may not be biologically feasible. When there are multiple such incompatible pairs interested in a living-donor kidney transplant, an opportunity arises if the potential recipients are willing to exchange their donors. Such an exchange can facilitate a match between the new recipient-donor pairs after the exchange. This is often referred to as the kidney exchange; see for example Zenios (2002), Roth et al. (2004, 2005), Segev et al. (2005), Ashlagi et al. (2011), and Glorie et al. (2014) for mechanism design and optimization approaches to facilitate kidney exchange. Although it is an active and important research area, see Figure 1, living-donor transplantation is beyond the scope of this chapter.

Figure 1: Total number of living organ donations over years. Based on OPTN data as of January 1, 2017.
Figure 2: The distribution of deceased-donor transplants over organs in 2016. Based on OPTN data as of January 1, 2017.

This chapter focuses on resource allocation problems arising in the deceased-donor kidney and liver transplant systems. A deceased-donor organ transplant is carried out by procuring donor’s organs after brain death or cardiac arrest.\footnote{In an effort to increase organ supply, donation after cardiac death is also permissible (Foley et al. 2005, Bernat et al. 2006).} It requires consent of the donors or their family. Although the deceased-donor transplants are performed for a range of organs such as heart, lung, pancreas, and intestines, kidney and liver transplants constitute the great majority of the total number of deceased-donor organ transplants (see Figure 2). As such, we will focus attention on the kidney and liver transplants.

\section{The Deceased-Donor Organ Allocation system: Stakeholders and their objectives}

The most prevalent aspect of the deceased-donor organ transplant system for our purposes is the severe organ shortage. Figures 3 and 4 show that the number of new patients in need of a transplant far exceeds the number of organs available for transplant. Organ allocation is an instrument to match the limited supply of organs with the demand for them. However,
the severe supply shortage turns the organ allocation problem essentially into a rationing problem. There are several studies considering initiatives to boost the organ supply so that more patients can receive transplants. For example, Dai et al. (2016) studies the effects of incentivizing living organ donation by prioritizing the donors in the case that they need an organ transplant in the future. Arikan et al. (2017) studies the impact of broader geographical sharing of the low quality organs on the deceased-donor organ procurement rates. Although such efforts can help to increase the organ supply, severe shortage of organs available for transplant remains a key challenge.

Figure 3: Number deceased-donor kidney donations and new registrations to the waitlist over the years. Based OPTN data as of January 1, 2017.

Figure 4: Number deceased-donor liver donations and new registrations to the waitlist over the years. Based OPTN data as of January 1, 2017.

Due to the imbalance in supply and demand of organs, the United States deceased donor
kidney wait list has been growing at an alarming rate. In 2016, there were 98,272 patients registered on the wait list, whereas only 13,431 candidates received transplants. A similar situation persists in the liver transplant waitlist with 14,361 new patients registering and only 7,469 candidates receiving transplants in the same year.

The deceased-donor transplantation system has various stakeholders with different objectives. The key stakeholders are patients/transplant candidates, hospitals/transplant centers, the central planner (The Organ Procurement and Transplant Network (OPTN) a federal contract held by the United Network of Organ Sharing (UNOS)), organ procurement organizations (OPOs), and the society.

The transplant candidates and their well being are the main focus of the deceased-donor organ transplant system. For the end-stage liver disease (ESLD) patients, transplantation is the only viable treatment. Without a transplant, the mortality rate of the ESLD patients is quite high. In contrast, the end-stage renal disease (ESRD) patients are perhaps more fortunate, because they may live up to ten years on dialysis. However, this requires the patients to visit a dialysis center up to three times a week, which imposes a significant burden, potentially limiting the patients’ opportunity of full-time employment. Also, from the medical perspective, the desired therapy for ESRD patients is transplantation.

Presumably, a patient’s primary objective is to live as long and well as possible. Although a variety of specific objective functions are consistent with that, the literature generally assumes that patients strive to maximize their QALY from the transplant. As such, an important consideration for patients is the fact that organs are heterogeneous. Not only do they vary in their quality, but also some organs may not even be suitable for a patient. Consequently, patients waiting for a transplant or transplant centers on their behalf may decline organ offers despite the severe shortage of available organs for transplant. In this regard, transplant candidates should carefully evaluate how often they will be receiving the organ offers of various quality and take that into consideration when making an accept/reject decision given an organ offer. Several researchers have studied dynamic programming for-
mulations of the patients’ accept/reject decisions for possible organ offers; see for example, Ahn and Hornberger (1996), Alagoz et al. (2007a,b) and Sandikci et al. (2008, 2013).

As mentioned above, organ donors are heterogeneous in terms of age or history of medical comorbidities like diabetes or hypertension. As a result, the deceased-donor organs vary in their graft failure risk and useful life after transplantation. The graft failure risk of a kidney can be quantified in terms of some donor characteristics. Israni et al. (2014) introduces kidney donor profile index (KDPI) which is derived from kidney donor risk index (KDRI). KDRI takes into account factors such as donor age, height, weight, ethnicity, history of hypertension and diabetes (Rao et al. 2009). KDPI is the percentile score of a kidney in terms of decreasing graft failure risk.

Graft failure risk of a deceased-donor liver can be predicted using several donor characteristics such as length of intensive care unit stay and antecedents of hypertension (Cuende et al. 2005); existence and degree of steatosis (Salizzoni et al. 2003); race, height, and involvement in a cerebrovascular accident (Feng et al. 2006); and age, blood type, and gender (Roberts et al. 2004). The transplant surgeons and candidates base their belief about graft survival of the organ mostly on these information. Accordingly, candidates seek to transplant an organ that will survive for sufficiently long. Consequently, the candidates may decline organ offers, if they are not satisfied with the organ quality.

Organ quality is not the sole predictor of a transplant candidate’s decision. Transplant candidates themselves are heterogeneous, in particular, in terms of their own health status. To be more specific, in the deceased-donor liver allocation system, transplant candidates are classified with respect to their likelihood of mortality. This classification also plays a key role in their prioritization by the liver allocation policy. If a candidate has a life expectancy of less than 7 days without a liver transplant, she is classified as Status 1A. Candidates who are not eligible for Status 1A are assigned a score that reflects the probability of death within a 3-month period. This scoring system is called the Model for End-Stage Liver Disease (MELD) scoring system which is first suggested by Malinchoc et al. (2000). MELD
score takes into account the serum concentrations of bilirubin and creatinine, international normalized ratio for prothrombin (INR) time, and the cause of the underlying liver disease as predictors of survival. The maximum MELD score is 40 which means the probability of death within 3 months is 97%. If a patient has MELD score of less than 6, they do not need a liver transplant. A patient’s MELD score evolves over time as she waits for a transplant. Although the evolution is not necessarily for the worse, it is more likely that health status of a ESLD patient will deteriorate over time. As a result, it is natural for the liver transplant candidate to lean more towards accepting an organ offer when the health condition gets more critical.

The mortality rate while waiting for a transplant does not vary as much across ESRD patients. However, the survival after a transplant depends on both the donor’s characteristics and the recipient’s health status (Clayton et al. 2014). The latter is quantified by estimated post-transplant survival (EPTS) score, developed by the Scientific Registry of Transplant Recipients (SRTR) contractor upon request of the OPTN Kidney Transplantation Committee. The EPTS score of a patient takes into account her age, dialysis duration, prior solid organ transplantation, and diabetes status (Israni et al. 2014). Candidates with lower EPTS scores have lower mortality risk after transplantation compared to those with higher EPTS scores. In addition, the EPTS score of a candidate gets worse with waiting, because it increases with the dialysis duration and age. This can have a significant effect on the transplant candidate’s tendency to accept organ offers. Even though the candidate may plan to wait for a high quality kidney at first, her aspirations may change as she waits longer because staying on dialysis for a long time may significantly lower the post-transplant graft survival as captured by the EPTS score.

Healthcare professionals monitor and guide the candidates throughout the entire transplantation process. In the case of deceased-donor kidney transplants, candidates continuously visit dialysis centers until they receive a transplant. Dialysis centers keep track of their patients’ schedule of visits, and monitor their health status closely. They decide the best
type of dialysis to offer according to health status of the patient, see for example Zenios and Fuloria (2000) and Lee et al. (2008). Because most patients wait for a long time to receive a transplant, dialysis centers and their interactions with the candidates constitute an important part of the overall process. The involvement of healthcare professionals with liver patients can be even more dramatic. Many liver transplant candidates are hospitalized while they wait for a transplant. In both the liver and kidney transplant systems, health care institutions devote significant resources for well-being of their patients before any transplant surgery.

Transplant centers are involved in various administrative tasks, the surgery as well as the pre- and post-transplant care of the patient. They register the transplant candidates to the waitlist and are responsible for assessing the candidate’s physical condition. The physicians and surgeons at a transplant center play a particularly important role. Since the candidates do not necessarily have the medical wisdom to assess their situation, physicians and surgeons evaluate the organ offers and guide candidates through accepting or rejecting them. If the candidate accepts an organ offer, the transplant center facilitates the transplant surgery.

The performance of transplant centers are measured by risk-adjusted post-transplant outcomes. In fact, the transplant centers are highly regulated under the Medicare Conditions of Participation (CoPs)\(^2\), and centers that do not meet the performance standards are flagged for performance review. Although it is intended for well being of the transplant candidates, CoPs may also force transplant centers to be more risk-averse (Arikan et al. 2016, Delasay and Tayur 2017).

To be specific, transplant centers are monitored on the short-term patient and graft survival. This may have unintended consequences both when the transplant centers list the patients, and when patients/surgeons make accept/reject decisions for organ offers. Patients with ESLD/ESRD go through an evaluation to decide their candidacy for organ transplantation. Moreover, once a patient is listed as a transplant candidate, he may need to undergo

periodic testing to determine eligibility. The evaluation process prior to listing a patient tries to identify those patients who may benefit the most from a transplantation as well as those patients who may be placed at risk. Listing practices vary significantly across different transplant centers while some transplant centers welcome risky patients, others do not.

Acceptance criteria for organ offers used by different transplant centers vary significantly as well. They may depend on a number of factors. The risk tolerances of the transplant centers and the clinicians are important factors. Acceptance criteria can also be affected by the performance monitoring of transplant centers. The performance reports of all transplant programs are publicly available and have been used by the insurance providers, prospective transplant candidates, the policy makers, and the public to evaluate transplant centers’ performance. This provides a serious disincentive for the transplant centers to use high-risk organs. On the one hand, poor short-term outcomes are harmful both to the patients and the transplant centers. They can even jeopardize the viability of a transplant center. On the other hand, the deceased donor transplant system in the United States suffers from a high rate of discarded organs. Many attribute this, in part, to the institutional risk aversion, in addition to the various inefficiencies of the allocation system discussed below.

OPOs procure donated organs after donor’s brain death. They assess the organ’s characteristics and report it for the transplant candidates’ evaluation. The procurement is done according to Final Rule\(^3\) issued by the Department of Health and Human Services (DHHS). The organ is procured unless one of the following occurs:

(i) The donor does not meet criteria for eligible donor,

(ii) The organ has been ruled out by basic donor information or by laboratory data prior to the donor entering the operating room for excision of organs,

(iii) The family does not agree to donate the organ,

(iv) The search for a recipient for that organ has ended unsuccessfully prior to the donor’s

entrance into the operating room.

If none of these four conditions is true, the DHHS Final Rule states that “intent” is present and the procurement may proceed.

Unfortunately, not every medically acceptable organ is procured and offered for transplantation, which is surprising given the severe organ shortage. Organ procurement itself involves a surgical operation and takes a significant time of healthcare personnel and facilities. The heterogeneity of the deceased-donor organs may cause some of them to be not procured. Organ procurement rates vary significantly across different locations. For example, the lowest quality kidney procured in New York is consistently of lower quality than the highest quality kidney not procured in Utah as observed by Arikan et al. (2017). Arikan et al. (2017) explores the reasons of these geographical differences in organ procurement rates and how changes to the geographical sharing may increase the organ procurement rates.

The Organ Procurement and Transplantation Network (OPTN) is the network of transplant centers and OPOs established by US Congress under the NOTA in 1984. OPTN facilitates the interaction among all professionals involved in organ donation and transplantation. United Network of Organ Sharing (UNOS) is a private nonprofit organization which administers the OPTN under contract with Health Resources and Services Administration of the US Department of Health and Human Services.

A primary function of UNOS is to allocate (scarce) deceased-donor organs to transplant candidates. Given the imbalance between supply of and demand for organs, any allocation system that UNOS uses is bound to favor some candidates over others. With such countereacting objectives of all stakeholders involved in the transplantation system, it is virtually impossible to base deceased-donor organ allocation rules on a single metric. The 1984 NOTA mandates that the deceased-donor organ allocation system takes into account both efficiency (i.e. patient and graft survival) and equity (i.e. fair allocation) (NOTA, 1984). There is also consensus in the transplant community that the overall objective of the allocation process should be to balance efficiency and equity (Kusserow 1991, Zenios et al. 2000, Bertsimas et al. 2011).
The equity can be achieved by providing all candidates with equal opportunity to receive a transplant. In other words, an equitable allocation policy should give patients with different demographics equal access to organs. Efficiency corresponds to maximizing the total QALYs from transplant for all candidates. One way to improve efficiency is to increase the overall post-transplant survival. This is one of UNOS’ primary concerns; and it directly affects UNOS’ choice of organ allocation policy. However, because the post-transplant survival depends on both the recipient’s health status/characteristics and the donor’s characteristics, it is not immediately obvious which policy will achieve this goal.

Another way to improve efficiency is to lower organ wastage, which occurs due, in part, to the perishable nature of the procured deceased-donor organs. The time lag between when organ is procured and when it is transplanted i.e. Cold Ischemia Times (CIT) is an important factor affecting graft survival of an organ (Rao et al. 2009). As CIT increases, the graft failure risk increases. Donated organs which are not transplanted to a recipient within reasonable time have to be discarded. Because of the severe organ shortage, minimizing organ wastage is important, yet remains challenging. One reason for this is that transplant candidates, for their own sake, reserve the right to reject organ offers. If an organ gets rejected by sufficiently many patients, CIT for the organ may exceed the maximum allowable duration that it can be stored and the organ has to be discarded. Therefore, addressing the organ wastage requires UNOS to predict the transplant candidates’ responses to organ offers, which itself is a challenging task.

As UNOS strives to balance efficiency and equity, there are also important biological constraints. In particular, a donated organ may not be a match for every transplant candidate on the waiting list. One reason for this is that a transplanted organ maybe perceived as a “foreign intrusion”, and human body’s immune system may put forth an effort to “destroy” the transplanted organ to protect itself. In order to avoid this, a prospective donor-recipient pair should satisfy certain match criteria (Weir and Lerma 2014, Busuttil and Klintmalm...
One basic matching criterion is ABO blood type: A, B, O, or AB. Candidates can receive organs from donors of identical blood type. Blood type AB candidates are compatible to receive organs from donors of all other blood types whereas blood type O donors are compatible to donate organs to candidates of all other blood types. If the donor-recipient pair is neither blood type identical nor compatible, they are ABO mismatched. ABO mismatched kidney transplantation is not allowed by UNOS. However, ABO mismatched liver transplantation is possible yet not advised (Gugenheim et al. 1990). Accordingly, only candidates of severe health conditions receive liver offers with ABO mismatch.

Blood type matching is not the only criterion for histocompatibility. Human body contains Human Leukocyte Antigens (HLAs) which define the familiarity of certain proteins to our organism. In the case of an organ transplant, the HLA antigens of the donor organ that do not match the recipient may be recognized as an intrusion by the recipient’s body upon transplantation. Corresponding anti-HLA antibodies are formed in recipient’s immune system which can cause acute and chronic rejection. In order to avoid this, the candidate is treated with immunosuppressive drugs which prevents anti-HLA production mechanism. This increases the candidates’ access to organs yet it may decrease the graft survival. Moreover, if the candidate has preformed HLA antibodies against the organ prior to the transplant, the donor-recipient pair is identified as a positive cross match and the transplantation is ruled out.

Upon every organ donation, UNOS determines the eligible pool of candidates according to above criteria. The eligible candidates can be located anywhere in the United States. To facilitate the allocation of organs, UNOS has established 11 geographic regions that further subdivided into 58 local donor service areas (DSAs). A DSA consists of potentially multiple transplant centers and one OPO. A donated organ is first offered to the candidates waitlisted in the DSA of the OPO that is procuring the organ. If no transplant candidate within the DSA accepts the offer, then the organ is offered to the regional list. Similarly, if no one
within the region accepts the offer, then it is offered to the national list.

![UNOS Regions](http://optn.transplant.hrsa.gov)

Figure 5: UNOS Regions, retrieved from: http://optn.transplant.hrsa.gov

At each step of the process, candidates are assigned points which depend on both the donor’s and candidate’s characteristics. UNOS follows two inherently different point systems for deceased-donor kidney and liver allocation. Both point systems exhibit variety of features promoting efficiency and equity.

Candidates who are listed for more than one organ transplant (e.g. kidney-pancreas) receive top priority. These patients are in high urgency in terms of their medical situation. In addition, as shown in Figure 2, the number of patients who need multiple organ transplants is far fewer than the number of those patients listed for a single organ transplant. Hence, their prioritization does not significantly impact the allocation system while providing efficiency by contributing to their survival. Liver allocation rule follows a similar principle by first offering organs to Status 1A candidates who otherwise will die in a week.

To further improve medical utility, ESRD patients with better EPTS scores are matched with kidneys of better KDPI scores. To be specific, candidates in the top 20th EPTS percentile are given priority to receive kidney’s of top 20th KDPI percentile (so called longevity matching). Pediatric candidates, since their EPTS score is better due to their age, are preferentially offered kidneys in the top 34th KDPI percentile. These practices attempt to
minimize the graft failure risk by exploiting the good health status of the candidate before they wait on dialysis for too long.

Pediatric candidates receive further prioritization. These candidates are awarded with extra points which presumably accelerates the process of receiving a transplant. This improves UNOS’ objective on efficiency since pediatric candidates have higher life expectancy. On the other hand, Bunzel and Laederach-Hofmann (2000) argues that post-transplant non-compliance rate, e.g. not adhering to immunosuppressive drug regimens, is high among pediatric recipients. This raises the question of whether prioritizing the pediatric candidates necessarily results in higher efficiency.

One way in which the deceased-donor transplantation system builds equity in the kidney allocation policy is to award priority points to the patients commensurate with their waiting times. In most service systems, serving people (who otherwise have identical characteristics) on a first-come-first served basis is considered fair. In a similar vein, the deceased-donor kidney candidates receive one point for each year they spend on the waiting list. The candidates start accruing waiting time points as soon as they are listed. All else being equal, the waiting time points ensure that whoever was listed earlier will also have access to organs earlier. The liver allocation system uses waiting time only as a tie breaker among patients who have identical MELD scores. Rather than accruing waiting time since the initial time they were listed, ESLD patients accrue waiting time for their historical MELD scores. In particular, the time they spend at each MELD category is recorded separately. Specifically, a candidate’s waiting time is the total waiting time spent at MELD scores higher than the current MELD score.

Sensitized patients (i.e. patients who have anti-HLA antibodies as a result of blood transfusion, pregnancy, or prior transplants) are at a disadvantage in terms of their likelihood of finding an eligible kidney and may wait twice as long as patients who are not sensitized. If a patient has anti-HLA antibodies that will counteract with at least one of the donor’s HLAs, the pair is identified as a positive cross match. In this case, the transplantation is ruled
out. Sensitized patients are more likely to have positive cross-match results. All transplant candidates are tested for the anti-HLA antibodies, and are assigned with a Calculated Panel Reactive Antibody (CPRA) score which is an estimate for how unlikely for a patient to find a matching kidney. For example, a patient of CPRA score 99 has only 1% chance of finding an organ without a positive crossmatch. Patients who have CPRA score greater than 20 are called sensitized and awarded extra points. Since they have a disadvantage in terms of finding a histocompatible organ, the extra points they receive stems from the desire to have an equitable allocation policy.

As discussed earlier, blood type compatibility is necessary for organ transplantation. On the other hand, the US population is not uniform in terms of ABO blood type distribution. This creates a discrepancy of organ supply and demand blood types for candidate of two blood types. Blood type O donors are compatible with all other blood types. However, blood type O candidates can only receive kidneys from blood type O donors. This raises the risk that blood type O patients will have less access to organs if the organs were distributed on compatibility basis. On the other hand, blood type B is the most rare ABO blood type in US population which directly decreases the donations of blood type B. In order to ensure blood type O and B candidates can receive transplants, donated kidneys with blood type O and B are first offered to blood type identical candidates on the local, regional, and national list. As a result, blood type O or B organs should be rejected by all the blood type identical candidates on the local, regional, and national list in order to be offered to any blood type compatible candidates. Exceptions occur only for transplant candidates with 0-HLA mismatch where deceased-donor kidneys of blood type O and B are offered to candidates who do not have identical blood type.
From an academic perspective, the interaction between UNOS and the transplant candidates can be viewed as one of strategic nature. Transplant candidates are forward looking and naturally seek to maximize their self interest. As such they may decline organ offers without penalty. In an allocation system where waiting time matters, this can crucially influence the way candidates respond to organ offers. In particular, the transplant candidates close to the top of the waiting list tend to be more selective and reject more offers (Sandikci et al. 2008, 2013). This creates a dilemma for UNOS because the candidates who receive a higher risk organ offer first will likely decline it. In addition, Leshno (2015) shows that candidates who are expecting long waiting times tend to accept offers with mismatch, decreasing efficiency. Taking into account such incentives of the transplant candidates, UNOS has been making parallel offers using the online software DonorNet since 2007. DonorNet intends to expedite the organ placement by a system of electronic organ offers for organs refused by all centers in a given OPO. Through this system, offers are transmitted to transplant candidates outside of the donating OPO, with only three open offers allowed at a time and up to 1 hour allowance to decline an offer (Massie et al. 2009).

Using historical data, UNOS studies patients’ past decisions to predict the responses to possible organ offers. Indeed, Scientific Registry of Transplant Recipients (SRTR) studies the transplant candidates’ decisions for specific organ offers and develops a prediction model.
that takes into account the donor and recipient characteristics. UNOS uses this model to evaluate the proposals for changes to allocation policy. To be more specific, Kidney Pancreas Simulation Allocation Model (KPSAM) and Liver Simulation Allocation Model (LSAM), which are also developed by SRTR, are used to test policy proposals in order to predict the number of transplantations, number of deaths while waiting, and several other performance measures under the proposed changes. As a result, UNOS takes into account patients choice as it strives to improve the allocation outcomes.

3 Research opportunities in the area

The complexity of the deceased-donor organ transplant system makes it challenging to come up with innovative solutions that improve the system and are broadly accepted by all stakeholders, especially given the inherent trade off between the efficiency and equity. Nonetheless, many researchers have been working on various aspects of the deceased-donor organ transplant system and have made important contributions over the last few decades. In what follows, we will discuss those as they relate to the resource allocation paradigm and operations research. We will also discuss some of the remaining challenges that are key to improving the deceased-donor kidney allocation system further.

3.1 Past research on the transplant candidate’s problem

In evaluating a proposed change to the allocation policy and the resulting outcomes, it is important to take into account the patient choice. Consider a transplant candidate who seek to optimize her total QALYs. She may decline some organ offers although organs are scarce. Interestingly, this may be in her best interest to do so. To elaborate on this, note that upon receiving an offer, the transplant candidate evaluates the expected life years from accepting this offer. Then, she weighs this against the alternative and the likelihood of receiving a better organ in the future. As mentioned above, this reasoning can be formalized as an
optimal stopping problem.

The organ quality is observable to the candidates when they are evaluating an offer. For kidneys, the graft failure risk is quantified by KDPI score. Therefore, candidate and the transplant surgeon can evaluate the organ in terms of the trade off mentioned above. In the case of livers, donor’s age as well as comorbidities can be used to estimate the graft survival, which the physician can assess and communicate to the transplant candidate.

The organ characteristics are not the only deciding factors when a candidate is evaluating an organ offer. If the transplant candidate rejects an organ, she should consider when she is going to receive another organ offer. The motivation for doing so may differ for ESLD and ESRD patients. Since mortality rate is high, the liver transplant candidates reject an organ offer only if they are convinced that they will stay alive until another organ offer arrives. For kidney transplant candidates, the mortality rate is less of a concern. However, spending more time on dialysis decreases their EPTS score, hence the utility from a transplant. In either the deceased-donor kidney transplant system or the deceased-donor liver transplant system, a patient waiting for a transplant rejects an organ offer only if the expected benefit of doing so outweighs the expected cost.

To build intuition, let us consider the simpler case of deciding the optimal timing of a liver transplant from a living donor. Considering a living donor-recipient pair provides significant insights on how recipient’s behavior is affected purely by their health status. Since there is a living donor involved, the candidates do not need to worry about the uncertainty in the timing of an organ offer from the waiting list. Additionally, the candidate does not need to account for uncertainty in organ quality. Alagoz et al. (2004) studies such a problem as a Markov Decision Process (MDP) where an ESLD patient decides on when to receive the transplant. They show that the decision of the candidate follows a threshold policy over the MELD score and age of the living donor. David and Yechiali (1985) studies a similar problem for an ESRD patient. They characterize the optimal stopping decision of the patient as a function of the HLA match level with the living donor and deteriorating health status of the
If the candidate does not have a living donor, she needs to wait for an organ offer from the waiting list. For deceased-donor liver candidates, the likelihood of receiving an organ offer can accurately be inferred from candidate’s MELD score. Alagoz et al. (2007a,b) model the deceased-donor liver offers to a specific candidate as a discrete time Markov Chain depending to their MELD score. Sandikci et al. (2008) builds on the earlier models using perfect information from the waitlist as well as the MELD score. In reality, candidates do not get to observe their exact position on the waitlist. However, the fact that a candidate receives organ offers gives them some information about her position on the waiting list. Therefore, Sandikci et al. (2013) models the decisions of the candidate as a partially observed Markov decision problem. The candidate seeks to maximize QALY while the MELD score also evolves as a random walk. Under certain assumptions, the authors show that the optimal policy is of threshold type with respect to the monotone likelihood order on the space of probability measures.

Ahn and Hornberger (1996) and Hornberger and Ahn (1997) develop an empirical model for the decision process of a deceased-donor kidney candidate. They model candidate’s health as a discrete time Markov chain where the patient can be on dialysis, ineligible for transplant, received a transplant, transplant failed, and deceased. They assume that candidates apply a threshold policy to accept the deceased-donor kidney offers according to one year graft survival rate. The authors estimate this threshold using logistic regression.

### 3.2 Challenges in modeling patient choice

A transplant candidate’s decision cannot be studied in isolation from the other candidates. For example, if the candidate has sufficient information about the wait list, then she should consider the behavior of candidates who are ahead of her. In particular, the candidate should note that an organ offer will be available to him only if all candidates who have higher points reject the current organ offer. In other words, patients’ choices should be studied in equilib-
rium. The specific equilibrium concept that is appropriate depends on both the informational assumptions and the tractability concerns. Sharpening these questions and further studying the patients’ accept/reject decisions in equilibrium is a fruitful future research direction.

Considering the concept of equilibrium in deceased-donor organ allocation system, one can reasonably believe that the candidates have very little knowledge about the other candidates on the waiting list. This imposes a great deal of uncertainty for a candidate to forecast how the other candidates on the waitlist will behave. In a recent study, Bandi et al. (2016) models the US deceased-donor kidney system as a multi-class multi-server queue where candidates have no information about other candidates and organ availability. The authors suggest a robust optimization solution methodology based on integer programming, and estimate waiting time given certain candidate characteristics.

Similar to most prior research, we postulate that a candidate’s discrete choice of accepting or rejecting an organ offer is based on the difference between QALY after transplantation and the cost of waiting until receiving the specific type of organ. However, it may be a strong position to take that the transplant candidate’s behavior can be predicted perfectly as the aforementioned analytical work suggests. In general, there may be idiosyncratic factors that the transplant candidate takes into account, which are unobservable to the researcher. Incorporating such idiosyncratic factors gives rise to the probabilistic discrete choice models that have been studied extensively in the literature, see for example, Ben-Akiva and Lerman (1985) and Anderson et al. (1992).

Under such idiosyncratic factors or shocks to utility, the dynamic nature of the problem can be modeled as follows. A candidate has two choices upon every organ offer she receives: accepting the current offer or rejecting it to wait for a better quality organ. The utility from accepting an organ offer is determined directly by the characteristics of the current organ under consideration whereas the utility of rejecting the organ offer needs to take into account the utility to be gained from a possible offer accepted in the future, the cost of waiting as well as the possibility of death. This setting can be studied using the framework of dynamic
discrete choice models. A closely related paper in that literature is Rust (1987) which uses an optimal stopping problem to study a maintenance manager’s decisions of either replacing the engine of a bus and incurring the cost of overhaul or not replacing the engine and incurring the cost of unexpected failure. More recently, in the operations research literature, Aksin et al. (2013, 2017) propose an optimal stopping model for empirically studying callers’ abandonment behavior in a call center. Ata et al. (2017c) and Ata and Peng (2017) lay out the theoretical foundations of studying such optimal stopping models for call centers in an equilibrium framework using queueing theory.

Ata et al. (2017b) uses a dynamic discrete choice model to empirically study the patients’ accept/reject decisions for deceased-donor kidney offers in an equilibrium framework. The authors also conduct counterfactual studies to assess potential policy changes taking into account possible changes in patient behavior.

3.3 Past research on the deceased-donor organ allocation policy

One aspect of the allocation problem UNOS faces is the geographic disparity. UNOS allocates deceased-donor organs according to the geographic location. As mentioned above, UNOS divides the country into 11 regions, which are further divided into 58 DSAs. To be specific, the deceased-donor kidney allocation system works as follows: A deceased-donor kidney is first offered to the waitlists in the DSA of the OPO. If the kidney is rejected by all candidates in the DSA, it is offered to the candidates in the region. Finally, if there are still no candidates willing to accept the offer, the kidney is offered to the national list. (The liver allocation system also uses a hierarchical geographical allocation rule.) Geographical hierarchy is at the heart of UNOS’ allocation policy. More than 70% of the procured deceased-donor kidneys are shared locally (Davis 2013). Although local sharing of organs may increase medical utility in some cases due to cold-ischemia time, volume of organ donations and recipient registrations vary significantly across DSAs due to variety of demographic factors. This disparity dramatically impact the waiting time of patients until they receive a transplant.
As a result, the fraction of candidates who receive a transplant within five years can be as high as 67.3% in some DSAs. This fraction can go as low as 25.5% for other DSAs as shown in Figure 7. This illustrates a severe equity issue, and addressing such issues may bring significant societal benefits (Ruth et al. 1985). This is in direct conflict with the 1998 final ruling of the Health and Human Services, which states:

“In principle, and to the extent technically and practically achievable, any citizen or resident of the United States in need of a transplant should be considered as a potential recipient of each retrieved organ on a basis equal to that of a patient who lives in the area where organs or tissues are retrieved.

Organs and tissues ought to be distributed on the basis of objective priority criteria, and not on the basis of accidents of geography.”

Figure 7: Percent of adult wait-listed patients, 2007, who received a deceased donor kidney transplant within five years, by DSA (Hart et al. 2017).

Several researchers used mathematical programming tools to improve upon the partitioning of the regions and DSAs; see for example Stahl et al. (2005), Kong et al. (2010), Gentry

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et al. (2013), and Davis et al. (2015). Although redistricting has promising result in terms of both equity and efficiency, such approaches have received strong resistance from regions which already have better supply/demand ratio. Washburn et al. (2011) summarizes this fact by saying “In general, any system that redistributes organs from areas of low need to high-need will be accepted by the high-need areas and rejected by low-need areas”. Consequently, redistricting does not seem to be a feasible way to overcome geographic disparities in the near future.

Interestingly, UNOS allows patients to multiple list in different DSAs. This raises an additional choice problem for candidates on where to join a waitlist. Although it is convenient for the candidates to register in a local transplant center, they may multiple list in transplant centers elsewhere to increase their chances of receiving a transplant and to lower their waiting time. The only requirement is that candidates should be able to travel to the transplant center within reasonable time. However, multiple listing requires the ability to travel and navigate the subtleties of the health care system. Therefore, it may not be a feasible option for many patients. Nevertheless, given the current geographical disparity, multiple listing offers a way to alleviate it as acknowledged by UNOS (Ardekani and Orlowski 2010).

Ata et al. (2016) suggests a model for making multiple listings available for a broader range of people. The authors study the service called OrganJet (also is an outgrowth of this research a startup company providing private jet services for multiple listing patients\(^5\) that brings people to the organs rather than bringing organs to people. The proposed operational solution does not require a policy change, and hence is politically feasible. The authors model the DSA choice of candidates for multiple listing as a congestion game using fluid and diffusion approximations, and identify the main routes that the jet service should be offered. As a result, they design a system that reduces geographic disparity via multiple listings which is implementable.

\(^5\)http://www.organjet.com

Within the geographical hierarchy, UNOS further assigns patients priority points, de-
terminating which transplant candidate will be offered the next available organ. Due to the stochastic nature of the organ and candidate arrivals, the allocation problem is non-trivial even if the candidates did not potentially decline organ offers. Because there are many candidate and donor attributes which need to be taken into account, the organ allocation problem has been viewed as a multi-dimensional stochastic dynamic optimization problem. Moreover, since waiting time is such an important contributor to organ allocation, queueing theory is extensively used in this area, see for example Zenios (1999), Gupta (2013), and Drekic et al. (2015).

Given the scarcity of resources, it is extremely important to allocate organs optimally. The early work by Righter (1989) and David and Yechiali (1995) consider non-stationary stochastic arrival of organs and patients where the candidates are not allowed to turn down offers. Righter (1989) proves that a threshold policy over value of transplant, which is determined by the candidate characteristics, is socially optimal. David and Yechiali (1995) suggests that the mismatched organs should be offered to candidates with most rare attributes. Zenios et al. (2000) builds on the earlier work and suggests an dynamic allocation model deceased-donor kidneys using a fluid approximation, see Alagoz et al. (2009) for a detailed discussion of the seminal work in the area.

Although these papers provide key insights, they do not incorporate patient choice i.e. the fact that organ offers may be declined. However, incorporating patients’ accept/reject decisions into the organ allocation problem gives rise to a model that is challenging to study. This is because of the fact that after an organ is rejected by a transplant candidate, it will be reallocated. Unfortunately, accounting for such phenomena is not always analytically tractable given the complexity of the system. However, simulating such allocation system is feasible. Zenios et al. (1999), Howard (2001), Su et al. (2004), Thompson et al. (2004), and Shechter et al. (2005) are among to first to incorporate candidate choice into allocation policies by simulation.

Under certain assumptions, the candidate choice can also be incorporated in analytical
models. Akan et al. (2012) develops an optimal liver allocation policy given probabilistic choices of candidates which are static. They model the waiting list as an overloaded multi-class queue, and account for MELD score evolution of liver candidates. Upon every organ arrival, they propose to allocate the organ to the patient class which will have the highest marginal benefit.

Su and Zenios (2004) investigates the effect of patient choice on the deceased-donor kidney transplant system. The authors incorporate patient heterogeneity and show that contrary to currently implemented deceased-donor kidney allocation, last-come-first-served policy will be more efficient in deceased-donor kidney allocation.

Su and Zenios (2005) studies a model where candidates and kidneys are partitioned into exclusive groups according to their EPTS and KDPI score, respectively. They match the deceased-donor organs and recipients based on longevity, disregarding the time that recipient spent on the wait list. Under such a policy, efficiency is maximized. Moreover, a patient has no incentive to reject an organ offer since waiting more does not necessarily increase the quality of an organ offer in the future.

Su and Zenios (2006) recognizes the fact that candidates may have private information about their life expectancy and life quality after transplantation. Consequently, a discrepancy emerges between the organ quality that a candidate is willing to transplant and the quality of organs that the allocation policy offers to him. As a remedy, candidates are allowed to specify a quality range for the organs that they are willing to accept when they join the waitlist. Therefore the waitlist is partitioned into multiple queues where candidates choose which queue to join. They prove that such system improve both efficiency and equity.

Bertsimas et al. (2013) develops a data-driven optimization model for a fundamentally different prioritization system. They construct an additive point system of the characteristics that UNOS takes into account, and determine optimal weight of each characteristic. The authors test their proposed policy by a simulation study which suggests an 8% improvement in QALY.
3.4 Challenges in modeling the deceased-donor organ allocation policy

UNOS evaluates proposals to change the allocation policy quantitatively to assess the potential impact. Simulation studies are commonly used in the academic literature to illustrate the effectiveness of a new solution approach; see for example Su et al. (2004), Stahl et al. (2005), Akan et al. (2012), Gentry et al. (2013), Davis et al. (2015), and Bertsimas et al. (2013). Similarly, UNOS uses the Liver Simulation Allocation Model (LSAM) and Kidney Pancreas Simulation Allocation Model (KPSAM) to study the impact of possible changes to the liver and kidney allocation policies, respectively. In particular, KPSAM has been used extensively to assess the impact of potential changes in the deceased-donor kidney allocation system during the decade prior to the implementation of the new policy which became effective in December 2014.

One key challenge of using simulation studies to compare alternative policy proposals for organ transplant system is the endogenous nature of the transplant candidates’ behavior. That is, as the policy changes, the candidates’ behavior may change too. Such changes in behavior have not been accounted for in previous simulation models. Rather, they use historical data and assume patients behavior remains the same. However, the historical data may fail to capture the change in patient behavior given the incentives provided by the new policy as articulated by Israni et al. (2014): “The KPSAM cannot account for changes in organ acceptance behavior. Therefore, if the new policy results in dramatic changes in organ acceptance behavior, the estimates of number of transplants from the simulations will differ from reality”. This can lead to erroneous conclusions regarding the potential impact or unintended consequences of a proposed policy change especially when one considers a major change. Incorporating patients’ accept/reject decisions (and their endogenous nature) is an important challenge. Although this research avenue is largely unexplored, recent work by Ata et al. (2017a,b) explore the effects of such endogenous patient behavior. A related issue arising in the study of callers’ abandonment behavior in call centers is explored by Ata et al.
3.5 Research problems from the perspective of other stakeholders

Transplant centers are also involved in their patients’ accept/reject decisions for organ offers. Transplant centers guide the patients through the process of receiving a transplant. Making an accept/reject decision upon receiving an organ offer involves assessing the quality (and match) of the current organ and forecasting the availability of the other organ offers in the future. How the patient’s health may evolve should also be considered. Given the complexity of the deceased-donor transplant system, this can be a daunting task for many patients. Therefore, the transplant candidates rely heavily on their physician’s guidance. In fact, Howard (2002) notes that the decision makers are surgeon-candidate pairs.

In this context, it is important to point out that a surgeon, and transplant centers in general, interact with multiple candidates on their waitlist. Then, it is not entirely clear whether a surgeon advices each patient for accept/reject decisions in isolation or she considers all her other patients collectively (Roberts 2016). Specifically, a surgeon may think that the current organ offer maybe a better fit for another candidate on the same waitlist. If the surgeon is considering the welfare of the entire waitlist, she may discourage the current candidate from accepting the organ offer. Schummer (2016) suggests that this practice can significantly increase the efficiency if the candidates are risk averse.

This discussion reasonably captures what may happen in a setting where there is only one transplant center in the DSA. The situation and the decision problem gets far more complex if there are multiple transplant centers in the same DSA. Such decisions involve the risk of losing the organ to the other transplant centers in the same local area. This constitutes an interesting decision problem for transplant centers, which is explored in Randa (2018).

In addition, transplant centers vary in the criteria they use to evaluate organ offers for their patients. For example, because level of HLA mismatch does affect the graft survival of the transplanted organ due to immunosuppressive drug use, transplant centers determine the
maximum mismatch level that they are willing to accept for their patients. Transplant centers that have long waitlists may be more lenient when they are offered with HLA mismatched organs and pass them along to their candidates. On the other hand, transplant centers with shorter waitlists may be more strict about accepting HLA mismatched organs to ensure high graft survival to their patients. The study of transplant center behavior offers a rich set of future research questions.

Organ procurement itself is a costly procedure and requires various resources (Jendrisak et al. 2002, Moazami et al. 2007). Therefore, the hospitals are reimbursed by the OPOs to procure organs. Arora and Subramanian (2017) studies the reimbursement scheme and suggest improvements taking into account the OPO’s financial objectives as well as the societal benefits of organ procurement. To the best of our knowledge, the financial aspects of the transplant operations is not explored much in the literature aside from few exceptions; see for example, Abecassis (2006), Axelrod et al. (2010a,b), and Lee and Zenios (2012). Further research on the financial aspects of and the incentives in the transplant operations can further improve the system and the outcomes.

As discussed above, the OPO procures a deceased-donor organ only if there is intent for transplantation. When the organ quality is low, it may not be procured. Arikan et al. (2017) observes that there is quite a bit variation in the quality threshold for procuring organs across different locations, which seems to be driven by the variation in waiting times and the transplant center competition. The authors show that broader sharing of low quality organs can increase the intent for them, and hence, improve their procurement rates and the supply more broadly can help improve the system significantly. Further research to increase the supply of organs can address the crux of the issue, i.e. the supply shortage (Tayur and Welsh 2016).
4 Concluding Remarks

The stakeholders of the deceased-donor transplant system include transplant candidates, UNOS, transplant centers, and the OPOs. The problems facing the transplant candidates and UNOS have been studied by several researchers. As mentioned above, most papers in the extant literature focus on a single decision maker, modeling other stakeholders passively. However, any major policy change affects the transplant candidates’ subsequent behavior. Therefore, research that take into account the change in patient behavior to assess the impact of possible changes can be a great assistance to policy makers.

The problems that transplant centers and OPOs are facing have received less research attention from the operations research community. The transplant centers’ performances are monitored on the short-term patient and graft survival. This arguably leads to institutional risk aversion. In particular, these performance reviews can influence who the transplant centers sign up to their wait lists and which organs they accept. Ultimately, these regulations may cause an increase in the organ wastage and discourage innovation. As such, this area deserves further research attention. Similarly, the OPOs make the organ procurement decisions; and further research on potential ways of increasing the deceased-donor procurement rates can help increase the organ supply. Needless to say, any increase on the organ supply will improve the well being of the transplant candidates.

Lastly, the availability of data makes it possible to utilize empirical/data-driven research methods such as machine learning, reduced form empirical methods, and structural estimation. The empirical research will help bridge the theory and practice.
References


