

Optimizing Organ Allocation and Acceptance

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1 Introduction

Since the first successful kidney transplant in 1954, organ transplantation has been an important therapy for many diseases. Organs that can safely be transplanted include kidneys, livers, intestines, hearts, pancreata, lungs and heart-lung combinations. The vast majority of transplanted organs are kidneys and livers, which are the focus of this chapter. Organ transplantation is the only viable therapy for patients with end-stage liver diseases (ESLD) and the preferred treatment for patients with end-stage renal diseases (ESRD). As a result of the the urgent need for transplantations, donated organs are very scarce. The demand for organs has greatly outstripped the supply. Thus organ allocation is a natural application area for optimization. In fact, organ allocation is one of the first application of medical optimization, with the first paper appearing twenty years ago.

The United Network for Organ Sharing (UNOS) is responsible for managing the national organ donation and allocation system. The organ allocation system is rapidly changing. For instance, according to the General Accounting Office, the liver allocation policy, the most controversial allocation system [14], has been changed four times in the last six years [17, 28]. The multiple changes in policy over a short time period is evidence of the ever-changing opinions surrounding the optimal allocation of organs. For example, although the new liver allocation policy is anticipated to “better identify urgent patients and reduce deaths among patients awaiting liver transplants” [28], anecdotal evidence suggests that there is some question among the transplant community as to whether the new allocation rules are satisfactory [10, 26].

UNOS manages the organ donation and procurement via Organ Procurement Organizations (OPOs), which are non-profit agencies responsible for approaching families about donation, evaluating the medical suitability of potential donors, coordinating the recovery, preservation, and transportation of organs donated for transplantation, and educating the public about the critical need for organ donation. There are currently 59 OPOs that operate in designated service areas;

these service areas may cover multiple states, a single state, or just parts of a state [28]. The national UNOS membership is also divided into 11 geographic regions, each consisting of several OPOs. This regional structure was developed to facilitate organ allocation and to provide individuals with the opportunity to identify concerns regarding organ procurement, allocation, and transplantation that are unique to their particular geographic area [28].

Organs lose viability rapidly once they are harvested, but the rate is organ-specific. The time lag between when an organ is harvested and when it is transplanted is called the *cold ischemia time* (CIT). During this time, organs are bathed in storage solutions. The limits of CIT range from a few hours for heart-lung combinations, to nearly three days for kidneys. Stahl et al. [24] estimated the relationship between CIT and liver viability. The Scientific Registry of Transplant Recipients states that the acceptable cold ischemia time limit for a liver is 12 to 18 hours [22], whereas the Center for Organ Recovery and Education gives the maximum limit as 18 to 24 hours [5].

There are two major classes of decision makers in organ allocation. The first class of decision makers is the individual patient, or the patient and his/her physician. Typically, the objective for such a perspective is to maximize some measure of that patient's benefit, typically life expectancy. The second class may be described as "society," and its goal is to design an organ allocation system so as to maximize some given criteria. Some examples of these criteria include total clinical benefit and some measure of equity. Equity is a critical issue in the societal perspective on organ allocation since there is considerable evidence that certain racial, geographic and socioeconomic groups have greater access to organs than others [27].

We limit our discussion to the U.S. organ allocation system. The remainder of this chapter is organized as follows. In Section 2 we describe the kidney allocation system, and in Section 3 we detail the liver allocation system. These two organs comprise the vast majority of organ transplantations; the details for other organs are described on the UNOS webpage [28]. Previous

research on the patient's perspective is discussed in Section 4, while the societal perspective is described in Section 5. We provide conclusions and directions for future work in Section 6.

2 Kidney Allocation System

Over 60,000 patients are on the nationwide kidney waiting list. In 2003, 15,000 patients received a kidney transplant, of which over 40% were from living donors [29]. The kidney waiting list and number of transplants are larger than those of all other organs combined. However, this need is somewhat mitigated by the fact that an alternate kidney replacement therapy (dialysis) is widely available. We describe the kidney allocation system as of late 2004 below. This allocation system is subject to frequent revision; readers are referred to the UNOS webpage [28] for updates to these and other allocation policies.

Kidneys are typically offered singly; however, there are certain cases when a high risk of graft failure requires the transplant of both kidneys simultaneously. UNOS defines two classes of cadaveric kidneys: standard and expanded. Kidneys in both classes have similar allocation mechanisms, as described below. Expanded-criteria kidneys have a higher probability of graft failure, and are distinguished by the following factors:

1. Age. Kidneys from some donors between 50-59 years, and kidneys from every donor older than 60 are expanded-criteria kidneys.
2. Level of creatinine in the donor's blood, which is a measure of the adequacy of kidney function.
3. Kidneys from donors who died of cardiovascular disease may be considered expanded-criteria.
4. Kidneys from donors with high hypertension may be considered expanded-criteria.

Patients who are willing to accept expanded-criteria kidneys do not have their eligibility for regular kidneys affected.

The *panel-reactive antibody (PRA)* level is a measure of how hard a patient is to match. It is defined as the percentage of cells from a panel of donors with which a given patient's blood serum reacts. This estimates the probability that the patient will have a negative reaction to a donor; the higher the PRA level, the harder the patient is to match.

A *zero-antigen mismatch* between a patient and a cadaveric kidney occurs when the patient and donor have compatible blood types, and have all six of the same HLA-A, B and DR antigens. There is mandatory sharing of zero-antigen-mismatched kidneys. When there are multiple zero-antigen-mismatched kidneys, there is an elaborate tie-breaking procedure that considers factors such as the recipient's OPO, whether the patient is younger than 18, and certain ranges of PRA level. One interesting concept is that of debts among OPOs. Except in a few cases, when a kidney is shared between two OPOs, the receiving OPO must then share the next standard kidney it harvests in that particular ABO category. This is called a *payback debt*. An OPO may not accumulate more than nine payback debts at any time. Priority for matching zero-antigen-mismatched kidneys is given to patients from OPOs that are owed payback kidneys. The full description of the tie-breaking procedure is available from the UNOS webpage [28].

If a kidney has no zero-antigen mismatches, kidneys with blood type O or B must be transplanted into patients with the same blood type. In general, kidneys are first offered within the harvesting OPO, then the harvesting region, and finally nationally. Within each of these three categories, patients who have an ABO match with the kidney are assigned points, and each kidney is offered to patients in decreasing order of points. A patient has the opportunity to refuse a kidney for any reason without affecting her subsequent access to kidneys.

Once minimum criteria are met, patients begin to acquire waiting time. One point is given to the patient who has been on the waiting list the longest amount of time. All other patients are accorded a fractional point equal to their waiting time divided by that of the longest-waiting

patient. A patient receives 4 points if she has PRA level 80% or greater. Patients younger than eleven years old are given 4 points, and patients between eleven and eighteen years of age are given 3 points. A patient is given 4 points if she has donated a vital organ or segment of a vital organ for transplantation within the United States. For the purposes of determining the priority within the harvesting OPO, a patient’s physician may allocate “medical priority points.” However, such points are not considered at the regional or national levels.

It is interesting to note that, excluding medical priority points, points based on waiting time can only be used to break ties among patients with the same number of points from other factors. In other words, kidneys are allocated lexicographically: the first factors are PRA level, age, and so on. Only among tied patients in the first factors is waiting time considered.

3 Liver Allocation System

This section describes the current liver allocation system. Basic knowledge of this system is necessary to understand the decision problem faced by the ESLD patients and the development of the decision models. The UNOS Board of Directors approved for implementation the new liver allocation procedure as of February 28, 2002 [28].

UNOS has different procedures for adult and for pediatric patients. Because researchers consider only the adult patients, we describe only the adult liver allocation procedure. UNOS maintains a patient waiting list that is used to determine the priority among the candidates. Under the current policy, when a liver becomes available, the following factors are considered for its allocation: Liver and patient OPO, liver and patient region, medical urgency of the patient, patient points, and patient waiting time.

The medical urgency of the adult liver patients is represented by UNOS Status 1 and MELD scores. According to the new UNOS policy, a patient listed as Status 1 “has fulminant liver failure

with a life expectancy without a liver transplant of less than 7 days” [28]. Patients who do not qualify for classification as Status 1 do not receive a status level. Rather, these patients will be assigned a “probability of pre-transplant death derived from a mortality risk score” calculated by the Model for End Stage Liver Disease (MELD) scoring system [28]. The MELD score, which is a continuous function of total bilirubin, creatinine and prothrombin time, indicates the status of the liver disease and is a risk-prediction model first introduced by Malinchoc et al. to assess the short-term prognosis of patients with liver cirrhosis [16, 30]. Wiesner et al. [30] develop the following formula for computing MELD scores:

$$\begin{aligned} \text{MELD Score} = & 10 \times [0.957 \times \ln(\text{creatinine mg/DL}) + 0.378 \times \ln(\text{bilirubin mg/DL}) \\ & + 1.120 \times \ln(\text{INR}) + 0.643 \times I_c] \end{aligned}$$

where INR, international normalized ratio, is computed by dividing prothrombin time (PT) of the patient by a normal PT value, and I_c is an indicator variable that shows the cause of cirrhosis, i.e., it is equal to 1 if the disease is alcohol or cholestatic related and it is equal to 0 if the disease is related to other etiologies. As Wiesner et al. [30] note, the etiology (cause) of disease is removed from the formula by UNOS. In addition to this, UNOS makes several modifications to the formula such as any lab value less than 1 mg/DL is set to 1 mg/DL, any creatinine level above 4 mg/DL is set to 4 mg/DL and the resulting MELD score is rounded to the closest integer [28]. By introducing these changes, UNOS restricts the range of MELD scores to be between 6 and 40, where a value of 6 corresponds to the best possible patient health and 40 to the worst.

Kamath et al. [15] developed the MELD system to more accurately measure the liver disease severity and to better predict which patients are at risk of dying. However, there are concerns about the accuracy of the MELD system. First, there were some biases in the data used to develop the model. For instance, the data available to the researchers were mostly based on patients with

advanced liver disease [16]. Furthermore, the MELD system was validated on the patients suffering from cirrhosis [30], therefore it is possible that the MELD system does not accurately measure the disease progression for other diseases, such as acute liver diseases. Moreover, as stated, although they presented data to indicate that the consideration of patient age, sex, and body mass is unlikely to be clinically significant, it is possible that other factors, such as a more direct measurement of renal function (iothalamate clearance), may improve the accuracy of the model [15]. Furthermore, the MELD system was validated on only three laboratory values: Creatinine and bilirubin levels, and prothrombin time. Thus, it is possible that the MELD system does not accurately consider patients with liver cancer because they would score as if they were healthy [10]. Consequently, relying mainly on laboratory results may not be the best solution for all patients [9].

Patients are stratified within Status 1 and each MELD score using patient “points” and waiting time. Patient points are assigned based on the compatibility of their blood type with the donor’s blood type. For Status 1 patients, candidates with an exact blood type match receive 10 points; candidates with a compatible, though not identical, blood type receive 5 points; and a candidate whose blood type is incompatible receives 0 points. As an exception, though type O and type A₂ (a less common variant of blood type A) are incompatible, patients of type O receive 5 points for being willing to accept a type A₂ liver. For non-Status 1 patients with the same MELD score, a liver is offered to patients with an exact blood type match first, compatible patients second, and incompatible patients last. If there are several patients having the same blood type compatibility and MELD scores, the ties are broken with patient waiting time. The waiting time for a Status 1 patient is calculated only from the date when that patient was listed as Status 1. Points are assigned to each patient based on the following strategy: “Ten points will be accrued by the patient waiting for the longest period for a liver transplant and proportionately fewer points will be accrued by those patients with shorter tenure” [28]. For MELD patients, waiting time is calculated as the time

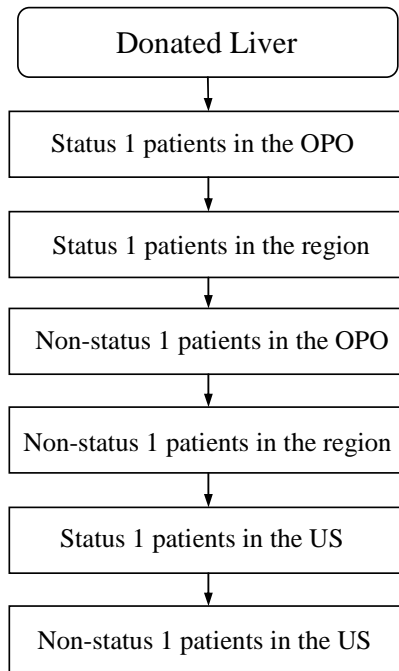


Figure 1: Current Liver Allocation System

accrued by the patient at or above her current score level from the date that she was listed as a candidate for liver transplantation.

Figure 1 shows a schematic representation of the liver allocation system. In summary, the current liver allocation system works as follows: Every liver available for transplant is first offered to those Status 1 patients located within the harvesting OPO. When more than one Status 1 patient exists, the liver is offered to those patients in descending point order where the patient with the highest number of points receives the highest priority. If there are no suitable Status 1 matches within the harvesting OPO, the liver is then offered to Status 1 patients within the harvesting region. If a match still has not been found, the liver is offered to all non-Status 1 patients in the harvesting OPO in descending order of MELD score. The search is again broadened to the harvesting region if no suitable match has been found. If no suitable match exists in the harvesting region, then the liver is offered nationally to Status 1 patients followed by all other patients in descending order of MELD scores.

UNOS maintains that the final decision to accept or decline a liver “will remain the prerogative of the transplant surgeon and/or physician responsible for the care of that patient” [14]. The surgeon and/or the physician have very limited time, namely one hour, to make their decision [28], because the acceptable range for cold ischemia time is very limited. Furthermore, as the Institute of Medicine points out, there is evidence that the quality of the organ decreases as cold ischemia time increases [14]. In the event that a liver is declined, it is then offered to another patient in accordance with the above-described policy. The patient who declines the organ will not be penalized and will have access to future livers. Organs are frequently declined due to low quality of the liver. For example, the donor may have had health problems that could have damaged the organ or may be much older than the potential recipient, making the organ undesirable [13].

4 Optimization from the Patient’s Perspective

This section describes the studies on the optimal use of cadaveric organs for transplantation that maximizes the patient’s welfare.

David and Yechiali [6] consider when a patient should accept or reject an organ for transplantation. They formulate this problem as an optimal stopping problem in which the decision maker accepts or reject offers $\{X_j\}_0^\infty$ that are available at random times $\{t_j\}_0^\infty$, where $\{X_j\}_0^\infty$ is a sequence of independent and identically distributed, positive bounded random variables with distribution function $F(x) = P(X \leq x)$. If the patient accepts the offer at time t_j , the patient quits the process and receives a reward $\beta(t_j)X_j$, where $\beta(t)$ is a continuous nonincreasing discount function with $\beta(0) = 1$. If the patient does not accept the offer, then the process continues until the next offer, or patient death. The probability that the decision maker dies before the new offer arrives at time t_{j+1} is given by the variable $1 - \alpha_{j+1} = P(T \leq t_{j+1} | T > t_j)$ defined by T , the lifetime of the underlying process. Their objective is to find a stopping rule that maximizes the

total expected discounted reward from any time t onward.

They first consider the case in which the offers arrive at fixed time points and there are a finite number of offers (n) available. In this case, they observe that the optimal strategy is a control-limit policy with a set of controls $\{\lambda_n^j\}_{j=0}^n$, and an offer X_j at time t_j is accepted if and only if $\beta_j X_j > \lambda_n^j$, where λ_n^j is the maximum expected discounted reward if an offer at time t_j is rejected. Because for each $j \leq n$, $\{\lambda_n^j\}_{n=0}^\infty$ is a nondecreasing bounded sequence of n , it has a limit l_j .

They extend their model to the infinite-horizon problem in which the offers arrive randomly. They prove that if the lifetime distribution of the decision maker is IFR [4], then the optimal policy takes the form of a continuous nonincreasing real function $\lambda(t)$ on $[0, \infty)$, such that an offer x at time t is accepted if and only if $\beta(t)x \geq \lambda(t)$. $\lambda(t)$ is equal to the future expected discounted reward if the offer is rejected at time t and an optimal policy is applied thereafter. They show that the IFR assumption is a necessary assumption in this setting.

They also consider the case where the arrivals follow a nonhomogeneous Poisson process. They consider several special cases of this model such as the organ arrival is nonhomogeneous Poisson with nonincreasing intensity and the lifetime distribution is IFR. In this case, they prove that the control limit function $\lambda(t)$ is nonincreasing, so that a patient becomes more willing to accept lower quality organs as time progresses. They obtain a bound for the $\lambda(t)$ for this special case.

They provide an explicit closed form solution of the problem when the lifetime distribution is Gamma with homogenous Poisson arrivals. They present a numerical example for this special case using data related to the kidney transplant problem.

Ahn and Hornberger [1] and Hornberger and Ahn [11] develop a discrete-time infinite horizon discounted MDP model for deciding which kidneys would maximize a patient's total expected (quality-adjusted) life. In their model, the patient is involved in the process of determining a threshold kidney quality value for transplantation. They use expected 1-year graft survival rate as

the criterion for determining the acceptability of a kidney. The state space consists of patient state which includes five states: Alive on dialysis and waiting for transplantation (S_1); not eligible for transplantation (S_2); received a functioning renal transplant (S_3); failed transplant (S_4); and death (S_5). They assume that the patient assigns a quality-of-life score to each state. They use months as their decision epochs because of the sparsity of their data. The patient makes the decision only when she is in state (S_1). The quality-adjusted life expectancy (QALE) of the patient in state (S_1) is a function of (1) QALE if a donor kidney satisfying eligibility requirements became available and the patient has the transplantation, (2) QALE if an ineligible donor kidney became available and the patient is not transplanted, and (3) the quality of life with dialysis in that month. Due to the small number of states, they provide an exact analytical solution for threshold kidney quality.

They use real data to estimate the parameters and solve the model for four representative patients. The minimum 1-year graft survival rate, d^* , differs significantly among the four patients. They compare their results with what might be expected by using the UNOS point system for four representative donor kidneys. They also perform a one-way sensitivity analysis to measure the effects of the changes in the parameters. Their results show that the important variables that affect the minimum eligibility criterion are: Quality of life assessment after transplant, immunosuppressive side effect, probability of death while undergoing dialysis, probability of death after failed transplant, time preference, and the probability of being eligible for retransplantation.

Howard [12] presents a decision model in which a surgeon decides to accept or reject a cadaveric organ based on the patient's health. He frames the organ acceptance decision as an optimal stopping problem. According to his model, a surgeon decides whether or not to accept an organ of quality $q \in (0, \bar{q}]$ for a patient in health state $h \in (0, \bar{h}]$, where the state $q = 0$ describes a period in which there is no organ offer and the state $h = 0$ corresponds to death. The organ offers arrive with distribution function $f(q)$. If the surgeon rejects the organ, the patient's health evolves according

to a Markov process described by $f(h'|h)$, where $f(h'|h)$ is IFR. If the surgeon accepts an organ offer, then the probability that the operation is successful in period $t + 1$ is a function of current patient health h and organ offer q and is denoted by $p(h, q)$. If the patient's single period utility when alive is u and the immediate reward of a successful operation is B , the total expected reward from accepting an organ at time t , $EV^{TX}(h, q)$, and from rejecting an organ at time t , $EV^W(h)$ are as follows :

$$EV^{TX}(h, q) = p(h, q)B, \quad \text{and}$$

$$EV^W(h) = \int_q \int_h V^W(h', q') f(h'|h) f(q') dh' dq',$$

where $V^W(h, q)$ is defined by the following set of equations:

$$V^W(h, q) = u + \delta \max \{EV^{TX}(h, q), EV^W(h)\}.$$

He estimates the parameters in his decision model using liver transplantation data in the U.S. However, he does not provide any structural insights or numerical solutions to this decision model. Instead, he provides statistical evidence that explains why a transplant surgeon may reject a cadaveric liver offer. His statistical studies show that as the waiting list has grown over time, the surgeons have faced stronger incentives to use lower quality organs. Similarly, the number of organ transplantations has increased dramatically in years when the number of traumatic deaths decreased.

He also discusses the trends in organ procurement in light of his findings and describes some options to the policy makers who believe that too many organs are discarded. One option is to use the results of a decision that calculates the optimal quality cut-off and enforce it via regulations. Another option is to penalize hospitals that reject organs that are subsequently transplanted successfully by other transplant centers. It is also possible to implement a dual list system in which the region maintains two waiting lists, one for patients whose surgeons are willing to accept low

quality organs and one for patients whose surgeons will accept only high quality organs.

Alagoz et al. [3] consider the problem of optimally timing a living-donor liver transplant in order to maximize a patient’s total reward such as life expectancy. Living donors are a significant and increasing source of livers for transplantation, mainly due to the insufficient supply of cadaveric organs. Living-donor liver transplantation is accomplished by removing an entire lobe of the donor’s liver and implanting it into the recipient. The non-diseased liver has a unique regenerative ability, so that a donor’s liver regains its previous size within two weeks. They assume that the patient does not receive cadaveric organ offers.

In their decision model, the decision maker can take one of two actions at state $h \in \{1, \dots, H\}$, namely, “Transplant” or “Wait for one more decision epoch,” where 1 is the perfect health state and H is the sickest health state. If the patient chooses “Transplant” in health state h , she receives a reward of $r(h, T)$, quits the process and moves to absorbing state “Transplant” with probability 1. If the patient chooses to “Wait” in health state h , she receives an intermediate reward of $r(h, W)$ and moves to health state $h' \in S = \{1, \dots, H + 1\}$ with probability $P(h'|h)$, where $H + 1$ represents death. The optimal solution to this problem can be obtained by solving the following set of recursive equations:

$$V(h) = \max \left\{ r(h, T), r(h, W) + \lambda \sum_{h' \in S} P(h'|h)V(h') \right\}, h = 1, \dots, H,$$

where $V(h)$ is the maximum total expected discounted reward that the patient can attain when her current health is h .

They derive some structural properties of this MDP model including a set of intuitive sufficient conditions that ensure the existence of a control-limit policy. They prove that the optimal value function is monotonic when the transition probability matrix is IFR and the functions $r(h, T)$ and $r(h, W)$ are nonincreasing in h . They show that if one disease causes a faster deterioration in patient health than another, and yet results in identical post-transplant life-expectancy, then the

control limit for this disease is less than or equal to that for the other. They solve this problem using clinical data. In all of their computational tests, the optimal policy is of control-limit type. In some of the examples, when the liver quality is very low, it is optimal for the patient to choose never to have the transplant.

Alagoz et al. [2] consider the decision problem faced by liver patients on the waiting list: Should an offered organ of a given quality be accepted or declined? They formulate a discrete-time, infinite-horizon, discounted MDP model of this problem in which the state of the process is described by patient state and organ quality. They consider the effects of the waiting list implicitly by defining the organ arrival probabilities as a function of patient state.

They assume that the probability of receiving a liver of type ℓ at time $t + 1$ depends only on the patient state at time t and is independent of the type of liver offered at time t . According to their MDP model, the decision maker can take one of two actions in state (h, ℓ) , where $h \in \{1, \dots, H + 1\}$ represents patient health and $\ell \in S_L$ represents current liver offer. Namely, “Accept” the liver ℓ or “Wait for one more decision epoch”. If the patient chooses “Accept” in state (h, ℓ) , she receives a reward of $r(h, \ell, T)$, quits the process and moves to absorbing state “Transplant” with probability 1. If the patient chooses to “Wait” in state (h, ℓ) , then she receives an intermediate reward of $r(h, W)$ and moves to state $(h', \ell') \in S$ with probability $\mathcal{P}(h', \ell' | h, \ell)$. The optimal solution to this problem is obtained by solving the following set of recursive equations [18]:

$$V(h, \ell) = \max \left\{ r(h, \ell, T), r(h, W) + \lambda \sum_{(h', \ell') \in S} \mathcal{P}(h', \ell' | h, \ell) V(h', \ell') \right\},$$

$$h \in \{1, \dots, H\}, \ell \in S_L, \quad (1)$$

where $V(h, \ell)$ is the maximum total expected discounted reward that the patient can attain when her current state is h and the current liver offered is ℓ .

They derive structural properties of the model, including conditions that guarantee the existence of a liver-based and a patient-based control-limit optimal policy. A *liver-based control-limit policy*

is of the following form: For a given patient state h , choose the “Transplant” action and “Accept” the liver if and only if the offered liver is of type $1, 2, \dots, i(h)$, for some liver state $i(h)$, called the *liver-based control limit*. Similarly, a *patient-based control-limit policy* is of the simple form: For a given liver state ℓ , choose the “Transplant” action and “Accept” the liver if and only if the patient state is one of the states $j(\ell), j(\ell) + 1, \dots, H$, for some patient state $j(\ell)$, called the *patient-based control limit*.

The conditions that ensure the existence of a patient-based control-limit policy are stronger than those that guarantee the existence of a liver-based control-limit policy. They compare the optimal control limits for the same patient listed in two different regions. They show that if the patient is listed in region A where she receives more frequent and higher quality liver offers than region B, then the optimal liver-based control limits obtained when she is listed in region A are lower than those obtained when she is listed in region B.

They use clinical data to solve this problem, and in their experiments the optimal policy is always of liver-based control-limit type. However, some optimal policies are not of patient-based control-limit type. In some regions, as the patient gets sicker, the probability of receiving a better liver increases significantly. In such cases, it is optimal to decline a liver offer in some patient states even if it is optimal to accept that particular liver offer in better patient states. Their computational tests also show that the location of the patient has a significant effect on liver offer probabilities and optimal control limits.

5 Optimization from the Societal Perspective

Righter [19] considers a resource allocation problem in which there are n activities each of which requires a resource, where resources arrive according to a Poisson process with rate λ . Her model can be applied to the kidney allocation problem, where resources represent the organs and activities

represent the patients. When a resource arrives its value X , a nonnegative random variable with distribution $F(\cdot)$, becomes known, and it can either be rejected or assigned to one of the activities. Once a resource is assigned to an activity, that activity is no longer available for further assignments. Activities are ordered such that $r_1 \geq r_2 \geq \dots \geq r_n \geq 0$, where r_i represents the activity value. Each activity has its own deadline that is exponentially distributed with rate α_i and is independent of other deadlines. When the deadline occurs, the activity terminates. The reward of assigning a resource to an activity is the product of the resource value and the activity value. The objective is to assign arriving resources to the activities such that the total expected return is maximized. If all activity deadlines are the same, i.e. $\alpha_i = \alpha$ for all i , then the optimal policy has the following form: Assign a resource unit of value x to activity i if $v_i(\alpha) < x \leq v_{i-1}(\alpha)$, where each threshold, $v_i(\alpha)$, represents the total expected discounted resource value when it is assigned to activity i under the optimal policy. She defines $v_0(\alpha) = \infty$ and $v_{n+1}(\alpha) = 0$. Furthermore, $v_0(\alpha) > v_1(\alpha) > \dots > v_n(\alpha) > v_{n+1}(\alpha)$, where $v_i(\alpha)$ does not depend on n for $n \geq i$, and $v_i(\alpha)$ does not depend on r_j for any j .

She analyzes the effects of allowing the parameters to change according to a continuous time Markov chain on the structural properties of the optimal value function. She first assumes that the arrival rate of resources change according to a continuous Markov chain while all other model parameters are fixed, and proves that the optimal policy still has the same structure, where the thresholds do not depend on the r_j but depend on the current system state (environmental state). She then considers the case in which the activity values and deadline rates change according to a random environment and proves that the thresholds and the total returns are monotonic in the parameters of the model. In this case, the thresholds depend on the r_j 's as well as the environmental state. She also provides conditions under which model parameters change as functions of the environmental state that ensure the monotonicity of the total returns.

David and Yechiali [7] consider allocating multiple organs to multiple patients, where organs and patients arrive simultaneously. That is, an infinite random sequence of pairs (patient and organ) arrive sequentially, where each organ and patient is either of Type I with probability p or of Type II with probability $q = 1 - p$. When an organ is assigned to the candidate, it yields a reward $R > 0$ if they match in type, or a smaller reward $0 < r \leq R$ if there is a mismatch. If an organ is not assigned it is unavailable for future assignments, however, an unassigned patient stays in the system until he/she is assigned an organ. The objective is to find assignment policies that maximize various optimality criteria.

They first consider the average reward criterion. A policy π is average-reward optimal if it maximizes the following equation:

$$\phi_\pi(s) = \liminf_{t \rightarrow \infty} \frac{E \left[\sum_{n=0}^{t-1} r_\pi(n) \mid \text{initial state} = s \right]}{t},$$

where $r_\pi(n)$ is the average reward earned in day n and states are represented by pairs (i, j) denoting i Type I and j Type II candidates waiting in the system ($0 \leq i, j < \infty$). They prove that when there are infinitely many organs and patients, the optimal policy is to assign only perfect matches for any $0 \leq p \leq 1$ and $0 \leq r \leq R$, and the optimal gain is the perfect-match reward, R . If there exist at most k patients, then the reasonable policy of order k is the optimal policy, where a reasonable policy of order k is defined as follows. A policy is a reasonable policy of order k if it satisfies the following conditions with k being the smallest number n_1 specified in (ii): (i) Assign a match whenever possible and (ii) Assign a mismatch when n_1 candidates are present prior to the arrival.

They then consider the finite- and infinite-horizon discounted models. They show that for a finite-horizon model, the optimal policy has the following form: Assign a perfect match when available. Assign a mismatch if and only if $r > r_{n,N}^*$, where $r_{n,N}^*$ is a control limit that changes with the optimal reward-to-go function when there are n Type I candidates and N periods to

go. Unfortunately, they could not find a closed-form solution for $r_{n,N}^*$. They also show that the infinite-horizon discounted-reward optimal policy is of the following form: Assign a perfect match when available. Assign a mismatch according to a set of controls

$$r_1^* \geq r_2^* \geq \dots \geq r_{k-1}^* \geq r_k^* \geq \dots$$

on r and according to k , where k represents the number of mismatching candidates in the system and r_k are a set of control limits on r .

David and Yechiali [8] consider allocating multiple (M) organs to multiple (N) patients. Assignments are made one at a time and once an organ is assigned (or rejected) it is unavailable for future assignments. Each organ and patient is characterized by a fixed-length attribute vector $X = (X_1, X_2, \dots, X_p)$, where each patient's attributes are known in advance and each organ's attributes are revealed only upon arrival. When an offer is assigned to a patient, the two vectors are matched and the reward is determined by the total number of matching attributes. There are at most $p + 1$ possible match levels. The objective is to find an assignment policy that maximizes the total expected return for both discounted and undiscounted cases. They assume that p equals 1, so that each assignment of an offer to a candidate yields a reward of R if there is a match and a smaller reward $r \leq R$ if there is a mismatch.

They first consider the special case in which $M \geq N$, each patient must be assigned an organ and a fixed discount rate (α) exists. They assume that $f_1 \leq f_2 \leq \dots \leq f_N$, where f_1, \dots, f_N are the respective frequencies $P\{X = a_1\}, \dots, P\{X = a_N\}$, the N realizations of the attribute vector. Using the notation (\mathbf{f}) for (f_1, \dots, f_{N+1}) and (\mathbf{f}_{-1}) for $(f_1, \dots, f_{i-1}, f_{i+1}, \dots, f_{N+1})$, the optimality equations are:

$$V_{N+1, M+1}(\mathbf{f})|X_1 = \max \begin{cases} R + \alpha V_{N, M}(\mathbf{f}_{-1})|\{X_1 = a_i\} & \text{(match);} \\ r + \alpha \max_k V_{N, M}(\mathbf{f}_{-k}) & \text{(a mismatch);} \\ \alpha V_{N+1, M}(\mathbf{f}) & \text{(rejection),} \end{cases}$$

where $V_{N,M}(\mathbf{f})$ is the maximal expected discounted total reward when there are N waiting patients with N attribute realizations (a_1, \dots, a_N) and M offers available. They prove that if $N < M$ and a_1, \dots, a_N are distinct, the optimal policy is to assign a match whenever possible and to reject a mismatch or assign it to a_1 depending on whether $\alpha\xi_1 \geq r$ or $\alpha\xi_1 < r$, where $\xi_1 = f_1R + (1 - f_1)r$.

They then consider the case where $M = N$ and no rejections are possible. In this case, the optimal policy is as follows: If an offer matches one or more of the candidates, it is assigned to one of them. Otherwise it is assigned to a candidate with the rarest attribute. Finally, they relax the assumption that all candidates must be assigned and $M \geq N$. In this case, they prove that the optimal policy is to assign the organs to one of the candidates if a match exists and to assign to a_1 when $f_1 < \varphi$, where φ is a function of f_i s and can be computed explicitly for some special cases.

Zenios et al. [31] consider the problem of finding the best kidney allocation policy with the three-criteria objective of maximizing total quality-adjusted life years (QALYs), and minimizing two measures of inequity. The first measures equity across various groups in terms of access to kidneys and the second measures equity in waiting times. They formulate this problem using a continuous-time, continuous-space deterministic fluid model, but do not provide a closed-form solution.

In their model, there are K patient and J donor classes. They assume that patients of class $k = 1, \dots, K_W$ are registered on the waiting list and patients of class $k = K_W + 1, \dots, K$ have a functioning graft. The state of the system at time t is described by the K -dimensional column vector $x(t) = (x_1(t), \dots, x_K(t))^T$, which represents the number of patients in each class. Transplant candidates of class $k \in \{1, \dots, K_W\}$ join the waiting list at rate λ_k^+ and leave the waiting list with rate μ_k due to death or due to organ transplantation. Organs of class $j \in \{1, \dots, J\}$ arrive at rate λ_j^- , from which a fraction $v_{jk}(t)$ is allocated to transplant candidates k . Note that $v_{jk}(t)$ is a control variable and $u_{jk}(t) = \lambda_j^- v_{jk}(t)$ is the transplantation rate of class j kidneys into class

k candidates. When a class j kidney is transplanted into a class k , $k \in \{1, \dots, K_W\}$ patient, the class k patient leaves the waiting list and becomes a patient of class $c(k, j) \in \{K_W + 1, \dots, K\}$. Furthermore, $c(k, j)$ patients depart this class at rate $\mu_{c(k, j)}$ per unit time; a fraction $q_{c(k, j)} \in [0, 1]$ of these patients are relisted as patients of class k as a result of graft failure, whereas $1 - q_{c(k, j)}$ of them exit the system due to death.

The system state equations are given by the following linear differential equations:

$$\frac{d}{dt}x_k(t) = \lambda_k^+ - \mu_k x_k(t) - \sum_{j=1}^J u_{jk}(t) + \sum_{j=1}^J q_{c(k, j)} \mu_{c(k, j)} x_{c(k, j)}(t); \quad k = 1, \dots, K_W, \quad (2)$$

$$\frac{d}{dt}x_k(t) = \sum_{j=1}^J \sum_{i=1}^{K_W} u_{ji}(t) 1_{\{c(i, j)=k\}} - \mu_k x_k(t); \quad k = K_W + 1, \dots, K, \quad (3)$$

and are subject to the state constraints

$$x_k(t) \geq 0; \quad k = 1, \dots, K. \quad (4)$$

The organ allocation rates $u(t)$ must satisfy the following constraints:

$$\sum_{k=1}^{K_W} u_{jk}(t) \leq \lambda_j^-; \quad j = 1, \dots, J, \quad (5)$$

$$u_{jk}(t) \geq 0; \quad k = 1, \dots, K_W \quad \text{and} \quad j = 1, \dots, J. \quad (6)$$

The authors note that this model ignores the three important aspects of the kidney allocation problem: Crossmatching between donor and recipient, unavailability of recipients, and organ sharing between OPOs. The model assumes that the system evolution is deterministic. They use the quality-adjusted life years (QALY) to measure the efficiency of the model. Namely, they assume that UNOS assigns a quality of life (QOL) score h_k to each patient class $k = 1, \dots, K$, and the total QALY over a finite time horizon T is found using

$$\int_0^T \sum_{k=1}^K h_k x_k(t) dt.$$

For a given allocation policy $u(t) = (u_1(t)^T, \dots, u_J(t)^T)$, where $u_j(t) = (u_{j1}(t), \dots, u_{jK_W}(t))^T$, their first measure of equity, *waiting time inequity* is calculated by

$$\frac{1}{2} \int_0^T \sum_{k=1}^{K_W} \sum_{i=1}^{K_W} \lambda_k(t, u(t)) \lambda_i(t, u(t)) \cdot \left(\frac{x_k(t)}{\lambda_k(t, u(t))} - \frac{x_i(t)}{\lambda_i(t, u(t))} \right)^2 dt,$$

where $\lambda(t, u(t)) = (\lambda_1(t, u(t)), \dots, \lambda_{K_W}(t, u(t)))$ represents the instantaneous arrival rate into class k under allocation policy $u(t)$.

The second measure of equity considers the likelihood of transplantation. They observe that

$$\lim_{T \rightarrow \infty} \frac{\int_0^T \sum_{j=1}^J u_{jk}(t) dt}{\lambda_k^+ T}$$

gives the percentage of class k patients who receive transplantation. Then the vector of likelihoods of transplantation is given by

$$\frac{\int_0^T \tilde{D}u(t) dt}{\lambda^+ T},$$

where $\tilde{D} \in \mathcal{R}^{K_W \times K_W, J}$ is a matrix with components

$$\tilde{D}_{ki} = \begin{cases} 1 & \text{if } i \bmod K_W = k; \\ 0 & \text{otherwise.} \end{cases}$$

Because this form is not analytically tractable, they insert the Lagrange multipliers $\gamma = (\gamma_1, \dots, \gamma_{K_W})^T$ into the objective function using the following expression in the objective function:

$$\int_0^T \gamma^T \tilde{D}u(t) dt.$$

They combine the three objectives and the fluid model to obtain the following control problem:

Choose the allocation rates $u(t)$ to maximize the tri-criteria objective of

$$\int_0^T \left(\beta \sum_{k=1}^K h_k x_k(t) - (1 - \beta) \sum_{k=1}^{K_W} \sum_{i=1}^{K_W} \lambda_k(t, u(t)) \lambda_i(t, u(t)) \cdot \left(\frac{x_k(t)}{\lambda_k(t, u(t))} - \frac{x_i(t)}{\lambda_i(t, u(t))} \right)^2 + \gamma^T \tilde{D}u(t) \right) dt,$$

subject to (2)-(6), where $\beta \in [0, 1]$.

Because there does not appear to be a closed-form solution to this problem, they employ three approximations to this model and provide a heuristic *dynamic index policy*. At time t , the dynamic index policy allocates all organs of class j to the transplant candidate class k with the highest index $G_{jk}(t)$, which is defined by

$$G_{jk} = \pi_{c(k,j)}(x(t)) - \pi_k(x(t)) + \gamma_k,$$

where $\pi_{c(k,j)}(x(t))$ represents the increase in

$$\beta \sum_{k=1}^K h_k x_k(t) - (1 - \beta) \sum_{k=1}^{K_W} \sum_{i=1}^{K_W} \lambda_k(t, u(t)) \lambda_i(t, u(t)) \cdot \left(\frac{x_k(t)}{\lambda_k(t, u(t))} - \frac{x_i(t)}{\lambda_i(t, u(t))} \right)^2$$

if an organ of class j is transplanted into a candidate of class k at time t .

They construct a simulation model to compare the dynamic index policy to the UNOS policy and an FCFT (first-come first-transplanted) policy. They evaluate the effects of dynamic index policy on the organ allocation system for several values of β and γ . They consider two types of OPOs: A typical OPO and a congested OPO, where the demand-to-supply ratio is much higher than a typical OPO. Their results show that the the dynamic index policy outperforms both the FCFT and UNOS policy.

Su and Zenios [25] consider the problem of allocating kidneys to the transplant candidates who have the right to refuse the organs. They use a sequential stochastic assignment model to solve variants of this problem. They assume that the patients do not leave the system due to pre-transplant death.

Their first model considers the case when the patient does not have the right to reject an organ. This model also assumes that there are n transplant candidates with various types to be assigned to n kidneys, which arrive sequentially-one kidney in each period. The type of kidney arriving at time t is a random variable $\{X_t\}_{t=1}^n$, where $\{X_t\}_{t=1}^n$ are independent and identically distributed with probability measure P over the space of possible types \mathcal{X} . There are m patient types where

the proportion of type i candidates is denoted by p_i . When a type x kidney is transplanted into a type i patient, a reward of $R_i(x)$ is obtained. The objective is to find an assignment policy $I = (i(t))_{t=1, \dots, n}$ that maximizes total expected reward, $E \left[\sum_{t=1}^n R_{i(t)}(X_t) \right]$, where $i(t)$ denotes the candidate type that is assigned to the kidney arriving at time t . The optimization problem is to find a partition $\{A_i^*\}_{i=1}^m$ to

$$\begin{aligned} & \max_{\{A_1, \dots, A_m\}} \sum_{i=1}^m E[R_i(X) 1_{\{X \in A_i\}}] \\ & \text{such that} \quad P(A_i) = p_i \quad \forall i, \end{aligned}$$

where $\{A_i\}_{i=1}^m$ is a partition of the kidney space \mathcal{X} .

They analyze the asymptotic behavior of this optimization problem and prove that the optimal partitioning policy is asymptotically optimal as $n \rightarrow \infty$. This result reduces the sequential assignment problem into a set partitioning problem. If the space \mathcal{X} consists of k discrete kidney types with probability distribution (q_1, \dots, q_k) , then the partition policy can be represented by the set of numbers $\{a_{ij}\}_{1 \leq i \leq m, 1 \leq j \leq k}$ such that when a kidney of type j arrives, it is assigned to a candidate of type i with probability $a_{ij} / \sum_{i=1}^m a_{ij}$, where a_{ij} is the joint probability of a type i candidate being assigned a type j kidney. Then the optimal partition policy is given by the solution $\{a_{ij}^*\}$ to the following assignment problem:

$$\begin{aligned} & \max_{\{a_{ij}\}} \sum_{i=1}^m \sum_{j=1}^k a_{ij} r_{ij} \\ & \text{such that} \quad \sum_{i=1}^m a_{ij} = q_j \quad \forall j \\ & \quad \quad \quad \sum_{j=1}^k a_{ij} = p_i \quad \forall i. \end{aligned}$$

They derive the structural properties of the optimal policy under different reward functions such as multiplicative reward structure and a match-reward structure, in which if the patient and kidney types match the transplantation results in a reward of R and if there is a mismatch then the transplantation results in a reward of $r < R$. They show that if the reward functions satisfy

increasing differences assumption, i.e. $R_i(x) - R_j(x)$ is increasing in x , then the optimal partition is given by $A_i^* = [a_{i-1}, a_i)$, where $a_o = -\infty, a_m = \infty$, and

$$Pr(X \leq a_i) = p_1 + \dots + p_i.$$

They then consider the problem of allocating kidneys to the patients when the patients have the right to refuse an organ offer and measure the effects of patient autonomy on the overall organ acceptance and rejection rates. In this model they assume that an organ rejected by the first patient will be discarded. They define a partition policy $A = \{A_i\}$ as incentive-compatible if the following condition holds for $i = 1, \dots, m$:

$$\inf_{x \in A_i} R_i(x) \geq \frac{\delta}{p_i} \cdot E[R_i(X)]1_{\{X \in A_i\}},$$

where δ is the discount rate for future rewards. Intuitively, a partition policy will be incentive-compatible if each candidate's reward from accepting a kidney offer is no less than their expected reward from declining such an offer. They add the incentive-compatibility constraint to the original optimization problem to model candidate autonomy. They find that the inclusion of candidate autonomy increases the opportunity cost each candidate incurs from refusing an assignment and make such refusals unattractive.

They perform a numerical study to evaluate the implications of their analytical results. Their experiments show that as the heterogeneity in either the proportion of candidates or the reward functions increases, the optimal partitioning policy performs better. They compared the optimal partitioning policy to a random allocation policy with and without the consideration of candidate autonomy. In general, the optimal partition policy performed much better than using a random allocation policy. Additionally, candidate autonomy can have a significantly impact on the performance of the kidney allocation system. However, the optimal partitioning policy with the inclusion of incentive-compatibility (IC) constraints performs almost as well as the optimal policy when

candidates are not autonomous. This is because the inclusion of IC constraints eliminates the variability in the stream of kidneys offered to the same type of candidates.

Roth et al. [20] consider the problem of designing a mechanism for direct and indirect *kidney exchanges*. A *direct kidney exchange* involves two donor-patient pairs such that each donor cannot give his/her kidney to his/her own patient due to immunological incompatibility, but each patient can receive a kidney from the other donor. An *indirect kidney exchange* occurs when a donor-patient pair makes a donation to someone waiting for a kidney, and the patient receives high priority for a compatible kidney when one becomes available. The objective is to maximize the number of kidney transplants and mean quality of match.

Let (k_i, t_i) be the donor-recipient pair where k_i denotes kidney i from live donor and t_i denotes patient t_i and K denote the set of living donors at a particular time. Each patient t_i has a set of compatible kidneys, $K_i \subset K$, over which the patient has heterogenous preferences. Let w denote the option of entering the waiting list with priority reflecting the donation of his donor's kidney k_i . Let P_i denote the patient's strict preferences over $K_i \cup \{k_i, w\}$, where P_i is the ranking up to k_i or w , whichever ranks higher. A kidney exchanging problem consists of a set of donor-recipient pairs $\{(k_1, t_1), \dots, (k_n, t_n)\}$, a set of compatible kidneys $K_i \subset K = \{k_1, \dots, k_n\}$ for each patient t_i , and a strict preference relations P_i over $K_i \cup \{k_i, w\}$ for each patient t_i . The objective is to find a *matching* of kidneys/wait-list option to patients such that each patient t_i is either assigned a kidney in $K_i \cup \{k_i\}$ or the wait-list option w , while no kidney can be assigned to more than one patient but the wait-list option w can be assigned to more than one patient. A kidney exchange mechanism selects a matching for each kidney exchange problem.

They introduce the *Top Trading Cycles and Chains* (TTCC) mechanism to solve this problem and show that TTCC mechanism always selects a matching among the participants at any given time such that there is no other matching weakly preferred by all patients and donors and strictly

preferred by at least one patient-donor pair. They use a Monte-Carlo simulation model to measure the efficiency of the TTCC mechanism. Their results show that substantial gains in the number and match quality of transplanted kidneys might result from the adoption of the TTCC mechanism. Furthermore, a transition to the TTCC mechanism would improve the utilization rate of potential unrelated living-donor kidneys and Type O patients without living donors.

In another work, Roth et al. [21] consider the problem of designing a mechanism for pairwise kidney exchange, which makes the following two simplifying assumptions to the model described in [20]: (1) They consider exchanges involving two patients and their donors and (2) They assume that each patient is indifferent between all compatible kidneys. These two assumptions change the mathematical structure of the kidney exchange problem, and the problem becomes a cardinality matching problem. Under these assumptions, the kidney exchange problem can be modeled with an undirected graph whose vertices represent a particular patient and her incompatible donor(s), and whose edges connect those pairs of patients between whom an exchange is possible, i.e. pairs of patients such that each patient in the pair is compatible with a donor of the other patient. Finding an efficient matching then reduces to finding a maximum cardinality matching in this undirected graph. They use results from graph theory to solve optimally this problem and give the structure of the optimal policy.

Stahl et al. [23] use an integer programming model to formulate and solve the problem of the optimal sizing and configuration of transplant regions and OPOs, in which the objective is to find a set of regions that optimizes transplant allocation efficiency and geographic equity. They measure efficiency by the total number of intra-regional transplants and geographic equity by the minimum OPO intra-regional transplant rate, which is defined as the number of intra-regional transplants in an OPO divided by the number of patients on the OPO waiting list.

They model the country as a simple network, in which each node represents an OPO and arcs

connecting OPOs indicate that they are contiguous. They assume that a region can consist of at most 9 contiguous OPOs, an OPO supplies its livers only to the region that contains it, and both transplant allocation efficiency and geographic equity could be represented as factors in a function linking cold-ischemia time (CIT) and liver transport distance. They also assume that the probability of declining a liver offer, which is measured by the liver's viability, is solely dependent on its CIT. Primary nonfunction occurs when a liver fails to work properly in the recipient at time of transplant. They use two functional relationships between primary nonfunction and CIT: Linear and polynomial.

They solve an integer program to find the optimal set of regions such that the total number of intra-regional transplants are maximized. They define the binary variable x_j for every possible region j such that it is equal to 1 if region j is chosen and is equal to 0 if region j is not chosen. Then, the integer program is as follows:

$$\left\{ \text{Max} \sum_{j \in J} c_j x_j : \sum_{j \in J} a_{ij} x_j = 1, i \in I; x_j \in \{0, 1\}, j \in J \right\}, \quad (7)$$

where I is the set of all OPOs; J is the set of all regions; $a_{ij} = 1$ if region j contains OPO i , and 0 otherwise; and c_j represents the total number of intra-regional transplants for region j . They provide a closed-form estimate of c_j . If the number of regions is constrained to be equal to 11, then the constraint $\sum_{j \in J} x_j = 1$ is added. The integer program defined in (7) does not consider the geographic equity. Let f_{ij} and λ_{min} represent the intra-regional transplant rate in OPO i , contained in region j and the minimal local transplant rate, respectively. Then, the integer program considering the geographic equity can be reformulated as follows:

$$\left\{ \text{Max} \sum_{j \in J} c_j x_j + \rho \lambda_{min} : \sum_{j \in J} a_{ij} x_j = 1, i \in I; \sum_{j \in J} f_{ij} x_j - \lambda_{min} \geq 0, i \in I; x_j \in \{0, 1\}, j \in J \right\}, \quad (8)$$

where ρ is a constant that indicates the importance the decision-makers place on the minimum transplant rate across OPOs versus intra-regional transplants. Hence, changing ρ will provide a

means for balancing the two conflicting factors, transplant allocation efficiency and geographic equity.

They conduct computational experiments using real data to compare the regional configuration obtained from their model to the current configuration. The optimal sets of regions tend to group densely populated areas. Their results show that the proposed configuration resulted in more intra-regional transplants. Furthermore, for all values of ρ , the minimum intra-regional transplant rate across OPOs is significantly higher than that in the current regional configuration. However, as ρ increases, the increase over the current configuration diminishes. They also perform sensitivity analyses, which show that the outcome is not sensitive to the relationship between CIT and primary nonfunction.

6 Conclusions

Organ allocation is one of the most active areas in medical optimization. Unlike many other optimization applications in medicine, it has multiple perspectives. The individual patient's perspective typically considers the patient's health and how she should behave when offered choices, such as whether or not to accept a particular cadaveric organ, or when to transplant a living-donor organ. The societal perspective designs an allocation mechanism to optimize at least one of several possible objectives. One possible objective is to maximize the total societal health benefit. Another is to minimize some measure of inequity in allocation.

Given the rapid changes in organ allocation policy, it seems likely that new optimization issues will arise in organ allocation. A critical issue in future research is modeling disease progression as it relates to allocation systems. The national allocation systems are increasingly using physiology and laboratory values in the allocation system (e.g., the MELD system described in Section 3). Furthermore, new technologies may mean more choices to be optimized for patients in the future.

For example, artificial organs and organ assist devices are becoming more common. Given the intense emotion that arises in organ allocation, more explicit modeling of the political considerations of various parties will yield more interesting and more applicable societal-perspective optimization models.

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