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Determining the Acceptance of Cadaveric Livers Using an Implicit Model of the Waiting List

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The only available therapy for patients with end-stage liver disease is organ transplantation. In the United States, patients with end-stage liver disease are placed on a waiting list and offered livers based on location and waiting time, as well as current and past health. Although there is a shortage of cadaveric livers, 45% of all cadaveric liver offers are declined by the first transplant surgeon and/or patient to whom they are offered. We consider the decision problem faced by these patients: Should an offered organ of a given quality be accepted or declined? We formulate a Markov decision process model in which the state of the process is described by patient state and organ quality. We use a detailed model of patient health to estimate the parameters of our decision model and implicitly consider the effects of the waiting list through our patient-state-dependent definition of the organ arrival probabilities. We derive structural properties of the model, including a set of intuitive conditions that ensure the existence of control-limit optimal policies. We use clinical data in our computational experiments, which confirm that the optimal policy is typically of control-limit type.

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1. Introduction

Human organs available for transplantation are scarce. Although the number of organ transplants performed annually has increased since the enactment of the National Organ Transplant Act of 1984, the number of patients waiting for an organ transplant and the number of deaths while waiting have also increased dramatically (Institute of Medicine (IOM) 1999). In many ways, livers represent the most urgent shortage. Although there are more kidney transplants than liver transplants, there is no alternative therapy for end-stage liver disease (ESLD), unlike dialysis for kidney patients. When Congress instructed the IOM to assess the impacts of the changes in the organ allocation procedures, it focused on liver transplantation because "much of the current debate has centered on the procurement and allocation of livers" (IOM 1999, p. 1). Table 1 shows the U.S. liver-transplant data for 1996–2002 (United Network for Organ Sharing (UNOS) 2004). As presented in the table, the number of patients waiting for a liver and the number of deaths while waiting have increased dramatically between 1996 and 2002. In 2002, nearly 4,962 Americans were transplanted with a liver; however, the organ waiting list contained nearly 16,974 patients, more than 1,800 of whom died while waiting (UNOS 2004). Unfortunately, each year approximately 6% of all donated livers are wasted, and 15% of all patients who receive transplants die within the first year. These data suggest that there is a need to improve the allocation and usage of available organs.

In the United States, patients with ESLD are placed on a liver waiting list maintained by UNOS, the organization responsible for managing the national organ donation and allocation system. When a cadaveric organ is harvested, UNOS offers this organ to the patients on the waiting list using a complex priority system. Patients are assigned priorities based on geographic location, time spent on the waiting list, as well as current and past health. We describe the current liver allocation system in detail in §2.

Much of the research on the optimal allocation of organs (particularly kidneys) focuses on designing an optimal allocation system that maximizes society's welfare. These researchers seek to provide an optimal match between

Table 1. U.S. liver data between 1996 and 2002.

	1996	1997	1998	1999	2000	2001	2002
Patients waiting	7,265	9,303	11,579	13,999	16,192	18,047	16,974
Deaths	992	1,181	1,424	1,827	1,791	2,034	1,818
Transplants[1]	3,951	4,031	4,377	4,478	4,579	4,662	4,962
Wasted organs[2]	280	313	283	306	301	264	187
Survival rate[3] (%)	83	85	85	83	84	85	87

[1]Transplants from deceased donors.
[2]An organ is assumed to be wasted only if it is donated by a cadaveric recipient, is viable for transplantation, but is not used for transplantation.
[3]One-year posttransplant survival rate for cadaveric organ recipients.

organs and patients that maximizes objectives such as mean expected quality-adjusted life years, average one-year graft survival probability, and quality of the prospective matches (Righter 1989; David and Yechiali 1990, 1995; David 1995; Zenios et al. 1999, 2000; Su and Zenios 2005). Roth et al. (2004) consider the problem of designing a mechanism for kidney exchanges, under which a donor in a noncompatible patient/donor pair may give the patient highest priority by donating one of his/her kidneys to another patient in the waiting list. Some issues arising in such research include ethical issues such as equity among various minority groups (London Health Sciences Center (LHSC) 2004) and patient prioritization (LHSC 2004), as well as political issues such as states' rights (Ubel and Caplan 1998). Furthermore, according to the current liver allocation procedure, 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" (IOM 1999, p. 184). However, most of the existing models that consider the optimal organ allocation problem ignore the fact that patients, and/or surgeons acting on their behalf, may decline organs.

Given the scarcity of donated livers, it may seem surprising that organs are frequently declined. However, Howard (2002) reports that 45% of livers are declined by the first surgeon to whom they are offered. Livers are typically declined due to poor quality. For instance, in some cases patients/transplant surgeons decline organs from donors with central nervous system malignancy (Collignon et al. 2004). Roberts et al. (2004) report that if the liver is from an elderly donor or if there is a blood type or gender mismatch, then the liver may be similarly regarded as poor quality. Alexander and Zola (1996) provide several other criteria that may render a donor undesirable: obesity, lengthy intensive-care unit stay, serious infection, or malignancy. Intuitively, a relatively healthy patient may decline a poor-quality organ now if the prospect of higher-quality organs in the near future is sufficiently high.

The research question addressed in this study is whether a patient and/or transplant surgeon should accept or decline a cadaveric liver offer, as a function of her current state, e.g., health and/or waiting time. That is, we seek a policy describing the patient-state/liver-type combinations in which transplantation should occur, and those combinations in which waiting is optimal. The accept/decline decision depends on two major components: the patient's current and likely future state as well as her current and future prospects for organ offers.

As we describe in §2, because UNOS offers organs to the patients on the waiting list using a complex priority system, the composition of the waiting list and the decision rules used by other patients on the waiting list have a significant impact on the likelihood/distribution of organ offers that the patient receives. Under the current UNOS policy, a patient does not have full knowledge about the composition of the waiting list; however, as we describe in §2, there is a strong correlation between patient health and her rank on the waiting list. Therefore, we capture the effects of the waiting list *implicitly* by defining the organ arrival probabilities as a function of patient state. Similarly, the policies of the other patients are also implicitly captured by the organ arrival rates. That is, we assume that the decisions made by the patient do not affect the policies of the other patients.

Several researchers investigate problems similar to ours (David and Yechiali 1985, Ahn and Hornberger 1996, Hornberger and Ahn 1997). However, these studies use simple and static models of patient health and do not consider the waiting list. Howard (2002) models the problem of when to decline a cadaveric liver and provides statistical evidence that explains why a transplant surgeon may reject a cadaveric liver offer, but does not provide any numerical solutions or structural insights. Furthermore, he does not consider the effects of the waiting list on the organ offers. Alagoz et al. (2004) consider the problem of optimally timing a *living-donor* liver transplant to maximize a patient's total life expectancy. They employ detailed models of patient health and solve the problem using clinical data. Their model does not consider the possibility of a cadaveric organ offer. In fact, their model can be viewed as a special case of our model with the appropriate liver arrival probability matrix (namely, the patient is offered the living-donor liver and not a cadaveric one at all decision epochs with probability one). Because organs from living donors represent a small portion (6% in 2003) of all transplanted organs (UNOS 2004) and few patients restrict their attention to living donors only, the decision model of Alagoz et al. (2004) applies to only a relatively few number of patients.

This research differs from previous studies in several ways. Unlike the previous studies in the literature, we consider the effects of the waiting list on the organ arrivals. In contrast to most of the existing literature, which considers kidneys, this research addresses livers. Additionally, we use a detailed model of patient health based on data gathered from clinical observation to estimate the parameters of our decision model. Unlike David and Yechiali (1985, 1990, 1995), our results do not depend on unrealistic assumptions such as that the number of organs is equal to the number of transplant candidates or that the patient will receive less frequent organ offers as time progresses. Unlike Alagoz et al. (2004), we consider the cadaveric liver transplantation problem. The cadaveric-donor problem is more general than the living-donor-only case because there is uncertainty regarding the future availability of livers and because there are multiple organ types as opposed to a single organ of known quality available to the patient in the living-donor-only problem.

The remainder of this paper is organized as follows. We describe the current liver allocation system in §2. Section 3 presents a Markov decision process (MDP) model of the problem. We derive several structural properties of this MDP model and its optimal policy in §4. In §5, we present and discuss computational results. We draw some conclusions and discuss future research directions in §6.

2. Current Liver-Allocation System

In this section, we describe the current liver-allocation system to understand the decision problem faced by patients with ESLD. The UNOS board of directors approved the new liver-allocation procedure on February 28, 2002 (UNOS 2005).

UNOS manages the organ donation and procurement via organ procurement organizations (OPOs), which are nonprofit agencies responsible for 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, which further comprise 11 regions (UNOS 2005).

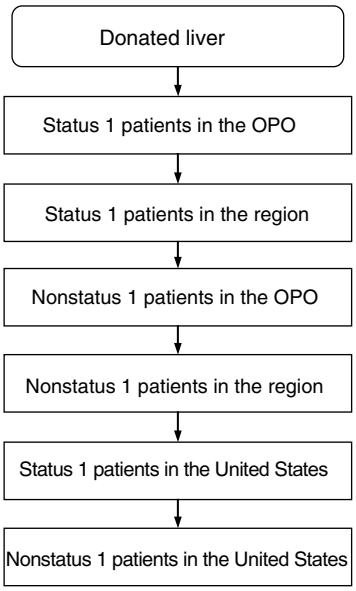
In this study, we only consider adult patients, and therefore do not describe the pediatric liver-allocation procedure, which is slightly different than the adult allocation procedure. UNOS maintains a waiting list that is used to prioritize patients for transplantation. When a liver becomes available, the following factors are considered for its allocation: liver and patient OPO, liver and patient region, medical urgency of the patient, liver and patient blood type, and patient waiting time.

The medical urgency of the adult liver patients is represented by UNOS Status 1 and model for end-stage liver disease (MELD) scores. A patient listed as Status 1 "has fulminant liver failure with a life expectancy without a liver transplant of less than 7 days" (IOM 1999, p. 190). Patients who do not qualify for classification as Status 1 are assigned a "probability of pre-transplant death derived from a mortality risk score" calculated by the MELD scoring system (UNOS 2005). The MELD score, a continuous function of three laboratory values (total bilirubin, creatinine, and prothrombin time), was first introduced by Malinchoc et al. to assess the short-term prognosis of patients with liver cirrhosis (Malinchoc et al. 2000, Wiesner et al. 2001). MELD is a decreasing function of patient health. UNOS uses a modified version of the original MELD formula that restricts the range of MELD scores to be integer values between 6 and 40. Our computational results exclude Status 1 patients because there are very few Status 1 patients. For instance, as of September 17, 2004, there were 15 Status 1 patients nationally, whereas there were a total of 17,856 MELD patients (UNOS 2004).

Patients are stratified within Status 1 using points, which are assigned based on the compatibility of the patient's blood type with the donor's blood type and waiting time within Status 1. 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 by patient waiting time. For MELD patients, waiting time is calculated as the time accrued by the patient at or above her current MELD score from the date that she was listed as a candidate for liver transplantation.

Figure 1 shows the operation of the current liver-allocation system in terms of geographical location. Every cadaveric liver is first offered to Status 1 patients located within the harvesting OPO in descending point order. If there are no suitable Status 1 matches or if all Status 1

Figure 1. Current liver-allocation system.



patients within the harvesting OPO decline the offer, the liver is then offered to Status 1 patients within the harvesting region. If a match still is not 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. Because patient health is dynamic and each organ induces its own priority queue, the composition of the waiting list and the ranking of the patients on this list change over time.

The final decision to accept or decline a liver is made by the transplant surgeon and/or physician responsible for the care of that patient (IOM 1999, UNOS 2005). The surgeon and/or the physician have very limited time (at most one hour) to make their decision (UNOS 2005) because the acceptable range for *cold ischemia time*, the time that the organ remains outside the body, is very limited. The Scientific Registry of Transplant Recipients (SRTR) states that the acceptable cold ischemia time limit for a liver is 12 to 18 hours (SRTR 2004). Furthermore, as the IOM points out, there is evidence that the quality of the organ decreases as cold ischemia time increases (IOM 1999). 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 is not penalized and maintains access to future livers. In general, however, if the patient declines an offered organ, she may anticipate advancing to a higher priority on the waiting list as her health deteriorates.

As discussed before, some patients receive a living-donor liver transplant. If a patient has access to a living donor, she can still be listed on the waiting list. Similarly, a patient on the waiting list can still seek a living donor.

3. Model Formulation

We formulate a discrete-time, infinite-horizon, discounted MDP model of this problem, in which the objective of the patient/physician is to maximize the patient's total expected discounted reward. Although we assume that the decision maker is both indifferent to the timing of the resolution of uncertainty and risk neutral, we recognize that these assumptions may not hold (Chew and Ho 1994). Considering these and other patient preference issues is left for future research. The transition probabilities and the reward function are assumed to be stationary. The notation used in the model is as follows:

- $N = \{1, \ldots, \infty\}$: time periods.
- λ: discount factor, $0 \leqslant \lambda \leqslant 1$.
- h_t: patient's state at time $t \in N$. Patient state consists of patient health and possibly patient waiting time, which are used to prioritize patients for transplantation. For instance, patient state could consist of laboratory values such as bilirubin and creatinine, and some measure of waiting time. A simplified patient-state definition may consist of only the MELD score. We discuss possible definitions of patient state in greater detail in §5. We assume that there exists a complete ordering of the patient states.
- S_H: patient-state space, i.e., $S_H = \{1, \ldots, H+1\}$, where $H+1$ represents death.
- l_t: quality of the liver offered to the patient at time $t \in N$. We assume that there exists a complete ordering of the liver qualities. We also assume that the liver quality does not change during a decision epoch.
- S_L: organ-state space, i.e., $S_L = \{1, \ldots, L, L+1\}$, where $L+1$ represents the case that no liver is offered and there are L possible cadaveric liver types. Note that $l_t \in S_L$, $t \in N$.
- $s_t = (h_t, ll_t)$: state of the process at time $t \in N$.
- S: state space, i.e., $S = S_H \otimes S_L$.
- $a^*(s)$: optimal decision when the state is s, which represents accepting the liver offer or equivalently quitting the process if $a^*(s)$ is T, and waiting for one more period or, equivalently, continuing the process if $a^*(s)$ equals W.
- $r(h, l)$: total expected discounted reward if the patient accepts the liver described by l while in state h. We define $r(h, l) = 0$ when $h = H+1$ or $l = L+1$, i.e., the total post-transplant reward is zero if the patient receives no organ offer or dies. Note that $r(h, l)$ is also a function of the disease group and patient type, i.e., gender and blood type. However, we suppress this dependency for notational convenience because we assume these factors are fixed.
- $c(h)$: expected intermediate reward accrued in the current time period when patient state is h and she chooses to wait. We define $c(H+1) = 0$.
- $\mathcal{H}(h' \mid h)$: probability that the patient will be in state h' at time $t+1$, given that she is in state h at time t and the liver is not transplanted at time t. We define $\mathcal{H}(h' \mid H+1) = 0$, $h' \in \{1, \ldots, H\}$ and $\mathcal{H}(H+1 \mid H+1) = 1$, i.e., the patient stays in the death state when she dies.
- $\mathcal{H}$: patient-state transition probability matrix $\mathcal{H} = [\mathcal{H}(h' \mid h)]$, $h, h' \in S_H$.
- $\mathcal{L}(l \mid h)$: probability that the patient will receive a liver offer l at time t, given that she is in state h at time t. We define $\mathcal{L}(l \mid H+1) = 0$, $l \in \{1, \ldots, L\}$ and $\mathcal{L}(L+1 \mid H+1) = 1$, i.e., the patient does not receive any organ offers when she dies.
- $\mathcal{L}$: organ arrival transition probability matrix $\mathcal{L} = [\mathcal{L}(l \mid h)]$, $l \in S_L$ and $h \in S_H$.
- $\mathcal{P}$: transition probability matrix of the MDP model when the "wait" action is selected, $\mathcal{P} = [\mathcal{P}(s' \mid h)]$, $s' \in S$ and $h \in S_H$, where $\mathcal{P}(s' = (h', l') \mid h) = \mathcal{H}(h' \mid h) \cdot \mathcal{L}(l' \mid h')$, $h, h' \in S_H$ and $l' \in S_L$.
- $V(h, l)$: maximum total expected discounted reward that the patient can attain when her current state is h and the current liver offered is l.

The above definitions imply 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. Note that $r(h, l)$ accounts for the possibility of death during the transplant operation. Furthermore, because patients often need to be retransplanted due to a number of severe posttransplant complications (Bilbao et al. 2003, Dudek et al. 2002, Yoo et al. 2003), we also incorporate the possibility and the reward of retransplantation into $r(h, l)$, which is explained in greater detail in §5.2. The difficulties of explicitly incorporating retransplantation into the model are discussed in §6.

According to the MDP model, the decision maker can take one of two actions in state (h, l), namely, "transplant" the liver l or "wait for one more decision epoch." If the patient chooses "transplant" in state (h, l), she receives a reward of $r(h, l)$, quits the process, and moves to absorbing state "transplant" with probability one. If the patient chooses to "wait" in state (h, l), then she receives an intermediate reward of $c(h)$ and moves to state $(h', l') \in S$ with probability $\mathcal{P}(h', l' \mid h)$. The optimal solution to this problem is obtained by solving the following set of recursive equations (Puterman 1994):

$$V(h,l) = \max\left\{ r(h,l), c(h) + \lambda \sum_{(h',l')\in S} \mathcal{P}(h',l' \mid h) V(h',l') \right\}, \quad h \in S_H,\ l \in S_L. \quad (1)$$

4. Structural Properties

In this section, we derive several structural properties of the cadaveric-donor-only model (CDM) given by (1). The following assumptions are common to all of the theorems:

Assumption 1. *The function $r(h, l)$ is nonincreasing in both h and l. That is, as the patient deteriorates and/or the liver quality drops, the patient's posttransplant reward does not increase.*

Assumption 2. *The function $c(h)$ is nonincreasing in h. That is, as the patient deteriorates, the intermediate reward does not increase.*

Theorem 1 proves that the above assumptions guarantee the monotonicity of the optimal value function in liver state for any patient state, without any additional assumptions on the transition probability matrices. The proof of this theorem is obvious and omitted.

Theorem 1. *$V(h, l)$ is monotonically nonincreasing in l, $l \in S_L$ $\forall\, h \in S_H$.*

While Assumptions 1 and 2 suffice to guarantee the monotonicity of $V(h, l)$ in l, we need additional assumptions to prove the monotonicity of $V(h, l)$ in h. Many researchers assume special structure on the transition probability matrix and/or the reward function to ensure the existence of structured policies. Below we define some concepts that are used to specify these special structures. Interested readers should refer to Barlow and Proschan (1965), Derman (1962, 1963a, b), and Pierskalla and Voelker (1976) for more details.

Definition 1 (Barlow and Proschan 1965). (a) A discrete distribution $\{p_k\}_{k=0}^{\infty}$ is increasing failure rate (IFR) if $p_k / \sum_{i=k}^{\infty} p_i$ is nondecreasing in $k = 0, 1, 2, \ldots$.

(b) A Markov chain is said to be IFR if its rows are in increasing stochastic order, that is,

$$b(i) = \sum_{j=h}^{H+1} P(j \mid i) \quad (2)$$

is nondecreasing in i for all $h = 1, \ldots, H+1$.

This definition is equivalent to the well-known notion of stochastic dominance and may be viewed intuitively as follows: The worse the patient, the more probable that the patient will become even worse. If the patient state consists of only patient health, then the IFR assumption is intuitive. On the other hand, the IFR assumption may not hold if the patient state includes waiting time.

Theorem 2 proves the monotonicity of $V(h, l)$ in h under a set of intuitive conditions. We first present two technical lemmas that are used in the proof of Theorem 2. Let $V^i(h, l)$ be the value, and $a^i(h, l)$ be the optimal action, associated with state (h, l) at the ith iteration of the value iteration algorithm, respectively. Then, noting that $a^i(h, L+1) = W$, Lemma 1 states that at the ith iteration of the value iteration algorithm the optimal value of the liver states for which the optimal action is to "wait" is equal to the optimal value of the no-offer state. The proof of Lemma 1 is obvious and is omitted. The proof of Lemma 2 is given in the online appendix at http://or.journal.informs.org/.

Lemma 1. *If $a^i(h, l) = W$, then $V^i(h, l) = V^i(h, L+1)$.*

Lemma 2. *If $V^i(h, l)$ is nonincreasing in h and l and*

$$\frac{\mathcal{L}(l \mid h+1)}{\mathcal{L}(l \mid h)} \leqslant \frac{r(h,l)}{r(h+1,l)} \quad \text{for } h = 1, \ldots, H-1 \text{ and } l = 1, \ldots, L, \quad (3)$$

then $z^i(h) = \sum_{l \in S_L} \mathcal{L}(l \mid h) V^i(h, l)$ is nonincreasing in h.

Condition (3) implies that for any given liver type, as the patient gets worse the increase in the probability of receiving an offer must be smaller than the reduction in the total expected discounted posttransplant reward. Theorem 2 imposes Condition (3) on $r(h, l)$ and $\mathcal{L}$ and proves the monotonicity of the optimal value function in h. Using Lemma 2, this theorem is a direct result of the infinite-horizon version of Lemma 3.9.4 in Topkis (1998) or, equivalently, Theorem 4.7.3 in Puterman (1994), and is omitted.

Theorem 2. *If $\mathcal{H}$ is* IFR *and* (3) *holds for all h and l, then $V(h, l)$ is nonincreasing in h.*

Theorems 3 and 4 establish sufficient conditions that ensure the existence of various optimal *control-limit policies*. A control-limit policy consists of decision rules of the form

$$d^*(s) = \begin{cases} a_1, & s < s^*, \\ a_2, & s \geqslant s^*, \end{cases}$$

where s is the state of the system, $d^*(s)$ is the optimal stationary decision rule for state s, a_1 and a_2 are distinct actions, and s^* is a control limit (Puterman 1994). This policy can be interpreted as follows: If the state of the system is less than s^*, it is optimal to take action a_1 otherwise, it is optimal to take action a_2. In many areas of application, such as maintenance optimization (Banjevic et al. 2001, Chen and Feldman 1997, Pierskalla and Voelker 1976, Valdez-Flores and Feldman 1989), inventory theory (Harrison and Taksar 1983, Weiss 1981), queueing (Bruns 2003, De Serres 1991, Weiss 1979, Weiss and Pliska 1982), and control theory (Kyriakidis 2004), authors derive sufficient conditions to ensure the existence of an optimal control-limit policy. If it is known that the optimal policy is of the control-limit type, the problem can typically be solved more efficiently. Such policies are also easier to implement (Puterman 1994). There are two types of control limits in the CDM: liver-based and patient-based.

DEFINITION 2. 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 $1, 2, \ldots, i(h)$ 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 $j(l), j(l)+1, \ldots, H$ for some patient state $j(l)$, called the *patient-based control limit*.

It can easily be shown that if a liver-based control-limit policy exists, then $i(h)$ is nondecreasing if and only if a patient-based control policy exists. The proof of Theorem 3 is given in the online appendix.

THEOREM 3. *There exists an optimal liver-based control-limit policy for each patient state $h \in S_H$.*

Theorem 4 provides a set of intuitive conditions that ensures the existence of an optimal patient-based control-limit policy. The proof of Theorem 4 is given in the online appendix. Before proving Theorem 4, we present two inequalities that hold for IFR matrices and nonincreasing functions. The proof of the following lemma is provided in Alagoz et al. (2004).

LEMMA 3. *Let $\mathcal{H}$ be an* IFR *transition probability matrix and $V(h)$ be a nonincreasing function. Then, the following hold*:

$$\text{(a)} \quad \sum_{h' \leqslant h} [\mathcal{H}(h' \mid h) - \mathcal{H}(h' \mid h+1)] V(h') \geqslant \sum_{h' \leqslant h} [\mathcal{H}(h' \mid h) - \mathcal{H}(h' \mid h+1)] V(h).$$

$$\text{(b)} \quad \sum_{h'' > h} [\mathcal{H}(h'' \mid h) - \mathcal{H}(h'' \mid h+1)] V(h'') \geqslant \sum_{h'' > h} [\mathcal{H}(h'' \mid h) - \mathcal{H}(h'' \mid h+1)] V(h+1).$$

THEOREM 4. *If $\mathcal{H}$ is* IFR, *$\mathcal{L}$ satisfies* (3),

$$\sum_{k=j}^{H} \mathcal{H}(k \mid h) \leqslant \sum_{k=j}^{H} \mathcal{H}(k \mid h+1) \quad \text{for } j = h+1, \ldots, H \text{ and } h = 1, \ldots, H, \quad \text{and} \quad (4)$$

$$\frac{r(h,l) - r(h+1,l)}{r(h+1,l)} \leqslant \lambda [\mathcal{H}(H+1 \mid h+1) - \mathcal{H}(H+1 \mid h)] \quad \text{for } h = 1, \ldots, H-1, \quad (5)$$

then there exists an optimal patient-based control-limit policy.

Note that (4) and Definition 1 have similar interpretations, but (4) is neither a consequence of, nor sufficient to establish, Definition 1. Condition (5) on the reward function has the intuitive explanation that as the patient gets worse, the reduction in the benefit of waiting is greater than the reduction in the benefit of performing the transplant. Alagoz et al. (2004) report maximum violations for Definition 1 as well as Conditions (4) and (5), which indicate that these conditions typically hold in practice. On the other hand, as we demonstrate in §5.3, Condition (3) often does not hold. Theorem 4 can be explained intuitively as follows: If the reduction in the benefit of waiting is larger than the reduction in the benefit of transplanting for each health state, then the optimal policy is of a patient-based control-limit type.

We next describe a plausible relationship between the transition probability matrices for two different diseases. Namely, if one of the transition probability matrices has a faster deterioration rate than another, then we say that that transition probability matrix is dominated by the other. In medical terms, this condition may arise when the progression of two diseases are different. The following definition and lemma are from Alagoz et al. (2004).

DEFINITION 3. Let $P = [P(j \mid i)]$, $i, j = 1, \ldots, n$ and $Q = [Q(j \mid i)]$, $i, j = 1, \ldots, n$ be two transition probability matrices. We say that P dominates Q, $P \succeq Q$, if $\sum_{j=k}^{n} P(j \mid i) \leqslant \sum_{j=k}^{n} Q(j \mid i)$, $1 \leqslant i, k \leqslant n$.

Consider the implications of this definition by letting the random variables $X(h)$ and $Y(h)$ be the time to death starting from patient state h under transition probability matrices P and Q if no transplant is performed, respectively. It can easily be shown that Definition 3 implies ordinary stochastic dominance between $X(h)$ and $Y(h)$, i.e., $X(h) \geqslant_{st} Y(h)$ for $h \in S_H$.

LEMMA 4. *Let P and Q be $n \times n$ transition probability matrices where $P \succeq Q$. Furthermore, let $V(j)$ be a monotonically nonincreasing function in j. Then, for any i, the following are true*:

$$\text{(a)} \quad \sum_{j \leqslant i} [P(j \mid i) - Q(j \mid i)] V(j) \geqslant \sum_{j \leqslant i} [P(j \mid i) - Q(j \mid i)] V(i), \quad \text{and}$$

(b) $\sum_{j>i}[P(j \mid i) - Q(j \mid i)]V(j) \geqslant \sum_{j>i}[P(j \mid i) - Q(j \mid i)]V(i+1)$.

Theorem 5 compares the optimal control limits of two identical patients who are listed in different OPOs, i.e., who have different liver-offer probability matrices. If Patient A receives more and better liver offers than Patient B, then Patient A's optimal patient-based control limits will be higher than those of Patient B. Similarly, the liver-based optimal control limits of Patient A will be lower than those of Patient B because Patient A will be more selective than Patient B. The proof of Theorem 5 is given in the online appendix.

THEOREM 5. *Let Π_1 and Π_2 be two problem instances with liver transition probability matrices $\mathscr{L}_1$ and $\mathscr{L}_2$, respectively. Let V_1 and V_2 be the optimal value functions of Π_1 and Π_2, respectively. If Π_1 and Π_2 have the same reward functions, $r(h, l)$ and $c(h)$, the same patient-state transition probability matrix $\mathscr{H}$ and $\mathscr{L}_1 \succeq \mathscr{L}_2$, then the following are true*:

(a) *$V_1(h, l) \geqslant V_2(h, l)$ for $h \in S_H$ and $l \in S_L$.*

(b) *Let $i_1(h)$ and $i_2(h)$, $h \in S_H$ be the liver-based control limits of Π_1 and Π_2, respectively. Then, $i_1(h) \leqslant i_2(h)$ for all $h \in S_H$.*

(c) *If both Π_1 and Π_2 have patient-based control-limit optimal policies with patient-based control limits $j_1(l)$ and $j_2(l)$, $l \in S_L$, then $j_1(l) \geqslant j_2(l)$ for all $l \in S_L$.*

Theorem 6 provides a similar result to Theorem 5, in which two patients having identical reward functions and liver-offer probabilities have different patient-state transition probability matrices. If Patient A deteriorates faster than Patient B, then Patient A has lower patient-based and higher liver-based control limits than Patient B. The proof of this theorem is similar to that of Theorem 5 and is omitted.

THEOREM 6. *Let Π_1 and Π_2 be two instances with patient-state transition matrices $\mathscr{H}_1$ and $\mathscr{H}_2$, respectively. Let V_1 and V_2 be the optimal value functions of Π_1 and Π_2, respectively. If Π_1 and Π_2 have the same reward functions, $r(h, l)$ and $c(h)$, the same liver transition probability matrix $\mathscr{L}$ and $\mathscr{H}_1 \succeq \mathscr{H}_2$, then the following are true*:

(a) *$V_1(h, l) \geqslant V_2(h, l)$ for $h \in S_H$ and $l \in S_L$.*

(b) *Let $i_1(h)$ and $i_2(h)$, $h \in S_H$ be the liver-based control limits of Π_1 and Π_2, respectively. Then, $i_1(h) \leqslant i_2(h)$ for all $h \in S_H$.*

(c) *If both Π_1 and Π_2 have patient-based control-limit optimal policies with patient-based control limits $j_1(l)$ and $j_2(l)$, $l \in S_L$, then $j_1(l) \geqslant j_2(l)$ for all $l \in S_L$.*

5. Computational Results

We solve the CDM using clinical data. We use the policy iteration algorithm, (Bellman 1957, Howard 1960) to solve the MDP model. Section 5.1 describes the data sources that are used in the computational experiments. We describe the estimation of parameters in §5.2. We provide numerical examples and computational tests in §5.3.

5.1. Data Sources

The data come from three sources. The first, UNOS1, is a publicly available data set from UNOS that covers 28,717 patients listed for their first liver transplant between 1990 and 1996 and contains data through 1999. UNOS1 is used to estimate $r(h, l)$.

The second data set, UPMC, comes from the Thomas E. Starzl Transplantation Institute at the University of Pittsburgh Medical Center (UPMC), one of the largest liver transplant centers in the world. Unlike data from UNOS, this data set is not publicly available. UPMC is used to estimate the $\mathscr{H}$ matrix. We examine the records of 3,009 patients who had ESLD and joined the waiting list between 1991 and 2000. After we exclude patients with incomplete data at listing and patients seen only once at UPMC, we are left with a sample of 1,997 individual patients. For each patient, our data set contains demographic and clinical data, including the type of liver disease that led to ESLD, the results of all laboratory testing done at UPMC, the location of the patient at the time of laboratory testing (at home, in a general hospital ward, or in an intensive care unit), information concerning the occurrence of death before transplantation, and information about the existence of clinical covariates such as the presence or absence of encephalopathy, a condition that occurs when toxic substances accumulate in the blood.

The third data set, UNOS2, was collected between February 27, 2002 and May 31, 2003. The data set does not include data prior to February 27, 2002 because UNOS did not record MELD scores of the patients before that date. We estimate $\mathscr{L}$ using UNOS2. The first part of UNOS2 includes information for 25,810 patients waiting for a liver transplant such as region, MELD scores, age, blood type, gender, race, and disease type. The second part of UNOS2 covers information for the cadaveric organ offers such as the patients that each organ has been offered to, the date of the offer, as well as information for the cadaveric donor such as gender, cause of death, age, and region number.

5.2. Estimating Parameters

We define the decision epochs as days in our computational experiments. Patient state consists of patient health and possibly waiting time. We use the MELD scores to represent patient health because UNOS uses MELD scores to determine the medical urgency of the patients with ESLD.

Because UPMC has only 1,997 patients, who are classified into five disease groups based on the underlying etiology (cause) of ESLD, it is necessary to perform some state-space aggregation. Otherwise, some states would contain too few observations for accurate transition probabilities. We define the patient state only through MELD score, and aggregate MELD scores into groups of two. Waiting time, while important, is used only as a tiebreaker among

patients with identical MELD scores. As described in §2, total waiting time at a MELD score is calculated as the time accrued by the patient at or above her current MELD score from the date that she was listed as a candidate for liver transplantation. As a result, the waiting-time component of the patient state would need to be a multidimensional measure. Therefore, the inclusion of waiting time into the state space would have necessitated a coarser aggregation of MELD scores, diminishing the clinical realism of the model.

We estimate the $\mathcal{H}$ matrix for each disease group separately because the progression of liver disease is highly disease dependent (Dienstag and Isselbacher 2001, Podolsky and Isselbacher 2001). For each group, we estimate the $\mathcal{H}$ matrix using the natural history model (NHM) of Alagoz et al. (2005). The NHM, an empirical stochastic model, employs cubic spline functions to estimate incomplete observations and uses the resulting data sets to predict values of the disease covariates of a particular patient at time $t+1$ given known values at time t.

The estimation of $\mathcal{L}$ includes the discretization of the liver quality, the classification of the liver types, and the computation of the organ arrival rates by recipient MELD score. The list of the donor characteristics that affect the posttransplant life expectancy is given in Roberts et al. (2004), which includes five donor characteristics. However, because UNOS2 includes information about only the age, the race, and the gender of the donor, we use these three factors to determine the quality of the liver. We define seven categories for the donor age groups: age < 20, $20 \leqslant$ age < 30, $30 \leqslant$ age < 40, $40 \leqslant$ age < 50, $50 \leqslant$ age < 60, $60 \leqslant$ age < 70, and age $\geqslant 70$. The donor race consists of two categories: white or not white. The donor gender either matches the recipient's gender or does not. As a result, there is a total of 28 categories for liver types. We use the coefficients of the Cox (1972) proportional hazards model of Roberts et al. (2004) to order the liver types. Note that the ordering of the liver types depends on the gender of the recipient. We consider only female patients throughout this study. Therefore, if the donor is a female, then there exists a gender match; otherwise, there exists a gender mismatch. Because the data are sparse, we group liver types into groups of two (e.g., 1 and 2, 3 and 4) and use 14 categories for livers.

To find the organ arrival rates, we first compute the total number of days that each patient waits at each MELD score. Then, by recipient MELD score, we calculate the total number of days that a liver is offered. Let $W_i(h)$ and $O_i(h,l)$ be the total number of days that patient i waits in MELD score h and the total number of days that the best offer that patient i receives is a type l liver given that her MELD score is h, respectively. Then, $\mathcal{L}$ is obtained using the following formulae:

$$\mathcal{L}(L+1 \mid h) = 1 - \frac{\sum_i \sum_l O_i(h,l)}{\sum_i W_i(h)}, \quad h \in \{1,\dots,H\}, \quad \text{and}$$

$$\mathcal{L}(l \mid h) = [1 - \mathcal{L}(L+1 \mid h)] \frac{\sum_i O_i(h,l)}{\sum_i \sum_l O_i(h,l)}, \quad h \in \{1,\dots,H\} \text{ and } l \in \{1,\dots,L\}.$$

Because $\mathcal{L}$ depends highly on geographical factors, we estimate 11 regional $\mathcal{L}$s as well as a national $\mathcal{L}$.

There are two types of rewards in the MDP model: pretransplant and posttransplant. Possible definitions include total discounted expected life days and total discounted quality-adjusted life days (QALD) of the patient, a common measure in medical decision-making research. The QALD measure is based on the assumption that the patient assigns a quality score between zero and one to each health state (Gold et al. 1996). Because we are unaware of any existing data on quality-adjusted rewards for MELD scores, we use total discounted life expectancy in days rather than total discounted QALD for $c(h)$ and $r(h,l)$ in our computational tests.

If the patient chooses to "wait," the patient accrues one day as the intermediate reward, i.e., $c(h) = 1 \; \forall h \in S$. If the patient chooses the "transplant" option, then she receives a posttransplant reward that is equal to the expected life days of the patient given her health status at the time of the transplant and the liver quality. We use the Cox proportional hazards model (Cox 1972) of Roberts et al. (2004) and Valenta (2002) to estimate the expected posttransplant life days of the patient, given her MELD score at the time of transplant and liver quality. The Cox model is typically used to describe survival as a function of a set of variables. However, it can also be used to create a patient-specific survival curve from which a pseudorandom observation can be generated to obtain the time of a particular event (e.g., patient death or graft failure). A simulation model based on this type of Cox model can be used to estimate the posttransplant life expectancy for a particular patient. Valenta (2002) presents such a simulation model, which estimates two survival times: one for the patient and another for the organ. If the graft survival is shorter than patient survival, then the patient needs a retransplantation. We use the patient survival-time estimates in our model, as opposed to graft survival-time estimates, and therefore implicitly capture the retransplantation possibility. Unfortunately, however, using these patient survival-time estimates assumes that the patient may use suboptimal policies after the graft failure. That is, we assume that the patient makes the accept/reject decisions for the retransplantation according to current practice.

In general, our parameter estimates demonstrate the following qualitative characteristics. The reward function monotonically decreases in liver type and MELD score. That is, as the liver quality decreases or MELD score increases, the posttransplant life expectancy decreases, which ensures the existence of an optimal liver-based control-limit policy, as shown in Theorem 3. We also observe that as the patient gets sicker, the patient receives more frequent organ offers. Furthermore, the health transition probability matrix satisfies the IFR assumption with minimal violations (see Alagoz 2004, Alagoz et al. 2004).

Figure 2. Transplant-wait decisions for annual discount rate = 0.99 ($\lambda = 0.999972$).

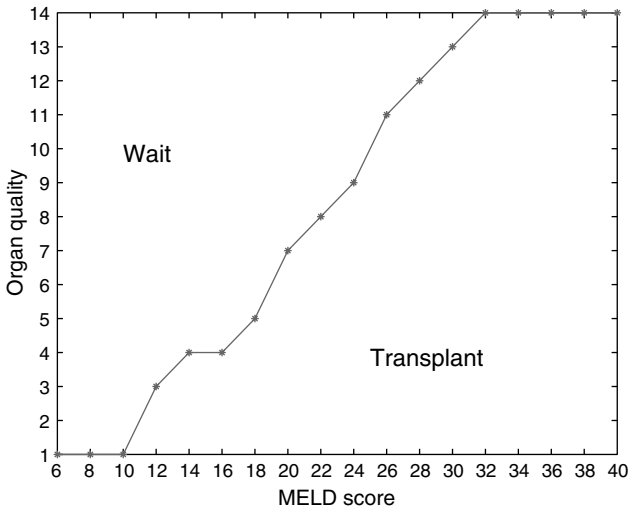
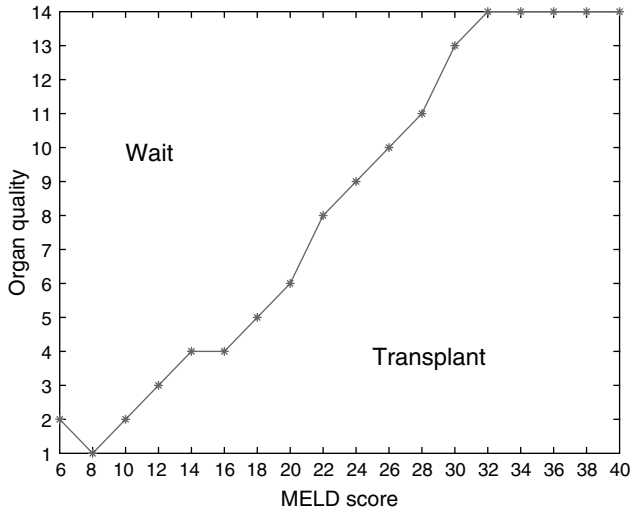


Figure 3. Example of a nonpatient-based control-limit policy.



5.3. Numerical Examples

We first consider a 60-year old female patient with primary biliary cirrhosis who has blood type A. We apply a 0.99 annual discount rate (daily $\lambda = 0.999972$) and use the national liver probability matrix. Recall that as the MELD score increases, the patient gets sicker. In Figure 2, the livers are ordered from highest to lowest quality, i.e., Liver Type 1 is the "best" liver and Liver Type 14 is the "worst" liver. As Figure 2 shows, the optimal action varies for different liver types. If the patient has a MELD score of 16, then the optimal policy for this particular patient is as follows: If she receives a liver offer that is of Type 4 or worse, then "wait;" otherwise, accept the liver and have the transplantation. This policy is an example of a liver-based control-limit policy. Similarly, if the patient receives a liver offer of Type 5, then the optimal action for this particular patient is as follows: If her MELD score is below 18, then "wait;" otherwise, accept the liver and have the transplantation. This policy is an example of a patient-based control-limit policy. For this particular patient, the optimal policy is of liver-based control-limit type for each h and is of patient-based control-limit type for each l.

In all of our computational tests, all of our data sets satisfy the hypotheses of Theorem 3, so all optimal policies are of liver-based control-limit type. However, some optimal policies do not have a patient-based control limit. Figure 3 shows the optimal policy for the same patient, but assumes that the patient is listed in Region 2 and experiences the corresponding liver probability matrix. As can be seen from the figure, for Liver Type 2, the patient does not have a patient-based control-limit policy. This result can be explained intuitively as follows: The allocation system implies that the sicker the patient is, the more likely it is that she receives higher-quality liver offers. As a result, if, as the patient gets sicker, the rate of increase in the liver-offer probability is sufficiently high, then it may be optimal for the patient to decline the low-quality livers in anticipation of higher-quality liver offers.

Neither the problem in Figure 2 nor the problem in Figure 3 satisfy the conditions of Theorem 4. While the maximum violation for Condition (3) is different, the maximum violations for all remaining conditions of Theorem 4, which are reported in Alagoz et al. (2004), are the same for both problems. To quantify the magnitude of the violation of Condition (3), we define the following metric:

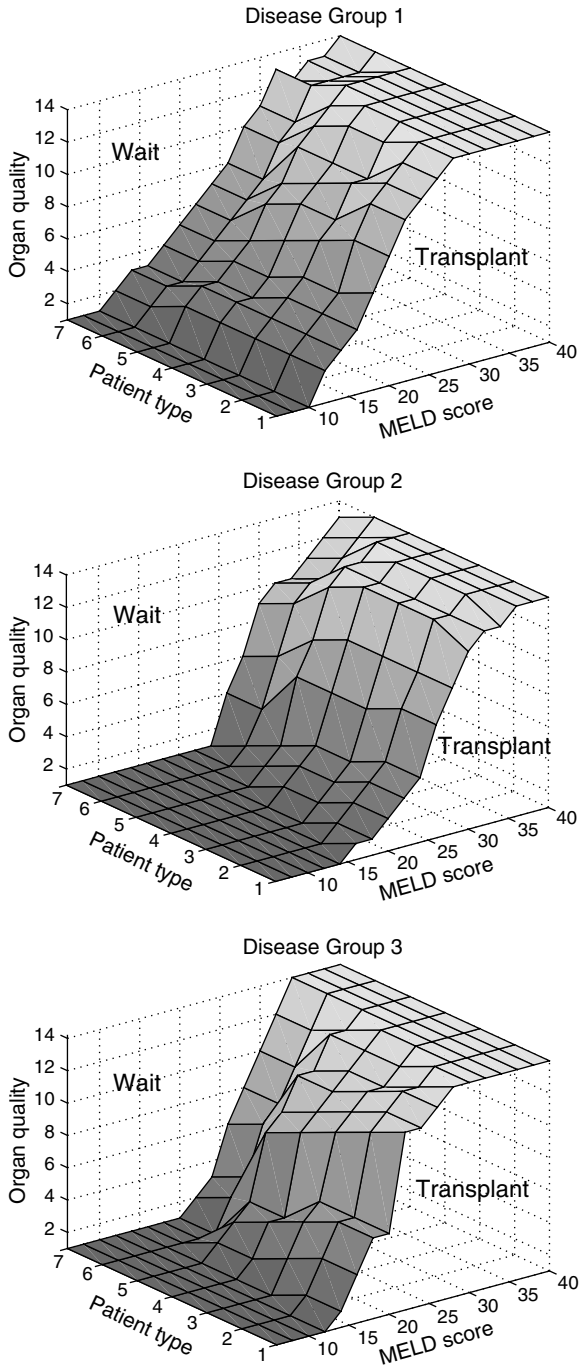
$$\epsilon_1 = \max_{h,l}\left\{0, \frac{\mathcal{L}(l \mid h+1)}{\mathcal{L}(l \mid h)} - \frac{r(h,l)}{r(h+1,l)}\right\},$$

the maximum violation of Condition (3). The value for ϵ_1 is 0.64 and 1.01 for the problems in Figure 2 and Figure 3, respectively. Although both of these values are high, the problem in Figure 3 has a larger ϵ_1 value, which shows that the sufficiency conditions in Theorem 4 may provide a good measure for the existence of a patient-based control-limit policy.

Disease and patient type affect the optimal policies. Figure 4 shows the optimal policy for seven patient types with an annual discount rate of 0.99. Note that MELD scores do not consider static patient characteristics such age, gender, and blood type, which affect the posttransplant life expectancy. Table 2 shows the static characteristics of the patient types that are used in generating Figure 4. In Figure 4, patients are in decreasing order with respect to their posttransplant expected life days for any given liver and MELD score. As the quality of the patient characteristics drops, it is optimal to "wait" in more states. Intuitively, this result makes sense because as the quality of patient characteristics drops, the ratio of pretransplant survival probability to posttransplant survival probability increases.

Liver-offer probabilities also affect the optimal policy. Recall that the liver-offer probability matrix depends on

Figure 4. Transplant-wait decisions when annual discount rate equals 0.99.



Notes. Disease Group 1 includes the following diseases: Primary biliary cirrhosis, primary sclerosing cholongitis, alcoholic liver disease, and autoimmune disorders. Disease Group 2 includes the following diseases: Hepatitis C virus and hepatitis B virus. Disease Group 3 includes the acute failure (fulminants) diseases.

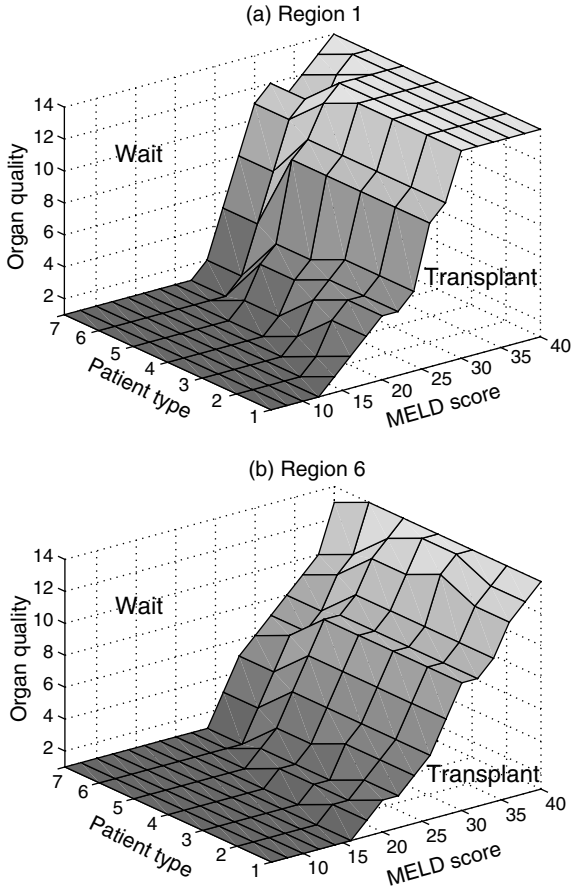
the location where the patient is listed. Figure 5 compares the optimal transplant-wait decisions for different patients when they are listed in two different regions. These patients have hepatitis, and the annual discount rate is 0.99. There is not a strict dominance relationship between the $\mathcal{L}$ matrices of Regions 1 and 6. In general, however, if a patient is listed in Region 6, then she receives more frequent and higher-quality liver offers. There are two factors that contribute to the probability of receiving more frequent and higher-quality livers in a particular region: the organ donation rate and the number of patients waiting for organs at that particular region. Region 6 has a higher organ dona-

Table 2. Patient characteristics.

Patient number[1]	Age	Sex	Blood type	CMVGR[2]	Encephel[3]	Priortx[4]
1	22	Female	A	No	No	No
2	30	Female	A	No	No	No
3	40	Female	A	No	Yes	No
4	50	Female	A	No	Yes	No
5	60	Female	A	No	Yes	No
6	65	Female	A	Yes	Yes	Yes
7	72	Female	A	Yes	Yes	Yes

[1]The patients are ordered according to their total life expectancies with a given organ, i.e., Patient 1 has the longest expected life and Patient 7 has the shortest life expectancy given the same liver.
[2]Indicates whether the patient has cytomegalovirus (CMVGR) or not.
[3]Indicates whether the patient has encephalopathy or not.
[4]Indicates whether the patient had a prior transplant or not.

Figure 5. Transplant-wait decisions for various regions.



tion rate and/or fewer patients on the waiting list than Region 1. To quantify the magnitude of the violation of the dominance criterion in Definition 3, we define the following metric:

$$\epsilon_{r_1, r_2} = \max_{h,\, 1 \leqslant k \leqslant L+1} \left\{ 0, \sum_{j=k}^{L+1} [\mathscr{L}_{r_1}(j \mid h) - \mathscr{L}_{r_2}(j \mid h)] \right\},$$

where $\mathscr{L}_{r_1}$ and $\mathscr{L}_{r_2}$ are the liver transition probability matrices of Region r_1 and Region r_2, respectively. $\epsilon_{1,6}$ equals 0.0117 for the problems in Figure 5. As can be seen from Figure 5, the optimal liver-based control limits in Region 1 are higher than those of Region 6. Similarly, the optimal patient-based control limits in Region 1 are lower than those of Region 6. This result is intuitive because as the patient receives more frequent liver offers with higher quality, she will be more selective.

6. Conclusions

This study considers the problem of sequentially accepting or declining cadaveric liver offers using an MDP model. We generalize the study by Alagoz et al. (2004), which considers the optimal timing of a living-donor liver transplantation. We derive structural properties of the model, including conditions that guarantee the existence of a patient-based and a liver-based control-limit policy. 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. We also compare the optimal control limits for the same patient listed in two different regions. We 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.

In all of our computational tests, the conditions of Theorem 3 hold and the optimal policy is of liver-based control-limit type. However, some optimal policies are not of patient-based control-limit type. In some regions, as the patient deteriorates, the probability of receiving a better liver increases sharply. 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. Our computational tests also show that the location of the patient has a significant effect on liver-offer probabilities and optimal control limits.

Admittedly, our study has some limitations. There is strong evidence that the graft-failure rate is correlated with cold ischemia time. Our computational experiments, however, do not consider the effect of cold ischemia time on posttransplant life expectancy because the UNOS data set does not include information about the cold ischemia time at the time of the offer, and the posttransplant survival model by Roberts et al. (2004) reports that cold ischemia time does not have a significant effect on the outcome of the transplantation. That is, we do not consider a possible change in the quality of the donated liver due to longer cold ischemia times. Our model can be used to account for the cold ischemia time effect on the posttransplant life expectancy if the posttransplant survival model includes the cold ischemia time at the time of the offer as part of the organ characteristics that affect the posttransplant life expectancy. Furthermore, patients with hepatoma (liver cancer) are typically assigned a higher MELD score (UNOS 2005) so that they move up the list faster than other patients with benign disease. As a result, a minor modification to the model is necessary for patients with hepatoma. We can incorporate this policy for patients with hepatoma into our model by expanding the patient health state space to include the clinical factors that cause patients to be assigned a higher MELD score and by using the corresponding $\mathscr{H}$ matrix.

As discussed earlier, our model captures the retransplantation possibility through the posttransplant survival model, which assumes that the patient makes retransplantation accept/decline decisions according to current practice. From a clinical perspective, the optimal timing of retransplantation is uninteresting for the majority of retransplant patients who, due to primary graft nonfunction, become Status 1 patients and require an immediate transplant. We could, in theory, model the retransplantation explicitly in the MDP with some modifications. The revised MDP model would require an additional set of postfailure health states because clinical evidence indicates that patients who experience transplant failure have significantly different clinical characteristics than patients with no prior transplant experience. In fact, the biostatistical question of modeling patient survival with the explicit inclusion of retransplantation remains unanswered; we are unaware of any such study. Furthermore, even if such a study were available, it is believed that the relevant factors explaining survival and retransplantation likelihood would not only include current health and liver quality, but also information describing all previous transplants, including liver qualities, the patient's health at the time of the previous transplants, and the age at which each transplantation occurred. Clearly, incorporating even some of these factors would render the resulting model impossible to calibrate, as well as explode the state space without substantial clinical benefit. Comparison of such a model with our current model would be an interesting extension of our work.

As discussed earlier, some patients on the waiting list may also have access to a living donor. Although these patients constitute a small portion of all patients (approximately 6%), their decisions regarding when to use (or not use) their living donors indirectly affect the rest of the waiting list. For instance, if a patient with a living donor opts to use that living donor at a very early stage of her liver disease, then when she is removed from the list at this early stage the candidates "below" her on the waiting list see an

increase in the likelihood of receiving an organ offer(s). Understanding the way in which this indirect effect impacts the optimal policies for wait-listed patients without living donors is left for future research.

Although this paper does not attempt to recommend any changes to the current liver-allocation system, the patient-perspective insights established here are a critical step in designing better liver-allocation systems. Because UNOS does not have any prior information about patients' preferences for different types of cadaveric organs, organs are offered to the top qualifying patients sequentially. That is, an organ is typically offered to several patients in sequence and then "wasted" (because of the limited allowable cold ischemia time) if none of these patients accept the offer. Approximately 6% of all donated livers are wasted because of this process. If transplant surgeons could use the results of our model to inform UNOS about their preferences in advance, then UNOS could "skip" patients who would decline a particular organ and offer it to patients with lower priority who would accept the offer. On the other hand, it is not clear whether the overall performance of the current liver allocation system would improve if all patients on the waiting list implement the optimal policies resulting from our model. Measuring the effects of this phenomenon requires a more complicated game-theoretic model, which is left for future research.

The decision model presented in this paper could be generalized to address the problem of acceptance/declination for the other organ transplants, given the following components: a measure for the patient health, the transition probabilities between patient health and organ offer states, a proxy for organ quality, and a reward function for a given organ and patient health characteristics. If there are additional treatment options (such as dialysis in kidney transplantation), then the action space and the state space could be expanded to include new actions.

Under the current UNOS policy, the composition of the waiting list and the actual position of the patient on this list have a significant impact on the liver offer(s) that the patient receives. Therefore, the waiting list must be considered in the cadaveric-donor liver transplant decision problem. However, the CDM neither includes the waiting list in the state space nor attempts to infer the patient's position on the waiting list. Instead, the CDM incorporates the effect of the composition of the waiting list and the patient's position on the list into the state transition probabilities. Modeling the waiting list explicitly requires a more complicated model. One possible method is to assume that a full description of the waiting list is available to the patient at all times and to include the description of the waiting list as part of the state space. However, under the current UNOS policy, the waiting list is only partially observable. As a result, the inclusion of the waiting list as part of the state space requires a partially observable MDP model, which is left for future research.

7. Electronic Companion

An electronic companion to this paper is available as part of the online version that can be found at http://or.journal.informs.org/.

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