ELICITING PATIENT PREFERENCES AND PLACING EXPEDITED ORGANS

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Submitted to the Graduate Faculty of

the Swanson School of Engineering in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

University of Pittsburgh

2011

UNIVERSITY OF PITTSBURGH

SWANSON SCHOOL OF ENGINEERING

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Liver transplantation plays a crucial role in saving lives when no other alternatives exist. Each year approximately 5,500 liver transplants are performed in the US. However, annually still 2,000 lives are lost due to lack of livers. Much effort has been spent on improving the organ allocation system. In this dissertation, we focus on patient preference elicitation which is an essential component of medical decision models and expedited organ placement which is relatively unexplored component of the organ allocation system.

When livers become available, they are offered to patients according to an order (match list) specified by a set of rules. Each patient can accept/reject the offer. Other researchers have considered this accept/decline decision. Estimating patient preferences over health states is an important component of these decision making models. Direct approaches, which involve asking patients abstract questions, have significant drawbacks. We propose a new approach that infers patient preferences based on observed decisions via inverse optimization techniques. We illustrate our method on the timing of a living-donor liver transplant.

If it appears that the standard allocation procedure will not result in a match before the organ becomes nonviable, the liver's placement can be expedited, meaning that it is offered to a transplant center instead of an individual patient. We study the subsequent decision problem faced by a transplant center, namely which, if any, of its patients should receive the organ independent of their positions on the match list. We develop a simulation model and compare different policies for expedited liver placement. Our study indicates that a policy

which gives higher priorities to patients whose likelihood of death is higher performs the best based on several metrics.

We also formulate the transplant center's decision problems as an average reward Markov Decision Process (MDP). Due to the complexity of the model, traditional methods used to solve MDP problems cannot be utilized for our model. Thus, we approximate the solution via Least Square Policy Iteration (LSPI) method. Despite the extensive search on basis functions, the LSPI method yields promising, yet not better outcomes than the policies found to be the best via simulation.

Keywords: expedited organ placement, Markov Decision Process, Least Square Policy Iteration, health care, inverse optimization, quality-adjusted life years.

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PREFACE

I would like to express my deepest gratitude to my advisor, Dr. Lisa M. Maillart, for her guidance and for supporting me through my doctoral studies. Her technical and editorial advice was essential to the completion of this dissertation. I also would like to thank the rest of my dissertation committee for their invaluable suggestions and insights. I am also grateful to Dr. Louis Luangkesorn for his input, guidance and insight.

I also owe a huge debt of gratitude to my friends in Pittsburgh. The years spent in Pittsburgh would not have been as wonderful without my dearest ones: Oya Andaçoğlu, Sakine Batun, Şebnem Eşsiz Gökhan, Nuri Mehmet Gökhan, Özlem Arısoy, Umut Özbek and Serdar Karademir.

I am forever indebted to my wonderful parents and sister for all their love and support.

Finally, I am very grateful to Mustafa Baz for his love, patience, support, and encouragement. He was always there cheering me up and stood by me through the good and bad times.

1.0 INTRODUCTION

The health care industry in the US has been growing rapidly and was one of the largest industries in 2008 [64]. It accounted for 10.3% of all industry wage and salary jobs by itself in 2008. The national health expenditures have reached to $2.5 trillion in 2009 accounting for 17.6% of Gross Domestic Product (GDP) [37]. The average growth in national health expenditures is expected to be 6.1% per year over the projection period (2009-2019) [37]. This growth is largely in response to the rapid growth of the elderly population. In 2004, the elderly constituted 12% of the population and accounted for 34% of spending [37]. They are expected to grow to be 19% of the population by 2030 [66]. Personal health care spending for the elderly population was $14,797 per person in 2004, which is 5.6 times higher than spending per child ($2,650) and 3.3 times higher than spending per working-age person ($4,511). While this shift in the population leads to higher expenditures, it draws attention to the efficiency and effectiveness issues in health care.

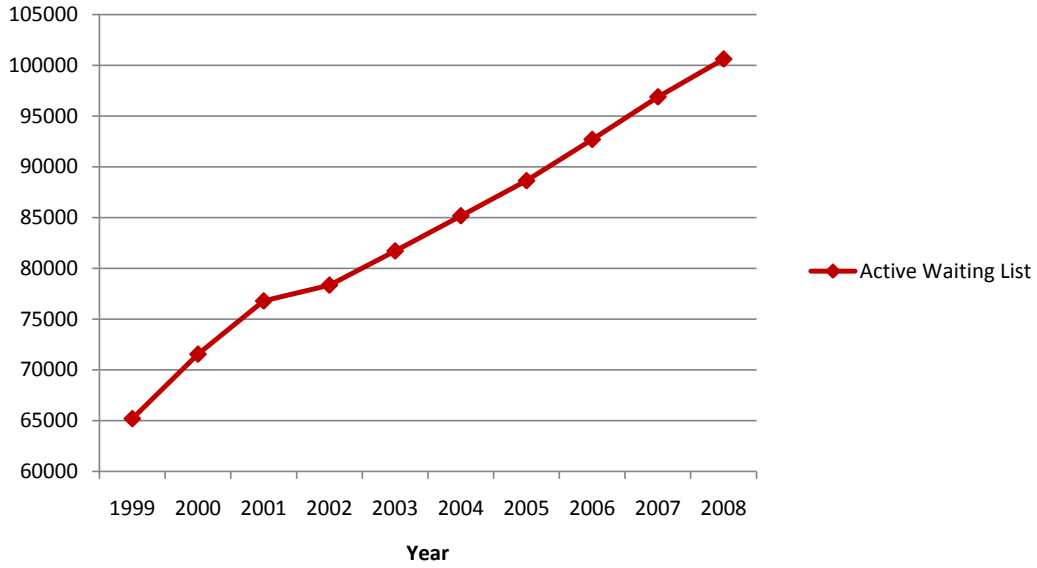
The health care spending per capita in the US is roughly twice as much as it is in Canada, France and the United Kingdom while the life expectancy in the US (i.e., 79) is slightly lower than it is in those countries (i.e., 81, 81 and 80, respectively) and the infant mortality rate (i.e., probability of dying by age 5 per 1000 live births) in the US (i.e., 8) is significantly higher than it is in those countries (i.e., 6, 4 and 5, respectively) [68]. These facts bring in criticism of every aspect of the US health care system.

Operations Research techniques have been widely utilized by researchers in the investigation of health care problems. Operating room scheduling [29, 62, 96, 100], ambulance locating [15, 54, 55], personnel/staff scheduling [20, 34, 56], vaccine selection [69, 101], cancer treatment optimization [47, 60, 71, 102] are examples of problems that have been extensively studied.

Organ transplantation is another health care operation that has attracted attention [1, 3, 28, 48, 58, 90]. The real issue related to organ transplantation is not the cost, but its life saving role in health care. For instance, for patients with end stage liver failure there is no alternative treatment than liver transplantation. More than 100,000 people currently need organ transplants and every 10 minutes another name is added to the national organ transplant waiting list [9]. However, supply cannot keep up with this demand. In Figure 1, the size of the waiting list for organ transplantation and the trends in organ donation, organ transplantation and deaths while waiting for organ transplantation over the period (1999-2008) can be seen [76]. Each day an average of 18 people die from the lack of available organs for transplant.

In this dissertation, we focus on liver transplantation. Liver transplantation is the only available treatment for end-stage liver disease (ESLD) patients. ESLD is an irreversible condition that is the final stage of many liver diseases such as cirrhosis, hepatitis, cancer in the liver, autoimmune disorders, etc. The liver is a unique organ which can regenerate itself. That is, transplantation from a living donor is a possibility which constitutes a way to increase the supply of livers.

Even though recent efforts (e.g., introduction of MELD/PELD system, which is utilized for prioritizing patients according to how urgent their need is, in 2002 and living donor liver transplantation) have modestly increased the supply of livers, the supply-demand imbalance still constitutes a problem in the US as can be seen in Figure 2 [76]. In the US, ESLD is the 12th leading cause of death [36]. Although many people are dying while waiting for a liver transplant, 11.3% of all donated livers are discarded due to excessive CIT, which is the amount of time that has elapsed since the organ is procured and a critical factor that affects the organ quality [42]. These facts emphasize the critical need to efficiently manage the scarce supply of livers.



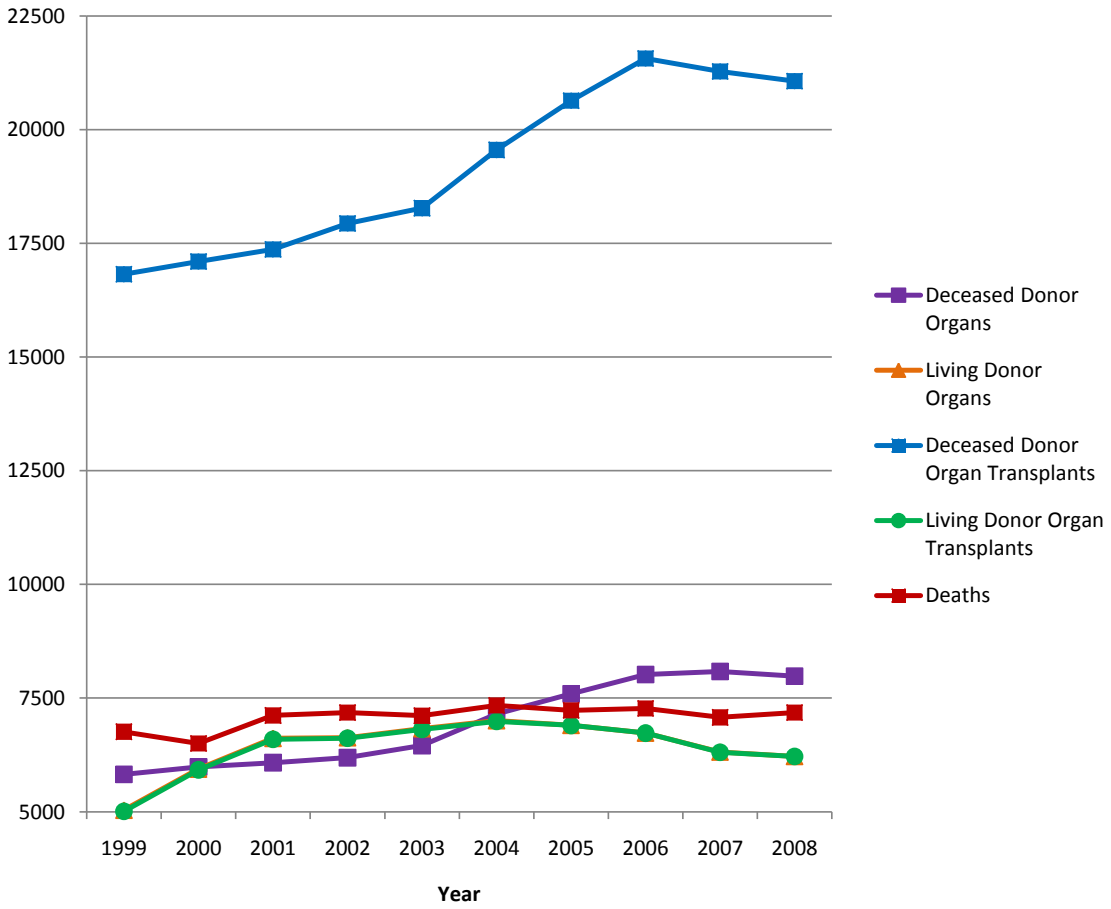


Figure 1: Trends in waiting list, donation, transplantation and deaths while waiting for organ transplant.

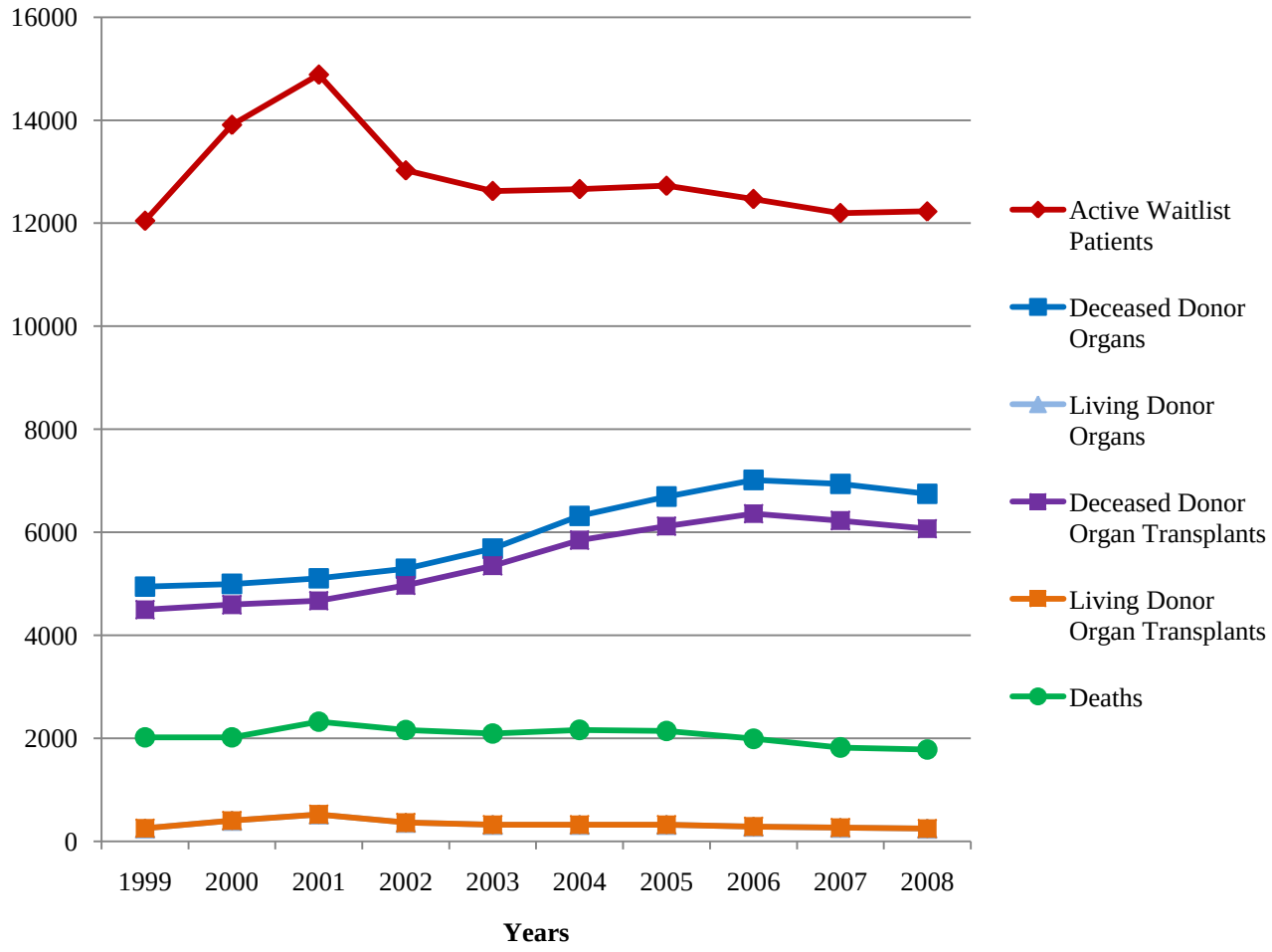


Figure 2: Trends in waiting list, donation, transplantation and deaths while waiting for liver transplant.

In different stages of the liver allocation system, there are multiple decision makers. Therefore, it is possible to evaluate the performance of the allocation system from different perspectives. Each perspective includes different concerns. Thus, each perspective utilizes different metrics for performance evaluation. For instance, post-transplant lifetime is one of the metrics utilized to describe how well the system is working. From a societal perspective, post-transplant lifetime might provide an acceptable metric. However, because for an individual the health status in which the post-transplant life will be spent is an important factor,

from an individual perspective solely post-transplant lifetime is not enough. Thus, from the perspective of a patient the outcome of a transplant is measured by Quality Adjusted Life Years (QALYs) gained as a result of the transplantation. QALYs consist of life years gained and the quality of life attributed to those life years. The quality of life spent in a health status is based on patient's preferences. Therefore, when an individual's perspective is being studied, patient's preference elicitation plays an important role.

Another decision maker in the liver allocation system is a transplant center. A transplant center faces a decision problem that hasn't been explored yet. In the organ allocation system, when livers become available, first they are offered to patients according to an order (match list) specified by a set of rules. Each patient (or physicians, acting on behalf of the patients) can accept/reject the offer based on their preferences. If it appears that this standard allocation procedure will not result in a successful match before the organ becomes nonviable, the liver's placement can be expedited, meaning that it is offered to a transplant center instead of an individual patient. Then, the center decides which, if any, of its patients should receive the organ independent of their positions on the match list. Expedited organ placement is accepted as a method of preventing organ discard [95]. Moreover, given that approximately 2,000 liver patients die per year while waiting for a transplant, expedited liver placement provides an opportunity that cannot be disregarded to save lives.

The rest of this chapter is organized as follows. In Section 1.1, we review the organ allocation system in the US. In Section 1.2, we describe the decision problems we study and state our contributions. We present an overview of the dissertation in Section 1.3.

1.1 LIVER ALLOCATION SYSTEM

United Network for Organ Sharing (UNOS) is the national organization which is responsible for organ allocation in the US. UNOS operates a private, non-profit entity called Organ Procurement and Transplantation Network (OPTN). OPTN is the expert in organ procurement and transplantation, and standardized the process of organ donation and allocation in the US. OPTN includes fifty eight organ procurement organizations (OPOs) that facilitate

organ donation, retrieval and transportation. Each OPO serves a specific region. There are 11 regions in the country [65].

UNOS has measured the degree of medical urgency of liver patients using the Model for End-Stage Liver Disease (MELD) score since 2002. Creatinine, bilirubin and prothrombin time (INR) are the prognostic factors taken into consideration in the calculation of a patient's MELD score. Creatinine is a measure of how well the kidney is functioning. Impaired kidney function is often a symptom of severe liver disease. Bilirubin is a measure of how effectively the liver excretes bile. Prothrombin time shows the liver's ability to make blood clotting factors. The MELD score is calculated using the following formula

$$\begin{aligned}\text{MELD Score} = {} & 0.957 \times \text{Log}_e(\text{creatinine mg/dL}) + 0.378 \times \text{Log}_e(\text{bilirubin mg/dL}) \\ & + 1.120 \times \text{Log}_e(\text{INR}) + 0.643.\end{aligned}$$

MELD scores range between 6 and 40. The higher the MELD score, the sicker the patient. For pediatric patients, a different version of MELD, i.e., PELD (Pediatric End Stage Liver Disease Model), is used to measure the severity of sickness [38].

There are patients who have fulminant liver failure with a life expectancy of less than 7 days if they do not receive a liver transplant. Instead of being assigned a MELD score, these patients are classified as Status 1A patients if they are adults (age $\geq$ 18) and Status 1B patients if they are pediatric patients. Status 1 patients constitute less than 1% of the liver patient population [38].

In 2007, UNOS launched DonorNet, a web-based system that facilitates a fast, convenient way of communication between the coordinators at the organ procurement organizations, i.e., procurement coordinators, and the coordinators at the transplant centers, i.e., transplant center coordinators. When a deceased donor becomes available, a transplant coordinator from an organ procurement organization enters the relevant donor information to DonorNet. Then, the system generates a ranked list of liver patients according to a set of matching rules. This list is called a match run or match list. The matching rules depend on both the donor and patient characteristics, i.e., degree of medical urgency, blood type, distance between the patient and the donor, waiting time, etc. Starting from the top of the ranked

list, the organ is offered to patients (Figure 3). The priority of patients is as follows (Figure 4):

1. Local Status 1 patients
2. Regional Status 1 patients
3. Local patients with MELD score equal to or greater than 15
4. Regional patients with MELD score equal to or greater than 15
5. Local patients with MELD score less than 15
6. Regional patients with MELD score less than 15
7. National Status 1 patients
8. National patients with MELD score equal to or greater than 15
9. National patients with MELD score less than 15

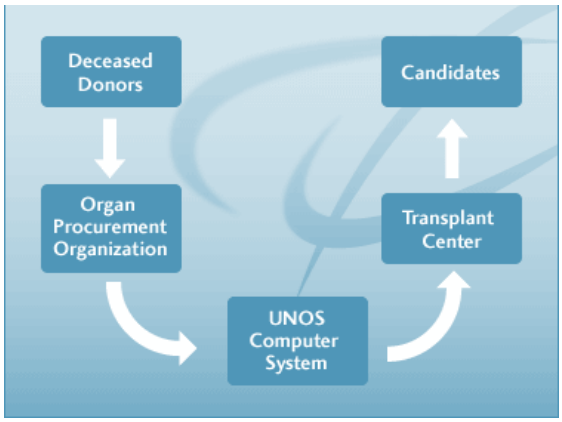


Figure 3: The flow of organ allocation [40].

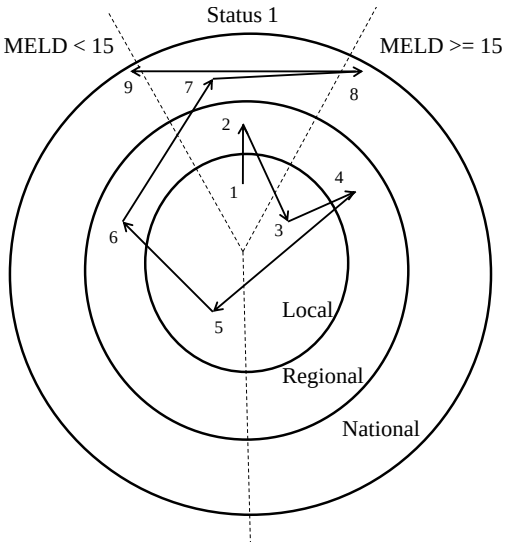


Figure 4: Order of patients in a match run (Adjusted Figure 1.3 of [28]).

Organ offers may be refused for one of several reasons, e.g., poor organ quality. One factor that affects organ quality is Cold Ischemia Time (CIT). CIT is the amount of time that has elapsed since the procurement surgery. Livers are generally considered nonviable after a maximum of 18 hours of CIT. As the CIT increases, the organ becomes less and less desirable, because of the decrease in the likelihood of graft survival. However, CIT is not necessarily the key factor for an organ to become an expedited organ. Based on the other attributes of the organ procurement coordinators might initiate expedited placement immediately after procurement.

As the standard placement procedure explained above continues, the organ ages and becomes less desirable. When the procurement coordinator senses that standard procedure cannot yield a match in a timely manner, she stops the prioritized matching procedure and offers the organ to a transplant center as an "expedited organ." Expedited liver placement is an escape mechanism used to avoid not placing a liver [21]. Once an expedited offer is made to a transplant center, it is no longer bound by the match list. That is, the transplant center may assign the expedited liver to any of its patients.

1.2 PROBLEM STATEMENT AND CONTRIBUTION

One of the purposes of this dissertation is to present an alternative to existing techniques used in patient preference elicitation. We propose an indirect, but rigorous approach to reveal patient preferences. Our new approach derives patient preferences from observed decisions via inverse optimization techniques. We apply our new approach to the timing of a living-donor liver transplantation.

The second purpose is to fulfill the need of guidelines on how transplant centers should act in the case of an expedited offer. Each transplant center coordinator bases her decision on her personal philosophy. With the launch of DonorNet, the need for expedited placement is expected to dissipate. However, as the OPTN/UNOS Organ Procurement Organization Committee Report to the Board of Directors [67] and Tuttle-Newhall et al. [95] point out, guidelines for developing expedited placement processes are still very much needed. Our goal in this dissertation is to provide such guidelines for transplant center coordinators.

When an expedited liver is offered to a transplant center, the center decides which, if any, of its patients should receive the organ regardless of their position on the match list. The fundamental trade-off in this decision problem is balancing medical urgency (e.g., pre-transplant likelihood of death) and anticipated outcomes (e.g., post-transplant likelihood of one-year graft survival) for the diverse, dynamic set of patients listed at the transplant center, while utilizing as many organs as possible.

In this decision making problem, we look at several metrics. One metric is the average transplant rate at the center. There are two facets of this metric. One is that as the transplant rate is being maximized, the waiting time of the patients listed at the center is expected to decrease. The other is that, transplant centers need to continue on their business to serve their patients and transplants serve this goal. The other metrics we consider are percentage of expedited livers unused, waiting time before transplant, expected life days after transplant, etc.

Our study is different from the existing studies because it focuses on the transplant center as the decision maker. Moreover, this study serves as a bridge between existing models of the patient-level accept/decline decision process, which is studied in different ways by several

authors [8, 26, 50, 84], and the societal-level liver allocation decision process, a common theme in recent work on organ allocation [88–90]. Results established at this micro-level, i.e., that of the transplant center, may provide insights applicable at the macro-level of the entire national allocation system.

1.3 OVERVIEW OF THE DISSERTATION

The remainder of this dissertation is organized as follows. Chapter 2 presents a review of the relevant literature on the research problems studied in this dissertation. Chapter 3 proposes a new approach that infers patient preferences based on observed decisions via inverse optimization techniques [33]. The method is applied to the timing of a living-donor liver transplant problem. Chapter 4 describes the expedited liver placement problem in detail and presents our simulation modeling approach to the problem. We explain our numerical study whose parametrization is based on clinical data. Chapter 5 develops an average reward Markov Decision Process model for the expedited liver placement problem of a transplant center. We examine two different objective functions. Chapter 6 concludes by summarizing and discussing our findings, limitations and possible future extensions.

2.0 LITERATURE REVIEW

In this chapter, we discuss the literature related to the problems and methodologies we use in this study. First, we briefly overview the literature on value assessment. We refer the reader to Section 3.2 for a detailed review. Second, we present a literature review on organ transplantation decision making.

2.1 VALUE ASSESSMENT

Value assessment, i.e., utility theory, is concerned with revealing people's preferences or choices. Researchers from various areas, i.e., psychology, statistics, etc., have a lot of input to the theory. However, its groundwork lies in economics. The basic motivation in economics is to understand the reactions of the society to changes in the commodity prices by examining the values of the individuals involved. Please refer to [35] for a detailed discussion on the various theories included under the general name "utility theory" and the relevant literature.

The economic evaluation in health care decision making requires value assessment, as well. Value assessment is utilized in the evaluation of the consequences of those decisions. The values are employed in the calculation of Quality Adjusted Life Years (QALYs), which combine life years and the quality of life attributed to those years. The quality of life spent in a health status is dependent on the patient's preferences. Thus, value assessment plays a crucial role in health care decision making problems.

Please refer to Section 3.2 for a detailed discussion of the value assessment in health care decision making.

2.2 TRANSPLANTATION DECISION MAKING

In this section, we discuss the literature on transplantation decision making. Transplantation decision making problems are modeled either from a societal perspective or an individual patient's perspective. Thus, we divide our review into two parts.

2.2.1 Organ Acceptance Literature

The accept/decline decision of a patient is an optimal stopping problem in which the patient makes a decision on when to accept the transplant and stop the process so as to maximize the total expected reward, i.e., quality adjusted life years. The patient base her decision on her current health status, underlying disease, location, presence or absence of a potential living donor, quality of organ offered, current UNOS organ allocation policy which implies the probability of receiving organ offers, and so on.

Research on organ acceptance problems are motivated by cadaveric kidney transplantation. David and Yechiali [26] model the accept/decline decision of a kidney patient. Patient health is assumed to be the time spent on dialysis, which translates into a health status that does not deteriorate over time. Moreover, the organ arrival rate decreases over time. They present under which conditions the optimal policy takes the control-limit form. Ahn and Hornberger [1] specifies the kidney types which yield the maximum post transplant quality adjusted life years. They define a minimum acceptable one year survival rate. Using this rate they incorporate patient preferences on the outcomes into their model. Their decision epoch is a month while patients make decisions more frequently in real life. They provide an exact analytical solution. Hornberger and Ahn [48] base the patient's kidney accept/decline decision on the one-year survival rate. They use real life data to estimate the survival rates. In their numerical work, they impose control-limit structure on the policies. Brand [14] models the optimal timing of a living-donor kidney transplant. Under the deterministic pre-transplant utilities, they show that the future rate of progression of the disease does not affect patient's accept/decline decision.

Howard [50] studies the accept/decline decision of a liver patient. He provides statistical evidence for the existence of optimal control-limit policy. The organ arrival process of his model does not depend on patient health. Alagoz et al. [5] provide a more detailed model for liver transplantation. They study the optimal timing in the living donor liver transplantation problem. Alagoz et al. [7] consider cadaveric liver offers only. They incorporate the effect of the waiting list into the patient's accept/decline decision via patient health dependent organ arrival probabilities. Alagoz et al. [8] combine the ideas in their previous two papers. They model the decision problem faced by a patient who has a living-donor liver and receives cadaveric liver offers. The stream of papers by Alagoz et al. [5, 7, 8] provides conditions under which the policy takes the optimal control limit structure for each decision problem they model.

2.2.2 Organ Allocation Literature

The societal perspective of the organ allocation policies of UNOS aims for equity and efficiency. The organ allocation policies are designed in such a way that individuals with the same level of medical urgency have equal access to organs independent of their age, race, gender, blood type or other physiological characteristics. They also target a maximum achievable number of quality adjusted life year gains through the transplantation activities.

Righter [78] models the organ allocation system as a discrete time sequential stochastic assignment problem. She shows the monotonicity of the optimal value function. New patient arrival is not allowed in her model. She assumes the post transplant rewards are independent of the organ quality. David and Yechiali [24], in their similar model, allow new patient arrivals. However, neither patients are allowed to die nor their health status are allowed to deteriorate over time. Moreover, patients and organs arrive at the system in pairs. The authors enhance their model in David and Yechiali [25] and increase the number of patient and organ types. In their enhanced model, they discard organs once they are rejected by a patient. Moreover, they do not let new patient arrivals. David [23] enhance the model further to a continuous time discounting case. They show structural properties of the optimal policy under a set of conditions. Zenios [104] models the waiting list as a queueing system. They

have multiple classes of patients and multiple classes of organs in their model. Patients renege due to death. They provide closed form expressions for waiting time metrics and fraction of patients who receive transplantation. Patients never decline offers. Zenios et al. [106] model the kidney allocation system as a continuous time, continuous state space deterministic fluid model. The control variable is the fraction of each class of organ to offer to each class of patient. The objective is maximizing efficiency, i.e., the total quality-adjusted life years, while minimizing two measures of inequity, i.e., access of various group of patients to kidneys and waiting time. They show that their suggested closed-form heuristic allocation policy performs better than the current UNOS allocation policy via simulation model of Zenios et al. [105]. In their fluid model, patient health does not change over time.

Zenios et al. [105] build a simulation model of kidney allocation system. They compare policies with different levels of emphasis on equity, i.e., average waiting time until transplant, and efficiency, i.e., quality adjusted life expectancy. They suggest policies which perform better than the current UNOS allocation policy in terms of their performance metrics. Their model does not let patient health progression over time. Howard [49] enhances the model of Zenios et al. [105]. In his model, patient health changes over time, but there are only three different health statuses. Ratcliffe et al. [74] make a cost-effectiveness analysis of various liver allocation policies via a simulation model. They find the policy that gives higher priority to healthiest patients as the most cost-effective one. Yuan et al. [103] build a simulation model of kidney allocation system. They compare a set of policies each of which give different weights to medical urgency and equity, i.e., waiting time, while prioritizing patients. They do not let patients die while waiting on the list. Shechter et al. [87] provides a more detailed simulation model of liver allocation system. They include a natural history component which models the patient health progression as a function of laboratory values [6]. They do not provide a comparison of various allocation policies.

Su and Zenios attempt to combine the societal and patient perspective in their stream of work [88–90]. In [88], they model the kidney allocation system as a queueing system with reneging. They let patients refuse the organ offers based on the expected outcome from the transplant. In [89], they have a a sequential stochastic assignment model of the system. New patients cannot arrive at the system. A rejected organ is immediately discarded. In [90],

they model the allocation system as a queueing system in which patients, depending on their type, choose to join a queue of different set of organs. The authors do not let patient health progression in any of their work.

3.0 ELICITING PATIENTS REVEALED PREFERENCES: AN INVERSE MARKOV DECISION PROCESS APPROACH

3.1 ACKNOWLEDGMENT

The following content is reprinted by the kind permission from the Institute for Operations Research and the Management Sciences: Z. Erkin, M. D. Bailey, L. M. Maillart, A. J. Schaefer, M. S. Roberts, "Eliciting Patients Revealed Preferences: An inverse Markov Decision Process Approach," *Decision Analysis*, 7(4), 358-365. © 2010, the Institute for Operations Research and the Management Sciences, 7240 Parkway Drive, Suite 300, Hanover, Maryland 21076 USA."

3.2 MOTIVATION

Quantitative models of patient-oriented decision making require values that map a variety of health outcomes to $\mathbb{R}_+$. If the patient seeks to maximize life expectancy, then these values are simply the expected survival time associated with each health outcome. However, patients do not value every living outcome equally; "perfect health" is preferred to paralysis. The most common approach to capturing these preferences is to assign a value to each health state, known as "quality-adjusted survival" or "quality-adjusted life years (QALYs)," [43]. A year in "perfect health" is worth one QALY, whereas death is given the value of zero QALYs.

It can be shown that the QALY measure does not necessarily correspond to a von Neumann-Morgenstern utility function [93, 99]. However, Garber and Phelps [41] claim

that QALYs well approximate utility functions. Culyer [22] argues that the QALY measure is closer to true patient preferences than von Neumann-Morgenstern utilities and is more useful in practice. For further details on the relationship between QALYs and von Neumann-Morgenstern utility functions, see Drummond et al. [32].

Researchers have devoted enormous effort to assess the values patients place on health states [43]. The most theoretically appealing and widely applied method for these purposes is the *standard gamble* [92, 97]. The standard gamble ascertains the probability p at which the patient is indifferent between staying in her current health state (e.g., severe fatigue and jaundice induced by hepatitis C) for the remainder of her life, and a lottery where she moves into "perfect health" with probability p and death with probability $1 - p$; the value associated with each year spent in her current state is then set equal to p years of perfect health. Another method is the *time tradeoff* [80, 94]. Under this method, the patient is asked to determine the amount of time spent in perfect health that is equivalent to a prespecified amount of time in her current health state. The time tradeoff method values the current health state as the ratio between the time spent in perfect health and that spent in the current health state.

These techniques have attracted criticism because the methods often produce inconsistent values when patients are reassessed and, not surprisingly, different techniques often produce different values. A summary of the drawbacks and potential biases of direct preference assessment techniques is found in Gold et al. [43], Arnold et al. [10], and recent behavioral economics research (c.f. Camerer et al. 18 and references therein).

Faced with a similar assessment problem in the context of utility theory, Samuelson [82, 83] proposed that utility functions be estimated through *revealed preferences*. Rather than eliciting utility functions from consumers directly, Samuelson suggested that inferences about utility functions may be made from consumer choices. For instance, when bundles A and B of goods are affordable, a consumer who purchases bundle A indicates that her utility of A is at least as much as her utility of B. As such, the consumer has revealed her preference of bundle A over B. In this manner, some of the decision maker's ordinal preferences may be observed.

We propose a similar approach to estimating patient preferences over health states based on a patient's observed behavior. We assume that a risk-neutral patient (or a physician acting on behalf of the patient) makes decisions that maximize her expected QALYs under health state valuations that are known only to herself. The assumption that a risk-neutral patient maximizes expected QALYs is common in the health state valuations assessment literature [43], and has been theoretically justified [13]. The goal is to find a set of health state valuations such that the patient's observed behavior is optimal. Of course, if there exists a set of health state valuations under which the observed behavior is optimal, there are infinitely many such sets (for example, the observed behavior will be optimal under any positive scalar multiple of these valuations). To mitigate this complication, we use non-quality adjusted expected survival as a base set of patient health state valuations. By considering restricted perturbations of these base valuations as a function of observed patient behavior, we arrive at a refined estimate of patient preferences. Such an approach can be categorized in the mathematical framework of *inverse optimization*. We caution that revealed preference approaches also appear to be subject to framing effects [98], which may limit the efficacy of our approach.

There are pragmatic reasons for our approach. Attempts to directly determine patient preferences are typically limited to no more than a few medical centers, and as few as several dozen patients. Using our approach, patient preferences can be assessed from deidentified data; the patient need not know that her preferences are being assessed. As such, our method can be applied to national datasets to estimate aggregate patient preferences. However, we caution that our method does not apply if limited or no data are available. In such a case, traditional methods of assessing patient preferences are the only option.

We illustrate our proposed inverse optimization technique on the optimal timing of living-donor liver transplantation. Applying the technique in this domain may support future research on how individual patients would react to changes in the national liver allocation system. Answering this question requires a model of the allocation system in which patients make accept/reject decisions when organs are offered to them, and therefore requires the specification of patients' health preferences. Recent work [5, 7, 8, 84] has analyzed this sequential decision making problem, however, because quality-adjusted data do not exist,

the valuations were not quality adjusted. Using the proposed revealed preference approach, we can more accurately parameterize the health state valuations of individual accept/reject decision models that consider patient health, organ quality and waiting list rank.

The remainder of the paper is organized as follows. In Section 3.3, we formalize our inverse optimization approach for a generic Markov decision process (MDP). We describe a specific MDP application concerning living-donor liver transplantation and present a numerical example in Section 3.4. We conclude in Section 3.5.

3.3 INVERSE MARKOV DECISION PROCESSES

An inverse optimization problem adjusts the parameters of a given optimization problem so that a particular feasible solution becomes an optimal solution. More specifically, consider an optimization problem P and a vector c. Given a feasible solution, x, and a nonnegative weight vector, w, an inverse optimization approach seeks to perturb the vector c to another vector d such that the solution x becomes an optimal solution to P with respect to the vector d and the weighted L_p norm $\|w(d-c)\|_p$ is minimized. Consistent with the existing literature, a vector for which the solution x is optimal is called *inverse-feasible*.

Inverse optimization has been widely applied in various areas, such as portfolio optimization [19], transportation networks [17, 31] and geophysical sciences (Tarantola 91 and references therein). Ahuja and Orlin [2] studied inverse problems under the weighted L_1 and L_∞ norms. Using duality, they established relationships between the optimization problem, P, and the inverse problem when P was a shortest path, assignment, minimum cost flow or minimum cut problem. A detailed survey of inverse combinatorial optimization problems is in Heuberger [46].

In the context of an MDP, given a stationary deterministic policy π°, the inverse optimization objective is to perturb the reward vector c to a new reward vector d, such that the policy π° is optimal and $\|d-c\|_p$ is minimized. Consider a discounted, infinite-horizon MDP with (finite) state space S. For every state $s \in S$, let the (finite) set of feasible actions be A_s. Furthermore, for each state-action pair, let $c(s,a)$ represent the corresponding immedi-

ate expected reward, $|c(s,a)| \leq M < \infty$. A transition from state s to state j when action $a \in A_s$ is chosen occurs with probability $p(j|s,a)$. Given these assumptions and a discount factor $0 \leq \lambda < 1$, it can be shown that there exists an optimal Markovian, deterministic, stationary policy [12]. Note, however, that many medical decision making problems include an absorbing state (reachable from all other states) that represents death, in which case discounting is not necessary, i.e. $\lambda = 1$ is possible. Let $v^\pi(s)$ be the total expected discounted reward under such a policy π when the system begins in state s, and similarly let v be the optimal value vector, which can be obtained by solving the optimality equations,

$$v(s) = \max_{a \in A_s} \left\{ c(s,a) + \lambda \sum_{j \in S} p(j|s,a) v(j) \right\} \text{ for all } s \in S. \tag{3.1}$$

For finite state and action models, (3.1) can be recast as a linear program [30]. Let $\gamma \in \mathbb{R}_+^{|S|}$ be such that $\gamma(i) \geq 0$ and $\sum_i \gamma(i) > 0$. If we require $\sum_i \gamma(i) = 1$ we may interpret γ as an initial probability distribution over S [73]. Then the linear program (LP) formulation of (3.1) is given by

$$\min_v \sum_{j \in S} \gamma(j) v(j) \tag{3.2a}$$

subject to

$$v(s) \;\geq\; c(s,a) \;+\; \lambda \sum_{j \in S} p(j|s,a) v(j), \;\; \forall \; s \in S, \;\; a \in A_s \tag{3.2b}$$

$$v(s) \text{ free}, \;\; \forall s \in S. \tag{3.2c}$$

Given a feasible stationary deterministic policy π° for the MDP defined by (3.1), we seek to perturb the reward vector c to a new set of rewards $d(s,a)$ such that the weighted L_1 norm, $\sum_{(s,a)} w(s,a)|d(s,a) - c(s,a)|$, is minimized and π° is optimal for the MDP defined by (3.1) when the vector c is replaced by the vector d. Specification of the weights, $w \in \mathbb{R}_+^{|S| \times |A|}$, is problem-specific and depends on the state definition (see, for example, Section 3.4.2). The new reward vector d determined through this approach is said to be *inverse feasible* with respect to π°.

By complementary slackness, π is the optimal solution for the MDP defined by (3.1) if and only if it is feasible and

$$\pi(s) = a \text{ implies } v^{\pi}(s) = c(s,a) - \lambda \sum_{j \in S} p(j|s,a) v^{\pi}(j), \ \forall s \in S. \tag{3.3}$$

In other words, if π is optimal for the MDP defined by (3.1), then the inequality constraints corresponding to the state-action pairs specified by π are satisfied as equalities. Hence we define the "*inverse MDP*" as

$$\min_{d} \quad \sum_{s \in S} \sum_{a \in A_s} w(s,a) |d(s,a) - c(s,a)| \tag{3.4a}$$

subject to

$$v(s) \geq d(s,a) + \lambda \sum_{j \in S} p(j|s,a) v(j), \ \forall s \in S, \ a \neq \pi^{\circ}(s), \tag{3.4b}$$

$$v(s) = d(s,a) + \lambda \sum_{j \in S} p(j|s,a) v(j), \ \forall s \in S, \ a = \pi^{\circ}(s), \tag{3.4c}$$

$$d \in D, \tag{3.4d}$$

$$v(s) \text{ free}, \ \forall \ s \in S, \tag{3.4e}$$

$$d(s,a) \geq 0, \quad \forall \ s \in S, \quad \forall \ a \in A_s, \tag{3.4f}$$

where the set D in (3.4d) is a (possibly polyhedral) set that represents additional requirements on the form of the rewards, e.g., monotonicity. By minimizing the weighted norm of the distance from a vector c, the inverse optimization problem finds the inverse-feasible vector d that is "closest" to c among all inverse-feasible vectors. Therefore, care must be given to the choice of both c and w.

Our approach makes the following assumptions:

Assumption 1: The patient is a risk-neutral decision maker who maximizes total expected discounted reward.

Assumption 2: The discount rate, λ, is known for each patient.

Assumption 3: All decisions are based on patient physiology alone.

Assumption 4: The patient has complete knowledge of the transition probabilities governing disease progression.

These assumptions ensure that the patients decision process is well modeled by the MDP framework. If the patient's MDP model is flawed because one of these assumptions is not adequately met, then the changes made to the rewards through the inverse optimization procedure may be due to these other deficiencies rather than simply the misspecification of the rewards, and hence not reflect the true rewards.

We recognize that these assumptions may not always hold in practice. Relaxing Assumption 1 would require modeling the inverse of a risk-sensitive MDP [51, 57, 70], and considering alternative optimality criteria. Relaxing Assumption 2 would introduce nonlinearities into the mathematical program given by (3.4) becoming a nonlinear program. Furthermore, adding additional parameters to be inferred (such as a patient's risk sensitivity or discount rate) would require additional terms in the objective function. Overcoming Assumptions 3 and 4 appears to be more difficult, particularly if our proposed inverse MDP approach is applied to deidentified patients.

3.4 NUMERICAL EXAMPLE: LIVING-DONOR LIVER TRANSPLANTATION

We describe a living-donor liver transplantation application that we use to illustrate the concepts described in Sections 3.2 and 3.3. The problem is to determine when, as a function of health, a patient should consent to a living-donor transplant. Alagoz et al. [5] studied this optimal stopping problem by formulating a discrete time, infinite horizon, discounted MDP model. Assuming that the patient is not entertaining deceased-donor organ offers, the state space S is comprised of a set of health states, $1, 2, ..., H$, and the absorbing death state, $H + 1$. Two actions, Wait (W) and Transplant (T), are available at each decision epoch, and the objective is to maximize the total expected discounted life days of the patient. The decision epochs are defined as days. Let $p(s'|s)$ be the probability that the patient will be in health state s' at time $t + 1$ given that she is in health state s at time t and the transplant does not occur. Let $c(s, T)$ be the total expected discounted post-transplant life days of the patient when the patient receives the transplant in health state s, and $c(s, W)$ be the

expected immediate reward accrued in the current period when the patient chooses to wait in health state s. An optimal solution to this problem is obtained by solving the following optimality equations

$$v(s) = \max\left\{c(s,T), c(s,W) + \lambda \sum_{s'=1}^{H+1} p(s'|s)v(s')\right\} \quad \text{for } s=1,..., H, \tag{3.5}$$

and $v(H+1) = 0$ where $v(s)$ is the maximum total expected discounted reward a patient in health state s can attain.

For this problem, the linear program given by (3.2a)-(3.2c) takes the following form

$$\min_{v} \sum_{j \in S} \gamma(j)v(j) \tag{3.6a}$$

subject to

$$v(s) \geq c(s,W) \ + \ \lambda \sum_{j \in S} p(j|s)v(j), \ \forall \ s \in S, \tag{3.6b}$$

$$v(s) \geq c(s,T), \ \forall \ s \in S, \tag{3.6c}$$

$$v(s) \text{ free}, \ \forall s \in S. \tag{3.6d}$$

Thus, given a policy π°, the inverse MDP formulation of the living-donor liver transplantation problem is given by

$$\min_{d} \sum_{s\in S} \sum_{a\in A_s} w(s,a)|d(s,a) - c(s,a)| \tag{3.7a}$$

subject to

$$v(s) \;=\; d(s,W) + \lambda \sum_{j\in S} p(j|s)v(j),\ \forall s \in S,\ \pi^\circ(s) = W, \tag{3.7b}$$

$$v(s) \;\geq\; d(s,T),\ \forall s \in S,\ \pi^\circ(s) = W, \tag{3.7c}$$

$$v(s) \;\geq\; d(s,W) + \lambda \sum_{j\in S} p(j|s)v(j),\ \forall s \in S,\ \pi^\circ(s) = T, \tag{3.7d}$$

$$v(s) \;=\; d(s,T),\ \forall s \in S,\ \pi^\circ(s) = T, \tag{3.7e}$$

$$d(s,a) \;\geq\; d(s+1,a)\ \forall\ s \in S,\ a \in \{W,T\}, \tag{3.7f}$$

$$d(s,W) \;\leq\; 1\ \forall\ s \in S, \tag{3.7g}$$

$$v(s) \text{ free},\ \forall\ s \in S, \tag{3.7h}$$

$$d(s,a) \geq 0,\ \forall\ s \in S,\ \forall\ a \in \{W,T\}. \tag{3.7i}$$

The set D in constraint (3.4d) is given by (3.7f) and (3.7g), which ensure that as the patient's health deteriorates both the post-transplant life expectancy as well as the reward associated with waiting an additional day decrease, and that the expected reward gained while waiting one day does not exceed one day.

3.4.1 Estimation of Parameters and Implemented Policies

We model patient health using Model for End-stage Liver Disease (MELD) scores. MELD scores map three laboratory values to an integer between 6 (healthiest) and 40 (sickest). Due to data scarcity, we aggregate consecutive MELD scores into groups of two. The transition probabilities and post-transplant rewards are derived using two data sets, one provided by the United Network for Organ Sharing and the other by the Thomas E. Starzl Transplantation Institute at the University of Pittsburgh Medical Center. The former includes 28,717 adult end stage liver disease patients and the latter 3,009 patients. Decision epochs correspond to days, hence the non-quality-adjusted immediate expected rewards $c(s,W)$, which we refer to

as the data-driven "wait" rewards, are set equal to 1 for all s. The health state transitions are modeled by the empiric disease-specific method of Alagoz et al. [6]. The post-transplant rewards $c(s, T)$, which we refer to as the data-driven "transplant" rewards, are calculated using the Cox proportional hazard model of Roberts et al. [79]. We refer to the optimal policy for the Alagoz et al. [5] model under these rewards as the "suggested" policy.

We assume that the policy used by the patient was a control-limit policy with threshold equal to the MELD score of the patient at the time of transplantation. That is, we assume that the patient's MELD score prior to transplantation was below this threshold, and transplantation was initiated the first time the MELD score met or exceeded the threshold. This assumption is mild given that MELD scores rarely jump by more than one from day to day and control-limit policies are almost always optimal in practice [5].

3.4.2 Numerical Results

Consider a 48-year old male patient with hepatitis C. According to the solution to (3.5), the optimal control-limit is MELD score 26. Suppose the implemented control-limit of this patient is MELD score 14. That is, the patient opts for transplantation earlier than the MDP model (3.5) suggests.

Table 1 includes the data-driven rewards, the suggested policy obtained by solving (3.5), the implemented policy, the weights used in the inverse MDP objective function and the policy-driven rewards obtained by solving the inverse MDP. Table 2 includes the value of waiting and transplanting in each state under the data-driven and policy-driven rewards, as well as their difference.

In the example presented, we use an annual discount rate of 0.97. Furthermore, for each state-action pair we set the corresponding weight, $w(s, a)$, equal to the reciprocal of the discounted expected number of times that that state-action pair would be realized under the suggested policy, starting from the healthiest MELD score. If $w(s, a)$ is viewed as a "penalty" per unit change in $c(s, a)$, (i.e., per unit of $|d(s, a) - c(s, a)|$) that is incurred every

Table 1: Policies, rewards and weights for the early transplanter

MELD Score	$c(s,W)$	$c(s,T)$	Suggested Policy	Implemented Policy	$w(s,W)$	$w(s,T)$	$d(s,W)$	$d(s,T)$
6-7	1	2039	W	W	0.003506		0.8022	2039
8-9	1	1994	W	W	0.002137		0.4924	1994
10-11	1	1945	W	W	0.002364		0.4924	1945
12-13	1	1896	W	W	0.003152		0.3792	1896
14-15	1	1843	W	T	0.004783		0.3792	1843
16-17	1	1795	W	T	0.008497		0.3792	1795
18-19	1	1751	W	T	0.018095		0.3792	1751
20-21	1	1701	W	T	0.025127		0.3792	1701
22-23	1	1650	W	T	0.045513		0.3792	1650
24-25	1	1597	W	T	0.081978		0.3792	1597
26-27	1	1536	T	T		2.033	0.3792	1536
28-29	1	1491	T	T		11.36	0.3792	1491
30-31	1	1447	T	T		117.11	0.3792	1447
32-33	1	1384	T	T			0.3792	1384
34-35	1	1341	T	T			0.3792	1341
36-37	1	1283	T	T			0.3792	1283
38-39	1	1226	T	T			0.3792	1226
40	1	1172	T	T			0.3792	1172

Table 2: Values of state-action pairs under the two sets of rewards for the early transplanter

MELD Score	$v_W(s)$ under reward $c(s,a)$	$v_T(s)$ under reward $c(s,a)$	$v_W(s)$ under reward $d(s,a)$	$v_T(s)$ under reward $d(s,a)$	difference in $v_W(s)$	difference in $v_T(s)$
6-7	2848.70	2039.04	2077.78	2039.04	770.92	0.00
8-9	2761.00	1994.12	1994.12	1994.12	766.88	0.00
10-11	2625.36	1944.81	1944.81	1944.81	680.55	0.00
12-13	2467.09	1896.11	1897.63	1896.11	569.46	0.00
14-15	2278.42	1842.93	1842.85	1842.93	435.57	0.00
16-17	2099.93	1795.43	1795.43	1795.43	304.50	0.00
18-19	1923.50	1751.13	1749.99	1751.13	173.51	0.00
20-21	1784.59	1701.48	1699.89	1701.48	84.70	0.00
22-23	1666.34	1649.87	1647.38	1649.87	18.96	0.00
24-25	1601.07	1597.13	1595.52	1597.13	5.55	0.00
26-27	1527.84	1536.28	1526.65	1536.28	1.18	0.00
28-29	1478.54	1490.84	1477.85	1490.84	0.68	0.00
30-31	1404.91	1446.97	1404.21	1446.97	0.70	0.00
32-33	1342.11	1384.36	1341.47	1384.36	0.64	0.00
34-35	1300.08	1340.93	1299.46	1340.93	0.62	0.00
36-37	1229.30	1283.04	1228.68	1283.04	0.62	0.00
38-39	1164.66	1225.74	1164.04	1225.74	0.62	0.00
40	1060.92	1171.74	1060.29	1171.74	0.62	0.00

time that state-action pair is realized, then setting the weights in this manner equates the total expected discounted penalty associated with each state-action pair and the magnitude of the change in the corresponding $c(s, a)$ value.

Consider, for example, the suggested policy reported in Table 1. The empty $w(s, a)$ entries correspond to state-action pairs that never occur under the suggested policy starting from the healthiest MELD score. Clearly, these state-action pairs include the suboptimal combinations, i.e., transplant (wait) actions for MELD scores below (at or above) 25. Additionally, due to the highly diagonal nature of the MELD score transition matrix, when starting from the healthiest MELD score it is impossible to reach MELD scores above 31 without first visiting a MELD score between 26 and 31. As a result, although it is optimal to transplant in MELD scores above 31, these state-action pairs will never occur when implementing this policy starting from the healthiest MELD score. For all of these "impossible" state-action pairs, we set $w(s, a)$ equal to an arbitrarily large value. The remaining weights are such that

$$\frac{1}{0.003506}\cdot 1+\frac{1}{0.002137}\cdot 1+\frac{1}{0.002364}\cdot 1+\frac{1}{0.003152}\cdot 1+\frac{1}{0.004783}\cdot 1+\frac{1}{0.008497}\cdot 1+\frac{1}{0.018095}\cdot 1+$$

$$\frac{1}{0.025127}\cdot 1+\frac{1}{0.045513}\cdot 1+\frac{1}{0.081978}\cdot 1+\frac{1}{2.033}\cdot 1536+\frac{1}{11.36}\cdot 1491+\frac{1}{117.11}\cdot 1447 = 2848.70,$$

which, as expected, is the total expected discounted reward starting from the healthiest MELD score under the suggested policy as reported in column 2 of Table 2.

As seen in Table 1, the revised transplant rewards, $d(s, T)$, are identical to the data-driven rewards. However, the revised wait rewards, $d(s, W)$, exhibit a stepwise non-increasing structure. This structure can be interpreted as a reflection of quality of life preferences across MELD scores, and/or a preference to end the optimal stopping problem sooner rather than later. That is, the patient places less value on days spent in sicker states and/or places less value on days spent living with uncertainty as to when the transplant will occur. Also noteworthy is the fact that the arbitrarily large weights need not be very large to produce the same result; indeed, any value greater than approximately 0.15 for these weights produces the same vector d.

An instance for a "late transplanter," i.e., a patient who opts for transplantation later than the MDP model (3.5) suggested, can be structured similarly. Intuition suggests that "late transplanters" value waiting (transplanting) more (less) than is reflected by the data-driven rewards.

3.5 CONCLUSION AND FUTURE RESEARCH

Estimating patient preferences is an important component of medical decision making models, but traditional techniques suffer from various drawbacks, namely the fact that it is difficult to obtain large samples, patients may find questionnaires hard to follow, and patients may provide logically inconsistent responses. We propose a new, indirect method for inferring patient preferences based on their observed policies. We formulate this problem as an inverse MDP, and use linear programming to solve it. We illustrate our techniques on the problem of timing a living-donor liver transplant as a proof of concept. More realistic models which include deceased-donor liver transplantation as an alternative to the living-donor liver [7, 8] could also be considered with proper modifications to the inverse MDP model.

Future work could include this method's application to different clinical decisions, and the use of the inferred patient preferences in societal decision models. Such a model could, for example, examine the effect of patients using the inferred patient preferences under a different liver allocation system. We also leave for future work the relaxation of the assumptions described in Section 3.3. While relaxing Assumptions 1 and 2 appears to be possible through more difficult optimization models, Assumptions 3 and 4 may be necessary for our approach, particularly with de-identified data.

4.0 A SIMULATION MODELING APPROACH TO PLACING EXPEDITED LIVERS

4.1 INTRODUCTION

As discussed in Chapter 1, expedited liver placement is an escape mechanism to avoid not placing a liver [21]. When a deceased organ donor is identified, standard placement procedure starts. The coordinator from the organ procurement organization contacts UNOS. Based on the characteristics of the donor and the patients waiting for a transplant, a ranked list of patients, i.e., a match list, is generated. The procurement coordinator attempts to place the organ with a recipient by proceeding down the match list. Once contacted, patients (or on behalf of them, their surgeons) have one hour to respond. The procurement coordinator can extend limited number of simultaneous local offers at a time to speed the match process. The responses of the patients who receive such an offer are considered according to the patients' positions on the match list. Patients frequently decline organs. Although approximately 2,000 listed patients die each year due to the scarcity of organs (Figure 2) [76], 45% of livers are declined by the first patient on their match list [50]. As the standard placement procedure continues, the organ ages and becomes less desirable due to the decrease in the quality. Therefore, to prevent the organ from being discarded at some point the procurement coordinator may stop the standard prioritized matching procedure and offer the organ to a transplant center as an "expedited organ."

In the liver allocation system, each liver might become an expedited liver depending on the attributes of the organ and attributes of the patients on the waiting list. Organs that

became an expedited organ constituted between 10% and 25% of all organs in 2006 [72]. Today expedited placement still attracts attention [77]. To prevent organs from being discarded, expedited placement is still suggested [67, 95].

When an expedited liver is offered to a transplant center, the center coordinator decides which, if any, of its patients should receive the organ regardless of their position on the match list. The transplant center coordinator aims to balance the trade-off between medical urgency (e.g., pre-transplant likelihood of death) and anticipated outcomes (e.g., post-transplant likelihood of one-year graft survival) for the diverse, dynamic set of patients listed at the transplant center, while utilizing as many organs as possible. When an expedited liver is allocated to an individual, she avoids the pre-transplant likelihood of death and earns an expected post-transplant lifetime. In the meantime, however, she also loses the opportunity of having a non-expedited liver transplant which would likely yield a better health outcome compared to the expedited liver transplant.

In this chapter, we build a discrete-time discrete-event simulation model for the expedited liver placement problem. We construct various expedited liver allocation policies based on the different aspects of the system at the transplant center. We compare and contrast these policies via our simulation model.

The chapter is structured as follows: Section 4.2 describes our simulation model (SIM1). Because we build multiple simulation models throughout this dissertation, we name them as SIMx in which x stands for the order in which it is presented. Section 4.3 reviews the datasets utilized in the parameter estimation and explains the parameter estimation methods. Section 4.4 presents the validation of the simulation model. Section 4.5 describes our numerical study and presents results. Section 4.6 concludes the section.

4.2 SIMULATION MODEL SIM1 DESCRIPTION

In our study, to define liver types we employ Alagoz [3]'s approach. We characterize each organ by its donor's age group, gender and ethnicity. Alagoz [3] uses the Cox proportional hazard model of Roberts et al. [79] to order the liver types. The author defines 28 categories.

Liver quality depends on the sex match between the donor and the recipient. Due to data sparsity, we aggregate the liver qualities. We assume there are two expedited liver qualities. In his study, Alagoz [3] considers only female patients. We extend his definition to include male patients, in addition to female ones, in our study. However, we use the same ordering of liver types. We do not incorporate CIT into our analysis. Because CIT is not found to be a significant factor in the regression analysis of Roberts et al. [79].

Because blood type compatibility between the donor and the patient decreases the risk of organ rejection and increases the post-transplant lifetime [39, 79], in addition to the attributes used to define the liver types we also employ blood type to characterize an organ.

Patient-level accept/decline decision process is always a part of an allocation system. The attributes of patients play a crucial role in this decision process. We group patient attributes, e.g., age, gender, etc., into patient types. We employ MELD (Model for End Stage Liver Disease) score, which measures patient's probability of death using a mortality risk score corresponding to the degree of medical urgency, to indicate patient's health status. We specify each patient listed at the transplant center by her MELD score and patient type.

While defining patient types, due to data sparsity, we aggregate patients with different blood types under the same patient type. We estimate model parameter values accordingly. However, the flexible structure of simulation modeling enables us to differentiate patients of the same type. In the simulation model, first the organ is assigned to a patient type-MELD score pair. Then, among the patients of that specific patient type-MELD score pair only blood compatible patients are considered for final assignment. That is, patients of the same type can have different blood types and they are treated differently in the simulation model during organ assignment depending on the blood type of the organ.

MELD scores have a range between 6 (healthiest) and 40 (sickest). Due to data scarcity, we aggregate consecutive MELD scores into groups of two. Our aggregated MELD scores have a range between 1 and 18. We do not consider Status 1 patients in our study. Because at any point of time there are fewer than a dozen of Status 1 patients nationwide.

Patient type is a function of disease group, age group, blood type, gender, whether the patient has a positive cytomegalovirus (CMV), encephalopathy and a prior transplant or

not. These attributes are the variables which are found to be significant in the regression analysis of Roberts et al. [79]. We consider only adult patients ($18 \leq \text{age} < 80$).

We assume that when offered an expedited organ, the patient accepts or declines the organ based on the optimal control limit introduced by Alagoz et al. [7]. The authors model the accept/decline decision of a patient as a discrete time, infinite horizon, discounted MDP model. Given an expedited organ offer of type $d \in \{1, 2, \ldots, D, D+1\}$ ($D+1$ denoting no offer), if a patient of type $i \in \{1, 2, \ldots, \tau\}$ has a MELD score less than the optimal control limit, $\mu_i^*(d)$, then she rejects the offer. Otherwise, she accepts the offer. The optimal control limit balances the expected post-transplant lifetime and the expected lifetime if the current liver offer is rejected. The sufficient conditions that ensure the existence of a control limit are listed as follows in the study of Alagoz et al. [7]:

- an increasing failure rate (IFR) health transition matrix,
- 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 post-transplant reward,
- as the patient gets worse, the reduction in the benefit of waiting is greater than the reduction in the benefit of performing the transplant,
- the worse the patient, the more probable that the patient will become even worse.

Please refer to the paper by Alagoz et al. [7] for details. The rewards utilized in the generation of the optimal control limits are the survival times calculated by the Cox proportional hazard model of Roberts et al. [79].

Patients with the same gender, disease group and optimal control limits for both liver qualities are grouped under the same patient type. Because patients with the same gender, disease group and different blood types might have the same optimal control limits for the liver types, a patient type includes patients with different blood types. In our model, we assume that patient type never changes during the process, patients of the same type and MELD score are indistinguishable and all patients are independent of each other.

The (random) events that take place at the transplant center on a daily basis are expedited transplant (if any), non-expedited transplant(s), health transitions including deaths,

arrival of new patients at the center. Due to the nature of these events, we construct a discrete-time discrete-event simulation model (SIM1). The time unit of the simulation model SIM1 is chosen to be days, because in our datasets utilized to estimate the model parameters expedited liver offers arrive at the center every four days on average (refer to Section 4.3.1). Because the events are modeled to take place on a daily basis, our model SIM1 takes the form of a discrete-time simulation model. The flow of the events in the simulation model SIM1 is presented in Figure 5.

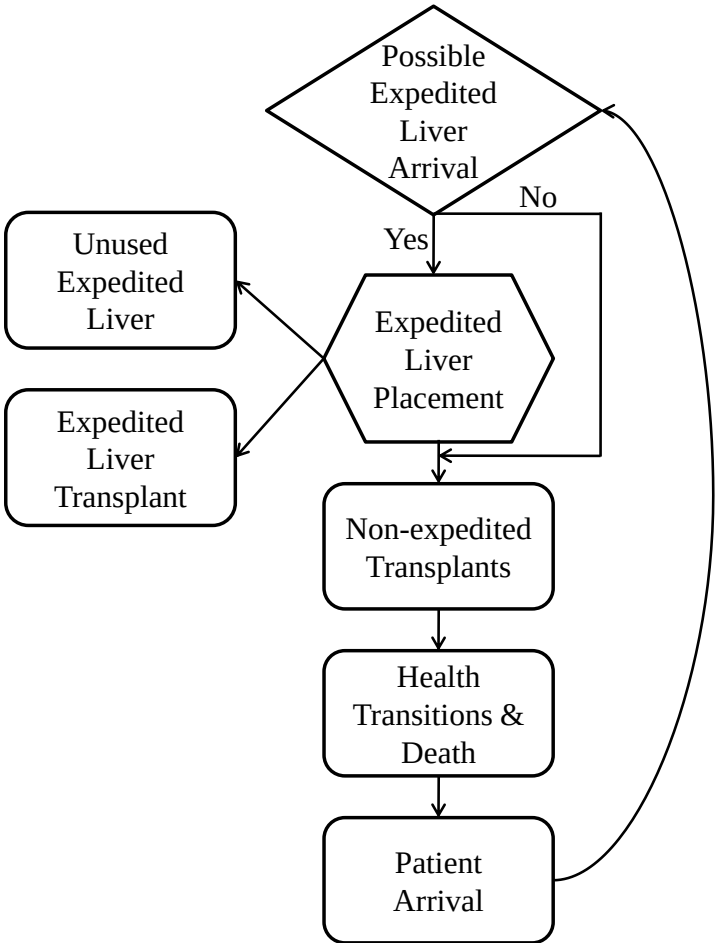


Figure 5: Simulation flow chart of daily events.

Each iteration, i.e., day, in the simulation starts with a probable expedited liver arrival. If there is an expedited liver offer on the current day, then the type of the expedited liver is specified and the transplant center coordinator attempts to match the liver with a pa-

tient. Given the liver is of type d and blood type $b \in \{\text{A, B, AB, O}\}$, the transplant center coordinator chooses a patient of type i among the blood compatible ones with a MELD score $j \geq \mu_i^*(d)$ to assign the liver to according to the expedited liver allocation policy being simulated. If the policy gives priority to a specific (i, j) pair patients over the other patients to receive the liver offer, but none of the (i, j) patients accept the offer according to their optimal control limits, then the organ is not assigned to those (i, j) patients and the next (i, j) pair patients with the highest priority receive the offer. If there is no patient who accepts the expedited liver, then the liver is rejected. Once the decision on the expedited liver placement is done, the non-expedited liver transplants take place. Patients who receive a non-expedited liver transplant leave the system. The remaining patients go under health transitions. Due to these health transitions, some patients might die. Finally, new patients join the waiting list at the center. Once joined, their patient type and initial MELD score are specified. The patient type defines the patient's gender and determines her blood type based on a distribution.

Because the datasets used to estimate the parameter values cover a 4-year long time horizon (see Section 4.3.1), we set each replication to a year. The warm-up period is set to last five replications, i.e., years. Through the end of the warm-up period it is observed that the patient population size at the center has reached steady state.

4.3 PARAMETER ESTIMATION

The parameters to be estimated are as the following.

- $r((i, j), d)$, the expected post-transplant lifetime that a patient of type i and MELD score j obtains when she receives an expedited liver transplant from an organ of type d, $i \in \{1, 2, \ldots, \tau\}$, $j \in \{1, 2, \ldots, 18\}$, $d \in \{1, 2, \ldots, D, D + 1\}$
- $H_i(j'|j)$, the probability that a patient of type i and MELD score j has a health transition to MELD score j' on a day, $i \in \{1, 2, \ldots, \tau\}$, $j \in \{1, 2, \ldots, 18\}$, $j' \in \{1, 2, \ldots, 18\}$
- $\mathcal{D}(d, b)$, the probability of receiving an expedited offer from an organ of organ type $d \in \{1, 2, \ldots, D, D + 1\}$ and blood type $b \in \{\text{A, B, AB, O}\}$ on a day

- the probability that k patients join the waiting list at the center on a day, $k \in \{0, 1, 2, \ldots\}$
- ρ_{ij}, the likelihood that when a new patient joins the list, she is of type $i \in \{1, 2, \ldots, \tau\}$ and MELD score $j \in \{1, 2, \ldots, 18\}$
- the probability that a new patient of type $i \in \{1, 2, 3 \ldots, \tau\}$ is of blood type $b \in \{A, B, AB, O\}$
- $\xi_i(j)$, the probability that a patient of type i and MELD score j receives a non-expedited transplant on a day, $i \in \{1, 2, \ldots, \tau\}$, $j \in \{1, 2, \ldots, 18\}$

4.3.1 Data Sources

The estimation of the parameter values is based on multiple datasets. We make use of the Cox proportional hazard model of Roberts et al. [79] to estimate the expected post-transplant lifetimes. The authors utilize a UNOS dataset including transplant information of 17,044 liver patients who received a transplant between 1990 and 1996. The health transition probabilities are based on the work of Alagoz et al. [4, 6] and Bryce et al. [16]. The authors develop a natural history model to estimate disease progression based on clinical and biological factors. Then, they estimate the health transition probabilities via simulation. They utilize a dataset coming from the Thomas E. Starzl Transplantation Institute at the University of Pittsburgh Medical Center (UPMC). The dataset includes information on 3,009 liver patients who joined the list between 1991 and 2000.

The rest of the parameter values are estimated using three datasets coming from the Thomas E. Starzl Transplantation Institute at the University of Pittsburgh Medical Center (UPMC). The first dataset includes information on 1,050 adult liver patients, i.e., date to join the list, age ($\geq$ 18), gender, primary reason for the need for transplantation, blood type, MELD score at listing, MELD score at transplant or death or the time datasets were generated, date of death (if any), date of transplant (if any), whether the patient received a prior transplant or not, whether the patient had CMVGR or not, whether the patient had encephalopathy or not. The second dataset includes information on 5,858 livers offered to patients at UPMC, i.e., the procurement date, the offer type (expedited/non-expedited), donor's age, donor's gender, donor's blood type, whether the organ was transplanted or not.

3,049 livers, out of 5,858, were offered to UPMC as a back-up offer. Back up offer is for a patient on the waiting list but is lower than the first patient. It is used to speed the match process. If the patient(s) prior to the patient who has received a back-up offer rejects the organ offer, then the patient who has received the back offer has the right to receive the transplant. In such a case, the back-up offer is not called a back-up offer anymore. That is, 3,049 livers were actually never offered to UPMC. The third dataset includes information on 813 liver-patient matches, i.e., organ identification number, patient identification number, date of transplant, offer type (expedited/non-expedited). The datasets cover the time period (2006, 2010). They were generated by UPMC upon request.

4.3.2 Estimation Methods

We assume the liver quality 1 corresponds to the highest quality liver and the liver quality 2 corresponds to the lowest quality liver. In Table 3, the liver qualities corresponding to different organ attributes and recipient genders are listed.

We group patients with the same gender, disease group and optimal control limits for both liver qualities under the same patient type. The information on gender determines the liver quality of the organ offered. The information on disease group specifies the health progression of the patient. Because we do not have health transition probabilities for liver patients whose primary reason for transplant is cancer, we exclude such patients from our study. We assume there are three disease groups. The first disease group includes primary biliary cirrhosis, primary sclerosing cholangitis, alcoholic liver disease, autoimmune disorders and metabolic disorders. The second disease group contains hepatitis B and C viruses. The third disease group includes acute diseases. The disease group classification is based on the study of Roberts et al. [79]. The optimal control limits specify how a patient behaves once offered an organ. We define 58 patient types. Due to data sparsity, we eliminate the patient types which do not have any appearance in the UPMC patient dataset and assume there are 32 patient types. In Table 4, patient types' attributes and frequency of observations in the patient dataset and match dataset are provided.

Table 3: Mapping of organ attributes to liver qualities

d	**age**	**race**	**gender**	**liver quality-female recipient**	**liver quality-male recipient**
1	0-20	White	Female	1	1
2	21-30	White	Female	1	1
3	31-40	White	Female	1	1
4	41-50	White	Female	1	1
5	51-60	White	Female	1	2
6	61-70	White	Female	1	2
7	71-...	White	Female	2	2
8	0-20	not White	Female	1	1
9	21-30	not White	Female	1	2
10	31-40	not White	Female	1	2
11	41-50	not White	Female	2	2
12	51-60	not White	Female	2	2
13	61-70	not White	Female	2	2
14	71-...	not White	Female	2	2
15	0-20	White	Male	1	1
16	21-30	White	Male	1	1
17	31-40	White	Male	1	1
18	41-50	White	Male	1	1
19	51-60	White	Male	2	1
20	61-70	White	Male	2	1
21	71-...	White	Male	2	2
22	0-20	not White	Male	1	1
23	21-30	not White	Male	2	1
24	31-40	not White	Male	2	1
25	41-50	not White	Male	2	2
26	51-60	not White	Male	2	2
27	61-70	not White	Male	2	2
28	71-...	not White	Male	2	2

Table 4: Patient type definitions and frequency of observations in datasets

Patient Type	Frequency of Observations in the Patient Dataset	Frequency of Observations in the Match Dataset	Control Limits 1	Control Limits 2	Gender	Disease Group
1	143	68	4	4	F	1
2	122	68	4	4	M	1
3	115	66	4	5	F	1
4	234	130	4	5	M	1
5	8	4	5	5	F	1
6	3	2	5	5	M	1
7	6	1	5	6	F	1
8	13	5	5	7	F	1
9	16	8	5	7	M	1
10	8	5	5	8	M	1
11	1	1	6	7	F	1
12	1	0	6	8	F	1
13	15	7	6	8	M	1
14	1	1	7	8	F	1
15	4	2	7	8	M	1
16	10	3	9	11	M	2
17	3	1	10	11	F	2
18	14	10	10	11	M	2
19	52	30	11	11	F	2
20	118	89	11	11	M	2
21	6	1	11	12	F	2
22	19	10	11	12	M	2
23	1	0	12	12	F	2
24	5	1	12	12	M	2
25	3	0	12	13	F	2
26	15	8	12	13	M	2
27	12	5	7	7	F	3
28	3	3	7	7	M	3
29	13	7	7	9	F	3
30	4	1	7	9	M	3
31	3	2	9	9	F	3
32	5	1	9	9	M	3

To estimate the probability of receiving an expedited offer from an organ of organ type $d \in \{1, 2, \ldots, D, D+1\}$ and blood type $b \in \{\text{A, B, AB, O}\}$, we assume that the time between expedited organ offers follows a geometric distribution with parameter p. Thus, the parameter p is calculated as the following.

$$p = \frac{1}{\text{mean days between expedited offers}}.$$

Then, the probability of an expedited offer from an organ of organ type d and blood type b is obtained using the following formula:

$$\begin{aligned}
\mathcal{D}(d,b) &= \Pr(\text{expedited organ arrives}) \cdot \\
&\quad \Pr(\text{offer is from organ of organ type } d \text{ and blood type } b | \text{expedited organ arrives}) \\
&= p \cdot \Pr(\text{offer is from organ of organ type } d \text{ and blood type } b | \text{expedited organ arrives}) \\
&= p \cdot \frac{\text{total number of expedited offers from organ of organ type } d \text{ and blood type } b}{\text{total number of expedited offers}}
\end{aligned}$$

In the UPMC liver dataset, the average time between 381 expedited organs' offer time is 3.86 days. That is, we calculate p as 0.26.

In the UPMC liver dataset, race information of donors is missing. Thus, we assume race is independent of donor's age, gender and blood type. According to 2009 OPTN/SRTR Annual Report (Figure 6), white donors constitute approximately 80% of the patient population [76]. Thus, we assume the probability that a donor is white is 0.80.

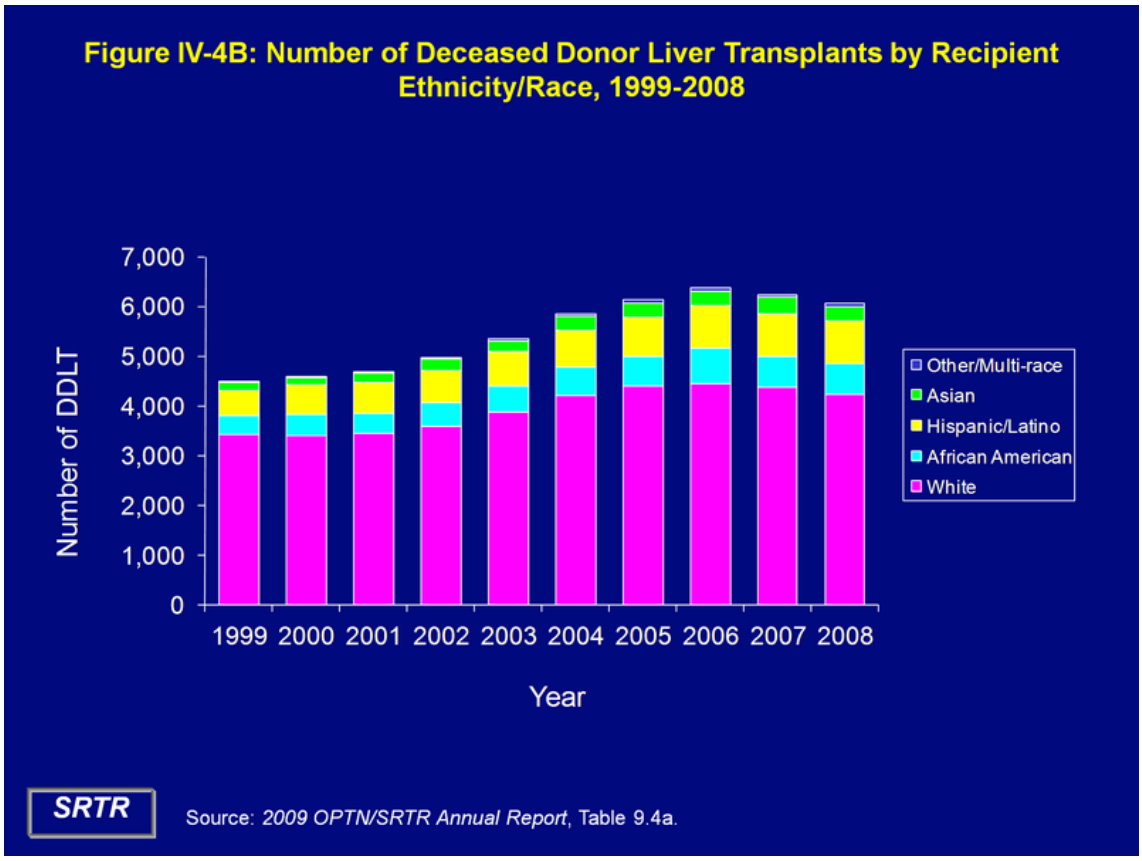


Figure 6: Distribution of race among the deceased donor liver transplants.

To estimate the probability that k patients join the list, $k \in \{1, 2, \ldots\}$, we count the number of arrivals on each day covered in the datasets. In the UPMC patient dataset, we observe maximum 5 arrivals at the center on a day. The dataset covers 1558 days. Table 5 presents the number of days in which k new patients, $k \in \{0, 1, 2, 3, 4, 5\}$, join the list at the center and the corresponding probabilities.

Relisting of a patient is possible when the graft transplanted fails after transplantation and before death of the patient. We do not explicitly model relisting of patients. Instead, we treat the patients who are relisted as new patients with a prior transplantation history. Relisted patients are included in the patient arrival probabilities as new patients.

Table 5: Patient arrival probabilities

k	**number of days**	**probability**
0	980	0.6290
1	384	0.2465
2	130	0.0834
3	49	0.0315
4	12	0.0077
5	3	0.0019

Next, consider the likelihood that when a new patient joins the list, she is of type i and MELD score j, ρ_{ij}. We use the following formula to calculate ρ_{ij}.

$$\rho_{ij} = \frac{\text{total number of patients who joined the list in } (i,\, j) \text{ pair}}{\text{total number of new patients}}.$$

Figure 7 shows the distribution of patient blood type independent of the patient types. In the simulation model SIM1, blood type is assumed to be dependent on the patient type. For each patient type, we count the number of patients from each blood type and divide that number to the total number of patients of the patient type under consideration to obtain the distribution.

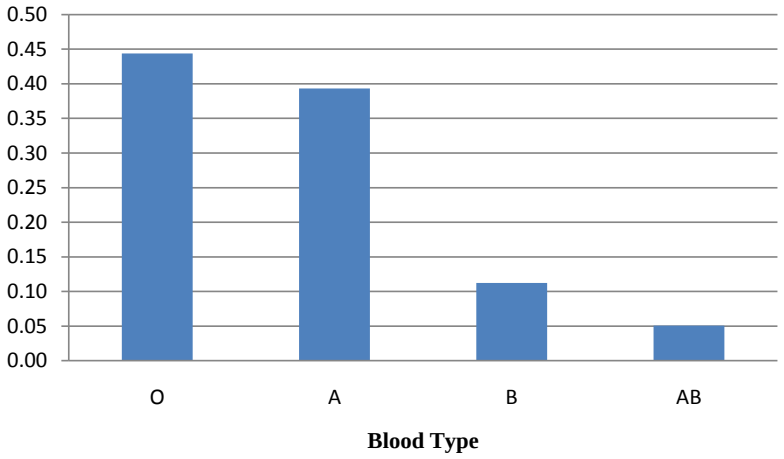


Figure 7: Patient blood type distribution.

Next, consider the probability that a patient of type i and MELD score j receives a non-expedited transplant, $\xi_i(j)$. It is actually a conditional probability, i.e., given there is a patient of type i and MELD score j, $\xi_i(j)$ is the probability that she receives a non-expedited transplant. It is obtained using the following formula:

$$\xi_i(j) = \frac{\text{number of non-expedited transplants received by patients of type } i \text{ and MELD score } j}{\text{total expected number of patient days of type } i \text{ in MELD score } j}. \tag{4.1}$$

In the calculations of the denominator of $\xi_i(j)$ (Equation 4.1), we assume that between additions/arrivals to the waiting list and transplants/departures from the waiting list (e.g., death) there exists a day. Then, given the patient type i, time on the waiting list T, MELD at listing M_0 and final MELD score M_T of the patient, the expected time spent in a MELD score j for an individual patient is calculated as

$$\mathbb{E}[T(j)] = \sum_{k=1}^{T-1} \frac{[(H_i)^k]_{M_0,j} \cdot [(H_i)^{T-k}]_{j,M_T}}{[(H_i)^T]_{M_0,M_T}},$$

where $[(H_i)^k]_{i,j}$ corresponds to $(i,j)^{\text{th}}$ entry of the $k-$step health transition matrix H_i. Once we calculate the expected time spent in a MELD score j for each individual patient, then,

depending on the patient type, summation of $\mathbb{E}[T(j)]$'s of all patients yield the total expected number of patient days in MELD score j.

We assume all patients are independent of each other. The independence assumption plays a crucial role in the random event non-expedited transplants. The non-expedited transplant probabilities calculated as described above are per patient day. Thus, on a day each (i, j) patient receives a non-expedited transplant with probability $\xi_i(j)$ independent of all the other patients.

Unfortunately, there is a large set of (i, j) pairs whose corresponding $\xi_i(j)$ values are zero. There might be two reasons of having these missing values. One would be that (i, j) patients did not receive transplant during the time period covered by the datasets. The other reason would be that we do not observe these (i, j) patients in the datasets. Both cases cannot provide sufficient proof on that these (i, j) patients never receive non-expedited transplant. It is unrealistic for an (i, j) patient not to receive a non-expedited transplant while patients from (i, j'), $j' \neq j$, pairs do so. Moreover, the expected time spent on a pair is non-zero for 97% of all (i, j) pairs. These missing values cause a bias on the policy comparison. That is, the performance of any expedited liver allocation policy favoring these (i, j) patients would be biased. Thus, we need to impute the missing $\xi_i(j)$ values.

Single imputation is a method to substitute a value for a missing value. For instance, each missing value can be imputed by the mean of the available data points. Single imputation method does not include the uncertainty on the predictions of the missing values. The multiple imputation procedure of Rubin [81], however, generates a set of plausible values for the missing values which represents the uncertainty on the right value to impute. In the multiple imputation procedure, the missing values are imputed multiple times and these values are combined for the inference.

Among the multiple imputation methods, we utilize the parametric regression method to impute the missing $\xi_i(j)$ values [81]. The regression method assumes that the missing values are missing at random (MAR). That is, the probability that a data point is missing may depend on the values of the available information about the missing data points, but not the values of the missing data points. For example, the probability that a specific $\xi_i(j)$ value is missing may be related to the patient type i and MELD score j, but not to the missing value

of $\xi_i(j)$. In addition to MAR, the parametric regression method also assumes multivariate normality. However, the method is proved to be robust to departures from the multivariate normality, as supported by the simulation studies found in [86] and the references therein.

In the parametric regression method, for each variable with missing values a regression model is fitted. Based on the estimated coefficients of the regression line and the associated covariance matrix, new estimates of the coefficients and the variance are drawn from the posterior predictive distribution of the parameters. The missing values are filled using the new estimates of the parameters of the regression line. The process is repeated k times, value of which is defined by the modeler.

The values of all model parameters can be seen in Appendix A.

4.4 MODEL VALIDATION

Model validation aims for building the right model. Its goal is to represent and correctly reproduce the behaviors of the real world system. There are various methods to validate a simulation model. For instance, subject matter experts' opinion on the model and its outputs is of great value for validation. Another method which we utilize to validate our simulation model SIM1 is historical validation. Historical validation uses historical data to replicate the past via simulation.

Because there is no specific rule for the expedited liver allocation followed by the transplant center coordinators, we run our simulation model SIM1 excluding the expedited liver placement component (SIM2). That is, no expedited liver offers arrive at the center. We compare the values of a set of performance measures generated via simulation and those calculated using the UPMC datasets. We take 5,000 replications so that the standard deviations of the performance measures are less than 10% of their corresponding mean. Table 6 includes the means and standard deviations of performance measures generated via simulation and their corresponding values calculated using UPMC datasets.

Simulation model SIM2 has, on average, more patients than the historical data. Even though the average number of patients at UPMC is approximately 189 patients, there is

Table 6: Historical validation of the simulation model SIM2

	simulation		historical
	mean	**std. deviation**	**data**
average non-expedited transplant rate	0.399198	0.034213	0.319641
average number of patients	215.51	14.0265	189.0745
percentage of patients died	0.272431	0.031441	0.221429
percentage of patients received transplant	0.727569	0.031441	0.778571

an increasing trend on the size of the patient population at UPMC. The average number of patients at UPMC was roughly 100 in 2006 while it has reached 250 by 2010. Because the simulation has more patients than the historical data, there is an increased opportunity for non-expedited transplants. Therefore, simulation model SIM2 has, on average, more transplants than the historical data. However, the number of transplants cannot keep up with the increase in the number of patients. Thus, we observe more deaths in the simulation results compared to the historical data. In conclusion, because we can provide intuitive explanations for the discrepancies in the performance measures, our simulation model SIM2 is a valid model of the system.

4.5 NUMERICAL STUDY

4.5.1 Expedited Liver Allocation Policies

Various expedited liver allocation policies that capture different aspects of the waiting list and patient characteristics are constructed. We consider policies which emphasize on non-expedited transplant probabilities, disease groups, waiting time, post-transplant survival, probability of mortality, etc. Below is the list of those policies and their descriptions. In Figure 8, we also present the summary of policy characteristics for ease of comparison.

- Policy A - Randomized policy. There is no specific way of ordering the patients. When there is an expedited liver offer, the patient to receive the organ is randomly chosen among the blood compatible ones.

- Policy B - UNOS allocation policy. First, patients are ordered according to their MELD score. The higher the MELD score is, the higher the priority of the patient is. Within each MELD score, patients are ordered according to their blood type compatibility with the donor. In Table 7, the ordering of the blood type matches is presented. Finally, ties are broken according to the waiting time. UNOS defines waiting time as the time accrued at or above the current MELD score. After the patients are ordered, the liver is allocated to the top patient who accepts it according to the optimal control limit.

- Policy C - The higher the difference between the likelihood of death and the likelihood of receiving a non-expedited transplant, the higher the priority of receiving an expedited transplant. The lifetime of each patient is modeled as a Markov Chain. The chain includes various transient health states and two absorbing states, i.e., death and transplant. We exclude the possibility of expedited liver transplant and calculate the limiting probabilities of the chain which is dependent on the current MELD score of each patient. We calculate the absorbing probabilities for every starting MELD score. The higher the probability that the system is absorbed in state death, the lower the probability that the system is absorbed in state transplant. We order the patients according to the absorbing probabilities of state death. The higher the absorbing probability of state death, the higher the priority of receiving an expedited transplant.

- Policy D - The lower the probability of receiving a non-expedited transplant, the higher the priority of receiving an expedited transplant. The lower the $\xi_i(j)$ is, the higher the priority of (i, j) patients is.

- Policy E - The higher the average number of (i, j) patients on any given day, the higher the priority of receiving an expedited transplant. The average number of (i, j) patients on a day is calculated via simulation (SIM2) in which expedited liver arrivals are excluded. We order the (i, j) pairs in descending order of their corresponding average number of patients on a day metric.

- Policy F - The lower the non-expedited transplant rate of an (i, j) pair, the higher the priority of receiving an expedited transplant. We simulate our model excluding the expedited liver arrivals (SIM2). We record the number of expedited transplants taking place on a day, i.e., non-expedited transplant rate, for each (i, j) pair. Then, we put the (i, j) pairs in descending order of these rates.
- Policy G - The lower the probability of receiving a non-expedited transplant, the higher the priority of receiving an expedited transplant. Contrary to Policy D, Policy G considers the competition among the (i, j) pairs for one non-expedited liver. Given there is a non-expedited liver offer, each (i, j) pair (not an (i, j) patient) has a probability of receiving that organ. We obtain these probabilities via simulation in which we eliminate the expedited liver arrivals (SIM2). We order the (i, j) pairs according to these probabilities whose sum over all (i, j) pairs is equal to one.
- Policy H - The higher the post-transplant expected lifetime, the higher the priority of receiving an expedited transplant. This policy orders patients according to the outcome of the transplant.
- Policy I - First, we order the patients according to their MELD score. The higher the MELD score is, the higher the patient's priority is. Within each MELD score, first blood type compatibility of the match and then whether the patient has an acute liver failure or not is considered. In this policy, we give higher priority to non-acute liver patients compared to acute ones.
- Policy J - This policy reverses the priority given to acute and non-acute liver patients under Policy I. We order the patients according to their MELD score. The higher the MELD score is, the higher the patient's priority is. Within each MELD score, first blood type compatibility of the match is considered. Within each blood type, acute liver patients have higher priority than non-acute liver patients.
- Policy K - First, we order the patients according to their MELD score. This policy gives higher priority to low MELD scores. The lower the MELD score is, the higher the patient's priority is. Within each MELD score, first blood type compatibility of the match and then whether the patient has an acute liver failure or not is considered. In this policy, we give higher priority to non-acute liver patients compared to acute ones.

- Policy L - This policy reverses the priority given to acute and non-acute liver patients under Policy K. We put patients in an ascending order of MELD scores. Within each MELD score, first blood type compatibility of the match is considered. Within each blood type, acute liver patients have higher priority than non-acute liver patients.

- Policy M - We order the patients according to their MELD score. Except aggregated MELD score 18, the priority assigned to MELD scores increases as the MELD score increases. We assign the lowest priority to MELD score 18. Within each MELD score, first blood type compatibility of the match and then whether the patient has an acute liver failure or not is considered as it is the case in previous policies. In this policy, we give higher priority to non-acute liver patients compared to acute ones.

- Policy N - This policy again reverses the priority given to acute and non-acute liver patients under the previous policy, Policy M.

Characteristics \ Policy	**A**	***B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**L**	**M**	**N**
MELD Score: sickest first		X							X	X				
MELD Score: healthiest first											X	X		
MELD Score: 17, 16, …, 1, 18													X	X
Acute priority over non-acute liver patients										X		X		X
Non-acute priority over acute liver patients									X		X		X	
Ordered blood type compatibility	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Waiting time on the list	X		X	X	X	X	X	X	X	X	X	X	X	X
Waiting time at or above the current MELD score		X												
Absorbing probability of death			X											
Absorbing probability of non-expedited transplant			X											
Daily probability of receiving a non-expedited transplant				X										
Daily average number of (*i, j*) patients					X									
Non-expedited transplant rate of (*i, j*) pairs						X								
Proportion of non-expedited transplants assigned to (*i, j*) pairs							X							
Post-transplant expected lifetime								X						

*Current UNOS liver allocation policy

Figure 8: Expedited Liver Allocation Policy Descriptions.

Under each policy, ties among patients for liver allocation are possible. Except Policy B in which we simulate the UNOS liver allocation policy, we use total waiting time on the list as a tie breaker. Each policy considers only blood type compatible matches as described in Table 7. For instance, if blood type of the donor is AB, then only blood type AB patients are assumed to be candidates for the expedited liver transplant. If no match can be found, then the organ is rejected.

Table 7: Ordering of the blood type matches

		recipient			
		A	**B**	**AB**	**O**
donor	**A**	1	-	2	-
	B	-	1	2	-
	AB	-	-	1	-
	O	3	2	3	1

Policy A aims to show that random assignment of the expedited liver to any patient is not the best strategy. A policy carefully constructed is expected to perform better than a randomized policy. Policy B follows the steps of the UNOS non-expedited liver allocation policy. UNOS policy considers solely the likelihood of mortality, MELD score, while ordering the patients. Policy C seeks for the balance between the likelihood of transplantation and that of death. It gives priority to patients who are more likely to die than to have transplant. Policy D takes only the probability of receiving non-expedited transplants into account. Policy E aims to capture the combined effect of the random events taking place in the transplant center via average number of patients metric. Policy F has a similar motivation to Policy E. In addition to the available number of (i, j) patients, policy F also considers the probability of receiving a non-expedited transplant. Non-expedited transplant rate of each (i, j) pair combines the average number of (i, j) patients metric and the probability that an (i, j) patient receives a non-expedited transplant. Policy G considers the competition among (i, j) pairs for a non-expedited liver. It aims to capture the effect of the waiting list. Policy H calculates the benefit that would be obtained from allocating the expedited liver

to each patient. Then, it puts the patients in a descending order of this benefit. Policies I-N mimic the UNOS policy. First they order the patients according to MELD score. Each policy pair, i.e., I-J, K-L, M-N, takes a different perspective on the MELD score ordering. Then, the policies take blood type and the primary reason for transplantation, namely acute liver diseases and non-acute liver diseases, into account. Acute liver failure which has various etiologies, i.e., viral hepatitis, severe sepsis, etc., is a rare condition in which rapid deterioration of liver leads to symptoms such as alteration in the mental status of a previously healthy individual [75]. In Figure 9 and Figure 10, the distribution of primary diseases and the number of deaths observed for each primary disease over the time horizon (1999, 2008) are presented [76]. Because acute liver patients are more prone to death, we construct policies that consider those patients separately.

Primary Diagnosis		Year									
		1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Total	**Patients**	20,965	23,390	25,517	26,131	25,677	26,330	26,585	26,695	26,503	26,407
	Deaths	2,018	2,019	2,325	2,161	2,094	2,164	2,141	1,991	1,822	1,782
Non-Cholestatic Cirrhosis	**Patients**	13,232	14,898	16,320	16,497	16,125	16,753	17,110	17,250	17,273	17,394
	Deaths	1,307	1,355	1,552	1,356	1,327	1,419	1,439	1,296	1,221	1,188
	% of Deaths	10%	9%	10%	8%	8%	8%	8%	8%	7%	7%
Cholestatic Liver Disease/Cirrhosis	**Patients**	2,206	2,371	2,469	2,539	2,475	2,452	2,406	2,395	2,315	2,212
	Deaths	177	164	180	165	140	146	132	136	124	118
	% of Deaths	8%	7%	7%	6%	6%	6%	5%	6%	5%	5%
Acute Hepatic Necrosis	**Patients**	1,262	1,407	1,485	1,532	1,435	1,431	1,388	1,289	1,249	1,122
	Deaths	170	142	156	178	148	149	127	133	104	82
	% of Deaths	13%	10%	11%	12%	10%	10%	9%	10%	8%	7%
Biliary Atresia	**Patients**	539	562	612	629	603	598	591	550	552	538
	Deaths	22	23	33	23	16	11	18	20	14	16
	% of Deaths	4%	4%	5%	4%	3%	2%	3%	4%	3%	3%
Metabolic Diseases	**Patients**	443	473	509	498	479	475	505	498	454	483
	Deaths	33	34	28	40	38	44	36	38	29	33
	% of Deaths	7%	7%	6%	8%	8%	9%	7%	8%	6%	7%
Malignant Neoplasms	**Patients**	306	340	423	512	509	619	720	823	931	1,212
	Deaths	27	26	43	45	31	29	28	28	33	52
	% of Deaths	9%	8%	10%	9%	6%	5%	4%	3%	4%	4%
Other	**Patients**	2,338	2,695	3,054	3,270	3,445	3,435	3,311	3,378	3,244	3,010
	Deaths	215	233	282	301	334	319	305	290	256	249
	% of Deaths	9%	9%	9%	9%	10%	9%	9%	9%	8%	8%
Not Collected	**Patients**	58	54	50	46	40	39	38	34	34	33
	Deaths	3	4	4	1	1	1	1	-	1	1
	% of Deaths	5%	7%	8%	2%	3%	3%	3%	-	3%	3%
Unknown	**Patients**	581	590	595	608	566	528	516	478	451	403
	Deaths	64	38	47	52	59	46	55	50	40	43
	% of Deaths	11%	6%	8%	9%	10%	9%	11%	10%	9%	11%

Figure 9: Number of patients and deaths by primary disease.

Primary Diagnosis	Year									
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Non-Cholestatic Cirrhosis	69.90%	70.00%	69.80%	70.30%	71.10%	72.20%	71.90%	73.00%	72.80%	72.60%
Cholestatic Liver Disease/Cirrhosis	12.20%	11.60%	11.10%	11.30%	11.20%	10.70%	10.60%	10.50%	9.80%	9.60%
Acute Hepatic Necrosis	4.70%	5.10%	4.90%	4.80%	4.80%	4.30%	4.00%	3.80%	3.40%	2.90%
Biliary Atresia	2.20%	1.90%	1.90%	2.00%	1.70%	1.70%	1.70%	1.20%	1.20%	1.20%
Metabolic Diseases	2.00%	1.80%	1.90%	1.70%	1.40%	1.50%	1.70%	1.40%	1.40%	1.50%
Malignant Neoplasms	1.20%	1.30%	1.30%	1.10%	1.30%	1.40%	1.50%	1.70%	2.30%	3.00%
Other	7.60%	8.10%	8.90%	8.60%	8.50%	8.20%	8.60%	8.40%	9.00%	9.30%
Unknown	0.30%	0.20%	0.20%	0.10%	0.10%	0.10%	0.10%	0.00%	0.00%	0.00%

Figure 10: Distribution of primary disease.

We coded our simulation model SIM1 in Microsoft Visual Studio .NET 2008. We obtained the numerical results on Intel Core2 Duo PC with processors running at 3.00 GHz and 2 GB memory. The runtime for 5,000 replications is on average 801 CPU seconds. The shortest run time is 573 CPU seconds and the longest is 1052 CPU seconds. Policies which perform sorting more compared to other policies are the ones which last the longest.

4.5.2 Performance Metrics

We base our comparison of the policies on a set of performance metrics. Below is the list and the calculation methods of those metrics.

- Average transplant rate

$$= \frac{\text{total number of expedited and non-expedited transplants}}{\text{total number of days}}$$

- Percentage of patients died

$$= \frac{\text{total number of patients died}}{\text{total number of patients who died or received a transplant}}$$

- Survival after departure

$$= \frac{\text{sum of the expected lifetimes of patients after transplant}}{\text{total number of patients who died or received a transplant}}$$

- Waiting time before transplant

$$= \frac{\text{sum of the waiting times until transplant of patients who received a transplant}}{\text{total number of patients who received a transplant}}$$

- Waiting time before death

$$= \frac{\text{sum of the waiting times until death of patients who died while waiting on the list}}{\text{total number of patients who died while waiting for a transplant}}$$

- Total survival

$$= \frac{\text{sum of the total expected lifetimes of patients}}{\text{total number of patients who died or received a transplant}}$$

The metric average transplant rate reflects the business perspective of the transplant center. Moreover, as the transplant rate is being maximized, the waiting time of the patients listed at the center is expected to decrease. However, the outcome of these transplants is also important. Therefore, we investigate the number of patients dying, waiting times and survival. Survival after departure combines the outcomes, the number of patients dying and the expected post-transplant lifetime. Please note that the survival after departure for patients who die is zero. Therefore, the numerator of the survival after departure metric contains only the expected post-transplant lifetime of patients who receive transplant.

4.5.3 Comparison Methods

We utilize two methods to compare the performance of the policies listed in Section 4.5.1. The first is Hsu's multiple comparison with the best method [52, 53]. Given the performance metric of the policy i is denoted by μ_i, Hsu's method compares μ_i with $\max_{j \neq i} \mu_j$ for all $i \in \{1, 2, \ldots, k\}$ in a maximization problem and constructs k simultaneous $100(1-\alpha)\%$ confidence intervals for $\mu_i - \max_{j \neq i} \mu_j$ where α is the significance level. The method eliminates the policies which are worse than the best. It sets negative upper bounds and positive lower bounds to zero. A policy with a negative upper bound cannot be the best while a policy with a positive bound is declared to be the best. If there are multiple policies with positive lower bounds set to zero, then this set of policies includes the best policy with $100(1-\alpha)\%$ confidence.

The second method is the work of Nelson et al. [63]. The authors combine the subset selection with indifference zone selection. The subset selection is the first stage of ranking and selection procedures [44] and aims to eliminate the noncompetitive policies. The indifference zone selection's goal is to select the best subset of policies such that the difference between the performance of the policies in the best subset and that of the eliminated policies is not less than some specified parameter $\delta > 0$ [11]. Nelson et al. [63], in their method's first stage, take a sample of observations for each policy. Depending on the variance in the samples and the practically significant difference δ, the authors eliminate the noncompetitive policies. For the remaining policies, the second stage sample sizes are determined. Additional observations are taken and the competitive policy with the highest performance measure is chosen as the best policy.

Type I and type II error are the experimental errors that are linked to each other. If a statistical test is conservative, that is, the probability of type I error is small, then it is likely to lack the power, that is, it has high probability of type II error. Thus, there is a trade-off between obtaining one incorrect rejection of the null hypothesis out of all the comparisons and missing the true bests. Multiple comparison methods generally put an emphasis on the control of type I error, instead of type II error [85]. However, type II error can be controlled

by imposing prescribed confidence interval widths, which is used in the determination of the sample sizes.

4.5.4 Validation of Statistical Assumptions

We simulate each policy listed in Section 4.5.1. We replicate each policy 5,000 times which corresponds to 5,000 years. Before investigating the results, we evaluate the validity of the statistical assumptions. Figures 11-19 present various plots used to validate these assumptions.

The methods utilized to make the policy comparison assume that the performance metric Y_{ij}, i.e., i^{th} observation of policy j, are mutually independent and have normal distribution with variance σ^2. They model Y_{ij}'s as

$$Y_{ij} = \mu + \gamma_i + \epsilon_{ij},$$

where $\gamma + \tau_i$ is the mean of the performance metric of policy i and ϵ_{ij} is the normally distributed error term with mean zero and variance σ^2. Therefore, we have to examine the fit of the model, and the independence, equal variance and normality assumptions. Plots in Figures 11-16 provide proof of the validity of the first three assumptions for all the performance metrics. Figures 17-19 present the normality plots.

In Figures 11-16, z denotes the standardized residuals and "ypred" denotes the fitted values. In each figure, the plot at the top refers to the fit of the model. The one in the middle refers to the independence assumption. The plot at the bottom refers to the equal variance assumption. The random pattern in the plots is a proof of the validity of the assumptions. The models for all the metrics except waiting time before transplant and waiting time before death satisfy the assumptions. However, the plots for these two metrics do not contain a random pattern to satisfy the equality of variance assumption. In addition to the plots, the ratio of maximum sample variance to minimum sample variance, i.e., s^2_{max}/s^2_{min}, provides a way to check the equal variance assumption [27]. The ratio is expected to be less than 3. The sample variance ratio is 2.49 and 4.16 for the waiting time before transplant and waiting time before death metrics, respectively.

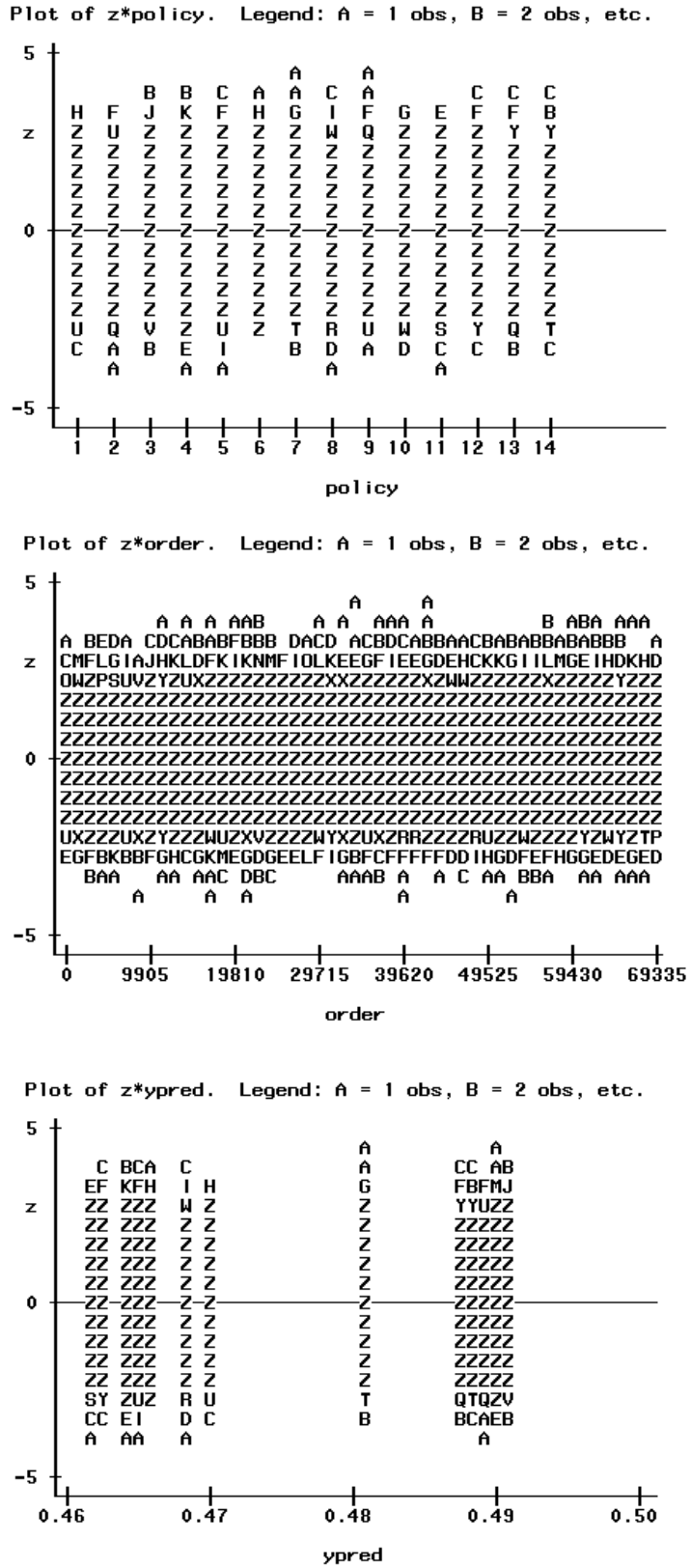


Figure 11: Plots for assumption validation for average transplant rate metric.

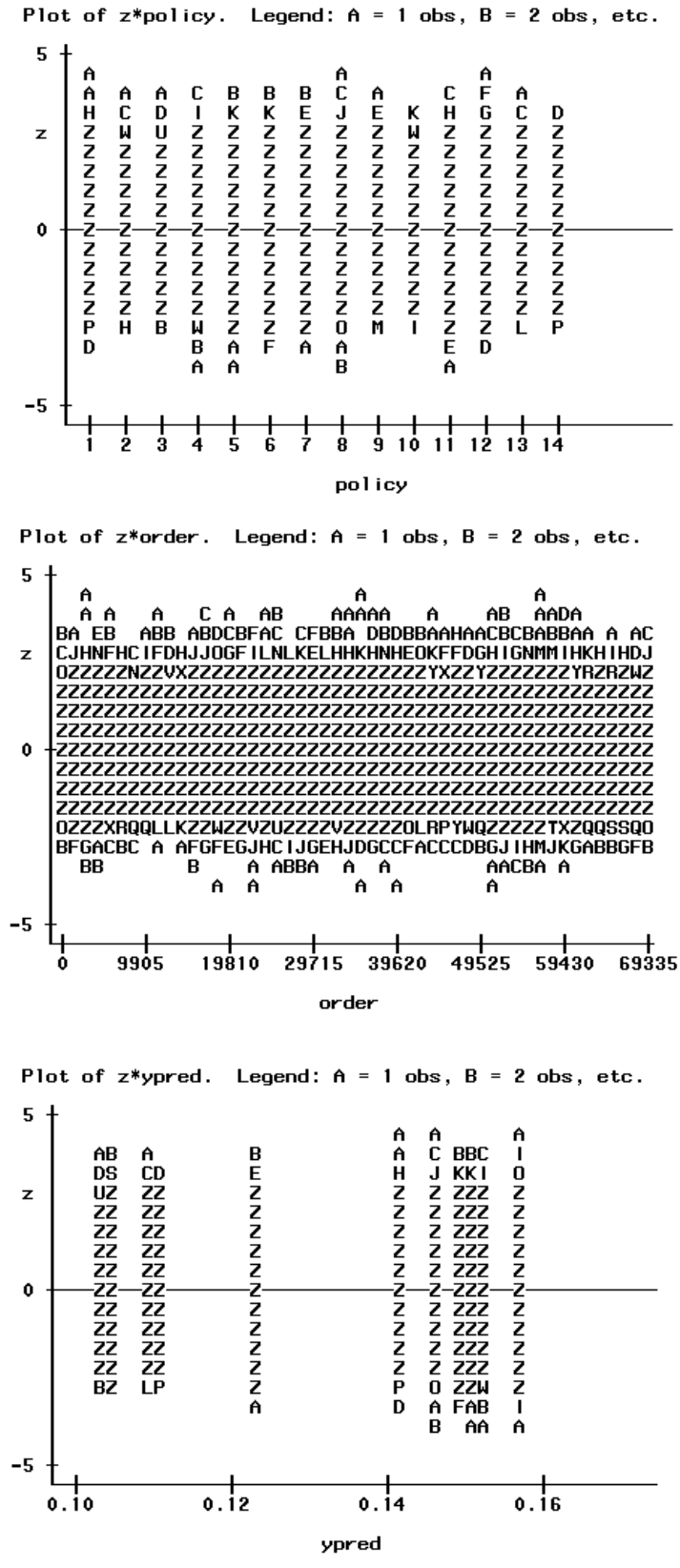


Figure 12: Plots for assumption validation for percentage of patients died metric.

Figures 17-19 provide the Anderson Darling Normality Test statistics and the corresponding p-values in addition to the normality plots. The Anderson Darling test is a valid test on normality; however, it is affected by the ties in the data. When there is significant amount of ties in the data, the Anderson Darling test rejects the data as non-normal regardless of how well the data fits the normal distribution. We have such a case in the plots of the average transplant rate and percentage of patients died. Due to the visual proof of the fit, we conclude that normality assumption is valid for these two metrics' models. The low Anderson Darling statistic values and high p-values of the survival after departure and total survival metrics provide sufficient proof for the validity of the normality assumption. We do not have sufficient proof for normality on the plots of waiting time before transplant and waiting time before death metrics. However, small deviations from normality is stated as not to badly affect the stated significance levels or confidence levels to be constructed [27].

When the equality of variance assumption fails to be satisfied, transformation of data is utilized. The data is transformed according to a function and then, if the transformed data satisfy the statistical assumptions, it is used for further analysis. We transform the data for the waiting time before transplant and waiting time before death metrics. We transform the data according to the function $h(y_{ij}) = y_{ij}^{1-(q/2)}$, where q is obtained via the following regression equation

$$\ln(s_i^2) = \ln(k) + q\ln(\bar{y}_{i\cdot}).$$

In the above equation, s_i^2 is the sample variance of the i^{th} policy, k is a constant and $\bar{y}_{i\cdot}$ is the mean of the performance metric for policy i. Figure 20 and Figure 21 present the plots for the first three model assumptions for the two metrics after transformation. The sample variance ratio for the waiting time before transplant metric becomes 1.09 and that for the waiting time before death metric becomes 1.23. Figure 22 provides the normality plots of the two metrics. Transformation improves our confidence on the normality assumption for both metrics. However, the waiting time before death metric still cannot provide sufficient proof for the validity of the normality assumption. Because small departures from normality do not have significant effect on the performance of the statistical tests, we assume the normality assumption is valid for the waiting time before death metric, as well.

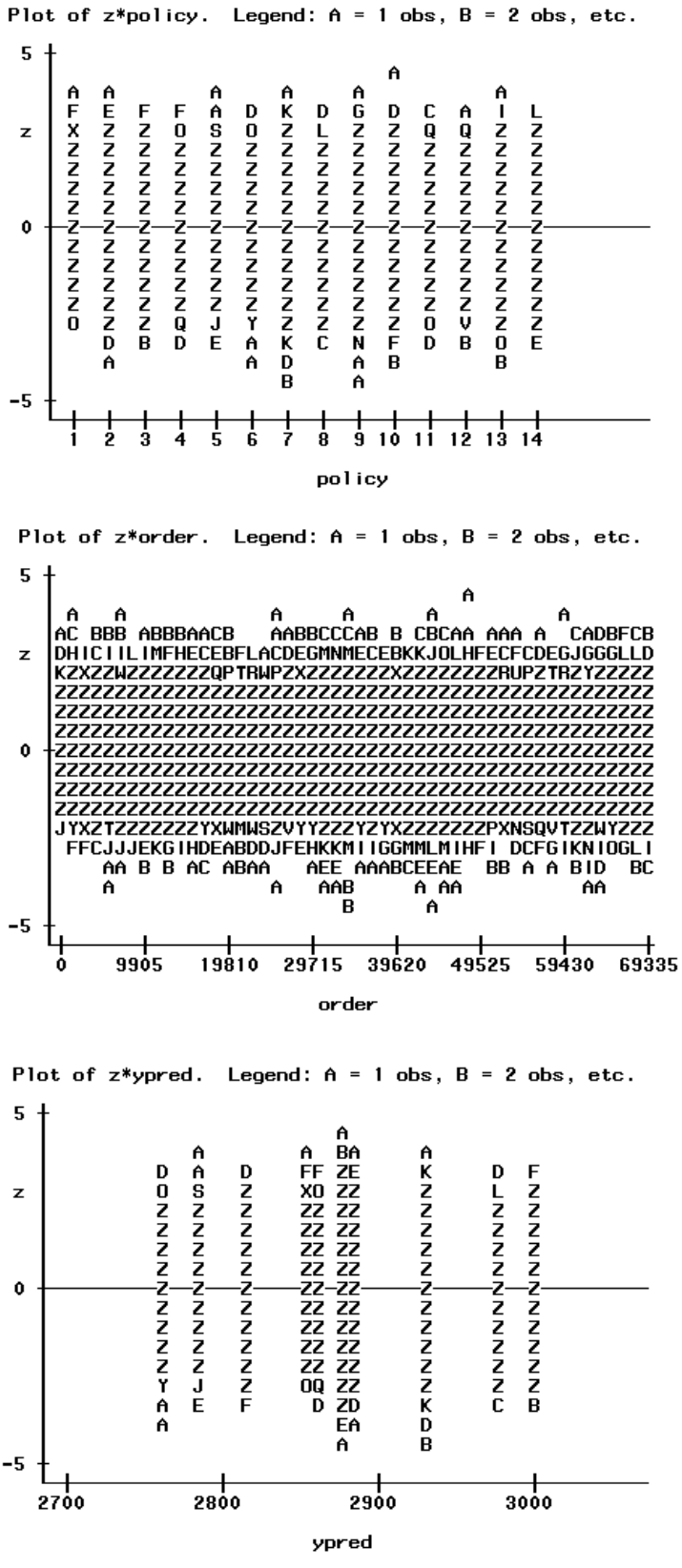
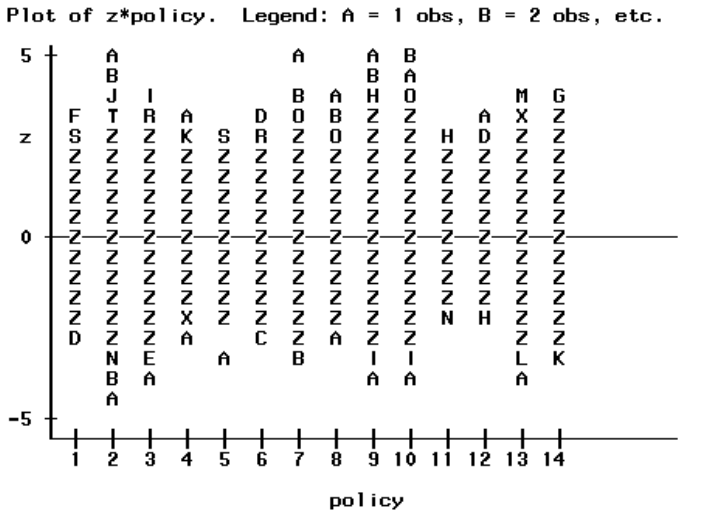
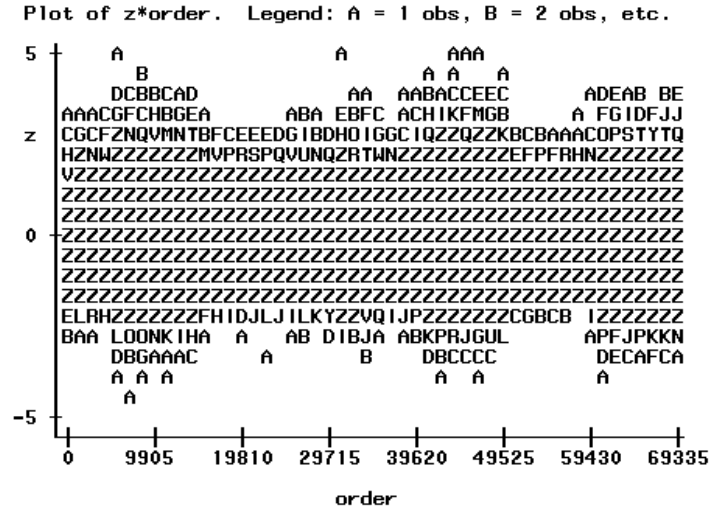


Figure 13: Plots for assumption validation for survival after departure metric.





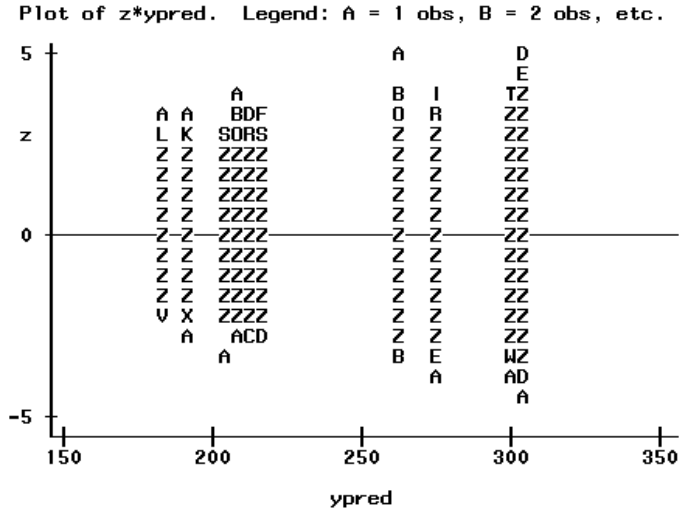


Figure 14: Plots for assumption validation for waiting time before transplant metric.

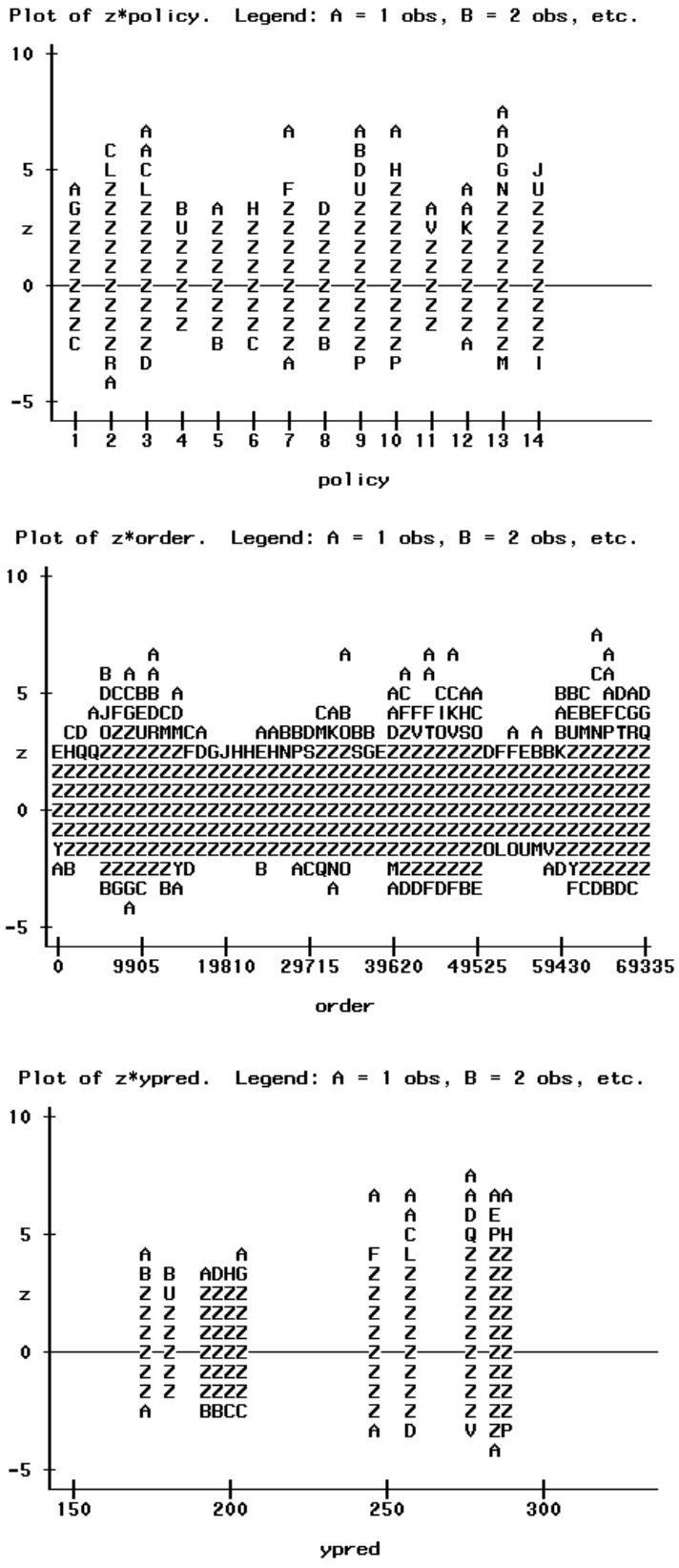


Figure 15: Plots for assumption validation for waiting time before death metric.

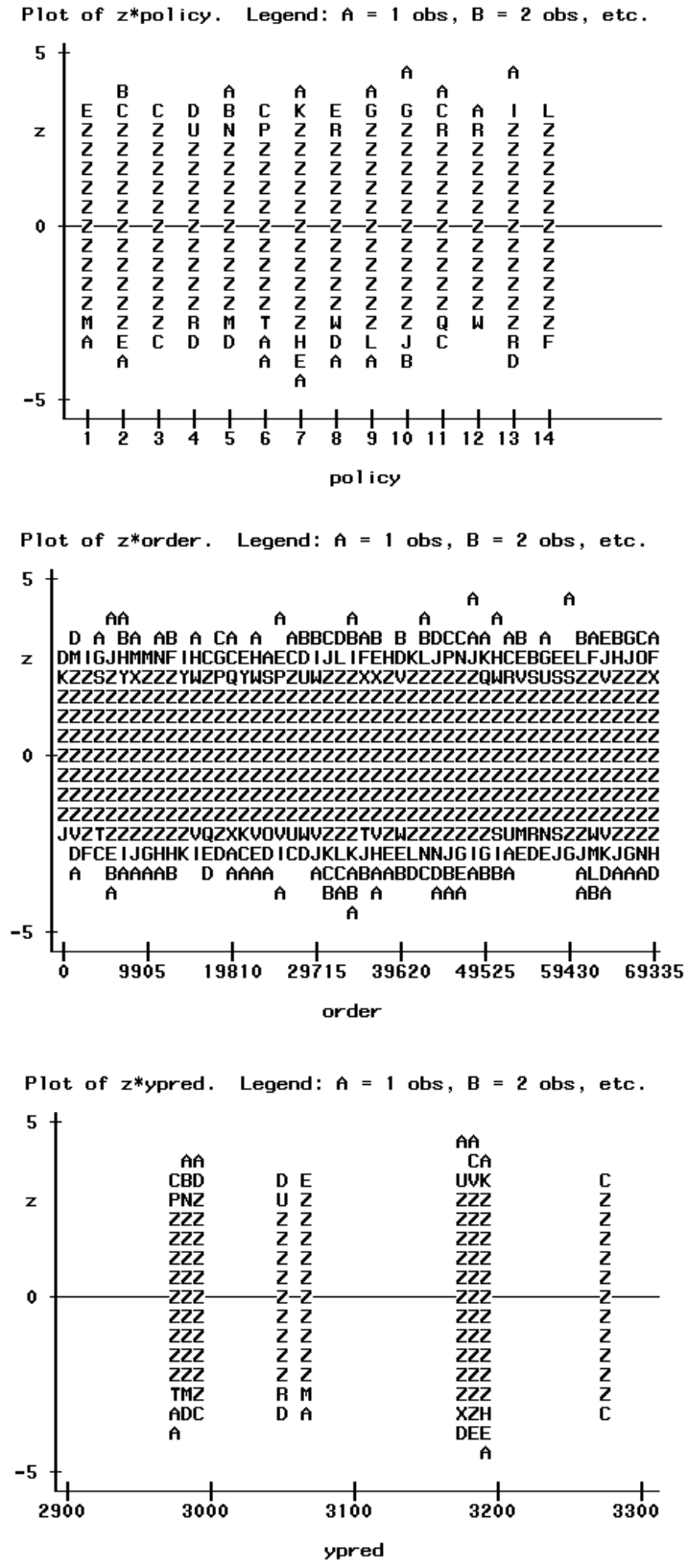


Figure 16: Plots for assumption validation for total survival metric.

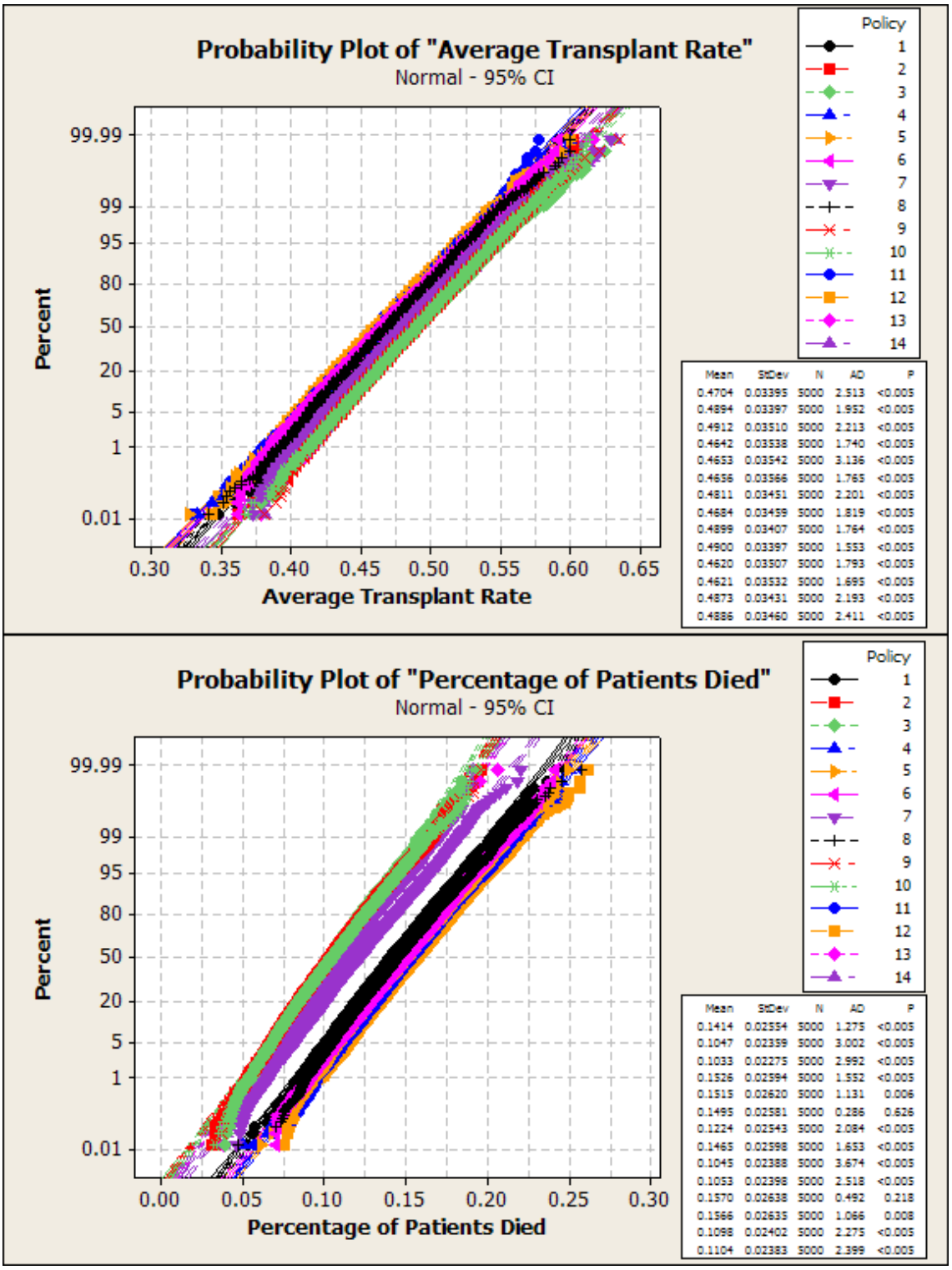


Figure 17: Probability plots for average transplant rate and percentage of patients died metrics.

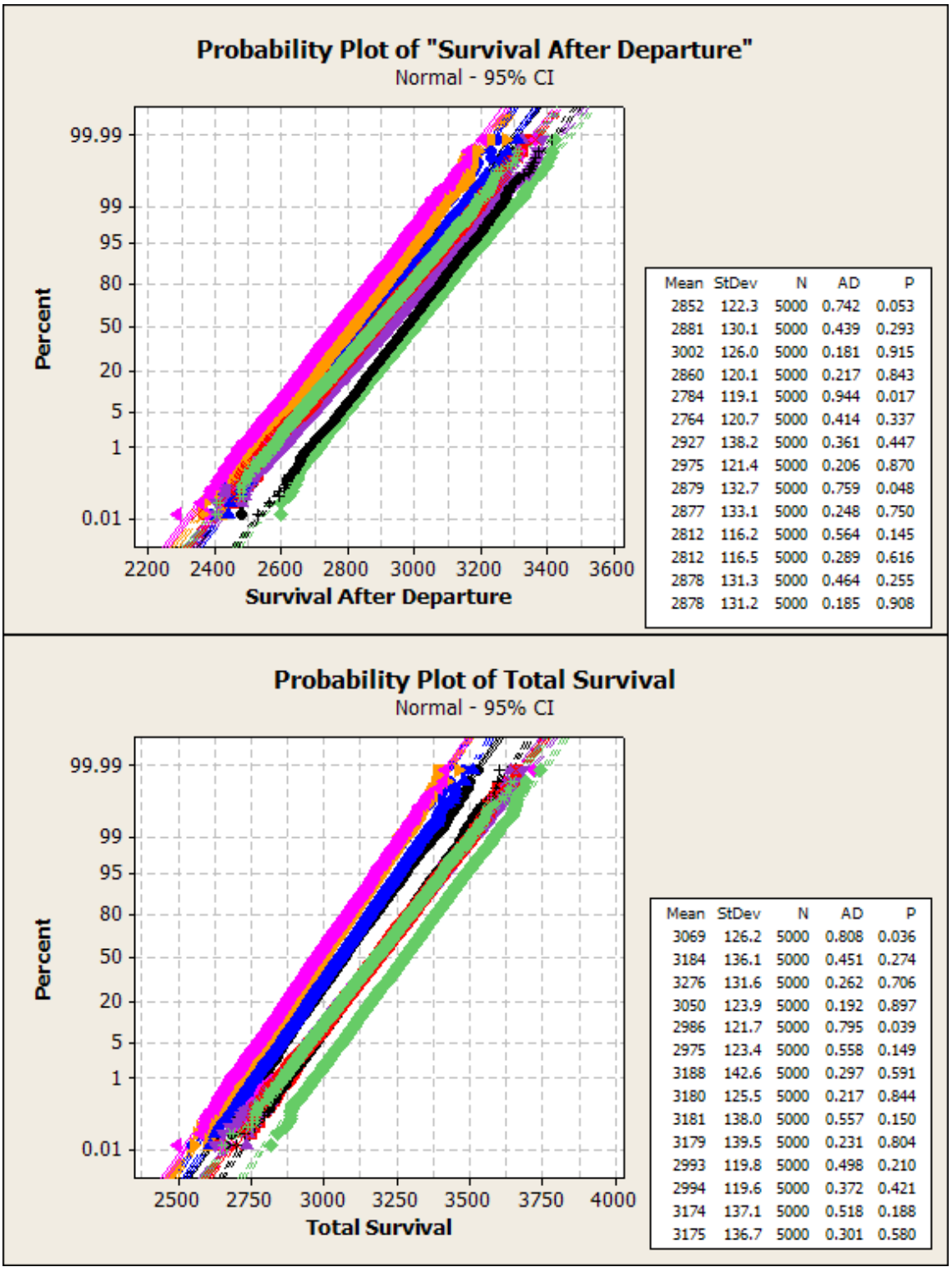


Figure 18: Probability plots for survival after departure and total survival metrics.

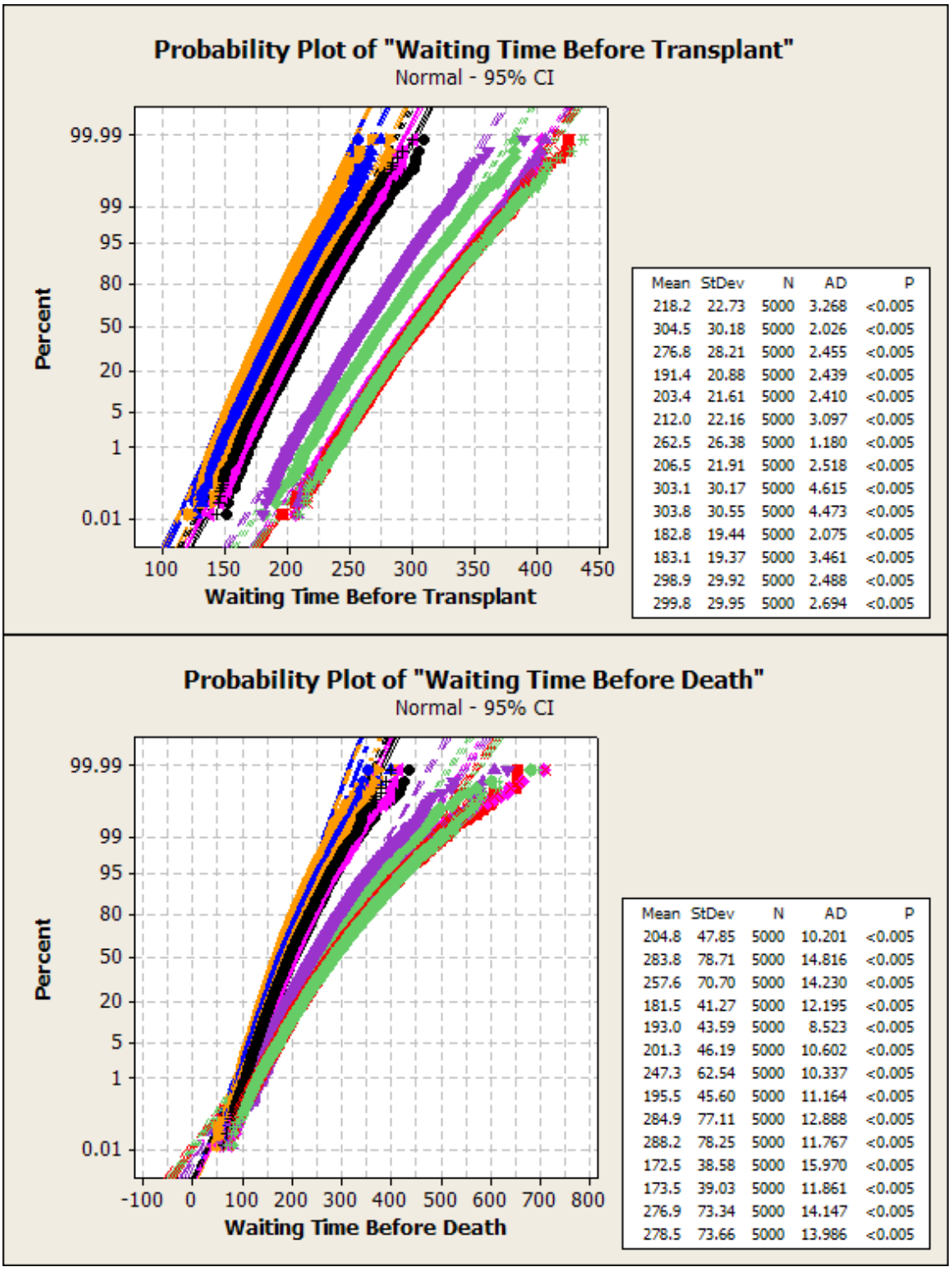


Figure 19: Probability plots for waiting time before transplant and waiting time before death metrics.

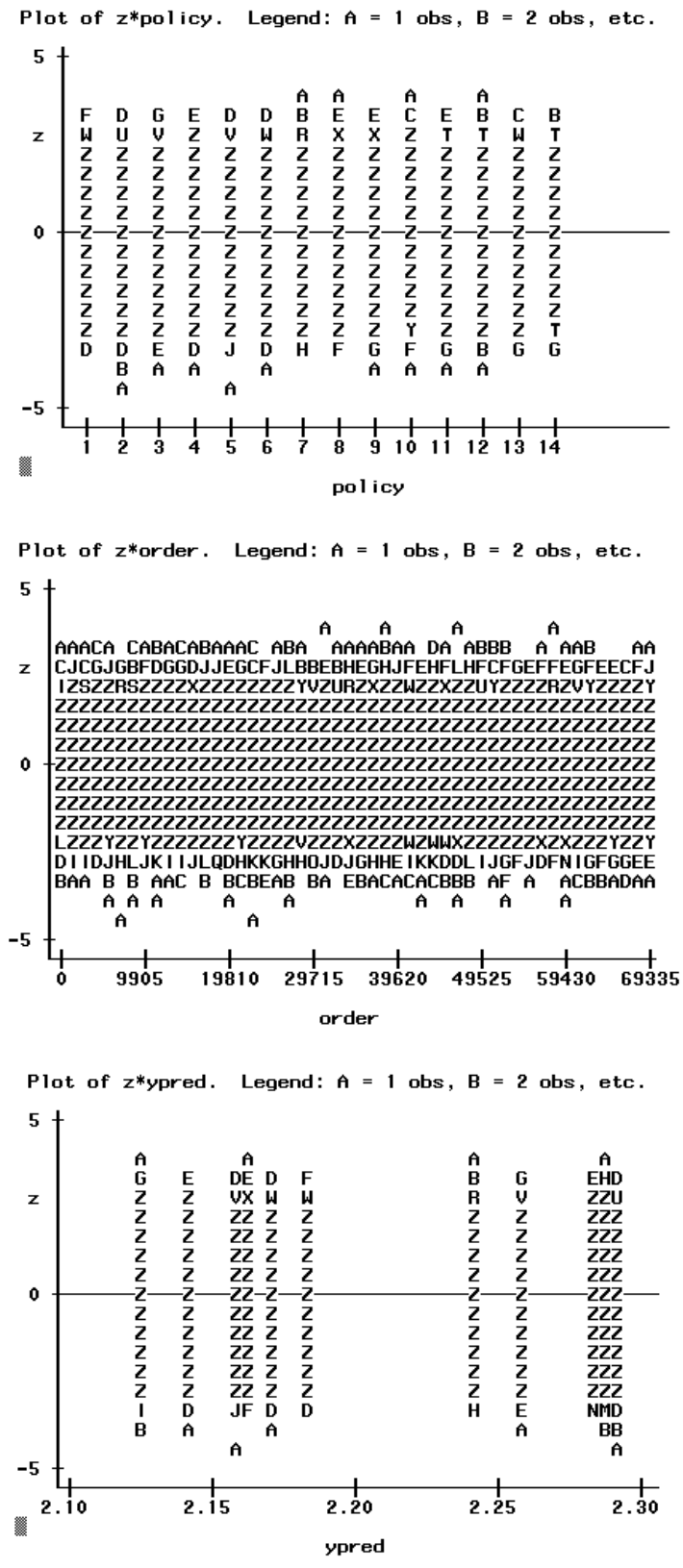


Figure 20: Plots for assumption validation for waiting time before transplant metric after transformation.

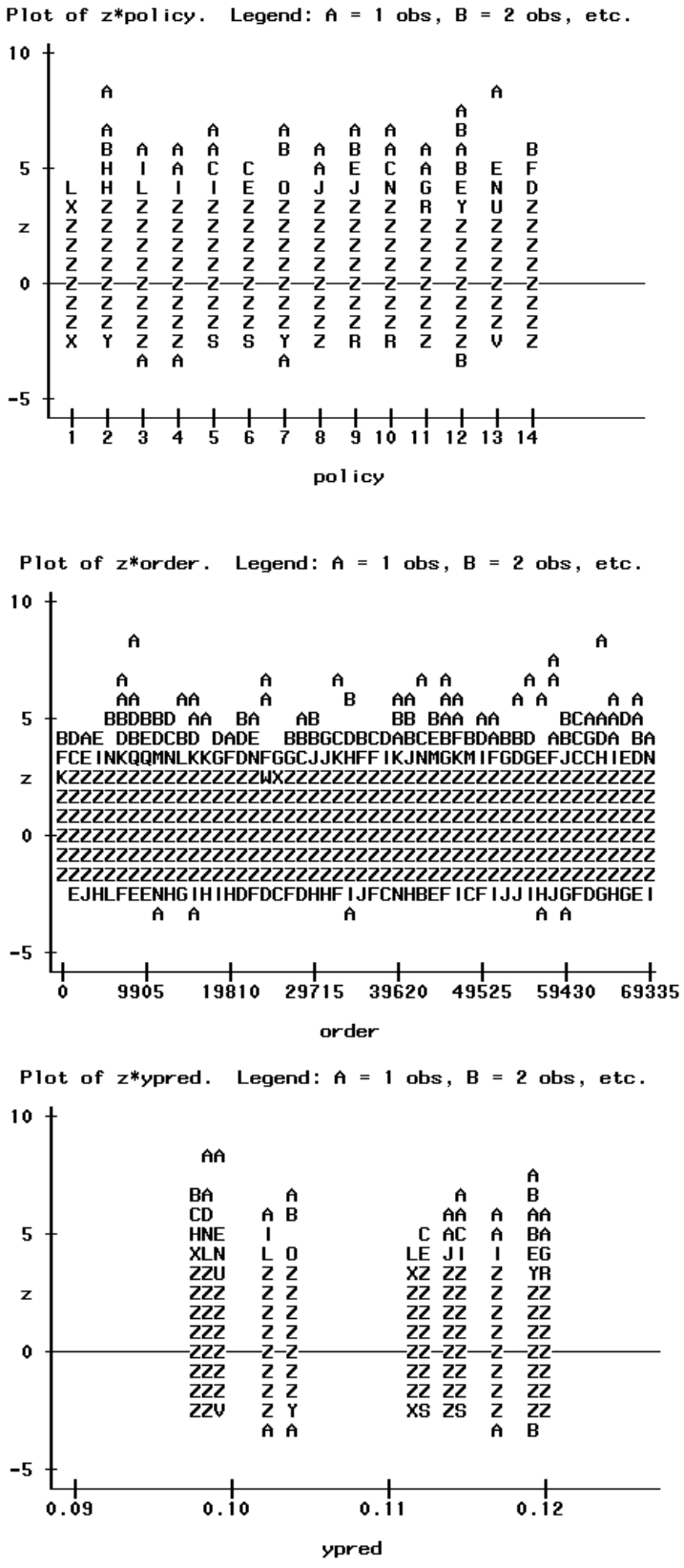


Figure 21: Plots for assumption validation for waiting time before death metric after transformation.

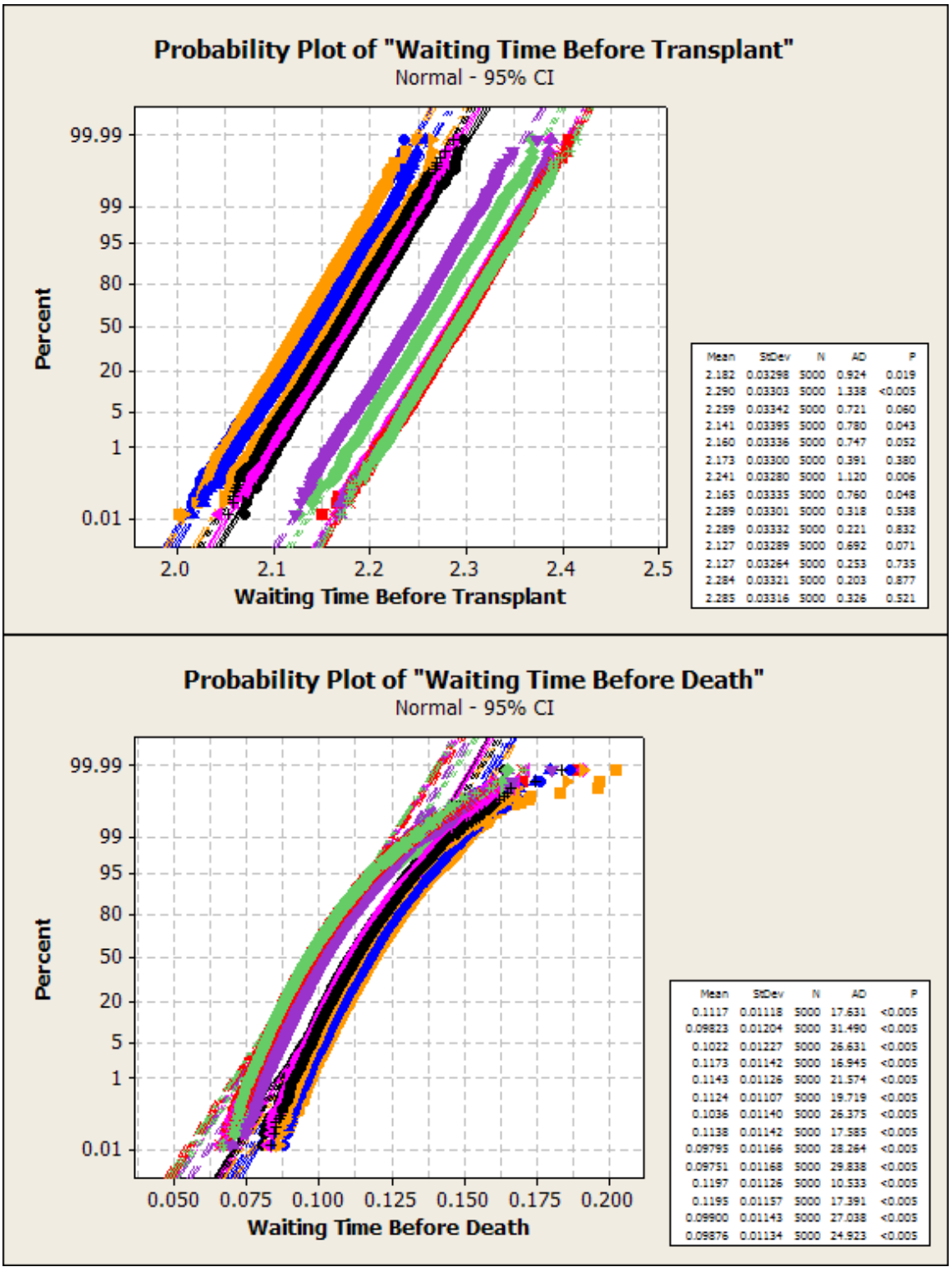


Figure 22: Probability plots for waiting time before transplant and waiting time before death metrics, after transformation.

4.5.5 Results

We compare the ten policies listed in Section 4.5.1 (Figure 8) using the methods of Hsu [52] and Nelson et al. [63]. We let the significance level be $\alpha = 0.05$. The results are presented in Figure 23 and Figure 24. The figures include the following information.

- Estimate - sample mean response of the policy
- Exact Estimate - sample mean response of the policy before data transformation (if any)
- StdErr - standard error of the sample mean for the policy
- cllo - lower bound of the confidence interval for the difference between the population mean of this policy and the best population mean
- clhi - upper bound of the confidence interval for the difference between the population mean of this policy and the best population mean
- rval - the smallest α level at which the population mean of this policy can be rejected as the best (generated for all groups but the one with the best sample mean)
- sval - the smallest α level at which the population mean of this policy can be selected as the best (generated for the policy with the best sample mean)

The highlighted policies on Figure 23 and Figure 24 are included in the best policy subsets chosen by Hsu's method. The best policy subsets are generated using Hsu's method. The policies whose policy number has a star next to it are the best policies chosen by Nelson et al. [63]'s method. The methods yield consistent results. That is, the best policy chosen by Nelson et al. [63]'s method is always included in the best policy subset chosen by Hsu's method.

Average Tx						
policy	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	0.4704	0.000491	-0.02255	0	0	.
B	0.4894	0.000491	-0.00352	0	0.04714	.
*C	0.4912	0.000491	-0.00061	0.002893	.	0.28167
D	0.4642	0.000491	-0.02869	0	0	.
E	0.4653	0.000491	-0.0276	0	0	.
F	0.4656	0.000491	-0.02733	0	0	.
G	0.4811	0.000491	-0.01181	0	0	.
H	0.4684	0.000491	-0.02447	0	0	.
I	0.4899	0.000491	-0.00303	0.000473	0.20539	.
J	0.49	0.000491	-0.00289	0.000613	0.28167	.
K	0.462	0.000491	-0.03091	0	0	.
L	0.4621	0.000491	-0.03076	0	0	.
M	0.4873	0.000491	-0.00565	0	0	.
N	0.4886	0.000491	-0.00428	0	0.00154	.

% of Patients Died						
policy	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	0.1414	0.000354	0	0.03935	0	.
B	0.1047	0.000354	0	0.002677	0.022392	.
*C	0.1033	0.000354	-0.00253	0	.	0.049581
D	0.1526	0.000354	0	0.050565	0	.
E	0.1515	0.000354	0	0.049519	0	.
F	0.1495	0.000354	0	0.047509	0	.
G	0.1224	0.000354	0	0.020338	0	.
H	0.1465	0.000354	0	0.044502	0	.
I	0.1045	0.000354	0	0.002527	0.049581	.
J	0.1053	0.000354	0	0.003235	0.000481	.
K	0.157	0.000354	0	0.055016	0	.
L	0.1566	0.000354	0	0.054598	0	.
M	0.1098	0.000354	0	0.007811	0	.
N	0.1104	0.000354	0	0.008377	0	.

Survival After Departure						
policy	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	2852.18	1.7794	-155.726	0	1.00E-12	.
B	2881.48	1.7794	-126.428	0	1.00E-12	.
*C	3001.55	1.7794	0	32.573	.	1.00E-12
D	2859.66	1.7794	-148.248	0	1.00E-12	.
E	2784.4	1.7794	-223.505	0	1.00E-12	.
F	2764.36	1.7794	-243.545	0	1.00E-12	.
G	2927.35	1.7794	-80.555	0	1.00E-12	.
H	2975.33	1.7794	-32.573	0	1.00E-12	.
I	2879.5	1.7794	-128.405	0	1.00E-12	.
J	2877.05	1.7794	-130.856	0	1.00E-12	.
K	2812.27	1.7794	-195.639	0	1.00E-12	.
L	2811.97	1.7794	-195.933	0	1.00E-12	.
M	2877.57	1.7794	-130.336	0	1.00E-12	.
N	2877.68	1.7794	-130.222	0	1.00E-12	.

Figure 23: Comparison of expedited liver allocation policies to identify the best one under various metrics.

Total Survival						
policy	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	3068.52	1.8435	-214.487	0	1.00E-12	.
B	3183.86	1.8435	-99.154	0	1.00E-12	.
*C	3276.43	1.8435	0	95.0237	.	1.00E-12
D	3049.55	1.8435	-233.457	0	1.00E-12	.
E	2986.26	1.8435	-296.75	0	1.00E-12	.
F	2974.75	1.8435	-308.259	0	1.00E-12	.
G	3187.99	1.8435	-95.024	0	1.00E-12	.
H	3180.26	1.8435	-102.749	0	1.00E-12	.
I	3180.79	1.8435	-102.217	0	1.00E-12	.
J	3179.31	1.8435	-103.698	0	1.00E-12	.
K	2993.45	1.8435	-289.557	0	1.00E-12	.
L	2993.56	1.8435	-289.446	0	1.00E-12	.
M	3174.07	1.8435	-108.942	0	1.00E-12	.
N	3175.13	1.8435	-107.88	0	1.00E-12	.

Waiting Time Before Transplant							
policy	**Exact Estimate**	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	218.21	2.182	0.000469	0	0.05707	0	.
B	304.54	2.2901	0.000469	0	0.16525	0	.
C	276.83	2.2586	0.000469	0	0.13372	0	.
D	191.39	2.1407	0.000469	0	0.01582	0	.
E	203.4	2.1598	0.000469	0	0.03487	0	.
F	211.99	2.1728	0.000469	0	0.04792	0	.
G	262.5	2.2413	0.000469	0	0.11641	0	.
H	206.52	2.1645	0.000469	0	0.03966	0	.
I	303.11	2.2886	0.000469	0	0.16369	0	.
J	303.83	2.2893	0.000469	0	0.16445	0	.
*K	182.79	2.1266	0.000469	-0.00218	0.00117	.	0.69368
L	183.08	2.1271	0.000469	-0.00117	0.00218	0.69368	.
M	298.86	2.2839	0.000469	0	0.15898	0	.
N	299.8	2.2849	0.000469	0	0.16003	0	.

Waiting Time Before Death							
policy	**Exact Estimate**	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	204.82	0.1117	0.000163	-0.00864	0	0	.
B	283.79	0.09823	0.000163	-0.02207	0	0	.
C	257.63	0.1022	0.000163	-0.01811	0	0	.
D	181.51	0.1173	0.000163	-0.003	0	0	.
E	193.05	0.1143	0.000163	-0.00595	0	0	.
F	201.32	0.1124	0.000163	-0.0079	0	0	.
G	247.34	0.1036	0.000163	-0.01673	0	0	.
H	195.51	0.1138	0.000163	-0.00646	0	0	.
I	284.94	0.09795	0.000163	-0.02235	0	0	.
J	288.22	0.09751	0.000163	-0.02279	0	0	.
*K	172.47	0.1197	0.000163	-0.00034	0.000818	.	0.57057
L	173.5	0.1195	0.000163	-0.00082	0.000344	0.57057	.
M	276.92	0.099	0.000163	-0.0213	0	0	.
N	278.49	0.09876	0.000163	-0.02154	0	0	.

Figure 24: Comparison of expedited liver allocation policies to identify the best one under various metrics.

Policy C is found to be the best policy under almost all metrics we consider. Policy C results in the highest average transplant rate while yielding the best outcome for the patient population. It saves as much as life possible, i.e., best policy in terms of minimizing the percentage of patients died, while balancing the pre- and post-transplant expected lifetime.

In the policy comparison, for the survival metrics we let the practically significant difference δ be 30 days. Given $\delta = 30$, Policy C dominates all other policies in terms of the survival times. Policy C results in 4% and 3% increase in the survival after departure and total survival metrics, respectively, compared to Policy B, i.e., the UNOS policy. Policy C leads to 3,002 expected lifedays after departure and 3,276 total expected lifedays while Policy B results in 2,882 expected lifedays after departure and 3,184 total expected lifedays. Moreover, policy C brings in a 1.3% decrease in the percentage of patients died while increasing the average transplant rate by 0.4% compared to Policy B.

Two policies other than Policy C are also found to be competitive under the average transplant rate metric. These are the versions of UNOS non-expedited liver allocation policies, Policy I and J. The difference between Policies I-J and the UNOS policy is that Policies I and J group patients according to their primary reason for transplant, namely acute patients versus non-acute patients. Notably, independent of which group of patients have the highest priority we obtain a better performance than that of UNOS policy, i.e., Policy B.

Policy J performs better than all the other policies under the waiting time before death metric. Policy J gives higher priority to acute liver disease patients with the highest MELD scores. Acute liver disease patients are the ones whose health progresses severely. Acute liver disease patients with high MELD scores are the patients whose probability of death is the highest. By favoring these patients, Policy J decreases the death rate among them. Thus, we obtain longer waiting times before death.

The policy found to be the best under the consideration of waiting time before transplant metric is different than the best policies under the consideration of the other metrics. This is due to the fact that the population which is addressed under this metric is just a portion of the overall liver patient population at the transplant center. The policy chosen to be the best, i.e., Policy K, gives higher priority to the healthiest patients, i.e., lowest MELD scores. The UNOS non-expedited liver allocation policy results in patients with lower MELD scores

wait until their health status become worse enough to receive a non-expedited transplant. Policy K removes these patients via expedited transplants from the system. Thus, it leads to a decrease in the waiting time before transplant.

In the light of the above discussion, the ultimate goal of the transplant center coordinator, i.e., the well-being of the patients and high transplant rate at the center, leads to the Policy C to be chosen to implement. Policy C considers the balance between the probability of receiving a non-expedited transplant and that of dying. While doing so, it prevents patients from dying. Moreover, it assigns organs to patients from whom the best outcome would be obtained.

Policy C gives higher priorities to non-acute liver patients with the highest MELD scores. In Figure 25, the priorities given to (i, j) pairs are presented. To differentiate the patient types, we also include the disease group of each patient type on Figure 25. Please refer to Table 4 for patient type definitions and to Section 4.3.2 for disease group definitions. For ease of search, the first 100 (i, j) pairs with the highest priority are highlighted with four different shades of grey in Figure 25. The darker the highlight, the higher the priority. We have only one highlighted (i, j) pair from patient type group including acute liver patients (disease group 3), i.e., pair $(27, 18)$. This is due to the their high likelihood of receiving non-expedited transplants. Even though acute liver patients are more prone to death, they also have high probability of receiving non-expedited transplants. In the simulation, we observe that Policy C assigns expedited livers mostly to patients with the lowest MELD scores (above the optimal control limits) and non-acute liver diseases. In Figure 26, the fraction of expedited livers assigned to each (i, j) pair is presented. We calculate these probabilities by taking the ratio of the number of expedited transplants that an (i, j) pair receives to the total number of expedited transplants. For ease of search, the first 100 (i, j) pairs with the highest values are highlighted. Four shades of grey are used. The darker the highlight, the higher the value. The reason of having higher values on lower MELD scores is that we generally do not observe many patients with high MELD scores. Even though the policy gives higher priorities to patients with high MELD scores, because there is generally no such patient to accept the offer, patients with lower MELD scores receive expedited liver transplants. Although the order of the MELD scores getting higher priorities changes, the

order of the disease groups stays the same. The sum of the probabilities of (i, j) pairs including acute liver patients (disease group 3) is 0.0016 and the sum of the probabilities of (i, j) pairs including non-acute liver patients with hepatitis (disease group 2) is 0.0476 while the sum is equal to 0.951 for (i, j) pairs including the rest of the non-acute liver patients (disease group 1).

Type\MELD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	disease group
1	169	166	150	147	149	138	122	113	101	80	63	49	41	47	45	14	7	26	1
2	246	231	209	173	154	135	121	114	108	86	78	67	43	21	18	15	8	25	1
3	212	204	197	195	162	153	136	123	116	97	83	70	54	53	51	52	40	32	1
4	225	230	227	213	206	181	158	140	137	118	89	61	42	30	19	13	11	5	1
5	279	293	283	271	270	257	249	220	178	160	152	126	98	71	88	117	73	91	1
6	350	364	335	331	319	323	311	278	284	229	156	104	58	31	23	4	3	1	1
7	372	389	360	343	348	336	302	264	223	185	141	100	65	37	33	16	20	17	1
8	402	423	392	378	370	345	287	239	219	217	194	145	107	60	28	10	12	2	1
9	411	429	408	410	387	369	358	338	299	267	179	110	75	44	24	29	50	27	1
10	441	466	445	427	436	416	394	346	301	263	236	207	203	111	151	103	69	85	1
11	453	478	459	440	448	442	403	354	291	256	182	119	96	56	79	131	62	90	1
12	451	487	468	458	464	430	412	320	273	210	159	134	109	64	59	68	34	6	1
13	479	542	498	493	484	465	415	321	251	234	167	144	95	74	87	76	82	36	1
14	471	533	500	491	497	457	409	332	298	241	180	142	120	105	128	208	81	46	1
15	496	550	501	492	470	438	385	326	266	238	228	196	106	92	77	55	39	9	2
16	490	509	510	541	506	477	456	418	390	368	308	265	216	193	254	143	94	48	2
17	504	520	523	548	517	499	417	396	349	339	328	337	242	187	146	112	132	72	2
18	521	516	515	514	483	454	388	355	310	288	281	245	215	252	202	133	125	93	2
19	507	476	352	334	312	276	253	235	226	214	201	139	115	124	155	157	102	22	2
20	357	367	365	361	351	333	307	286	295	261	218	176	164	84	57	38	35	66	2
21	524	529	526	552	532	519	475	428	450	391	314	255	184	170	199	189	258	172	2
22	522	528	462	488	480	512	467	434	375	363	382	243	177	168	174	163	175	232	2
23	472	489	531	551	544	536	482	481	455	452	399	381	274	282	306	248	221	148	2
24	505	474	503	556	546	534	485	461	406	384	272	250	205	200	233	297	316	277	2
25	525	511	538	557	527	535	473	447	431	469	380	342	260	300	393	285	268	222	2
26	508	547	540	539	486	432	359	327	322	374	240	198	171	165	190	289	192	191	3
27	566	559	554	530	495	424	377	449	341	362	309	315	275	292	237	400	183	99	3
28	574	570	564	549	513	460	437	421	329	325	304	395	317	366	433	518	211	130	3
29	575	571	568	560	553	537	463	435	356	330	318	305	303	290	262	247	224	161	3
30	572	563	562	545	502	425	371	407	294	340	444	405	419	439	376	280	324	129	3
31	576	569	567	558	543	443	401	404	296	347	398	414	426	386	244	269	188	127	3
32	573	565	561	555	494	446	413	422	373	379	344	397	420	383	313	259	353	186	3

Figure 25: Priorities assigned to (i, j) pairs by Policy C.

Because the allocation rules specified by Policy C depend on patient types and MELD scores, the implementation of Policy C requires the assignment of patient types to patients listed at the center. We suggest the transplant center coordinator assigns a patient type to each patient on her list using the scheme we describe in Section 4.2 and 4.3.2 and bases her decision on the priorities of the patient type-MELD score pairs specified by Policy C.

Type\MELD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	0	0	0	0.045136	0.015840	0.014136	0.030547	0.052041	0.027883	0.020882	0.009128	0.006418	0.006516	0.001524	0.001851	0.003525	0.003352	0.003513
2	0	0	0	0.026638	0.021407	0.026654	0.026099	0.033420	0.025493	0.017700	0.009084	0.009155	0.006276	0.001728	0.001929	0.001230	0.001512	0.001253
3	0	0	0	0.022746	0.022157	0.015383	0.021733	0.015683	0.019451	0.015981	0.010260	0.006608	0.005821	0.001916	0.001105	0.001059	0.002285	0.003401
4	0	0	0	0.020834	0.035202	0.029104	0.029129	0.034980	0.023517	0.025688	0.019765	0.012553	0.011901	0.005718	0.007789	0.007977	0.007448	0.013551
5	0	0	0	0	0.000503	0.000523	0.000333	0.000153	0.000404	0.000313	0.000166	0.000294	0.001128	0.000286	0.000125	0.000035	0.000042	0.000012
6	0	0	0	0	0.000118	0.000056	0.000022	0.000019	0.000013	0.000071	0.000188	0.000248	0.000142	0.000054	0.000082	0.000295	0.001243	0.000349
7	0	0	0	0	0.000478	0.000332	0.000401	0.000102	0.000029	0.000025	0.000045	0.000057	0.000083	0.000032	0.000158	0.001085	0.000276	0.000092
8	0	0	0	0	0.000050	0.000095	0.000508	0.000501	0.000350	0.000265	0.000335	0.000513	0.001591	0.000511	0.000580	0.002444	0.000876	0.001476
9	0	0	0	0	0.000344	0.000189	0.000304	0.000091	0.000031	0.000029	0.000247	0.001503	0.002108	0.001271	0.001068	0.002838	0.001595	0.001572
10	0	0	0	0	0.000116	0.000037	0.000014	0.000018	0.000033	0.000061	0.000019	0.000011	0.000008	0.000076	0.000051	0.000847	0.001228	0.000982
11	0	0	0	0	0	0.000055	0.000374	0.000093	0.000018	0.000011	0.000009	0.000016	0.000007	0.000004	0.000001	0.000001	0	0
12	0	0	0	0	0	0.000002	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0.000043	0.000015	0.000124	0.000068	0.000130	0.000216	0.000453	0.001003	0.001023	0.001083	0.001320	0.000405	0.001110
14	0	0	0	0	0	0	0	0	0	0	0	0.000002	0.000224	0.000116	0.000012	0	0.000021	0.000009
15	0	0	0	0	0	0	0	0.000003	0.000006	0.000013	0.000029	0.000035	0.000497	0.000756	0.001062	0.000477	0.000158	0.000052
16	0	0	0	0	0	0	0	0	0.000003	0.000001	0.000005	0.000004	0.000001	0.000002	0.000001	0.000035	0.000616	0.000335
17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0.000318	0.000150	0.000086	0.000067	0.000015	0.000035	0.000084	0.000088	0.000933
19	0	0	0	0	0	0	0	0	0	0	0.001513	0.002761	0.003415	0.000758	0.000193	0.000287	0.002014	0.002397
20	0	0	0	0	0	0	0	0	0	0	0.001290	0.002343	0.001057	0.006236	0.004895	0.003550	0.003726	0.007304
21	0	0	0	0	0	0	0	0	0	0	0.000041	0.000015	0.000033	0.000040	0.000033	0.000130	0.000032	0.000021
22	0	0	0	0	0	0	0	0	0	0	0.000044	0.000040	0.000048	0.000020	0.000014	0.000006	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0.000047	0.000023	0.000009	0.000015	0.000032	0.000006	0.000001
25	0	0	0	0	0	0	0	0	0	0	0	0.000001	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0.000082	0.000098	0.000074	0.000117	0.000010	0.000012	0.000006
27	0	0	0	0	0	0	0.000023	0.000012	0.000021	0.000012	0.000023	0.000019	0.000044	0.000012	0.000007	0.000002	0.000010	0.000375
28	0	0	0	0	0	0	0.000002	0.000001	0.000001	0.000007	0.000011	0.000001	0.000011	0.000002	0	0	0.000004	0.000191
29	0	0	0	0	0	0	0.000024	0.000078	0.000027	0.000073	0.000081	0.000038	0.000069	0.000055	0.000033	0.000011	0.000017	0.000145
30	0	0	0	0	0	0	0.000010	0.000006	0.000031	0.000013	0.000001	0.000003	0	0.000001	0	0	0	0
31	0	0	0	0	0	0	0	0	0.000002	0.000001	0	0.000005	0.000002	0	0.000001	0.000001	0	0
32	0	0	0	0	0	0	0	0	0.000001	0	0.000001	0.000004	0.000006	0.000001	0.000011	0.000001	0	0.000003

Figure 26: The fraction of expedited livers assigned to each (i, j) pair.

In addition to seeking for the best expedited liver allocation policy, we also look for the allocation policies which should be avoided. We repeat our policy comparison, but this time we take the inverse of our objectives. That is, if we have been maximizing a metric beforehand, we make a policy comparison in which we minimize the metric. We present the results in Figure 27 and Figure 28. The results of the comparison under the average transplant rate and percentage of patients died metrics indicate that priority on receiving expedited livers shouldn't be given to the healthiest patients. Given that UNOS gives higher priority to the sickest patients in the non-expedited liver allocation, following the opposite strategy to UNOS's non-expedited liver allocation policy in the expedited liver allocation not only decreases the average transplant rate at the center, but also increases the death rate.

Average Tx						
policy	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	0.4704	0.000491	0	0.010112	0	.
B	0.4894	0.000491	0	0.029137	0	.
C	0.4912	0.000491	0	0.030906	0	.
D	0.4642	0.000491	0	0.003969	0.00748	.
E	0.4653	0.000491	0	0.005061	0.00001	.
F	0.4656	0.000491	0	0.005327	0	.
G	0.4811	0.000491	0	0.020845	0	.
H	0.4684	0.000491	0	0.008185	0	.
I	0.4899	0.000491	0	0.029627	0	.
J	0.49	0.000491	0	0.029766	0	.
*K	0.462	0.000491	-0.0019	0.001609	.	0.88584
L	0.4621	0.000491	-0.00161	0.001896	0.88584	.
M	0.4873	0.000491	0	0.027014	0	.
N	0.4886	0.000491	0	0.028376	0	.

% of Patients Died						
policy	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	0.1414	0.000354	-0.01693	0	0	.
B	0.1047	0.000354	-0.0536	0	0	.
C	0.1033	0.000354	-0.05502	0	0	.
D	0.1526	0.000354	-0.00571	0	0	.
E	0.1515	0.000354	-0.00676	0	0	.
F	0.1495	0.000354	-0.00877	0	0	.
G	0.1224	0.000354	-0.03594	0	0	.
H	0.1465	0.000354	-0.01178	0	0	.
I	0.1045	0.000354	-0.05375	0	0	.
J	0.1053	0.000354	-0.05304	0	0	.
*K	0.157	0.000354	-0.00085	0.00168	.	0.66258
L	0.1566	0.000354	-0.00168	0.000845	0.66258	.
M	0.1098	0.000354	-0.04847	0	0	.
N	0.1104	0.000354	-0.0479	0	0	.

Survival After Departure						
policy	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	2852.18	1.7794	0	94.173	1.00E-12	.
B	2881.48	1.7794	0	123.471	1.00E-12	.
C	3001.55	1.7794	0	243.545	1.00E-12	.
D	2859.66	1.7794	0	101.651	1.00E-12	.
E	2784.4	1.7794	0	26.394	1.00E-12	.
*F	2764.36	1.7794	-26.3939	0	.	1.00E-12
G	2927.35	1.7794	0	169.344	1.00E-12	.
H	2975.33	1.7794	0	217.326	1.00E-12	.
I	2879.5	1.7794	0	121.494	1.00E-12	.
J	2877.05	1.7794	0	119.043	1.00E-12	.
K	2812.27	1.7794	0	54.26	1.00E-12	.
L	2811.97	1.7794	0	53.966	1.00E-12	.
M	2877.57	1.7794	0	119.563	1.00E-12	.
N	2877.68	1.7794	0	119.677	1.00E-12	.

Figure 27: Comparison of expedited liver allocation policies to identify the worst one under various metrics.

Total Survival						
policy	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	3068.52	1.8435	0	100.354	1.00E-12	.
B	3183.86	1.8435	0	215.687	1.00E-12	.
C	3276.43	1.8435	0	308.259	1.00E-12	.
D	3049.55	1.8435	0	81.384	1.00E-12	.
E	2986.26	1.8435	0	18.092	6.33E-05	.
F	*2974.75	1.8435	-18.0915	0	.	6.33E-05
G	3187.99	1.8435	0	219.817	1.00E-12	.
H	3180.26	1.8435	0	212.092	1.00E-12	.
I	3180.79	1.8435	0	212.624	1.00E-12	.
J	3179.31	1.8435	0	211.143	1.00E-12	.
K	2993.45	1.8435	0	25.284	1.00E-12	.
L	2993.56	1.8435	0	25.395	1.00E-12	.
M	3174.07	1.8435	0	205.899	1.00E-12	.
N	3175.13	1.8435	0	206.961	1.00E-12	.

Waiting Time Before Transplant							
policy	**Exact Estimate**	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	218.21	2.182	0.000469	-0.10986	0	0.00E+00	.
*B	304.54	2.2901	0.000469	-0.00087	0.002481	.	0.47782
C	276.83	2.2586	0.000469	-0.03321	0	0.00E+00	.
D	191.39	2.1407	0.000469	-0.15111	0	0.00E+00	.
E	203.4	2.1598	0.000469	-0.13206	0	0	.
F	211.99	2.1728	0.000469	-0.11901	0	0	.
G	262.5	2.2413	0.000469	-0.05052	0	0.00E+00	.
H	206.52	2.1645	0.000469	-0.12727	0	0.00E+00	.
I	303.11	2.2886	0.000469	-0.00324	0.000112	7.45E-02	.
J	303.83	2.2893	0.000469	-0.00248	0.000867	4.78E-01	.
K	182.79	2.1266	0.000469	-0.16525	0	0.00E+00	.
L	183.08	2.1271	0.000469	-0.16475	0	0.00E+00	.
M	298.86	2.2839	0.000469	-0.00795	0	0.00E+00	.
N	299.8	2.2849	0.000469	-0.0069	0	0.00E+00	.

Waiting Time Before Death							
policy	**Exact Estimate**	**Estimate**	**StdErr**	**cllo**	**clhi**	**rval**	**sval**
A	204.82	0.1117	0.000163	0	0.014728	0	.
B	283.79	0.09823	0.000163	0	0.001298	0.0095	.
C	257.63	0.1022	0.000163	0	0.005257	0	.
D	181.51	0.1173	0.000163	0	0.020366	0	.
E	193.05	0.1143	0.000163	0	0.017413	0	.
F	201.32	0.1124	0.000163	0	0.015465	0	.
G	247.34	0.1036	0.000163	0	0.006633	0	.
H	195.51	0.1138	0.000163	0	0.016904	0	.
I	284.94	0.09795	0.000163	-0.00014	0.001021	0.18231	.
*J	288.22	0.09751	0.000163	-0.00102	0.000141	.	0.18231
K	172.47	0.1197	0.000163	0	0.022786	0	.
L	173.5	0.1195	0.000163	0	0.022549	0	.
M	276.92	0.099	0.000163	0	0.002069	0	.
N	278.49	0.09876	0.000163	0	0.001831	0	.

Figure 28: Comparison of expedited liver allocation policies to identify the worst one under various metrics.

4.6 CONCLUSION

Expedited liver allocation is an important, yet relatively unexplored problem of the liver allocation system. The expedited liver placement problem faced by a transplant center has never been studied. Our study is motivated by the need of guidelines on this allocation decision. In this chapter, we build a simulation model SIM1 for a transplant center's decision problem on the expedited liver placement. We compared various expedited liver allocation policies.

Our study indicates that an allocation policy which gives higher priority to patients with higher likelihood of death compared to the likelihood of receiving a non-expedited transplant performs better than all the other policies we examine in terms of both the health outcomes, percentage of patients died and average transplant rate metrics. Such a policy increases the average survival times, i.e., 4% increase compared to UNOS's non-expedited liver allocation policy applied to expedited liver allocation. This increase translates to almost 200 days.

Possible future work is duplicating the study using UNOS datasets instead of transplant center-based datasets. The analysis of the datasets obtained from UPMC and the statistics published on UNOS website indicates some discrepancies. This might due to the quality of data collected at various levels of the system. Moreover, due to the lack of data we have a restricted patient type and liver quality definition. An extensive UNOS dataset might help on extending the level of detail we capture in both patient types and liver qualities. In addition, more expedited liver allocation policies can be constructed and tested via our simulation model SIM1.

5.0 A LARGE SCALE DYNAMIC PROGRAMMING APPROACH TO PLACING EXPEDITED LIVERS

5.1 INTRODUCTION

In Chapter 4, to provide guidance to transplant centers we compare various intuitive expedited liver allocation policies via simulation. Simulation is a powerful tool to model systems with complex structures. It provides flexibility and ability to model the dynamic behaviors of the systems more accurately than analytical models. However, as it is the case in Chapter 4, how well the policy space is spanned is uncertain. Therefore, how well the policies evaluated would perform compared to the optimal policy is unknown.

In this chapter, we introduce an alternative model of the expedited liver allocation problem faced by a transplant center. We develop a large scale dynamic programming approach, namely an average reward Markov Decision Process model. We keep most of the modeling framework developed in Chapter 4 intact. Due to the complexity of the problem, we assume the significance of blood type match between donor and recipient away. To compensate the assumption, we adjust the organ arrival rates. We utilize an approximate dynamic programming approach to solve the expedited liver allocation problem faced by the transplant center.

The chapter is structured as follows: Section 5.2 describes our average reward Markov Decision Process model formulation of expedited liver placement problem faced by the transplant center. We present two different objectives. Section 5.3 explains the model parameter estimation methods. Section 5.4 reviews the Least Square Policy Iteration algorithm. Section 5.5 presents our numerical study. Section 5.6 concludes the section.

5.2 MARKOV DECISION PROCESS MODEL FORMULATION

We extend the notation used in Chapter 4. We still specify each patient by her MELD score and patient type. We utilize the same patient type definition as in Chapter 4. That is, even though we assume the blood type match between donor and patient away, we continue on assigning blood types to patients because it is one of the factors included in patient type definition. However, in this chapter blood type does not play any role. We represent the entire transplant center waiting list by a matrix whose entries indicate the number of patients of each type and MELD score. To decrease the size of the state space, we eliminate (type, MELD) pairs in which the patients would reject even the best possible expedited organ offer. The (type, MELD) pairs to be eliminated are specified by the optimal control limit policies (Section 4.2). Let μ_i^* be the optimal control limit for patients of type i, given the best possible expedited organ offer, i.e.,

$$\mu_i^* = \min_d \mu_i^*(d),$$

where $\mu_i^*(d)$ is the optimal control limit of patients of type i for an expedited organ offer of type d. In our model, we only consider the patients who have a MELD score at or above μ_i^*. That is, we remove the (type, MELD) pairs that would always reject any expedited organ offer.

When we eliminate (type, MELD) pairs that would never accept an expedited organ, a "partial matrix" of potentially eligible patients is left. The patients in our "partial matrix" are just potentially eligible to receive an expedited liver transplant because, depending on the type of the current donor, the eligible patients who are willing to accept that specific offer constitutes just a subset of the patients included in the "partial matrix." Let the "partial matrix" be N. Let the entry in the i^{th} row and j^{th} column of N be n_{ij}, which is the number of patients of type $i \in \{1, 2, \ldots, \tau\}$ and MELD score $j \in \{\mu_i^*, \mu_i^* + 1, \ldots, H\}$ listed in the waiting list of the transplant center. Then, the state S of the process is (N, d), where d stands for the donor type defined by its age group, gender and ethnicity. To ensure a finite

state space, we assume in steady state there is an upper bound on the number of potentially eligible patients that can be listed at the transplant center at any time, i.e.,

$$\sum_{i=1}^{\tau} \sum_{j=\mu_i^*}^{H} n_{ij} \leq m < \infty.$$

For ease of notation, in the rest of the document, we use i, j within the summation and product notations to indicate all (type, MELD) pairs which are included in the "partial matrix" N, i.e.

$$\begin{aligned} \sum_{i,j} \dots &= \sum_{i=1}^{\tau} \sum_{j=\mu_i^*}^{H} \dots \\ \prod_{i,j} \dots &= \prod_{i=1}^{\tau} \prod_{j=\mu_i^*}^{H} \dots \quad . \end{aligned}$$

First, we study the expedited placement problem faced by the transplant center with the objective of maximizing the long-run transplant rate at the transplant center. There are two facets of this objective. One is that as the transplant rate is being maximized, the waiting time of the patients listed at the center is expected to decrease. The other is that a transplant center is a business. It needs to continue on its business to survive and transplants serve this goal. Second, we study the same decision problem with the objective of maximizing the average survival gain per patient. For an individual we define the survival gain as the lifetime gained over death on any given day. Therefore, the survival gain is a day for a patient who doesn't leave the system due to transplant. It is the post-transplant expected lifetime for a patient who receive a transplant. For a patient who dies, survival gain is equal to zero. There may be alternative multi-criteria objective functions, such as maximizing the transplant rate and the expected lifetime at the same time, which might require different modeling approaches.

The objective of maximizing transplant rate only considers the number of transplants performed. It does not take the outcome of the transplants into account. However, liver allocation decisions based on the optimal control limits incorporate the consideration of the outcomes into the objective. Thus, including the optimal control limits in the decision process the objective of maximizing transplant rate does not only consider the performance of the transplant center, but also the well-being of the individual patients.

In state (N, d), the center can decline the expedited offer, action "0," or allocate it to a patient of type i and MELD score j. If no expedited offer is made, then the only option is "0"; otherwise, any patient whose MELD score is at or above the optimal control limit, $\mu_i^*(d)$, is a candidate to receive the expedited organ, i.e.,

$$A_{(N,d)} = \begin{cases} 0, & \text{if } d = D+1; \\ \{0\} \cup \{(i,j) : \ j \geq \mu_i^*(d) \text{ and } n_{ij} > 0\}, & \text{otherwise.} \end{cases}$$

For a given donor type, the set of possible actions, namely $A_{(N,d)}$, is a subset of the (type, MELD) pairs in N and constitutes the eligible patient set.

Decision epochs are defined as days. To specify the transition probabilities, we assume the same order of events as in Chapter 4 within each day: expedited transplant (if any), non-expedited transplant(s), health transitions including deaths, arrival of new potentially eligible patients. In order to define the one-step transition probabilities, we specify the transition probabilities given how many potentially eligible patients experience each of these four events. Let $\bar{n}_{ij}$ be the number of patients of type i and MELD score j listed at the transplant center after the (potential) expedited transplant, $\tilde{n}_{ij}$ be the number of patients of type i and MELD score j after the non-expedited transplants occur, $\hat{n}_{ij}$ be the number of patients of type i and MELD score j after the health transitions including death occur and n'_{ij} be the the number of patients of type i and MELD score j after the arrivals occur. Let $I_{\{a=(i,j)\}}$ be an indicator function which takes a value of one if the expression in the parenthesis holds and zero otherwise, i.e.,

$$I_{\{a=(i,j)\}} = \begin{cases} 1, & \text{if } a = (i,j); \\ 0, & \text{otherwise.} \end{cases}$$

Let X_{ij} be the random number of potentially eligible patients of type i and MELD score j who receive a non-expedited transplant, $\boldsymbol{X}$ be the "partial matrix" whose entries are X_{ij}, and $\mathcal{X}$ be the set of all feasible realizations of $\boldsymbol{X}$, i.e.,

$$\mathcal{X} = \{X : x_{ij} \leq \bar{n}_{ij}, \forall\, i \in \{1, 2, \ldots, \tau\} \text{ and } j \in \{\mu_i^*, \mu_i^* + 1, \ldots, H\}\},$$

where X, i.e., $X = [x_{ij}]_{i=1,\ldots,\tau; j=\mu_i^*,\ldots,H}$, is a realization of $\boldsymbol{X}$ and $\bar{n}_{ij} = n_{ij} - I_{\{a=(i,j)\}}$.

Let $\hat{\xi}_i(j)$ be the probability that a patient of type i and MELD score j receives a non-expedited transplant. Given the initial state (N, d) and action $a \in A_{(N,d)}$ the probability of observing a specific realization X of $\boldsymbol{X}$, $X \in \mathcal{X}$, is

$$\Pr(\boldsymbol{X} = X|(N,d),a) = \prod_{i,j}\Big[\binom{\bar{n}_{ij}}{x_{ij}}\hat{\xi}_i(j)^{x_{ij}}(1-\hat{\xi}_i(j))^{\bar{n}_{ij}-x_{ij}}\Big].$$

Let $Y^i_{j,j'}$ be the random number of potentially eligible patients of type i and MELD score j who transition to MELD score j', Y^i_j be the $(H+1)$-dimensional vector whose j'^{th} entry is $Y^i_{j,j'}$, $j' \in \{1, 2, \ldots, H, H+1\}$ ($H+1$ denoting death), $\boldsymbol{Y}$ be the array whose $(i, j, j')^{\text{th}}$ entry is $Y^i_{j,j'}$, and $\mathcal{Y}$ be the set of all feasible realizations of $\boldsymbol{Y}$, i.e.,

$$\mathcal{Y} = \{\, Y : \sum_{j'=1}^{H+1} y^i_{j,j'} = \tilde{n}_{ij} \ ,\ \forall\, i \in \{1, 2, \ldots, \tau\} \text{ and } j \in \{\mu^*_i, \mu^*_i + 1, \ldots, H\}\},$$

where Y, i.e., $Y = [y^i_j]_{i=1,\ldots,\tau;j=\mu^*_i,\ldots,H}$, is a realization of $\boldsymbol{Y}$ and $\tilde{n}_{ij} = \bar{n}_{ij} - x_{ij}$.

We have defined $H_i(j'|j)$ as the daily probability of a health transition from MELD score j to MELD score j' for a patient of type i. Given the initial state (N, d), action a and the realization X of $\boldsymbol{X}$, the probability of observing a specific realization Y of $\boldsymbol{Y}$, $Y \in \mathcal{Y}$, is

$$\Pr(\,\boldsymbol{Y} = Y|X,(N,d),a) = \prod_{i,j}\Big[\Big(\frac{\tilde{n}_{ij}!}{(y^i_{j,1})!(y^i_{j,2})!\ldots(y^i_{j,H+1})!}\Big)\prod_{k=1}^{H+1} H_i(k|j)^{y^i_{j,k}}\Big].$$

Lastly, let Ψ be the random total number of new potentially eligible patients and $\hat{\rho}_{ij}$ be the likelihood that a new potentially eligible patient is of type i and MELD score j. Let Z_{ij} be the random number of new potentially eligible patients of type i and MELD score j, $\boldsymbol{Z}$ be the "partial matrix" whose entries are Z_{ij} and $\mathcal{Z}$ be the set of all feasible realizations of $\boldsymbol{Z}$, i.e.,

$$\mathcal{Z} = \Big\{Z : \sum_{i,j} z_{ij} \le m - \sum_{i,j}\hat{n}_{ij}\Big\},$$

where Z, i.e., $Z = [z_{ij}]_{i=1,\ldots,\tau;j=\mu^*_i,\ldots,H}$ is a realization of $\boldsymbol{Z}$ and $\hat{n}_{ij} = \tilde{n}_{ij} - \sum_{j'=1,j'\neq j}^{H+1} y^i_{j,j'} + \sum_{k=\mu^*_i,k\neq j}^{H} y^i_{k,j}$. Because we are only modeling patients with MELD scores above the optimal control limits, the new potentially eligible patients might be patients who are newly listed at the transplant center with a MELD score at or above the optimal control limit for the

best expedited liver or patients who have already listed, but are having a health transition into a MELD score at or above the optimal control limit for the best expedited liver.

Given the total number of new potentially eligible patients, the probability that new potentially eligible patients are characterized by a realization Z of $\boldsymbol{Z}$, $Z \in \mathcal{Z}$, is

$$\Pr(\boldsymbol{Z} = Z|\Psi = \psi) = \frac{\psi!}{z_{11}!z_{12}!\dots z_{\tau H}!}\prod_{i,j}\hat{\rho}_{ij}^{z_{ij}}.$$

Given the initial state (N, d), action a and realizations of X and Y of $\boldsymbol{X}$ and $\boldsymbol{Y}$, respectively, the probability of observing a specific realization Z of $\boldsymbol{Z}$ is

$$\Pr(\boldsymbol{Z} = Z|\, Y, X, (N, d), a) = \Pr(\Psi = \psi) \cdot \Pr(\boldsymbol{Z} = Z|\Psi = \psi).$$

After all the events occur, the number of potentially eligible patients of type i and MELD score j becomes

$$n'_{ij} = \hat{n}_{ij} + z_{ij}.$$

Let N' whose entries are n'_{ij}s be the new "partial matrix" obtained after the observation of X, Y and Z. Given N, there is a unique "partial matrix" N' characterized by X, Y and Z. We do not explicitly define one-step transition probabilities, because given an initial N, there are multiple observations of the action taken and realizations of $\boldsymbol{X}$, $\boldsymbol{Y}$ and $\boldsymbol{Z}$ that lead to N'. Instead, we define the probability of observing X, Y and Z, given an initial state (N, d) and action a as

$$\begin{aligned}\Pr(\boldsymbol{X} = X, \boldsymbol{Y} = Y, \boldsymbol{Z} = Z|(N, d), a) = \Pr(\boldsymbol{Z} = Z|\, Y, X, (N, d), a)\\ \cdot \Pr(\boldsymbol{Y} = Y|X, (N, d), a)\\ \cdot \Pr(\boldsymbol{X} = X|(N, d), a).\end{aligned}$$

Although the definition of "partial matrix" N provides computational advantages, it adds some challenges, as well. Due to this definition, the patients' movements between MELD scores outside of the state space are not modeled explicitly. For instance, we cannot capture the likely event that a potentially eligible patient transitions to a MELD score below μ_i^* and then back to a MELD score above μ_i^*. Therefore, the resulting policies will not be a function of the number of patients in MELD scores below μ_i^*. We address this issue in Section 5.3.

Let $r_k((N,d),a)$ be the expected reward associated with taking action a in state (N,d) for the decision problem with the objective k. Our objective of maximizing transplant rate $(k=1)$ gives a reward of one for each transplant, i.e.,

$$r_1((N,d),a) = (1 - I_{\{a=0\}}) + \sum_{i,j}[\bar{n}_{ij} \cdot \hat{\xi}_i(j)].$$

The first term in the definition of $r_1((N,d),a)$ corresponds to the reward obtained from the decision made and the second term corresponds to the expected reward obtained from the non-expedited transplants. The objective of maximizing average survival gain per patient $(k=2)$ yields a reward that depends on the survival times generated by the Cox model of Roberts et al. [79] for patients who receive a transplant, a reward equal to zero for patients who die and a reward equal to one for patients who stay on the waiting list, i.e.,

$$r_2((N,d),a) = \frac{L_{exp}(a,d) + \sum_{i,j}[\bar{n}_{ij} \cdot \hat{\xi}_i(j) \cdot L_{non\_exp}(i,j)] + \sum_{i,j} \tilde{n}_{ij} \cdot [1 - H_i(\Delta|j)]}{\sum_{i,j} n_{ij}},$$

where $L_{exp}(a,d)$ is the expected post-transplant life days of an $a=(i,j)$ patient who receives an expedited transplant of an organ type d, $L_{non\_exp}(i,j)$ is the expected post-transplant life days of an (i,j) patient who receives a non-expedited transplant, Δ stands for death and $H_i(\Delta|j) = 1 - \sum_{j'=1}^{18} H_i(j'|j)$. Because we do not explicitly model the non-expedited liver arrivals, we cannot specify the organ types that result in non-expedited transplants. Therefore, in the calculation of the post-transplant expected life days which are caused by the non-expedited liver transplants we aggregate all liver qualities into one and generate the survival times accordingly.

Given $\mathcal{D}(d')$ is the probability of receiving an expedited liver from a donor of type d', the value function for the objective k with t days remaining can be written as

$$V_t^k((N,d)) = \max_{a \in A_{(N,d)}} \left\{ r_k((N,d),a) + \mathbb{E}[V_{t-1}^k((\dot{N},\dot{d}))] \right\}, \tag{5.1}$$

where the expectation is given by

$$\mathbb{E}[V_{t-1}^k((\dot{N},\dot{d}))] = \sum_{d'=1}^{D+1}\sum_{X\in\mathcal{X}}\sum_{Y\in\mathcal{Y}}\sum_{Z\in\mathcal{Z}}\Pr(\boldsymbol{X}=X,\boldsymbol{Y}=Y,\boldsymbol{Z}=Z|(N,d),a) \cdot \mathcal{D}(d')\cdot V_{t-1}^k((N',d')),$$

and the terminal reward is zero.

Given that the above MDP model has finite state space, bounded and stationary rewards, stationary transition probabilities and a single irreducible class under all stationary policies, as $t\to\infty$ we obtain

$$W^k((N,d)) = \max_{a\in A_{(N,d)}}\left\{r_k((N,d),a) + \mathbb{E}[W^k((\dot{N},\dot{d}))] - \gamma_k\right\}, \tag{5.2}$$

where γ_k is the maximum attainable transplant rate or average survival gain per patient for $k=1,2$, respectively, and $W^k((N,d))$ is the bias associated with starting in state (N,d).

5.3 PARAMETER ESTIMATION

To estimate the model parameter values, we utilize the same datasets as in Chapter 4 and employ similar calculation methods. Contrary to the parameters in Chapter 4, the ones in this chapter are defined for only (i,j) pairs included in the "partial matrix" N.

First, consider the expedited liver arrival probabilities. To estimate the probability of an expedited offer from a donor of type $d\in\{1,2,\ldots,D,D+1\}$, we follow the same steps as in Chapter 4. We assume that the time between expedited organ offers follows a geometric distribution with parameter p. We obtain $\mathcal{D}(d)$ using the following formula:

$$\mathcal{D}(d) \;=\; p\cdot\frac{\text{total number of expedited offers from donor type } d}{\text{total number of expedited offers}},\ \forall\ d.$$

In Chapter 4, the blood compatibility of the donor and the patient is a factor in the allocation decision of expedited livers. Therefore, in the simulation model SIM1 of Chapter 4, we observe cases in which a liver cannot be matched to any patients due to the lack of blood compatibility. However, in this chapter we assume the effect of blood compatibility

away. Therefore, independent of the blood type match any patient might accept any liver as long as the optimal control limits permit. To prevent the number of transplants from being artificially increased, we adjust the liver arrival probabilities. For each policy studied in Chapter 4, we examine the percentage of cases in which no match is found for an expedited liver due to blood type incompatibility in the simulation model SIM1. On average, 12% of the time a match cannot be found for a liver. Thus, we decrease the organ arrival probabilities by 12%.

Second, consider the probability that a patient of type i and MELD score j receives a non-expedited transplant, $\hat{\xi}_i(j)$. The estimated values of $\hat{\xi}_i(j)$ are the same as of $\xi_i(j)$ for patients of type $i \in \{1, 2, \ldots, \tau\}$ and MELD score $j \in \{\mu_i^*, \mu_i^* + 1, \ldots, H\}$.

Third, consider the likelihood that when a new potentially eligible patient joins the list, she is of type i and MELD score j, $\hat{\rho}_{ij}$. Due to the construction of the "partial matrix" N, we partition the estimation method into two parts. First, consider the patients who are "new" to the transplant center. Using patients' MELD score at listing, gender, race, etc., we can determine which (type, MELD) pair a patient belonged to when she joined the waiting list. Then, on a given day the expected number of arrivals of newly listed patients to the pair (i, j) is

$$\varphi_{ij} = \frac{\text{total number of patients who joined the list in } (i,j) \text{ pair}}{\text{total number of days covered within the dataset}},$$

and the expected number of arrivals of newly listed patients to MELD scores at or above μ_i^* is

$$\varphi = \sum_{i,j} \varphi_{ij} = \frac{\text{total number of patients who joined the list in any } (i,j) \text{ pair}}{\text{total number of days covered within the dataset}}.$$

Now, consider the existing patients having health transitions from the MELD scores below μ_i^*. A patient of type i and MELD score k is assumed to have transitions to MELD score j with probability $H_i(j|k)$. Then, $H_i(j|k)$ multiplied by the expected number of patients of type i and MELD score k gives us the expected number of arrivals from (i, k) pair to (i, j) pair. Let β_k^i be the expected number of patients of type i and MELD score k and ζ_{ik}^j be the expected number of arrivals from (i, k) pair to (i, j) pair. Then,

$$\zeta_{ik}^j = H_i(j|k) \cdot \beta_k^i,$$

where

$$\beta_k^i = \frac{\text{total average number of days patients of type } i \text{ spent in MELD score } k}{\text{total number of days covered within the dataset}}.$$

Then, for type i, the expected number of arrivals from MELD scores below μ_i^* to MELD score j is

$$\sum_{k=1}^{\mu_i^*-1} \zeta_{ik}^j,$$

and the total expected number of arrivals from MELD scores below μ_i^* to MELD scores at or above μ_i^* is

$$\sum_{j=\mu_i^*}^{H} \sum_{k=1}^{\mu_i^*-1} \zeta_{ik}^j.$$

Then, $\hat{\rho}_{ij}$ is obtained using the following formula:

$$\hat{\rho}_{ij} = \frac{\varphi_{ij} + \sum_{k=1}^{\mu_i^*-1} \zeta_{ik}^j}{\varphi + \sum_{i=1}^{\tau} \sum_{j=\mu_i^*}^{H} \sum_{k=1}^{\mu_i^*-1} \zeta_{ik}^j}.$$

Lastly, consider the rate at which new eligible patients join the list. We need to consider both the new patients to the system and the patients who have been listed with MELD scores below μ_i^* and having a health transition to MELD scores at or above μ_i^*. We utilize a simulation model (SIM3) to estimate the arrival probabilities. We construct a similar simulation model (SIM3) to the one in Chapter 4 (SIM1). However, we model the expedited transplants as we model the non-expedited transplants. That is, we do not simulate an expedited liver allocation policy. Instead, we calculate the probability that a patient of type i and MELD score j receives an expedited transplant for all $i \in \{1, 2, \ldots, \tau\}$ and MELD score $j \in \{1, 2, \ldots, H\}$. Contrary to the probability that a patient of type i and MELD score j receives a non-expedited transplant, $\xi_i(j)$, we do not impute the missing probability values. In the simulation model SIM3, we consider the effect of the events, i.e., patient arrivals, transplants, and health transitions, to all (i, j) pairs, $i \in \{1, 2, \ldots, \tau\}$, $j \in \{1, 2, \ldots, H\}$. The parameters whose estimation methods explained in Section 4.3.2 are utilized in the simulation model SIM3. We let the number of replications be 5,000. We count the number of arrivals to MELD scores at or above μ_i^*'s on each iteration, sum the number of iterations

on which a specific number of arrivals is observed and divide these sums by the number of iterations in a replication, i.e., 365.

The values of all model parameters can be seen in Appendix B.

5.4 SOLUTION TECHNIQUE

The number of states is calculated using a balls and bins approach. The cells, i.e., (type, MELD) pairs of N, are thought of as bins and the patients in the cells are thought of as balls. The number of ways of distributing k identical balls over n bins, if one or more bins may remain empty, is given by $\binom{k+n-1}{k}$ [45]. Then, because at the center we might have $k, k \in [0, m]$, patients on any day, the number of states is given by

$$|S| = (D+1) \cdot \sum_{k=0}^{m} \binom{k + \sum_{i=1}^{\tau}(H - \mu_i^* + 1) - 1}{k}.$$

Not surprisingly, the number of states explodes for realistically sized problems. Thus, our numerical experiment in which we obtain optimality is restricted to very small instances.

Under both objectives, i.e., maximizing transplant rate at the transplant center and average survival gain per patient, it is never optimal to decline an expedited offer of type d if there is a patient with a MELD score at or above $\mu_i^*(d)$, $i = 1, \ldots, \tau$. This behavior is also confirmed in our numerical experimentation on small instances for which we obtain the optimal solution. It intuitively makes sense that as long as there is a benefit to obtain for any patient, it cannot be optimal to reject an offer under these two metrics.

Our model suffers from the "curse of dimensionality." A one unit increase in the model parameters' sizes, e.g., $m \rightarrow m + 1$, leads to an exponential increase in difficulty in solving the problem. For realistically sized problems, we have enormous state spaces. It is even impossible to store them. For instance, for the instance with model parameters $D = 2$, $m = 50$, $H = 18$, $\tau = 4$, $\mu_1^* = 8$, $\mu_2^* = 9$, $\mu_3^* = 9$, $\mu_4^* = 10$, the size of the state space is equal to 1.8×10^{26}. Furthermore, the transition probabilities quickly become intractable. Thus, we cannot utilize traditional methods, i.e., policy iteration, to solve our model. Instead, we explore different approximate dynamic programming approaches.

Given the two problems that exhibit the curse, i.e., the size of the state space and the difficulty in the generation of transition probabilities, we have selected Least-Squares Policy Iteration (LSPI) [59] as the most suitable approach. LSPI is an approximate dynamic programming approach for control problems which combines value-function approximation with linear architectures and approximate policy iteration as a solution technique. To be able to incorporate the policy improvement step into the algorithm, LSPI approximates the state-action values, i.e., $Q(s,a)$, instead of the value function. Q values are the estimates of the expressions that are maximized in the right hand side of Bellman's equation. To represent the Q values, LSPI uses a linear combination of nonlinear basis functions or features, given by the vector $\phi(s,a)$, i.e.,

$$\hat{Q}(s,a,\omega) = \sum_{k=1}^{\kappa} \phi_k(s,a)\omega_k,\ s \in S,\ a \in A_s$$

where the ω_k's are the parameters to be estimated. Because it only requires that the Q values are generated as needed, it overcomes the dimensionality issue related to the state space. By just storing the values of the ω_k's, any Q value can be obtained for any state-action pair at any time. LSPI evaluates the values of the linear architecture via simulation. In this manner, it eliminates the need of calculation of one-step transition probabilities. The optimal action at state s is obtained by maximizing the Q value over all actions $a \in A_s$.

The steps of LSPI algorithm follow

1. Decide on the κ basis functions, i.e., what they represent.
2. Let the initial policy $\pi = \pi^0$.
3. Calculate the parameters $\tilde{\omega}$.
   - Let $s_t = (N_t, d_t)$. Draw a sample $D = \{(s_t, a_t, r(s_t,a_t), s'_t) | t = 1, 2, \ldots, T\}$. Once s_t and a_t are known, $r(s_t,a_t)$ and s'_t can be generated via simulation. The observations, $(s_t, a_t, r(s_t,a_t), s'_t)$, in sample D are not specific to a policy π. (s_t, a_t) are chosen uniformly from the state-action space. All states should be observed in sample D.
   - Let $\tilde{A}^{(0)}$ and $\tilde{b}^{(0)}$ be zero.
   - If $\tilde{A}$ is not full rank, instead of zero, initialize $\tilde{A}^{(0)}$ and $\tilde{b}^{(0)}$ to νI, where ν is a positive small number.

- For $t = 1$ to T,

$$\tilde{A} \leftarrow \tilde{A} + \phi(s_t, a_t)\Big(\phi(s_t, a_t) - \lambda\phi(s'_t, \pi(s'_t))\Big)'$$
$$\tilde{b} \leftarrow \tilde{b} + \phi(s_t, a_t)r$$

  where $\lambda,\ 0 < \lambda \leq 1$, is the discount factor.

4. Calculate $\tilde{\omega}$ using $\tilde{b} = \tilde{A}\tilde{\omega}$.
5. Let $\pi'(s) = \underset{a \in A_s}{\arg\max}\ \hat{Q}(s, a) = \underset{a \in A_s}{\arg\max}\ \sum_{k=1}^{\kappa} \phi_k(s, a)\tilde{\omega}_k$, for all $s \in S$.
6. If $\pi \approx \pi'$, stop. Otherwise, go to step 3.

The goal of LSPI is to mimic the behavior of the value function to be approximated. Numerical estimation of the right value of the value function is not intended. By mimicking the upward and downward trends in the value function, LSPI aims at choosing the optimal action at each state.

LSPI has two issues which are common to most algorithms of approximate dynamic programming. One is the exploration-exploitation trade-off problem. Should it take suboptimal actions to explore new rewards? Or should it focus on gained knowledge to improve the current reward? Because LSPI utilizes sample data generated from any reasonable sampling distribution, with appropriate approaches, like that of Li et al. [61], it is possible to overcome this issue. The second problem is feature selection. Feature selection is suggested to be done using insight [59]. Especially linear architectures are claimed to give insight to how they fail to provide good fit. The selection of basis functions that can fit the Q values properly becomes easier with linear architectures because, for instance, it is easier to understand how an architecture fails via plots if a linear architecture is employed. A key point in the selection of the basis functions is the functional behavior. The performance of LSPI is highly dependent on the basis functions, i.e., $\phi_k(s, a),\ k \in \{1, 2, \ldots, \kappa\}$, chosen. Depending on the choice made the algorithm might even oscillate between policies or ω values and never converge.

5.5 NUMERICAL STUDY

5.5.1 Maximizing Transplant Rate

To be able to understand the behavior of the value function, we first study very small problems. To find the appropriate basis functions, we investigate the effect of various properties of state and action pairs. We utilized the estimated values of the model parameters in the basis function definitions. For instance, we consider the number of patients in each (i, j) pair, the number of patients in each MELD score j, the number of patients in each patient type i, their likelihood of death on a day, their likelihood of receiving a non-expedited transplant on a day, their long run probability of receiving a transplant, the existence of an expedited liver on any given day, the total number of patients who are willing to accept an expedited liver offer on any given day, the outcome of a match of an expedited liver and a patient, the benefit of allocating an expedited liver to a patient instead of the other patients as the components of the basis functions. We utilize different functional forms. We experiment on the linear combinations of linear and non-linear basis functions. We study polynomial terms with various degrees and many functional forms, i.e., exponential function, probability density function of gamma distribution, probability density function of log-normal distribution, etc. After observing the performance of the basis functions on small instances, we repeat the experiments on real size instances.

The basis function found to yield the best outcomes in terms of the performance metrics, i.e., average transplant rate, survival after departure, has the following form:

$$\phi(s,a) = \left(exp\left(\left(-\sum_{i,j} (n_{ij} - I_{\{a!=0\}}) \cdot \hat{\xi}_i(j) \cdot \frac{1}{1-(1-\hat{\xi}_i(j))\cdot(1-H_i(\Delta|j))} \right) /2 \right) \right)^{\mathcal{B}(a,d)},$$

where $\mathcal{B}(a,d)$ is defined as the following.

$$\mathcal{B}(a,d) = \begin{cases} \max\limits_{(i',j')\neq(i,j)} \{L_{exp}((i,j),d) - L_{exp}((i',j'),d)\}, & \text{if } (L_{exp}((i,j),d) - L_{exp}((i',j'),d)) \\ & \text{is non-negative for all comparisons;} \\ \min\limits_{(i',j')\neq(i,j)} \{L_{exp}((i,j),d) - L_{exp}((i',j'),d)\}, & \text{otherwise.} \end{cases}$$

The first component of the basis function is a constant term. The second component incorporates the expected number of non-expedited liver transplants that the patients listed at the center would receive. Excluding the expedited transplant option, the probability that a patient receives a non-expedited transplant is given by

$$\hat{\xi}_i(j) \cdot \frac{1}{1-(1-\hat{\xi}_i(j)) \cdot (1-H_i(\Delta|j))} =$$
$$\hat{\xi}_i(j) + (1-\hat{\xi}_i(j)) \cdot (1-H_i(\Delta|j)) \cdot \hat{\xi}_i(j) + (1-\hat{\xi}_i(j))^2 \cdot (1-H_i(\Delta|j))^2 \cdot \hat{\xi}_i(j) + \ldots$$

The third component is the benefit of allocating the expedited liver to an (i, j) patient instead of an (i', j') patient, $i \neq i'$, $j \neq j'$. If the outcome of another match of the liver and a patient is higher, the benefit function $\mathcal{B}(a, d)$ represents the loss in terms of life days.

The sample size utilized in step 3 of the LSPI algorithm is chosen to be 30,000 to increase the probability of visiting all feasible state-action pairs. Given the above basis functions, the LSPI algorithm repeats steps 3 through 6 five times and converges to the following values.

$$\omega = \begin{pmatrix} 1442691.551 \\ 184.9864309 \\ 0.000205571 \end{pmatrix}.$$

Due to the size of the state space, generation of an expedited liver allocation policy based on the results of the LSPI algorithm is only possible via simulation. The values of ω obtained via LSPI algorithm are fed into a simulation model of the system (SIM4) which is similar to the one in Chapter 4 (SIM1). In this simulation model SIM4, not the whole transplant center, but only patients that fall into the "partial matrix" N are simulated. Moreover, blood type match between the donor and the patient is not important. The expedited liver allocation decisions are based on the Q values calculated using the ω values, i.e., $\pi'(s) = \underset{a \in A_s}{\arg\max}\ \hat{Q}(s, a) = \underset{a \in A_s}{\arg\max} \sum_{k=1}^{\kappa} \phi_k(s, a)\tilde{\omega}_k$. While choosing the optimal action generated via the Q values, we might observe ties between multiple state-action pairs. In the simulation SIM4, we observe such a tie 10% of the time. In the case of a tie, we prioritize patients with the highest MELD scores and acute liver disease (disease group 3). In Table 8, various performance metrics obtained via the simulation model SIM4 are presented.

Table 8: Performance metrics obtained via LSPI - I

	mean	**std. deviation**
average transplant rate	0.36936	0.02857
average non-expedited transplant rate	0.14212	0.02501
average expedited transplant rate	0.22724	0.02169
percentage of livers unused	0.00047	0.00357
percentage of patients died	0.18889	0.03131
expected life days after departure	2973.4	144.5
waiting time before death (in days)	37.172	11.324
waiting time before transplant (in days)	37.546	9.624
total expected lifedays	3010.8	143.5

To be able to comment on how well we approximate the optimal solution we utilize the policies constructed in Chapter 4 (Figure 8). We feed those policies into the simulation model mentioned above (SIM4), instead of the ω values. In Figure 29 and Figure 30, the performance metrics obtained by simulating those policies and the ω values are presented. We perform policy comparison analysis for the metrics in Figure 29. We utilized Hsu's method. The highlighted policies are the ones in the best policy subset. In Figure 30, we put the means in order for ease of comparison.

Average Transplant Rate						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	0.3682	0.000396	-0.0121	0	0	.
B	0.3664	0.000396	-0.01384	0	0	.
C	0.3702	0.000396	-0.01007	0	0	.
D	0.3769	0.000396	-0.00336	0	0.003366	.
E	0.3788	0.000396	-0.00014	0.002713	.	0.088681
F	0.3682	0.000396	-0.01207	0	0	.
G	0.3682	0.000396	-0.01207	0	0	.
H	0.3775	0.000396	-0.00271	0.000138	0.088681	.
I	0.3667	0.000396	-0.01355	0	0	.
J	0.3667	0.000396	-0.01354	0	0	.
K	0.3769	0.000396	-0.00334	0	0.003679	.
L	0.3768	0.000396	-0.00346	0	0.001739	.
M	0.3653	0.000396	-0.01493	0	0	.
N	0.3648	0.000396	-0.0154	0	0	.
LSPI	0.3694	0.000396	-0.01089	0	0	.

% of Patients Died						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	0.1749	0.000431	0	0.072771	1.00E-12	.
B	0.1117	0.000431	0	0.009649	1.00E-12	.
C	0.1036	0.000431	-0.00955	0	.	1.00E-12
D	0.1879	0.000431	0	0.085777	1.00E-12	.
E	0.1907	0.000431	0	0.088628	1.00E-12	.
F	0.1515	0.000431	0	0.049433	1.00E-12	.
G	0.1515	0.000431	0	0.049433	1.00E-12	.
H	0.1753	0.000431	0	0.07323	1.00E-12	.
I	0.1116	0.000431	0	0.009551	1.00E-12	.
J	0.1119	0.000431	0	0.009854	1.00E-12	.
K	0.1968	0.000431	0	0.094746	1.00E-12	.
L	0.1971	0.000431	0	0.095046	1.00E-12	.
M	0.1209	0.000431	0	0.018768	1.00E-12	.
N	0.1202	0.000431	0	0.018146	1.00E-12	.
LSPI	0.1889	0.000431	0	0.086803	1.00E-12	.

Average Non-expedited Transplant Rate						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	0.1411	0.000352	-0.01195	0	0	.
B	0.1389	0.000352	-0.01414	0	0	.
C	0.1427	0.000352	-0.01035	0	0	.
D	0.1501	0.000352	-0.00295	0	0.0043	.
E	0.1518	0.000352	0	0.002786	.	0.012251
F	0.1408	0.000352	-0.01233	0	0	.
G	0.1408	0.000352	-0.01233	0	0	.
H	0.1503	0.000352	-0.00279	0	0.012251	.
I	0.1388	0.000352	-0.01427	0	0	.
J	0.1396	0.000352	-0.01353	0	0	.
K	0.1499	0.000352	-0.0032	0	0.000671	.
L	0.1497	0.000352	-0.00337	0	0.000157	.
M	0.1381	0.000352	-0.01501	0	0	.
N	0.137	0.000352	-0.01606	0	0	.
LSPI	0.1421	0.000352	-0.01097	0	0	.

Survival After Departure						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	2946.77	2.1876	-254.617	0	1.00E-12	.
B	2820.05	2.1876	-381.332	0	1.00E-12	.
C	3164.71	2.1876	-36.676	0	1.00E-12	.
D	3017.08	2.1876	-184.307	0	1.00E-12	.
E	2929.09	2.1876	-272.294	0	1.00E-12	.
F	2939.96	2.1876	-261.43	0	1.00E-12	.
G	2939.96	2.1876	-261.43	0	1.00E-12	.
H	3193.51	2.1876	0	36.6765	.	1.00E-12
I	2819.16	2.1876	-382.227	0	1.00E-12	.
J	2818.99	2.1876	-382.398	0	1.00E-12	.
K	2929.06	2.1876	-272.33	0	1.00E-12	.
L	2928.57	2.1876	-272.812	0	1.00E-12	.
M	2812.39	2.1876	-388.994	0	1.00E-12	.
N	2818.58	2.1876	-382.807	0	1.00E-12	.
LSPI	2973.37	2.1876	-228.016	0	1.00E-12	.

Average Expedited Transplant Rate						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	0.227	0.000289	-0.0019	0.000181	0.13335	.
B	0.2275	0.000289	-0.00145	0.000632	0.59736	.
C	0.2274	0.000289	-0.00147	0.000606	0.56675	.
D	0.2268	0.000289	-0.00216	0	0.02953	.
E	0.001038	0.000289	-0.22788	0	0	.
F	0.2274	0.000289	-0.00149	0.000587	0.54371	.
G	0.2274	0.000289	-0.00149	0.000587	0.54371	.
H	0.001034	0.000289	-0.22788	0	0	.
I	0.2279	0.000289	-0.00099	0.001093	.	0.90932
J	0.2272	0.000289	-0.00176	0.000321	0.24385	.
K	0.227	0.000289	-0.0019	0.00018	0.133	.
L	0.2271	0.000289	-0.00184	0.000237	0.17247	.
M	0.2272	0.000289	-0.00168	0.000403	0.32798	.
N	0.2278	0.000289	-0.00109	0.000987	0.90932	.
LSPI	0.2272	0.000289	-0.00168	0.000401	0.3256	.

Total Survival						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	3000.38	2.1853	-264.532	0	1.00E-12	.
B	2941.34	2.1853	-323.563	0	1.00E-12	.
C	3257.04	2.1853	0	30.4849	.	1.00E-12
D	3050.39	2.1853	-214.522	0	1.00E-12	.
E	2968.56	2.1853	-296.344	0	1.00E-12	.
F	3029.29	2.1853	-235.618	0	1.00E-12	.
G	3029.29	2.1853	-235.618	0	1.00E-12	.
H	3234.42	2.1853	-30.485	0	1.00E-12	.
I	2940.5	2.1853	-324.408	0	1.00E-12	.
J	2940.46	2.1853	-324.445	0	1.00E-12	.
K	2962.21	2.1853	-302.703	0	1.00E-12	.
L	2961.85	2.1853	-303.054	0	1.00E-12	.
M	2931	2.1853	-333.906	0	1.00E-12	.
N	2937.18	2.1853	-327.724	0	1.00E-12	.
LSPI	3010.84	2.1853	-254.068	0	1.00E-12	.

Figure 29: Performance metrics obtained for various allocation policies A-I.

percentage of livers unused			waiting time before death			waiting time before transplant		
policy	**mean**	**std dev.**	**policy**	**mean**	**std dev.**	**policy**	**mean**	**std dev.**
B	0	0.00E+00	J	117.8	35.35	K	33.03	9.396
C	0	0	I	116.77	34.37	L	33.169	9.547
F	0	0	B	116	34.77	D	33.243	9.826
G	0	0	M	113.14	32.03	LSPI	37.546	9.624
I	0	0	N	112.16	31.98	E	39.402	9.828
J	0	0.000000	F	88.187	22.421	H	40.729	11.13
M	0	0	G	88.187	22.421	A	54.035	10.929
N	0	0	C	87.102	27.881	F	89.525	12.081
A	0.000043	0.001026	A	51.5	14.317	G	89.525	12.081
LSPI	0.000469	0.003571	H	41.789	13.575	C	92.94	14.72
E	0.00061	0.004280	E	39.77	11.661	M	119.34	14.72
H	0.000888	0.005369	LSPI	37.172	11.324	N	119.46	14.68
L	0.001669	0.007284	L	33.739	11.065	I	121.88	14.7
K	0.001696	0.007083	K	33.678	10.768	B	121.92	14.49
D	0.002167	0.008316	D	33.595	11.352	J	121.93	14.52

Figure 30: Performance metrics obtained for various allocation policies A-II.

The results of the Hsu's method and the visual comparison made for the metrics in Figure 30 indicate that there is still room for improvement for the LSPI method. Under none of the metrics, LSPI method's policy is picked as the best policy. However, further investigation of Figure 29 reveals that the non-expedited transplants are the actual factor which affect the order of the policies. Moreover, we perform a t-test to compare the performance of Policy E, which is one of the best policies according to Hsu's method, and the performance of LSPI method under the average transplant rate metric. The test results in a p-value less than 0.0001 indicating that there is no sufficient evidence to reject the equality of the performances.

The values in Figure 29 show that we cannot easily differentiate the expedited liver allocation policies based on the objective of maximizing average transplant rate at the center.

Therefore, we construct another average reward MDP model with the objective of maximizing average survival gain per patient.

5.5.2 Maximizing Average Survival Gain per Patient

We perform a similar search for basis functions for the expedited liver placement problem with the objective of maximizing average survival gain per patient as we do in the previous section. Our extensive basis function search yields the following form as the best basis function in terms of the performance metrics obtained.

$$\phi(s,a) = \begin{pmatrix} 1 \\ -\sum_{i,j}(n_{ij} - I_{\{a!=0\}}) \cdot H_i(\Delta|j) \\ \mathcal{B}(a,d) \end{pmatrix}.$$

The first and third components of the basis function are the same as in the previous section. However, the second component captures purely the expected number of deaths. We would like to prevent the patients from dying, because a patient who dies affects all the performance metric negatively. Thus, the second component has a negative sign.

The sample size utilized in step 3 of the LSPI algorithm is again chosen to be 30,000 to increase the probability of visiting all feasible state-action pairs. Given the above basis function, the LSPI algorithm repeats steps 3 through 6 three times and converges to the following values:

$$\omega = \begin{pmatrix} 176233982.9 \\ -4632.20056 \\ 0.031210671 \end{pmatrix}.$$

The negative effect we impose via the expected number of deaths is converted to be a positive one by the negative coefficient ω_2.

The simulation model of the system (SIM4) is fed by the values of ω obtained via LSPI algorithm. Contrary to the case in the previous section, we do not observe any ties between state-action pairs while choosing the optimal actions. In Table 9, the performance metrics obtained via the simulation model SIM4 are presented. Even though the objective is to maximize the average survival gain per patient, not only this metric but also the average

transplant rate has been improved compared to the results obtained for the average reward model of Section 5.5.1. This might be due to the fact that policies' average transplant rates are very close to each other. The basis functions explored cannot detect these small differences. However, the average survival gain per patient has different values from policy to policy. Thus, the basis functions explored yield more satisfactory results.

Table 9: Performance metrics obtained via LSPI - II

	mean	**std. deviation**
average transplant rate	0.37598	0.02906
average non-expedited transplant rate	0.14909	0.02542
average expedited transplant rate	0.2269	0.02154
percentage of livers unused	0.00178	0.0073
percentage of patients died	0.18872	0.03140
expected life days after departure	3016.6	139.2
waiting time before death	33.878	11.196
waiting time before transplant	32.751	9.319
total expected lifedays	3049.6	138.3

In Figure 31 and Figure 32, we present the comparison of the results of the LSPI method with that of the policies constructed in Chapter 4 (Figure 8). Unfortunately, the policy generated via LSPI method still do not perform better than the other policies under all metrics except the waiting time before transplant metric. The policy generated via LSPI method yields the smallest waiting time before transplant. Moreover, when the average transplant rate metric is investigated, we observe that even though statistically the policy generated via LSPI method is not chosen to be the best policy, it's performance is very close the best, i.e., 0.376 vs. 0.379. In addition, the policy generated via LSPI method performs better than all policies, except Policies A, C and D, under the total survival metric.

Average Transplant Rate						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	0.3682	0.000396	-0.0121	0	0	.
B	0.3664	0.000396	-0.01384	0	0	.
C	0.3702	0.000396	-0.01007	0	0	.
D	0.3769	0.000396	-0.00336	0	0.003416	.
E	0.3788	0.000396	-0.00014	0.002715	.	0.089222
F	0.3682	0.000396	-0.01207	0	0	.
G	0.3682	0.000396	-0.01207	0	0	.
H	0.3775	0.000396	-0.00272	0.00014	0.089222	.
I	0.3667	0.000396	-0.01356	0	0	.
J	0.3667	0.000396	-0.01354	0	0	.
K	0.3769	0.000396	-0.00334	0	0.003733	.
L	0.3768	0.000396	-0.00346	0	0.001768	.
M	0.3653	0.000396	-0.01493	0	0	.
N	0.3648	0.000396	-0.0154	0	0	.
LSPI	0.376	0.000396	-0.00427	0	0.000003	.

% of Patients Died						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	0.1749	0.000431	0	0.072771	1.00E-12	.
B	0.1117	0.000431	0	0.00965	1.00E-12	.
C	0.1036	0.000431	-0.00955	0	.	1.00E-12
D	0.1879	0.000431	0	0.085778	1.00E-12	.
E	0.1907	0.000431	0	0.088628	1.00E-12	.
F	0.1515	0.000431	0	0.049433	1.00E-12	.
G	0.1515	0.000431	0	0.049433	1.00E-12	.
H	0.1753	0.000431	0	0.073231	1.00E-12	.
I	0.1116	0.000431	0	0.009552	1.00E-12	.
J	0.1119	0.000431	0	0.009854	1.00E-12	.
K	0.1968	0.000431	0	0.094746	1.00E-12	.
L	0.1971	0.000431	0	0.095046	1.00E-12	.
M	0.1209	0.000431	0	0.018768	1.00E-12	.
N	0.1202	0.000431	0	0.018146	1.00E-12	.
LSPI	0.1887	0.000431	0	0.086628	1.00E-12	.

Average Non-expedited Transplant Rate						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	0.1411	0.000352	-0.01196	0	0	.
B	0.1389	0.000352	-0.01414	0	0	.
C	0.1427	0.000352	-0.01035	0	0	.
D	0.1501	0.000352	-0.00295	0	0.004355	.
E	0.1518	0.000352	0	0.002787	.	0.012378
F	0.1408	0.000352	-0.01233	0	0	.
G	0.1408	0.000352	-0.01233	0	0	.
H	0.1503	0.000352	-0.00279	0	0.012378	.
I	0.1388	0.000352	-0.01427	0	0	.
J	0.1396	0.000352	-0.01353	0	0	.
K	0.1499	0.000352	-0.0032	0	0.000683	.
L	0.1497	0.000352	-0.00337	0	0.00016	.
M	0.1381	0.000352	-0.01501	0	0	.
N	0.137	0.000352	-0.01607	0	0	.
LSPI	0.1491	0.000352	-0.004	0	0	.

Survival After Departure						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	2946.77	2.183	-254.6	0	1.00E-12	.
B	2820.05	2.183	-381.315	0	1.00E-12	.
C	3164.71	2.183	-36.66	0	1.00E-12	.
D	3017.08	2.183	-184.29	0	1.00E-12	.
E	2929.09	2.183	-272.277	0	1.00E-12	.
F	2939.96	2.183	-261.413	0	1.00E-12	.
G	2939.96	2.183	-261.413	0	1.00E-12	.
H	3193.51	2.183	0	36.6597	.	1.00E-12
I	2819.16	2.183	-382.21	0	1.00E-12	.
J	2818.99	2.183	-382.381	0	1.00E-12	.
K	2929.06	2.183	-272.313	0	1.00E-12	.
L	2928.57	2.183	-272.795	0	1.00E-12	.
M	2812.39	2.183	-388.977	0	1.00E-12	.
N	2818.58	2.183	-382.791	0	1.00E-12	.
LSPI	3016.63	2.183	-184.737	0	1.00E-12	.

Average Expedited Transplant Rate						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	0.227	0.000289	-0.0019	0.00018	0.13306	.
B	0.2275	0.000289	-0.00145	0.000631	0.59711	.
C	0.2274	0.000289	-0.00147	0.000606	0.56648	.
D	0.2268	0.000289	-0.00216	0	0.02941	.
E	0.001038	0.000289	-0.22788	0	0	.
F	0.2274	0.000289	-0.00149	0.000586	0.54343	.
G	0.2274	0.000289	-0.00149	0.000586	0.54343	.
H	0.001034	0.000289	-0.22788	0	0	.
I	0.2279	0.000289	-0.00099	0.001093	.	0.90931
J	0.2272	0.000289	-0.00176	0.00032	0.2435	.
K	0.227	0.000289	-0.0019	0.00018	0.13271	.
L	0.2271	0.000289	-0.00184	0.000236	0.17215	.
M	0.2272	0.000289	-0.00168	0.000403	0.32762	.
N	0.2278	0.000289	-0.00109	0.000986	0.90931	.
LSPI	0.2269	0.000289	-0.00202	5.88E-05	0.07052	.

Total Survival						
policy	Estimate	StdErr	cllo	clhi	rval	sval
A	3000.38	2.1808	-264.516	0	1.00E-12	.
B	2941.34	2.1808	-323.547	0	1.00E-12	.
C	3257.04	2.1808	0	30.4687	.	1.00E-12
D	3050.39	2.1808	-214.506	0	1.00E-12	.
E	2968.56	2.1808	-296.328	0	1.00E-12	.
F	3029.29	2.1808	-235.601	0	1.00E-12	.
G	3029.29	2.1808	-235.601	0	1.00E-12	.
H	3234.42	2.1808	-30.469	0	1.00E-12	.
I	2940.5	2.1808	-324.392	0	1.00E-12	.
J	2940.46	2.1808	-324.428	0	1.00E-12	.
K	2962.21	2.1808	-302.687	0	1.00E-12	.
L	2961.85	2.1808	-303.038	0	1.00E-12	.
M	2931	2.1808	-333.89	0	1.00E-12	.
N	2937.18	2.1808	-327.708	0	1.00E-12	.
LSPI	3049.59	2.1808	-215.298	0	1.00E-12	.

Figure 31: Performance metrics obtained for various allocation policies B-II.

percentage of livers unused			waiting time before death			waiting time before transplant		
policy	**mean**	**std dev.**	**policy**	**mean**	**std dev.**	**policy**	**mean**	**std dev.**
B	0	0.00E+00	J	117.8	35.35	LSPI	32.751	9.319
C	0	0	I	116.77	34.37	K	33.03	9.396
F	0	0	B	116	34.77	L	33.169	9.547
G	0	0	M	113.14	32.03	D	33.243	9.826
I	0	0	N	112.16	31.98	E	39.402	9.828
J	0	0.000000	F	88.187	22.421	H	40.729	11.13
M	0	0	G	88.187	22.421	A	54.035	10.929
N	0	0	C	87.102	27.881	F	89.525	12.081
A	4.28E-05	0.001026	A	51.5	14.317	G	89.525	12.081
E	0.00061	0.004280	H	41.789	13.575	C	92.94	14.72
H	0.000888	0.005369	E	39.77	11.661	M	119.34	14.72
L	0.001669	0.007284	LSPI	33.878	11.196	N	119.46	14.68
K	0.001696	0.007083	L	33.739	11.065	I	121.88	14.7
LSPI	0.001776	0.007282	K	33.678	10.768	B	121.92	14.49
D	0.002167	0.008316	D	33.595	11.352	J	121.93	14.52

Figure 32: Performance metrics obtained for various allocation policies B-I.

5.5.3 Structure and Performance of the Policies

In this section, first we examine the structure of the policies generated via LSPI method under the objectives, maximizing transplant rate and maximizing average survival gain per patient. Second, we compare the performances of these policies with those of the policies constructed in Chapter 4.

We feed the policies generated via LSPI into the simulation model (SIM1) of Chapter 4 which simulates the whole matrix instead of the "partial matrix" N. In Figure 33 and Figure 34, we present the fraction of expedited livers assigned to each (i, j) pair for the objectives, maximizing transplant rate and maximizing average survival gain per patient, respectively. These fractions include information on both the expedited liver allocation policy being simulated and the patient distribution among the (i, j) pairs, because the allocation

of the expedited organ is also dependent on which (i, j) pairs are populated and which (i, j) pairs are empty. In each figure, we highlight one hundred (i, j) pairs with the highest fractions. The darker the highlight, the larger the fraction.

Type\MELD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	0	0	0	0.090046	0.046806	0.018139	0.032351	0.040202	0.021969	0.010064	0.004439	0.002840	0.002561	0.000521	0.000324	0.000550	0.000400	0.000419
2	0	0	0	0.071247	0.047942	0.018372	0.023162	0.028992	0.025493	0.009116	0.005078	0.006799	0.002971	0.000755	0.000494	0.000244	0.000236	0.000156
3	0	0	0	0.063590	0.041268	0.015516	0.007231	0.005010	0.004099	0.002185	0.001361	0.000820	0.000707	0.000246	0.000176	0.000151	0.000225	0.000259
4	0	0	0	0.117644	0.088873	0.034402	0.019526	0.013145	0.008914	0.004716	0.002072	0.001090	0.001156	0.000582	0.000739	0.000834	0.000786	0.001135
5	0	0	0	0	0.002124	0.002109	0.001481	0.000423	0.000147	0.000080	0.000058	0.000049	0.000151	0.000010	0.000011	0.000012	0	0
6	0	0	0	0	0.000571	0.000178	0.000097	0.000085	0.000068	0.000292	0.000069	0.000020	0.000025	0.000013	0.000017	0.000051	0.000101	0.000047
7	0	0	0	0	0.000907	0.000456	0.000757	0.000133	0.000075	0.000020	0.000004	0.000007	0.000019	0.000005	0.000056	0.000116	0.000063	0.000023
8	0	0	0	0	0.000213	0.000334	0.001664	0.001154	0.000926	0.000672	0.000320	0.000141	0.000178	0.000054	0.000102	0.000201	0.000096	0.000122
9	0	0	0	0	0.001902	0.001087	0.001098	0.000243	0.000097	0.000125	0.000278	0.000240	0.000261	0.000160	0.000131	0.000291	0.000193	0.000163
10	0	0	0	0	0.000848	0.000177	0.000082	0.000072	0.000067	0.000216	0.000049	0.000017	0.000017	0.000008	0.000034	0.000120	0.000128	0.000116
11	0	0	0	0	0	0.000100	0.000698	0.000172	0.000029	0.000015	0.000005	0.000005	0.000003	0.000008	0.000002	0	0	0
12	0	0	0	0	0	0.000020	0.000002	0.000002	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0.000257	0.000065	0.000431	0.000207	0.000450	0.000154	0.000183	0.000147	0.000069	0.000105	0.000127	0.000058	0.000086
14	0	0	0	0	0	0	0	0	0.000003	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0.000003	0.000010	0.000027	0.000038	0.000104	0.000045	0.000060	0.000085	0.000074	0.000043	0.000007	0.000008
16	0	0	0	0	0	0	0	0	0.000093	0.000034	0.000098	0.000009	0.000005	0.000012	0	0.000010	0.000020	0.000014
17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0.000815	0.000371	0.000173	0.000180	0.000052	0.000013	0.000015	0.000015	0.000100
19	0	0	0	0	0	0	0	0	0	0	0.002081	0.000975	0.000597	0.000241	0.000200	0.000240	0.000291	0.000280
20	0	0	0	0	0	0	0	0	0	0	0.002861	0.001627	0.000774	0.000623	0.000491	0.000459	0.000480	0.000767
21	0	0	0	0	0	0	0	0	0	0	0.000087	0.000059	0.000008	0.000030	0.000038	0.000109	0.000042	0.000030
22	0	0	0	0	0	0	0	0	0	0	0.000145	0.000082	0.000042	0.000011	0.000008	0.000003	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0.000076	0.000015	0.000013	0	0.000053	0.000010	0
25	0	0	0	0	0	0	0	0	0	0	0	0.000003	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0.000081	0.000066	0.000051	0.000128	0.000037	0.000012	0.000017
27	0	0	0	0	0	0	0.000083	0.000059	0.000062	0.000032	0.000061	0.000069	0.000084	0.000067	0.000016	0.000010	0.000008	0.000029
28	0	0	0	0	0	0	0.000015	0.000020	0.000020	0.000036	0.000104	0.000030	0.000086	0.000043	0.000007	0	0.000010	0.000045
29	0	0	0	0	0	0	0.000181	0.000377	0.000134	0.000194	0.000288	0.000102	0.000184	0.000213	0.000095	0.000015	0.000016	0.000084
30	0	0	0	0	0	0	0.000037	0.000031	0.000125	0.000040	0.000008	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0.000038	0.000007	0.000010	0.000061	0.000005	0	0.000003	0	0	0
32	0	0	0	0	0	0	0	0	0.000008	0.000005	0.000002	0.000003	0.000030	0.000011	0.000038	0.000007	0.000002	0.000003

Figure 33: Fraction of expedited livers assigned to each (i, j) pair under the objective of maximizing transplant rate.

Type\MELD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	0	0	0	0.102684	0.038865	0.019150	0.030248	0.040844	0.017329	0.009001	0.003355	0.001404	0.000673	0.000126	0.000209	0.000317	0.000285	0.000276
2	0	0	0	0.073472	0.045823	0.023497	0.021861	0.029921	0.020355	0.009033	0.004353	0.003553	0.001336	0.000178	0.000220	0.000189	0.000167	0.000141
3	0	0	0	0.059459	0.053007	0.014646	0.008117	0.004865	0.004119	0.002067	0.001401	0.000838	0.000609	0.000199	0.000135	0.000156	0.000231	0.000199
4	0	0	0	0.137476	0.078541	0.027711	0.019471	0.014150	0.008921	0.004823	0.002101	0.001135	0.001023	0.000478	0.000732	0.000799	0.000728	0.000936
5	0	0	0	0	0.002073	0.002315	0.001569	0.000463	0.000167	0.000075	0.000038	0.000027	0.000097	0.000033	0.000011	0.000013	0.000005	0.000002
6	0	0	0	0	0.000708	0.000196	0.000108	0.000084	0.000084	0.000291	0.000060	0.000028	0.000007	0.000019	0.000018	0.000044	0.000124	0.000042
7	0	0	0	0	0.000848	0.000476	0.000779	0.000180	0.000053	0.000024	0.000014	0.000008	0.000005	0.000000	0.000034	0.000128	0.000060	0.000032
8	0	0	0	0	0.000204	0.000357	0.001634	0.001422	0.001154	0.000721	0.000407	0.000191	0.000210	0.000064	0.000081	0.000219	0.000128	0.000123
9	0	0	0	0	0.002151	0.001084	0.001062	0.000229	0.000073	0.000116	0.000298	0.000289	0.000267	0.000148	0.000126	0.000292	0.000197	0.000155
10	0	0	0	0	0.000858	0.000195	0.000081	0.000081	0.000107	0.000193	0.000056	0.000030	0.000020	0.000003	0.000023	0.000111	0.000112	0.000087
11	0	0	0	0	0	0.000114	0.000772	0.000127	0.000040	0.000012	0.000010	0.000000	0.000000	0.000003	0	0	0	0
12	0	0	0	0	0	0.000032	0.000010	0.000003	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0.000293	0.000114	0.000412	0.000209	0.000472	0.000174	0.000158	0.000094	0.000077	0.000132	0.000123	0.000081	0.000075
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0.000003	0.000027	0.000030	0.000049	0.000115	0.000043	0.000048	0.000066	0.000091	0.000057	0.000023	0.000007
16	0	0	0	0	0	0	0	0	0.000101	0.000065	0.000075	0.000028	0.000002	0	0	0.000013	0.000044	0.000009
17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0.000958	0.000345	0.000191	0.000167	0.000046	0.000023	0.000012	0.000031	0.000147
19	0	0	0	0	0	0	0	0	0	0	0.002380	0.001190	0.000695	0.000249	0.000185	0.000202	0.000294	0.000277
20	0	0	0	0	0	0	0	0	0	0	0.003575	0.001890	0.000766	0.000642	0.000569	0.000435	0.000494	0.000845
21	0	0	0	0	0	0	0	0	0	0	0.000098	0.000065	0.000023	0.000030	0.000046	0.000166	0.000022	0.000020
22	0	0	0	0	0	0	0	0	0	0	0.000123	0.000092	0.000044	0.000011	0.000007	0	0.000003	0
23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0.000072	0.000020	0.000010	0.000012	0.000042	0.000015	0.000006
25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0.000103	0.000062	0.000037	0.000117	0.000022	0.000007	0
27	0	0	0	0	0	0	0.000108	0.000110	0.000059	0.000051	0.000057	0.000087	0.000108	0.000072	0.000012	0.000005	0.000015	0.000032
28	0	0	0	0	0	0	0.000013	0.000023	0.000010	0.000039	0.000050	0.000029	0.000103	0.000030	0.000003	0.000000	0.000002	0.000033
29	0	0	0	0	0	0	0.000083	0.000379	0.000124	0.000171	0.000250	0.000088	0.000133	0.000167	0.000056	0.000031	0.000029	0.000076
30	0	0	0	0	0	0	0.000055	0.000026	0.000112	0.000037	0.000010	0.000002	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0.000026	0.000008	0.000007	0.000021	0.000018	0	0.000005	0	0	0
32	0	0	0	0	0	0	0	0	0	0.000003	0.000000	0.000005	0.000023	0.000012	0.000033	0.000005	0.000003	0.000003

Figure 34: Fraction of expedited livers assigned to each (i, j) pair under the objective of maximizing average survival gain per patient.

In Figure 35 and Figure 36, we also present the priority of each (i, j) pair for receiving the organ of a white female donor who is younger than 20 years old and of blood type O if there is one patient listed at the center from each (i, j) pair. We assume all patients are female and of the blood type O. We highlight the first one hundred (i, j) pair with the highest priorities. The darker the highlight, the higher the priority. As the figures indicate we mostly favor disease group 1 patients, i.e., patient types 1-15, over disease group 2 patients, i.e., patient types 16-26. When we compare Figure 33-34 and Figure 35-36, we observe that while disease group 3 patients, i.e., patient types 27-32, have high priorities for receiving expedited livers,

the fraction of the expedited livers assigned to them is low. The reason of that is at any time we do not observe many disease group 3 patients listed at the center.

Type\MELD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	0	0	0	2	4	6	8	10	13	14	17	19	21	25	29	31	37	39
2	0	0	0	1	3	5	7	9	11	12	15	16	18	20	23	26	32	34
3	0	0	0	24	28	33	38	43	47	53	60	68	76	89	93	94	95	96
4	0	0	0	22	27	30	36	42	46	51	58	64	70	81	86	97	98	99
5	0	0	0	0	49	54	61	67	79	90	100	101	102	103	104	105	106	107
6	0	0	0	0	52	57	65	74	83	108	109	110	111	112	113	114	115	116
7	0	0	0	0	63	72	82	92	117	118	119	120	121	122	123	124	125	126
8	0	0	0	0	127	128	129	130	131	132	133	134	135	136	137	138	139	140
9	0	0	0	0	69	80	91	141	142	143	144	145	146	147	148	149	150	151
10	0	0	0	0	152	153	154	155	156	157	158	159	160	161	162	163	164	165
11	0	0	0	0	0	166	167	168	169	170	171	172	173	174	175	176	177	274
12	0	0	0	0	0	178	179	180	181	182	183	184	185	186	187	188	278	284
13	0	0	0	0	0	189	190	191	192	193	194	195	196	197	198	199	200	279
14	0	0	0	0	0	0	201	202	203	204	205	206	207	208	209	280	295	299
15	0	0	0	0	0	0	210	211	212	213	214	215	216	217	275	288	301	307
16	0	0	0	0	0	0	0	0	218	219	220	221	222	223	224	225	282	287
17	0	0	0	0	0	0	0	0	0	226	227	228	229	230	231	232	283	289
18	0	0	0	0	0	0	0	0	0	233	234	235	236	277	285	291	297	302
19	0	0	0	0	0	0	0	0	0	0	237	238	276	281	286	292	300	305
20	0	0	0	0	0	0	0	0	0	0	293	298	303	308	309	311	314	318
21	0	0	0	0	0	0	0	0	0	0	290	294	296	304	306	310	312	315
22	0	0	0	0	0	0	0	0	0	0	317	320	322	324	326	330	336	339
23	0	0	0	0	0	0	0	0	0	0	0	313	316	319	321	323	327	331
24	0	0	0	0	0	0	0	0	0	0	0	333	335	341	343	347	352	353
25	0	0	0	0	0	0	0	0	0	0	0	325	329	334	338	342	345	349
26	0	0	0	0	0	0	0	0	0	0	0	348	350	355	357	358	360	362
27	0	0	0	0	0	0	328	332	337	340	344	346	351	354	356	359	361	363
28	0	0	0	0	0	0	41	45	50	56	62	71	75	87	239	240	241	242
29	0	0	0	0	0	0	35	40	44	48	55	59	66	73	77	88	243	244
30	0	0	0	0	0	0	78	85	245	246	247	248	249	250	251	252	253	254
31	0	0	0	0	0	0	0	0	84	255	256	257	258	259	260	261	262	263
32	0	0	0	0	0	0	0	0	264	265	266	267	268	269	270	271	272	273

Figure 35: Priority of each (i, j) pair under the objective of maximizing transplant rate.

Type\MELD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	0	0	0	2	4	6	8	10	14	24	32	66	159	285	232	258	283	338
2	0	0	0	1	3	5	7	9	11	22	27	61	155	282	228	257	279	337
3	0	0	0	13	16	18	20	30	40	80	92	124	180	299	241	261	286	339
4	0	0	0	12	15	17	19	28	39	78	91	119	176	298	240	262	287	340
5	0	0	0	0	25	29	33	45	77	93	104	128	188	300	242	263	288	341
6	0	0	0	0	26	31	35	62	79	94	105	129	187	301	243	264	289	342
7	0	0	0	0	34	38	43	68	81	95	106	130	189	302	244	265	290	343
8	0	0	0	0	47	48	54	69	82	96	107	131	190	303	245	266	291	344
9	0	0	0	0	37	42	46	70	83	97	108	132	191	304	246	267	292	345
10	0	0	0	0	49	50	55	71	84	98	109	133	192	305	247	268	293	346
11	0	0	0	0	0	51	56	72	85	99	110	134	193	306	248	269	294	347
12	0	0	0	0	0	52	57	73	86	100	111	135	194	307	249	270	311	349
13	0	0	0	0	0	53	58	74	87	101	112	136	195	308	250	271	295	348
14	0	0	0	0	0	0	59	75	88	102	113	137	196	309	251	296	312	350
15	0	0	0	0	0	0	60	76	89	103	114	138	197	310	274	297	313	351
16	0	0	0	0	0	0	0	0	67	63	115	120	177	200	198	205	259	324
17	0	0	0	0	0	0	0	0	0	64	116	121	178	201	199	206	260	325
18	0	0	0	0	0	0	0	0	0	65	117	122	179	214	209	236	272	327
19	0	0	0	0	0	0	0	0	0	0	118	123	204	217	210	237	273	328
20	0	0	0	0	0	0	0	0	0	0	151	163	208	224	216	239	276	330
21	0	0	0	0	0	0	0	0	0	0	150	158	207	222	212	238	275	329
22	0	0	0	0	0	0	0	0	0	0	164	166	213	231	223	253	278	332
23	0	0	0	0	0	0	0	0	0	0	0	165	211	229	220	252	277	331
24	0	0	0	0	0	0	0	0	0	0	0	170	219	234	226	255	281	334
25	0	0	0	0	0	0	0	0	0	0	0	168	218	233	225	254	280	333
26	0	0	0	0	0	0	0	0	0	0	0	171	221	235	230	256	284	335
27	0	0	0	0	0	0	154	147	202	186	215	181	203	227	336	326	357	363
28	0	0	0	0	0	0	41	23	148	127	169	139	152	182	320	315	352	358
29	0	0	0	0	0	0	36	21	146	125	167	126	149	175	319	314	353	359
30	0	0	0	0	0	0	90	44	156	143	172	140	160	183	321	316	354	360
31	0	0	0	0	0	0	0	0	153	144	173	141	161	184	322	317	355	361
32	0	0	0	0	0	0	0	0	157	145	174	142	162	185	323	318	356	362

Figure 36: Priority of each (i, j) pair under the objective of maximizing average survival gain per patient.

We investigate how the policies generated via LSPI method perform if we consider all the patients listed at the center, not only the ones included in "partial matrix" N. This examination will enable us to compare the results of Chapter 4 with that of this and previous sections. However, one detail that has to be kept in mind is that while SIM1 differentiates among the blood type matches between donor and patients, the construction of the LSPI policy has no such consideration. The consideration of blood type matches affects the patient population attributes, i.e., who is the right person to leave the system. Thus, the patient populations in the simulation model and the analytical model do not match completely.

We feed the policies generated via LSPI method into the simulation model (SIM1) of Chapter 4. We call the resulting policy of Section 5.5.1 LSPI_I and that of Section 5.5.2 LSPI_II. Please refer to Figure 8 for the descriptions of policies of Chapter 4. In Figure 37, the values obtained for various performance metrics are presented. We observe that LSPI methods cannot compete with the policies constructed in Chapter 4. This might be attributed to the high rate of unused organs and the discrepancy in the patient population attributes in the simulation model and the analytical model.

Average Transplant Rate

policy	Estimate	StdErr	cllo	clhi	rval	sval
A	0.4704	0.000492	-0.02258	0	0	.
B	0.4894	0.000492	-0.00356	1.69E-05	0.05308	.
C	0.4912	0.000492	-0.00065	0.002926	.	0.30295
D	0.4642	0.000492	-0.02872	0	0	.
E	0.4653	0.000492	-0.02763	0	0	.
F	0.4656	0.000492	-0.02737	0	0	.
G	0.4811	0.000492	-0.01185	0	0	.
H	0.4684	0.000492	-0.02451	0	0	.
I	0.4899	0.000492	-0.00307	0.000507	0.22317	.
J	0.49	0.000492	-0.00293	0.000646	0.30295	.
K	0.462	0.000492	-0.03094	0	0	.
L	0.4621	0.000492	-0.0308	0	0	.
M	0.4873	0.000492	-0.00568	0	0	.
N	0.4886	0.000492	-0.00432	0	0.00182	.
LSPI_I	0.4691	0.000492	-0.02384	0	0	.
LSPI_II	0.4665	0.000492	-0.02643	0	0	.

Survival After Departure

policy	Estimate	StdErr	cllo	clhi	rval	sval
A	2852.18	1.7727	-155.804	0	1.00E-12	.
B	2881.48	1.7727	-126.506	0	1.00E-12	.
C	3001.55	1.7727	0	32.6508	.	1.00E-12
D	2859.66	1.7727	-148.326	0	1.00E-12	.
E	2784.4	1.7727	-223.583	0	1.00E-12	.
F	2764.36	1.7727	-243.623	0	1.00E-12	.
G	2927.35	1.7727	-80.633	0	1.00E-12	.
H	2975.33	1.7727	-32.651	0	1.00E-12	.
I	2879.5	1.7727	-128.483	0	1.00E-12	.
J	2877.05	1.7727	-130.933	0	1.00E-12	.
K	2812.27	1.7727	-195.717	0	1.00E-12	.
L	2811.97	1.7727	-196.011	0	1.00E-12	.
M	2877.57	1.7727	-130.414	0	1.00E-12	.
N	2877.68	1.7727	-130.3	0	1.00E-12	.
LSPI_I	2969.83	1.7727	-38.148	0	1.00E-12	.
LSPI_II	2944.26	1.7727	-63.725	0	1.00E-12	.

% of Patients Died

policy	Estimate	StdErr	cllo	clhi	rval	sval
A	0.1414	0.000355	0	0.039374	0	.
B	0.1047	0.000355	0	0.002702	0.025566	.
C	0.1033	0.000355	-0.00255	0.000022	.	0.055793
D	0.1526	0.000355	0	0.050589	0	.
E	0.1515	0.000355	0	0.049543	0	.
F	0.1495	0.000355	0	0.047533	0	.
G	0.1224	0.000355	0	0.020362	0	.
H	0.1465	0.000355	0	0.044526	0	.
I	0.1045	0.000355	-2.2E-05	0.002551	0.055793	.
J	0.1053	0.000355	0	0.003259	0.000576	.
K	0.157	0.000355	0	0.05504	0	.
L	0.1566	0.000355	0	0.054622	0	.
M	0.1098	0.000355	0	0.007835	0	.
N	0.1104	0.000355	0	0.008401	0	.
LSPI_I	0.1468	0.000355	0	0.044804	0	.
LSPI_II	0.15	0.000355	0	0.048023	0	.

Total Survival

policy	Estimate	StdErr	cllo	clhi	rval	sval
A	3068.52	1.8372	-214.569	0	1.00E-12	.
B	3183.86	1.8372	-99.237	0	1.00E-12	.
C	3276.43	1.8372	0	95.1064	.	1.00E-12
D	3049.55	1.8372	-233.54	0	1.00E-12	.
E	2986.26	1.8372	-296.832	0	1.00E-12	.
F	2974.75	1.8372	-308.341	0	1.00E-12	.
G	3187.99	1.8372	-95.106	0	1.00E-12	.
H	3180.26	1.8372	-102.832	0	1.00E-12	.
I	3180.79	1.8372	-102.3	0	1.00E-12	.
J	3179.31	1.8372	-103.781	0	1.00E-12	.
K	2993.45	1.8372	-289.64	0	1.00E-12	.
L	2993.56	1.8372	-289.529	0	1.00E-12	.
M	3174.07	1.8372	-109.025	0	1.00E-12	.
N	3175.13	1.8372	-107.963	0	1.00E-12	.
LSPI_I	3175.46	1.8372	-107.635	0	1.00E-12	.
LSPI_II	3146.33	1.8372	-136.759	0	1.00E-12	.

Figure 37: Comparison of the performances of the policies of Chapter 4 and the LSPI methods.

5.6 CONCLUSION

In this chapter, we present another solution approach to the expedited liver placement problem of a transplant center. We build two average reward Markov Decision Process (MDP) models. The only difference between the models is their objective function. The size of the state space and the intractable transition probabilities make the use of the traditional solution methods, i.e., policy iteration, impossible. Thus, we utilize an approximate dynamic programming approach, Least Squares Policy Iteration (LSPI).

Our extensive search on basis functions yields better results for the average reward MDP model with the objective of maximizing average survival gain per patient compared to the one with the objective of maximizing average transplant rate. This might be due to the fact that small differences in the objective function of maximizing average transplant rate are more difficult to detect compared to the larger differences in the objective function of maximizing average survival gain per patient.

Unfortunately, the statistical comparison of the performance of the policies generated via LSPI method with the policies constructed in Chapter 4 shows that the basis functions explored are insufficient to approximate the optimal policy. However, in terms of practical significance the results of the policy generated via LSPI method, specifically of the model with the objective of maximizing average survival gain per patient, is competitive with the other policies.

Independent of how practically or significantly well the policy generated via LSPI method performs based on the performance metrics, it always defines the optimal actions indirectly, i.e., via the Q values. Therefore, the policies of Chapter 4 are always more transparent compared to the policies of the LSPI method.

A possible direction for future research is the extension of the basis function set explored. Because the performance of the policies generated via LSPI method is highly dependent on the basis functions chosen, it is difficult to claim that the method is insufficient to approximate the optimal solution.

6.0 CONCLUSIONS AND FUTURE RESEARCH

6.1 CONCLUSIONS

In this dissertation, we examine fundamental and essential questions embedded in the liver allocation system. Namely, we study the decision problems faced by the two decision makers of the system, a patient and a transplant center.

In Chapter 3, we address a fundamental component of patient based accept/decline decision making models. Such models utilizes Quality Adjusted Life Years (QALYs) to evaluate the outcomes of decisions. Patient preferences constitutes a critical ingredient of QALYs. There exists direct approaches, which involve asking patients various abstract questions, to elicit patient preferences. However, they have significant drawbacks. We propose a new approach that infers patient preferences based on observed decisions via inverse optimization techniques. We illustrate our methods on the timing of a living-donor liver transplant.

In Chapter 4 and Chapter 5, we study the decision problem faced by a transplant center. The livers which are appeared not to be matched to a patient in a timely manner by the standard allocation procedure are offered to transplant centers. Then, the center makes a decision on the acceptance and allocation of the liver to its patients. Namely, the center decides which, if any, of its patients should receive the organ independent of their position on the match list. Such livers are called expedited livers. No one has considered optimizing the transplant centers decision on the expedited liver placement. We present two approaches to this decision problem.

We build a simulation model for the expedited placement problem faced by a transplant center in Chapter 4. We construct various allocation policies for the expedited liver placement. We parameterize our model using clinical data. We compare the allocation policies

via simulation. Our numerical study reveals that a policy which gives higher priorities to patients whose likelihood of death is higher than likelihood of receiving a non-expedited transplant performs the best based on several metrics, i.e., average transplant rate, total survival times.

We also develop a dynamic programming approach to the transplant center's decision problem. In Chapter 5, we construct two average reward Markov Decision Process models. The models differ in their objective function. One maximizes the average transplant rate and the other maximizes the average survival gain per patient. Due to the curse of dimensionality embedded in our models, we resort to approximate dynamic approaches to solve the decision problem. We utilize Least Square Policy Iteration (LSPI) method. The policies generated via the LSPI method statistically do not perform better than the allocation policies constructed in Chapter 4. However, they are practically competent compared to the allocation policies of Chapter 4.

6.2 FUTURE RESEARCH

The possible extensions to this dissertation are as follows.

In Chapter 3, we employ multiple assumptions in the construction of the model. Assumptions 1 and 2 can be relaxed through more complex optimization models. In addition, our model can be applied to different clinical decisions. Lastly, the inferred patient preferences can be utilized in societal decision models. Such a model , for example, could examine the effect of a different liver allocation system utilizing the inferred patient preferences.

The expedited organ placement problem is not unique to livers. For instance, such placement is frequently encountered in the allocation of lungs. Our decision models for expedited liver placement can be applied to different expedited organ placement problems. More allocation policies for the expedited liver placement can be constructed to increase the coverage of the feasible policy region. Moreover, our studies can be repeated using UNOS data. Such a study would increase the confidence in the datasets we use. Moreover, if different transplant centers are studied, the change in the outcome which depends on the

dynamics at the transplant center can be examined. A comprehensive dataset might also enable us to increase the level of detail we capture in liver and patient type definitions. We might also include blood type compatibility issue in our average reward MDP models. Lastly, the search on the basis functions fed into the LSPI method can be extended.

APPENDIX A

CHAPTER 4 - SIMULATION MODEL SIM1 PARAMETER VALUES

d			b	D(d,b)	d			b	D(d,b)	d			b	D(d,b)
age	**gender**	**race**	**blood type**		**age**	**gender**	**race**	**blood type**		**age**	**gender**	**race**	**blood type**	
<20	female	white	O	0.0038	31-40	female	non-white	B	0.0003	51-60	male	white	A	0.0065
<20	female	non-white	O	0.0010	31-40	female	white	AB	0.0005	51-60	male	non-white	A	0.0016
<20	female	white	A	0.0049	31-40	female	non-white	AB	0.0001	51-60	male	white	B	0.0038
<20	female	non-white	A	0.0012	31-40	male	white	O	0.0054	51-60	male	non-white	B	0.0010
<20	female	white	B	0	31-40	male	non-white	O	0.0014	51-60	male	white	AB	0.0022
<20	female	non-white	B	0	31-40	male	white	A	0.0054	51-60	male	non-white	AB	0.0005
<20	female	white	AB	0.0005	31-40	male	non-white	A	0.0014	61-70	female	white	O	0.0065
<20	female	non-white	AB	0.0001	31-40	male	white	B	0.0027	61-70	female	non-white	O	0.0016
<20	male	white	O	0.0044	31-40	male	non-white	B	0.0007	61-70	female	white	A	0.0065
<20	male	non-white	O	0.0011	31-40	male	white	AB	0.0011	61-70	female	non-white	A	0.0016
<20	male	white	A	0.0054	31-40	male	non-white	AB	0.0003	61-70	female	white	B	0.0011
<20	male	non-white	A	0.0014	41-50	female	white	O	0.0082	61-70	female	non-white	B	0.0003
<20	male	white	B	0.0011	41-50	female	non-white	O	0.0020	61-70	female	white	AB	0
<20	male	non-white	B	0.0003	41-50	female	white	A	0.0054	61-70	female	non-white	AB	0
<20	male	white	AB	0.0011	41-50	female	non-white	A	0.0014	61-70	male	white	O	0.0044
<20	male	non-white	AB	0.0003	41-50	female	white	B	0.0044	61-70	male	non-white	O	0.0011
21-30	female	white	O	0.0016	41-50	female	non-white	B	0.0011	61-70	male	white	A	0.0071
21-30	female	non-white	O	0.0004	41-50	female	white	AB	0.0011	61-70	male	non-white	A	0.0018
21-30	female	white	A	0	41-50	female	non-white	AB	0.0003	61-70	male	white	B	0.0033
21-30	female	non-white	A	0	41-50	male	white	O	0.0098	61-70	male	non-white	B	0.0008
21-30	female	white	B	0.0011	41-50	male	non-white	O	0.0024	61-70	male	white	AB	0.0005
21-30	female	non-white	B	0.0003	41-50	male	white	A	0.0174	61-70	male	non-white	AB	0.0001
21-30	female	white	AB	0	41-50	male	non-white	A	0.0044	>71	female	white	O	0.0044
21-30	female	non-white	AB	0	41-50	male	white	B	0.0038	>71	female	non-white	O	0.0011
21-30	male	white	O	0.0027	41-50	male	non-white	B	0.0010	>71	female	white	A	0.0044
21-30	male	non-white	O	0.0007	41-50	male	white	AB	0.0049	>71	female	non-white	A	0.0011
21-30	male	white	A	0.0022	41-50	male	non-white	AB	0.0012	>71	female	white	B	0.0022
21-30	male	non-white	A	0.0005	51-60	female	white	O	0.0065	>71	female	non-white	B	0.0005
21-30	male	white	B	0.0016	51-60	female	non-white	O	0.0016	>71	female	white	AB	0.0005
21-30	male	non-white	B	0.0004	51-60	female	white	A	0.0071	>71	female	non-white	AB	0.0001
21-30	male	white	AB	0.0016	51-60	female	non-white	A	0.0018	>71	male	white	O	0.0082
21-30	male	non-white	AB	0.0004	51-60	female	white	B	0.0027	>71	male	non-white	O	0.0020
31-40	female	white	O	0.0016	51-60	female	non-white	B	0.0007	>71	male	white	A	0.0060
31-40	female	non-white	O	0.0004	51-60	female	white	AB	0.0027	>71	male	non-white	A	0.0015
31-40	female	white	A	0.0022	51-60	female	non-white	AB	0.0007	>71	male	white	B	0.0016
31-40	female	non-white	A	0.0005	51-60	male	white	O	0.0114	>71	male	non-white	B	0.0004
31-40	female	white	B	0.0011	51-60	male	non-white	O	0.0029	>71	male	white	AB	0.0005
										>71	male	non-white	AB	0.0001

Figure 38: Expedited liver arrival probabilities, $\mathcal{D}(d, b)$.

type\MELD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	0.009346	0.007009	0.015187	0.017523	0.01285	0.003505	0.011682	0.024533	0.011682	0.007009	0.002336	0.002336	0.003505	0	0.001168	0.002336	0.002336	0.003505
2	0.009346	0.01285	0.016355	0.005841	0.016355	0.007009	0.007009	0.016355	0.014019	0.005841	0.002336	0.007009	0.002336	0	0.001168	0	0.001168	0.001168
3	0.004673	0.011682	0.018692	0.01986	0.011682	0.010514	0.007009	0.003505	0.011682	0.002336	0.004673	0.002336	0.002336	0.001168	0	0	0.002336	0.003505
4	0.010514	0.018692	0.026869	0.029206	0.045561	0.017523	0.016355	0.015187	0.021028	0.008178	0.003505	0.001168	0.003505	0.003505	0.005841	0.003505	0.004673	0.01285
5	0	0	0.001168	0.001168	0	0.002336	0.002336	0	0	0	0	0	0.001168	0	0	0	0	0
6	0	0.001168	0	0	0	0	0	0	0	0.001168	0	0	0	0	0	0	0.001168	0
7	0	0	0.001168	0.001168	0	0	0.001168	0	0	0	0	0	0	0	0	0.001168	0	0
8	0	0	0	0	0	0	0.002336	0.001168	0.002336	0.001168	0.001168	0	0.001168	0	0	0.002336	0	0.001168
9	0	0	0.001168	0.001168	0.002336	0.001168	0.001168	0	0	0	0.001168	0.001168	0.001168	0.001168	0	0.002336	0.001168	0.001168
10	0	0	0.001168	0.001168	0.001168	0	0	0	0	0.001168	0	0	0	0	0	0.001168	0.001168	0.001168
11	0	0	0	0	0	0	0.001168	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0.001168	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0.002336	0.001168	0	0.001168	0	0.002336	0	0.001168	0	0.001168	0.001168	0.001168	0	0.001168
14	0	0	0	0	0	0	0	0	0	0	0	0	0.001168	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0.001168	0	0	0.001168	0.001168	0	0	0
16	0	0	0	0.002336	0	0.001168	0	0	0.001168	0	0.001168	0	0	0	0	0	0.001168	0
17	0	0.002336	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	0.001168	0	0.001168	0.002336	0	0	0.002336	0.002336	0.002336	0.001168	0	0	0.001168	0	0	0	0	0.001168
19	0.001168	0.005841	0.010514	0.004673	0.008178	0.004673	0.003505	0.004673	0.002336	0	0.001168	0	0.002336	0	0	0.001168	0.002336	0.001168
20	0.008178	0.010514	0.011682	0.017523	0.018692	0.010514	0.005841	0.005841	0.008178	0.001168	0.004673	0.004673	0.002336	0.004673	0.001168	0.001168	0.001168	0.008178
21	0	0	0	0.001168	0.001168	0.001168	0	0	0	0.002336	0	0	0	0	0	0.001168	0	0
22	0	0.001168	0.005841	0.003505	0.002336	0.001168	0.001168	0.001168	0.002336	0.001168	0.001168	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0.001168	0	0	0	0	0	0	0	0	0
24	0	0	0.001168	0	0	0.001168	0.001168	0	0.001168	0	0.001168	0	0	0	0	0.001168	0	0
25	0	0	0	0	0	0.003505	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0.004673	0.002336	0.001168	0	0	0.001168	0.001168	0.001168	0	0	0	0.001168	0	0	0
27	0	0	0	0	0.002336	0	0	0.001168	0.001168	0	0.001168	0.001168	0.002336	0.001168	0	0	0	0.001168
28	0	0	0	0	0	0	0	0	0	0	0.001168	0	0.001168	0	0	0	0	0.001168
29	0	0	0	0	0	0	0	0.002336	0	0.001168	0.003505	0	0.001168	0.002336	0.001168	0	0	0.002336
30	0	0	0	0	0.001168	0	0	0	0.001168	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0.001168	0	0	0.001168	0	0	0	0.001168	0	0	0	0	0	0
32	0	0	0	0	0.002336	0	0	0	0	0	0	0	0.001168	0	0.001168	0	0	0

Figure 39: The likelihood that when a patient joins the list, she is of type i and MELD score j, ρ_{ij}.

type\MELD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	0.000289	0.000326	0.00014	0.000301	0.001259	0.001019	0.000912	0.0042	0.00799	0.006479	0.008011	0.00511	0.01266	0.06017	0.062299	0.021958	0.017661	0.08643
2	0.000931	0.000448	0.000799	0.000741	0.001159	0.00033	0.00076	0.003239	0.00957	0.004269	0.00931	0.02278	0.0215	0.03485	0.021422	0.0308	0.021319	0.085171
3	0.000449	0.000141	0.000261	0.001279	0.00077	0.001371	0.00048	0.00399	0.007921	0.00828	0.009629	0.01642	0.01371	0.05443	0.039569	0.054691	0.04585	0.08458
4	0.00023	0.00011	0.00081	0.00066	0.00143	0.00184	0.00163	0.0022	0.011	0.01613	0.01152	0.01245	0.0144	0.05465	0.02683	0.02821	0.03744	0.05474
5	0.000308	0.000382	0.001156	0.000842	0.002362	0.00189	0.006352	0.006654	0.00793	0.013408	0.024892	0.028966	0.03906	0.030676	0.038148	0.13873	0.033946	0.154724
6	0.000894	0.000914	0.000896	0.00203	0.00131	0.004218	0.006422	0.008572	0.05547	0.03269	0.028776	0.030074	0.014976	0.041892	0.058706	0.00732	0.03476	0.012206
7	0.000758	0.001636	0.001248	0.00156	0.004298	0.006518	0.007724	0.016768	0.011496	0.022524	0.024408	0.024724	0.025792	0.034342	0.047474	0.017218	0.045598	0.065438
8	0.001016	0.00239	0.001904	0.003576	0.00501	0.010186	0.009462	0.00331	0.00576	0.025768	0.03763	0.035296	0.056148	0.071178	0.029732	0.02161	0.049752	0.032322
9	0.001516	0.001662	0.001826	0.006766	0.00503	0.00207	0.00732	0.028192	0.035954	0.060236	0.035542	0.01906	0.029418	0.04555	0.011266	0.02821	0.07722	0.07675
10	0.002066	0.002882	0.004168	0.005144	0.010404	0.011876	0.01571	0.027028	0.030086	0.033072	0.02955	0.025046	0.12346	0.02586	0.16127	0.09215	0.03132	0.14686
11	0.003218	0.002338	0.007388	0.005002	0.011926	0.02151	0.0156	0.03273	0.030894	0.047116	0.03035	0.015994	0.043612	0.00339	0.013924	0.1785	0.008638	0.158004
12	0.002488	0.00283	0.006818	0.010044	0.022806	0.01273	0.038684	0.018416	0.036474	0.0147	0.016918	0.028172	0.055588	0.044512	0.027668	0.086042	0.044348	0.051376
13	0.005444	0.017118	0.010646	0.021864	0.02734	0.039504	0.039904	0.024962	0.00695	0.037112	0.01333	0.046774	0.027672	0.04041	0.0752	0.05134	0.11109	0.072958
14	0.004314	0.010832	0.01159	0.020328	0.037974	0.032084	0.026586	0.016764	0.048946	0.024798	0.022044	0.01605	0.043846	0.052942	0.043104	0.28304	0.040798	0.084082
15	0.00822	0.024582	0.013838	0.023992	0.024358	0.021326	0.015846	0.024416	0.016274	0.01708	0.04625	0.08041	0.018608	0.09631	0.062834	0.050892	0.0562	0.053792
16	0.008446	0.016842	0.014272	0.02653	0.021484	0.00946	0.035548	0.032952	0.029372	0.024692	0.060648	0.06236	0.061782	0.022086	0.237432	0.08642	0.059958	0.05469
17	0.012782	0.024638	0.02462	0.02715	0.028324	0.049158	0.010688	0.025982	0.008216	0.009568	0.051838	0.177294	0.105684	0.08272	0.056086	0.022538	0.132066	0.07135
18	0.02535	0.021134	0.021164	0.009764	0.017282	0.022092	0.00893	0.015158	0.00721	0.00464	0.066278	0.02888	0.040636	0.216588	0.096362	0.042828	0.095862	0.09916
19	0.024608	0.026642	0.00033	0.00092	0.00275	0.00164	0.00259	0.00137	0.00672	0.00437	0.037182	0.00921	0.01509	0.02693	0.081868	0.147748	0.0872	0.03116
20	0.00099	0.00135	0.0014	0.00056	0.00241	0.00237	0.00407	0.00285	0.02521	0.01316	0.01529	0.02439	0.117894	0.01649	0.01417	0.01635	0.01553	0.09298
21	0.028054	0.033888	0.02648	0.036788	0.040974	0.04131	0.059948	0.01333	0.108178	0.042652	0.06584	0.05845	0.036808	0.03957	0.084238	0.03242	0.296422	0.177812
22	0.024644	0.044064	0.00254	0.00323	0.00337	0.051654	0.050852	0.048622	0.01272	0.00601	0.221054	0.024022	0.04205	0.051222	0.076536	0.066362	0.10185	0.28047
23	0.005636	0.007998	0.038038	0.016642	0.060132	0.05793	0.034904	0.09713	0.054954	0.084304	0.109454	0.192266	0.087284	0.162554	0.247256	0.1571	0.159038	0.152378
24	0.018976	0.005208	0.012436	0.062158	0.06565	0.062082	0.059582	0.090024	0.02938	0.062508	0.01732	0.052242	0.044264	0.031314	0.071652	0.264226	0.326672	0.36825
25	0.032298	0.01458	0.045596	0.049974	0.025926	0.08595	0.040062	0.034242	0.026424	0.178348	0.090964	0.118668	0.045082	0.160196	0.46361	0.196384	0.230824	0.241896
26	0.012792	0.072204	0.050932	0.036166	0.024434	0.019052	0.00153	0.00179	0.00241	0.102816	0.00657	0.01093	0.045268	0.03351	0.02805	0.380262	0.07354	0.21192
27	0.047802	0.022024	0.030228	0.027006	0.04209	0.04367	0.01553	0.211292	0.12089	0.18661	0.13506	0.150244	0.069488	0.253786	0.22369	0.776014	0.337362	0.27208
28	0.012314	0.100176	0.075732	0.046514	0.030252	0.044976	0.132164	0.057966	0.109594	0.082088	0.08054	0.407598	0.031948	0.263984	0.82073	0.97096	0.361108	0.34375
29	0.050718	0.019942	0.037582	0.02072	0.079782	0.60426	0.21961	0.02297	0.18582	0.068068	0.181158	0.077496	0.15826	0.21357	0.37029	0.29669	0.405738	0.4217
30	0.033942	0.030726	0.091554	0.04672	0.063942	0.086338	0.020458	0.09312	0.037324	0.03479	0.61927	0.157626	0.408198	0.607912	0.656622	0.296258	0.666034	0.30567
31	0.072212	0.023466	0.075212	0.07686	0.25078	0.044312	0.064582	0.04178	0.033424	0.091842	0.36726	0.33056	0.516526	0.481878	0.26104	0.416778	0.337362	0.342284
32	0.032906	0.024498	0.014828	0.208882	0.01057	0.041284	0.073954	0.040512	0.188894	0.189642	0.124118	0.222348	0.496212	0.391404	0.472216	0.21192	0.720076	0.432508

Figure 40: The daily probability that a patient of type i and MELD score j receives a non-expedited transplant, $\xi_i(j)$.

APPENDIX B

CHAPTER 5 - AVERAGE REWARD MARKOV DECISION PROCESS MODEL PARAMETER VALUES

d			D(d)	D(d) - adjusted
age	**gender**	**race**		
<20	female	white	0.0081	0.0092
<20	female	non-white	0.0020	0.0023
<20	male	white	0.0105	0.0119
<20	male	non-white	0.0026	0.0030
21-30	female	white	0.0024	0.0027
21-30	female	non-white	0.0006	0.0007
21-30	male	white	0.0071	0.0081
21-30	male	non-white	0.0018	0.0020
31-40	female	white	0.0048	0.0054
31-40	female	non-white	0.0012	0.0014
31-40	male	white	0.0128	0.0146
31-40	male	non-white	0.0033	0.0037
41-50	female	white	0.0167	0.0190
41-50	female	non-white	0.0041	0.0047
41-50	male	white	0.0315	0.0358
41-50	male	non-white	0.0079	0.0090
51-60	female	white	0.0167	0.0190
51-60	female	non-white	0.0041	0.0047
51-60	male	white	0.0210	0.0239
51-60	male	non-white	0.0053	0.0060
61-70	female	white	0.0124	0.0141
61-70	female	non-white	0.0031	0.0035
61-70	male	white	0.0134	0.0152
61-70	male	non-white	0.0033	0.0038
>71	female	white	0.0100	0.0114
>71	female	non-white	0.0025	0.0028
>71	male	white	0.0143	0.0163
>71	male	non-white	0.0036	0.0041

Figure 41: Expedited liver arrival probabilities, $\mathcal{D}(d)$.

Type\MELD	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1	0.05616	0.01701	0.00479	0.01291	0.02710	0.01291	0.00774	0.00258	0.00258	0.00387	0.00000	0.00129	0.00258	0.00258	0.00387
2	0.03867	0.02041	0.00855	0.00774	0.01807	0.01549	0.00645	0.00258	0.00774	0.00258	0.00000	0.00129	0.00000	0.00129	0.00129
3	0.06097	0.01576	0.01259	0.00774	0.00387	0.01291	0.00258	0.00516	0.00258	0.00258	0.00129	0.00000	0.00000	0.00258	0.00387
4	0.08325	0.05402	0.02064	0.01807	0.01678	0.02323	0.00903	0.00387	0.00129	0.00387	0.00387	0.00645	0.00387	0.00516	0.01420
5	-	0.00304	0.00280	0.00264	0.00000	0.00000	0.00000	0.00000	0.00000	0.00129	0.00000	0.00000	0.00000	0.00000	0.00000
6	-	0.00001	0.00000	0.00000	0.00000	0.00000	0.00129	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00129	0.00000
7	-	0.00277	0.00023	0.00134	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00129	0.00000	0.00000
8	-	0.00181	0.00012	0.00262	0.00129	0.00258	0.00129	0.00129	0.00000	0.00129	0.00000	0.00000	0.00258	0.00000	0.00129
9	-	0.00958	0.00180	0.00142	0.00000	0.00000	0.00000	0.00129	0.00129	0.00129	0.00129	0.00000	0.00258	0.00129	0.00129
10	-	0.00578	0.00032	0.00009	0.00000	0.00000	0.00129	0.00000	0.00000	0.00000	0.00000	0.00000	0.00129	0.00129	0.00129
11	-	-	0.00000	0.00129	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
12	-	-	0.00043	0.00006	0.00001	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
13	-	-	0.00635	0.00048	0.00140	0.00006	0.00258	0.00000	0.00129	0.00000	0.00129	0.00129	0.00129	0.00000	0.00129
14	-	-	-	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00129	0.00000	0.00000	0.00000	0.00000	0.00000
15	-	-	-	0.00183	0.00016	0.00004	0.00001	0.00129	0.00001	0.00000	0.00129	0.00129	0.00000	0.00000	0.00000
16	-	-	-	-	-	0.00357	0.00026	0.00140	0.00008	0.00000	0.00000	0.00000	0.00000	0.00129	0.00000
17	-	-	-	-	-	-	0.00161	0.00026	0.00009	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
18	-	-	-	-	-	-	0.01355	0.00161	0.00036	0.00129	0.00000	0.00000	0.00000	0.00000	0.00129
19	-	-	-	-	-	-	-	0.02261	0.00306	0.00299	0.00000	0.00000	0.00129	0.00258	0.00129
20	-	-	-	-	-	-	-	0.03128	0.00907	0.00306	0.00516	0.00129	0.00129	0.00129	0.00903
21	-	-	-	-	-	-	-	0.00209	0.00032	0.00004	0.00000	0.00000	0.00129	0.00000	0.00000
22	-	-	-	-	-	-	-	0.00912	0.00111	0.00015	0.00000	0.00000	0.00000	0.00000	0.00000
23	-	-	-	-	-	-	-	-	0.00142	0.00017	0.00002	0.00000	0.00000	0.00000	0.00000
24	-	-	-	-	-	-	-	-	0.00504	0.00057	0.00007	0.00000	0.00129	0.00000	0.00000
25	-	-	-	-	-	-	-	-	0.00117	0.00012	0.00001	0.00000	0.00000	0.00000	0.00000
26	-	-	-	-	-	-	-	-	0.01445	0.00164	0.00018	0.00129	0.00000	0.00000	0.00000
27	-	-	-	0.00559	0.00219	0.00129	0.00000	0.00129	0.00129	0.00258	0.00129	0.00000	0.00000	0.00000	0.00129
28	-	-	-	0.00000	0.00000	0.00000	0.00000	0.00129	0.00000	0.00129	0.00000	0.00000	0.00000	0.00000	0.00129
29	-	-	-	0.00043	0.00265	0.00000	0.00129	0.00387	0.00000	0.00129	0.00258	0.00129	0.00000	0.00000	0.00258
30	-	-	-	0.00525	0.00083	0.00129	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
31	-	-	-	-	-	0.00013	0.00000	0.00000	0.00129	0.00003	0.00000	0.00000	0.00000	0.00000	0.00000
32	-	-	-	-	-	0.00106	0.00000	0.00000	0.00000	0.00143	0.00000	0.00129	0.00000	0.00000	0.00000

Figure 42: The likelihood that when a patient joins the list, she is of type i and MELD score j, $\hat{\rho}_{ij}$.

k	prob.
0	0.619978
1	0.276911
2	0.079831
3	0.019068
4	0.003607
5	0.000549
6	0.000053
7	0.000003
8	0.000001

Figure 43: The probability that k patients join the list on a day.

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